UNIVERSITAT DE BARCELONA

Emotions in Eating Disorders: The Interplay of Emotion Regulation and Inhibitory Control in Appetite and Eating Behaviour

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Doctoral Thesis

Emotions in Eating Disorders:

The Interplay of

Emotion Regulation and Inhibitory Control

in

Appetite and Eating Behaviour

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Ph.D. in

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You cannot find peace
By avoiding life.

Virginia Woolf (*1882 †1941)

Los seres humanos no nacen para siempre
el día en que sus madres los alumbran,
sino que la vida los obliga a parirse
a sí mismos una y otra vez.

Gabriel García Márquez (*1927 †2014)

Wenn ein Tier oder ein Mensch seine ganze
Aufmerksamkeit und seinen ganzen Willen
auf eine bestimmte Sache richtet,
dann erreicht er sie auch.

Hermann Hesse (*1877 †1962)

La paciència comença amb llàgrimes i,
al final, somriu.

Ramón Llull (*1232 †1316)

To those who animated me

And to the most wonderful and inspiring city I have known.

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MERCI! DANKE!

Table of Contents

Index of tables and figures

Abstract

Introduction: In recent years, a steady rise in the prevalence of obesity and eating disorders (ED), including Anorexia Nervosa (AN), Bulimia Nervosa (BN) and Binge-Eating Disorder (BED), has been observed (NCD Risk Factor Collaboration, 2016; Qian et al., 2013). This is partly attributable to changes in the food environment, offering plenty of food products high in sugar and/or fat which often are consumed without physiological hunger, and can lead to behaviour reminding on addictive processes (Schulte et al., 2015). Further biopsychosocial risk factors for the development and maintenance of EDs constitute among others, dysfunctional personality traits, difficulties in emotion regulation, an emotionally deprived or weight-focused social environment, and genetic and neurobiological predispositions (Culbert et al., 2015). Emotion regulation models of disordered eating show the functionality of starving in AN and of bingeing in BN and BED for the regulation of negative emotions (Macht, 2008; Fox et al., 2013). In the case of BN and BED, patients often have to struggle with strong stimulus-induced cravings, which may be intensified through incentive sensitization of these stimuli (Berridge, 2009). Incentive sensitization of specific rewarding stimuli is related to neuroadaptations in the appetite regulation and reward circuits, which can lead to attentional biases towards these stimuli and may cause compulsive food intake, similar to drug addiction (Franken et al., 2005). Therefore, the attentional processing of food stimuli may be an important indicator of processes underlying psychopathology. Due to similarities between drug addiction and some forms of disordered eating, the possibility of food addiction (FA) has become a topic heavily discussed in research on EDs and overeating in the past years (Meule, 2015).

Objectives: The main goals of this thesis were to examine the link between the regulation of emotions and disordered eating to obtain insights into the processes underlying ED psychopathology. More specifically, this work aimed to expand upon previous knowledge on emotion regulation in ED patients and upon the effects of these difficulties on eating patterns and craving. An additional aim was to advance the research regarding addiction-like eating and to contribute to the discussion about the validity and usefulness of the FA concept. Since incentive sensitization is related to the attribution of motivational meaning to potentially addictive stimuli, another aim was to

investigate whether incentive salience of food cues is altered in ED patients compared to healthy individuals.

Results: *Study 1: Facial expression to emotional stimuli in mental disorders*. A systematic review of a total of 39 studies showed alterations in emotional facial expression across different mental disorders (obsessive-compulsive disorder, depression, bipolar disorder, borderline personality disorder, AN, BN, autism spectrum disorder, and disruptive behaviour disorder). A meta-analysis showed decreased facial expressivity in response to positive and negative stimuli in patients with AN, with a higher summary effect size for positive (d=1.01) than for negative (d=.58) stimuli. With respect to BN, results of included studies were inconsistent; there is evidence for less expression of negative emotions, but regarding positive emotions some studies show higher and others lower expressivity in BN patients compared to healthy controls (HC). There were no studies on facial expressivity for patients with BED.

Study 2: Personality and emotion regulation in eating disorders. The validation of the Spanish version of the Difficulties in Emotion Regulation Scale conducted as a first part of this study showed a factor structure similar to the original version and good internal consistency in adults with and without EDs. The discriminant validity of the scale was good: ED patients had higher values than HC in the total score and in all subscales of difficulties in emotion regulation (lack of emotional awareness, lack of emotional clarity, non-acceptance of emotions, lack of emotion regulation strategies, impulse control difficulties, problems to direct behaviour towards goals)**.** Moreover, emotion regulation capacity appeared to be different depending on diagnostic category; the AN group had comparably less problems than the BN group. Results furthermore showed that difficulties in emotion regulation mediate the influence of harm avoidance and self-directedness on ED severity. While for self-directedness an indirect and a direct effect on ED was found, the effect of harm avoidance was fully explained through the level of difficulties in emotion regulation.

Study 3: Personality profiles related to addictive eating patterns. This study on predictors of FA in ED patients showed that those patients with higher levels of FA are characterized by lower self-directedness, more negative urgency and less perseverance. The probability of receiving an FA “diagnosis” was predicted by higher reward

dependence, higher negative urgency and higher premeditation. Negative urgency was the strongest predictor of FA in patients with an ED.

Study 4: A model to predict addictive eating patterns. Hypothesis-driven structural equation modelling was conducted to test a comprehensive model of FA including previously proposed predictors (self-directedness, negative urgency, emotion regulation), while accounting for ED symptomatology. Results suggest that of the variables included the only independent predictor of FA might be negative urgency. Self-directedness and emotion regulation predicted negative urgency and were highly related to ED symptomatology in general, but not to FA.

Study 5: Food cue processing – electrophysiological evidence for motivated attention towards food in abnormal eating behaviours. A systematic review of 26 studies on attentional processing of food stimuli as measured through electrophysiological potentials involved seven studies on participants with an ED diagnosis (six samples with AN, two with BN, one with BED), six studies on individuals with obesity or overweight and 13 studies on participants with subclinical forms of abnormal eating. Most of the studies used a picture presentation paradigm of food and control pictures. Results consistently show high motivated attention towards food pictures compared to neutral pictures in all participants. A comparison of published data regarding differences between individuals with abnormal eating behaviour and healthy eating participants in electrophysiological measures of attention to food shows inconsistencies between study results. Obesity seems to be related to a bias in attentional orienting towards food stimuli, but regarding later time windows the evidence suggests that obese people might try to avoid further processing of food. Individuals with binge-eating, external or emotional eating seem to have increased maintenance of attention in response to high-caloric food when compared to healthy eating individuals which might be an indicator of incentive sensitization of food in people who experience loss of control over eating. This review shows that the type of eating pathology and other factors such as the availability of food and the type of stimuli have an influence on the attentional processing of food cues; however, further research is needed for a better understanding of the subject.

Study 6: Craving and brain response of binge-eating patients to visual and olfactory chocolate cues. In this study on stimulus-induced chocolate craving patients with binge-

eating pathology reported higher craving than controls; both groups experienced a significant increase in craving when exposed to the smell and sight of chocolate. Amplitudes of electrophysiological event-related potentials were higher for chocolate than for neutral pictures. The Late Positive Potential as measure of motivated attention did not differ between groups. Patients compared to HC had lower baseline amplitudes of an electrophysiological potential related to inhibitory control (N2) in neutral trials but showed a higher relative increase in N2 amplitudes related to chocolate pictures. Patients with higher craving levels tended to have lower N2 amplitudes while in healthy individuals this relation was inverted. Priming chocolate pictures by chocolate odour compared to neutral odour led to a slightly increased craving response and to an increased activation of inhibitory control resources in binge-eating patients.

Discussion: The studies conducted to adress the aims formulated for this doctoral thesis were concentrated on emotional and cognitive aspects of ED psychopathology and addictive eating. Different measures of emotion regulation such as facial expressivity and self-reported measures of difficulties in emotion regulation were shown to be related to all kinds of ED, but not specifically to FA. The observed results of this thesis further suggest that some temperamental traits such as harm avoidance and self-directedness are likely to affect an individual's capacity to adequately regulate emotions and are related to negative urgency. Negative urgency and inhibitory control were shown to be related to FA and binge-eating, including BN and BED. Results altogether suggest that difficulties in emotion regulation lead to increased and undifferentiated negative affect, and that the lack of adequate emotion regulation strategies is associated to disordered eating behaviour. With regard to addictive eating, results indicate that people with high negative urgency may abuse the rewarding properties intrinsic to some food products in order to attain an associated brain reward response. The repeated intake of these foods can then lead to incentive sensitization of food related cues such as the sight or smell of food, or a specific situation or environment, which predict this reward. Incentive sensitization supposedly increases craving, attentional bias and compulsive food intake which results in behaviour similar to substance use disorders.

The results of this thesis have some important implications for prevention and treatment of EDs and FA. Emotion- and urgency- based strategies should be included

into treatment and brain-based complements should be used in order to target alterations in attentional processing, inhibitory control and craving regulation. Regarding prevention, there are two main areas where interventions are advised to set in: improving emotional well-being in the general population and new policies targeting the modern food environment.

Future work should concentrate on longitudinal studies, momentary assessment and experimental data in order to better understand the relations between emotion regulation and symptomatology in everyday life and the interrelations between emotion regulation, negative urgency, inhibitory control, craving and food intake.

Conclusions: Alterations in facial emotional expressivity and self-reported difficulties in emotion regulation point towards emotional problems underlying ED psychopathology. Unregulated affect and decreased facial emotional expressivity might explain difficulties to recognize own and other's emotions and thus constrain satisfactory social relations. Negative urgency is a form of impulsivity related to negative affect and is shown to be specifically associated to addictive eating patterns in patients with EDs. There is a possible incentive sensitization of food cues, which is seen in that food stimuli lead to more motivated attention than neutral stimuli. Increased attentional bias to food in different forms of abnormal eating is confirmed mainly in attentional orienting; later time windows in the attentional processing stream seem to be affected by cognitive strategies which are used by individuals in order to control their eating behaviour. The smell of chocolate is a potent stimulus to induce craving and might increase the response to visual stimuli. Patients with binge-eating seem to be lower in baseline cognitive control, but may make a stronger effort to increase control when confronted with chocolate images.

Resumen

Introducción: En los últimos años se ha observado un aumento constante en la prevalencia de la obesidad y de los trastornos de la conducta alimentaria (TCA), tales como Anorexia nerviosa (AN), Bulimia nerviosa (BN) y Trastorno por atracón (TA) (NCD Risk Factor Collaboration, 2016; Qian et al., 2013). Siguiendo un modelo explicativo biopsicosocial, varios factores ambientales, sociales e individuales estarían influyendo en la aparición y/o mantenimiento de estos trastornos. Algunos de estos factores ambientales serían hábitos y patrones alimentarios, en sociedades opulentas, que favorecerían la ingesta de alimentos con alto contenido de azúcar y/o grasa, consumidos muchas veces sin hambre y sin que existiera ninguna necesidad de hacerlo, desde un punto de vista fisiológico, y que se asociarían a comportamientos de sobreingesta similares a los descritos en procesos adictivos (Schulte, Avena, & Gearhardt, 2015). Otros factores implicados en el desarrollo y mantenimiento de un TCA serían ciertos rasgos disfuncionales de personalidad, dificultades en la regulación de las emociones, entornos sociales emocionalmente desfavorecidos y/o centrados en el peso, así como predisposiciones genéticas y neurobiológicas específicas (Culbert, Racine, & Klump, 2015). En este sentido, los modelos de regulación emocional en TCA, explicarían la funcionalidad que puede tener la restricción alimentaria (mayoritariamente en AN) y/o los atracones de comida (mayoritariamente en pacientes con BN y TA), como mecanismos de regulación de las emociones negativas (Fox et al, 2013; Macht, 2008). En el caso de la BN y los TA, los pacientes a menudo tienen que luchar contra deseos muy intensos de ingerir ciertos tipos de alimentos, inducidos por estímulos externos, que podrían incrementarse por una sensibilización incentivada ante estos estímulos (Berridge, 2009). Esta sensibilización ante estímulos específicos, con un alto nivel de recompensa, estaría relacionada con neuroadaptaciones en circuitos cerebrales, relacionados a la regulación del apetito y la recompensa. Esto podría conducir a sesgos atencionales hacia estos estímulos, favoreciendo la ingesta compulsiva de alimentos, similar a la adicción a las drogas (Franken, Booij, & van den Brink, 2005). Por lo tanto, el procesamiento atencional, de los estímulos alimenticios, puede ser un indicador importante de los procesos que subyacen a la psicopatología del TCA. En los últimos años y debido a las similitudes entre la adicción a las drogas y

algunas formas de trastornos de la alimentación, la existencia de una posible adicción a la comida (AC) se ha convertido en un tema muy discutido en la investigación sobre el TCA y el comer en exceso (Meule, 2015).

Objetivos: Los objetivos principales de esta tesis doctoral fueron el análisis de la relación entre la regulación emocional y los TCA, para incrementar el entendimiento de los procesos que subyacen a la psicopatología del TCA. Más concretamente, este trabajo tuvo como objetivo ampliar los conocimientos sobre la regulación emocional, en los pacientes con TCA, y sobre los efectos de estas dificultades en los patrones de alimentación y el deseo por la comida. Otro objetivo fue avanzar en la investigación relacionada con hábitos alimentarios similares a la adicción, contribuyendo a la discusión sobre la validez y la utilidad del concepto de la AC. Teniendo en cuenta que la sensibilización incentivada está relacionada con la atribución de significado motivacional a los estímulos potencialmente adictivos, otro objetivo fue investigar si la prominencia de incentivación de alimentos claves, está alterada en pacientes con TCA en comparación con individuos sanos.

Resultados: *Estudio 1: Expresión facial asociada a estímulos emocionales en trastornos mentales*. Una revisión sistemática, de un total de 39 estudios, mostró alteraciones en la expresión emocional facial en diferentes trastornos mentales (trastorno obsesivo-compulsivo, depresión, trastorno bipolar, trastorno límite de la personalidad, AN, BN, trastorno del espectro autista y trastorno de comportamiento disruptivo). Un meta-análisis mostró disminución de la expresividad facial en respuesta a los estímulos positivos y negativos en pacientes con AN, con un tamaño del efecto global mayor para estímulos positivos (d = 1,01) que negativos (d = .58). Con respecto a la BN, los resultados de los estudios incluidos fueron contradictorios. Es decir, existen evidencias de menor expresión de las emociones negativas, pero en relación con las emociones positivas algunos estudios demuestran más y otras menos expresividad, en pacientes con BN, en comparación con los controles sanos (CS). No se han encontrado estudios sobre la expresividad facial en personas afectadas de TA.

Estudio 2: Personalidad y regulación emocional en los trastornos alimentarios. La validación de la versión española de la Escala de Dificultades en la Regulación Emocional, realizada como primera parte de este estudio, demostró una estructura factorial similar a la versión original y una buena consistencia interna en adultos con y

sin TCA. La validez discriminante de la escala era buena: los pacientes con TCA obtuvieron valores más altos que los CS en la puntuación total y en todas las subescalas de dificultades en la regulación emocional (falta de conciencia emocional, falta de claridad emocional, no aceptación de las emociones, falta de estrategias de regulación emocional, dificultades de control de impulsos ante las emociones, problemas para dirigir la conducta hacia metas ante las emociones). Además, la capacidad de regulación emocional parecía ser diferente dependiendo de la categoría de diagnóstico; el grupo de AN tenía comparativamente menos problemas que el grupo de BN. Los resultados demostraron, además, que las dificultades de regulación emocional mediaban la influencia entre evitación del daño y autodirección y gravedad del TCA. Mientras que para la autodirección se encontró un efecto indirecto y un efecto directo sobre el TCA, el efecto de evitación del daño se explicaba únicamente por el nivel de dificultades en la regulación emocional.

Estudio 3: Perfiles de personalidad relacionados con los patrones de alimentación adictivos. Este estudio sobre indicadores de la AC, en pacientes con TCA, demostró que aquellos pacientes con niveles más altos de AC se caracterizan por una menor autodirección, mayor urgencia negativa y menor perseverancia. Una mayor dependencia a la recompensa, mayor urgencia negativa y mayor capacidad de premeditación fueron factores predictores de recibir el diagnóstico de AC. Finalmente, la urgencia negativa fue el indicador más robusto de la presencia de AC, en los pacientes con TCA.

Estudio 4: Un modelo para predecir los patrones de alimentación adictivos. Para poner a prueba un modelo global de AC, incluyendo indicadores anteriormente encontrados por la investigación (autodirección, urgencia negativa, regulación emocional), se llevó a cabo un modelaje de ecuaciones estructurales, basado en determinadas hipótesis y controlando por la sintomatología del TCA. Los resultados sugirieron que, entre las variables incluidas, el único indicador independiente de la AC era la urgencia negativa. La autodirección y la regulación emocional fueron factores predictores de la urgencia negativa, estando al mismo tiempo estrechamente relacionados con la sintomatología TCA en general, pero no con la AC.

Estudio 5: Procesamiento de estímulos alimentarios - pruebas electrofisiológicas para la atención motivacional hacia la comida en los comportamientos alimentarios anormales.

Una revisión sistemática de 26 estudios, sobre el procesamiento atencional electrofisiológico de los estímulos alimentarios, incluyó siete estudios que incorporaban participantes con diagnóstico de TCA (seis con AN, dos con BN, una con TA), seis estudios con muestras de individuos con obesidad o con sobrepeso y 13 estudios con participantes que presentaban cuadros sub-clínicos de alimentación anormal. La mayoría de los estudios usaron un paradigma de presentación de imágenes de alimentos y fotografías control. Los resultados demostraron consistentemente una alta atención motivacional hacia las imágenes de alimentos, en comparación con las imágenes neutras en todos los participantes. Al comparar los datos publicados sobre las diferencias entre individuos con comportamiento de alimentación anormal y los participantes con alimentación saludable, en las medidas electrofisiológicas de atención a la comida, se observaron inconsistencias en los resultados de los estudios. La obesidad parecía estar relacionada con un sesgo en la orientación atencional hacia los estímulos alimentarios, pero al considerar intervalos de tiempo aplazados, las evidencias sugerían que las personas obesas podrían tratar de evitar el procesamiento posterior. Los individuos con atracones, o los que comían de forma externa o emocional, parecían tener un mantenimiento de la atención aumentado, en respuesta a estímulos de comida alta en calorías, en comparación con los individuos que comían de forma saludable. Este hallazgo podía ser un indicador de una sensibilización incentivada ante los alimentos, en aquellas personas que experimentan pérdida de control sobre la alimentación. Esta revisión demuestra que tanto el tipo de patología alimentaria como otros factores, tales como la disponibilidad de alimentos y el tipo de estímulos utilizado, tienen una influencia destacada en el procesamiento atencional de los estímulos alimentarios. Sin embargo, es necesaria más investigación para una mejor comprensión del tema.

Estudio 6: Deseo de comer y respuesta cerebral de pacientes con atracones ante estímulos visuales y olfativos de chocolate. En este estudio, sobre el deseo por el chocolate inducido por estímulos externos, los pacientes con atracones refirieron un deseo mayor que los controles; aunque ambos grupos experimentaron un aumento significativo en el deseo después de estar expuestos al olor y la vista de chocolate. Las amplitudes de los potenciales electrofisiológicos fueron mayores ante imágenes de chocolate que ante imágenes neutras. El "Late Positive Potential" como medida de atención motivada no difirió entre los grupos. Los pacientes, en comparación con CS, obtuvieron menores amplitudes de un potencial electrofisiológico relacionado con el control inhibitorio

(N2), ante estímulos neutros, pero demostraron un aumento en amplitudes de la N2, relativamente más alto que los CS ante imágenes de chocolate. Los pacientes con altos niveles de deseo a la comida tendían a presentar menores amplitudes de la N2, mientras que en individuos sanos se invertía esta relación. Las imágenes de chocolate precedidas por su olor, en comparación con un olor neutro, se relacionaron con un ligero aumento del deseo y con un aumento en la activación de recursos de control inhibitorio, en los pacientes con atracones.

Discusión: Los estudios llevados a cabo para analizar los objetivos formulados en esta tesis doctoral, se centraron en los aspectos emocionales y cognitivos de la psicopatología de los TCA y de la adicción a la comida. Se demostró que diferentes medidas de regulación emocional, como la expresividad emocional facial y las medidas de auto-informe sobre las dificultades en la regulación emocional, estaban relacionadas con todos los subtipos de TCA, pero no específicamente con la AC. Los resultados de esta tesis sugieren, además, que algunos rasgos de personalidad como la evitación del daño y la autodirección pueden afectar a la capacidad para regular adecuadamente las emociones, estando asimismo relacionados con la urgencia negativa. Se demostró que la urgencia negativa y un bajo nivel de control inhibitorio están relacionados con la AC y con los atracones, incluyendo BN y TA. Los resultados, en conjunto, sugieren que las dificultades en la regulación emocional pueden conducir a un afecto negativo aumentado e indiferenciado, y que la falta de estrategias adecuadas de regulación emocional se asocia con TCA. Con respecto a la conducta alimentaria adictiva, los resultados indican que las personas con altos niveles de urgencia negativa pueden abusar de determinados alimentos, con un elevado componente gratificante, con el fin de lograr una respuesta asociada de recompensa en el cerebro. La ingesta repetida de estos alimentos puede conducir a la sensibilización incentivada de estímulos relacionados con este tipo de alimentos, tales como la vista o el olor de la comida, una situación específica o el entorno, que predicen esta recompensa. La sensibilización al incentivo supuestamente aumenta el deseo, el sesgo atencional y la ingesta compulsiva de alimentos que se traduce en un comportamiento similar a los trastornos por uso de sustancias.

Las implicaciones más importantes de los resultados obtenidos en esta tesis, para la prevención y el tratamiento de los TCA y la AC, son la inclusión de estrategias

terapéuticas orientadas a la mejora de la regulación emocional y del manejo de la urgencia, así como a la utilización de técnicas complementarias, centradas en el cerebro, con el fin de modificar alteraciones en el procesamiento atencional, el control inhibitorio y la regulación del deseo a comer. En cuanto a la prevención, existen dos áreas principales en las que se aconseja iniciar las intervenciones: mejorar el bienestar emocional de la población general y el desarrollo de políticas de regulación alimentaria en las sociedades actuales.

La investigación futura debe centrarse en los estudios longitudinales, la evaluación momentánea y los datos experimentales, con el fin de comprender mejor las relaciones entre la regulación emocional y la sintomatología en la vida cotidiana. Asimismo, debe explorarse en profundidad la relación entre la regulación emocional, la urgencia negativa, el control inhibitorio, el deseo y la ingesta de alimentos.

Conclusiones: Las alteraciones en la regulación emocional, identificadas a través de la expresión facial y de las medidas de autoinforme apuntan a los problemas emocionales que subyacen la psicopatología de los TCA. El afecto mal regulado y la disminución de la expresividad emocional facial, podrían explicar las dificultades para reconocer las propias emociones y los emociones de otros, limitando el establecimiento y mantenimiento de relaciones sociales satisfactorias. La urgencia negativa es una forma de impulsividad relacionada a las emociones negativas, demostrándose que está específicamente asociada a los patrones de alimentación adictivos, en los pacientes con TCA. Existe una posible sensibilización a los incentivos ante determinados estímulos alimentarios. Cuando éstos se comparan con estímulos neutros se identifica la presencia de una atención motivacional alterada. Se confirmó un elevado sesgo atencional frente a la comida, en distintos patrones de alimentación anormal, principalmente referente a la orientación atencional. Además, los intervalos de tiempo posteriores parecían estar afectados por estrategias cognitivas que los individuos utilizarían con el fin de controlar su conducta alimentaria. El olor del chocolate es un potente estímulo para inducir deseo de comer y podría aumentar la respuesta a los estímulos visuales. Los pacientes con atracones parecían tener un menor control cognitivo de base, pero podrían hacer un mayor esfuerzo para aumentar el control, cuando se confrontaban ante imágenes de chocolate.

Zusammenfassung

Einleitung: In den letzten Jahren wurde ein stetiger Anstieg in der Prävalenz von Adipositas und Essstörungen, einschließlich Anorexia Nervosa (AN), Bulimia Nervosa (BN) und Binge-Eating Störung (BES), beobachtet (NCD Risk Factor Collaboration, 2016). Dies ist teilweise auf Veränderungen im Lebensmittelbereich zurückzuführen welche eine Vielzahl an zucker- und/oder fettreichen Produkten bietet, die oft ohne physiologischen Hunger konsumiert werden, was zu suchtähnlichem Verhalten führen kann (Schulte et al., 2015). Zu weiteren bio-psycho-sozialen Risikofaktoren für die Entstehung und Aufrechterhaltung von Essstörungen gehören u.a. dysfunktionale Persönlichkeitseigenschaften, Schwierigkeiten in der Emotionsregulation, ein emotional armes oder gewichtfokussiertes soziales Umfeld und genetische und neurobiologische Veranlagung (Culbert et al., 2015). Emotionsregulationsmodelle zur Psychopathologie von Essstörungen zeigen die Funktionalität des Hungerns bei AN und der Essanfälle bei BN und BES in der Regulation negativer Emotionen (Fox & Power, 2009; Macht, 2008). Im Falle von BN und BES haben betroffene Patientinnen oft mit starkem stimulus-induziertem Verlangen zu kämpfen, was durch Anreizsensibilisierung (engl. *„incentive sensitization"*) dieser Stimuli noch verstärkt werden kann (Berridge, 2009). Die Anreizsensibilisierung bestimmter mit Belohnung verbundener Reize ist mit neuronalen Anpassungen im Appetitregulations- und Belohnungssystem verbunden, was zu Aufmerksamkeitsverzerrungen gegenüber diesen Reizen führen und somit zwanghaftes Essverhalten ähnlich einer Drogensucht hervorrufen kann (Franken et al., 2005). Demzufolge kann die Aufmerksamkeitsverarbeitung von Essensreizen einen wichtigen Hinweis auf die den Essstörungen zugrundeliegenden Prozesse bieten. Aufgrund der Ähnlichkeiten des Suchtervehaltens und der neuronalen Prozesse bei Substanzmissbrauch mit manchen Formen gestörten Essverhaltens ist die Möglichkeit einer Essenssucht in den vergangenen Jahren zu einem vieldiskutierten Thema in der Forschung zu Essstörungen und Überernährung geworden (Meule, 2015).

Ziele: Eines der Hauptziele dieser Arbeit war, den Zusammenhang zwischen Schwierigkeiten in der Emotionsregulation und gestörtem Essverhalten zu untersuchen, um ein besseres Verständnis der mit den Essstörungen verbundenen Mechanismen zu bekommen. Insbesondere sollte das Wissen bezüglich Schwierigkeiten in der

Emotionsregulation bei Patientinnen mit Essstörungen und deren Effekte auf das Essverhalten und Verlangen erweitert werden. Ein weiteres Ziel war die Forschung mit Bezug auf sucht-ähnliches Essverhalten voranzubringen und zur Diskussion über die Gültigkeit und Brauchbarkeit des Konzepts der Essenssucht beizutragen. Da Anreizsensibilisierung mit der Zuschreibung von motivationaler Bedeutung zu potentiell suchterzeugenden Reizen verbunden ist, war ein weiteres Ziel dieser Arbeit Veränderungen in der Salienz von Essensreizen bei Patientinnen mit Essstörungen im Vergleich zu gesunden Individuen zu untersuchen.

Ergebnisse: *Studie 1: Emotionaler Gesichtsausdruck gegenüber emotionalen Stimuli bei psychischen Erkrankungen*. Eine systematische Übersichtsarbeit mit insgesamt 39 Studien zeigte Veränderungen im emotionalen Gesichtsausdruck bei Patienten mit verschiedenen psychischen Erkrankungen (Zwangsstörung, Depression, Bipolare Störung, Borderline-Persönlichkeitsstörung, AN, BN, Autismus-Spektrum-Störung und disruptive Verhaltensstörung). Eine Metaanalyse zeigte verminderten emotionalen Ausdruck bei Patientinnen mit AN angesichts positiver und negativer Reize mit einer höheren Gesamteffektstärke für positive (d=1.01) im Vergleich zu negativen (d=.58) Stimuli. Bezüglich BN waren die Ergebnisse der einbezogenen Studien jedoch uneinheitlich; es liegen Hinweise für einen verringerten emotionalen Gesichtsausdruck von negativen Emotionen vor, mit Bezug auf positive Emotionen zeigen jedoch manche Studien mehr und andere weniger Mimik bei Patientinnen mit BN im Vergleich zur Kontrollgruppe (KG). Es wurden keine Studien zum Gesichtsausdruck bei Patientinnen mit BES gefunden.

Studie 2: Persönlichkeit und Emotionsregulation bei Essstörungen. Die Validierung der Spanischen Version der Skala zu Emotionsregulationsschwierigkeiten („*Difficulties in Emotion Regulation Scale*“), welche als erster Teil dieser Studie durchgeführt wurde, zeigte eine der Originalversion ähnliche Faktorstruktur und eine gute interne Konsistenz in einer Stichprobe von Erwachsenen mit und ohne Essstörung. Die Diskriminanzvalidität der Skala war gut: Essstörungspatientinnen hatten höhere Werte als die KG im Gesamtergebnis und in allen Unterskalen der Skala zu Emotionsregulationsschwierigkeiten (Mangel emotionalen Bewusstseins, Mangel emotionaler Klarheit, nicht-Akzeptanz von Emotionen, Mangel an Emotionsregulationsstrategien, Schwierigkeiten der Impulskontrolle, Probleme

zielgerichteten Verhaltens). Außerdem zeigte sich ein Unterschied in der Emotionsregulationsfähigkeit abhängig von der diagnostischen Kategorie der Essstörung. Die Gruppe mit AN hatte vergleichsweise weniger Probleme als die Gruppe mit BN. Die Ergebnisse zeigten weiterhin eine Mediation von Emotionsregulationsschwierigkeiten zwischen dem Einfluss von Schadensvermeidung (engl. *„harm avoidance"*) und Selbstbestimmung (engl. *„self-directedness"*) auf die Essstörungsschwere. Während für Selbstbestimmung ein indirekter und ein direkter Effekt auf die Essstörungssymptomatik gefunden wurde, wurde der Einfluss von Schadensvermeidung vollständig durch den Grad der Emotionsregulations-schwierigkeiten erklärt.

Studie 3: Persönlichkeitsprofile im Zusammenhang mit addiktivem Essverhalten. Diese Studie zu Prädiktoren von Essenssucht bei Essstörungspatientinnen zeigte, dass sich Patientinnen mit einem höheren Grad an Essenssucht durch eine geringere Selbstbestimmung, höhere Negativdringlichkeit (engl. *„negative urgency"*) und geringere Ausdauer beschreiben lassen. Die Wahrscheinlichkeit des Vorliegens einer „Diagnose" Essenssucht wurde durch höhere Belohnungsabhängigkeit, höhere Negativdringlichkeit und höhere Planungsfähigkeit vorhergesagt. Negativdringlichkeit war der stärkste Prädiktor für Essenssucht bei Essstörungspatientinnen.

Studie 4: Ein Modell zur Vorhersage addiktiven Essverhaltens. Zur Testung eines übergreifenden Modells der Essenssucht wurde ein hypothesengeleitetes Strukturgleichungsmodell unter Einbezug zuvor gefundener Variablen (Selbstbestimmung, Negativdringlichkeit, Emotionsregulation) und Kontrolle der Essstörungssymptomatologie berechnet. Die Ergebnisse deuten darauf hin, dass von den einbezogenen Variablen die Negativdringlichkeit der einzige von der Essstörungsschwere unabhängige Prädiktor der Essenssucht ist. Selbstbestimmtung und Emotionsregulation waren mit Negativdringlichkeit und höherer Essstörungssymptomatologie im Allgemeinen verbunden, aber nicht mit Essenssucht.

Studie 5: Verarbeitung von Essensreizen – elektrophysiologische Nachweise für motivierte Aufmerksamkeit gegenüber Lebensmitteln bei abnormem Essverhalten. Eine systematische Übersichtsarbeit mit 26 Studien zur elektrophysiologischen Aufmerksamkeitsverarbeitung von Essensstimuli beinhaltete sieben Studien über Patienten mit einer Essstörungsdiagnose (sechs Stichproben mit AN, zwei mit BN, eine

mit BES), sechs Studien über Individuen mit Adipositas oder Übergewicht und 13 Studien über Teilnehmer mit subklinischen Formen gestörten Essverhaltens. Die meisten der Studien verwendeten ein Bildpräsentationsparadigma mit Essens- und Kontroll-Bildern. Die Ergebnisse zeigen durchweg bei allen Gruppen eine hohe motivationale Aufmerksamkeit gegenüber Essensbildern im Vergleich zu neutralen Bildern. Ein Vergleich der veröffentlichten Daten zu Unterschieden zwischen Personen mit abnormem Essverhalten und gesund essenden Teilnehmern bezüglich elektrophysiologischer Potentiale der Aufmerksamkeit gegenüber Essensstimuli zeigt Inkonsistenzen zwischen den Studienergebnissen. Adipositas scheint mit einer Verzerrung in der Aufmerksamkeitsorientierung verbunden zu sein, Ergebnisse bezüglich späterer Zeitfenster weisen darauf hin, dass adipöse Personen allerdings versuchen könnten die weitere Verarbeitung von Essensreizen zu vermeiden. Individuen mit Essanfällen, externalem oder emotionalem Essverhalten im Vergleich zu gesund essenden Individuen scheinen eine verstärkte Aufrechterhaltung der Aufmerksamkeit gegenüber hochkalorischem Essen zu haben. Diese Übersichtsarbeit zeigt, dass die Art der Essstörung und andere Faktoren wie die Erreichbarkeit von Essen und die Art des präsentierten Reizes einen Einfluss auf die Aufmerksamkeitsverarbeitung von Essensreizen haben. Es werden jedoch weitere Forschungsarbeiten zum besseren Verständnis der Thematik benötigt.

Studie 6: Appetitives Verlangen und neuronale Aktivität von Patientinnen mit Essanfällen in Reaktion auf visuelle und olfaktorische Schokoladenreize. In dieser Studie zum stimulus-induzierten Verlangen nach Schokolade berichteten Patientinnen mit Essanfällen ein höheres Verlangen als die KG. Beide Gruppen erlebten eine signifikante Zunahme im Verlangen, wenn sie dem Geruch und dem Anblick von Schokolade ausgesetzt wurden. Die Amplitude der ereigniskorrelierten Potentiale war höher für Schokoladen- als für neutrale Bilder. Das Späte Positive Potential (engl. *„Late Positive Potential*“) als Maß motivationaler Aufmerksamkeit unterschied sich nicht signifikant zwischen den Gruppen. Patientinnen im Vergleich zur KG hatten niedrigere Ausgangsamplituden bei neutralen Trials eines elektrophysiologischen Potentials (N2) welches mit inhibitorischer Kontrolle in Verbindung gebracht wird, zeigten jedoch eine relativ höhere Zunahme in N2 Amplituden als die KG in Reaktion auf Schokoladenbilder. Patientinnen mit höherem appetitivem Verlangen neigten zu niedrigeren N2 Amplituden während dieser Zusammenhang in gesunden Individuen umgekehrt war.

Wenn vor den Schokoladenbildern der Geruch von Schokolade im Vergleich zu neutralem Geruch präsentiert wurde, wurde ein leicht erhöhtes Verlangen und eine erhöhte Aktivierung inhibitorischer Kontrolle bei Patienten mit Essanfällen gemessen.

Diskussion: Die zur Erreichung der für diese Doktorarbeit aufgestellten Ziele durchgeführten Studien waren auf emotionale und kognitive Aspekte der Psychopathologie von Essstörungen gerichtet. Es wurde gezeigt, dass verschiedene Maße der Emotionsregulation wie der emotionale Gesichtsausdruck und selbstberichtete Emotionsregulationsschwierigkeiten mit allen Arten von Essstörungen, jedoch nicht speziell mit Essenssucht, verbunden sind. Die Ergebnisse dieser Arbeit legen weiterhin nahe, dass Persönlichkeitsmerkmale wie Schadensvermeidung und Selbstbestimmung die Fähigkeit eines Individuums zur adäquaten Emotionsregulation beeinträchtigen könnten und auch die Negativdringlichkeit beeinflussen. Ferner wurde der Einfluss von Negativdringlichkeit und inhibitorischer Kontrolle auf Essenssucht und Essanfälle bei BN und BES gezeigt. Im Ganzen betrachtet lassen die Ergebnisse darauf schließen, dass Emotionsregulationsschwierigkeiten zu erhöhtem und undifferenziertem negativem Affekt führen und dass der Mangel an adäquaten Emotionsregulationsstrategien mit gestörtem Essverhalten in Verbindung steht. Mit Bezug zu addiktivem Essen weisen die Ergebnisse darauf hin, dass Personen mit hoher Negativdringlichkeit die in manchen Lebensmitteln enthaltenen Eigenschaften missbrauchen könnten um eine damit verbundene Belohnungsreaktion im Gehirn auszulösen. Der wiederholte Konsum dieser Lebensmittel kann dann zu einer Anreizsensibilisierung der damit verbundenen Hinweisreize, wie dem Geruch oder Anblick von Essen, oder einer bestimmten Situation oder Umgebung, welche diese Belohnung vorhersagt, führen. Eine potentielle Anreizsensibilisierung erhöht vermutlich das Verlangen nach Essen, die Aufmerksamkeitsverzerrung und zwanghafte Nahrungszufuhr was zu sucht-ähnlichem Verhalten führt.

Die für die Prävention und Therapie von Essstörungen und Essenssucht wichtigsten Implikationen der in dieser Arbeit gefundenen Ergebnisse sind der Einbezug von Strategien zur Verbesserung der Emotionsregulation und Negativdringlichkeit und die Verwendung von auf neurowissenschaftlichen Befunden basierenden Therapie-Ergänzungen, welche auf Abweichungen in der Aufmerksamkeitsverarbeitung, der inhibitorischen Kontrolle und der Regulation des Verlangens abzielen.

Zukünftige Forschung sollte auf Längsschnitts-Studien, ambulantes Assessment und experimentelle Studien fokussieren, um das Verständnis des Zusammenhangs zwischen Emotionsregulation und Essstörungssymptomatologie im Alltag und des Zusammenspiels von Emotionsregulation, Negativdringlichkeit, inhibitorischer Kontrolle, Verlangen und Nahrungsaufnahme weiter zu verbessern.

Fazit: Veränderungen im emotionalen Gesichtsausdruck und selbstberichtete Emotionsregulationsschwierigkeiten weisen auf der Essstörungspsychopathologie zugrunde liegende emotionale Probleme hin. Unregulierter Affekt und verminderter emotionaler Gesichtsausdruck könnten die Schwierigkeiten in der Erkennung der eigenen Emotionen und der Emotionen Anderer erklären und zufriedenstellende soziale Beziehungen erschweren. Negativdringlichkeit ist eine Art der Impulsivität die durch negative Emotionen hervorgerufen wird und es wurde gezeigt, dass sie insbesondere mit addiktivem Essverhalten bei Essstörungspatientinnen verbunden ist. Essensreize sind möglicherweise mit Anreizsensibilisierung verbunden, was sich in erhöhter motivationaler Aufmerksamkeit gegenüber Essensreizen im Vergleich zu neutralen Reizen zeigt. Eine erhöhte Aufmerksamkeitsverzerrung gegenüber Essen bei unterschiedlichen Formen abnormalen Essverhaltens wurde hauptsächlich für die Aufmerksamkeitsorientierung bestätigt. Spätere Zeitfenster im Aufmerksamkeitsfluss scheinen durch kognitive Strategien, welche Personen zur Kontrolle ihres Essverhaltens einsetzen, beeinflussbar zu sein. Der Geruch von Schokolade ist ein wirksamer Stimulus um Verlangen hervorzurufen und kann möglicherweise die Reaktion auf visuelle Stimuli erhöhen. Patientinnen mit Essanfällen scheinen geringere Ausgangswerte in der kognitiven Kontrolle zu haben, könnten aber eine größere Anstrengung machen um die Kontrolle zu erhöhen, wenn sie mit Schokoladenbildern konfrontiert werden.

Introduction

1 Introduction

> *"It's amazing how pervasive food is. Every second commercial is for food. Every second TV episode takes place around a meal. In the city, you can't go ten feet without seeing or smelling a restaurant. There are 20 foot high hamburgers up on billboards. I am acutely aware of food, and its omnipresence is astounding."*
>
> Adam Scott, comedian (2006)

Typing "food addiction" into an online search machine, more than 16 million results are found: information, tests, treatments, support groups and much more are provided for "food addicts". An awareness of the addictive properties of food and its rewarding qualities is also represented in many quotes of famous or anonymous people, found in the internet. Quotes such as "*You can't buy happiness, but you can buy chocolate, and that's kind of the same thing*" (anonymous) or "*All you need is love, but a little chocolate from time to time doesn't hurt*" (Charles Schulz, cartoonist) shows the popular opinion that chocolate can help to feel better and even plays in the same league as love. Other quotes show the functionality especially sweet food can have in the regulation of stress and negative emotions: "*When you're stressed, you eat ice-cream, cakes and chocolate. Why? Because stressed spelled backwards is desserts*" (anonymous), the hedonic component of food: "*Nothing would be more tiresome than eating and drinking if God had not made them a pleasure as well as a necessity"* (Voltaire, philosopher), or the difficulty to cut down food intake once started: *"Strength is the capacity to break a bar of chocolate into four pieces with your bare hands - and then eat just one of the peaces"* (Judith Viorse, journalist).

Folk psychology has picked up many aspects about food and its hedonic and in some sense seducing aspects, which research associates to the development of problematic eating habits, obesity and eating disorders (ED). According to the world health organisation (WHO, 2016), worldwide obesity prevalence has more than doubled since the 1980s; in Europe almost half of the population struggles with overweight (Body Mass Index [BMI] 25-30 kg/m^2) and in almost all European countries more than 20% of people are considered obese (BMI > 30 kg/m^2), which is associated with cardiovascular diseases, diabetes and some types of cancer (NCD Risk Factor Collaboration, 2016). This rise in obesity and in EDs (Qian et al., 2013) relates to changes in our food environment:

food is omnipresent and easily accessible, many products are intensely processed and include a high amount of sugar and fat, which fosters food intake disconnected from physiological hunger (Schulte et al., 2015; Volkow et al., 2012). As Kent Berridge (professor of biopsychology) puts it: "*Perhaps it is the prevalence of normal body weights, rather than obesity, that should be most surprising in affluent modern societies where tasty foods abound*" (Berridge, 2009, *p*. 17).

In spite of the apparent link between emotions and eating, research into EDs has neglected this relationship for a long period of time. Only recently, increasing evidence emerged that shows a substantial influence of emotions on eating behaviour and recognizes the interaction of emotional and appetite regulating systems in the pathogenesis of EDs. Particularly those people with high stress reactivity or who lack strategies to sufficiently regulate negative emotions are susceptible to use food in the hope to ease their negative affect (Macht, 2008); this can then lead to loss of control over food intake and the development of an ED. However, still more research is needed to understand the complex interactions between emotions and eating behaviour (Treasure, 2012). Furthermore and besides emotional aspects, a return to eating as a crucial aspect of EDs and an emphasis on research into processes underlying appetite and food intake has recently been postulated (Treasure et al., 2012).

This doctoral thesis focuses on the interplay of emotions, emotion regulation and appetite in the development and maintenance of EDs. In the following chapters, the theoretical background for the studies conducted to this regard will be introduced. First of all, the state of the art regarding diagnostic criteria, prevalence, general risk and maintenance factors as well as treatment possibilities will be outlined. Thereafter, emotion regulation models of eating will be explained in more detail. The last chapter of the introduction gives a description of processes underlying craving and incentive sensitization of food stimuli. To complete the scientific background, an overview and discussion of research on addiction-like eating, including results from neurobiological and psychological studies on appetite regulation and food addiction (FA), will be given.

After introducing the scientific background, the global goals and hypotheses of this thesis and each study's main aim will be outlined. Specific goals and methods will be explained in more detail for each of the included studies in the empiric part of this thesis, whereupon the results of each of these studies will be presented. Having done

this, results will be discussed in a global context, considering also the strengths and limitations of the studies and of this thesis as a whole. Finally, this thesis closes by pointing out general conclusions, clinical and research implications and discussing possibilities for future research.

1.1 Eating disorders

Eating Disorders are mental disorders mainly found in females (female:male ratio = 4.2:1) with a peak onset in late adolescence or early adulthood, and often present with an illness duration of many years or even result in chronification (Stice et al., 2013; Qian et al., 2013; Zipfel et al., 2015). EDs typically lead to a significantly reduced quality of life and functional impairment and are often associated with comorbid disorders such as substance abuse, mood, anxiety and personality disorders (Allen et al., 2013; Stice et al., 2013; Hudson et al., 2007; Herzog et al., 1995; Lilenfeld et al., 2008; Krug et al., 2008; Fernandez-Aranda et al., 2007; Fernández-Aranda et al., 2016b). According to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; (American Psychiatric Association, 2013)), EDs comprise a group of disorders including Anorexia Nervosa (AN), Bulimia Nervosa (BN), Binge-Eating Disorder (BED), Other Specified Feeding or Eating Disorders (OSFED) and Unspecified Feeding or Eating Disorders (UFED) (American Psychiatric Association, 2013; Stice et al., 2013; Qian et al., 2013). However, a high crossover between diagnostic groups, especially from BED to BN and from BN to OSFED and vice versa (Allen et al., 2013; Stice et al., 2013), suggests similar risk and maintenance factors of different ED subcategories. See Table 1 (*p*. 4) for an overview of diagnostic subgroups according to DSM-5 criteria.

1.1.1 Epidemiology and diagnostic categories

With the change from DSM-IV to DSM-5 criteria, prevalence rates of EDs have changed; this is explained partly by the inclusion of BED as an official diagnosis, and partly by the fact that individuals who formerly were categorized in the “others” category “Eating Disorders Not Otherwise Specified” (EDNOS) do now receive a full threshold ED diagnosis (Machado et al., 2013). Thus, these individuals now enter into AN or BN categories, wherefore especially for AN and BN higher prevalence rates are observed (Call et al., 2013; Hoek, 2013). In Western countries, the prevalence of any ED is reported with numbers as high as 15.2% in female *adolescents* (Allen et al., 2013) and

estimates for lifetime prevalence in *adults* are between 3% and up to 9% (Smink et al., 2013; Qian et al., 2013). There are relatively low remission rates and high mortality rates: considering DSM-IV criteria, highest mortality rates are found for AN (5.1%), followed by EDNOS (3.3%) and then BN (1.7%) (Smink et al., 2013; Arcelus et al., 2011).

Table 1. Diagnosis of eating disorders according to DSM-5 criteria.

Diagnosis	Core Symptoms	Severity	Subtypes
Anorexia Nervosa	❖ Persistent restriction of energy intake leading to significantly low body weight ❖ Intense fear of gaining weight/ becoming fat ❖ Body-image disturbance and undue influence of body shape and weight on self-evaluation	BMI (kg/ m²) Mild:>17 Moderate:16-17 Severe:15-16 Extreme:<15	Restricting type Binge-purging type
Bulimia Nervosa	❖ Recurrent objective binge-eating ❖ Compensatory behaviours such as vomiting, abuse of laxatives or hard exercising ❖ Over-evaluation of body shape and weight	Compensatory behaviour/week Mild: 1-3 Moderate: 4-7 Severe: 8-13 Extreme: >14	
Binge-Eating Disorder	❖ Recurrent objective binge-eating ❖ Significant distress/shame over binge-eating ❖ No compensatory behaviour	Binges/week Mild: 1-3 Moderate: 4-7 Severe: 8-13 Extreme: >14	
Other Specified Feeding or Eating Disorders	AN symptomatology with BMI >18.5 kg/m²		Atypical AN
	BN symptomatology with < 1 binge-purge/ week		Low frequ. BN
	BED symptomatology with < 1 binge/ week		Low frequ. BED
	Recurrent episodes of night eating together with significant distress/ impairment		Night eating syndrome
	Recurrent purging without binge-eating		Purging disorder

AN = Anorexia Nervosa; BED = Binge-Eating Disorder; BN = Bulimia Nervosa; BMI = Body Mass Index

Anorexia Nervosa, according to DSM-5 criteria (American Psychiatric Association, 2013), is characterized by significantly low body weight due to food restriction, a strong fear of gaining weight, disturbance of the body-image, and an abnormal importance of the own shape and weight (see Table 1, *p.* 4). Estimates of lifetime prevalence rates for females at age 20 are 0.6-0.8% (males <0.1%) (Allen et al., 2013; Stice et al., 2013), 12-month prevalence is estimated 0.4% in young female adults (American Psychiatric Association,

2013). Meta-analytic results including samples of 14-65 year old European participants estimate a lifetime prevalence of 0.2-0.5% for AN, using DSM-IV criteria (Wittchen et al., 2011; Qian et al., 2013).

A diagnosis of *Bulimia Nervosa* is given with at least one objective binge-episode occurring at least once per week over a period of at least three months, including the feeling of loss of control over eating, and accompanied by compensatory behaviours such as self-induced vomiting, use of laxatives or hard exercising, an over-evaluation of weight/shape and usually a BMI higher than 18.5 kg/m^2. Lifetime prevalence rates for females at age 20 range from 2.6% to 9.5% (males 1.6%) (Allen et al., 2013; Stice et al., 2013), 12-month prevalence among young females is 1-1.5% (American Psychiatric Association, 2013). Meta-analytic results of studies referring mainly to DSM-IV criteria and including a higher age range indicate lower numbers, with a 12-month prevalence of 0.1-0.9% of BN in the general population (Wittchen et al., 2011; Qian et al., 2013).

Diagnostic criteria for *Binge-Eating Disorder* include recurrent objective binge-eating defined as "eating an unusually large amount of food accompanied by loss of control over eating" at least once a week over at least three month, going along with significant distress and/or shame over binge-eating. Individuals diagnosed with BED have a BMI > 18.5 kg/m^2 and do not use any compensatory strategies such as self-induced vomiting, laxatives or hard exercising. Lifetime prevalence rates at age 20 for females range between 3.0% and 4.8% (males 0.7%) when using DSM-5 criteria (Allen et al., 2013; Stice et al., 2013), 12 months prevalence in adults is 1.6% in females and 0.8% in males (American Psychiatric Association, 2013). Meta-analytic results for population based studies with a broader age range indicate with 1.25% for females and 0.46% for males a lower 12-month prevalence of BED (Qian et al., 2013).

The OSFED category includes among others *purging disorder* (characterized by over-evaluation of weight/shape, self-induced vomiting without binge-eating and a BMI > 18.5 kg/m^2), *atypical AN* (characterized by intense fear of weight gain and body image disturbance, but with a BMI > 18.5 kg/m^2), *low frequency/duration BN and BED* (less than one binge per week or shorter than 3 month duration) and *night eating syndrome*. Lifetime prevalence rates at age 20 for females are 3.3-14.2% (males 0.6%) (Allen et al., 2013; Stice et al., 2013).

1.1.2 Etiopathogenesis: general risk, vulnerability and maintenance factors

The etiopathogenesis of EDs can be understood in a biopsychosocial frame, which proposes that psychological factors such as low self-esteem, perfectionism and difficulties in emotion regulation alongside biological and social factors can predispose individuals to the development of an ED and contribute to the maintenance of the disorder (Harrist et al., 2013; Keel and Forney, 2013; Frank, 2015). Since most research regarding correlates of EDs is based on retrospective or cross-sectional studies and there is a lack of longitudinal studies, it is often difficult to differentiate between predisposing risk and maintenance factors. Hereafter, an overview of pathogenic factors associated with the diagnosis of EDs is provided (see also Table 2, *p.* 6); the influence of emotions and emotion regulation on disordered eating will be described in more detail in chapter 1.2.

Table 2. Biopsychosocial risk factors related to the development and maintenance of eating disorders.

Psychological	Socio-Cultural	Biological
❖ **Personality** 🡅 Harm avoidance 🡇 Self-directedness 🡅 Perfectionism (AN) 🡅 Novelty seeking (BN/BED) ❖ **Emotions** 🡅 Emotion regulation difficulties ❖ **Cognitive functions** 🡇 Inhibitory control (BN/BED) 🡇 Cognitive flexibility (AN) ➲ Attentional processing of food/body related stimuli	❖ **Family environment** 🡇 Regular meals 🡅 Dieting behaviour 🡇 Family connectedness 🡅 Emotional/physical abuse ❖ **Peer environment** 🡅 Fat talking 🡅 Weight teasing ❖ **Culture** 🡅 Internalization of the thin ideal ➲ Food environment	❖ **Brain function** ➲ Neurotransmitters (e.g. dopamine, serotonin, opioids) ❖ **Brain structure** ➲ White matter ➲ Grey matter (e.g. areas related to appetite regulation, emotion regulation, interoceptive perception) ❖ **Hormones** ➲ Gut hormones (e.g. leptin, insulin, ghrelin) ➲ Sex hormones (e.g. estrogen) ❖ **Genetic predisposition**

AN = Anorexia Nervosa; BED = Binge-Eating Disorder; BN = Bulimia Nervosa.
🡇 Lower scores of this trait are related to higher eating disorder psychopathology.
🡅 Higher scores of this trait are related to higher eating disorder psychopathology.
➲ There is a relation of this trait to eating disorder psychopathology, but its direction depends on various influencing factors.

1.1.2.1 Psychological factors

Psychological pathogenic factors related to EDs include emotional, cognitive and personality-related factors. Regarding personality, EDs in general have been associated to behavioural inhibition, negative emotionality, fear of uncertainty and punishment

sensitivity (harm avoidance), low goal-directedness and lack of self-confidence (self-directedness), and perfectionism (Agüera et al., 2012; Krug et al., 2011; Atiye et al., 2015; Harrison et al., 2010a; Keel and Forney, 2013). Furthermore and more specifically, for pathologies on the binge-eating spectrum high novelty seeking and reward sensitivity were found to be related to the disorder (Harrison et al., 2010a). In contrast, for patients with AN – who are better described by high reward dependence and persistence – novelty seeking is lower than in healthy individuals (Harrison et al., 2010a). Notably, more *dysfunctional personality traits* have been found to predict not only higher ED severity, but also worse therapy response and prognosis (Hintsanen et al., 2012; Abbate-Daga et al., 2011; Rodríguez-Cano et al., 2014).

Box 1. Preclinical forms of morbid eating constituting risk for eating disorders.

Childhood *obesity* is an important predicting factor in the development of body dissatisfaction with subsequent dieting behaviour and restriction of food intake (Snoek et al., 2008; Munkholm et al., 2016; Forrester-Knauss et al., 2012). Research furthermore shows that *restrained eaters*, who confine their eating habits by cognitive rules (e.g. a restricted number of calories per day, forbidden foods etc.), are also jeopardized to lose control over food intake under conditions of cognitive load or stress, and following caloric preload or food-related priming (Herman & Mack, 1975; Polivy, Herman, & Deo, 2010; Ward & Mann, 2000; Wardle, Steptoe, Oliver, & Lipsey, 2000). Another pre-clinical morbid eating pattern is found in *external eating*, which refers to an eating behaviour characterised by the desire for and intake of food in response to environmental stimuli such as the sight and smell of food (Burton, Smit, & Lightowler, 2007; Rodin & Slochower, 1976). Eating in response to external triggers has become more and more important as a result of an obesogenic environment with an omnipresence of food. *Emotional eaters* on the other hand eat in response to emotional distress, intending to regulate negative emotions or stress through their food intake (Macht, 2008; Stice et al., 2002; Van Strien, Schippers, & Cox, 1995).

Since personality manifests early in life (Ferguson et al., 2012; Ando et al., 2002; Kim et al., 2006), it seems likely that personality characteristics form a base for an individual's vulnerability towards other risk factors, such as difficulties in emotion regulation but also the internalization of the "thin ideal" (Rodgers et al., 2015) and the development of an idealization of thinness (Keel and Forney, 2013; Homan, 2010). This can then lead to body dissatisfaction and body image disturbance (Sepúlveda et al., 2002; Liechty and Lee, 2013), and result in disturbed eating behaviours such as restrained, external or emotional eating (see Box 1, *p*. 7).

Further psychological vulnerability factors of EDs are found in *dysfunctional cognitive processes* such as biases in attention, impaired decision making, inflexible cognitive

styles, and a lack of inhibitory control (Claes et al., 2012; Fagundo et al., 2012; Svaldi et al., 2014a; Treasure and Schmidt, 2013). ED patients, but also obese individuals, restrained, emotional and external eaters, show alterations in the attentional processing of food cues, body shape, social and emotionally negative stimuli (Nijs and Franken, 2012; Schmidt et al., 2013; Werthmann et al., 2014b; van Elburg and Treasure, 2013). Impulsivity and low inhibitory control are related to unhealthy eating, such as overeating, external eating and emotional eating (Jasinska et al., 2012), and to stimulus-induced craving and attentional biases to food stimuli (Hou et al., 2011) (see also chapter 1.3.1). Corroborating this link, experimental data has shown that impulsive reactions to food stimuli predict subsequent food cravings, i.e. low inhibitory control in response to appetitive stimuli is associated with higher craving and thus might lead to overeating (Meule et al., 2014a). Rigidity and high levels of cognitive control on the other hand are related to restrained eating and AN (van Elburg and Treasure, 2013; Claes et al., 2012). These cognitive alterations reflect processes underlying disordered eating behaviour and certainly contribute to the maintenance of the disorder; therefore, cognitive deficits have been proposed as an endophenotype of EDs (Kanakam et al., 2013, 2012).

1.1.2.2 Social and cultural factors

Regarding social risk and maintenance factors, the literature emphasizes the importance of both family and peer environment in the development of body-dissatisfaction and dieting behaviour (Quiles Marcos et al., 2013; Neumark-Sztainer et al., 2007). Especially for girls, the *peer environment* may shape the development of restrained eating and binge-eating behaviour, through teasing on one side and encouragement to diet on the other. Typical topics in appearance conversation or 'fat-talking' between youngsters are self-comparisons with ideals and peers, the fear of becoming over-weight, and strategies for meal-replacement and exercising; participating in these kinds of conversations augments body-dissatisfaction and dieting behaviour (Sharpe et al., 2013).

Longitudinal studies show that among male and female adolescents, exposure to weight loss magazine articles, higher weight importance, and unhealthy weight control behaviours predict disordered eating at five-year follow up, while *family connectedness*, body satisfaction, high self-esteem and *regular meals* are protective factors (Neumark-

Sztainer et al., 2009, 2007). The importance of regular meals in the prevention of EDs is underlined by another prospective study showing that female adolescents who ate family dinner at least most days of the week were less likely to start purging, binge-eating, or restrained eating than those who didn't usually sit down with their families to eat dinner (Haines et al., 2010). This association might be mediated on the one hand by the facilitation of a more regular food intake which prevents binge-eating (Masheb and Grilo, 2006); on the other hand family dinners might help to improve the *parent-child relationship*, which is another important factor in the pathogenesis of EDs (Neumark-Sztainer et al., 1998; Tasca and Balfour, 2014). ED patients often have lower parental bonding than their healthy peers; this may contribute to the development of unhealthy core beliefs about themselves and their social relations, such as feelings of abandonment, functional dependence, mistrust, emotional deprivation and social undesirability (Leung et al., 1999, 2000). Children grown up in a deprived family environment, or who even had to suffer emotional or sexual abuse, are often incapable to develop an effective and emotionally stable self, form inadequate core beliefs about themselves and their social environment and are therefore at high risk for the development of an ED (Wonderlich et al., 2000; Molinari, 2001; Sanci et al., 2008; Waller et al., 2001; Groleau et al., 2012).

1.1.2.3 Biological factors

Biological factors related to EDs include genetic predispositions (Yilmaz et al., 2015), dysregulations in neurotransmitter systems (Kaye, 2008; Frank and Kaye, 2013; Phillipou et al., 2014), alterations in functional brain activity, connectivity (Kaye et al., 2011; Friederich et al., 2013) and brain structure (Van den Eynde et al., 2011; Frank, 2015), and abnormalities in the neuropeptide and hormone system (Fernández-Aranda et al., 2016a; Monteleone, 2011; Schwartz et al., 2000). The attribution of a cause and effect relation to biological risk or maintenance factors is of particular difficulty due to methodological and ethical limitations to study protocols. This has to be kept in mind when considering the presented results. Furthermore, the (dys)regulation of appetite is part of a complex system, where different parts of the central nervous system (CNS) and the autonomic nervous system interact. Therefore, the reader is also referred to chapter 1.3.2 for a deeper understanding of the neurobiological basis of food intake, craving and appetite regulation.

As a whole, research regarding alterations in the brain structure of patients with an ED was inconsistent in the past, and it was difficult to rule out effects of acute starvation, malnutrition, dehydration, medication and exercising. A recent review however reports for AN and BN *increased gray matter* volume in the orbitofrontal cortex (OFC, related to food intake control) and in the insula (related to interoceptive awareness and taste perception) and *reduced gray matter* in the striatum (related to reward sensitivity) (Frank, 2015). The same review points out reductions in fornix *white matter* of patients with ED, but altogether evidence on white matter alterations is limited to a very small number of studies. Abnormalities in *neurocircuit function* are consistently found in areas related to *reward function* (OFC, amygdala, striatum, medial prefrontal cortex [PFC], and mid-brain), *emotional processing* and *emotion regulation* (ventral circuit: amygdala, insula, ventral striatum, and ventral regions of the anterior cingulate cortex [ACC] and PFC; dorsal circuit: hippocampus, dorsal regions of the caudate, dorsolateral PFC [DLPFC], parietal cortex, and other regions), *gustatory processing* and *interoceptive awareness* (anterior insula and striatal regions) and *cognitive control* (DLPFC); thereby, AN in general is related to low reward function and high levels of control and BED and BN to low levels of inhibitory control, while results regarding reward function are inconsistent for binge-type disorders (Kaye et al., 2011; Friederich et al., 2013). For AN, an overactivation of the fear-network (left insula, ACC, left amygdala-hippocampal region) specifically in response to food stimuli and correlated to intense calorie fear might explain their aversive reactivity towards food stimuli or food phobia (Ellison et al., 1998; Friederich et al., 2013).

The most important *neurotransmitter systems* in the context of disordered eating behaviour are the *dopamine* system, which is implicated in the seeking of appetitive stimuli and signals reward, and the *serotonin* system, related to behavioural inhibition, aversive reactivity and negative emotionality (Phillipou et al., 2014; Frank and Kaye, 2013). Both systems are known to interact, and an imbalance between the two neurotransmitter systems might explain a great part of the personality and behavioural traits found in ED patients.

Genetic predispositions are a possible explaining factor for interindividual differences in neurotransmission and for the high familial accumulation of ED, with more than 50% of variation in phenotype being explained by genetic factors (Yilmaz et al., 2015). Genes

such as the serotonin transporter polymorphism 5HTTLPR, associated with vulnerability to psychopathology in general and with dysfunctional personality traits (van Ijzendoorn et al., 2012; Clauss et al., 2015; Kim et al., 2006), or genes related to dopamine functioning certainly influence the development of EDs (Karwautz et al., 2011; Yilmaz et al., 2015); however, consistency of results are rather limited (Solmi et al., 2016). To date, it no genes have been directly and robustly associated with ED psychopathology in linkage studies, candidate gene or genome-wide association studies (Boraska et al., 2014; Yilmaz et al., 2015). There is preliminary evidence that underweight and obesity have a shared genetic base and may be understood as a continuum in the phenotypical expression of variations in the same genetic variants (Jacquemont et al., 2011). But the genetic influence on psychiatric disease seems to be a complex interaction between different genes and in any case it is also moderated by environmental factors such as adverse life events (Akkermann et al., 2012; van Ijzendoorn et al., 2012) and by epigenetic changes (e.g. DNA methylation) which moderate gene expression (Yilmaz et al., 2015).

Further important players in biological factors of ED psychopathology are hormones regulating appetite and influencing brain functioning. The dopamine system is part of a feedback loop with appetite regulating *hypothalamic neuropeptides* (e.g. endocannabinoides and opioids) and the peripheral *gut hormones* ghrelin, insulin, and leptin (van Zessen et al., 2012; Monteleone, 2011; Davis, 2015). Leptin is known to signal adiposity to the brain and shown to be related to the development of obesity when under-expressed. Ghrelin stimulates food intake by signalling the need for energy and is associated with the anticipation of feeding behaviour and food reward processing (Egecioglu et al., 2011). Patients with AN have increased levels of circulating ghrelin, which normalizes with weight restoration, for BN an association of the disorder with ghrelin is not clear (Monteleone, 2011). Furthermore, the female *sex hormone* estrogen and its increased release during puberty may be an explaining factor for the increased female risk for EDs and its pubertal onset. Its mode of action is explained through a moderating effect of estrogen on brain development and organization in adolescence, which in adulthood influences the phenotypic expression of psychopathology (Klump, 2013). Altogether, alterations in brain and endocrine functioning may influence or explain dysregulated appetitive processes. The neurobiological foundations of appetite regulation and food craving will be explained in further detail in chapter 1.3.2.

1.1.3 Treatment of eating disorders

There are a range of different, more or less standardized and evaluated interventions for the treatment of patients with EDs. The treatment of choice with the best evidence base regarding adherence and outcome is cognitive-behaviour therapy (CBT) for BN and BED, for adolescent AN patients family-based treatments were also found effective (Hay, 2013) and for adult AN focal psychodynamic therapy has been recommended as well (Zipfel et al., 2013). A combined pharmacological treatment with antidepressants (fluoxetine, serotonin-reuptake inhibitors) is helpful in some cases, and for BED interpersonal psychotherapy has also proven effective (Brown and Keel, 2012). In recent years, during the so-called "third wave" of psychotherapy (Kahl et al., 2012), the importance of targeting emotions and affect regulation in CBT has become clear. New, integrative therapy manuals such as cognitive remediation and emotion skills training (CREST) for AN or dialectical behaviour therapy (DBT) for binge-eating have been proposed for the treatment of ED; although these therapy modules need further evaluation, pilot studies have already shown promising results (Tchanturia et al., 2015b; Schmidt et al., 2015; Klein et al., 2013; Fernandez-Aranda et al., 2015). Nevertheless, remission rates remain low and therapy approaches still need further improvement. There is a call for more research into brain functioning of patients with an ED in order to base treatments to a greater extend on knowledge about neurobiological processes underlying disordered eating behaviour (Schmidt et al., 2013).

1.2 Emotion regulation models of eating disorders

1.2.1 Emotions and emotion regulation

First of all, to start the topic of emotion regulation in disordered eating, a proper working definition of emotions seems to be expedient. From a psychological perspective, *emotions* can be defined as the combination of changes in physiological parameters (e.g. skin conductance, heart rate, blood pressure) on the one hand, and of a cognitive attribution of meaning (appraisal), which results in negative or positive affect, on the other. Normally, emotions are also accompanied by changes in facial expression and at least most of basic emotions have distinct and universal nonverbal signs (Weisfeld and Goetz, 2013; Ekman, 2016). Emotions can be evoked by *external* or

internal stimuli and have a shorter duration than mood, which usually refers to an ongoing emotional state. Emotions not only inform about personal needs, prepare an individual to adapt its behaviour to the environment, and lead to specific motivated behaviour with protecting aims (Ekman, 1992), but they also have a social function in that they inform about a person's intentions or wants (Fridlund, 1994). The *evolutionary significance* of emotions is highlighted by their neuronal structure, which is based in subcortical brain regions developed comparatively early in brain evolution (e.g. amygdala, periaqueductal grey, insula) (Panksepp, 2011).

Panksepp (2011) proposes a three-level model of how emotions are processed in the brain, starting with a sub-neocortical level for sensory (pleasant vs. unpleasant), homeostatic (hunger, thirst etc.) and emotional (fear, lust, seeking, care, panic/grief and play) affects. Next, according to the model, emotions reach a secondary process level in the basal ganglia, where classical and operant conditioning and emotional habit learning takes place under inclusion of memory. Finally, in a third level in the neocortex emotions are brought to awareness, are consciously regulated and can be controlled by "free will". LeDoux however criticises this approach of a global emotional system devoted to basic emotions and indicates that *emotion-specific brain circuits* have attained more scientific support (LeDoux, 2012). In his work on fear processing he advocates the view that basic emotional information enters the brain through the thalamus and cortex which project to the amygdala. From these brain regions, threat information is transmitted to the hypothalamus, brain stem and motor systems to initiate a respective behavioural reaction (LeDoux, 2014, 2000). According to this conceptualization, emotions cannot be consciously "felt" without cortex activation; the amygdala merely creates an emotion-specific motivational state which, when brought to consciousness through neocortical (DLPFC) processing, is interpreted as the respective emotion and then leads to the emotion-specific subjective feeling. Research on emotions other than fear shows that the amygdala is implicated in the processing of a range of emotions (Cardinal et al., 2002), including reward processing and reward learning (Holland and Gallagher, 2004; Murray, 2007; Everitt et al., 1999). Furthermore, evolutionarily younger regions such as the parietal cortex, the ACC and the PFC are part of the emotion brain system; they are involved in emotion regulation (Etkin et al., 2015) and the explicit use of emotion regulation strategies (McRae et al., 2010; Ochsner et al., 2004).

Emotion regulation as a basic psychological concept refers to automatic and controlled processes used to influence the duration, intensity, valence, and expression of emotions (Gross, 1998b). As proposed by Gratz and colleagues (2004), for an adequate regulation of emotions, first of all, a person needs to be aware about his/her own emotions and able to identify, experience and differentiate the full range of emotions (emotional clarity). Furthermore, the ability to accept strong (negative) emotions is crucial for an appropriate regulation, which also alludes to the notion that a *modulation of the emotional effect* of a given emotion might be more appropriate than the attempt to eliminate it. Adequate regulation achieves to direct behaviour towards long-term goals even under strong emotional states, to adapt behaviour to the specific demands of a situation, and to control impulses which go against these goals (Gratz and Roemer, 2004).

The *process model* of emotion regulation developed by Gross and colleagues (Gross, 1998b, 1998a) posits that emotion regulation can set in either before or after the onset of an emotional response and can therefore be divided into *antecedent- or response-focused strategies* (see Figure 1, *p*. 15). Antecedent-focused strategies aim on situation selection and modification through attentional deployment (e.g. distraction, rumination, concentration) and cognitive framing (e.g. reappraisal). Response-focused strategies are used to intensify or decrease the emotion after its emergence, by influencing its duration or by suppressing the emotional expressive, physiological, experiential or behavioural response.

Evidence shows that instructions to use specific emotion regulation strategies are helpful to cope with the emotional content of pictures or movies (Gross & John, 2003; Hajcak, MacNamara, & Olvet, 2010). Thereby, antecedent-focused strategies such as reappraisal seem to be more effective than response-focused strategies such as suppression or distraction (Asnaani, Sawyer, Aderka, & Hofman, 2014; Evers, Marijn Stok, & de Ridder, 2010; McRae et al., 2010; Svaldi, Tuschen-Caffier, Trentowska, Caffier, & Naumann, 2014; Thiruchselvam, Blechert, Sheppes, Rydstrom, & Gross, 2011). For example, it has been shown that expressive suppression of negative emotions can lead to higher psychophysiological activation and thus to the opposite effect of what was initially intended by suppressing the emotion (Gross and Levenson, 1993). Still, it seems crucial that depending on the emotion and situation, each emotion regulation strategy

has different advantages and can have more or less adequate consequences, wherefore flexibility in choosing different strategies depending on context may be the most effective and healthy way of regulating ones emotions (Bonanno and Burton, 2013; Birk and Bonanno, 2016; Kashdan et al., 2014; Aldao and Nolen-Hoeksema, 2012; Farmer and Kashdan, 2012).

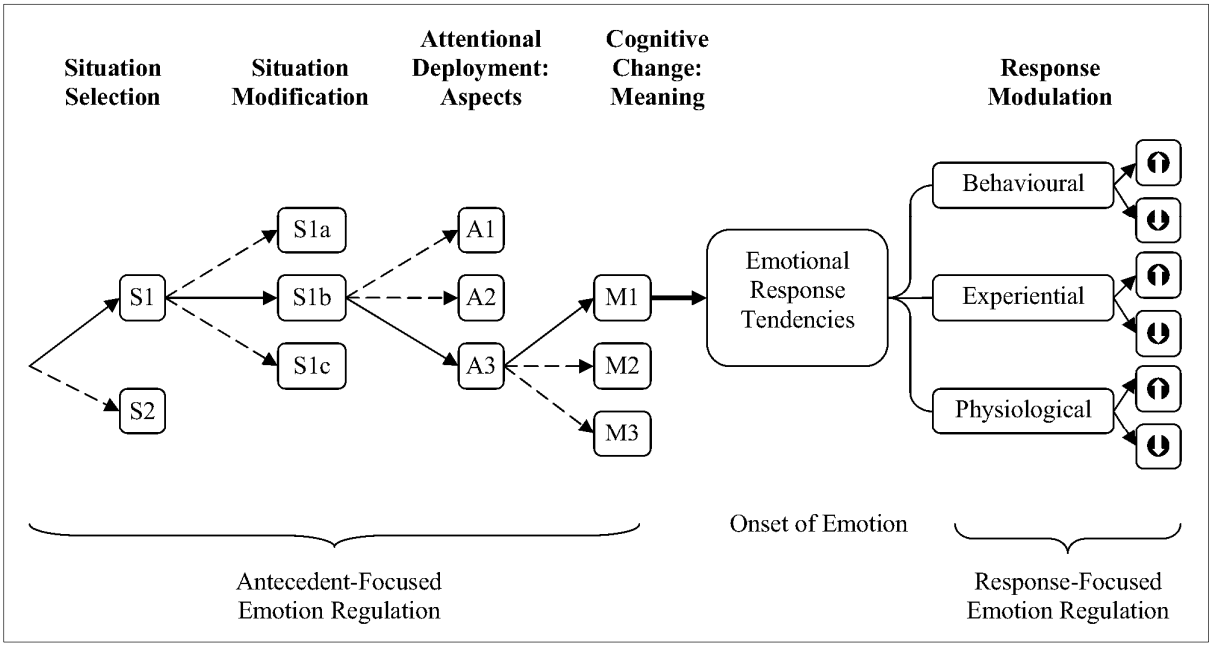

Figure 1. Process model of emotion regulation as developed by Gross and colleagues (Gross, 1998a).

Interindividual differences in emotion regulation are explained by a combination of temperamental factors and strategies learned in the family environment (Calkins and Fox, 2002; Calkins et al., 2013; Soussignan et al., 2009; Cyders and Smith, 2008). Temperament is a relatively stable trait and greatly heritable: many studies have looked at the genetic base of personality and found specific genetic variants and polygenetic interactions to be associated with these behavioural phenotypes (Clauss et al., 2015; Ando et al., 2002; Amin et al., 2013; De Moor, 2015; van den Berg et al., 2016). Therefore, personality traits can be seen as endophenotypes affecting behaviour and emotional functioning. In this context, some specific gene variants (e.g. short allele of the serotonin transporter gene 5HTTLPR) are of overriding interest because of their influence on serotonergic neurotransmission, which in turn is implied in the control of stress reactivity through modulation of the hypothalamic-pituitary-adrenal-(HPA) and hypothalamic-spinal-adrenal-axes (Lowry, 2002). The 5HTTLPR short allele genotype is

phenotypically expressed in the neuroticism/harm avoidance personality traits (Sen et al., 2004), which are characterized by behavioural inhibition, emotional reactivity, mistrust, negative affectivity and anxiousness (Cloninger et al., 1993; Costa and McCrae, 1997). Other ways of action in which genes are expressed in temperamental traits and thus relate to differences in emotion regulation are found for example in genes influencing oxytocin (rs53576 polymorphism) (Li et al., 2015) and dopamine functioning (Clauss et al., 2015), related to sociality and novelty seeking, respectively.

Already very early in *childhood development*, i.e. in infancy, these heritable temperamental differences present themselves in levels of attentional control, motor reactivity and trait physiological arousal, which predict self-regulation capacity in toddlerhood and effortful control later in life (Derryberry and Rothbart, 1988; Sheese et al., 2009; Johansson et al., 2015; Smith et al., 2016; Sheese et al., 2012). A child's reactivity towards environmental stimuli shows its self-regulation capacities, an important component of psychosomatic well-being, stress resistance and acquisition of adequate emotion regulation (Calkins and Fox, 2002). However, research has shown that there is a gene-by-environment interaction in the development of emotion regulation. While in a protective family environment a child carrying genotypic risk can still develop normal psychological functioning without problems, a child with the same genotype in an adverse environment or insecurely attached may lose out on learning appropriate emotion regulation and is at risk of developing any kind of psychopathology, including EDs (Akkermann et al., 2012; Choe et al., 2013; Kochanska et al., 2009; Sheese et al., 2007). The parents' own emotion regulation skills and expressiveness of positive emotions are certainly an important influencing factor in the attachment-relationship and emotion socialization, and by this means may contribute to shape the child's emotional responding and regulation capacity (Gratz et al., 2014; Are and Shaffer, 2015; Jones et al., 2014; Eisenberg et al., 2001).

1.2.2 Dysfunctional emotion regulation and eating behaviour

A lack of adequate emotion regulation strategies can result in the feeling that emotions are overwhelming and that nothing can be done about it, wherefore some people may use other, but less appropriate strategies, such as deliberate self-harm, drug consumption, or food intake, in order to modify unpleasant emotions (Gross, 1998b; Linehan, 1993). *Dysfunctional emotion regulation* is associated to a range of psychiatric

disorders and is therefore considered a transdiagnostic risk and/or maintenance factor for psychopathology (Aldao et al., 2010; Svaldi et al., 2012). Self-report indicates that BED (Svaldi et al., 2014b; Danner et al., 2014), AN (Davies et al., 2012b; Danner et al., 2014) and BN (Davies et al., 2012b; Danner et al., 2014) patients habitually use more frequently suppression as a strategy to regulate emotions than healthy individuals. Furthermore, ED patients exhibit fewer adequate emotion regulation strategies, they *feel more* negative emotions but *express less* emotions than healthy controls (HC), and at the same time they exhibit increased problems in recognizing their own and other's emotions (Kanakam et al., 2013; Svaldi et al., 2012; Caglar-Nazali et al., 2014).

There are various models of possible links between emotions and eating. As proposed by Fox and Power in their multi-level model of emotions, negative emotions in general and specifically anger are critical to ED psychopathology (Fox and Power, 2009; Fox et al., 2013). The authors suggest that adverse childhood experiences give rise to schematic models (e.g. "Feeling anger is dangerous.", "I'm a worthless person.", "Better not trust anybody.") and an attribution of emotional events to the own body and to food intake; these schemes, together with dysfunctional emotion regulation styles, lead to a suppression of negative emotions and a subsequent coupling of these to *disgust* directed at the self. This can evoke depression and in turn can bring along ED symptomatology as a strategy of passive inhibition of these negative feelings (Fox and Power, 2009; Fox et al., 2013).

Macht (Macht, 2008) proposed a model composed of five pathways in which emotions can affect food intake: 1) emotions evoked by food stimuli influence food choice, 2) emotions very high in arousal suppress food intake, 3) in restrained eaters, negative and positive emotions enhance food intake through disinhibition, 4) emotional eaters try to regulate negative mood states through the intake of high-palatable food, and 5) in normal eating individuals the influence of emotion on food intake is congruent with cognitive and motivational features of the emotional state.

Other authors underline the *emotion regulation function of starvation* and exercising in patients with AN (Brockmeyer et al., 2012; Frank, 2015; Haynos and Fruzzetti, 2011). Qualitative interview data suggest that AN patients are aware of this link between emotions, body dissatisfaction, and disordered eating behaviour: patients report that they use food restriction and purging in order to cope with or avoid overwhelming

negative emotions such as sadness, fear and anger. According to the patients' statements, anorexic behaviour distracts from emotional problems and helps them to regain a sense of control over their lives; eating or body awareness on the other hand makes them feel disgusted about themselves which in some patients may raise the desire to purge (Espeset et al., 2012). Ecological momentary assessment (EMA) shows that AN patients in a naturalistic setting restrict more on days following these with higher negative affect. While exercising and caloric restriction decreased negative feelings, negative affect increased after other ED behaviours such as loss of control over food intake, purging or weighing (Engel et al., 2013). Several recent studies found that inducing negative mood in an experimental setting increases ED behaviour and the desire to restrict food intake (Wildes et al., 2012; Naumann et al., 2014). Furthermore, emotion regulation problems are found a maintaining factor in longitudinal studies of AN, with more difficulties to regulate emotions predicting higher ED symptom severity over a one-year period (Racine and Wildes, 2015). Regarding the persistence of emotion regulation problems, weight gain alone is not sufficient to reduce these difficulties (Haynos et al., 2014), but there is evidence to suggest that emotion regulation capacity increases and is similar to healthy individuals after a 1-year recovery from the disorder (Harrison et al., 2010b; Treasure, 2012).

Emotional eating refers to an *increased* food intake in response to strong emotions and can be found as well in healthy populations as in ED patients, ranging from emotion related snacking to bingeing and loss of control over eating (Macht, 2008). A recent meta-analysis concludes that a significant increase of food intake following negative mood induction is found in restrained eaters and BED, but not in healthy or obese populations, while an increase in food consumption through positive mood induction can also be seen in HC (Cardi et al., 2015b). It has been proposed that negative emotions together with high levels of impulsivity increase emotional eating (Bekker et al., 2004; Alpers and Tuschen-Caffier, 2001). However, there is also evidence to suggest that it is rather *the way* in which emotions are regulated than the emotion *per se* which influences eating; for example, the use of rumination and suppression were found to evoke higher desire to binge and higher emotion-related food intake than distraction or reappraisal (Evers et al., 2010; Svaldi et al., 2014b; Naumann et al., 2015; Svaldi et al., 2010a).

Emotional triggers such as feelings of loneliness, anxiety or depression are – besides cognitive (e.g. negative thoughts about self, weight/shape, future) and physiological (e.g. craving) components – important contributing factors to the maintenance of binge-eating (Vanderlinden et al., 2004), while food intake might be used as an intent to regulate these negative emotions. A longitudinal study shows that adolescents with higher negative urgency (defined as the need to act rashly in response to negative emotions) are more prone to developing binge-eating, which was mediated by the belief that food intake helps to feel better (Pearson et al., 2012). Experimental and EMA studies however suggest that although negative mood is a common antecedent of binge-eating in both BN and BED, binge-eating does *not* effectively decrease negative mood states; quite the contrary, negative feelings might even increase after binge-eating episodes (Haedt-Matt and Keel, 2011; Hilbert and Tuschen-Caffier, 2007; Leehr et al., 2015).

A reinforcement model of binge-eating, originally conceptualized for drug-addiction, predicts that negative mood leads to biased information processing and thus increases the salience of appetitive stimuli such as drugs or food (Baker et al., 2004). This increase in salience leads to selective attentional processing of these stimuli and goes along with higher desire to consume the respective drug or food (Hepworth et al., 2010; Bradley et al., 2007). The following chapters describe the neurobiological processes underlying stimulus-induced craving and incentive sensitization of food, and discuss neurobiological and behavioural similarities of disordered eating behaviour to substance abuse and other addictive disorders.

1.3 Craving and appetite regulation: can food be addictive?

Craving is a term initially conceptualized in the area of alcohol and drug addiction research, with a largely physical connotation, despite the definition brought out by a WHO conference in the 1950s which also included psychological components (Skinner and Aubin, 2010). The definition of the term has changed throughout the years and nowadays refers to a multidimensional concept including principles from classic conditioning, cognitive science, neurobiology, and motivation psychology. Generally, craving refers to a strong and seemingly *irresistible desire* to consume a particular substance, which is often triggered by external stimuli like the smell or sight of a drug or food ("cue-elicited craving") and – the stronger the more – frequently leads to loss of

control over the intake of the craved substance. Food intake, however, is not always preceded by craving and cravings do not always lead to consumption (Hill, 2007).

In *classic conditioning theories*, withdrawal is an important concept related to craving (withdrawal-elicited craving), whereby it is suggested that the intolerance of aversive states (withdrawal symptoms) engendered by abstinence leads to an increase in craving and thus to possible relapse through negative reinforcement (Skinner and Aubin, 2010; Drummond, 2000; O'Brien et al., 1992). Craving can, however, also be related to positive reinforcement, when a specific situation or cue is associated with the positive consequences of consumption, such as an increase in positive states through dopamine release (Stewart et al., 1984). *Cognitive theories* of craving incorporate the effects of mood (Baker et al., 2004), expectations and beliefs about consequences of substance consumption (Marlatt and Donovan, 2005; Tiffany, 1999), and emphasize the basic concept of self-efficacy (Bandura, 1977), the belief that one can resist one's own cravings. *Motivational models* of craving underline the importance of choice and claim that a substance is only consumed if the expected positive consequences surpass the benefits expected from abstinence (Cox and Klinger, 1988); here, the ratio between approach and avoidance tendencies related to a stimulus or substance determines craving (Breiner et al., 1999). *Neurobiological models* explain craving through individual differences and changes in the neurotransmitter and neurocircuit function, mainly referring to the reward system (Skinner and Aubin, 2010); one of these models, the incentive sensitization model of craving (Robinson and Berridge, 1993, 2001), will be described in more detail hereafter (chapter 1.3.1).

1.3.1 Stimulus salience and incentive sensitization

If you are a smoker and you are stressed, nervous, anxious or sad, you long for a cigarette. If you are an alcoholic in the same situation, you think about having a drink. And if you are an emotional eater, you think about your favourite food, you see it everywhere, you smell it, you would make an effort to get and consume it. Why is that the case? – The reasons for these specific cravings and selective attentional processes can be explained by incentive sensitization of these particular stimuli, which will be explained hereafter.

Some stimuli in the human environment with high motivational significance *automatically* attract more attention than others, which is referred to as *salience*. Seen

from an evolutionary perspective, the salience of certain stimuli is meaningful for considerations of fitness since it trains the individual towards stimuli crucial for survival (Weisfeld and Goetz, 2013). For instance, emotional stimuli with positive and negative valence have been shown to be more salient than neutral stimuli, evoke more attention and are preferentially processed (Carretié, 2014). Studies using event-related potentials (ERP) measured by electroencephalogram (EEG) show that emotional compared to neutral stimuli are related to higher electrophysiological brain activity shortly after the sight of these cues (Hajcak et al., 2010; Schupp et al., 2000), which has been denominated as "*motivated attention*" (Schupp et al., 2004).

The salience of external objects is however *not* totally *stimulus-driven*, it also varies depending on ongoing emotional states and subjective momentary or long-term goals, whereby *mood- or goal-congruent cues are preferentially processed* (Brosch et al., 2011; Becker and Leinenger, 2011). While positive mood is related to a broadening of the attentional focus, negative mood has been shown to reduce it (Dhinakaran et al., 2013), leading to an enhanced salience and attentional processing of negative stimuli, which is referred to as *mood-congruent attentional bias* (Yuan et al., 2014; Becker and Leinenger, 2011). In an extreme, biases can permanently orient the attention of an individual towards particular and selective environmental cues, as has been found for threatening information in anxiety disorders (Van Bockstaele et al., 2014). Further evidence showing the influence of subjective concerns on salience is brought forth by EEG studies showing that drug stimuli lead to more pronounced ERPs in addicts compared to non-addicts, which is specific for the respective substance of abuse, related to subjective craving and referred to as *incentive* salience (Field et al., 2010; Littel et al., 2012). Increased motivated attention towards *personally relevant* drugs has been shown for nicotine addiction (Bradley et al., 2004) and addiction to other substances such as cocaine or heroin (Franken et al., 2003, 2008), showing heightened incentive salience in people using these drugs.

The *incentive sensitization* theory put forth by the neuroscientists Robinson and Berridge explains how in the process of drug addiction formerly neutral stimuli can achieve incentive salience through enduring changes in brain reward systems (Robinson and Berridge, 2001, 1993). Through this process, brain circuits get trained to be hypersensitive towards drug (-related) cues. A key aspect of the theory is the

distinction between "*liking*" and "*wanting*", the first referring to (intrinsic) *hedonic aspects* of rewarding stimuli and the second referring to (learned) *motivational aspects* of stimuli related to craving and drug seeking behaviour. Strong "wanting" may drive behaviour unconsciously and can lead to compulsive consumption of addictive substances even without being accompanied by the hedonic feeling of "liking". Sensitization is, however, not an inevitable, automatic or mere pharmacological process, but rather is influenced by environmental factors and inter-individual differences in susceptibility; possible mediating factors are genetic predispositions, hormones and stressful life events (Robinson, 1988).

An important driver for reward signalling is the *mesocorticolimbic dopamine system* which actuates incentive sensitization through neuroadaptive processes in response to rewarding stimuli, and thus renders the addictive substance increasingly attractive (Franken et al., 2005). Reciprocal projections from the amygdala and nucleus accumbens (NAc) to the OFC are of importance for associative reward learning through instrumental and classical conditioning processes; thus, the mesolimbic dopaminergic pathway is crucial for predicting the sensory, affective and motivational reward of stimuli, for including these reinforcing aspects into decision making, and for directing behaviour accordingly (Holland and Gallagher, 2004; Murray, 2007; Everitt et al., 1999). Importantly, associative learning in the OFC is also mediated by serotonergic and glutamatergic inputs, wherefore abnormalities in the glutamate and serotonin systems may contribute to imbalanced reward learning and altered "wanting" of addictive substances (Robinson et al., 2009; Clarke et al., 2007; Kelley and Berridge, 2002; Geisler and Wise, 2008).

Following this model firstly described for drug addiction, Berridge applied their theory of incentive sensitization to food reward and broadened its focus towards the understanding of normal and abnormal eating behaviour (Berridge, 2009). According to this approach, both "wanting" and "liking" are necessary for *normal food reward*. Since food is essential for survival and a *naturally* rewarding stimulus, it automatically leads to higher salience and higher motivated attention than neutral stimuli (Kelley and Berridge, 2002; Gable and Harmon-Jones, 2010). Neuroimaging studies using functional magnetic resonance imaging (fMRI) consistently find an increased response of the OFC and the insula in response to food stimuli compared to neutral stimuli in the healthy

brain, even in satiated states (Wang et al., 2004; Simmons et al., 2005). Especially sweet foods generally elicit hedonic "liking" due to the activation of brain reward systems such as the OFC which scales the experienced sensory pleasure (Rolls, 2016). Through associative learning as described for the incentive sensitization process in drug addiction, some food stimuli can however become *overly attractive* and attention grabbing, which leads to strong motivational "wanting", possibly even in the absence of hedonic "liking".

"Wanting" is related to the experience of craving and can be modulated by mood and physiological states – analogue to mood-congruent biases to emotional stimuli. Thus, it has been shown that the brain reward response to food is potentiated under physiological hunger (LaBar et al., 2001; Porubská et al., 2006). In a similar way, experimental neurophysiology found that *food deprivation* modulates the brain response towards food pictures in healthy individuals, hunger leading to selective visual attention towards food stimuli due to higher incentive salience of the same (Stockburger et al., 2008, 2009; Mogg et al., 1998). Furthermore, it has been shown that negative mood modulates brain activity to food cues (Killgore and Yurgelun-Todd, 2006) and can increase attentional bias towards food stimuli (Hepworth et al., 2010). This is important for the conceptualization of models of emotional eating and binge-eating. As mentioned earlier in the section on emotion regulation models of EDs (chapter 1.2), the negative reinforcement model (Baker et al., 2004) indicates that negative mood activates the reward system, which entails an attentional bias towards rewarding stimuli. A possible link between attentional bias towards food and subsequent food intake is supported by experimental (Werthmann et al., 2014a, 2014c) and longitudinal studies (Calitri et al., 2010).

Altogether, this raises the question if food may be sensitized in patients with an ED in a similar manner as are drugs in addiction and if motivated attention to food is altered in ED patients compared to normal eating individuals. Behavioural studies point towards an attentional bias for food in ED patients which might indicate a higher incentive salience of these stimuli in ED patients; this is however more clearly pronounced in BN than in AN patients and evidence as a whole is inconsistent (Brooks et al., 2011; Giel et al., 2011). For BED, a recent study reported an increased preference for food in attentional processing during a behavioural task (Schmitz et al., 2014) which is also

supported by electrophysiological data showing heightened motivated attention towards high caloric food in BED patients (Svaldi et al., 2010b). In summary, these results indicate that incentive sensitization of food may be an important vulnerability or maintenance factor for ED, but the exact course of events is not yet totally understood. It may be crucial to differentiate between diagnostic categories when looking at incentive sensitization and motivated attention. On all accounts, an understanding of the neurobiology underlying food processing, craving and appetite regulation seems necessary in order to get more insight into mechanisms underlying disordered eating behaviour.

1.3.2 Neurobiological basis of food intake, craving and appetite regulation

The regulation of appetite and feeding is a complex process influenced by many different endogenous and exogenous factors, such as time of the day, emotions, hormones, and stress. Although the amount of food intake may be variable between individuals, usually within an individual a *homeostasis* is reached over time between energy expenditure and intake. Evidence suggests that homeostatic parameters are balanced primarily by influencing *meal size* as opposed to *meal frequency*, which in turn is seen to be more strongly affected by external factors and habits (Schwartz et al., 2000; Woods, 2009). While a complete overview and description of the biological substrates and processes underlying energy homeostasis goes beyond the scope of this work, the most important players in appetite regulation will be briefly introduced hereafter (see also Figure 2 for a graphical representation, *p*. 26).

At the sight, smell, or taste of food, the body initiates a response in preparation for food intake, which is called *cephalic phase response* (CPR) (Nederkoorn et al., 2000; Smeets et al., 2010). A CPR can be initiated by stimuli with primary (innate) or secondary appetitive components, the latter referring to learned conditioned responses which can be attributed even to non-food stimuli which are associated to food (Mattes, 1997). The CPR is known to prepare the body to tolerate larger amounts of food and increases the feeling of hunger through an augmentation in salivation (Epstein et al., 1996), gastric activity (Stern et al., 1989), as well as the release of pancreatic polypeptides (Teff, 2000, 2011) and the gastric hormones ghrelin and insulin (Smeets et al., 2010). Experimental data show that food exposure increases hunger and craving in healthy individuals, which is accompanied by a rise in salivation, heart rate, body temperature and gastric

activity; the magnitude of the increase in physiologic reactivity is however not necessarily related to food intake (Nederkoorn et al., 2000). In this same study, the CPR in restrained eaters was enhanced compared to participants who did not usually control their food intake, which leads to the assumption that changes in CPR may be related to dieting and abnormal eating behaviour. However, the evidence regarding CPR in response to food exposure in binge-eating compared to healthy normal-weight individuals is inconclusive, some results showing an enhanced or prolonged response (Legenbauer et al., 2004; LeGoff et al., 1988; Monteleone et al., 2010; Wisniewski et al., 1997) while others show normal (Moyer et al., 1993; Karhunen et al., 1997) or even reduced (Bulik et al., 1996) CPR in BN and BED. In AN there may be a diminished CPR (LeGoff et al., 1988), but evidence is weak and there are also studies pointing towards the opposite (Broberg and Bernstein, 1989; Monteleone et al., 2008).

The maintenance of energy homeostasis is, however, a more sophisticated process going beyond the described CPR, which is controlled by the CNS through a complex interplay of neuropeptides, neurotransmitters and gastric hormones, building feedback loops on different levels of action. Adiposity signalling hormones such as *leptin* and *insulin*, which circulate in the blood in proportion to body fat, act on the brain in order to *decrease* hunger and energy intake (Schwartz et al., 2000). Thereby, leptin seems to have a more significant role in energy homeostasis than insulin, it declines with depletion of energy stores; its absence leads to extreme obesity in rats and leptin resistance is often found in obese humans (Morton et al., 2006). These two adiposity signals act on the brain through their inhibiting influence on *hypothalamic neuropeptides* such as neuropeptide Y (NPY), melanocortins and orexins, which stimulate food intake and decrease energy expenditure (Alcaraz-Iborra and Cubero, 2015; Schwartz et al., 2000; Reichelt et al., 2015). *Orexin A* is an *appetite enhancing* neuropeptide released from the lateral hypothalamus, it has been related to the pursuit of rewarding stimuli, food craving and binge-eating (Pich and Melotto, 2014; Mahler et al., 2012; Alcaraz-Iborra and Cubero, 2015). *Ghrelin* is another important gastrointestinal hormone which acts as a hunger signal and *increases* food intake through its releasing effect on NPY and through its stimulating effect on the dopamine reward system (Abizaid et al., 2006; Egecioglu et al., 2011), it elevates before food intake and rapidly decreases afterwards (Cummings et al., 2001).

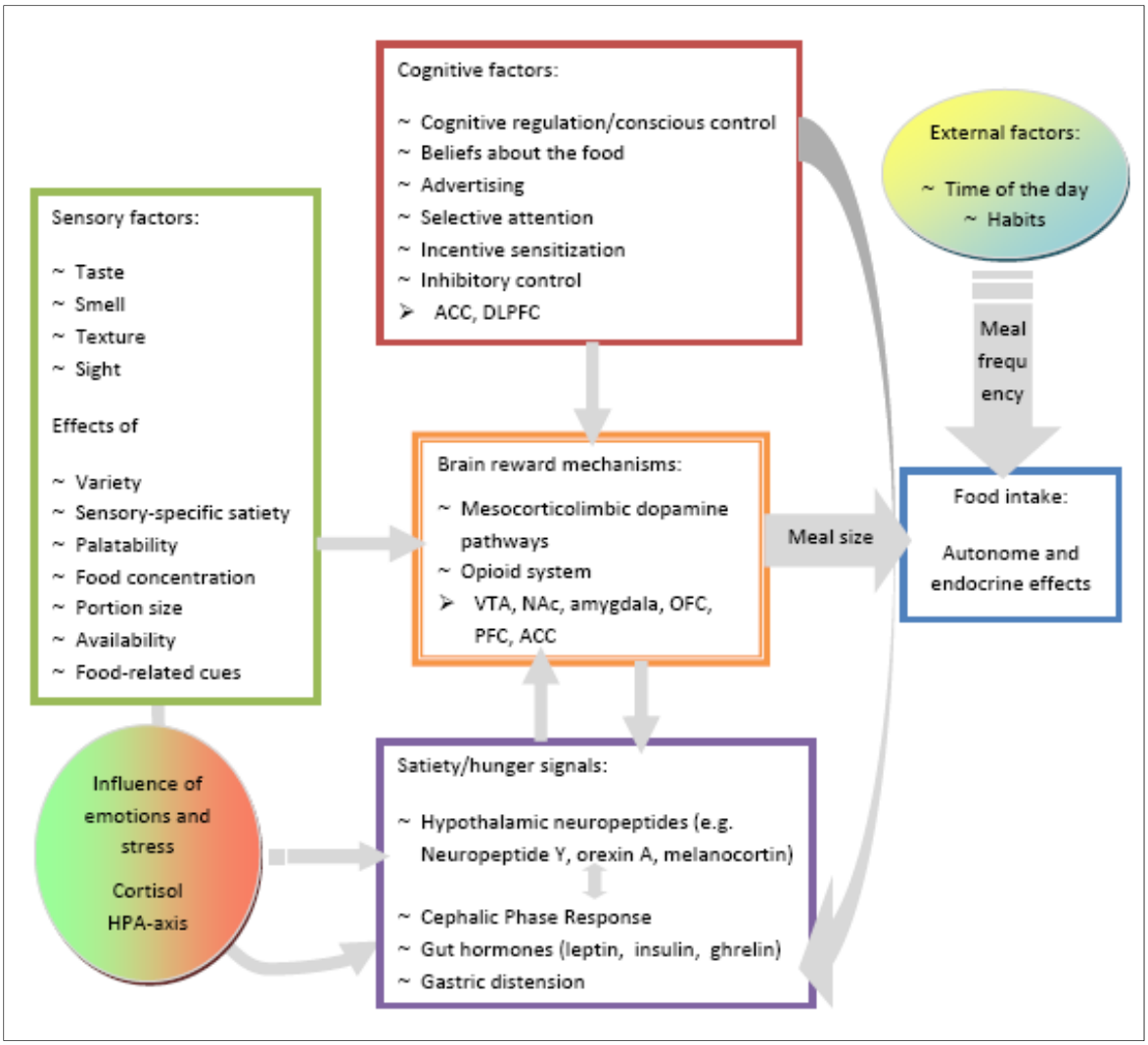

Figure 2. Most important factors for energy homeostasis and their interrelations in the regulation of craving and appetite. Figure modified from Rolls (Rolls, 2016).

ACC: Anterior Cingulate Cortex; DLPFC: Dorso-Lateral Prefrontal Cortex; HPA-axis: Hypothalamus-pituitary adrenal axis; NAc: Nucleus Accumbens; OFC: Orbitofrontal Cortex; PFC: Prefrontal Cortex; VTA: Ventral Tecmental Area

Another hormone, which is released in times of (dis)stress and initiates behavioural, autonomic and endocrinological adaptations, namely *cortisol*, also has its impact on appetite regulation (Adam and Epel, 2007). Depending on individual psychological stress reactivity, stressors can differ in the effect on food intake. This is mediated by interindividual differences in stress-related cortisol release (Stone and Brownell, 1994). In line with this, individuals who have higher cortisol release in response to stress react with more food intake (Kirschbaum et al., 1993). People with BED have been found to react to stress more sensitively and with higher cortisol release than healthy individuals (Gluck, 2006), which could be an explaining factor to their stress-related intake of large amounts of food. Glucocorticoids including cortisol and its interplay with the HPA axis

influence the release of leptin, insulin and NPY, building a feedback loop by which stress manipulates appetite regulation and reward circuits (Cavagnini et al., 2000). Thus, chronic stress and increased cortisol levels may lead to a dysregulation of the CNS control over appetite and food intake. Besides, activation of the HPA axis induces *opioid* release (O'Hare et al., 2004), which in a negative feedback loop decreases HPA activity in order to terminate the stress response (Drolet et al., 2001). However, at the same time opioids increase hedonic food intake (Castro and Berridge, 2014), which perpetuates the opioid response and its influence on the HPA axis; thus, eating may be an effective means to reduce the physiological stress response (Adam and Epel, 2007).

Neurotransmitters associated with the regulation of food intake include noradrenaline, serotonin, opioids, cannabinoids and dopamine. Dopamine is related to the rewarding function of food when released in mesolimbic pathways, but decreases food intake in other brain areas (Morton et al., 2006; Volkow et al., 2013). Endogenous cannabinoids and opioids in the NAc are important for both motivational incentive salience and hedonic aspects of food intake (Cota et al., 2006), whereby an anatomical dissociation differentiates between the opioid signalling of "wanting" versus "liking" (Kelley and Berridge, 2002; Berridge, 2009; Castro and Berridge, 2014). The lateral hypothalamus and ventral pallidum play important roles in food reward through opioid neurotransmission, lesion of the latter leads to "disliking" instead of "liking" in response to sweetness (Berridge, 2009; Castro et al., 2015).

As described in chapter 1.3.1, the mesocorticolimbic dopamine pathway is an important driver of reward, related to "liking" as well as "wanting" of rewarding stimuli and implicated in reward learning (Berridge, 2009; Schultz et al., 1997). It may, however, be more important to the *motivational* than the hedonic aspects of food reward: its release in the ventral tegmental area (VTA) towards the NAc, amygdala, PFC and other prosencephalic regions leads to an increase in food *"wanting"*. Thus, dopamine is thought to mediate the incentive sensitization of drug and food stimuli and to facilitate association learning with subsequent attribution of motivated attention to these and other related stimuli (e.g. smell of food, but also specific situations or objects in the environment), which can then lead to cue-induced craving and food-seeking behaviour (Franken et al., 2005; Berridge, 2009). The dopamine reward pathway is thought to increase the ingestion of rewarding food (Kelley et al., 2005) by acting on the lateral

hypothalamus and its neuropeptides with orexigenic function (e.g. NPY, orexin A). The lateral hypothalamus on the other hand also stimulates dopamine reward functioning through the release of orexin A (Korotkova et al., 2006). For instance, the facilitated response to pleasure stimulation during food deprivation may be explained through reduced levels of leptin and insulin when food deprived and their influence on hypothalamic neuropeptides (i.e. orexin A), which disinhibits mesocorticolimbic dopamine release towards the OFC (Morton et al., 2006; Berridge, 2009; Narita et al., 2006). By this means, hunger influences the reward value of food processed in the OFC and increases "wanting" through facilitation of hypothalamic neuropeptide release.

Considering all presented results, it nevertheless remains clear that the amount of food intake is not merely a result of interacting hormones and neurotransmitters, but rather depends to a great extent on the type of food presented on a plate and, most importantly, on its *flavour*. Corroborating this assumption, it has been shown that food placed directly into the stomach does not lead to the same feeling of satiety and reward as food eaten and tasted through the mouth (Rolls, 2016). To this effect, it is known that the combination of odour and taste together create flavour, which is crucial for food reward (Rolls, 2015). *Taste* is transmitted from the tongue receptors through cranial nerves to the thalamus and from there to the primary taste cortex comprising the frontal operculum and the anterior insula (Kaye et al., 2011; Rolls, 2012). The insula in addition receives information on gastric distension detected by mechanoreceptors in the stomach via vagal and spinal nerves (Craig, 2009; Cummings and Overduin, 2007), and thus is related to the perception of satiety and fullness (Wang et al., 2008). From this primary taste cortex, projections lead to higher order appetite-processing brain areas, such as the OFC and ACC, and also to the amygdala which incorporates affective value to stimuli (Rolls, 2015). *Olfaction* is processed from olfactory receptors in the nasal cavity, which connect to the olfactory bulb from where axons project to the amygdala and the primary olfactory cortex, comprising the piriform cortex, entorhinal cortex and olfactory tubercule (Keller, 2011). From there, information is relayed via the mediodorsal thalamic nucleus to the amygdala and the OFC where gustatory, olfactory, visual and sensory (texture, temperature) information converge (Rolls, 2016).

In contrast to the primary olfactory cortex, which represents the identity and intensity of odours, the activity in the OFC is potentiated by the hedonic value ("liking") of a given

smell (Rolls, 2015). Furthermore, activation to odour and taste stimuli has been shown to decrease with sensory-specific satiety, i.e. while for one specific flavour of a food eaten to satiety brain activation decreases, for another food the hedonic response may still be high (Rolls, 2016). Thus, the reward value of both taste and olfaction is coded in the OFC and ACC, where activation correlates with subjective pleasantness. While taste can act as a primary reinforcer, the reinforcing properties of the smell of a given food are assumed to be learned through the association of olfaction with taste in the OFC (Rolls et al., 1996). In a similar way, *visual* input from the inferior temporal visual cortex can become attributed to the taste of food and its rewarding components by associative learning in the OFC (Thorpe et al., 1983; Rolls et al., 1996), under influence of the amygdala (Murray, 2007). This explains why the OFC is consistently activated in individuals viewing pictures of food in fMRI studies, both in the satiated (Simmons et al., 2005) and deprived state (Wang et al., 2004). The OFC and amygdala in turn project to the hypothalamus and thus influence its appetite regulating function (Rolls, 2013).

The appetite regulation circuit does, however, not end here. The same group around Edmund Rolls has shown that the hedonic value of food can be affected by *cognitive top-down control*: in one of their studies, priming subjects with the words "cheddar cheese" let to significantly more liking of the same odour and respectively more OFC activation, than when preceded by the words "body odour" (De Araujo et al., 2005). These and other similar findings (Siep et al., 2012; Giuliani et al., 2013; Rolls et al., 2008; Grabenhorst et al., 2008) suggest, that appetite regulation can be influenced through top-down processes; there is even evidence suggesting that the transmission of the gut hormone ghrelin varies depending on cognitive framing (Crum et al., 2011). The DLPFC has been related to this type of self-control (Rolls, 2013) and to the use of strategies aimed at altering the desire for food (Siep et al., 2012).

Differences in cognitive control abilities is one explaining factor why some individuals are more prone to hedonic eating and loss of control over eating than others. Furthermore, the magnitude of the brain's response to food is related to trait *reward sensitivity* (Beaver et al., 2006), which makes individuals with this personality profile more susceptible to incentive sensitization and increased "wanting" of food. Moreover, modern food is omnipresent, highly palatable and disposes of a kaleidoscope of tastes, odours and textures which produces reward more easily than "natural", non-processed

food and may reinforce prolonged eating and excessive demands of the brain reward system (Rolls, 2016). Typical binge foods are highly-palatable products high in fat, sugar, and carbohydrates (Schulte et al., 2015), which lead to a release in the opioid reward system (NAc, medial PFC) and subsequent neuroadaptations (Blasio et al., 2014; Berridge, 2009; Nathan and Bullmore, 2009).

1.3.3 Functional alterations of appetite regulation circuits in eating disorders

Neuroimaging studies have found alterations in the brain reward and food processing system in patients with an ED compared to HC. For example, an fMRI study found *heightened* activity in the medial OFC and ACC in response to food stimuli in both AN and BN patients compared to HC, and differences between AN and BN in the anterior and lateral PFC, which is associated to *cognitive control* over food intake (Uher et al., 2004). Similarly, another study found increased activation of the OFC, ACC and insula towards food compared to neutral stimuli in BED, BN, overweight- and normal-weight individuals. However, the OFC activation was even higher in BED patients and was positively related to self-reported reward sensitivity; BN patients had increased activation in the ACC and insula and also reported higher arousal levels when watching food pictures (Schienle et al., 2009). An over-activation (fMRI) in response to both pleasant and aversive food stimuli was found even in recovered AN, which shows that an increased salience of food stimuli could be a trait biological marker of the illness (Cowdrey et al., 2011). Abnormalities in fMRI insula activation may reflect disturbed *interoceptive awareness* in AN (right insula) and *difficulties to perceive fullness* in BN patients (left insula) (Frank, 2015).

Furthermore, across studies it was found that during repeated stimulation with sweet taste, AN patients tend to show reduced activity in the reward circuitry, while BN patients seem to have an over-reactive reward system in response to these stimuli. Interestingly, when sweet taste stimuli are presented at random and are not predictable, the reaction pattern of the two patient groups is reversed, which suggests that cognitive mechanisms to down-regulate reward when exposure to food is anticipated may play a role in AN, while BN patients may have an underactive dopamine reward system at baseline which over-reacts through repeated stimulation (Frank, 2015). This view is compatible with the finding of *increased* dopamine receptor binding in *AN* and *decreased* binding in obesity and *BN*, although the cause-effect relation is not

clear and alterations in the dopamine system may as well be a risk, as a consequence and/or maintenance factor of the illness. A down-regulation of dopamine receptors in obesity may be due to an ongoing over-activation of the reward system and is also found in drug tolerance, while the increase of dopamine receptor binding in AN may facilitate starving (Berridge, 2009; Frank, 2015).

Alterations in the *opioid system* are likely to contribute to the pathogenesis and maintenance of BED (Giuliano and Cottone, 2015) and BN (Bencherif et al., 2005). Reward dysfunction may lead to abnormalities in "liking" of food, which could be either too strong or too weak, and might be explained by dysfunctions in the opioid system (Berridge, 2009). A strong incentive sensitization of food could lead to "wanting" without "liking" and thus to forms of compulsive eating which are not accompanied by pleasure. In this line of thinking, it has been proposed that overeating – similar to drug addiction – at the beginning is associated with hedonic reward, but that this kind of reinforcement is lost quite quickly and motivational, cue-driven aspects take control over food intake; while the hedonic aspects get lost, the behaviour gets more and more compulsive (Egecioglu et al., 2011; Everitt and Robbins, 2005).

This leads us to the last chapter of the introduction – the discussion about addiction-like eating patterns and the debate about whether or not there is an actual FA.

1.3.4 The debate about "food addiction" and addiction-like eating patterns

"Food addiction" is a nowadays widely discussed concept (Meule, 2015; Gearhardt et al., 2011; Davis et al., 2011; Ziauddeen and Fletcher, 2013), with a scientific history going back 60 years (Randolph, 1956). In the former chapters, a parallel between substance addictions and specific forms of disordered eating has become clear; there are similarities, for example, with regard to incentive sensitization of cues, brain circuits, craving and behaviour patterns. On one hand, there are behavioural characteristics in some types of abnormal food intake reminiscent of substance addictions; for example, craving is a strong component and catalyst of both binge-eating and addictive drugs (Hill, 2007; Skinner and Aubin, 2010). On the other hand, the consumption of both addictive drugs and food is related to similar brain structures (Hoebel et al., 2009); therefore, research into obesity and EDs has increasingly concentrated on a comparison of substance abuse and abnormal eating behaviour. Cumulating research on biological

similarities between drug and food intake have reinforced this concept. There are similar alterations in brain activation patterns and impairments in neurobiological functioning (Volkow et al., 2013; Michaelides et al., 2012), and animal models looking at the development of addictive eating patterns of sugar intake in rodents suggest that some underlying processes are comparable to drug abuse (Avena et al., 2008, 2012; Johnson and Kenny, 2010).

Substance use disorders (SUS) according to the DSM-5 (American Psychiatric Association, 2013) are diagnosed by checking a range of criteria (twelve altogether); these include consuming more of the substance than intended and despite of negative consequences (on physical, emotional, interpersonal levels), being unable to cut down, giving up activities, failure in role obligation and spending substantial time for drug seeking. Furthermore, the development of tolerance, withdrawal, and craving and the feeling of impairment or distress due to the addictive behaviour are important for the diagnosis of SUD. Applying these criteria to food intake, Gearhardt and colleagues developed the *Yale Food Addiction Scale* (YFAS) as a behavioural measure of FA (Gearhardt et al., 2009b). With the increasing use of the YFAS, FA has become a "diagnosis", although researchers have not yet reached an agreement on whether or not it is a *valid construct* (Ziauddeen and Fletcher, 2013). Even under the assumption that hedonic food intake can convert into FA, the question of why some people develop these addiction-like eating patterns while others don't, still remains unanswered. This same question can, however, also be asked with respect to SUD, because many people consume drugs (e.g. alcohol) but do not get addicted, while others do. To this effect, personality traits known to predispose addiction have been related to behavioural addictions and to FA, leading to the proposal of an "*addictive personality*" (Lent and Swencionis, 2012). Traits related to susceptibility to abuse and addiction and also to non-homeostatic food intake include low inhibitory control, low self-directedness, high reward/novelty seeking, delay discounting and stress reactivity (Volkow et al., 2013; Barry et al., 2009; Jiménez-Murcia et al., 2015; Appelhans et al., 2012).

However, other authors advocate the use of "*eating addiction*" instead of FA, stating that there is not sufficient evidence supporting the importance of chemical properties of food in the reinforcement of addiction-like eating patterns (Hebebrand et al., 2014). These authors propose that it is rather a matter of *addictive behaviour patterns*, without

disclaiming, however, the rewarding properties some specific foods of high sugar – high fat combinations might have. Hebebrand in his article warns about the consequences the attribution of overeating to FA in the sense of chemical dependence might have, pointing out that disturbed eating behaviour might then be viewed as a passive, externally influenced process. The effects of naming behaviour in different ways is shown in another study where participants informed that "FA is real" were more likely to self-diagnose to *actually have* an addiction to food than when they were told that "FA is a myth" (Hardman et al., 2015). Furthermore, there is a hazard of *stigmatization* of obese individuals as "addicts" despite the fact that physical appearance can be ascribed to many different causes. On the other hand, there is also evidence suggesting that a FA model of obesity might have *positive consequences* in that it reduces prejudice and blaming (Latner et al., 2014). These results underline the importance to advance research in the area of FA, but they also show that caution should be exercised when making the communicating about FA to media and the public.

Objectives

2 Objectives

The global goals of this doctoral thesis project were to assess the link between emotion and appetite and their respective regulation in order to get more insight into the explanation of ED psychopathology. More specifically, this work aimed to expand upon the knowledge on emotion regulation in ED patients and investigate the effects of these difficulties on disordered eating patterns and craving. It was further aimed to advance the research regarding addiction-like eating and to contribute to the discussion on the validity and usefulness of the FA concept. Since incentive sensitization is an important process related to the attribution of motivational meaning to potentially addictive stimuli, another aim was to investigate the incentive salience of food stimuli in healthy compared to individuals with an ED. Altogether, six studies were designed and conducted in order to pursue the following main goals:

I. To investigate differences in facial emotional expression in response to positive and negative emotional stimuli in individuals with mental disorders compared to healthy individuals (study 1);
II. To reach a better understanding of the relation between ED-specific personality traits, difficulties in emotion regulation and their shared influence on ED psychopathology (study 2);
III. To examine whether the fulfilment of the FA criteria is related to a distinguishable personality profile in ED patients (study 3);
IV. To find independent predictors of FA in a comprehensive model under consideration of ED severity (study 4);
V. To study processes related to a possible incentive sensitization of food stimuli such as increased motivated attention and low inhibitory control in response to food in people with abnormal eating behaviour (study 5), and to broaden especially the knowledge regarding these processes in patients with disorders on the binge-eating spectrum (study 6);
VI. To investigate the influence of the combination of olfactory and visual chocolate stimuli on cue-induced craving, motivated attention and inhibitory control (study 6).

Hypotheses

3 Hypotheses

Considering the theoretical background, the following hypotheses were put forth:

I. Patients with an ED have more difficulties to show and regulate emotions than HC; this is seen in alterations in facial emotional expressions in response to emotional stimuli (study 1) and in self-reported difficulties in emotion regulation (study2);

II. The established relationship between specific personality traits known to predispose ED, namely harm avoidance and self-directedness, is partly mediated by difficulties in emotion regulation (study 2);

III. FA in ED patients is related to a distinguishable personality profile, which is similar to other addiction disorders (study 3);

IV. Self-directedness, emotion regulation and negative urgency interact in their shared explanation of FA and explain variance over and above ED severity (study 4);

V. Food stimuli are processed with more motivated attention than neutral stimuli (study 5);

VI. There are differences in motivated attention to food depending on eating behaviour; patients with binge-eating show higher motivated attention to food than HC (study 5 and 6);

VII. Patients with binge-eating dispose of less inhibitory control when presented with visual food stimuli than HC participants (study 6);

VIII. Cue-induced chocolate craving, motivated attention and inhibitory control induced through visual stimuli are potentiated when primed by a chocolate odour as compared to a neutral odour (study 6).

Methods

4 Methods

Although the specific methodology for each study is delineated in the respective section, the main questionnaires used in most of the studies and relevant assessment methods are explained hereafter.

4.1 Self-report questionnaires

4.1.1 Symptom Chech-List 90 Revised (SCL-90-R)

The SCL-90-R (Derogatis, 1994) is a 90-item self-report questionnaire, it is commonly used to measure psychological distress and general psychopathology. The questionnaire comprises of nine primary symptom dimensions: *somatization*, *obsessive-compulsive symptoms, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation* and *psychoticism*. Furthermore, the questionnaire yields a global score, denominated as *Global Severity Index (GSI)*, which is a widely used index of psychopathological distress. The SCL-90 has been validated in a Spanish sample and obtained a mean internal consistency of α =.75 (Derogatis, 2002).

4.1.2 Eating Disorders Inventory-2 (EDI-2)

The EDI-2 (Garner et al., 1983) is a 91-item self-report questionnaire used to assess characteristics of AN, BN, BED and OSFED. ED behaviour and thoughts are evaluated regarding the dimensions *drive for thinness, bulimia* (binge-eating episodes), *body dissatisfaction, ineffectiveness, perfectionism, interpersonal distrust, interoceptive awareness, maturity fears, asceticism, impulse regulation* and *social insecurity*. The EDI-2 has been validated in a Spanish population (Garner, 1998), obtaining a mean internal consistency of α =.63.

4.1.3 Temperament and Character Inventory-Revised (TCI-R)

The TCI-R (Cloninger, 1994) is a 240-item self-report questionnaire measuring personality on four temperament and three character dimensions. The temperament dimensions are *harm avoidance*, *novelty seeking, reward dependence* and *persistence*. Character covers *self-directedness, cooperativeness* and *self-transcendence*. High scores in *harm avoidance* indicate behavioural inhibition, passiveness and introversion. *Novelty seeking* is characterized by approach to signals of reward and impulsivity. A

person high in *reward dependence* is sociable and dependent on others, while a person low in this trait is tough-minded and socially insensitive. *Persistence* is characterized by perseverance and ambition. *Self-directedness* refers to the ability to act responsibly and direct behaviour towards long-term goals. *Cooperativeness* is a continuum from helpful/ empathic to hostile/ aggressive. Finally, *self-transcendence* refers to imaginative/ unconventional versus controlling/ materialistic traits. The original questionnaire and the Spanish version of the revised questionnaire are validated and show good psychometric properties (Cloninger, 1994; Gutiérrez-Zotes et al., 2004).

4.1.4 Difficulties in Emotion Regulation Scale (DERS)

The DERS (Gratz and Roemer, 2004) is a 36-item self-report measure designed according to the formerly described emotion regulation model by Gratz and colleagues (see chapter 1.2). It assesses an individuals' difficulties in emotion regulation across six domains: *non-acceptance of emotional responses, difficulties pursuing goal-directed behaviours when experiencing negative emotions, difficulties controlling impulsive behaviours when experiencing negative emotions, lack of emotional awareness, limited access to emotion regulation strategies,* and *lack of emotional clarity*. Higher values indicate greater difficulties in emotion regulation. The DERS demonstrates good reliability (Cronbach's α =.93; test–retest reliability over a period ranging from 4 to 8 weeks = .88) and adequate construct and predictive validity and is significantly associated with objective measures of behavioural, physiological, and neurological components of emotion regulation (Goodman et al., 2014; Gratz & Roemer, 2004; Gratz et al., 2007, 2006; Gratz & Tull, 2010; Vasilev et al., 2009). A Spanish version of the DERS has been validated in the Spanish general adolescent population (Gómez-Simón et al., 2014).

4.1.5 Yale Food Addiction Scale (YFAS)

The YFAS (Gearhardt et al., 2009b) measures FA using 25 items which are assigned to seven scales, referring to the seven criteria for substance dependence defined by the DSM-IV: (1) tolerance, (2) withdrawal, (3) substance taken in a larger amount/ period of time than intended, (4) persistent desire/ unsuccessful efforts to cut down, (5) great deal of time spent to obtain substance, (6) important activities given up to obtain substance, (7) use continued despite psychological/ physical problems (American Psychiatric Association, 2000). The YFAS was translated into Spanish and validated in

the Spanish adult and ED population, with good validity and reliability scores (Granero, Hilker, Agüera, Jiménez-Murcia, et al., 2014).

4.1.6 Impulsive Behaviour Scale (UPPS-P)

The UPPS-P (Whiteside and Lynam, 2001; Cyders et al., 2007) measures five facets of impulsive behaviour through self-report on 59 items: *positive* and *negative urgency* (defined as the tendency to act rashly in response to positive mood or to distress), *lack of perseverance* (inability to remain focused on a task), *lack of premeditation* (tendency to act without thinking of the consequences of an act) and *sensation seeking* (tendency to seek out novel and thrilling experiences). The Spanish translation shows good reliability (Cronbach's α between .79 and .93) and external validity (Verdejo-García et al., 2010).

4.2 PRISMA guidelines

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; (Moher et al., 2009; Liberati et al., 2009)) provides an evidence-based guideline for the realization and reporting of systematic reviews and meta-analyses.

4.3 Electroencephalography and event-related potentials

Hans Berger (Berger, 1929) was the first to use and publish about human electroencephalography, the use of electrodes applied to the scalp to measure *fluctuations of current* arising from neuronal brain activity. Since then, both the hardware such as electrodes and amplifiers and the software have developed to a great extend, which now not only permits to assess and analyse large sets of EEG data, but also allows for *quantification* and *averaging* of the data. Normal brain activity usually fluctuates in frequencies of 1-40 Hertz (Hz); amplitudes can change in a range from -100 to 100 microvolt (μV) (Rugg and Coles, 1995).

In quantitative EEG analysis (QEEG), the electrophysiological activity is decomposed into its underlying frequency bands: delta ~ 1-4 Hz, theta ~ 4-8 Hz, alpha ~ 8-13 Hz, beta ~ 13-30 Hz and gamma ~ 36-44 Hz (Pizzagalli, 2007). QEEG can be helpful for example to conclude on covert activity or to investigate brain activity changes produced by the transition between two states (e.g. from sleep to awake state). The most important advantage and potential in using EEG is, however, its ability to inform about the exact timing of activity in stimulus processing, since its signal has an exactitude in

the millisecond (ms) range. ERPs are time-locked deflections in the EEG signal acquired through averaging of various trials of the same type, related to the onset of specific externally presented stimuli or to a particular response. ERPs have typical time windows and scalp distributions and can be used as electrophysiological measures of attentional processes and to deduce underlying emotional processing. The N2 is an anterior-frontal negativity appearing about 200 ms after stimulus onset and scales attentional resources needed during response conflict or behavioural inhibition (Nieuwenhuis, Yeung, van den Wildenberg, & Ridderinkhof, 2003; Pollatos, Herbert, Schandry, & Gramann, 2008). The P300 and Late Positive Potential (LPP) are both positive deflections measured at posterior electrodes, peaking around 300 ms after stimulus onset (the LPP may have a later peak) and have been ascribed to measures of motivated attention and emotional salience (Cuthbert, Gilchrist, Hicks, MacDougall, & Curthoys, 2000; Franken et al., 2008; Hajcak, MacNamara, & Olvet, 2010; Schienle, Schäfer, & Naumann, 2008; Stockburger, Schmälzle, Flaisch, Bublatzky, & Schupp, 2009).

Results

5 Results

5.1 Studies on emotions and emotion regulation in ED

Two studies were conceptualized with regard to emotional functioning and emotion regulation in patients with EDs. The first one looks at differences between ED patients, patients with other psychological disorders and healthy individuals with regard to their facial expression of emotions. The second study includes a comprehensive model of personality traits and emotion regulation in ED patients and their interaction in the influence on ED severity.

Study 1: Facial expression to emotional stimuli in mental disorders

Objectives: Research on alterations in facial expressivity in psychiatric disorders can not only help us to better understand processes underlying these disorders, but may also be a target for new therapeutic approaches. Altered facial expressivity could be a vulnerability factor to the pathogenesis of ED, contributing to social isolation and difficulties in emotion regulation. Therefore, this study aimed to give a systematic overview and integrate results by use of meta-analytical statistics and to compare automatic facial expressivity in patients with non-psychotic disorders between diagnostic categories of psychological disorders and in comparison to HC, with a special focus on EDs.

Results: A total of 39 studies show alterations in emotional facial expression across all included disorders (obsessive-compulsive disorder, depression, bipolar disorder, borderline personality disorder, AN, BN, autism spectrum disorder, disruptive behaviour disorder), except anxiety and post-traumatic stress disorders. In ED, a meta-analysis showed decreased facial expressivity in response to positive and negative stimuli in patients with AN, with a higher summary effect size for positive stimuli (d = 1.01). Regarding BN, results are more inconsistent, there seems to be evidence for less expression of negative emotions but with regard to positive emotions some studies show higher and others lower expressivity in BN patients compared to healthy participants. There were no studies found on facial expressivity for patients with BED.

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Facial expression to emotional stimuli in non-psychotic disorders: A systematic review and meta-analysis

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Abstract

Facial expression of emotion is crucial to social interaction and emotion regulation; therefore, altered facial expressivity can be a contributing factor in social isolation, difficulties with emotion regulation and a target for therapy. This article provides a systematic review and meta-analysis of the literature on automatic emotional facial expression in people with non-psychotic disorders compared to healthy comparison groups. Studies in the review used an emotionally salient visual induction method, and reported on automatic facial expression in response to congruent stimuli.

A total of 39 studies show alterations in emotional facial expression across all included disorders, except anxiety disorders. In depression, decreases in facial expression are mainly evident for positive affect. In eating disorders, a meta-analysis showed decreased facial expressivity in response to positive and negative stimuli. Studies in autism partially support generally decreased facial expressivity in this group.

The data included in this review point towards decreased facial emotional expressivity in individuals with different non-psychotic disorders. This is the first review to synthesise facial expression studies across clinical disorders.

Keywords: facial expression; emotion regulation; anxiety; obsessive-compulsive; eating disorders; borderline personality disorder; depression; autism

1 Introduction

Facial expressions have a culturally invariant basis in how they are performed and perceived (Darwin, 1872; Ekman and Friesen, 1971). Developmental studies support this idea (Reissland et al., 2011; Rinn, 1984) as well as studies which have shown that children born deaf and blind display facial expressions such as anger and smiles in circumstances that would be plausible occasions for the corresponding emotion (Eibl-Eibesfeldt, 1989).

Cultural and developmental studies suggest that all humans have the same facial musculature and move them in a similar way under similar circumstances, denoting facial expression as a behavioural phenotype (Schmidt and Cohn, 2001). However, within this

phenotype there is individual and group variation in people's ability and tendency to produce facial expressions based on factors such as culture (Chentsova-Dutton et al., 2007; Jack et al., 2012), age (Chapell, 1997), gender (Chaplin and Aldao, 2013; Hess et al., 2000), and psychopathology (e.g. Bylsma et al., 2008; Fagundo et al., 2013; Kring and Moran, 2008; Rosenthal et al., 2008).

This broad repertoire of invariant emotional facial expressions is crucial for emotional communication, social connectedness and rapport (Schmidt and Cohn, 2001). For example, facial mimicry of emotion, which is the visible or non-visible use of facial musculature by an observer to match the facial gestures in another person's expression (Hess and Bourgeois, 2010), often occurs at an unconscious level and seems to be related to enhancing levels of empathy between recipients (Nummenmaa et al., 2012). This can have important implications for effective and efficient communication.

To convey or communicate emotion is a key function of facial expression, but there are other theories, for example concerning regulation of emotion (facial feedback theory; e.g. Davis et al., 2010); social motives (Fridlund, 1994); dimensions of affect (Russell and Fernandez-Dols, 1997) and indications of direction of attention (Rutter, 1987). It has been argued that none of these theories alone is right and that the essence of facial function is hard to distil into a single theory (Parkinson, 2005); however, clearly facial expression is an important function in these processes.

Altered emotionality, social cognition and difficulties in interpersonal functioning are an integral part of many mental disorders (e.g. Aldao et al., 2010; Bylsma et al., 2008; Oldershaw et al., 2011; Tchanturia et al., 2013). Decreased emotion recognition abilities were found in a broad range of mental disorders (Kret and Ploeger, 2015), and research has shown that voluntary and involuntary facial expression of emotions plays a key role in the recognition of others' emotions (Künecke et al., 2014; Schneider et al., 2013; Sel et al., 2015). This process has been referred to as "embodiment of emotions", meaning that the perceiver simulates the emotion on a motor, somatosensory and affective level and thus deduces its meaning and reward value (Niedenthal et al., 2010; Zajonc et al., 1989). Therefore, the exploration of the nature and prevalence of facial expression alterations in mental disorders as compared to healthy control groups is a useful line of enquiry in order to better understand the mechanisms underlying difficulties in the recognition of emotions and in the emotion regulation process in general.

There are different methods for assessing facial expressions in a standardized way. One possibility is the use of electromyography (EMG), which assesses electrical activity of facial muscles, whereby corrugator supercilii (frowning), levator labii (disgust) and zygomaticus major (smiling) are the muscles of interest often assessed in emotion research (Dimberg, 1990; Sato et al., 2008; Whitton et al., 2014). Another method is coding systems to identify specific facial movements, which are then categorized into emotional expressions. The most commonly used and validated coding systems are the Facial Action Coding System (FACS; Ekman and Friesen, 2003) with its special version for emotional expressions (EMFACS; Ekman and Friesen, 1978), the Facial Expression Coding System (FACES; Kring and Sloan, 2007) and the Emotional Expressive Behaviour Coding System (EEB; Gross and Levenson, 1993).

A front runner in respect of published studies in emotional expressivity in mental disorders is the psychosis field. A

review of emotional responding, including facial expression in schizophrenia summarised 62 studies (Kring and Moran, 2008). Using a wide range of elicitation techniques, these studies showed that individuals with schizophrenia display less observable expressiveness in positive and negative emotion than individuals without schizophrenia. This has a number of interpersonal drawbacks. For example, people with schizophrenia, who are least expressive, show the poorest interpersonal relationships and poorest adjustment at home and in other social domains (Bellack et al., 1990).

Attenuated emotion expression has been observed among people with schizophrenia both on and off medication and cannot be explained by a neuromotor deficit, as electromyography recordings have shown congruent responses to stimuli (Kring and Moran, 2008). Kring and Moran suggest that patients with schizophrenia have a different threshold for producing observable displays and do so only when stimuli are of sufficient intensity (Kring and Moran, 2008). Only a few studies have looked at trait related factors and there seems to be a bias towards attenuated expression in people in remission from the illness and those at risk (Mattes et al., 1995; Walker et al., 1993).

Furthermore, a meta-analysis of emotion responses including facial expressions has been undertaken in depression (Bylsma et al., 2008). This included seven studies which measured facial expressivity using either EMG or observational coding in response to stimuli including pictures or film clips. The key findings were that people with major depressive disorder demonstrated reduced emotional reactivity to both positive and negative valenced stimuli, with the larger reduction for positive stimuli (medium effect size (ES) d=.53) than for negative stimuli (small ES d=.25) (Bylsma et al., 2008).

Very little is known about emotional expressivity in psychiatric disorders other than schizophrenia or depression. The main aims of the present review were (1) to synthesize the evidence from empirical studies exploring emotional facial expression in individuals with non-psychotic mental disorders in order to identify alterations in comparison to healthy control groups (2) to examine possible similarities and differences across disorders and (3) to assess whether facial emotion expression is related to state or trait factors.

2 Method

This review follows the guidelines in the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses; Liberati et al., 2009; Moher et al., 2009), which was developed to improve the standard of reporting of systematic reviews and meta-analyses.

2.1 Eligibility Criteria

The article focuses on automatic facial expressions elicited by emotional and social stimulus material as the main outcome. Since facial expression to neutral stimuli and incongruent responses are very rarely observed, the review concentrates on congruent responses to positive and negative emotions.

For inclusion in this review, studies were required to fulfil the following criteria: 1) a healthy control group had to be present, 2) the clinical group was diagnosed according to DSM criteria, 3) there were a minimum of 10 people in each group, 4) participants could be adolescent or adult, 5) the stimulus material to elicit facial expressions elicited positive and/or negative emotions and had to be a visual induction method, 6) the primary outcome measure was congruent automatic facial emotional expression as measured by EMG activity (zygomaticus to positive stimuli; corrugator supercilii or levator labii superioris activity to negative

stimuli) or observation [e.g. through FACES (Kring and Sloan, 2007), FACS (Ekman and Friesen, 2003), EMFACS (Ekman and Friesen, 1978) or other (e.g. automated) emotion coding programs], and 7) the study was reported in English in a peer reviewed journal.

The criterion for inclusion for meta-analysis was the use of a visual emotion induction method clearly distinguishable into positive or negative valence and the availability of means and standard deviations for the main outcomes, separated for positive and negative emotions.

2.2 Search Strategy

The following electronic databases were searched: Embase, Medline/PubMed and PsychInfo. The search covered the period from 1962 to January 2016. This start date was chosen as the empirical study of facial expression began in 1962 with the publication of books on emotion by Tomkins and by Plutchik (Russell and Fernandez-Dols, 1997).

The following search terms were used ($ denotes truncation): Facial express$ OR emotion express$ OR emotion response$ OR non verbal behave$ OR facial behav$ OR EMFACS OR facial action coding system AND clinical OR mood OR mental OR psych$ OR borderline personality disorder OR post traumatic stress OR PTSD OR anxiety OR addiction OR anorex$ OR bulimi$ OR binge eating OR obsessive$ OR bipolar OR autis$ OR personality$ OR depression OR psychosis OR schizoph$.

2.3 Study Selection

Two authors (HD and IW) screened all titles and abstracts in the electronic databases. The abstracts of potentially eligible articles were saved to an electronic reference manager. Bibliographic references from these articles were systematically searched. Eligible records then had a full text screening by two reviewers (HD and IW) and were promoted to the next stage of the process by categorising as 'yes', 'no' or 'maybe'. The next stage was to have a consensus meeting and to call in external opinions as to whether any 'maybe' records should be included in the review. From each included study, information on participants (clinical group, number of participants, age, medication status), elicitation method, coding method, outcome measure and ES was extracted by the shared first authors (HD and IW) and summarized in a table. In order to control for bias caused by the inclusion of multiple reports of the same study, authors were contacted in cases where an overlap of the sample was suspected.

2.4 Risk of bias and quality assessment

The Newcastle-Ottawa Quality Assessment Tool (Wells et al., 2014) for case control studies was applied to assess for the quality of the studies, in particular risk of bias. This tool has been used in previous studies, shows content validity and inter-rater reliability. Selection bias is assessed on four items and thus can receive a total score of 4 (definition and representativeness of cases and controls), comparability between groups is scored with a maximum of two points (depending on group matching and/or adjustments) and validity of the exposure procedure is assessed by the use of three items (ascertainment of exposure, same method for cases and controls, no-response rate). In addition to this scale, studies were rated according to the presence of a power calculation (one point if reported) and the reporting of statistical parameters necessary for meta-analysis, receiving two points if means and standard deviations were available and one point if only the ES was reported.

2.5 Data Synthesis

Due to the heterogeneous nature of the groups and methodologies in some areas and to missing statistical parameters in

others it was not feasible to undertake a quantitative meta-analysis approach in most of the diagnostic categories. For one diagnostic subcategory (eating disorders (ED)), it was possible to meta-analyse the existing data; one analyses was conducted for positive emotions and one for negative emotions. Results of all studies were summarized in a table as well as being qualitatively reviewed (IW, JL, KT and HD).

2.6 Statistical Data Analysis

Where possible, Cohen's *d* ES were calculated based on means and standard deviations. If these were not reported in the published article, corresponding authors were contacted by e-mail (IW) with the request to provide these data. In case of lack of response/unavailability of the data, ES estimations were based on the reported *t*- or *F*-statistic, when possible. ES can be interpreted as: negligible (≥−0.15 and >0.15), small (≥0.15 and >0.40), medium (≥0.40 and >0.75), large (≥0.75 and >1.10), very large (≥1.10 and >1.45) and huge (≥1.45).

Meta-analysis was based on a random effects model and computed with Stata 11.0 (Stata Corporation, College Station, TX, USA) with the user-contributed commands metan (Bradburn et al., 1998), metabias, metatrim (Steichen, 1998) and metareg (Sharp, 1998). Cohen's *d* ES and 95% confidence intervals (CI) were calculated. Assessment of consistency was done by assessing the I^2-value as an index of heterogeneity, as it is a more powerful measure for a small number of studies than Cochran's Q test (Higgins et al., 2003). The I^2 index of heterogeneity goes from 0% to 100%, indicating low (25%), moderate (50%) and high (75%) heterogeneity. When heterogeneity was moderate or high, meta-regressions for related variables such as age, depression and anxiety were calculated as an attempt to explain the inconsistency. To assess for a possible publication bias, funnel plots were visually inspected and Egger's tests (Egger et al., 1997) were calculated.

3 Results

3.1 Risk of bias

The results of the quality assessment are shown in Table 1. No studies were excluded post-hoc based on quality. This is most likely related to the strict inclusion and exclusion criteria of this review (e.g. studies which did not have a healthy control group or not clearly defined cases were excluded beforehand). It is nevertheless noted that very few studies conducted a power analyses; therefore, the possibility that some effects were not detected due to insufficient power has to be considered when interpreting the results of this systematic review.

3.2 Main study findings

A total of 39 articles (35 independent samples) were included in this review, results are shown in Table 2. Twenty-three of these studies were identified through electronic database searching and the remainder through scanning of reference lists. Figure 1 shows a flow chart of the study selection process as recommended by Moher et al. (2009). During the search, systematic reviews of emotional responding (which included facial expression) in depression (Bylsma et al., 2008) and borderline personality disorder (BPD) (Rosenthal et al., 2008) were identified. Inclusion criteria were different to the current review; therefore, studies meeting the criteria of the present review were included into the following data synthesis.

As a result of the final selection of studies included in the review, the following clinical groups were represented: post-traumatic stress disorder (PTSD; *n*=4), generalised anxiety disorder (GAD; *n*=1), social phobia (*n*=1), obsessive-compulsive disorder (OCD; *n*=3), depression (*n*=7), bipolar disorder (*n*=1), ED (*n*=11), BPD

(*n*=4), autism spectrum disorders (ASD; *n*=6) and disruptive behaviour disorder (DBD; *n*=1). There were no studies including patients diagnosed to the remaining categories of mental disorders, such as attention-deficit hyperactivity disorder, substance abuse, somatoform disorders, sleep disorders, or personality disorders other than BPD.

Table 1. Assessment of bias and study quality of included studies.

Study	Selection	Compar-ability	Exposure	Data availability	Power-Analysis
PTSD					
Carlson (1997)	♦♦♦		♦♦♦	♦♦	
Litz (2000)	♦♦		♦♦♦	♦♦	
Orsillo (2004)	♦♦♦♦		♦♦♦	♦♦	
Kirsch (2007)	♦♦♦	♦♦	♦♦♦	♦♦	
OCD					
Mergl (2003)	♦♦	♦	♦♦♦	♦♦	
Bersani (2012)	♦	♦	♦♦	♦♦	
Valeriani (2015)	♦♦		♦♦	♦♦	
Other AD					
Hubert (1990)	♦	♦♦	♦♦♦		
Baker (2002)	♦♦♦		♦♦♦	♦♦	
MD					
Berenbaum (1992)	♦♦♦	♦	♦♦♦	♦♦	
Sloan (2001)	♦	♦♦	♦♦♦	♦	
Rottenberg (2002)	♦♦♦		♦♦♦		
Tsai (2003)	♦	♦	♦♦		
Rottenberg (2005)	♦♦♦♦		♦♦♦	♦♦	
Renneberg (2005)	♦♦♦	♦♦	♦♦♦	♦♦	
Chentsova-Dutton (2007)	♦♦♦	♦	♦♦		
Bersani (2013)	♦	♦♦	♦♦	♦♦	
ED					
Soussignan (2010)	♦♦	♦	♦♦♦	♦	
Soussignan (2011)	♦♦	♦	♦♦♦	♦	
Davies (2011)	♦♦♦♦	♦♦	♦♦♦	♦♦	♦
Claes (2012)	♦♦		♦♦♦	♦♦	
Davies (2013)	♦♦♦♦	♦♦	♦♦♦	♦♦	♦
Rhind (2013)	♦♦	♦♦	♦♦	♦♦	♦
Tárrega (2014)	♦	♦	♦♦♦	♦♦	
Cardi (2014)	♦♦		♦♦	♦♦	
Cardi (2015)	♦♦		♦♦	♦♦	
Dapelo (2015)	♦♦		♦♦♦	♦♦	♦
Lang (2016)	♦♦♦	♦♦	♦♦	♦♦	
BPD					
Herpertz (2001)	♦♦♦	♦♦	♦♦♦		
Renneberg (2005)	♦♦♦	♦♦	♦♦♦	♦♦	
Staebler (2011)	♦♦♦	♦♦	♦♦♦	♦	
Matzke (2014)	♦♦♦	♦♦	♦♦♦		
ASD					
McIntosh (2006)	♦♦	♦♦	♦♦♦		
Stel (2008)	♦♦♦	♦♦	♦♦♦	♦♦	
Grossman (2013)	♦♦♦		♦♦	♦♦	
Mathersul (2013)	♦♦♦		♦♦		
Rozga (2013)	♦♦♦		♦♦	♦♦	
Yoshimura (2014)	♦♦	♦♦	♦♦♦	♦♦	
DBD					
De Wied (2012)	♦♦♦	♦♦	♦♦♦	♦	

AD = Anxiety Disorders; ASD = Autism Spectrum Disorder; BPD = Borderline Personality Disorder; DBD = Disruptive Behaviour Disorder; ED = Eating Disorders; MD = Mood Disorders; OCD = Obsessive Compulsive Disorder; PTSD = Post-Traumatic-Stress Disorder.

Newcastle-Ottawa Quality Assessment Tool (Wells et al., 2014): one point is given each for definition and representativeness of cases and controls, respectively (selection bias, total of 4), matched groups, adjustments between groups (comparability, total of 2), validity and ascertainment of exposure procedure, same method for cases and controls, low no-response rate (exposure, total of 3). Additionally, one point is given for: the presence of a power calculation, availability of means and standard deviations, availability of effect size.

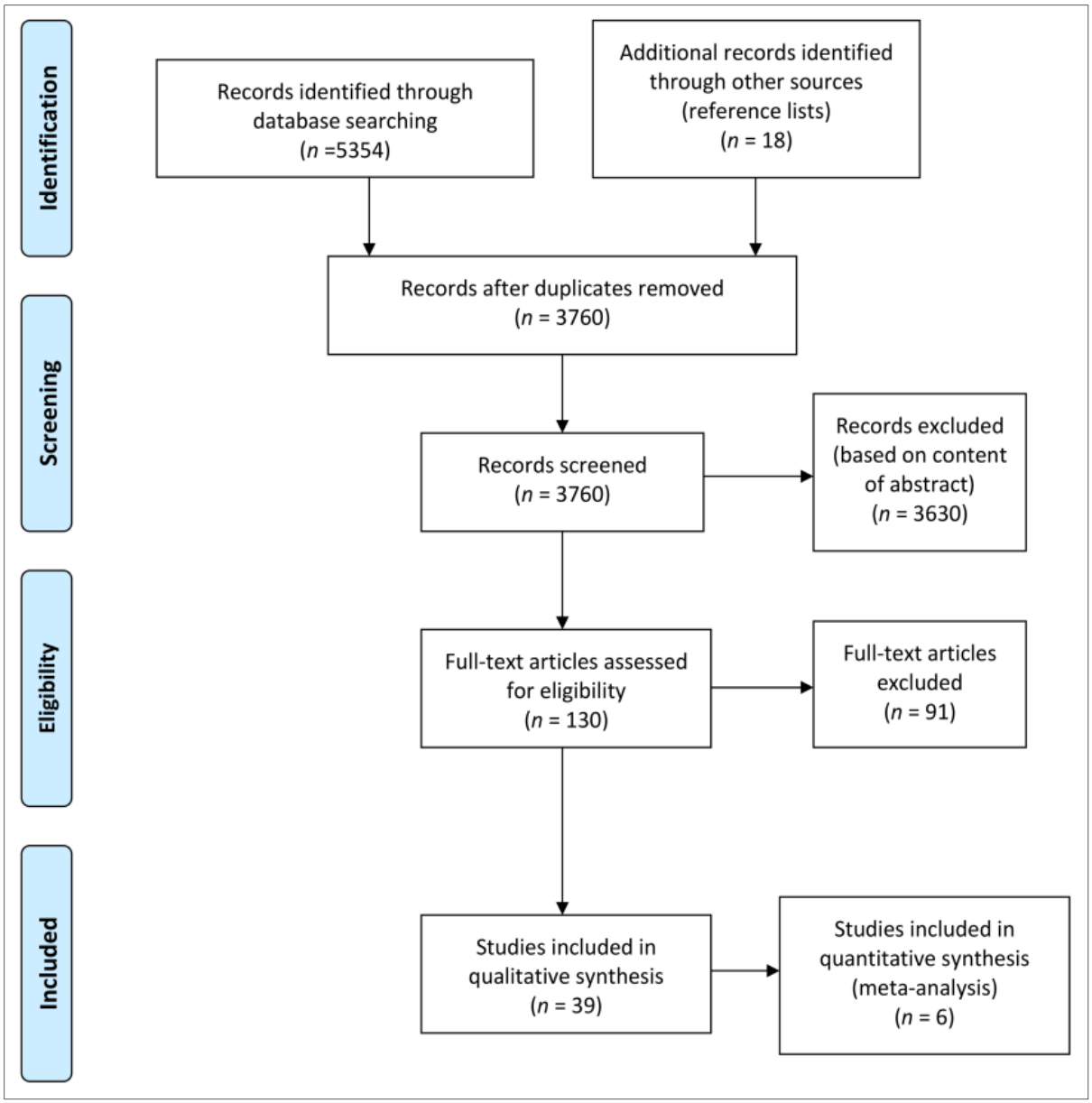

Figure 1. PRISMA flow chart of study selection process (Moher et al., 2009).

3.2.1 Evocation and coding methods

The included studies utilised different methods to evoke emotional response and different measures to record the facial expressions. With regard to the method used to evoke emotion, ten studies used pictures, 24 studies used film clips (all clinical groups), three studies used social interaction (PTSD, anxiety, BPD) and two studies used a video game (ED). Twelve of the studies used EMG to record facial expression, three studies used automated emotion recognition techniques and the remainder utilised an observational coding technique, of these twelve used FACS/ EMFACS, nine FACES and two EEB.

Table 2. Summary of studies included into the systematic review of emotional facial expression in non-psychotic DSM Axis I and II disorders.

Authors[1]	Clinical Group	Nr of partici pants	Age in years Mean (SD)	Psychoact. Medication (N/group)	Emotion Elicitation Method	Coding Method	Outcome Measure	Result and Effect Size (magnitude)
Post-Traumatic Stress Disorder								
Carlson (1997)	PTSD (war veterans)	PTSD: 10 HC: 10	PTSD & HC 49.4	Not monitored	Pictures[2]	EMG	Negative (corrugator)[3]	NS 0.66[++]
Litz (2000)	PTSD (war veterans)	PTSD: 32 HC: 29	PTSD: 49.5 (2.8) HC: 52.3 (5.3)	Not reported	Pictures[4]	EMG	Positive (zygomaticus)[5] Negative (corrugator)	NS .06[+-] NS .08[+-]
Orsillo (2004)	PTSD (sexual trauma)	PTSD: 18 HC: 17	PTSD & HC: 35.4 (14.1)	Not reported	Film clips[6]	FACES	Positive expression[7] - Amusement film - Contentment film Negative expression - Sadness film - Fear film - Anger film	 NS 0.59[++] NS 0.36[+-] NS 0.45[++] NS 0.11[+-] NS 0.26[+-]
Kirsch (2007)	PTSD (sexual trauma)	PTSD:15 HC: 15	PTSD: 44.9 HC: 46.7	Not reported	Social interaction[8]	EMFACS	Positive expression - Duchenne smiles - Non-Duchenne smiles Negative expression (anger)	 PTSD<HC 1.59 PTSD<HC 1.23 PTSD>HC 0.97
Obsessive Compulsive Disorder								
Mergl (2003)	OCD	OCD: 34 HC: 34	OCD: 35.8 (11.5) HC: 37.5 (13.1)	OCD (at baseline): 0 HC: 0	Film clips[9]	Kinematical analysis and video-recording	Positive (laughing)[10] 1. Frequency 2. Initial velocity - left eye - right eye - left angle of the mouth - right angle of the mouth	 OCD < HC 1.17 OCD < HC .68 OCD < HC .62 OCD < HC .74 OCD < HC .62
Bersani (2012)	OCD	OCD: 10 HC: 10	OCD: 40.22 (13.49) HC: 40.20 (10.49)	OCD: min 7 HC: 0	Film clips[11]	FACS	Congruent emotional expression[12]	OCD < HC 2.45
Valeriani (2015)	OCD	OCD: 10 MildOCD: 11 HC: 15	OCD: 40.61 (6.21) MildOCD: 37.77 (8.21) HC: 41.71 (12.53)	Not reported	Film clips[13]	FACS	Congruent emotional expression[12]	OCD < HC 3.09 MildOCD < HC 2.74
Other Anxiety Disorders								
Hubert (1990)	Generalized Anxiety Disorder	GAD: 12 HC: 12	GAD & HC: 30	GAD: 0 HC: 0	Film clips[14]	EMG	1. Positive film clip 2. Negative film clip	NS[*+-] NS [*+-]
Baker (2002)	Social Phobia and Clinical anxiety	CA:10 SP: 10 HC: 10	CA: 48.3 (11.4) SP: 42.3 (12.2) HC: 50.9 (8.0)	Not reported	Social[15] interaction	Observation	Positive (relative amount of time spent smiling)	SP vs HC NS .05[+-] CA vs HC NS .25[++]
Mood Disorders								
Berenbaum (1992)	Depression	DPN: 17 HC: 20	DPN: 38.9 (11.3) HC: 36.1 (10.8)	DPN: 6 HC: 0	Film clips[16]	EMFACS	Positive expression[17] Negative expression[17]	DPN < HC .91 NS .17[+-]
Sloan (2001)	Depression	DPN: 20 HC: 20	DPN: 40.4 (9.2) HC: 42.5 (6.0)	DPN: 20 HC: not reported	Pictures[18]	FACES	Positive expression[19] - Frequency - Intensity Negative expression - Frequency - Intensity	 DPN < HC 3.63 DPN < HC 2.66 NS .25[++] NS .23[++]

Authors[1]	Clinical Group	Nr of participants	Age in years Mean (SD)	Psychoact. Medication (N/group)	Emotion Elicitation Method	Coding Method	Outcome Measure	Result and Effect Size (magnitude)
Rottenberg (2002)	Depressions	DPN: 72 HC: 33	DPN: 33.4 (10.5) HC: 32.3 (11.7)	DPN: 31 HC: 0	Film clips[20]	EEB	Positive expression[21] Negative expression	NS*+- NS*+-
Tsai (2003)	Depression	DPN: 12 HC: 10	DPN & HC: 28.28 (7.45)	Not reported	Films clips[22]	FACS	Positive expression[23] - Duchenne smile - Non-Duchenne smile Negative expression	 NS*+- DPN < HC 1.09 NS*+-
Rottenberg (2005)	Depression	DPN: 19 RecDPN: 22 HC: 26	DPN: 35.7 (7.5) RecDPN: 33.7 (9.3) HC: 33.6 (10.7)	DPN: 6 RecDPN: 7 HC: 0	Film clips[24]	EMG	Positive (zygomaticus)[25] Negative (corrugator)	DPN > HC .72 RecDPNvsHC NS .57-- DPNvsRecDPN NS .12+- DPN vs HC NS .24-- RecDPN vs HC NS .37-- DPN vs RecDPN NS.16+-
Renneberg (2005)	Depression	DPN: 27 HC: 30	DPN: 39.1 (8.0) HC: 28.3 (8.6)	Not reported.	Film clips[26]	EMFACS	Positive expression[27] - Frequency (happiness) - Frequency (surprise) - Intensity Negative expression (frequency)	DPN < HC .73 DPN < HC .8[a] NS .1[a]+- DPN < HC .82[a] DPN < HC .87[a]
Chentsova-Dutton (2007)	Depression	DPN: 27 HC: 29	DPN EA: 28.7 (8.4) DPN AA: 26.8 (9.1) HC EA: 32.0 (9.8) HC AA: 26.3 (4.9)	DPN: 12 HC: 0	Film clips[28]	EEB	Positive expression[29] Negative expression - Likelihood of crying	NS*++ NS*+- DPN EA < HC OR .34 DPN AA > HC OR 6.5
Bersani (2013)	Bipolar Disorder	BD: 15 HC: 15	BD: 48.13 (10.60) HC: 41.80 (12.50)	BD: 15	Film clips[30]	FACS	Congruent emotional expression[31]	BD < HC 1.84
Eating Disorders								
Soussignan (2010)	AN	AN: 16 HC: 25	AN: 26.6 ± 7.3 HC: 24.6 ± 6.0	AN: 0 HC: 0	Pictures[32]	EMG & FACS	Positive[33] - Zygomaticus - Smiles Negative - Corrugator - Expression	 AN < HC .78 AN < HC .78 NS*-- NS*+-
Soussignan (2011)	AN	AN: 17 HC: 27	AN: 26.5 ± 7.1 HC: 24.7 ± 6.1	AN: 0 HC: 0	Pictures[34]	EMG	Positive (zygomaticus)[35] - Food - Objects Negative (corrugator) - Food - Objects	 AN < HC .64[a] AN < HC .78[a] NS*-- NS*+-
Davies (2011)	AN	AN: 30 HC: 34	AN 24.5 (19-33.5) HC 23 (19-31.5)	Not reported	Film clips[36]	FACES	Positive expression Negative expression[37]	AN<HC 1.78 AN<HC .99
Claes (2012)	AN BN	AN: 11 BN: 12 HC: 11	AN: 32.5 (9.7) BN: 29.2 (10.5) HC: 28.1 (5.1)	Not reported	Videogame[38]	Facial Recognition software	Expression of joy[39] Expression of anger	AN vs. HC NS .22++ BN vs. HC NS .16-- AN < HC 1.02 BN vs. HC NS .92++

Authors[1]	Clinical Group	Nr of participants	Age in years Mean (SD)	Psychoact. Medication (N/group)	Emotion Elicitation Method	Coding Method	Outcome Measure	Result and Effect Size (magnitude)
Davies (2013)	AN RecAN	AN: 49[38] RecAN: 21 HC: 53	AN: 25.9 (6.8) RecAN: 28.4 (8.7) HC: 26.4 (8.4)	AN: 19 RecAN: 4 HC: 0	Film clips[36]	FACES	Positive expression Negative expression[41]	AN < HC 1.72 AN < RecAN 1.10 RecAN vs HC NS .50[++] AN < HC 1.13 AN vs RecAN .46[++] RecAN vs HC .61[++]
Rhind (2013)	AN	AN: 16 HC: 17	AN: 14.75 (1.65) HC: 14.41 (1.28)	Not reported	Film clips[42]	FACES	Positive expression[43] Negative expression	AN < HC 1.7 AN < HC 1.6
Tárrega (2014)	BN RecBN	BN: 22[42] RecBN: 22 HC: 19	BN: 28.9 (7.8) RecBN: 27.2 (8.6) HC: 29.4 (8.1)	Not reported	Videogame[38]	Facial Recognition software	Expression of joy Expression of anger[45]	BN > HC 8.96 RecBN vs HC NS 1.13[++] BN > RecBN 10.26 BN < HC 53.54 RecBN < HC 29.08 BN < RecBN 27.18
Cardi (2014)	AN BN	AN: 49 BN: 16 HC: 73	AN: 28.2 (10) BN: 23.4 (5.7) HC: 26.4 (7.8)	AN: 26 BN: 9 HC: N/A	Pictures[46]	FACES	Positive expression[47] Negative expression - Sadness - Frustration	ED < HC .79 NS .2[++] NS .1[++]
Cardi (2015)	AN BN	AN: 49[48] BN: 16 HC: 73	AN: 28.2 (10) BN: 23.4 (5.7) HC: 26.4 (7.8)	AN: 26 BN: 9 HC: N/A	Film clips[49]	FACES	Positive expression[50] Negative expression - Sadness - Anger	ED < HC .8 ED < HC .2 ED < HC .52
Dapelo (2015)	AN BN	AN: 20 BN: 20 HC: 20	AN: 28.85 (9.75) BN: 26.85 (6.75) HC: 26.40 (7.60)	AN: 12 BN: 5 HC: 0	Film clips[51]	FACS	Duchenne Smile[52] - Duration - Intensity Non-Duchenne Smile - Duration - Intensity	 AN < HC 1.13 BN vs HC NS .78[++] AN < HC 1.6 BN vs HC .36[++] AN < HC 1.32 BN < HC .92 AN < HC 1.67 BN vs HC NS .85[++]
Lang (2016)	AN	AN: 36 HC: 38 AN: 30 HC: 38	AN: 26.03 (6.82) HC: 24.79 (7.08) AN: 15.08 (1.79) HC: 15.05 (1.93)	Not reported	Film clips[36]	FACES	Positive expression[53] Negative expression Positive expression Negative expression	NS .26[++] NS .09[+-] AN < HC .61 NS .07[+-]
Borderline Personality Disorder								
Herpertz (2001)	BPD (criminal offenders)	BPD: 18 HC: 24	BPD: 33.3 (6.9) HC: 32.5 (10.8)	BPD: 0 HC: 0	Pictures[54]	EMG	Negative (corrugator)[55]	BPD < HC*
Renneberg (2005)	BPD	BPD: 30 HC: 30	BPD: 28.5 (9.1) HC: 28.3 (8.6)	Not reported	Film clips[26]	EMFACS	Positive expression[27] - Frequency (happiness) - Frequency (surprise) - Intensity Negative expression (frequency)	BPD < HC .64 NS .45[a++] BPD < HC .93[a] NS .45[a++] BPD < HC .71

Authors[1]	Clinical Group	Nr of partici pants	Age in years Mean (SD)	Psychoact. Medication (N/group)	Emotion Elicitation Method	Coding Method	Outcome Measure	Result and Effect Size (magnitude)
Staebler (2011)	BPD	BPD: 35 HC: 33	BPD: 27.9 (8.3) HC: 27.9 (8.6)	BPD: 23 HC: 0	Social Interaction[56]	EMFACS	Positive expression[57] Negative expression	BPD<HC 0.92 BPD>HC 0.74
Matzke (2014)	BPD	BPD: 28 HC: 28	BPD: 24.93 (5.81) HC: 24.81 (5.40)	BPD: 0 HC: 0	Pictures[58]	EMG	Positive (zyogamaticus)[59] Negative (corrugator) - Anger - Sadness - Disgust - Fear Negative (levator labii)	NS* BPD > HC .7[a] BPD > HC .69[a] BPD > HC .49[a] NS* NS*
Autism Spectrum Disorder								
McIntosh (2006)	ASD	ASD:14 HC: 14	ASD: 27 (13.8) HC: 24 (8.6)	Not reported	Pictures[60]	EMG	Congruent facial expressions[61]	ASD < HC .82[a]
Stel (2008)	ASD	ASD: 23 HC: 21	ASD: 14.6 (0.6) HC: 15.7 (0.4)	Not reported	Films clip[62]	Observation	Positive expression[63]	ASD < HC 1.34
Grossman (2013)	ASD	ASD: 14 HC: 12	ASD: 13.1 (3.4) HC: 15 (3.6)	Not reported	Film clips[64]	Observation	Congruent expressions[65] Intensity of expression	NS .39 NS .67
Mathersul (2013)	ASD	ASD: 18 HC: 18	ASD: 36.7 (17.1) HC: 44.6 (15.5)	Not reported	Pictures[66]	EMG	Positive (zygomaticus)[67] Negative (corrugator)	NS*+- NS*++
Rozga (2013)	ASD	ASD: 17 HC: 17	ASD: 16.6 (9.2) HC: 15.2 (5.4)	Not reported	Film clips[68]	EMG	Positive (zygomaticus)[69] Negative (corrugator) - Anger - Fear	NS .24++ NS .47++ ASD < HC .50
Yoshimura (2014)	ASD	ASD: 15 HC: 15	ASD: 26.2 (6.9) HC: 24.1 (4.0)	ASD: 0 HC: 0	Film clips[70]	FACS & FACES	Positive expressions[71] - Dynamic - Static Negative expressions - Dynamic - Static	 ASD < HC .81 NS .19++ ASD < HC 1.02 NS .00+-
Disruptive Behaviour Disorder								
De Wied (2012)	DBD	DBD/CU+: 14 DBD/CU-: 17 HC: 32	DBD/CU+: 13.93 (1.17) DBD/CU-: 13.29 (0.85) HC: 13.75 (0.76)	DBD: 14 HC: 0	Film clips[72]	EMG	Positive (zygomaticus)[73] Negative (corrugator) - Sadness - Anger	DBD/CU- < HC .73 DBD/CU+ vs. HC NS .5 DBD/CU+ < HC .48 DBD/CU- < HC .52 NS .07a+-

NS: non-significant; results in bold indicate significant differences between groups.
* indicates that mean/standard deviations or f statistic were unobtainable to calculate effect size.
[a] The effect size is an approximation of the real effect size, calculated through the "Practical Meta-Analysis Effect Size Calculator" by David B. Wilson
++ indicates a trend to more facial expression in the HC group; -- indicates a trend to less facial expression in the HC group; +- indicates where the direction of the effect is unclear.

AA: Asian Americans of East Asian descent; AN: Anorexia Nervosa; ASD: Autism Spectrum Disorder; BPD:Borderline Personality Disorder; CA: Clinical Anxiety; CU: callous unemotional traits; DBD: Disruptive Behaviour Disorder; DPN: Depression; EA: East Asians; EEB: Emotional Expressive Behavior Coding System (Gross & Levenson, 1993); EMFACS: Emotional Facial Action Coding System (Ekman & Friesen, 1978); EMG: Electromyography; FACS: Facial Action Coding System (Ekman & Friesen, 2003); FACES: Facial expression coding system (Kring & Sloan, 2007); GAD: Generalised anxiety disorder; HC: Healthy Control; IAPS: International Affective Picture System (Lang, Bradley & Cuthbert, 1999); OCD: Obsessive Compulsive Disorder; OR: Odds Ratio; PTSD: Post Traumatic Stress Disorder; Rec: Recovered; SP: Social phobia.

[1] First authors stated only.
[2] 15 combat-related and 15 neutral pictures
[3] PTSD patients had significantly higher values than HC on a subjective measure of distress.

[4] Positive, negative and neutral IAPS pictures, 8/category. Trauma related and neutral priming videos were shown prior to pictures. The results shown are based on the neutrally primed blocks.
[5] Groups did not differ in subjective ratings of valence or arousal. The combat prime increased corrugator activity to negative stimuli in both groups similarly.
[6] The Money Pit (amusement; 4:31m), The Champ (sadness; 2:44m), Cat's Eye (fear; 1:42m), Cry Freedom (anger; 2:36m), waves breaking on a beach (contentment; 1:04m)
[7] PTSD patients had significantly higher values than HC on a subjective measure of negative feelings towards all of the film clips and of positive feelings towards the anger and fear film clips.
[8] Participants were filmed during a psychodynamic interview.
[9] Mr. Bean (amusement; max. 9m).
[10] Groups did not differ in voluntary facial movement or subjective ratings of amusement.
[11] MGM introduction (neutral; 0:10m), When Harry met Sally (amusement; 2:35m), The Shining (fear; 1:22m), Capricorn one (surprise; 0:49m), Cry Freedom (anger; 2:36m), The Champ (sadness; 2:51m), Pink Flamingos (disgust; 0:30m), Roberto Benigni and Massimo Troisi video interview (amusement; 1:30m)
[12] Facial expression values are not reported separately for positive and negative emotions. OCD patients had significantly lower values than HC on a subjective measure of emotions. Bersani 2012: OCD patients did not differ significantly on emotional measures when compared to a group of patients with schizophrenia.
[13] Color Bars (neutral; 0:08m), When Harry met Sally (amusement; 2:35m), The silence of the lambs (fear; 3:29m), Sea of love (surprise; 0:09m), Cry Freedom (anger; 2:36m), The Champ (sadness; 2:51m), Pink Flamingos (disgust; 0:30m)
[14] Indiana Jones (Anxiety/disgust; 9m) and Peanuts cartoon (Joy; 9m)
[15] 9 minute talk with a confederate of the experimenters.
[16] Chinatown/Marathon Man (negative), The Godfather (negative), Bill Cosby: Himself (positive), Alt Baba Bunny (positive), all films had a length between 2:47m and 3:32m.
[17] Groups did not differ in voluntary facial movement or subjective ratings of happiness and disgust. Patients with depression did not differ in negative emotional expression from a group of patients with non-blunted schizophrenia, but showed less positive emotions these patients.
[18] Positive (happiness and contentment), negative (sadness and disgust) and neutral IAPS pictures, 16/category.
[19] Depressed patients rated positive pictures as less pleasant and less arousing than the HC group, groups did not differ in their rating of negative pictures. Neutral slides did not elicit notable facial expressions.
[20] Landscape (neutral; 3m), airplane turbulence (fear; 2:20m),. boy mourning father (sadness, 2:50m), slapstick comedy (amusement; 2m).
[21] Depressed patients reported more sadness and less amusement during neutral and amusing films, but there were no differences for the fear or sadness films.
[22] Two sad (one human; 3:35m, one animal; 2m), two amusing film clips (one human; 4:07m, one animal; 1:12m), neutral (colour sticks; 1m)
[23] Groups did not differ significantly in self-report of emotional experience.
[24] Landscape (neutral; 3m), airplane turbulence (fear; 2:20m), boy mourning father (sadness, 2:50m), boy with family (happiness; 3:57m). The study also used idiographic stimuli, but for comparability here only data to these normative clips is reported.
[25] Reported is the difference score of change between neutral and emotional pictures. The DPN group reported less happiness and more sadness in response to all stimuli than the HC and RecDPN groups.
[26] Cry Freedom (negative), French Kiss (positive).
[27] Depressed patients did not differ significantly in facial expression of negative and positive emotion from patients with BPD (63% also had a comorbid depression). Medication status had no effect on the outcome.
[28] Natural scenery (neutral; 3m), The Champ (sadness; 2:50m), Mr. Bean (amusement; 2m), shown in this order.
[29] EA depressed patients reported significantly less sadness to the negative film than HC, AA depressed patients did not differ from HC. There were no group differences in the subjective ratings of the positive film clip. Medication did not have any effect on emotional reactivity for either of the groups.
[30] Color Bars (neutral; 1:30m), When Harry met Sally (amusement; 2:35m), The Shining (fear; 1:22m), Capricorn One (surprise; 0:49m), Cry Freedom (anger; 2:36m), The Champ (sadness; 2:51m), Pink Flamingos (disgust; 0:30m), Roberto Benigni and Massimo (amusement; 1:30m).
[31] Facial expression values are not reported separately for positive and negative emotions. Patients with BD showed significantly more congruent emotion expressions than schizophrenia patients. BD patients had significantly lower values than HC on a subjective measure of emotions.
[32] 32 IAPS pictures of food. The pictures were preceded by subliminal emotional and neutral face primes, results shown are based on the main effects of group regarding facial expression. Participants were tested in a hungry and in a satiated state, results show main effects of facial expression.
[33] AN patients reported significantly less hedonic liking in response to food pictures than HC in both states and lower wanting in the hunger state. For emotional primes, only fear induced more corrugator activity in AN compared to HC (in the hunger state only), for zygomaticus activity, smiles and negative expression there was no priming effect.
[34] 6 food and 6 object pictures matched for hedonic rating. There were no differences between AN patients and HC in the subjective rating of the pictures.
[35] Participants were tested once in a hungry state and once in a satiated state, the table shows main effects. There was an interaction effect for food pictures in corrugator activity in that patients had higher activity than HC during the

hungry state only. Also, for the time window between 400 and 600ms post stimulus, AN patients had less corrugator activity for picture stimuli.
[36] Four Weddings and A Funeral (amusement; 2m), Shadowlands (sadness; 2m), waves (neutral; 2m).
[37] AN patients looked away significantly more often than HC during the negative film, for the positive film there was no difference in frequency of looking away. AN patients reported significantly less positive affect in response to the positive film clip than HC, groups did not differ for ratings of the negative film clip.
[38] Playmancer video game designed to train emotion regulation, set on an island and consisting of three mini-games including different challenges. Emotions are coded during the game, but the stimulus valence is not clearly assignable to the coded expressions.
[39] AN and BN patients did not differ significantly, but AN patients tended to express less. BN patients self-reported significantly more state anger than HC, there were no differences in anger between HC and AN.
[40] One part of the patients of the AN group was included in Davies (2011).
[3941] During the negative film AN patients looked away significantly more often than HC and RecAN (which did not differ), for the positive film there was no difference in frequency of looking away. AN patients reported significantly less positive affect in response to the positive film clip than HC, RecAN did not differ significantly from neither of both groups, groups did not differ for ratings of the negative film clip.
[42] The Bare Necessities from the Jungle Book (amusement), The Death of Mufasa from Lion King (sadness), ocean waves (neutral).
[43] Groups did not differ in subjective ratings of positive and negative effect in response to the according film clips.
[44]One part of the patients of the BN and of the HC groups was included in Claes (2012).
[45] BN patients self-reported significantly more state anger than HC and than RecBN, RecBN reported more anger than HC.
[46] Four film clips (1m each) showing infants displaying discrete emotions: happiness, sadness, anger and neutrality.
[47] AN and BN groups did not differ significantly on the main outcome measures, wherefore they were pooled into one ED group. Groups did not differ in frequency of looking away. AN patients reported more negative emotions in response to sad film clips, groups did not differ in subjective emotion ratings of the other film clips.
[48] Same sample as included in Cardi (2014)
[49] Four film clips (1m each) showing adults displaying discrete emotions: happiness, sadness, anger and neutrality.
[50] AN and BN groups did not differ significantly on the main outcome measures, wherefore they were pooled into one ED group. Participants with ED looked away more frequently than HC in response to both of the films. Groups did not differ in subjective ratings of positive and negative emotions experienced during the film clips.
[51] Waves (neutral; 0:30m), Four Weddings and A Funeral (amusement; 2m).
[52] Groups did not differ in subjective ratings of positive mood in response to the positive film clip. AN patients had significantly lower values than BN in duration and intensity of duchenne smiles and in intensity (but not duration) of non-duchenne smiles.
[53] AN patients looked away significantly more often than HC during the negative film, for the positive film there was no difference in frequency of looking away. AN patients reported significantly more negative emotions during the negative and the positive film clip than HC, groups did not differ for ratings of the positive film clip.
[54] Positive, negative and neutral IAPS pictures, 8/category.
[55] The outcome is measured as corrugator activity change from neutral to unpleasant pictures. BPD patients did not differ from a group of psychopaths in negative stimulus evoked corrugator activity. Groups did not differ in self-report ratings of valence and arousal in response to the pictures.
[56] Participants facial expressions were observed when playing Cyberball, a virtual ball-tossing game that reliably induces social exclusion.
[57] Compared to HC and to an objective measure, BPD patients felt more excluded while playing the game, they also reported more self-focused negative and less positive emotions (independent from playing) and more increase in other focused negative emotions after being excluded. Depression and medication did not significantly change outcomes.
[58] NimStim Face Stimulus set: 5 male and 5 female faces depicting happiness, sadness, anger, surprise, disgust, fear, 10/category morphed into dynamic facial expressions.
[59] BPD patients did not differ from HC in recognition of facial expressions, nor on subjective intensity ratings of the pictures.
[60] Pictures depicting angry and happy facial expressions, 8/category.
[61] Results are not reported separately for positive and negative stimuli. Groups did not differ in voluntary mimicry of facial expressions.
[62] Student talking about his adventures (amusement; 5m).
[63] Groups did not differ in voluntary mimicry of facial expressions. Facial expression during the video correlated with reported emotion experience in HC, but not in ASD.
[64] Four videotaped stories told by "Safari Bob", depicting happy, fearful, angry and positive surprise emotions (0:25-0:32m).
[65] Results were not reported separately for positive and negative emotions.
[66] Positive, negative and neutral IAPS pictures, 18/category.
[67] Groups did not differ in subjective ratings of valence and arousal in response to the pictures.
[68] Actors depicting sentences in angry, fearful, or happy valence, 8/category (0.9-2s).
[69] Groups did not differ in an emotion recognition task.

[70] Male and female faces displaying facial expressions, dynamic (evolving from neutral to angry and neutral to happy expressions) vs. static (1.5s).
[71] Results for FACS and FACES coding were comparable, effect sizes are shown for FACES data since it seemed to be the more conservative measure. Groups did not differ in voluntary mimicry of facial expressions.
[72] Boys and girls in everyday situations creating sadness, anger and happiness, 2/category (2:04m-2:37m).
[73] Medication had a significant effect on the outcome and was therefore entered as covariate. Groups did not differ in an emotion recognition task. The high CU group reported less empathy in response to the films than the low CU and the HC groups, which did not differ. DBD groups did not differ in facial expressivity.

3.2.2 Anxiety Disorders:

3.2.2.1 Post-Traumatic Stress Disorder (PTSD)

Four studies were retrieved for PTSD. Three of these used emotional pictures or film clips to induce emotion and did not find group differences of negative expressivity to negative stimuli or positive expressivity to positive stimuli (Carlson et al., 1997; Litz et al., 2000; Orsillo et al., 2004). One of these studies used disorder specific stimuli (combat related pictures in war veterans; Carlson et al., 1997); results were comparable to those studies using generic emotional stimuli (Litz et al., 2000, Orsillo et al., 2004). The one study using a social interaction to evoke emotion found less positive and more negative facial expressions in PTSD patients compared to HC, with large to very large ES (*d*=.97-1.59) (Kirsch and Brunnhuber, 2007).

3.2.2.2 Obsessive Compulsive Disorder (OCD)

Three studies found reduced facial expressivity in patients with OCD in response to film clips with positive versus negative valence. Two of them reported one total score for congruent emotional expression to negative and positive stimuli (Bersani et al., 2013; Valeriani et al., 2015); therefore, it is not known if blunted facial expression was due to negative or positive valence or both. The third study used only positive stimulus material, showing that OCD patients express positive emotions less frequently and with decreased velocity than HC (Mergl et al., 2003). ES ranged from medium (*d* = .62) to huge (*d* = 3.09), evidencing robustness of these results.

3.2.2.3 Other Anxiety Disorders

Two studies were retrieved which included clinically anxious groups (Baker and Edelmann, 2002; Hubert and De Jong-Meyer, 1990). These found no significant differences regarding automatic facial expression of congruent emotions in response to emotional film clips or a social interaction paradigm.

3.2.3 Mood Disorders

3.2.3.1 Depression

Seven studies in depression were found to fulfil our inclusion criteria; three of these had been included in the meta-analysis by Bylsma (2008). Six of these studies used film clips to induce emotions (Berenbaum and Oltmanns, 1992; Chentsova-Dutton et al., 2007; Renneberg et al., 2005; Rottenberg et al., 2005, 2002; Tsai et al., 2003) and one used emotional pictures (Sloan et al., 2001). Renneberg et al. (2005) was the only study to use EMG, the others used an observational coding system in order to assess emotional expression.

Regarding positive emotions, four studies (Berenbaum and Oltmanns, 1992; Renneberg et al., 2005; Sloan et al., 2001; Tsai et al., 2003) found fewer facial expressions in the clinical group for at least one of the outcome variables, with ES ranging from *d*=.8 to *d*=3.6. One study found more positive expressions in depressed patients compared to HC with a medium effect (Rottenberg et al., 2005) and two studies found no effects of group on expression of positive emotions (Chentsova-Dutton et al., 2007; Rottenberg et al., 2002). Regarding negative emotions, one study found that the depressed group expressed less facial

emotions than HC with a medium ES (*d*=.71) (Renneberg et al., 2005), but the other six studies found no significant effects of depression on facial expression of negative emotions.

A group of individuals recovered from depression did not show any significant difference in emotional expression to positive or negative stimuli when compared to patients with acute depression or HC (Rottenberg et al., 2005).

Chentsova-Dutton et al. (2007) compared facial expressivity of depressed and non-depressed people of European American (EA) and Asian Americans of East Asian (AA) descent. Depressed EAs showed a pattern of diminished reactivity (likelihood of crying) to the sad film compared to non-depressed participants. In contrast, depressed AAs showed a pattern of heightened emotional reactivity compared to non-depressed participants. This suggests that there is cultural specificity of altered facial expression in depression.

3.2.3.2 Bipolar Disorder

The one study in bipolar disorder (Bersani et al., 2013) used film clips to induce emotions and the FACS coding system. Results are reported as a global score of congruent expressivity and show blunted affect in patients with bipolar disorder compared to HC.

3.2.4 Eating Disorders (ED)

Eleven studies were retrieved in ED which investigated facial expression. In anorexia nervosa (AN) *n*=6; bulimia nervosa (BN) *n*=1; AN/BN *n*=4 (Cardi et al., 2015, 2014; Claes et al., 2012; Dapelo et al., 2015; Davies et al., 2013, 2011; Lang et al., 2016; Rhind et al., 2014; Soussignan et al., 2011, 2010; Tárrega et al., 2014).

Seven of these studies used similar emotion elicitation methods and outcome measures, more precisely they used either pictures or film clips reliably evoking either positive or negative emotions and they used one of the two most common coding systems (FACS or FACES) in order to measure positive and negative facial emotional expressions. While five of these studies used pretested segments of movies (Dapelo et al., 2015; Davies et al., 2013, 2011; Lang et al., 2016; Rhind et al., 2014), two used film clips of humans displaying facial expressions (Cardi et al., 2015, 2014). Two of these studies were excluded from the meta-analysis because they had overlapping samples (Cardi et al., 2014; Davies et al., 2011) and one article included two samples, one with adolescents and the other with adults (Lang et al., 2016). One study focused specifically on the expression of positive emotions (Dapelo et al., 2015), comparing Duchenne-smiles (real smiles) and Non-Duchenne-smiles (social smiles). Results were similar for both outcome measures, but since Duchenne-smiles are considered a more authentic expression of positive emotion, these outcome values were included in the meta-analysis. This resulted in six ES for quantitative synthesis for positive emotions and five for negative emotions (Dapelo et al. (2015) analysed positive emotions only).

Meta-analytic results for positive expression showed a large and significant summary effect for reduced facial expression in patients with AN when compared to HC (ES -1.01; CI -1.50, -0.52). Heterogeneity was high (I^2 = 80.7%) and significant (p<.001); therefore, meta-regression analyses including the factors anxiety, depression and age were conducted. For positive expression, results showed that anxiety (residual I^2 = 79.57%; adj. R^2 = -0.3%; p = .38) and age (residual I^2 = 82.18%; adj. R^2 = -23.35%; p = .77) did not explain a significant amount of between-studies variance, but depression reduced heterogeneity to I^2 = 12.35% (adj. R^2 = 100%; p <.05). There was no evidence of publication bias when

inspecting the funnel plot or according to Egger's test (t = .80; p = .47).

A meta-analysis including studies on negative emotions shows reduced expressivity in the clinical group for negative emotions as well, with medium ES (ES = -.58; 95% CI -1.09, -0.07). Heterogeneity was high (I^2 = 82.6%) and significant (p<.001). Meta-regressions for negative expressivity showed that age (residual I^2 = 86.22%; adj. R^2 = -41.03%; p = .38) and anxiety (residual I^2 = 69.53%; adj. R^2 = 22.72%; p = .86) did not explain heterogeneity, depression accounted for R^2 = 100% of between studies variance, which reduced I^2 to 0%. There was no evidence of publication bias when inspecting the funnel plot or according to Egger's test (t = .45; p = .69).

The remaining four studies in ED (Claes et al., 2012; Soussignan et al., 2011, 2010; Tárrega et al., 2014) used different methodologies. In Soussignan et al. (2010), participants were shown pictures of food preceded by different subliminal faces expressing emotions (including happiness, disgust, fear and neutral). Facial response of participants was measured both by EMG and observational coding. The authors found reduced positive facial expression in the AN group in both EMG recording (d=0.8) and observational coding (d=0.8). For negative expression there was no main effect on neither of the outcome measures. However, increased muscle tension of the corrugator muscle was demonstrated when subliminal 'fear faces' were shown prior to the food pictures (d=0.9). Soussignan et al. (2011) also used food stimuli in comparison to non-food stimuli with comparative hedonic value and measured EMG response of zygomaticus and corrugator activity. There was a stronger zygomatic reaction in HC compared to AN to both kinds of stimuli (d=.64) with no main effects found for corrugator activity.

The studies by Claes and colleagues (2012) and Tárrega and colleagues (2014) were conducted in the same laboratory, measuring facial expression of joy and anger through an automatic emotion detection software, during a video game (Playmancer) designed for emotion regulation training. Unfortunately, the stimulus valence is not obvious; or rather, it cannot be defined exactly what was going on in the game in the moment a specific emotion was displayed; therefore, it was not possible to include these studies into the quantitative synthesis. Interestingly, the results of the first study show that AN patients expressed less anger than HC during the game (d=1.0), the BN group did not differ from HC (although there was a trend in the same direction) and there were no differences for the expression of joy. The second study (Tárrega et al., 2014) increased the power of the BN sample and found significantly more expression of joy (d=8.9) and less expression of anger (d=53.5) in BN patients compared to controls.

There were two studies in ED including a recovered group. Davies et al. (2013) found that individuals recovered from AN had more expression of positive emotions than acute AN patients (d=1.1), while these groups did not differ in the expression of negative emotions. The recovered AN group was comparable to the HC group on both negative and positive expression of emotion. A recovery from altered emotional expression after remission from BN was also found by Tárrega et al. (2014), the recovered group being more similar to HC than the BN group, although they still had significantly less expression of anger.

3.2.5 Borderline Personality Disorder (BPD)

A systematic review of emotional responses, which included two studies exploring facial expression, had previously been undertaken in BPD (Rosenthal et al.,

2008). The two studies described in the review used positive and negative pictures and films to elicit emotion and EMG and observational coding to measure outcomes (Herpertz et al., 2001; Renneberg et al., 2005), respectively. Both studies reported an attenuation of positive and negative facial expression in BPD groups.

Subsequent to Rosenthal's review (2008) two further studies were retrieved in BPD (Matzke et al., 2014; Staebler et al., 2011). Matzke and colleagues (2014) used a design similar to the above-mentioned studies (emotional pictures) and EMG to measure emotional expression. They found no group differences for zygomaticus activity during positive emotions, but for negative emotions corrugator activity was increased during pictures displaying disgust, anger and sadness, but not during fear evoking pictures. Activity of the levator labii (muscle of the upper lip, related to disgust) did not differ between groups. Staebler et al. (2011) used a social interaction paradigm inducing social exclusion. Consistent with Herpertz et al. (2001) and Renneberg et al. (2005), an attenuation of positive facial expression was observed (*d*=0.9); however, there was an increase in negative expression (*d*=0.7), in keeping with the findings by Matzke and colleagues (2014). Reasons for these increases in negative facial expression are outlined in the discussion.

3.2.6 Autism Spectrum Disorders (ASD)

Six studies were identified comparing facial expression in people with ASD to typically developing individuals (TD) (Grossman et al., 2013; Mathersul et al., 2013; McIntosh et al., 2006; Rozga et al., 2013; Stel et al., 2008; Yoshimura et al., 2014).

The studies by McIntosh et al. (2006) and Mathersul et al. (2014) used pictures to induce emotions, the other four studies used emotional film clips. Three studies used EMG as a measure of emotional expression (Mathersul et al., 2013; McIntosh et al., 2006; Rozga et al., 2013) and three used observation through FACS/FACES (Yoshimura et al., 2014) or specifically developed scales (Grossman et al., 2013; Stel et al., 2008).

Two studies reported global scores for expression of congruent emotions, one found less expression in ASD with a large ES (*d*=0.8) (McIntosh et al., 2006) and one found no significant group differences (Grossman et al., 2013). Regarding positive expression, two studies found very large ES (*d*=1.15-1.34) for a reduction of facial expression in ASD compared to TD (Stel et al., 2008; Yoshimura et al., 2014), but two studies found no group differences (Mathersul et al., 2013; Rozga et al., 2013). This may partly be explained by the elicitation method, since Yoshimura and colleagues (2014) found that the effect was only significant for dynamic stimuli, but not for static ones. Mathersul et al. (2013) used pictures and Rozga et al. (2013) used film clips, but also of relatively small duration (< 2 seconds of length).

Three studies reported results on facial expression in response to negative stimuli. There seemed to be a trend towards lower values in ASD than TD (Mathersul et al., 2013; Rozga et al., 2013; Yoshimura et al., 2014), but only two studies reported significant differences with medium ES (*d*= .5 - .78) and each only in one of their two outcome measures (Rozga et al., 2013; Yoshimura et al., 2014).

3.2.7 Disruptive Behaviour Disorder (DBD)

One study assessing emotion expressivity in people with DBD was identified (De Wied et al., 2012). It used film clips to induce positive and negative emotions. Facial expression was measured by EMG. Results show that adolescents with DPD

have less facial expression of positive and negative emotions compared to healthy peers, although this may be moderated by unemotional traits and dependent on the specific emotion, since the differences were only significant for sadness, but not for anger.

3.3 Manipulation and validity checks

Five studies reported voluntary facial expression of participants and most of the studies assessed subjective experience of emotions. Although it is beyond the focus of this review to look at these outcomes, both are important for a deeper understanding of the causes and meanings of altered facial expressivity and are therefore shortly summarized hereafter.

None of the five studies reporting on voluntary movement or explicit mimicry of facial expressions found significant differences between clinical (OCD, depression, ASD) and control groups; therefore, facial expression differences are unlikely to be attributable to problems in facial muscle movement.

Regarding self-report of positive vs. negative emotions experienced during exposure to positive vs. negative stimuli, of the 21 studies reporting this outcome, most reported that there were no group differences for subjective experience of emotions (twelve for positive and eleven for negative emotions). Conversely, eight studies reported more self-reported negative emotions during negative stimulus exposure in clinical groups and six studies reported less subjective experience of positive emotions during positive stimuli in clinical groups.

Some studies in ED also coded the frequency of looking away and found that AN patients looked away more often during a negative (sad) film (Davies et al., 2013; Lang et al., 2016) or during negative and positive films of adults expressing emotions (Cardi et al., 2015), but they did not differ in frequency of looking away during a film of infants' facial expressions; one of the possible explanation for this was that patients found it hard to identify infants' facial expressions (Cardi et al., 2014).

4 Discussion

The aims of the current review were to analyse differences between individuals with a non-psychotic disorder and control participants in the automatic, stimulus-related facial expression of emotions. Since the importance of facial expression for the recognition of others' emotions has been shown (Künecke et al., 2014; Sel et al., 2015), a lack of automatic facial emotional expressivity in patient groups could be an explanation for shortcomings in social interaction (e.g. Harrison et al., 2014; Jeung and Herpertz, 2014; Lavelle et al., 2014; Tchanturia et al., 2013). To investigate this assumption, it is important to first answer the question whether individuals with psychological disorders have altered facial expressions of emotions when compared to controls.

The results show that there are alterations in emotional facial expression in DSM non-psychotic Axis I and II disorders in the acute phase of the illness. The review highlights that, although compared to the large body of research on this topic in schizophrenia (Kring and Moran, 2008), research of facial expression in non-psychotic mental disorders is in its infancy; however, it has notably grown in recent years.

4.1 Alterations in facial expression within and across clinical groups

The evidence from studies in PTSD summarized in this review does not suggest altered facial expression in response to emotional stimuli in individuals with this diagnosis. It is of note that patients with PTSD nevertheless show problems in the recognition of emotional expressions (Kret and Ploeger, 2015), which suggests that this patient

group may have problems in some domains of social emotional interaction, i.e. in deciphering socially significant emotional signals in others, but that they are as competent as healthy individuals when communicating their own emotions through facial expressions. However, earlier studies (Davis et al., 1996; Pitman et al., 1987; Shalev et al., 1993) using trauma-related imagery had found increased expressivity in patients compared to controls. Therefore, it can be concluded that individuals suffering from PTSD have 'heightened' facial expression in response to stimuli related to their trauma, but not in general to emotional stimuli. There might be some alteration during social interaction, but this has to be consolidated by further studies.

Although there were not enough studies in OCD to conduct a meta-analysis, the present results support the hypothesis of blunted facial emotional expressivity in patients with OCD, which were found to be comparable to patients with schizophrenia with regard to facial expression of emotions (Valeriani et al., 2015).

In other anxiety disorders, the evidence is quite limited; there were only two studies reporting no differences between healthy controls and patients with generalised anxiety disorder or social phobia/clinical anxiety. More studies are needed to better understand emotional processing in anxiety disorders, and to distinguish processes related to disorder-related and general emotional stimuli.

Findings from studies of depression, ED and BPD mostly show a general attenuation in facial expression. In depression and BPD this particularly manifests in attenuation of positive expression. One hypothesis for this result in depression was explored in a study by Reed et al. (2007). The authors examined whether the attenuated response to positive stimuli was related to how depressed people appraise emotional stimuli (based on research which suggests that appraisals of emotional stimuli may be different to non-depressed individuals). The study explored 'dynamic' facial expression to positive stimuli, thus looking at patterns of response (e.g. does a frown follow a smile?) rather than simply counting each expression. Results showed that depressed people were more likely to show affect-related shifts in expression in response to the positive film clip, specifically initial smiles were followed by negative affect-related expressions. As anhedonia, which is associated with lowered motivation to engage in pleasurable events, is a prominent feature of the illness (Rottenberg and Vaughan, 2008), this response pattern is unsurprising. Depression and anhedonia are common features in AN (Davis and Woodside, 2002; Harrison et al., 2014; Hudson et al., 2007; Tchanturia et al., 2012) and in BPD (Marissen et al., 2012).

Regarding ED, the main conclusion of the meta-analysis for facial expression in adult patients with AN is that diminished positive facial expression can be seen as a robust finding (ES = -1.01; CI -1.41, -0.53). Negative emotions are also diminished (ES = -.58; CI -1.09, -0.07) although results are less strong. For adolescent AN patients, and for BN and binge eating disorder more research is needed in order to examine whether there is an effect of psychopathology on facial emotional expression (see Figures 2 and 3). Depression is an important influencing factor which should be controlled for in future studies.

In some of the studies of people with ED in this review (Cardi et al., 2015; Davies et al., 2011; Lang et al., 2016) depression was shown to be negatively associated with positive facial expression, whereas it did not correlate with the attenuation of negative expression or looking away. Attenuating negative facial expression or

looking away may be explained as a way of regulating threatening or indeed any social interaction (Oltmanns and Gibbs, 1995). For example, studies have shown that people with AN report that they perceive the expression of negative emotion as unacceptable and believe that it should not be expressed for fear of being criticized and/or rejected (Hambrook et al., 2011; Oldershaw et al., 2015). This is supported by an fMRI study reporting that AN patients may react over-sensitively to social rejection (Via et al., 2015). The expressive suppression of emotions might then be further amplified by the patients being unclear of their proper emotion and its adequacy, having less emotional clarity and general problems in emotion regulation (Wolz et al., 2015). Recent research further suggests that AN patients also have problems in deliberate facial expression of emotions, seen in less accuracy when posing and imitating facial emotions, and underlining their difficulties to convey emotional meaning (Dapelo et al., 2016).

In contrast to the above results in ED, one study reported increased facial expression of joy in patients with BN (Tárrega et al., 2014), which may be explained by the nature of the evocation method and the capacity of patients to inhibit or avoid negative emotions and to increase positive emotions, in order to obtain social reward.

The finding of attenuated facial expression in BPD is more unexpected, as dysregulated emotion manifesting in high sensitivity to emotional stimuli and strong emotional reactivity, is a central feature of the disorder (Herpertz et al., 2001; Renneberg et al., 2005). One explanation for attenuated expression is that these individuals may have learned to hide their facial expressions as negative emotional expressions were ignored or punished in the social contexts they were raised in (Linehan, 1993). Applying Fridlund's theory (Fridlund, 1994) of facial expression as a communication of intention, a neutral face could be a way of making oneself invisible by suggesting 'I do not wish to take part in this interaction' and may be an attempt to reduce threat, as showing signs of emotion leaves the person vulnerable if the emotion displayed is not reciprocated or dismissed by others as invalid or inappropriate.

Conversely, Staebler and colleagues (2011) found conflicting findings in BPD compared to the other BPD studies in the review. They employed a social interaction task inducing social exclusion. Although an attenuation of positive facial expression was observed, there was in fact an increase in negative expression as well as 'blends' of emotions (the expressions of at least two facial expressions at the same time), indicating an asynchrony of facial expression in BPD rather than a general attenuation. Another study, using pictures of faces to induce emotions, did not find differences in positive expression, but supported a heightened response to negative stimuli (Matzke et al., 2014). Since pictures of facial expressions are more similar to a real social interaction than emotional scenes used in the former two studies, it is possible that the theme elicited more intense emotional reactions in patients with BPD than the negative but 'non-disorder' stimuli used in the other two investigations of facial expression in BPD. Alternatively, a social situation task may just be more ecologically valid and thus more engaging. Clearly there is some way to go in untangling the effects of social context on display of facial expression.

The research questions have been different for the ASD studies thus making it difficult to draw comparisons with the other studies in this review. Although many studies in ASD explicitly addressed whether deficits were in automatic versus voluntary emotional mimicry, this review focused on automatic facial expression

and only these results were summarized. Mimicry (doing what others do) often occurs at an unconscious level thus enabling smooth and effective interactions, aiding emotion recognition and creating empathy between people (e.g. Stel et al., 2008) – although a recent study questions the place of emotion mimicry in emotion recognition (Rives Bogart and Matsumoto, 2010). It seems that in ASD, alterations in facial expressivity are related more to automatic than voluntary processes as participants could mimic facial expressions if instructed to. Automatic expression was found to be decreased with medium to very large ES (*d*=.5 to 1.34) in some of the studies, but in others no group differences were found. Insignificant results may be explained by small sample sizes (none of the studies reported a power analysis) or by the nature of the stimulus material (social vs. emotional scenes).

Research in autism suggests that imitation may involve two different processes, one comprising 'an affective mechanism modulating social exchanges' and the second 'a more executively constructed cognitively mediated intentional imitation system'. It is suggested that people with ASD rely on the second (McIntosh et al., 2006). Difficulties with automatic emotional mimicry may mediate the ability to empathise, something which has been shown to be lowered in ASD (Baron-Cohen and Wheelwright, 2004; Kret and Ploeger, 2015).

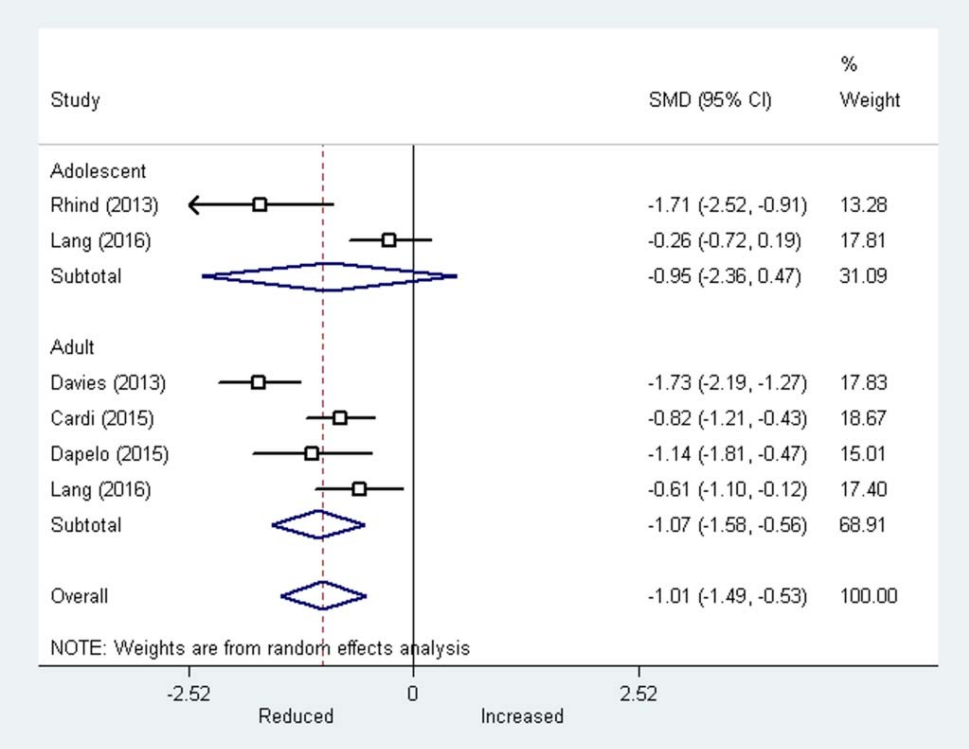

Figure 2. Forest plot of the meta-analysis for facial emotional expression in response to positive affect in patients with AN.

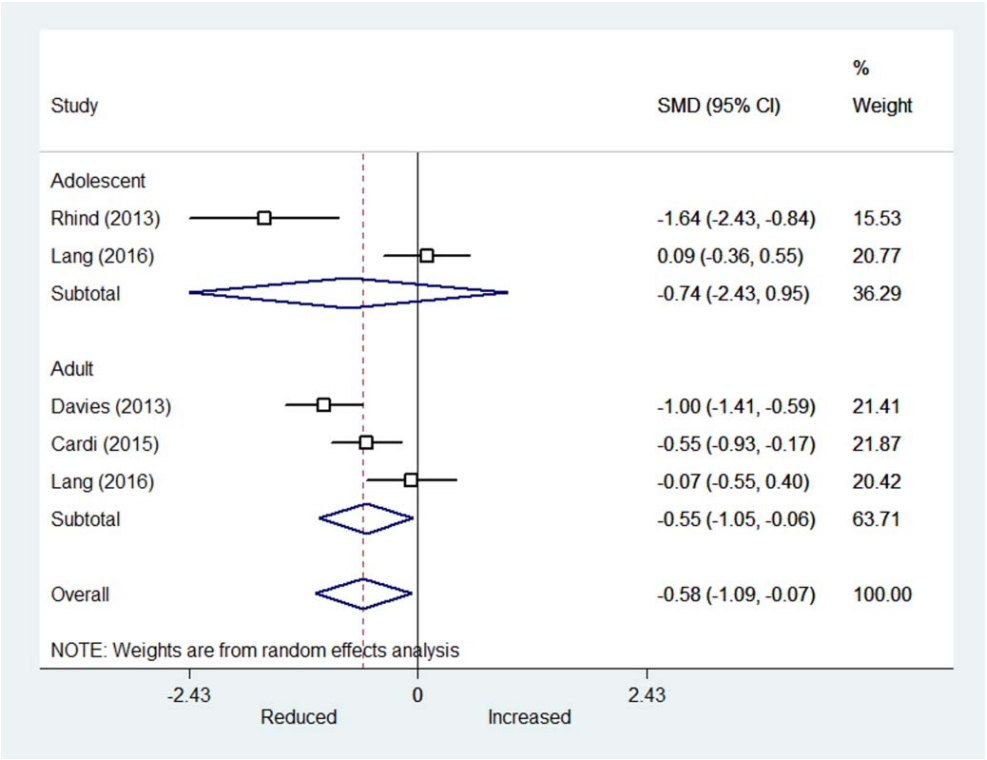

Figure 3. Forest plot of the meta-analysis for facial emotional expression in response to negative affect in patients with AN.

4.3 Trait related alterations

Three studies in this review addressed state and trait related factors of facial expressivity by including a recovered (not acutely ill) sample (Davies et al., 2013; Rottenberg et al., 2005; Tárrega et al., 2014). The studies by Davies and colleagues (2013) and by Tárrega and colleagues (2014) found an intermediate profile in recovered individuals between people with current ED (AN and BN, respectively) and controls. The third study in depression (Rottenberg et al., 2005) showed no differences between the recovered and the healthy group for both positive and negative expressivity. In schizophrenia, only a few studies have looked at trait related factors and there seems to be a bias towards attenuated expression in people in remission from the illness and those at risk (Mattes et al., 1995; Walker et al., 1993). To conclude, therefore, studies which have addressed the issue of trait alterations in facial expression in ED and depression have found evidence for facial expression improvement in recovered groups. However, longitudinal studies are needed to clarify state/trait influences of facial expressivity in people with axis I and II disorders.

4.4 Limitations

4.4.1 Limitations at review level

This review focussed on congruent facial expression; therefore, some of the outcomes available in the literature – such as mixed or incongruent facial expressions – were not included into data synthesis. Moreover, we were unable to conduct a global meta-analysis including different mental disorders due to the lack of statistical parameters in some studies.

4.4.2 Limitations at study/outcome level

Cultural and educational background, age, gender and medication may have an important influence on facial emotional expression. Most of the studies reported at

least some of these variables, but statistic tests of mean differences may not be enough to control for the influence and there were very few studies to use well matched groups.

Finally, many of the studies did not report means and standard deviations, which is crucial for doing an exact calculation of a summary effect size. Furthermore, some studies analysed positive and negative expressions as one common effect, which probably blurs the results, since the pattern of reactivity in clinical groups has been found to differ between positive versus negative stimuli. Therefore, results should be reported as separate values, where possible.

4.4.3 Limitations of the literature

Aside from the limited number of studies, one of the major limitations of the literature in this review is the heterogeneity of methodologies across studies. This is in part due to the wide ranging methods available to elicit emotion but also due to the range of theories which drive research questions in this area of study. A wide variety of stimuli was used ranging from pictures and films to social interaction and within each of these there was variability. For example, across studies different pictures and films were used. This may result in differences in the salience of stimuli e.g. in the degree of sadness induced by different stimuli or trauma related stimuli compared to generic affective stimuli.

With regard to assessment methods, it is important to bear in mind the possible differences depending on the technique. Only one of the studies included in this review used a combination of both EMG and manual coding and showed that alterations were consistent across coding methods (Soussignan et al., 2010). Finally, the review aimed to investigate whether alterations are related to trait factors; however, there is a complete absence of studies which have addressed state and trait questions using longitudinal groups.

4.5 Clinical Implications

Emotional facial expressions contribute to the regulation of both social interactions and individual emotion regulation (Butler et al., 2003; Davis et al., 2010; Gross and Levenson, 1997, 1993). Therefore, alterations can have negative consequences for the individual and their social functioning (Tchanturia et al., 2015a).

Attenuated facial expression can have negative social consequences as emotional responses or typical communicatory signals are not available to others (Srivastava et al., 2009). This could cause therapeutic difficulties because obvious markers of emotion are not available (Buhl, 2002). Suppression or avoidance of emotion is suggested to lead to a rebound effect whereby the emotion becomes increasingly more intense (Gross and John, 2003). Expressive suppression of emotions leads to decreased sensitivity in recognizing facial expressions, while deliberate mimicry increases this capacity (Schneider et al., 2013).

Emotional constraint or suppression has been associated with heightened depressive symptoms primarily, but also symptoms of anxiety (Barr et al., 2008); therefore, there are important health benefits to enabling patients to express how they feel. Furthermore, attenuated facial expression may not be representative of the felt experience. For example, in schizophrenia, AN, BN and BPD, although facial expression is attenuated, experiences of emotion have been shown to be comparable or stronger than in healthy controls (Dapelo et al., 2015; Davies et al., 2013; Kring and Moran, 2008; Tárrega et al., 2014). Therefore, the expected responses in social interactions may not be given, for example, the evocation of sympathy and

distress, thus perpetuating further negative effects. Interventions that help patients better match their expressions with their subjective emotion may have positive effects on intra- and inter-personal adjustment (Davies et al., 2012; Money et al., 2011; Schmidt et al., 2015, 2012; Tchanturia et al., 2015b, 2014).

4.6 Research Implications

The review highlights the patchiness of elicitation methodologies used, and the need for replication of methods within and across disorders. As already mentioned in the limitations section, one crucial point in research on facial expression is that the outcome is strongly dependent on two factors: the stimuli used to evoke emotions and the assessment methods. To develop a full picture of facial emotional expression in healthy and in clinical populations and its impact on emotion recognition and regulation, additional studies will be needed which combine different methods and compare these. For example, there are not always consistencies between EMG and manual coding results. In the schizophrenia literature, where facial expression has been studied extensively, discontinuances have been shown between outcomes in EMG and manual coding results. Although people with schizophrenia are less outwardly expressive than people without schizophrenia as shown through observable studies, their facial muscles are still responding in a way that is consistent with the valence (positive, negative) of the stimuli, as shown through studies using EMG (Kring and Elis, 2013). It is suggested that this difference may be in part related to medication effects and/or social skills deficits, motivation and effort (Kring and Elis, 2013). However, further studies need to be undertaken to understand these differences. Particularly it would be beneficial if studies used both EMG and observational methods in the same group for measuring facial expression as this could reveal discontinuities and consistencies in the transition from covert to overt expressions (Cacioppo et al., 1992). A few studies which have done so e.g in people experiencing pain (Karmann et al., 2015) and in this review looking at facial expression in eating disorders (Soussignan et al. 2010) found consistency in results in EMG activity and manual coding results.

Going beyond these conventional methods, automatic coding systems could be helpful to improve reliability, validity and comparability of results, yielding a more detailed coding of intensity, duration and fine-grained variety of facial movements (Ahn et al., 2003), and additionally alleviating the time consuming nature of manual coding. Automatic face analysis systems based on the FACS coding system use automatic face recognition for an evaluation and more detailed analyses of facial movements and have been found to be highly reliable (Girard et al., 2014a; Mohammadi et al., 2015; Tian et al., 2001). Although these techniques have been available for years, they are only recently finding their way into clinical research (Hamm et al., 2011; Wu et al., 2014). A study with participants having different degrees of depression and following these individuals over time used both automatic and manual coding and found comparable and consistent results (Girard et al., 2013).

With regard to stimuli, many studies have used the International Affective Picture System (Lang et al., 2005) set , which is a validated battery of emotional and neutral pictures. Attempts at standardising film clips have been made (e.g. Rottenberg et al., 2007) and should be referred to in future studies. Going beyond this type of 2D-stimuli, the review also highlights how ecological methods, such as social interaction, can produce results which

differ from less ecological methods e.g. pictures (e.g. Kirsch and Brunnhuber, 2007; Staebler et al., 2011). Although social interaction paradigms come with problems of standardisation, and can increase the number of dependent variables, some novel virtual reality methods are being used (e.g. Cyberball, see Staebler et al., 2011) and could provide alternatives to "real-life", less standardised paradigms. Future studies using virtual reality paradigms for emotion elicitation are therefore recommended to create ecologically valid and standardized social situations and thus increase generalizability of results and transferability. Virtual environment systems have advanced to a great extent in the last few years, becoming less expensive, more user-friendly and more reliable (Parsons, 2015). Therefore, these paradigms can be seen as a useful method to induce emotions and produce "life-like" social interaction, creating a higher feeling of "presence" as compared to traditional stimuli such as film clips or pictures and thus increasing the intensity of the evoked emotion (Riva et al., 2007). 3D interactive virtual reality thereby enhances this feeling of "presence" compared to 2D paradigms due to higher immersion, but there are also other associated factors that may influence the participants' "presence" such as movement and spatial distribution (Kober et al., 2012; Wilson et al., 2015).

In these paradigms, factors such as gaze direction and mutual eye contact could be systematically varied to study their effect in social interaction and differences between clinical and non clinical groups in this respect (Marschner et al., 2015; Soussignan et al., 2013). Multidimensional systems such as the Empathy Enhancing Virtual Evolving Environment (Jackson et al., 2015) could be used to create specific emotional situations and at the same time measure emotional reactions on different levels (i.e. facial expression, psychophysiology, gaze dynamics) in a standardized manner. Additionally, virtual environment systems can be used to give real time feedback to patients on their emotional responses and thus to have the capacity to train immediately some emotion regulation skills (Fernandez-Aranda et al., 2012), as shown in recently published research with impulse related disorders (Fernandez-Aranda et al., 2015; Tárrega et al., 2015).

Another important factor on stimulus level is if it depicts emotional scenes or facial expressions, where participants' expression may rather be mimicry than really felt emotions. Results of the meta-analyses nevertheless point out that both could have a comparable effect, since one of the included studies (Cardi et al., 2015) used facial expressions for emotion elicitation and the others used emotional scenes. Cardi and colleagues study (2015) supported the outcomes from the other studies regarding group differences in emotional expression.

In terms of future directions, researchers in this area should also consider whether they wish to look at general affect or discrete emotions. An example of why this is an issue comes from two studies in AN (Davies et al., 2011; Soussignan et al., 2010), where it is debatable whether attenuated expression may be related to specific emotions or general negative affect. Thus using a range of discrete emotion elicitation methods or a coding system which accounts for coding discrete emotions (e.g. EMFACS, automated systems) could resolve this issue. Furthermore, future studies should look at the effects of pathology relevant stimuli (e.g. food in eating disorders, phobia-related cues in anxiety) in order to compare the effects of general emotional processing versus emotional processing related to disorder specific material. One study in this review (Soussignan et al., 2011), which compared general and specific stimuli, points towards a generally

flat emotional expressivity in AN patients, but this finding needs to be corroborated by further studies and expanded to other diagnoses.

The research summarized in this work is not exhaustive with regard to non-verbal expression of emotions; future work has to bring clarity to other related functions and its relationship to facial expression. A recent article postulates the importance of including more subtle affective signals (e.g. gaze direction or blushing, pupil dilation), which go beyond muscular reactions and may be less susceptible to top-down regulation, into research on facial emotional expression (Kret, 2015). Gaze dynamics for example are not only an indicator of emotional involvement versus avoidance, but are also important to inform on attentional allocation and thus identify the environmental cues that shape emotion evocation and facial expression; therefore, eye tracking methods should be included in future research on facial expression of emotions. Gaze dynamics might reveal whether alterations in facial expressivity in psychiatric patients are due to patients focussing on different information or cues (e.g. not focusing on most informative/ emotional parts of a scene) than healthy controls, or if these findings may be rather explained by emotional numbing regardless of attentional biases or avoidance. In social situations for instance, direct eye contact is a vital social signal which entices others into social interaction (Theeuwes and Van Der Stigchel, 2006) and also is important for the embodiment of emotions (Niedenthal et al., 2010). However, the use of another's face to obtain social and emotional information may vary in clinical populations (Cipolli et al., 1989; Watson, 2010) and, additionally, direct eye contact seems to have differing effects on emotional reactions (Wieser et al., 2009), which could influence facial expressivity. Furthermore, other channels of expression like body posture and body contact should also be taken into account (App et al., 2011). It is possible that patients with less facial expression display their emotions through other channels. Regarding the rebound effect of emotional suppression, physiological parameters should be used in combination with measures of facial expression in order to investigate the physiological cost of expressive suppression of facial emotion (Fagundo et al., 2014).

4.7 Conclusions

In conclusion, this review has shown that facial expression of emotion is altered in people with mental health problems with broad similarities across certain clinical groups. There is tentative support for recovered individuals having a facial expression profile more similar to non clinical controls; however, longitudinal studies are required to understand whether alterations in facial expression are a trait vulnerability factor to mental disorders or rather a state of the illness. Given the multiple functions of facial expression, altered expression in clinical disorders can be explained from as many different standpoints. For example, the impact of social presence could be a particularly useful line of enquiry in untangling causes of disrupted expression in disorders such as BPD and AN. With regard to future directions relating to research methods, emotion elicitation and coding methods need standardisation (e.g. Girard et al., 2014; Rottenberg et al., 2007) to make comparison within and between groups more reliable.

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Study 2: Personality and emotion regulation in eating disorders

Objectives: Both personality traits and emotion regulation are important and possibly interacting facets of biopsychosocial models of EDs. Developmental models of emotion regulation suggest that heritable personality traits may predispose individuals to the acquisition of more or less adequate emotion regulation capacities, depending also on family environment (Calkins et al., 2013). The aims of the study were two-fold: since the DERS had not yet been validated in the Spanish adult population, the study aimed at validating the scale in a sample of Spanish adults with and without ED. Furthermore and more importantly, this study aimed at increasing the understanding of the clinical representation of emotion regulation in EDs and the interaction of dysfunctional personality traits and difficulties in emotion regulation in the explanation of this disorder.

Results: The Spanish version of the DERS showed a factor structure similar to the original version and good internal consistency in adults with and without ED. Discriminative validity was good: HC had fewer difficulties in emotion regulation than patients with EDs**.** Moreover, emotion regulation capacity of ED patients appeared to be different depending on diagnostic category, the AN group having comparably less problems than the BN group. A path model showed that difficulties in emotion regulation mediate the influence of harm avoidance and self-directedness on ED severity.

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Emotion regulation in disordered eating: Psychometric properties of the Difficulties in Emotion Regulation Scale among Spanish adults and its interrelations with personality and clinical severity

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Abstract

Objective: The aims of the study were to 1) validate the Difficulties in Emotion Regulation Scale (DERS) in a sample of Spanish adults with and without eating disorders, and 2) explore the role of emotion regulation difficulties in eating disorders, including its mediating role in the relation between key personality traits and ED severity **Methods**: 134 patients (121 female, mean age = 29 years) with anorexia nervosa (n = 30), bulimia nervosa (n = 54), binge eating (n = 20), or Other Specified Feeding or Eating Disorders (n = 30) and 74 healthy control participants (51 female, mean age = 21 years) reported on general psychopathology, eating disorder severity, personality traits and difficulties in emotion regulation. Exploratory and confirmatory factor analyses were conducted to examine the psychometrics of the DERS in this Spanish sample (Aim 1). Additionally, to examine the role of emotion regulation difficulties in eating disorders (Aim 2), differences in emotion regulation difficulties across eating disorder subgroups were examined and structural equation modeling was used to explore the interrelations among emotion regulation, personality traits, and eating disorder severity. **Results:** Results support the validity and reliability of the DERS within this Spanish adult sample and suggest that this measure has a similar factor structure in this sample as in the original sample**.** Moreover, emotion regulation difficulties were found to differ as a function of eating disorder subtype and to mediate the relation between two specific personality traits (i.e., high harm avoidance and low self-directedness) and eating disorder severity. **Conclusions:** Personality traits of high harm avoidance and low self-directedness may increase vulnerability to eating disorder pathology indirectly, through emotion regulation difficulties.

Keywords: Eating disorder; Emotion regulation; Difficulties in Emotion Regulation Scale; Personality types; Harm Avoidance; Self-Directedness; Vulnerability to psychopathology

1 Introduction

Difficulties in emotion regulation have been identified as a transdiagnostic risk factor for the development and maintenance of numerous forms of psychopathology (Aldao et al., 2010; Hechtman et al., 2013), including eating disorders (ED; Svaldi et al., 2012). In male and female student populations, emotion regulation abilities are related to disordered eating and body-dissatisfaction (Ambwani et al., 2014; Cooper et al., 2014; Lavender and Anderson, 2010). Moreover, literature suggests that inhibited or disinhibited food intake and, thus, the development of an ED, may function to regulate emotions in the absence of more adaptive emotion regulation strategies (Brockmeyer et al., 2012; Fox and Power, 2009; Haynos & Fruzzetti, 2011; Leehr et al., 2015; Macht, 2008; Naumann et al., 2014). This is supported by experimental data showing that the suppression of negative emotions leads to increased food intake in both healthy normal weight students and obese individuals with and without binge eating disorder (BED; Evers et al., 2010; Svaldi et al., 2014). Importantly, negative emotions and their maladaptive regulation are considered key contributing factors to anorexia nervosa (AN; Davies et al., 2012; Harrison et al., 2009), bulimia nervosa (BN; Lavender et al., 2014; Southward et al., 2013), and BED (Brockmeyer et al., 2014; Vanderlinden et al., 2004).

Notably, there is a lack of data on the relevance of emotion regulation difficulties to the group of patients diagnosed as Eating Disorder Not Otherwise Specified/Other Specified Eating or Feeding Disorders (EDNOS/OSFED, as characterized in the 4th and 5th editions of the Diagnostic and Statistical Manual of Mental Disorders, respectively; American Psychiatric Association, 2000, 2013). Because this category includes patients who do not meet full criteria for AN, BN or BED, individuals included in this category may be more functional, showing subthreshold or less severe forms of ED. Nonetheless, studies using the DSM-IV criteria highlighted the clinical severity of patients diagnosed as EDNOS, demonstrating that individuals who receive this diagnosis do not differ from those with full ED diagnoses in eating pathology, clinical severity, or general psychopathology (Thomas et al., 2009). Likewise, research suggests that individuals with EDNOS have levels of alexithymia (Nowakowski et al., 2013) and depression (Schmidt et al., 2008) similar to or even higher than those meeting full ED criteria. Thus, although the criteria for ED in general have changed and OSFED differs from EDNOS, evidence suggests emotion regulation difficulties may be just as relevant to OSFED as to the full syndrome ED.

ED have also been related to specific personality traits, including high harm avoidance and low self-directedness for all ED diagnostic subtypes, high novelty seeking for BED and BN, and high reward dependence and persistence for AN (Agüera et al., 2012; Bulik et al., 1998; Krug et al., 2011; Atiye et al., 2015). Notably, more dysfunctional personality traits have been found to predict not only higher ED severity, general psychopathology, and self-harm behaviors, but also worse therapy response and prognosis (Hintsanen et al., 2012; Abbate-Daga et al., 2011; Claes et al., 2012; Rodríguez-Cano et al., 2014).

Research suggests that one pathway through which these personality traits may relate to ED is emotion regulation difficulties. For example, evidence suggests that high levels of neuroticism, behavioral inhibition, and harm avoidance, together with low levels of extraversion, are related to self-report, physiological, and neurological indices of emotion regulation difficulties (Baeken et

al., 2014; Di Simplicio et al., 2012; John and Gross, 2004; Kokkonen and Pulkkinen, 2001; Ng and Diener, 2009; Picket et al., 2012). Likewise, some of these traits (e.g., behavioral inhibition, avoidant personality traits) have been found to be associated with behavioral indices of emotion regulation difficulties, including the unwillingness to experience distress (Gratz et al., 2013; Tull et al., 2010). This association is also evident on a neurobiological level, as high harm avoidance is related to stronger resting state activation and white matter microstructural organization of brain networks associated with emotion regulation (Taddei et al., 2012; Baeken et al., 2014), and correlates with amygdala activation to emotional images (Most et al., 2006; Schuerbeek et al., 2014; Baeken et al., 2009). Furthermore, both high levels of harm avoidance and low levels of self-directedness are associated with lower μ-opioidergic neurotransmission in emotion-related brain regions (which is involved in the modulation of emotional reactions; Tuominen et al., 2012). Overall, this research suggests that certain personality traits may increase the risk for emotion regulation difficulties, which, in turn, may increase the risk for various forms of psychopathology, including ED.

Although basic research points to a relation between personality and emotion regulation, there is limited research on the relations between personality and emotion regulation in specific psychiatric disorders. Moreover, most research on the interrelations of personality and emotional functioning in ED has focused on emotional responding versus emotion regulation per se. For example, one such study (Brownstone et al., 2013) found that the relation between affect lability and over-exercising in BN is moderated by compulsive personality traits. Additionally, there is research on the mediating role of anger in the relation between certain personality traits and ED (Amianto et al., 2012; Krug et al., 2008). Research on the interrelations of personality traits and emotions in ED notwithstanding, a growing body of research emphasizes the importance of considering responses to emotions (i.e., emotion regulation) rather than the nature or quality of emotions per se when examining psychopathology, both in general (e.g., Gratz et al., 2013; Gratz and Tull, 2010) and with regard to ED in particular (Fox and Power, 2009; Evers et al., 2010). This is a particularly understudied area within the ED literature. One frequently used questionnaire to measure emotion regulation is the Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004), which is based on the multidimensional conceptualization of emotion regulation as maladaptive ways of responding to emotions, including a lack of awareness, understanding, and acceptance of emotions, difficulties controlling impulsive behaviors and engaging in goal-directed behaviors when experiencing negative emotions, and a lack of access to effective strategies for modulating emotions. Although the original version of this measure has been shown to have good reliability and adequate validity in both adults and adolescents (Gratz and Tull, 2010), the Spanish translation of this measure has not yet been validated in the Spanish adult population.

The aims of this study were twofold. Aim 1 was to provide data on the factor structure and validity of the Spanish version of the DERS within a combined clinical-nonclinical sample of Spanish adults with ED and healthy controls (HC). To this end, we examined the factor structure of the DERS within this sample, tested its capacity to discriminate between ED patients and HC, and examined its relations to ED severity, personality traits, and general psychopathology. Aim 2 was to explore

the role of emotion regulation difficulties in ED by examining differences in emotion regulation difficulties across ED subtypes (with special attention to OSFED) and exploring the mediating role of emotion regulation difficulties in the relation between key personality traits and ED severity. Based on the existing ED literature, we hypothesized that ED patients would report higher levels of emotion regulation difficulties than HC. We also hypothesized that difficulties in emotion regulation would be associated with higher levels of dysfunctional personality traits, ED severity, and general psychopathology. Finally, consistent with past research indicating an association between certain personality traits (i.e., high harm-avoidance and low self-directedness) and emotion regulation difficulties, we hypothesized that the relation between these personality traits and ED symptoms would be mediated by difficulties in emotion regulation.

2 Methods

2.1 Participants

The current study was conducted between April and November 2014. The HC group consisted of 74 undergraduate volunteer students of the University of Barcelona. Students were approached by their professors after course completion to assess their interest in participating in the study. They received course credit in exchange for their participation. An exclusion criterion for the HC group was a self-reported lifetime diagnosis of any ED (Aim 1). Patients (n = 134) were recruited from consecutive referrals to the ED unit of Bellvitge University Hospital (Aims 1 and 2). AN (n = 30), BN (n = 54), BED (n = 20), and OSFED (n = 30) patients were diagnosed according to the DSM-IV-TR criteria (American Psychiatric Association, 2000) by means of a semi-structured interview [Structured Clinical Interview for DSM Disorders-I] (First, Gibbon, Spitzer, & Williams, 1996) conducted by experienced psychologists and psychiatrists. These diagnoses were reanalyzed *post hoc* using the recent DSM-5 criteria (American Psychiatric Association, 2013).

Table 1 provides data on the socio-demographic variables of participants in the study, as well as for their age and Body Mass Index (BMI). Most participants in both groups were single. The mean age of the HC group was 21.1 years (SD = 4.5) and their mean BMI was 22.1 kg/m^2 (SD = 3.1). The mean age of the ED group was 28.8 years (SD = 10.4) and their mean BMI was 25.0 kg/m^2 (SD = 9.1). Analyses revealed statistically significant differences between the HC and ED groups in all socio-demographic variables presented in Table 1. As for differences in these variables across the ED subtypes, results revealed no significant between-group differences for sex, marital status, educational level, or employment status. However, the mean age of participants was higher for the BED group than the other groups, and the mean BMI was higher for the BED group and lower for the AN group, relative to all other ED subtypes.

2.2 Measures

Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004). The DERS is a 36-item self-report measure that assesses individuals' typical levels of emotion dysregulation across six domains: nonacceptance of emotional responses; difficulties pursuing goal-directed behaviors when experiencing negative emotions; difficulties controlling impulsive behaviors when experiencing negative emotions; lack of emotional awareness; limited access to emotion regulation strategies; and lack of emotional clarity. Higher values indicate greater difficulties in emotion regulation. The DERS has been found to demonstrate good reliability (Cronbach's α =.93; test–retest reliability over a period ranging

from 4 to 8 weeks = .88) and adequate construct and predictive validity and is significantly associated with objective (i.e., behavioral, physiological, and neurological) measures of emotion regulation (Goodman et al., 2014; Gratz & Roemer, 2004; Gratz et al., 2007, 2006; Gratz & Tull, 2010; Vasilev et al., 2009). A Spanish version of the DERS was previously validated in the Spanish general adolescent population (Gómez-Simón et al., 2014), and found to have satisfactory fit of the 36 item and 6 factor model. Internal consistency in this sample was adequate (α between .71 and .84) with the exception of the Awareness subscale (α = 62).

Table 1. Demographic and selected clinical data for the sample.

		HC		ED sample			AN		BN		BED		OSFED		*p*
		(n=74)		(n=134)		*p*	(n=30)		(n=54)		(n=20)		(n=30)		
Sex; *n-%*	*Female*	51	68.9%	121	90.3%	<.001	25	83.3%	50	92.6%	16	80.0%	30	100%	.054
	Male	23	31.1%	13	9.7%		5	16.7%	4	7.4%	4	20.0%	0	0%	
Marital status;	*Single*	72	97.3%	98	73.1%	<.001	23	76.7%	40	74.1%	10	50.0%	25	83.3%	.076
n-%	*Married*	0	0.0%	28	20.9%		4	13.3%	12	22.2%	9	45.0%	3	10.0%	
	Divorced	2	2.7%	8	6.0%		3	10.0%	2	3.7%	1	5.0%	2	6.7%	
Educational level[a];	*Primary*	0	0%	54	40.3%	<.001	7	23.3%	27	50.0%	5	25.0%	15	50.0%	.078
n-%	*Secondary*	74	100%	51	38.1%		14	46.7%	16	29.6%	12	60.0%	9	30.0%	
	University	0	0%	29	21.6%		9	30.0%	11	20.4%	3	15.0%	6	20.0%	
Employment; *n-%*	*Employed*	38	51.4%	96	71.6%	.003	20	67.7%	38	70.4%	6	30.0%	6	20.0%	.690
Age (years-old)	*Mean-SD*	21.10	4.47	28.76	10.43	<.001	28.20	11.21	27.65	8.96	36.65	10.86	26.07	9.82	.002
BMI (kg/m^2)	*Mean-SD*	22.07	3.81	24.95	9.13	.010	16.84	1.85	25.27	5.96	39.54	10.33	22.80	4.56	<.001

Note. AN = anorexia nervosa; BED = binge eating disorder; BMI = Body Mass Index; BN = bulimia nervosa; ED = eating disorder; HC = healthy control; OSFED: other specified eating and feeding disorders; SD = standard deviation.
[a]Primary educational level = no qualification/first qualification age 16; Secondary educational level = qualification for admission to university, age 16-19; University = degree or higher degree.

Eating Disorders Inventory-2 (EDI-2; Garner et al., 1983): The EDI-2 is a 91-item self-report questionnaire that assesses characteristics of AN and BN on the dimensions of drive for thinness, bulimia, body dissatisfaction, ineffectiveness, perfectionism, interpersonal distrust, interoceptive awareness, maturity fears, asceticism, impulse regulation, and social insecurity. This scale has been validated in a Spanish population (Garner, 1998), obtaining a mean internal consistency of α =.63. Internal consistency in the current sample ranged from moderate (ascetic scale, α=.70) to excellent (total scale, α=.96).

Symptom Check-List 90 revised (SCL-90-R; Derogatis, 1994): The SCL-90-R is a 90-item self-report questionnaire measuring psychological distress and psycho-pathology. The items load on nine symptom dimensions: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. The global score (Global Severity Index, GSI), is a widely used index of psychopathological distress. The SCL has been validated in a Spanish population obtaining a mean internal consistency of α =.75 (Derogatis, 2002). Internal consistency in this sample was between good (paranoid ideation scale, α=.83) and excellent (global indexes, α=.98).

Temperament and Character Inventory revised (TCI-R; Cloninger, 1994): The TCI-R is a 240-item self-report questionnaire measuring personality on four temperament and three character dimensions. The temperament dimensions

include harm avoidance (e.g., inhibited/ passive vs. energetic/ outgoing), novelty seeking (e.g., reward-seeking/ impulsive vs. uninquiring/ reflective), reward dependence (e.g., sociable/ socially dependent vs. tough-minded/ socially insensitive), and persistence (e.g., perseverant/ ambitious vs. inactive/ erratic). The character dimensions assess self-directedness (e.g., responsible/goal-directed vs. insecure/ inept), cooperativeness (e.g., helpful/ empathic vs. hostile/ aggressive), and self-transcendence (e.g., imaginative/ unconventional vs. controlling/ materialistic). The original questionnaire and the Spanish version of the revised questionnaire were validated and showed good psychometric properties (Cloninger, 1994; Gutiérrez-Zotes et al., 2004). Internal consistency in the current sample was good (novelty seeking scale, α=.83) to excellent (harm avoidance scale, α=.93).

2.3 Procedure

All participants provided written informed consent; the study was conducted according to the Declaration of Helsinki and was approved by the local ethical committee. Patients were evaluated and diagnosed at the ED Unit of the University Hospital of Bellvitge by experienced psychologists and psychiatrists during two assessment sessions. The first assessment session consisted of a face-to-face interview that provided information about current ED symptoms and antecedents, as well as other psychopathological data of interest. The second assessment session involved weight/eating monitoring and the completion of self-report measures (see Measures section). HC participants were assessed in one session, during which they had their weight and height recorded and completed the relevant self-report measures, as well as a written survey on socio-demographic data, core symptoms of ED, history of psychopathology, and family psychopathology.

2.4 Data Analyses

Statistical analyses were carried out with SPSS20 and Stata13 for Windows. The analysis plan included multiple statistical comparisons. In order to control for Type I error inflation, and because the classical Bonferroni's correction method has been criticized for being too conservative, an improved modified procedure was used here: the Holm-Bonferroni method (see, e.g., Gratz and Roemer, 2004; Weinberg and Klonsky, 2009; Cooper et al., 2014). This method has the advantage of being more powerful and especially useful when several highly-correlated test statistics are involved. Additionally, because p-values are strongly dependent on sample sizes, we included effect sizes for all comparisons, including partial eta^2 for ANCOVA models and Cohen's d coefficient for mean differences. Mean differences were considered medium for $|d| > 0.5$ and large for $|d| > 0.8$. Correlation coefficients were considered medium for $|r| > 0.30$ and large for $|r| > 0.50$.

2.4.1 Aim 1

First, an Exploratory Factor Analysis (EFA, with Varimax-rotation) and a Confirmatory Factor Analysis (CFA, selecting the Maximum Likelihood and the Robust estimation method) were conducted to examine the internal structure of the Spanish version of the DERS. For the EFA analyses, sample adequacy was based on the Kaiser-Meyer-Olkin measure (for ease of interpretation, 0.90 is considered excellent, 0.80 is considered good, 0.70 is considered moderate, 0.60 is considered low, 0.50 is considered poor. and below 0.50 is considered unacceptable), and Bartlett's test of sphericity was used to test the hypothesis that the correlation matrix is an identity matrix ($p < .05$ is indicative that the data set included correlations

appropriate for the factor analysis). For the CFA analysis, goodness-of-fit was assessed using the Standardized Root Mean Squared Residuals (SRMR, adequate fit was considered for SRMR limited to .10), as well as the Root Mean Squared Error of Approximation (RMSEA), Comparative Fit Index (CFI), and Tucker-Lewis Index (TLI).

Second, analyses of covariance (ANCOVAs), controlling for participants' age, sex, and education level, were conducted to explore the discriminative capacity of the DERS scores in differentiating between controls and ED patients. Third, Pearson-correlation coefficients were conducted to assess the linear associations between DERS scores and the measures of ED (EDI-2 scales), general psychopathology (SCL-90-R), and personality traits (TCI-R dimensions).

2.4.2 Aim 2

Analyses of covariance (ANCOVAs), controlling for participants' age, sex, and education level, were conducted to examine group differences in DERS scores between ED subtypes. Structural Equation Modeling (SEM) was used to examine the hypothesized mediating role of emotion regulation difficulties in the relation between personality traits and ED severity. Robust standard errors were estimated and overall goodness-of-fit was assessed through the RMSEA, CFI, TLI and SMSR. Adequate fit was considered for RMSE < .08, CFI > .90, TLI > .90 and SRMR < .10. Global predictive utility of the model was estimated with the Coefficient of Determination (CD).

3 Results

3.1 Preliminary analyses

Data was screened for outliers in the DERS scale, with an exclusion criterion of a deviation of more than 3 SD from the sample mean. No outliers were detected. The DERS scores were normally distributed, as shown by non-significant Shapiro-Wilk normality tests (*p*-values > .05 for all subgroups and subscales).

Preliminary analysis to identify possible covariates indicated that the demographic factors sex, age and education were each significantly related to some of the dependent variables (DERS, TCI-R and EDI-2) in the whole sample and partly also in the ED sample. Therefore, these variables were controlled for in the following analyses to ensure that any observed associations between the variables of interest are not due to their shared associations with these demographic variables. Nevertheless, since in the ED sample the demographic variables were not significantly related to all of the dependent variables, we run each analyses of Aim 2 without covariates. For the path model, standardized coefficients obtained in the model not adjusted by age and sex were quite similar to those obtained in the adjusted model, but goodness-of-fit was clearly poorer (RMSEA and TLI did not achieve the threshold for adequate fitting, see Figure S1.1). For the ANOVAS, evidence remained similar wherefore we report the adjusted results for all analyses. Unadjusted results can be consulted in the supplementary material (Tables S2 and S3 and Figure S1).

3.2 Aim 1

3.2.1 Internal structure of the DERS: factor analyses

Table S1.1 (supplementary) shows the factor loadings obtained in the EFA for the one-dimensional factor solution and the six-factor solution, as well as the standardized coefficients of the CFA for the Spanish version of the DERS for the whole sample. Prior to the factor analyses, inverse items (1, 2, 6, 7, 8, 10, 17, 20, 22, 24, 34) were reversed so that higher scores indicate greater emotion regulation difficulties. Sample adequacy for the EFA was excellent (Kaiser-Meyer-Olkin =.927,

Bartlett's test p<.001). The one-dimension factor solution in the EFA was acceptable, providing a factor with high loadings for all the DERS items, excellent internal consistency (Cronbach's alpha α=0.96), and a moderate percentage of explained variance (41.1%). The six-factor solution was also acceptable and corresponded closely to the original six-factor solution identified in Gratz and Roemer's (2004) paper (with a few exceptions involving high cross-loadings of items on the Strategies and Clarity factors with other factors; i.e., items 1, 9, 22, 28, 30, 31 and 36). All factors in the six-factor solution had good internal consistency (α coefficients ranging from 0.81 for the Impulse factor and 0.92 for the Non-acceptance factor), and accounted for 64.0% of the cumulative explained variance. Additionally, all factors were significantly correlated with one another (with correlations between factors ranging from r = .49 to r = .77), with the exception of the Awareness factor (see Table S1.1 for intercorrelations between the factors).

Results of the CFA support the acceptability of the 6-factor solution; the standardized coefficients for all DERS items on their respective (and theorized) dimension were significant and moderate to high in magnitude. Additionally, the 6-factor solution demonstrated adequate goodness of fit across all indices (RMSEA=.076, CFI=.903, TLI=.900, SRMR=.088), supporting the adequacy of this factor solution.

The following analyses were performed using the DERS raw scores (obtained as the direct sum of the items) for the six original subscales and the DERS total scale.

3.2.2 Discriminative capacity of the DERS

Table 2 shows the results of the ANCOVAs comparing the mean DERS scores for the HC and ED groups, adjusted for participants' sex, age, and educational level. As expected, participants in the ED group reported greater difficulties in emotion regulation across all dimensions; all effect sizes accompanying these mean differences were medium to large. These results provide support for the discriminative capacity of the DERS in differentiating between HC and ED cases. Furthermore, we explored the sensibility of the DERS to discriminate each specific ED subgroup from HC (see Supporting Information, Table S1.4). The Goals subscale was the only one which couldn't successfully discriminate HC from two ED subgroups, namely AN and BED. All the other subscales had good discriminative capacity for each ED diagnostic subtype.

Table 2. Discriminative capacity of the DERS scores to differentiate between controls and ED patients

	HC (n=74)		ED (n=134)		Means comparison:ANCOVA				
DERS-scale	Mean	SD	Mean	SD	MD	F-stat	[1]p	η^2	|d|
Nonacceptance of emotional responses	12.3	5.01	18.3	6.84	6.02	31.15	<.001	.135	1.00**
Difficulties engaging in goal directed behavior	13.8	4.42	16.3	4.95	2.44	8.72	.004	.042	0.52*
Impulse control difficulties	10.7	3.63	15.9	6.14	5.20	30.56	<.001	.133	1.03**
Lack of emotional awareness	14.9	4.44	18.3	5.06	3.48	16.89	<.001	.078	0.73*
Limited access to emotion regulation strategies	15.9	5.88	23.6	8.27	7.65	34.26	<.001	.147	1.07**
Lack of emotional clarity	10.3	3.91	14.9	5.02	4.56	31.72	<.001	.137	1.01**
Total score	78.0	18.39	107.3	27.69	29.34	46.54	<.001	.190	1.25**

Note. Results of all analyses are adjusted for participant age, sex, and educational level.
ED = eating disorder; HC = Healthy Control; MD = mean difference; SD = standard deviation; η^2 = Partial eta2; |d| = Cohen's d. [1]p-values are adjusted for multiple testing using the Holm-Bonferroni method. *Medium effect size for d>0.50 and **large effect size for d>0.80.

Table 3. Correlations of the DERS scores with the clinical measures for the control and ED samples.

	ED sample (n=134)							Control sample (n=74)						
	N-acc.	Goals	Impulse	Aware	Strategies	Clarity	Total	N-acc.	Goals	Impulse	Aware	Strategies	Clarity	Total
Body mass index	.09	.00	-.03	.10	.14	.11	.10	-.06	.04	-.06	.01	-.01	-.07	-.03
EDI: Total score	.49	.49	.50	.15	.59	.55	.62	---	---	---	---	---	---	---
SCL-90-R: Somatization	.33	.35	.35	.11	.48	.37	.45	.30	.19	.14	-.14	.27	.17	.24
SCL-90-R: Obs./comp.	.45	.52	.43	.05	.54	.36	.53	.34	.27	.08	-.03	.27	.37	.33
SCL-90-R: Interp. sen.	.54	.54	.48	.18	.69	.53	.66	.30	.20	.13	-.11	.40	.41	.34
SCL-90-R: Depressive	.56	.56	.54	.14	.69	.50	.68	.39	.25	.26	-.17	.50	.24	.39
SCL-90-R: Anxiety	.46	.48	.50	.10	.56	.37	.56	.42	.22	.22	-.19	.38	.29	.35
SCL-90-R: Hostility	.36	.48	.53	.16	.55	.38	.55	.35	.16	.33	-.05	.22	.32	.33
SCL-90-R: Phobic anx.	.40	.42	.35	.13	.51	.31	.48	.30	.22	.13	-.20	.30	.16	.24
SCL-90-R: Paranoid	.46	.48	.44	.13	.58	.45	.57	.17	.11	.15	.01	.30	.25	.25
SCL-90-R: Psychotic	.49	.44	.48	.10	.52	.42	.55	.38	.16	.19	-.05	.36	.42	.37
SCL-90-R: GSI score	.53	.55	.53	.13	.67	.48	.65	.41	.24	.22	-.12	.43	.34	.39
SCL-90-R: PST score	.50	.48	.47	.18	.60	.46	.60	.42	.26	.27	-.02	.44	.45	.46
SCL-90-R: PSDI score	.50	.48	.46	.06	.59	.41	.57	.31	.20	.11	-.22	.33	.13	.23
TCI-R: Novelty seeking	-.07	.03	.06	-.03	-.02	.03	-.01	-.05	.05	.09	-.01	-.03	.17	.04
TCI-R: Harm avoid.	.37	.43	.32	.10	.51	.41	.48	.29	.28	.06	.04	.47	.25	.37
TCI-R: Reward depen.	-.09	-.05	-.09	-.28	-.04	-.21	-.15	.02	-.10	-.10	-.41	-.08	-.37	-.24
TCI-R: Persistence	-.16	-.33	-.26	-.12	-.37	-.23	-.33	.05	-.04	.08	-.37	-.08	-.29	-.16
TCI-R: Self-directedn.	-.42	-.46	-.46	-.20	-.54	-.54	-.59	-.18	-.14	-.18	-.09	-.39	-.47	-.37
TCI-R: Cooperativen.	-.08	-.16	-.16	-.17	-.17	-.24	-.21	.01	-.14	-.23	-.22	-.11	-.24	-.22
TCI-R: Self-Transc.	.09	.02	.01	-.18	-.04	-.11	-.04	.18	-.01	.17	-.14	.02	.11	.08

Bold: Medium to large effect size for correlation |r|>.30. --- Not available for this group.

3.2.3 Associations of the DERS with ED severity, psychopathology, and personality traits

Table 3 shows the correlations of the DERS scale scores with the clinical measures of ED symptom severity (EDI-2), general psychopathology (SCL-90-R), and personality (TCI-R). In the ED group, all of the DERS scales were significantly positively correlated with the EDI-2 total score and all the SCL-90-R scale scores (such that greater emotion regulation difficulties were associated with higher ED severity and greater psychopathology), with the exception of the DERS Awareness scale (which was not significantly associated with the other clinical measures).

All DERS scales (except Awareness) were also significantly correlated with the personality traits of harm avoidance (positive association) and self-directedness (negative association). The DERS Goals, Strategies, and Total scale scores were also negatively correlated with persistence. BMI was not significantly correlated with any of the DERS scales in either the ED or HC groups (see Table 3). Moreover, BMI was not significantly correlated with the DERS total score in any of the ED subtypes. However, within the BED subgroup, BMI was significantly correlated with the Goals

(r = -.31) and Awareness (r = .39) scales of the DERS. The pattern of associations within the HC group was somehow different. The DERS scales demonstrating the most robust associations with the clinical measures were as follows: a) the Nonacceptance scale correlated significantly with most SCL-90-R scales (excluding somatization and paranoid); b) the total DERS score and the Strategies and Clarity subscales correlated with many SCL-90-R scores; c) the Awareness scale correlated negatively with the TCI-R reward dependence and persistence scales; d) the DERS total score and the Strategies subscale correlated positively with TCI-R harm avoidance and negatively with TCI-R self-directedness; and e) the Clarity scale correlated negatively with the TCI-R reward dependence and self directedness scales. Figure 1 contains the scatter-plots of the distribution of DERS total score with TCI-R self-directedness and harm avoidance scales.

3.3 Aim 2

3.3.1 Differences in emotion regulation difficulties across ED subtypes

Results of an ANCOVA (controlling for sex, age, and educational level) comparing mean differences in emotion regulation difficulties across the four ED subtypes (AN, BN, BED and OSFED) revealed significant differences between ED subtypes for the DERS total scale and the Strategies, Goals and Nonacceptance subscales (*t*-values and effect sizes see Table 4, $p < .05$). Scores on the Awareness, Clarity and Impulse subscales did not differ between groups (*p*s > .10). The AN group reported lower mean scores than the BN group on the Nonacceptance, Goals and Strategies subscales. The AN group also reported lower mean scores than the OSFED group on the Goals and Strategies subscales. Table 4 presents both the mean DERS-scores for the ED subtypes (AN, BN, BED and OSFED) and the pairwise comparisons between the ED subtypes.

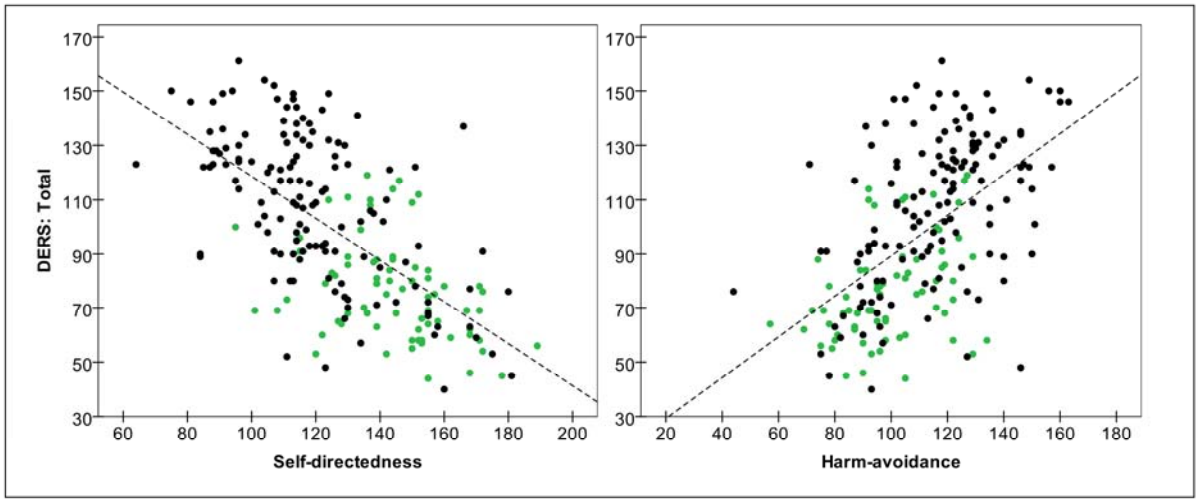

Figure 1. Scatter-plot of the DERS total score with TCI-R self-directedness and harm avoidance scales. ED patients are in black and HC participants are in green. Dashed line represents total line fit.

3.3.2 Path analysis of the interrelations between personality traits, emotion regulation difficulties, and ED

Figure 2 contains the results of the path analysis of the theorized associations among the personality traits (self-directedness and harm-avoidance), emotion regulation difficulties (DERS total score) and ED severity (EDI-2-total score), adjusted for patient sex and age. Including these factors as covariates allows us to

examine the interrelations of personality, emotion regulation, and ED symptoms when accounting for their shared associations with sex and age. This model shows that the DERS total score mediates the relation between the personality traits and ED severity; specifically, low scores on the self-directedness scale and high scores on the harm avoidance scale predicted higher scores on the DERS total scale, and high scores on the DERS total scale were associated with higher EDI-2 total scores. In addition, self-directedness had a direct effect on EDI-2 total scores (such that lower levels of this personality trait were related to higher scores on the EDI-2 total scale). Adequate goodness-of-fit of the path model was demonstrated across all fit indices (RMSEA=.061, CFI=.994, TLI=.975 and SRMR=.026), and the global predictive capacity was high (Coefficient of Determination = .59).

Table 4. Comparison of the DERS scores between different ED subtypes.

	Adjusted means and standard deviations								ANOVA adjusted by age, education and sex				
	AN (n=30)		BN (n=54)		BED (n=20)		OSFED (n=30)		Significant pairwise comparisons				
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Contrast	MD	t	*p*	|d|
Non acceptance of emotions	16.39	7.52	19.61	6.00	17.99	6.46	19.36	7.59	AN-BN	-3.22	2.01	.047	0.50*
Difficulties in goal directed behavior	14.43	4.81	17.23	5.11	15.64	3.80	17.30	4.99	AN-BN	-2.80	2.43	.017	0.56*
									AN-OSF	-2.87	2.16	.032	0.59*
Impulse control difficulties	14.22	5.58	16.57	5.49	15.62	6.64	17.06	7.18	---	---	---	---	---
Lack of emotional awareness	18.07	5.43	17.99	4.86	19.82	5.46	17.63	4.95	---	---	---	---	---
Limited emotion regulation strategies	20.00	7.52	25.37	7.91	24.21	7.52	24.46	9.14	AN-BN	-5.37	2.79	.006	0.70*
									AN-OSF	-4.46	2.01	.046	0.53*
Lack of emotional clarity	14.41	5.45	14.96	4.86	15.16	4.69	15.40	5.19	---	---	---	---	---
Total score	97.52	30.08	111.74	24.91	108.45	23.19	111.20	30.73	AN-BN	-14.22	2.19	.030	0.51*

MD: mean difference. |d|: Cohen's d. AN: anorexia. BN: bulimia. BED: binge eating disorder. OSF: other specified eating and feeding disorders.
Note. HC = healthy controls; AN = anorexia; BN = bulimia; BED = binge eating disorder; OSF = other specified eating and feeding disorders; MD = mean difference; |d| = Cohen's d. Bolded text indicates significant pairwise comparisons. *Medium (d>0.50) and large (d>0.80) effect sizes.

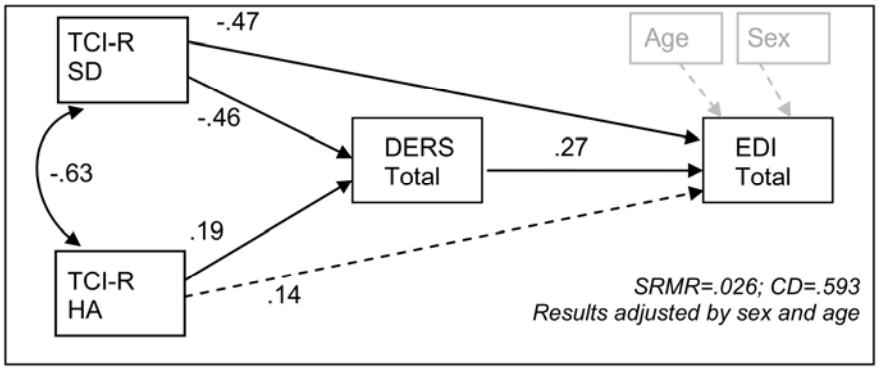

Figure 2. SEM of the proposed mediation model of emotion regulation difficulties mediating the relation of personality traits and eating disorder severity.

Note: CD = Coefficient of Determination; DERS = Difficulties in Emotion Regulation Scale; EDI = Eating Disorders Inventory; HA = Harm Avoidance; SD = Self-Directedness; SRMR = Standardized Root Mean Squared Residuals; TCI-R = Temperament and Character Inventory – Revised

4 Discussion

The aims of the present study were to examine the factor structure and validity of the Spanish version of the DERS in a combined clinical and nonclinical sample of Spanish adults, and to examine the role of emotion regulation difficulties in ED by examining differences in emotion regulation difficulties across ED subtypes (with special attention to OSFED) and exploring the mediating role of emotion regulation difficulties in the relation between key personality traits and ED severity.

The factor structure of the DERS in our adult Spanish sample was comparable to that obtained in the original study, with support provided for the original six-factor solution. Furthermore, consistent with previous studies with Anglo-Saxon samples (Brockmeyer et al., 2014; Lavender et al., 2014; Harrison et al., 2009), the DERS and its subscales demonstrated good internal consistency and convergent validity. Results also support the discriminative capacity of the DERS, as the DERS total score and each subscale differentiated between the healthy controls and ED patients, with ED patients reporting significantly greater difficulties in emotion regulation than the HC group (consistent with past research using the DERS in ED samples; Brockmeyer et al., 2014; Harrison et al., 2009; Lavender et al., 2014).

Greater difficulties in emotion regulation were associated with higher self-reported general psychopathology in both the HC and ED groups, although the associations were smaller in the HC group. Furthermore, although BMI was not significantly associated with emotion regulation difficulties in either the ED or HC groups, greater difficulties in emotion regulation were associated with greater ED severity among the ED patients. Indeed, with the exception of difficulties in emotional awareness, all DERS subscales were significantly correlated with ED severity. Positive correlations between measures of emotion regulation difficulties and ED severity have been found in former studies (Gianini et al., 2014; Gupta et al., 2008; Lavender et al., 2014; Svaldi et al., 2012). Likewise, the absence of a significant association between difficulties in emotional awareness (as assessed with the DERS Awareness subscale) and ED was found previously in BN patients (Lavender et al., 2014). One possible explanation for the lack of significant relations between the Awareness subscale and ED pathology may be that being aware of one's emotions is a necessary but not sufficient condition for adaptive emotion regulation, with emotional awareness alone not automatically resulting in more adequate emotion regulation and fewer psychiatric difficulties. Nevertheless, another study found a small association between deficits in emotional awareness and ED symptoms (Svaldi et al., 2012). Further research is needed to draw conclusions about the exact relations among awareness of emotions, adequate emotion regulation, and psychopathology.

Our hypothesis that certain personality traits would be associated with emotion regulation difficulties was also supported by our findings. Greater difficulties in emotion regulation in the ED group were related to more dysfunctional personality traits. More specifically, high harm avoidance, low self-directedness, and low persistence were associated with greater difficulties engaging in goal-directed behavior when experiencing negative emotions and with less access to adaptive emotion regulation strategies. Moreover, higher levels of harm avoidance and lower levels of self-directedness were related to greater nonacceptance of emotions, greater difficulties controlling impulses when experiencing negative emotions, and lower emotional clarity. Lack of emotional awareness was not associated with harm

avoidance or self-directedness in the ED sample. Thus, the personality traits reflected in self-directedness (i.e., poor resourcefulness, helplessness, irresponsibility) and harm avoidance (i.e., behaviorally and socially inhibited, fear of uncertainty, easily tired) are associated with difficulties in all dimensions of emotion regulation assessed by the DERS, with the exception of emotional awareness

Although the DERS has been used to assess emotion regulation difficulties among ED patients in past studies, this is the first study to our knowledge to include the category of OSFED. Within our sample, the greatest difficulties in emotion regulation were found in the BN and the OSFED groups, which did not differ from one another. Additionally, the AN group reported lower difficulties in emotion regulation than both the BN and OSFED groups. Findings that the OSFED patients in our sample reported levels of emotion regulation difficulties comparable to those reported by the BN patients and greater than those reported by the AN patients provide preliminary support for the relevance of emotion regulation difficulties to this particular ED subtype. These findings are consistent with past research demonstrating that patients diagnosed as EDNOS do not differ from those with full ED diagnoses in clinical severity or overall psychopathology (Thomas et al., 2009), and provide further evidence for the clinical relevance of the OSFED subtype. Conversely, findings that the AN patients reported lower levels of emotion regulation difficulties than the BN or OSFED groups differ from previous findings suggesting that AN patients report levels of emotion regulation difficulties comparable to BN patients, with BED patients reporting fewer problems with emotion regulation (Brockmeyer et al., 2014; Svaldi et al., 2012). Given that the AN patients in this sample reported levels of emotion regulation difficulties comparable to those previously reported by patients with AN (Brockmeyer et al., 2012; Harrison et al., 2010), findings of lower levels of emotion regulation difficulties among the AN (vs. BN and OSFED) patients in this sample may reflect the greater severity of the BN and OSFED groups in our study (relative to past studies), rather than a lack of emotion regulation difficulties in the AN group. Specifically, differences in the sampling or recruitment methods across studies in this area may influence the nature of the ED sample. Alternatively, these findings may reflect cultural differences in the clinical presentation and severity of ED.

Results of the SEM suggest that the relation of the personality traits of harm avoidance and self-directedness to ED severity is mediated by difficulties in emotion regulation. More specifically, results suggest that whereas self-directedness influences ED severity through both direct and indirect pathways, harm avoidance may only have an indirect effect on ED severity through difficulties in emotion regulation. Although the cross-sectional nature of our study precludes conclusions about the precise nature and direction of the observed relationships, there is sufficient evidence to support our proposed model. For example, twin studies suggest that a substantial proportion (~30-40%) of the variance in temperament and personality traits is explained by genetic components (Ando et al., 2002; Garcia et al., 2013; Gillespie et al., 2003; Heath et al., 1994) and longitudinal studies suggest that personality predicts emotion regulation (Kokkonen and Pulkkinen, 2001; Xia et al., 2014). Furthermore, research suggests that maladaptive emotion regulation predicts psychopathology rather than the other way around (Bardeen et al., 2013; Berking et al., 2014; Goodwin et al., 2014; McLaughlin et al., 2011; Wirtz et al., 2014).

Thus, research suggests that a biologically-based and heritable temperament predisposes the development of more or less adaptive emotion regulation strategies. Notably, although Cloninger's (1993) original model of personality distinguished between temperament and character (with the former referring to genetically determined traits, such as harm avoidance, and the latter corresponding to environmentally-determined traits that are thought to emerge over time, such as self-directedness), evidence suggests that the hypothesis of a neurobiological distinction between temperament and character cannot be upheld (Farmer and Goldberg, 2008) and provides support for a genetic basis of character traits as well (Garcia et al., 2013; Ando et al., 2002; Gillespie et al., 2003). Thus, both harm avoidance and self-directedness traits – through biological mechanisms such as hypothalamic–pituitary–adrenal axis and autonomic nervous system functioning – may play a central role in how an individual will respond to and manage environmental influences. Resiliency to psychopathology has been suggested to be associated with the development of a stable emotion regulation network (Cisler et al., 2013), whereas the absence of adaptive emotion regulation can result in various psychopathological symptoms (Aldao et al., 2010). With regard to ED in particular, the biopsychosocial model of ED proposes that biologically- and genetically-based vulnerabilities (which are seen in personality traits) influence reactivity to external stimuli, integration of childhood experiences, storage of emotional schemas, and the acquirement (or lack thereof) of adaptive emotion regulation strategies (Kochanska et al., 2009; Shapero and Steinberg, 2013; Calkins et al., 2013), with the lack of adaptive regulation strategies resulting in the use of maladaptive strategies, such as starvation, binge eating, or self-injurious behavior, to avoid or escape unwanted or overwhelming negative emotions (Fox and Power, 2009; Haynos & Fruzzetti, 2011; Ivanova et al., 2015; Lavender et al., 2015)

There are some limitations of this study that warrant mention. First, the cross-sectional nature of this study precludes conclusions about the direction or temporal ordering of the observed relationships, or the development and interrelations of the constructs of interest over time. Second, the sample size was relatively small, particularly for some of the specific ED subgroups. Thus, results of the within-ED group comparisons need to be interpreted with caution. In addition, the patient groups were too small to subdivide the AN group into binge-purging and restrictive subtypes, which may influence results. Third, our sample did not include a sufficient number of male participants to examine gender effects or the moderating role of gender in the observed relations. Fourth, we relied exclusively on the DERS to assess emotion regulation difficulties. Although the DERS is based on a multidimensional conceptualization of emotion regulation difficulties (Gratz and Roemer, 2004) and, thus, assesses several distinct dimensions of emotion regulation difficulties, it is not exhaustive and other dimensions of emotion regulation difficulties (including emotion regulation strategy use and emotional avoidance) remain unexamined. Thus, future studies would benefit from the use of multiple self-report measures of emotion regulation difficulties (in addition to objective behavioral and/or physiological measures of emotion regulation) in order to examine emotion regulation deficits in ED and their mediating role in the personality-ED relation.

Finally, longitudinal studies beginning earlier in the lifespan are needed to fully understand the influence of inherited

temperament on the acquisition of emotion regulation strategies and the development of adaptive emotion regulation. There is preliminary evidence to suggest that harm avoidance is an endophenotype (Gottesman et al., 2003) for psychological illness (Choe et al., 2013; Markett et al., 2013; Calati et al., 2014), whereas difficulties in emotion regulation are learned responses to emotions that may be attributed to environmental influences to a greater extent (Kanakam et al., 2013). However, the precise nature of the relation between harm avoidance and emotion regulation remains unclear. Further research in this area would also be helpful in developing new intervention strategies for ED patients. Training in emotion regulation may be one way to influence temperament and character phenotypes and improve treatment outcomes (Bulik et al., 1998; Kaye et al., 2015; Fagundo et al., 2013). Cognitive behavioral therapy teaches patients to identify and label thoughts and feelings, as well as to decrease avoidance behavior and promote more adaptive behavioral choices. As we have seen in a previous study (Agüera et al., 2012), these learned strategies during treatment help to change personality traits, and, as a result, may promote the development of more adaptive emotion regulation strategies. Treatments focused specifically on promoting more adaptive emotion regulation, such as emotion regulation group therapy (Gratz et al., 2014, 2015) could lead to even better results and target more directly and efficiently both emotion regulation difficulties and the psychopathology stemming from those difficulties.

Abbreviations

AN = Anorexia Nervosa
ANCOVA = Analysis of Covariance
ANOVA = Analysis of Variance
BED = Binge Eating Disorder
BMI = Body Mass Index
BN = Bulimia Nervosa
CD = Coefficient of Determination
CFA = Confirmatory Factor Analysis
CFI = Comparative Fit Index
DERS = Difficulties in Emotion Regulation Scale
ED = Eating Disorder
EDI-2 = Eating Disorders Inventory
EDNOS = Eating Disorder Not Otherwise Specified
EFA = Exploratory Factor Analysis
HC = Healthy Control
OSFED = Other Specified Eating or Feeding Disorders
RMSEA = Root Mean Squared Error of Approximation
SCL-90-R = Symptom Check List
SEM = Structural Equation Modeling
SD = Standard Deviation
SRMR = Standardized Root Mean Squared Residuals
TCI-R = Temperament and Character Inventory
TLI = Tucker-Lewis Index

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Conflict of Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

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5.2 Investigation of the "food addiction" concept

Two studies were conceptualized in order to investigate the processes underlying addictive eating, to find correlates related to FA and to detect indicators distinguishable from ED *severity*. The first study measured personality traits and impulsivity in ED patients with and without FA, which only had been done in healthy student populations until then. The second study extended by the first one by including all of these variables together with difficulties in emotion regulation and measures of ED severity into one model in order to find independent predictors of *addictive eating* in ED patients with binge-eating psychopathology.

Study 3: Personality profiles related to addictive eating patterns

Objectives: FA has been firstly mentioned in the scientific literature in the year 1956 (Randolph, 1956) and since then there was a consistent discussion on the topic, with an explosive increase in publications from 2009 (Meule, 2015). The high prevalence of obesity and EDs in our society show that the constant availability of a variety of food is problematic to some individuals, a fact that has led to an increase on research into overeating and loss of control over food intake. The finding that addictive drugs use to some extend similar brain circuits as rewarding food (Volkow et al., 2012) and the development of the YFAS (Gearhardt et al., 2009b) have fuelled the discussion further. To conclude on the separability of FA and ED severity, this study aimed to investigate if a "diagnosis" of FA in ED patients is related to a distinguishable personality profile and to differences in impulsivity when compared to ED patients without FA.

Results: Compared to patients who did not fulfil the criteria for FA, patients with FA had lower self-directedness, more negative urgency and higher lack of perseverance. The probability of receiving a FA "diagnosis" was predicted by high reward dependence, high negative urgency and low scores in lack of premeditation.

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"Food addiction" in patients with eating disorders is associated with negative urgency and difficulties to focus on long-term goals

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Abstract

Objectives: The present study aimed to investigate if eating disorder patients differ in specific personality traits depending on a positive screening of food addiction and to find a model to predict food addiction in eating disorder patients using measures of personality and impulsivity. **Methods**: 278 patients having an eating disorder self-reported on food addiction, impulsivity, personality, eating and general psychopathology. Patients were then split into two groups, depending on a positive or negative result on the food addiction screening. Analysis of variance was used to compare means between the two groups. Stepwise binary logistic regression was used to obtain a predictive model for the presence of food addiction. **Results:** Patients with food addiction had lower self-directedness, and more negative urgency and lack of perseverance than patients not reporting addictive eating. The probability of food addiction can be predicted by high negative urgency, high reward dependence, and low lack of premeditation. **Conclusions:** Eating disorder patients who have more problems to pursue tasks to the end and to focus on long-term goals seem to be more likely to develop addictive eating patterns.

Keywords: Eating disorder; food addiction; personality; impulsivity; negative urgency

1 Introduction

Until now there is no clear agreement about the question if food addiction (FA) is a valid and necessary concept, specifically in the domain of eating disorders (ED). On the one hand, different components of food have been studied using animal models, providing evidence that sugar consumption – and to some extend also high fat food – can lead to addictive behaviors, similar to other substances of abuse (Avena et al., 2008; Gold and Avena, 2013; Avena et al., 2012; Teegarden and Bale, 2007). Hyperpalatable foods, characterized by high levels of sugar, fat and salt are potentially addictive for humans (Davis,

2014; Schulte et al., 2015; Gearhardt et al., 2011a). Apart from this, neuroimaging techniques have shed light over neural correlates of FA, as well as on the similarities between substance dependence and addictive-like eating behavior in humans in terms of reward value and incentive value of respective stimuli (Davis et al., 2013; Gearhardt, Yokum, et al., 2011; Imperatori et al., 2014; Smith & Robbins, 2013; Volkow, Wang, Fowler, Tomasi, & Baler, 2012). On the other hand, the FA construct seems to overlap with common eating psychopathology, namely bingeing, and seems to have collinearity with severity of disordered eating. Furthermore, a much debated question is whether addictive properties intrinsic to specific foods (physical dependence) or rather the eating behavior per se (psychological dependence) play a major role in the explanation of addictive-like eating, wherefore the term "eating addiction" has been proposed in order to underline the behavioral component of these symptoms (see Hebebrand et al., 2014 for a review). This shows the need for more research on psychological processes underlying FA.

The Yale Food Addiction Scale (YFAS) was developed in 2009 with the aim to apply the diagnostic criteria for substance dependence of the fourth revision of the Diagnostic and Statistical Manual of Mental Disorders (DSM; (American Psychiatric Association, 2013)) to eating behavior (Gearhardt et al., 2009a). Since the development of this first validated tool for the measurement of addictive behaviors towards food, the number of publications about FA has experienced a constant growth (Gearhardt et al., 2011a). In DSM-5, the chapter on addictions has undergone reorganization, including now not only substance related disorders, but also behavioral addictions. FA could be included in this new category in future revisions of the DSM.

A meta-analysis including 23 studies using the YFAS reports a mean prevalence of FA of 19.9% in adult samples ranging from healthy normal weight, over obesity, to binge eating disorder (BED), and bulimia nervosa (BN), in which the highest prevalence of up to 100% was found (Pursey et al., 2014). In a recent study using the YFAS in ED patients, 72.8% of the sample fulfilled the criteria for FA compared to 2.4 % of healthy controls, those ED patients who report FA showing higher ED severity and more general psychopathology (Granero et al., 2014). If ED patients with and without FA differ on basic psychological measures, such as personality and impulsivity traits, focused approaches to treatment may be helpful. However, there is a lack of literature analyzing personality vulnerabilities underlying FA.

The idea, that personality characteristics implicated in addictive processes could also contribute to ED, is not a new concept and has been confirmed by empiric data (Davis & Claridge, 1998; Lent & Swencionis, 2012). ED patients are more likely than healthy controls to use addictive substances such as tobacco, but also illicit drugs (Krug et al., 2008), which supports the notion of an "addictive personality". Yet, it is possible that this association is explained by those patients fulfilling the criteria of FA, rather than being typical to all ED patients. Assuming that FA is comparable to other (substance and/or behavioral) addictions, it is expectable that, after controlling for ED subtypes, patients having a positive FA screening will have more addictive-like personality traits than those who do not fulfill the YFAS criteria for FA.

A recent meta-analysis on temperament in ED (Atiye et al., 2015) shows high harm avoidance in all ED-types compared to controls, high novelty seeking in BN patients, high persistence in anorexia nervosa (AN), BN and Other Not Specified

Eating or Feeding Disorders (OSFED), and no differences in reward dependence between patient and control groups. Furthermore, all types of ED-patients were found to have lower scores in self-directedness than healthy controls (Fassino et al., 2004). By comparison, the personality profile found in individuals with substance related and non-substance related addictive disorders, namely gambling disorder, shows similarities but also differences: high novelty seeking and low self-directedness was reported transdiagnostically for different drugs (Pedrero Pérez and Rojo Mota, 2008; Le Bon et al., 2004) and non-substance related addictions (Alvarez-Moya et al., 2007), harm avoidance in contrast may vary depending on the substance consumed (Schneider et al., 2015) and on sex (Granero et al., 2014; Clinton et al., 2004; Claes et al., 2012a). When comparing behavioral addictions (gambling disorder, compulsive buying) to BN, high novelty seeking is more specifically related to the former group, whereas low self-directedness is associated to both groups and reward dependence is not clearly related to either of the groups (Jiménez-Murcia et al., 2015; Alvarez-Moya et al., 2007). Harm avoidance in general is high in both clinical groups, but may be a more gender specific trait, with lower values in males than in females (Claes et al., 2012a; Alvarez-Moya et al., 2007).

Since impulsivity is an important characteristic common to behavioral and substance addictions (Alvarez-Moya et al., 2011; Di Nicola et al., 2015; Jiménez-Murcia et al., 2013; Kaiser et al., 2012; Lawrence et al., 2009; Ochoa et al., 2013; Torres et al., 2013), heightened levels could also be associated with FA. However, high impulsivity has also been found in ED patients (Davies et al., 2009; Claes et al., 2015, 2012b), wherefore a clarification is needed of whether this correlate is related to ED in general, or if it relates specifically to addictive-like eating. In studies using different self-report measures (UPPS, Barratt Impulsivity Scale) in student populations, high impulsivity was related to higher scores on the YFAS (Davis et al., 2011); more specifically, negative urgency, lack of perseverance (Murphy et al., 2014; Pivarunas and Conner, 2015) and attentional impulsivity (Raymond and Lovell, 2015; Meule et al., 2012), while motor and non-planning impulsivity were related to FA only in one (Raymond and Lovell, 2015) of these studies. Regarding behavioral response inhibition tasks, FA was not consistently related to task performance (Meule et al., 2012, 2014a). These results show that the term "impulsivity" has been referred to in different ways and with varying meanings, which may explain the discrepant results of self-report measures of impulsivity when compared to behavioral impulsivity tasks (Cyders and Coskunpinar, 2011; Meule et al., 2014a) and shows that a clear definition of this construct is needed. In the following, impulsivity will be defined according to a five factor-model (Cyders et al., 2007) incorporating the facets lack of premeditation, lack of perseverance, sensation seeking, positive urgency and negative urgency.

The objectives of the present study were 1) to investigate if ED patients differ in specific personality traits depending on a positive FA screening according to the YFAS; and 2) to find a model to predict FA in ED patients using measures of personality and impulsivity. More specifically, starting from the literature on addictive personality traits, it was hypothesized that ED patients with FA would have more novelty seeking, similar self-directedness, reward dependence and harm-avoidance (1a), and higher negative urgency and lower perseverance than ED patients without FA (1b). The second objective was more explorative, therefore

we did not make specific hypotheses on which variables would best predict FA.

2 Material and Methods

2.1 Participants

Participants (*n* = 278, 20 males) were recruited from consecutive referrals to the ED Unit of the Department for Psychiatry of Bellvitge University Hospital during a period comprised from September 2013 until March 2015. AN (n = 68), BN (n = 110), BED (n = 39), and OSFED (n = 61) patients were originally diagnosed according to DSM-IV-TR (American Psychiatric Association, 2000) criteria by means of the Structured Clinical Interview for DSM Disorders-I (First et al., 1996), conducted by experienced psychologists and psychiatrists. DSM-IV diagnoses were reanalyzed *post hoc* using the recent DSM-5 criteria to ensure diagnoses reflected the current diagnostic criteria (American Psychiatric Association, 2013). See Table 1 for sociodemographic variables, for further information on the sample characteristics see Table S2.1 and Table S2.2 in the supplementary material.

Table 1. Demographic and selected clinical data for the sample.

	Total		AN		BN		OSFED		BED				
	n=278		*n*=68		*n*=110		*n*=61		*n*=39		χ^2	df	*p*
Gender *Females*	92.8%		89.7%		96.4%		95.1%		84.6%		7.46	3	.059
Employed	69.4%		58.8%		70.0%		78.7%		71.8%		6.19	3	.103
Tobacco use	30.6%		29.4%		31.8%		39.3%		15.4%		6.57	3	.087
Alcohol abuse	10.1%		7.4%		17.3%		6.6%		0%		12.1	3	.007
Other drugs use	12.9%		10.3%		19.1%		9.8%		5.1%		6.75	3	.080
Food addiction: screening positive	74.8%		55.9%		89.1%		62.3%		87.2%		33.08	3	<.001
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*F*	df	*p*
Age (yrs-old)	29.1	10.4	26.7	9.2	28.7	9.4	26.6	10.2	38.3	10.9	14.4	3; 274	<.001
Age of onset (yrs-old)	19.7	8.4	17.7	5.1	19.0	7.0	19.8	9.9	24.6	11.8	5.8	3; 274	.001
Duration of illness (yrs)	9.3	9.0	8.3	9.1	9.8	8.7	6.9	6.9	13.6	11.1	4.6	3; 274	.004
BMI (kg/m^2)	24.5	8.7	16.8	1.5	25.2	6.4	22.7	4.2	38.9	9.1	125.0	3; 274	<.001
Food addiction: total criteria	4.76	1.89	3.51	1.71	5.69	1.46	3.74	1.72	5.92	1.36	42.93	3; 274	<.001

* Primary educational level = no qualification/first qualification age 16; Secondary educational level = qualification for admission to university, age 16-19; University = degree or higher degree.

Note. AN = anorexia nervosa; BED = binge eating disorder; BMI = Body Mass Index (kg/m^2); BN = bulimia nervosa; OSFED = Other Not Specified Eating or Feeding Disorders; SD = Standard Deviation.

2.3 Assessment

Yale Food Addiction Scale-Spanish Version -YFAS-S (Gearhardt et al., 2009b; Granero et al., 2014). The YFAS measures FA using 25 items which are assigned to seven scales, referring to the seven criteria for substance dependence defined by the DSM-IV: (1) tolerance, (2) withdrawal, (3) substance taken in larger amount/period of time than intended, (4) persistent desire/unsuccessful efforts to cut down, (5) great deal of time spent to obtain substance, (6) important activities given up to obtain substance, (7) use continued despite psychological/physical problems (American Psychiatric Association, 2000). The YFAS was translated into Spanish and

validated in the Spanish adult and ED population, with good validity and reliability scores (Granero, Hilker, Agüera, Jiménez-Murcia, et al., 2014).

For the following analyses, we either used the "FA total criteria", which indicates the number of fulfilled subscales, or the positive versus negative screening result. If at least three of the seven criteria are met for a period of the last 12 month and the person feels significantly impaired and/or suffers due to the described behavior, this is referred to as "positive YFAS screening score". Internal consistency for the YFAS in our sample was excellent, Cronbach's α = .92.

UPPS-P Impulsive Behavior Scale-UPPS (Whiteside and Lynam, 2001; Cyders et al., 2007). The UPPS-P measures five facets of impulsive behavior through self-report on 59 items: positive and negative urgency (tendency to act rashly in response to positive mood or to distress), lack of perseverance (inability to remain focused on a task), lack of premeditation (tendency to act without thinking of the consequences of an act) and sensation seeking (tendency to seek out novel and thrilling experiences). The Spanish translation shows good reliability (Cronbach's α between .79 and .93) and external validity (Verdejo-García et al., 2010). Reliability as measured by Cronbach's α for the UPPS-P in the study sample ranged from very good (negative urgency α = .83) to excellent (positive urgency α = .91).

Temperament and Character Inventory-Revised-TCI-R (Cloninger, 1994). The TCI-R is a 240-item self-report questionnaire measuring personality on four temperament and three character dimensions. The temperament dimensions are harm avoidance (inhibited, passive vs. energetic, outgoing); novelty seeking (approach to signals of reward, impulsivity vs. uninquiring, reflective); reward dependence (sociable, socially dependent vs. tough-minded, socially insensitive) and persistence (perseverant, ambitious vs. inactive, erratic). Character covers self-directedness (responsible, goal-directed vs. insecure, inept); cooperativeness (helpful, empathic vs. hostile, aggressive) and self-transcendence (imaginative, unconventional vs. controlling, materialistic). The original questionnaire and the Spanish version of the revised questionnaire were validated and show good psychometric properties (Cloninger, 1994; Gutiérrez-Zotes et al., 2004). Internal consistency for the TCI-R in the study sample ranged from very good (novelty seeking α = .80) to excellent (harm avoidance α = .91).

Eating Disorders Inventory-2-EDI-2 (Garner et al., 1983). The EDI-2 is a 91-item self-report questionnaire that assesses characteristics of AN and BN on the dimensions drive for thinness, bulimia, body dissatisfaction, ineffectiveness, perfectionism, interpersonal distrust, interoceptive awareness, maturity fears, asceticism, impulse regulation and social insecurity. This scale has been validated in a Spanish population (Garner, 1998), obtaining a mean internal consistency of α =.63.

Symptom Check-List 90-Revised-SCL-90-R (Derogatis, 1994): The SCL-90-R is a self-report questionnaire measuring psychological distress and psychopathology through 90 items. The items load on nine symptom dimensions: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. The global score (Global Severity Index, GSI), is a widely used index of psychopathological distress. The SCL has been validated in a Spanish sample obtaining a mean internal consistency of α =.75 (Derogatis, 2002).

Behavioral and substance addictions: gambling, kleptomania, stealing and

buying behavior and the abuse of alcohol, the use of tobacco (smoking on an at least a daily basis) and drugs (lifetime use of any drug other than alcohol and tobacco) were assessed in a clinical interview conducted by psychologists and psychiatrists experienced in the field of addictive behaviors.

2.4 Procedure

This study was approved by the local ethics committee and was conducted according to the Declaration of Helsinki. After participants signed informed consent, they were evaluated and diagnosed at the ED Unit of the University Hospital of Bellvitge by experienced psychologists and psychiatrists, who conducted two semi-structured face-to-face interviews. The first interview provided information about current ED symptoms, antecedents and other psychopathological data of interest. The second interview comprised psychometrical assessment, and weight (assessment of body mass index and body composition) and eating monitoring (through daily reports completed at home on food intake, purges, and binges).

2.5 Statistical Data Analyses

Statistical analyses were conducted with SPSS20 for windows. Since age significantly differed between groups and ED subtype is known to influence the probability of FA (Granero et al., 2014), these two variables were entered as covariates. Analysis of variance (ANOVA), adjusted by participants' age and ED subtype, was used to compare the means of the seven TCI-R and the five UPPS-P subscales between participants classified into the two FA groups (positive and negative screening score).

Regarding missing data, statistical analyses were performed for subjects with complete information on each instrument (pair-wise procedure). The number of missing data was very low in this study: only data of one SCL-90R questionnaire was missing (for 1 patient in the YFAS-negative group), one TCI-R (also for one patient in the YFAS-negative group) and eight UPPS (2 patients of YFAS-negative and 6 patients of YFAS-positive group).

Stepwise binary logistic regression was used to obtain a predictive model for the outcome presence of a "positive YFAS screening score" (more than three criteria fulfilled), considering three blocks: the first block included and fixed the participants' sex, age and diagnostic subtype, the second block automatically selected the TCI-R scales with a significant prediction on the dependent variable, and the third block selected the UPPS-P scales with significant contribution. The predictive capacity of each block was measured through the increase in the Nagelkerke's pseudo-R^2 coefficient and the goodness-of-fit of the final model through the Hosmer and Lemeshow test (Hosmer et al., 2013). Due to the multiple statistical comparisons, Bonferroni-Finner correction was included to avoid the increase in Type-I errors. The measure of the effect size for mean and proportion comparisons was done through the 95% confidence interval of the parameters and the Cohen's-*d* coefficient (moderate effect size was considered for $|d|>0.50$ and high effect size for $|d|>0.80$).

3 Results

3.1 Temperament, character and impulsivity traits in ED patients with and without food addiction

Table 2 shows the results of the ANOVA comparing the temperament and character (TCI-R) and impulsivity (UPPS-P) traits mean scores between patients with positive versus negative YFAS screening score, adjusted by age and ED subtype. The analysis was carried out in two steps. In the first step the interaction parameter "positive YFAS screening score" by ED-subtype was included into

the ANOVA to assess whether differences between individuals with positive and negative YFAS screening score were related to the different ED subtypes. Since this interaction term was not statistically significant, it was excluded from the model and the main effects of a "positive YFAS screening score" were estimated and interpreted. Results show that ED patients with positive FA screening compared to patients without FA have lower self-directedness (p <.01), while novelty seeking (p = .915), harm-avoidance (p =.08) and reward dependence (p = .56) do not differ significantly between groups. For a graphical representation and norm comparisons, see Figure S2.1 in the supplementary material.

Table 2. Differences on mean scores of personality traits and impulsivity for patients with or without food addiction: ANOVA adjusted by age and ED subtype.

	Adjusted means; SD				ANOVA						
	FA=negative		FA=positive		FA×ED		(adjusted by age and ED subtype)				
	n=70		*n*=208		$F_{df=3;275}$	^1p	$F_{df=1;275}$	^1p	eta^2	MD	|*d*|
TCI-R: Novelty seeking	100.39	15.07	100.71	15.83	0.36	.781	0.02	.915	.000	0.32	0.02
TCI-R: Harm avoidance	112.89	19.54	119.91	21.08	1.33	.266	5.24	.080	.019	7.02	0.35
TCI-R: Reward dependence	99.40	16.89	101.78	15.62	0.23	.876	0.99	.562	.004	2.38	0.15
TCI-R: Persistence	105.90	18.37	106.24	22.68	0.42	.739	0.01	.915	.000	0.34	0.02
TCI-R: Self-directedness	125.32	21.63	115.37	20.46	0.59	.622	11.17	.007	.040	-9.95	0.47
TCI-R: Cooperativeness	136.49	17.33	134.07	16.24	0.29	.835	1.02	.562	.004	-2.43	0.14
TCI-R: Self-Transcendence	63.32	13.28	63.88	14.27	2.00	.114	0.07	.915	.000	0.57	0.04
UPPS: lack premeditation	23.48	6.08	23.38	6.24	0.07	.974	0.01	.912	.000	-0.10	0.02
UPPS: lack perseverance	21.44	5.45	23.54	5.96	0.79	.500	6.22	.033	.023	2.10	0.37
UPPS: sensation seeking	27.50	8.01	25.27	8.80	0.71	.546	3.41	.110	.013	-2.23	0.26
UPPS: positive UR	27.07	8.79	29.13	8.99	0.21	.892	2.34	.159	.009	2.05	0.23
UPPS: negative UR	29.68	6.70	34.39	6.56	0.22	.881	24.50	<.001	.085	4.70	0.71*

FA: food addiction. ED: eating disorder. FA×ED: interaction parameter. MD: mean difference. eta^2: Partial eta^2.
^1p: includes Bonferroni-Finner correction for multiple statistical comparisons.
Bold: significant comparison (.05 level). *Bold: moderate (|*d*|>0.50) to high ((|*d*|>0.80) effect size.

There were significant differences on the UPPS-P subscales lack of perseverance (p <.05) and negative urgency (p <.001), with higher values in FA patients compared to patients without "positive YFAS screening score" (see Table 2). Lack of premeditation, sensation seeking and positive urgency did not differ as a function of FA.

3.2 Predictive capacity of personality in the explanation of food addiction

Table 3 includes the final predictive model of the presence of a positive YFAS screening score. The first block, including the covariates sex, age, and diagnostic subtype, obtained an initial predictive capacity equal to R^2=.22. In the second block, the TCI-R reward-dependence and self-directedness scale scores were selected and fixed, with an increase in the predictive capacity equal to R^2=.08, while the other TCI-R traits didn't explain further variance. In the third block, the UPPS-P lack of premeditation and negative urgency scores were included, and the new increase in the predictive ability was R^2=.08, while the other UPPS-P subscales did not add additional explanative power. The final predictive model contained in the third block of the logistic regression indicates that after adjusting for sex, age, and ED subtype, the odds of a "positive YFAS screening score"

is increased by high scores in the reward-dependence and negative urgency scales and low scores in the lack of premeditation scale, while negative urgency can be seen as the strongest predictor of FA. This model achieved goodness-of-fit (Hosmer-Lemeshow test: p=.408).

Table 3. Predictive model for the dependent variable: positive screening of food addiction.

Criterion: FA "positive YFAS screening score"		B	SE	Wald	*p*	OR	95%CI (OR)	
First block (ΔR^2=.221)								
Sex (0=female. 1=male)		-0.369	0.596	0.383	.536	0.69	0.22	2.22
Age (years-old)		0.001	0.018	0.006	.938	1.00	0.97	1.04
Diagnostic subtype	*AN vs OSFED*	-0.293	0.398	0.541	.462	0.75	0.34	1.63
BN vs OSFED		1.674	0.450	13.829	<.001	5.33	2.21	12.88
BED vs OSFED		2.258	0.813	7.707	.006	9.57	1.94	47.11
Second block (ΔR^2=.078)								
Sex (0=female. 1=male)		-0.039	0.658	0.004	.953	0.96	0.26	3.49
Age (years-old)		0.001	0.019	0.002	.964	1.00	0.97	1.04
Diagnostic subtype	*AN vs OSFED*	-0.011	0.420	0.001	.978	0.99	0.43	2.25
	BN vs OSFED	1.644	0.470	12.239	<.001	5.18	2.06	13.00
	BED vs OSFED	2.064	0.828	6.208	.013	7.88	1.55	39.95
TCI-R: Reward-dependence		0.023	0.011	3.897	.048	1.02	1.00	1.05
TCI-R: Self-directedness		-0.030	0.009	12.154	<.001	0.97	0.95	0.99
Third block (ΔR^2=.079)								
Sex (0=female. 1=male)		0.095	0.709	0.018	.894	1.10	0.27	4.41
Age (years-old)		0.000	0.020	0.000	.999	1.00	0.96	1.04
Diagnostic subtype	*AN vs OSFED*	-0.048	0.452	0.011	.916	0.95	0.39	2.31
	BN vs OSFED	1.517	0.486	9.757	.002	4.56	1.76	11.81
	BED vs OSFED	2.004	0.843	5.658	.017	7.42	1.42	38.70
TCI-R: Reward-dependence		0.026	0.012	4.531	.033	1.03	1.00	1.05
TCI-R: Self-directedness		-0.016	0.011	2.209	.137	0.98	0.96	1.01
UPPS: Lack premeditation		-0.069	0.033	4.235	.040	0.93	0.87	1.00
UPPS: Negative UR		0.124	0.034	12.992	<.001	1.13	1.06	1.21
Constant		-2.439	2.358	1.070	.301	0.09		

OSFED: Other Not Specified Eating or Feeding Disorders. AN: anorexia. BN: bulimia. BED: binge eating disorder

4 Discussion

Our first goal was to determine if ED patients with FA differ in personality traits when compared with ED Patients without FA, after controlling for ED subtypes and age. Prevalence of FA is high in ED (Granero et al., 2014; Meule et al., 2014b; Gearhardt et al., 2013), in our sample 74.8% of participants met criteria for FA. Those with comorbid FA indeed showed a distinct personality profile, although it was different than expected from the literature regarding "addictive personality traits". Food addiction was not related to higher values in novelty seeking, but exclusively to lower self-directedness (1a). With regard to impulsivity, the hypothesis that ED patients with FA would have higher lack of perseverance and lower negative urgency was supported by our data (1b).

Lower self-directedness has been found to be a characteristic trait both in individuals with substance related and non-substance related addictive disorders, and seems to identify individuals more vulnerable to develop addictive behavior patterns (Schneider et al., 2015; Alvarez-Moya et al., 2007). In ED patients, low self-directedness is also a characteristic trait (Fassino et al., 2002; Cassin and Von Ranson, 2005; Alvarez-Moya et al., 2007), but those with FA seem to be even more marked in this regard. Further support for our results is provided by another study (Bégin et al., 2012), that examined personality differences between overweight/obese women with and without FA and found that women with FA were more similar to women with substance use disorder than women without FA, particularly in regard to impulsivity and self-directedness.

Research has shown that harm avoidance is common to all ED subtypes and significantly higher in patients compared to controls (Atiye et al., 2015; Lilenfeld et al., 2006; Cassin and Von Ranson, 2005). In our study, both ED groups had values beyond the norms of general population (see Figure S2.1), but no significant association was found between this temperament factor and a higher rate of FA. According to this data, we can thus infer that patients high in FA seem to have more problems with goal-orientation and accountability (as measured by self-directedness) compared to ED patients without FA, but both groups are comparable in behavioral and social inhibition and fear of uncertainty (as measured by harm-avoidance). Low self-directedness in patients high in FA implicates that this group has poor resourcefulness; this may present itself in problems to realistically adapt behavior to environmental requirements and to remain in accord with individual goals at the same time. Patients low in self-directedness may also be blaming and unreliable, which could lead to interpersonal problems in this patient group.

The results of this study further indicate that patients reporting addictive eating patterns have more difficulties to pursue tasks to the end and to focus on long-term goals, especially when they are in a negative mood. This is reflected by their high lack of perseverance and high values of negative urgency and is consistent with the results reported for non-clinical populations (Murphy et al., 2014; Pivarunas and Conner, 2015). It is interesting to note that FA patients show high impulsivity related to the regulation of *negative* emotions (as measured by negative urgency), but do not show elevated values in impulsivity related to *positive* emotions (as measured by positive urgency). Negative emotions may signal a discrepancy between personal needs and present conditions, which for individuals with high negative urgency is hard to bear (Cyders and Smith, 2008). This suggests that patients with FA feel a strong pressure to act immediately when having negative emotions instead of enduring until a moment more suitable to change. Since the need by itself all too often cannot be fulfilled immediately, ingestion of rewarding food can be seen as an attempt to escape these unbearable emotions by other means, which - depending on subjective expectancies - could also be a drug or another behavior (Fischer et al., 2012; Torres et al., 2013). Previous research shows that FA is also related to difficulties in emotion regulation (Gearhardt et al., 2012; Pivarunas and Conner, 2015), which corroborates the results on impulsive acts related to negative mood states.

Unexpectedly, ED patients with FA did not show elevated levels of novelty seeking when compared to ED patients without FA. In general, therefore, it seems that the approach to appetitive stimuli (reward seeking), which is implied by novelty/sensation seeking, does not differ between ED patients with and without addictive eating behavior. This points out that FA as assessed by the YFAS is more related to negative rather than to positive reinforcement, which is in line with results of a former study in normal weight participants (Meule & Kübler, 2012). It has been proposed that sensation seeking may be related rather to non-clinical drug use, than to an actual addiction (Torres et al., 2013), which would explain why patients with FA do not necessarily show elevated levels of sensation/novelty seeking.

In regard to the study's second objective, higher values in reward dependence, negative urgency and lack of premeditation and lower values in self-directedness together explained about 15% of the variance on having or not a positive FA screening, over and above sex, age, and diagnostic subtype, while negative urgency was the most important predictor and reduced the predictive power of the other variables to very small effects. Until now, risk factors for suffering FA have been established in different samples, e.g. students (Murphy et al., 2014; Pivarunas and Conner, 2015), obese women with overeating problems (Bégin et al., 2012) or in ED patients (Meule et al., 2014b; Gearhardt et al., 2013; Granero et al., 2014), but no study has explored which would be the highest risk population for presenting FA. Our prediction model suggests that individuals with a high disposition to act rashly to negative emotions are highly vulnerable for FA and would benefit from a specific approach for treating FA symptoms.

It is important to bear in mind the cross-sectional nature of our study; we cannot definitely conclude if the personality traits found to be related to FA precede or succeed FA symptoms, or if both have one common cause. Further work is required to confirm the interrelations between different predictors of FA in ED patients. Another limitation of this study is the small sample size, especially for male patients, wherefore results on effects of gender in FA should be investigated in future studies with higher sample power. Furthermore, our study only included one self-report measure of food addiction, which could be completed by measures of craving, daily assessments and behavioral food ingestion tests in future studies.

Regarding the YFAS, a key issue is the high prevalence rates of FA in AN patients, which seems counterintuitive. Nevertheless, looking at the "total criteria fulfilled" (see Table 1), it appears that AN patients have a smaller number of total criteria fulfilled compared to BN and BED; this may indicate to some part a problem of the cut-off criteria of the YFAS. In addition to this, our results show that the criteria most frequently fulfilled in AN patients are "important activities given up" (60.3%) and "unable to cut down/stop" (89.7%) (see Table S2.3). Some of the items of the YFAS, such as those loading on "important activities given up" and "impairment or distress" may apply to AN in a similar way as to patients on the bulimic spectrum, wherefore this patient group also scores high on these criteria. On the other hand, the subscale "unable to cut down or stop" seems to be systematically misunderstood by AN patients, possibly due to their subjective feeling of eating too much. This could be addressed in future revisions of the scale and should be born in mind when employing the YFAS in this patient group.

It has been formerly suggested that FA may merely be an index of ED severity (Davis, 2013; Gearhardt et al., 2014). The

data at hand suggests that ED patients with FA apart from showing a more severe symptomatology may differ from those without FA in the reward value they expect from food intake. Rather than enjoying the hedonic value of food in good mood, ED patients scoring high on FA mainly use food to regulate their negative emotions. It can be hypothesized that the relation between negative emotional states and food intake is mediated by impulsive personality traits and problems to focus on basic values or personal goals.

To improve the described emotional dysregulation and inhibition of responses, a training of emotion regulation strategies such as acceptance of emotional states could be helpful (Murakami et al., 2015). The importance to integrate work on emotions and emotion regulation skills into cognitive behavioral psychotherapy has reached increasing recognition in the last years (Kahl et al., 2012; Moyal et al., 2015), and new therapy approaches for ED patients have been developed. One example is the Cognitive Remediation and Emotion Skills Training (CREST), a manualized brief psychotherapy addressing emotion regulation and recognition (Tchanturia et al., 2015; Money et al., 2011), where patients learn to differentiate between different emotions and are taught about the communicative function of negative emotions. Patients with addictive-like eating patterns might benefit from this kind of training; the findings of our study further suggest that work on value-oriented behavior is important for patients with FA. Furthermore, this patient group might benefit to a great extend from learning to endure negative emotions by the use of strategies other than food intake and by this means they may be able to gradually reduce their dependence on food/eating in order to regulate negative mood states.

The psychological basis of addictive-like eating compared to mere ED, e.g. the importance ascribed to body shape, food-related cognitions, emotion regulation, should be further investigated in future studies. Which situations and emotional states lead to uncontrolled food intake in each group and the cognitions going along with this behavior could be investigated in experimental studies or ecological momentary assessment studies.

Conflict of Interests

None.

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Study 4: A model to predict addictive eating patterns

Objectives: Previous studies found characteristic correlates of FA in patients with an ED and in HC such as high negative urgency, emotion regulation difficulties and low self-directedness, but it seems difficult to disentangle effects independent from ED severity. The debate on whether a separate diagnostic category would be helpful for the characterization and treatment of patients with addictive eating patterns is ongoing. Therefore, this study aimed to test a comprehensive model of FA and known underlying correlates (urgency, emotion regulation difficulties and self-directedness), under control of ED psychopathology, in order to find independent predictors of FA.

Results: Hypothesis-driven structural equation modelling was conducted to test this comprehensive model. Results suggest that of the included variables the only independent predictor of FA is negative urgency. Self-directedness and emotion regulation predicted negative urgency and were highly related to ED symptomatology in general, but not to FA.

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A comprehensive model of food addiction in patients with binge-eating symptomatology: the essential role of negative urgency

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Abstract

Food addiction has been widely researched in past years. However, there is a debate on the mechanisms underlying addictive eating and a better understanding of the processes associated to these behaviours is needed. Previous studies have found characteristic psychological correlates of food addiction in eating disorder patients and healthy adults such as high negative urgency, emotion regulation difficulties and low self-directedness. Still, it seems difficult to disentangle effects independent from general eating disorder psychopathology. Therefore, this study aimed to test a comprehensive model under control of eating disorder severity, in order to find independent predictors of food addiction. To this aim, 315 patients with eating disorder diagnoses on the binge-eating spectrum were assessed in personality, emotion regulation, negative urgency, eating disorder symptomatology, and food addiction by self-report. Hypothesis-driven structural equation modelling was conducted to test the comprehensive model. The only independent predictor found for food addiction was negative urgency, while self-directedness and emotion regulation predicted negative urgency and were highly related to eating disorder symptomatology, but not to food addiction. Altogether the model suggests that low self-directedness and difficulties in emotion regulation are related to higher eating disorder symptomatology in general. Those patients who, in addition to these traits, tend to act impulsively when in negative mood states, are at risk for developing addictive eating patterns. Urgency-based treatments are therefore recommended for this subgroup of patients.

Keywords: binge-eating; bulimia nervosa; food addiction; emotion regulation; personality; path model

1 Introduction

In the modern world, food is omnipresent. This is especially the case for products which are highly processed, high in sugar and/or fat content, and therefore potentially addictive (Schulte et al., 2015; Volkow et al., 2012). Increased consumption of rewarding food can lead to increased compulsive intake associated with a loss of its hedonic properties (Berridge, 2009; Davis, 2013b); this type

of eating behaviour has been referred to as "food addiction" (FA) (Meule, 2015; Gearhardt et al., 2009a). FA can lead to becoming overweight and is associated with eating disorders (ED), especially binge-eating disorder (BED) and bulimia nervosa (BN), but possibly also binge-eating behaviour in patients diagnosed with Other Specified Feeding or Eating Disorders (OSFED) (Davis, 2013b; Wolz et al., 2016; Granero et al., 2014). Excess weight, in turn, is associated with cardiovascular disease, cancer, and diabetes (Llewellyn et al., 2015). Therefore, research into addictive eating patterns is important and a better understanding of the processes underlying these behaviours would be helpful in improving prevention programmes and treatments for obesity and ED.

As former research has shown, FA is related to high negative urgency (defined as the urge to act rashly under the influence of negative emotions), low self-directedness (defined as self-confidence and capacity to direct behaviours to long-term goals) and difficulties in emotion regulation in both healthy controls (Pivarunas and Conner, 2015; Murphy et al., 2014) and ED patients (Wolz et al., 2016). Furthermore, the relationship between self-directedness and eating disorder psychopathology has been shown to be moderated by emotion regulation difficulties (Wolz et al., 2015). There is a growing body of literature that recognises the importance of FA; however, until now there is no comprehensive model testing the interplay of personality and emotion related factors in addictive eating behaviours. Furthermore, it seems important to find psychological correlates of FA and to identify possible specificities of ED patients scoring high in FA, since it is possible that FA and binge-eating might represent two sides of the same coin and almost all patients with BN receive a "diagnosis" of FA according to the commonly used self-report Yale Food Addiction Scale (Meule et al., 2014b; Granero et al., 2014). In order to conclude if FA significantly differs from other ED, or if it might be better placed on the far end of a continuum from homeostatic eating to severe binge-eating (Davis, 2013b; Imperatori et al., 2014; Davis, 2013a), further understanding is needed.

Therefore, the objectives of the current study were to test a comprehensive model of FA and related constructs while controlling for ED severity and other potential cofounders such as sex, age, and ED duration. Starting from a theoretical background (Murphy et al., 2014; Pivarunas and Conner, 2015; Wolz et al., 2016, 2015), it was hypothesized that FA would be influenced through three ways, over and above ED symptomatology. Firstly, low scores in the personality trait self-directedness would predispose subjects to higher scores on FA. Secondly, it was expected that more difficulties in emotion regulation and higher negative urgency would predict higher FA scores in the model. And thirdly, self-directedness was expected to additionally have an indirect effect by mediating difficulties in emotion regulation and negative urgency, which again were expected to be highly related.

2 Methods

2.1 Participants

A total of 315 patients (292 females, 23 males) were recruited for study participation as consecutive referrals from the ED Unit of the Department for Psychiatry at Bellvitge University Hospital during a time period from September 2013 to May 2016. All patients meeting diagnostic criteria for BN (*n*=176) or BED (*n*=61), and OSFED (*n*=78) patients with binge-eating symptomatology, were included. Patients were diagnosed according to the criteria of the fifth edition of the Diagnostic and Statistical Manual of

Mental Disorders (DSM-5) (American Psychiatric Association, 2013), by means of a face-to-face, semistructured interview. See Table 1 for sociodemographic information and clinical characteristics of the total sample (Table S3.1 contains detailed descriptive statistics for each diagnostic subtype group).

Table 1. Sample characteristics and scores of psychometric measures for the whole sample (n=315).

Gender: Females; *n-%*	292	92.7%
Quantitative variables; mean-SD		
Age (years-old)	30.50	10.79
Onset (years-old)	20.18	8.74
Evolution-duration	10.29	9.03
TCI-R: Self-directedness	114.31	20.42
Food addiction: total criteria	5.36	1.67
UPPS-P: Negative urgency	34.78	6.30
DERS: total score	113.5	22.37
EDI: Total score	111.1	40.79

Note. SD: Standard Deviation; TCI-R: Temperament and Character Inventory-Revised; UPPS-P: Negative Urgency, Premeditation, Perseverance, Sensation Seeking – Positive Urgency; DERS: Difficulties in Emotion Regulation Scale; EDI-2: Eating Disorders Inventory-2.

2.2 Assessment

Internal consistency for all the measures analyzed in this study was between very good (α=.81 for the UPPS-P negative urgency scale) to excellent (α=.95 for EDI-2-total scale) (Table S3.1 contains the α-values for each scale).

The *Yale Food Addiction Scale* (YFAS-S) (Gearhardt et al., 2009b) is a self-report measure with 25 item, which are assigned to seven scales, referring to the DSM-IV (American Psychiatric Association, 2000) criteria for substance dependence: (1) tolerance, (2) withdrawal, (3) substance taken in larger amount/ period of time than intended, (4) persistent desire/ unsuccessful efforts to cut down, (5) great deal of time spent to obtain substance, (6) important activities given up to obtain substance, (7) use continued despite psychological/ physical problems. The YFAS was translated into Spanish and validated in Spanish adult and ED populations, with good validity and reliability scores (Granero, Hilker, Agüera, Jiménez-Murcia, et al., 2014). For the following analyses, the patients' score of total fulfilled FA criteria was used.

The *UPPS-P Impulsive Behaviour Scale* (Whiteside and Lynam, 2001; Cyders et al., 2007) measures five facets of impulsive behaviour through self-report on 59 items. In this study, only the negative urgency subscale, which measures the tendency to act rashly in response to distress and is related to the engagement in risky behaviour under negative emotional states, was used. The Spanish translation shows good reliability (Cronbach's α between .79 and .93) and external validity (Verdejo-García et al., 2010).

The *Temperament and Character Inventory-Revised* (TCI-R) (Cloninger, 1994) is a 240-item self-report questionnaire measuring personality on four temperament and three character dimensions. For the current study, only

the self-directedness subscale – measuring responsible/ goal-directed versus insecure/ inept behaviour – was used. The original questionnaire and the Spanish version of the revised questionnaire were validated and show good psychometric properties (Cloninger, 1994; Gutiérrez-Zotes et al., 2004).

The *Eating Disorders Inventory-2* (EDI-2) (Garner et al., 1983) is a 91-item self-report questionnaire that assesses characteristics of ED on the dimensions drive for thinness, bulimia, body dissatisfaction, ineffectiveness, perfectionism, interpersonal distrust, interoceptive awareness, maturity fears, asceticism, impulse regulation and social insecurity, which compose the EDI-2 total score, an index of ED severity. This scale has been validated in a Spanish population, obtaining a mean internal consistency of α =.63 (Garner, 1998).

The *Difficulties in Emotion Regulation Scale* (DERS; Gratz & Roemer, 2004) is a 36-item self-report measure to assess difficulties in emotion regulation across six subscales, which can be integrated into a total score: non-acceptance of emotions; difficulties pursuing goals when experiencing negative emotions; difficulties controlling impulses when experiencing negative emotions; lack of emotional awareness; limited access to regulation strategies; and lack of emotional clarity. The DERS demonstrates excellent reliability (Cronbach's α =.93; test–retest = .88) and construct and predictive validity (Gratz et al., 2006; Vasilev et al., 2009). A Spanish version of the DERS has been validated in clinical populations with good psychometric properties (Wolz et al., 2015).

2.3 Procedure

The study was conducted according to the Declaration of Helsinki and approved by the Bellvitge University Hospital ethics committee. Participants were evaluated and diagnosed at the ED Unit at the University Hospital of Bellvitge by experienced psychologists and psychiatrists. After having signed informed consent, participants completed the psychometric questionnaires.

2.4 Statistical Data Analyses

Analyses were carried out with Stata13.1 for Windows. Structural Equation Modelling (SEM) was conducted to test the hypothesized model for FA. The Maximum Likelihood method of parameter estimation was used and results were obtained under inclusion of participants' sex, age and duration of the ED (given the strong association reported in the scientific literature between these variables and dependent measures (see e.g. Pursey et al., 2014), their inclusion was aimed at avoiding potential biases caused by confounding effects). Goodness-of-fit was assessed by the following indices and criteria (Barrett, 2007): non-significant (p>.05) chi-square test χ^2, Root Mean Square Error of Approximation (RMSEA) <.08, Bentler's Comparative Fit Index (CFI) >.90, Tucker-Lewis Index (TLI) >.90, and Standardized Root Mean Square Residual (SRMR) <.1. The global predictive capacity of the model was measured with the Coefficient of Determination (CD).

3 Results

Table S3.2 (supplementary material) includes the correlation-matrix (Pearson's-correlation coefficients, r) for the variables included in the SEM. Relevant associations (i.e. *r-values* in the moderate to good effect size range) to FA were found for UPPS-P negative urgency, DERS-total and EDI-total scores.

Figure 1 contains the path-diagram with the standardized coefficients obtained in the SEM analysis (Table S3.3 shows the complete results of this model). Goodness-of-fit was adequate: χ^2=8.137 (p=.420), RMSEA=.007, CFI=1.000, TLI=.999 and

SRMR=.026. Global predictive capacity was also very good: CD=.516. Results of the SEM indicate that high levels in self-directedness predicted low negative urgency, low difficulties in emotion regulation and low ED severity. ED severity mediated the relationship between negative urgency and FA, and also the relationship between difficulties in emotion regulation and FA: high negative urgency levels and high difficulties in emotion regulation predicted high ED levels, which is also a significant and positive predictor of high FA levels. A direct effect was found for negative urgency to FA, but not for emotion regulation and self-directedness to FA levels. As expected, men achieved lower mean scores of ED severity, sex was however not directly related to FA level. Regarding age and evolution of the illness, FA intensity was increased for older patients, but it was not associated to ED duration.

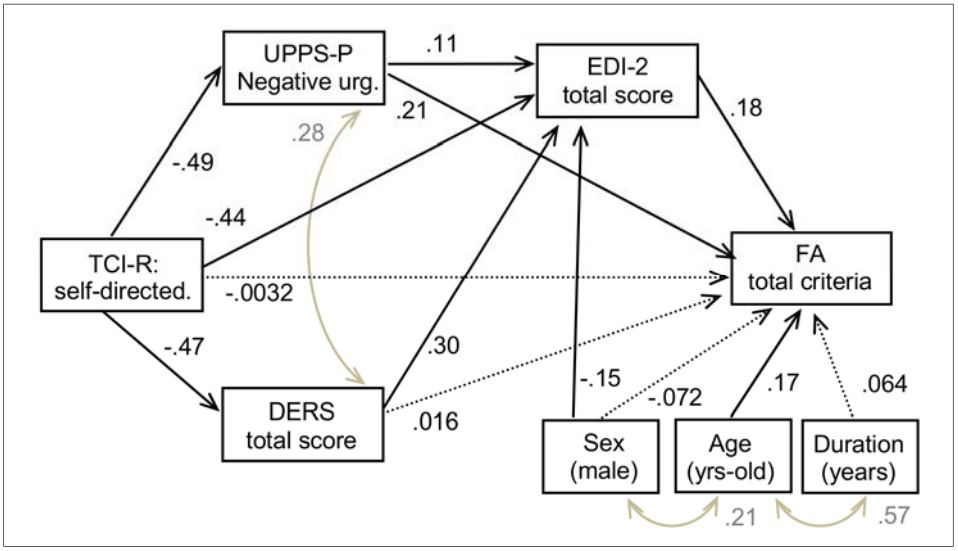

Figure 1. Path-diagram with standardized coefficients for the Structural Equation Modelling (SEM). (Dashed lines: non-significant parameter; grey color: covariances).

Note. TCI-R: Temperament and Character Inventory-Revised; UPPS-P: negative Urgency, Premeditation, Perseverance, Sensation seeking – Positive urgency; DERS: Difficulties in Emotion Regulation Scale; EDI-2: Eating Disorders Inventory-2; FA: Food Addiction

4 Discussion

The main aim of the current study was to test if FA in ED patients can be predicted by related psychological traits, i.e. self-directedness, negative urgency and emotion regulation, over and above ED severity. Our hypotheses that self-directedness would directly relate to FA and through its influence on emotion regulation and negative urgency was not supported by the data; self-directedness was not directly related to FA, through it was when mediated by negative urgency. Apart from ED severity, the only direct predictor of FA in ED patients was negative urgency, which in this comprehensive model was related more strongly to FA than to ED severity. Contrary to expectations, emotion regulation was not directly related to FA, when taking into account ED severity as a mediator. As expected, negative urgency and emotion regulation were highly positively interrelated; both were predicted by low scores in self-directedness. This can be expected, since both constructs are related to managing negative emotions; while negative urgency specifically measures rash action in negative emotional states, i.e. impulsive behaviour under distress, the DERS total score is a multifactorial measure including

different aspects of emotion dysregulation.

The relations of personality traits and emotion regulation with FA found in bivariate analyses in former studies were only partly replicated by this study. Negative urgency, a predictor found in all of the studies concerning this matter (Wolz et al., 2016; Murphy et al., 2014; Pivarunas and Conner, 2015), was confirmed as a direct predictor of FA, while controlling for ED severity. Apart from this, the results of our model highlight that the association between emotion regulation difficulties and FA found in student samples (Pivarunas and Conner, 2015) and in patients with obesity (Baldofski et al., 2016; Gearhardt et al., 2012) might be diminished when accounting for ED psychopathology and negative urgency. Likewise, the link between low self-directedness and FA found in earlier research (Wolz et al., 2016) is likely explained by the mediators negative urgency and ED severity. This suggests that a large part of FA variation is explained by ED symptomatology, which mediates the influence of personality and emotion regulation on FA. Self-directedness and emotion regulation are risk factors closely related to general and ED psychopathology, but not specifically to FA. Interestingly, the variable sex had no significant impact on FA scores in the model, although past studies have shown a higher prevalence in female than in male adults without ED (Pursey et al., 2014). When considering ED severity as a mediator, the only variable adding predictive power to the explanation of FA in ED patients was negative urgency. This may suggest that ED patients who are more prone to act impulsively when in a negative mood state might be at higher risk of developing eating patterns analogue to addictive behaviour.

Taken together, the results of this study support the view that the FA construct as measured by the YFAS might mainly be an indicator of higher ED severity, as has proposed in the case of BED before (Davis, 2013b). The model shows that ED patients suffering from addictive-like eating have more problems with rash action under distress. Looking at the results from a different perspective, they indicate that the inability to endure and accept negative emotional states and the tendency to engage in risky behaviour under emotional distress might lead to food intake becoming a means of self-medication and thus entail addictive-like eating patterns. Negative urgency is described as a phenotypical expression of low 5HT serotonin and high dopamine levels in the brain and is also an important predictor of drug use, alcohol consumption and pathological gambling; therefore, negative urgency seems to be decisive for the development of addictive behaviours in general and might be seen as a marker of addictive disorders (Cyders and Smith, 2008; Yeh et al., 2016). Negative urgency has been found a unique predictor of alcohol and cannabis addiction in a sample of individuals with childhood maltreatment, while other forms of impulsivity were not associated with substance use (Wardell et al., 2016). On the other hand, those patients who are able to keep calm and consider their actions even under distress may have fewer problems with addictive-like eating. Self-directedness in turn is clearly related to ED severity only, i.e. individuals with poor resourcefulness are prone to develop disordered eating behaviour, but not necessarily to higher FA severity when controlling for the mediating effect of ED severity. The same can be said for difficulties in emotion regulation, which are related to ED psychopathology in general, but not to higher scores of FA. The most important role of emotion regulation in this model might be to influence the frequency and intensity of negative emotional states and by this the

probability to emotion-provoked disinhibition, but it does not have a direct effect on addictive-like eating. This corroborates earlier results showing that negative affect was not directly related to binge-eating, but mediated by negative urgency (Lavender et al., 2015); the relation between negative affect and negative urgency was moderated by thought suppression, which can be a component or consequence of emotion regulation difficulties. Urgency-based interventions such as distress tolerance skills training (Linehan, 1993) might be helpful for this patient group. Therapy approaches such as Cognitive Remediation and Emotion Skills Training (Money et al., 2011), primarily developed for the treatment of cognitive and emotional deficits of patients with anorexia nervosa, have also shown promising results (Tchanturia et al., 2015b, 2014). Adaptations of these approaches specific for binge-eating patients with addictive eating patterns, aiming at their individual cognitive profile, are needed.

Although the study has the strength to combine different correlates formerly found for FA in one model and to investigate these relations in a powerful sample of binge-eating ED patients, there are also some limitations to be borne in mind when generalizing the results. This model was proposed according to theoretical background and evidence (Murphy et al., 2014; Pivarunas and Conner, 2015; Wolz et al., 2016, 2015), but it is not exhaustive and there certainly are other important predictors of FA which are not taken into account here. Furthermore, the sample was composed of male and female patients, but since women form a greater part of the ED population than men, males are underrepresented in this model. Another limitation of this study is that the results are based merely on self-report measures. Future studies could add other correlates common to addiction such as related cognitive deficits (Franken et al., 2016), incentive sensitization of cues (Robinson and Berridge, 2001) or behavioural measures of emotion regulation and impulsivity, in order to assess the interrelations between cognitive, emotional and behavioural facets in the explanation of FA.

Abbreviations: BED = Binge-Eating Disorder; BN = Bulimia Nervosa; CD = Coefficient of Determination; CFI = Comparative Fit Index; DERS = Difficulties in Emotion Regulation Scale; DSM = Diagnostic and Statistical Manual of Mental Disorders; ED = Eating Disorder; EDI-2= Eating Disorders Inventory-2; FA = Food Addiction; OSFED = Other Specified Feeding or Eating Disorders; RMSEA = Root Mean Square Error of Approximation ; SEM = Structural Equation Modelling; SRMR = Standardized Root Mean Square Residual; TCI-R = Temperament and Character Inventory- Revised; TLI = Tucker-Lewis Index; UPPS-P = negative Urgency, Premeditation, Perseverance, Sensation seeking – Positive urgency; YFAS = Yale Food Addiction Scale

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Conflict of interests

None**.**

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5.3 Stimulus induced craving and motivated attention to food

Increased motivated attention in response to food and related cues is considered an indicator of incentive sensitization of visual food-related stimuli. To investigate incentive sensitization and stimulus induced craving in ED patients compared to HC, two studies were conducted. The first study was aimed at systematically synthesizing research on attentional processing of food stimuli in different forms of disordered eating behaviour. The second study was designed in order to investigate the impact of olfactory and visual chocolate stimuli on stimulus-induced craving, inhibitory control and motivated attention of patients with binge-eating symptomatology.

Study 5: Food cue processing – electrophysiological evidence for motivated attention towards food in abnormal eating behaviours

Objectives: Due to their evolutionary significance, food stimuli automatically attract more attention than neutral stimuli (Gable and Harmon-Jones, 2010). The preferred processing of specific, subjectively relevant stimuli has been referred to as "motivated attention" (Schupp et al., 2004), which is seen in higher amplitudes of electrophysiological components. It is, however, unclear, how differences in eating behaviour might affect the attentional processing of food. On the one hand, ED patients might show incentive sensitization of food stimuli and therefore have an increased attentional bias towards food, but on the other hand some individuals with an ED might try to avoid the processing of food. To this regard, attentional EEG markers could be of help to conclude on differences between ED subgroups and HC. The aims of this study were therefore to update and summarize the knowledge on attentional processing of food stimuli as measured by electrophysiological ERPs, focusing on differences between individuals with abnormal as compared to normal eating behaviour.

Results: Of the 26 included studies seven, involved participants with an ED diagnosis (six samples with AN, two with BN, one with BED), six studies reported on individuals with obesity or overweight and 13 studies comprised participants with subclinical forms of abnormal eating. Most of the studies used a picture presentation paradigm of food and control pictures, analyzing early and late ERPs related to sensory processing and motivated attention, respectively. Results consistently show high motivated attention towards food pictures compared to neutral pictures in all participants. Group

comparisons of individuals with different abnormal eating habits to healthy eating participants show inconsistencies in results. Obesity is seen to be related to a bias in attentional orienting towards food stimuli, but regarding later time windows the evidence suggests that obese people might try to avoid the processing of food. Individuals with binge-eating, external or emotional eating are likely to have increased motivated attention in response to high-caloric food when compared to healthy-eating individuals, but more research is needed to confirm these results.

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The processing of food stimuli in abnormal eating: A systematic review of electrophysiology

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Abstract

To update the knowledge about attentional processing of food stimuli, a systematic review of electrophysiological studies was conducted using PubMed, PsychInfo and Web of Knowledge (2000-2014). 21 studies were included into qualitative synthesis. Presentation of food and control pictures was used to analyze event-related potentials related to sensory processing and motivated attention. Results show consistent attentional bias towards food pictures compared to neutral pictures for patient and control groups. Group comparisons between individuals with abnormal eating and healthy eating participants were more inconsistent. Results suggest that temporal differences in the millisecond range are essential for the understanding of visual food processing. In obesity, early attention engagement to food is followed by relative disengagement. Loss of control eating, as well as external and emotional eating, are associated with a sustained maintenance of attention towards high-caloric food. There is a lack of studies in anorexia nervosa, bulimia nervosa and binge-eating disorder.

1 Introduction

Eating disorders (ED) are complex and heterogeneous mental disorders, with nutritional and physical consequences, that comprise a group of disorders including anorexia nervosa (AN), bulimia nervosa (BN), binge eating disorder (BED) and other specified and unspecified feeding or eating disorders (OSFED/ UFED) (American Psychiatric Association, 2013). The last categories were formerly (DSM-IV criteria) named 'eating disorders not otherwise specified' (EDNOS); the prevalence of this residual category was effectively reduced by the new criteria of DSM-5 and the inclusion of BED as an official diagnosis (Smink, van Hoeken, & Hoek, 2013). Although obesity has not been considered a mental disorder in DSM-5, there is discussion about the degree to which this condition can be seen as a form of disordered eating (Devlin, 2007; Jauch-Chara & Oltmanns, 2014). Obesity is often mentioned and considered in the literature along with specific eating disorders, sharing genetic and environmental risk factors (Fagundo et al., 2012; Jacquemont et al., 2011; Krug et al., 2013). In addition, childhood obesity has been shown to be a risk factor for the development of restrained and abnormal eating behaviors (Fairburn et al., 1998; Forrester-Knauss, Perren, & Alsaker, 2012; Snoek, Engels, van Strien, & Otten, 2008).

Biopsychosocial models propose that low self-esteem, perfectionism and difficulties

in emotion regulation can predispose individuals to the development of eating disorders alongside biological and social risk factors (Harrist, Hubbs-Tait, Topham, Shriver, & Page, 2013; Keel & Forney, 2013; Svaldi, Griepenstroh, Tuschen-Caffier, & Ehring, 2012). In conjunction with an overvaluation of the importance of shape and weight, these risk factors can lead to the development of eating patterns such as restrained, external and emotional eating. These eating traits can be seen as pre-clinical morbid eating or even precursors of the development of EDs (Neumark-Sztainer et al., 2006; Racine, Burt, Iacono, McGue, & Klump, 2011; Stice, Presnell, & Spangler, 2002). The term 'restrained eating' was put forth in the 1970s and denotes an eating style whereby food intake is restricted and regulated by cognitive rules (e.g. number of calories per day, forbidden foods). Disinhibited eating has been found in restrained eaters under conditions of cognitive load or stress, and caloric preload or food-related priming was followed by increased food intake (Herman & Mack, 1975; Polivy, Herman, & Deo, 2010; Ward & Mann, 2000; Wardle, Steptoe, Oliver, & Lipsey, 2000). This seesaw between restriction and disinhibition mirrors processes found in BN and also in binge-eating/purging type AN. 'External eating' refers to an eating pattern responsive to environmental stimuli, the availability, sight and smell of food and is accompanied by high food craving (Burton, Smit, & Lightowler, 2007; Rodin & Slochower, 1976). Eating in response to external triggers has become more and more important as a result of the 'obesogenic' environment. Although external and emotional eating are related concepts, there are some important differences. Emotional eaters eat in response to emotional distress, food intake functions as regulator of emotions or stress (Macht, 2008; Stice et al., 2002; Van Strien, Schippers, & Cox, 1995).

Psychological treatment for people with an ED have limited efficacy and may benefit from treatment modules targeting core underpinning processes (Schmidt & Campbell, 2013). To this effect, research on attentional processing is of interest. People with disordered eating have attentional biases towards food, body shape and emotional negative stimuli (Brooks, Prince, Stahl, Campbell, & Treasure, 2011; Giel et al., 2011; Harrison, Tchanturia, & Treasure, 2010). Furthermore, laboratory induced attentional bias can alter food intake (Smith & Rieger, 2009; Werthmann, Field, Roefs, Nederkoorn, & Jansen, 2014). Attentional orienting, selection and maintenance are influenced by stimulus-inherent factors, and also by momentary situational context (e.g. physiological and emotional state, availability of food), subjective preferences and learning history (e.g. drug addiction). The amygdala and the mesolimbic dopamine system play an important role in altering the incentive value of specific stimuli, thus leading to increased craving of these stimuli and heightened visual attention, which is also referred to as 'motivated attention' (Berridge, 2009; Schupp et al., 2004; Stockburger et al., 2009). Attentional biases towards food stimuli could act as a predisposing or perpetuating factor in the psycho-pathology of ED and may augment relapse-probability. Attentional bias modification approaches, which are established in anxiety disorders and addictive behaviors (Cox, Fadardi, Intriligator, & Klinger, 2014; Renwick, Campbell, & Schmidt, 2013), may be of use for prevention and treatment of EDs. The use and training of cognitive regulation strategies could help patients to counter the increased salience of food stimuli and to regulate craving and food intake (Giuliani, Calcott, & Berkman, 2013; Yokum & Stice, 2013).

Recent reviews of behavioral attention tasks (Brooks et al., 2011; Giel et al., 2011) report a consistent attentional bias towards food in patients with BN but the evidence is more inconclusive for anorexia nervosa. Most of the behavioral studies on attentional processing included in the former mentioned reviews used a modified Stroop-Task (Stroop, 1935), where the color naming of disorder related and unrelated words is compared. One important limitation of this task is that it is difficult to conclude if heightened reaction times are due to avoidance or selective processing of these stimuli (De Ruiter & Brosschot, 1994; Lee & Shafran, 2004). The Dot-Probe Task (MacLeod, Mathews, & Tata, 1986), where the participant has to react to a probe appearing in the location of a neutral vs. motivationally salient word or picture, allows more conclusions about the direction of biased processing. Two studies using this task showed that ED-patients avoided stimuli with low-caloric food and processed stimuli with high-caloric food with more attentional resources (Lee & Shafran, 2008; Shafran, Lee, Cooper, Palmer, & Fairburn, 2007). Another recent study using a similar paradigm found that healthy participants as well as patients with AN avoided the processing of high-caloric food pictures in a medium time window (500 ms), while there was no difference between high- and low-caloric food in earlier (300 ms) and later (1000 ms) time windows (Veenstra & Jong, 2012). An eye tracking study in turn showed that healthy control participants as well as patients with AN have an early attentional bias towards food, while maintenance of attention was different between groups in that controls (particularly when hungry) attended longer to the food pictures than AN patients (Giel et al., 2011). The results from these two studies show clearly, that timing is an important factor in the allocation of attentional resources to food stimuli.

Temporal aspects of attentional allocation can be measured by electro-encephalographic event-related potentials (ERP). Hans Berger (1929) in the early 20th century developed the use of electroencephalography (EEG) to measure shifts in voltage produced by neuronal activity through electrodes attached to the human scalp. When time-locked to the repeated presentation of a stimulus (ERP), EEG-activity can be used as a direct and temporally exact measure of information processing (Rugg & Coles, 1995). Electrophysiological measures of attention can be divided into short-, midterm- and long-latency potentials (see Table 1). Potentials in early time windows (N100/P100; 100-300 ms after stimulus onset) correspond to early sensory processing and quantify attentional orienting and selection processes; midterm potentials (e.g. early posterior negativity, EPN/P200/N200; 200-300 ms) have been related to the degree of arousal of stimuli, scaling the selective processing of emotional stimuli even under conditions of cognitive load (Coull, 1998; Olofsson, Nordin, Sequeira, & Polich, 2008; Schupp, Junghöfer, Weike, & Hamm, 2003). 'Motivated attention' and subjective emotional salience and arousal is scaled by later ERPs (> 300 ms) denoted as P300/Late Positive Potential (LPP)/slow positive wave (SPW) (Coull, 1998; Hajcak, MacNamara, & Olvet, 2010; Schienle, Schäfer, & Naumann, 2008; Schupp et al., 2000; Stockburger, Weike, Hamm, & Schupp, 2008).

EEG has superior temporal resolution compared to functional Magnetic Resonance Imaging (fMRI) or Positron Emission Tomography (PET) and can offer new insights into abnormal eating behaviors. A literature review of studies on EEG in ED was published in 2011 (Jauregui-Lobera, 2011), and was focused

on sleep and resting state. The objectives of the present review are to summarize electrophysiological research on the visual attentional processing of eating disorder related cues in abnormal eating and weight conditions. To this aim, the following questions were raised:

a) Do patients with ED show an attentional bias towards food stimuli?
b) Is this bias also present in extreme weight conditions and in non-clinical groups with risk factors of ED (i.e. restrained, external and emotional eating, obesity, underweight)?
c) Are there differences between diagnostic groups in the attentional processing of food stimuli?
d) Is there evidence that processing differences are diminished after symptom reduction/remission?

Table 1. Summary of ERP outcome measures.

Outcome measure	Temporality*	Related Functions	Studies included into the review reporting results on the respective outcome measure	
N1(00)	150-200	Early sensory processing; automatic orienting	Meule et al., 2013 Sarlo et al., 2013	
N2(00) (Anterior Negativity, AN)	180-300	Cognitive control under conditions of conflict or response inhibition	Asmaro et al., 2012 Watson & Garvey, 2013	
P2(00) (Anterior Positivity, AP)	180-300	Early attentional processing; automatic orienting to stimuli	Asmaro et al., 2012 Hachl et al., 2003 Nijs, Franken et al., 2010	
Early Posterior Negativity (EPN)	200-300	Attention allocation; affective valence of stimuli	Blechert et al., 2011 Sarlo et al., 2013	
P3(00)	250-500	Visual attention towards stimuli with personal relevance and/or negative or positive emotional salience; motivated attention	Babiloni et al., 2009 a, b Babiloni et al., 2011 a, b Hachl et al., 2003 Hill et al, 2013 Nijs et al., 2008 Nijs et al., 2009	Nijs et al., 2010 a, b Nikendei et al., 2012 Novosel et al., 2014 Sarlo et al., 2013 Watson & Garvey, 2013
Late Positive Potential (LPP)	450-1000		Asmaro et al., 2012 Blechert et al., 2010 Blechert et al., 2014 Hanlon et al., 2012 Meule et al., 2013	Nijs et al., 2008 Novosel et al., 2014 Sarlo et al., 2013 Svaldi et al., 2012
Slow (Positive) Wave (SPW)	500- 6000	Sustained attention	Svaldi et al., 2012 Watson & Garvey, 2013	

* Approximate latency in ms after stimulus onset

2 Methods

A systematic review was conducted according to the PRISMA-guidelines (Liberati et al., 2009; Moher, Liberati, Tetzlaff, & Altman, 2009); objectives, methods, inclusion and search criteria were defined in advance. Relevant studies were identified by searching three electronic databases: PubMed, PsychInfo and Web of Knowledge. The reference lists of the existing literature were screened for additional resources. The search terms for PubMed are stated below; for PsychInfo and Web of Knowledge, the same search terms (organized in three groups: ERP-terms, eating-related terms, stimuli-related terms) were used.

(Electroencephalogram OR EEG OR Event-related Potential OR neurophysiology) AND (eating disorder OR anorexia OR bulimia OR

binge eating OR obesity OR restrained eating OR emotional eating OR external eating) AND food

2.1 Inclusion and exclusion criteria

- Participants: included were studies with humans, with a recognized disorder (AN, BN, BED, EDNOS/OSFED/UFED, according to DSM-IV, resp. DSM-5) and/or obesity (exclusion: sleep disordered breathing/ sleep apnea syndrome), and/or healthy participants with abnormal eating traits (restrained eating, external eating, emotional eating, binge eating etc.).
- Interventions: inclusion of paradigms evaluating the processing of food stimuli (exclusion of studies on resting-state or sleep-EEG).
- Outcomes: ERP amplitudes (exclusion of structural outcomes or EEG complexity and power spectrum analysis of alpha, beta and theta frequencies).
- Study design: original studies (exclusion: case studies); reviews.
- Report characteristics: studies published in English, French, German or Spanish in peer-reviewed journals between 2000 and July 2014 and available during the research period (December 2013-July 2014).

The process of inclusion and exclusion of studies is shown in Fig. 1. After the exclusion of repeated results, all abstracts were screened for inclusion and exclusion criteria. Most studies excluded in this first step either investigated processes/ illnesses other than eating disorders, did not use human subjects, had a dependent variable other than EEG or were published in a language other than English, French, German or Spanish. For all studies identified for inclusion, a full text version was retrieved and all studies were reviewed with regard to their quality and eligibility for the review. In case of exclusion of studies, reasons were documented. Included studies were read thoroughly and the former defined outcomes were extracted and guarded into tables.

2.2 Assessment of quality and risk of bias

Risk of bias in individual studies and quality appraisal was done using the Effective Public Health Practice Project Quality Assessment Tool (EPHPP; National Collaborating Centre for Methods and Tools; 2008). The EPHPP is a guide to systematically appraise study quality in seven ambits: selection bias, study design, confounders, blinding, data collection methods, withdrawal and dropouts, intervention integrity and analyses. The tool can be used to evaluate the study quality of observational, cross sectional, before and after studies and randomized controlled trials and has good content and construct validity and adequate test-retest reliability (Armijo-Olivo, Stiles, Hagen, Biondo, & Cummings, 2012; Thomas, Ciliska, Dobbins, & Micucci, 2004). The scales 'withdrawal and dropouts' and 'intervention integrity' were omitted in our quality assessment since they were not applicable to the studies at hand. Two authors (ABF and IW) independently rated the quality of each study.

3 Results

Altogether, 21 studies were included into the review. Four studies in eating disorders were found, one with AN and BN patients, two with only AN and one with BED patients. Furthermore, six studies on obesity/overweight and twelve studies measuring subclinical forms of abnormal eating traits like restrained, external and emotional eating were analyzed. Summaries of all studies, including sample descriptions, paradigms and stimuli, outcome measures and results can be found in the supporting information (Table S4.1).

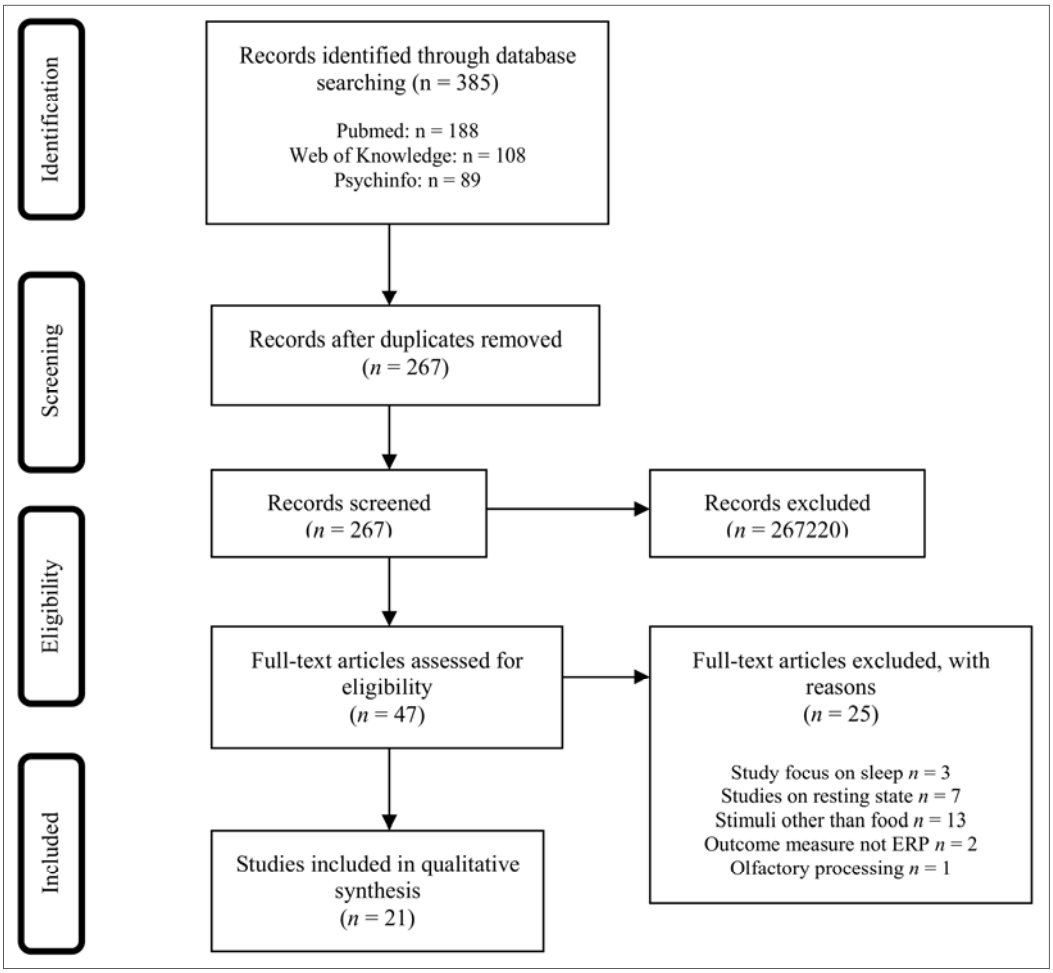

Figure 1. PRISMA flow chart. This flow chart shows the process of identification, screening and selection of the studies included into the systematic review (*from:* Moher et al., 2009).

3.1 Early processing of food stimuli

Patients with BN and AN patients had higher amplitudes of the EPN for both high-calorie and low-calorie food compared to neutral pictures during a rapid serial visual presentation of food, neutral and emotional pictures. Healthy controls showed an attentional orienting bias only for high calorie pictures. People with AN processed high-calorie pictures more extensively than low-calorie food while the BN-group did not process those two categories differentially (Blechert, Feige, Joos, Zeeck, & Tuschen-Caffier, 2011).

For obesity, one study (Nijs, Franken, & Muris, 2010) found higher early electrophysiological processing (P200) of high-caloric food stimuli in a group of obese participants compared to the normal-weight group. People with chocolate craving had higher amplitudes of an anterior positivity (AP/P200) towards chocolate than towards neutral stimuli in the left hemisphere, which persisted after satiation with chocolate (Asmaro et al., 2012). The source of this early frontal positivity was localized in the left orbito-frontal cortex (OFC), which has been associated with craving and individual preferences (Koeneke, Pedroni, Dieckmann, Bosch, & Jäncke, 2008; Rolls & McCabe, 2007). In contrast, for non-cravers the amplitude of an anterior negativity (AN/N200) was modulated by chocolate intake in that it was higher for chocolate than for neutral stimuli before

eating chocolate and was attenuated after subjects had eaten chocolate to satiety. This modulation of chocolate intake was not found for chocolate cravers.

Emotional and restrained eaters did not differ from the respective control groups in their processing of food pictures in early time windows (Blechert, Goltsche, Herbert, & Wilhelm, 2014; Blechert, Feige, Hajcak, & Tuschen-Caffier, 2010).

3.2 Later processing of food stimuli

Measuring P300 signals it was shown that food pictures (Hill, Wu, Crowley, & Fearon, 2013; Nijs, Franken, & Muris, 2008; Nijs, Muris, Euser, & Franken, 2010; Nikendei et al., 2012; Sarlo, Übel, Leutgeb, & Schienle, 2013) and food words (Nijs, Franken, et al., 2010; Nikendei et al., 2012) are processed with more attentional resources than neutral stimuli are, both in subjects with healthy and abnormal eating. The effect is stronger with pictorial stimuli as compared to word stimuli (Nikendei et al., 2012). This bias towards food is seen in all subjects, but may be influenced by an external eating style (Nijs, Franken, & Muris, 2009). One study which did not find a bias towards food stimuli in a sample of restrained and unrestrained eaters used a subliminal presentation of food-related and -unrelated word stimuli (Hachl, Hempel, & Pietrowsky, 2003). Four more studies, all from the same group and using the same oddball paradigm, did not find a main effect of picture category when comparing control, food and face pictures, which could be due to the presentation method (Babiloni, Del Percio, De Rosas, et al., 2009; Babiloni, Del Percio, Triggiani, Marzano, Valenzano, De Rosas, et al., 2011; Babiloni, Del Percio, Triggiani, Marzano, Valenzano, Petito, et al., 2011; Babiloni, Del Percio, Valenzano, et al., 2009). In one study, the differences between processing of food and neutral pictures were not reported (Novosel et al., 2014)

The results with P300 are mirrored by the findings reporting LPP amplitude, where a general bias towards food is also observed (Asmaro et al., 2012; Hanlon, Larson, Bailey, & LeCheminant, 2012; Meule, Kübler, & Blechert, 2013; Nijs et al., 2008; Sarlo et al., 2013), with the exception of one study which did not find this general effect (Blechert et al., 2010).

This bias towards food items was shown to be reduced after doing exercise in obese and in normal-weight subjects (Hanlon et al., 2012). Attentional processing of food as measured by P300/LPP amplitude correlated with hunger and food intake in people within the normal weight range (Nijs et al., 2008, 2009; Nijs, Muris, Euser, & Franken, 2010; Nijs, Franken, et al., 2010).

Obesity and overweight: This coherent response of correlation between attentional resources to food, hunger, and food intake is not persistently found in obese individuals: there was a correlation between attentional bias and hunger, but this was not related to food intake (Nijs, Franken, et al., 2010; Nijs, Muris, et al., 2010; Svaldi, Tuschen-Caffier, Peyk, & Blechert, 2010). There is some consistent evidence that obese and normal-weight subjects do not diverge in P300/LPP amplitude to high-calorie food stimuli in a satiated state (Hanlon et al., 2012; Nijs et al., 2008; Nijs, Franken, et al., 2010). When food-deprived though, normal-weight individuals reacted with an increase in amplitude, whereas the obese group showed a decrease in attention to food when hungry compared to satiated (Nijs, Muris, et al., 2010).

In healthy normal- and overweight children, BMI correlated negatively with P300 amplitude towards food stimuli during a visual oddball-paradigm, suggesting that children with higher BMI process high-caloric food with less attentional resources (Hill et al., 2013). Additional authors show less attentional

resources (P300) in an obese group as compared to normal weight adults for both food and face stimuli during an oddball-task. The neuronal source of this potential was localized in the medial prefrontal cortex (mPFC), activation of the mPFC was negatively correlated with body fat percentage (Babiloni, Del Percio, Valenzano, et al., 2009). Using the same task in normal weight participants, P300 amplitude to rare food stimuli was not related to body fat or dieting status (Babiloni, Del Percio, Triggiani, Marzano, Valenzano, De Rosas, et al., 2011; Babiloni, Del Percio, Triggiani, Marzano, Valenzano, Petito, et al., 2011). Results of another study show non-significant correlations between BMI and ERP amplitudes to food pictures in normal weight individuals (Sarlo et al., 2013).

Anorexia nervosa: In a study presenting pictures of neutral, negative and positive scenes and of high-caloric and low-caloric food, it was found that patients with AN process pictures of low-caloric food with more attentional resources than healthy controls (Novosel et al., 2014). In the processing of high-calorie food, emotional and neutral pictures, no significant differences were found between groups. There was also a main effect of food category in that low-calorie food stimuli yielded higher P300 and LPP amplitudes than high-calorie food pictures.

Another study compared patients with AN to healthy controls in a satiated versus hungry state during a recognition task of food and body stimuli. Results show lower P300 amplitudes in individuals with AN independent of stimulus category. Hungry controls processed food stimuli with more motivated attention than neutral stimuli, while satiated controls and AN patients processed both stimulus categories in the same manner and less than hungry controls (Nikendei et al., 2012). In contrast, underweight individuals without ED had P300 amplitudes in response to food pictures similar to normal weight individuals (Babiloni, Del Percio, Triggiani, Marzano, Valenzano, Petito, et al., 2011).

Binge eating disorder: People with BED had, compared to a healthy overweight group, enhanced LPP amplitudes evoked by pictures with high-caloric content, but not for pictures with low-caloric content. This effect was found for the LPP and persisted until a late time-window (SPW). For obese individuals with and without binge-eating disorder, food pictures yielded a higher LPP when the food presented had been announced for a later taste test, than in simple picture presentation (Svaldi et al., 2010).

Subclinical abnormal eating: High-external eaters allocated more attentional resources during food picture processing (higher P300 amplitude) than low-external eaters (Nijs et al., 2009). High emotional eaters showed higher LPP amplitudes towards food stimuli than low emotional eaters, both in neutral and negative emotional states (Blechert, Goltsche, et al., 2014). No differences depending on emotional state were found on the usual parietal distribution, but there was a right-frontal negativity in the same time-window, which showed a modulation by affect state in the high-emotional eaters group but not in low emotional eaters. High-emotional eaters had a strong negativity in the neutral condition, which was attenuated in the negative condition. The neuronal generators of the effect of emotion on food processing were localized in frontal and occipital regions.

In healthy normal-weight individuals, Watson & Garvey (Watson & Garvey, 2013) did not find any correlation between attentional processing of food pictures and external, emotional or restrained eating. Only in the female subsample of this study, a relation between food image processing and BMI as well as external eating was found.

For high restrained eaters the LPP response to food was reduced if food was available for consumption rather than merely as visual images, for unrestrained eaters the LPP did not differ for pictures of available and unavailable food (Blechert et al., 2010). Another study found increased P300 in restrained compared to unrestrained eaters, similarly for food, neutral and erotic words (Hachl et al., 2003). Trait chocolate craving was not associated with a larger LPP to chocolate pictures when compared to neutral food (uncooked food) pictures (Asmaro et al., 2012).

Table 2. Summary of the critical appraisal of study quality conducted using the EPHPP assessment tool.

Authors	Selection bias	Study Design	Confounders	Blinding	Data collection methods	Appropriate statistical tests	Global Rating
Asmaro et al., 2012	+	+	++	+	++	++	++
Babiloni et al., 2009a	--	--	n.a.	+	++	++	--
Babiloni et al., 2009b	--	+	--*	+	++	+	--
Babiloni et al., 2011a	--	+	+	+	++	++	+
Babiloni et al., 2011b	--	+	+	+	++	+	+
Blechert et al., 2010	+	+	++	+	++	++	++
Blechert et al., 2011	+	+	+	+	++	++	++
Blechert et al., 2014	+	+	++	+	++	++	++
Hachl et al., 2003	--	++	++	+	+	++	+
Hanlon et al., 2012	--	+	++	+	++	++	+
Hill et al., 2013	+	--	n.a.	+	++	++	+
Meule et al., 2013	+	--	n.a.	+	++	++	+
Nijs et al., 2008	+	+	++	+	++	++	++
Nijs et al., 2009	+	+	++	+	++	++	++
Nijs, Muris et al., 2010	+	++	++	+	++	++	++
Nijs, Franken et al., 2010	+	+	++	+	++	++	++
Nikendei et al., 2012	+	+	++	+	++	++	++
Novosel et al., 2014	+	+	+	+	++	++	++
Sarlo et al., 2013	+	--	n.a.	+	++	++	+
Svaldi et al., 2010	+	+	+	+	++	++	++
Watson & Garvey, 2013	+	--	n.a.	+	++	++	+

n.a. = not applicable; -- weak quality; + moderate quality; ++ high quality
*In this study, confounding effects of age and gender were controlled for, but effects of hunger and eating attitudes were not controlled for/reported

3.3 The effect of cognitive regulation on the processing of food stimuli

Only two studies have so far investigated the effect of regulation strategies on the processing of food cues. Both studies found that electrophysiological processing of food can be influenced by cognitive regulation strategies in a later time window (P300, LPP), but not in an earlier one (N100, EPN) (Meule et al., 2013; Sarlo et al., 2013). Sarlo and colleagues (2013) found that long latency ERPs were generally more pronounced when subjects were instructed to increase the appetitive value towards high-calorie food pictures.

Contrary to the expectations, the amplitudes were not down-regulated by a 'decrease' instruction. The amplitudes in the 'decrease' condition were positively correlated with self-reported scores of fear of weight gain, binge eating and purging, which was not found in the increase or maintain condition. In the study of Meule et al. (2013), participants were instructed to think about immediate or long-term consequences of high-, and low-calorie food pictures, a positive correlation between emotional eating and LPP amplitudes across all conditions was reported.

3.4 Study quality assessment

The results of the systematic assessment of study quality conducted by means of the EPHPP assessment tool (National Collaborating Centre for Methods and Tools; 2008) are shown in table 2. Inter-rater agreement was given for almost all of the scales for all studies, in the cases of disagreement, evaluations were discussed and revised. The global ratings are generally moderate to high quality with the exception of two studies. Those two studies were included into data analysis, but they are not likely to have a great influence on the conclusions drawn from the study results.

4 Discussion

The current review shows evidence for altered electrophysiological processing of food stimuli related to abnormal eating traits and extreme weight conditions. The evidence suggests that abnormal eating behaviors are related to increased early orienting to food stimuli. An increased attentional engagement to food stimuli was found for people with AN, BN, obesity and chocolate craving (Asmaro et al., 2012; Blechert et al., 2011; Nijs, Franken, et al., 2010). For restrained and emotional eaters no food-specific processing differences were found in this early time window (Blechert, Goltsche, et al., 2014; Blechert et al., 2010).

Assuming that the P300 and the LPP represent the same underlying cognitive processes (Polich, 2007), for the time frame thought to relate to 'motivated attention' it can be concluded that there is a general processing bias for food stimuli compared to neutral stimuli independent of eating behavior. In healthy normal weight individuals, the processing of food stimuli was not related to body fat or dieting (Babiloni, Del Percio, De Rosas, et al., 2009; Babiloni, Del Percio, Triggiani, Marzano, Valenzano, De Rosas, et al., 2011; Sarlo et al., 2013). Obese people process food stimuli similarly or even with less attention as persons in the normal weight range (Babiloni, Del Percio, Valenzano, et al., 2009; Hanlon et al., 2012; Hill et al., 2013; Nijs et al., 2008; Nijs, Franken, et al., 2010; Nijs, Muris, et al., 2010).

For AN, the number of studies is limited and too small to draw final conclusions. There may be a bias in maintenance of attention to low-caloric food stimuli, but not for high-caloric food (Novosel et al., 2014). The effects of AN probably aren't explained merely by underweight, since underweight and normal-weight individuals did not differ in their P300 to food (Babiloni, Del Percio, Triggiani, Marzano, Valenzano, Petito, et al., 2011). Another study suggests that individuals with AN process food stimuli similarly to satiated controls, namely without selective processing of food compared to neutral stimuli, while hungry healthy individuals processed food pictures with more visual attention than neutral pictures (Nikendei et al., 2012).

There was only one study in BED, showing a processing bias towards high-caloric food but not for low-caloric food (Svaldi et al., 2010). Emotional and external eating relates to higher electrophysiological processing of high-caloric food stimuli

mainly in females (Blechert, Goltsche, et al., 2014; Nijs et al., 2009; Watson & Garvey, 2013). Restrained eaters did not show an attentional bias specific to food stimuli, when food was available, they avoided the processing of food pictures (Blechert et al., 2010; Hachl et al., 2003).

Two studies on appetite regulation suggest that attention towards food is influenceable through cognitive strategies, whilst people with bulimic tendencies seem to have more problems in this kind of regulation (Meule et al., 2013; Sarlo et al., 2013).

ERPs usually originate from multiple neuronal generators. Combined fMRI-EEG studies and results of source localization relate P300 and LPP activity to the inferotemporal, occipital and parietal cortex, speaking for an involvement of visual areas in the generation of these ERPs (Hajcak et al., 2010; Keil et al., 2002; Sabatinelli, Lang, Keil, & Bradley, 2007). Visual attention is modulated by the amygdala, which communicates to extrastriate visual areas and thus emphasizes the processing of emotional and motivationally salient stimuli (Hajcak et al., 2010; Pourtois, Schettino, & Vuilleumier, 2013). It is suggested that the increased preoccupation with body shape and food intake, together with the omnipresence and excessive supply of food, leads to the incentive salience of food stimuli. Increased negative emotionality may also contribute to higher salience of rewarding stimuli like food (Baker, Piper, McCarthy, Majeskie, & Fiore, 2004; Hepworth, Mogg, Brignell, & Bradley, 2010). This leads to selective sensory attention to these stimuli, which may automatically lead to higher food intake, but also to higher food restraint, especially when preoccupations with body image are present (Smith & Rieger, 2009; Werthmann et al., 2014).

While ERPs in early time windows reflect rather automatic bottom-up attentional processes, later processing stages reflect subjective preferences and motivational significance ('motivated attention'), but can also be influenced by top-down processes (Ferrari, Codispoti, Cardinale, & Bradley, 2008). The evidence at hand suggests that obese people process food stimuli more extensively than people in the normal weight range in an early processing stage. Later during stimulus processing, they seem to regulate this bias as seen in attentional disengagement. Similarly, patients with AN and patients with BN show increased visual attention to high- and low-caloric food in an early time window. In a later time window individuals with AN show attentional bias to low-caloric foods only. People with AN may avoid the processing of high-caloric food after an early attentional orienting bias (Giel et al., 2011; Veenstra & Jong, 2012). The relative avoidance of high-caloric compared to low-caloric food seen in AN is in line with the hypothesis that patients with AN show phobic avoidance of food stimuli (Friederich, Wu, Simon, & Herzog, 2013).

Early attentional bias and later avoidance of food stimuli in obesity may reflect an ambiguous relation to food, with strong engagement and craving on the one hand and an attempt to regulate attentional resources in order to control food intake on the other. These regulation processes may distinguish BED patients from overweight people without BED, as the BED group showed an attentional bias towards high-calorie food stimuli even in a later time window. This could be also true for emotional and external eaters, who show higher ERP amplitudes in later time windows. Support for this interpretation comes from studies on appetite regulation showing that the success in regulating attention towards food pictures was negatively correlated with scores of emotional eating, fear of weight gain, binge eating and purging (Meule et al., 2013; Sarlo et al., 2013).

These results indicate increased difficulties in the down-regulation of motivated attention towards food in subjects with bulimic tendencies.

The ability to intentionally modulate selective attention has been associated with cognitive control capacities and difficulties in emotion regulation: fMRI studies show that the willful use of craving and affect regulation strategies is correlated with increased activation in regions of top-down cognitive control (Giuliani, Mann, Tomiyama, & Berkman, 2014; Ochsner et al., 2004; Siep et al., 2012). Higher P300 amplitudes to negative pictures were related to decreased activation of regions related to emotion regulation and the down-regulation of bodily sensations (Pollatos & Gramann, 2012). Thus, prefrontal and anterior regions supposedly contribute to attentional regulation and by this means to the attenuation of P300/LPP-amplitudes (Petersen & Posner, 2012). Cognitive inhibitory control may also be reflected in anterior potentials (Nieuwenhuis, Yeung, van den Wildenberg, & Ridderinkhof, 2003) like the anterior negativity observed by Asmaro and colleagues (2012) in non-chocolate-craving individuals in response to chocolate images and the frontally distributed increased negativity found by Blechert et al. (2010) in high restrained eaters when confronted with food available to eat.

The methodology, participants and outcome measures in the studies included in the review differ, which made the conduction of a meta-analysis impossible. Therefore, it is desirable that future studies try to replicate and validate findings using similar paradigms and methods. Diverging results in former studies could be due to factors such as paradigm used, caloric content of depicted food, gender, satiety and emotional state of participants, availability of food, electrode measured and time interval used for analysis (Kamijo et al., 2012; Stockburger et al., 2009, 2008; Svaldi et al., 2010; Watson & Garvey, 2013). These factors should be controlled for, varied and reported in future studies; standardized image sets (Blechert, Meule, Busch, & Ohla, 2014; Foroni, Pergola, Argiris, & Rumiati, 2013; Miccoli et al., 2014) should be used for the sake of comparability. Another important factor to be addressed in future studies is the current treatment status of participants, since it was shown that treatment can have an influence on electrophysiological processing of disorder-related material in alcohol-dependent subjects (Noel et al., 2006; Townshend & Duka, 2007). Pharmacological treatment may also have an influence on electrophysiological activity, although it was controlled for in most of the studies and no influence was reported.

Our research question about remission of attentional bias after treatment could not be answered due to the cross-sectional designs of the studies. The chicken-or-egg question cannot be dissolved until now, but there is some evidence from fMRI showing that attentional bias towards food predicts BMI increase over a one-year period (Yokum, Ng, & Stice, 2011). In addition, former mentioned studies showed that laboratory induced attentional bias leads to changes in food intake. There is a need for longitudinal studies and for more studies with subjects having an actual eating disorder.

Finally yet importantly, the quality of studies and risk of publication bias have to be considered. The EPHPP assessment tool (National Collaborating Centre for Methods and Tools; 2008) led to generally moderate to high global study quality ratings. Nevertheless, it has to be mentioned that many studies were conducted using student populations, which leads to reduced

representativeness of the data. Furthermore, in some cases, recruiting of the sample was not reported (Babiloni, Del Percio, De Rosas, et al., 2009; Babiloni, Del Percio, Triggiani, Marzano, Valenzano, De Rosas, et al., 2011; Babiloni, Del Percio, Triggiani, Marzano, Valenzano, Petito, et al., 2011; Babiloni, Del Percio, Valenzano, et al., 2009; Hachl et al., 2003). As for study design, most studies were rated with low or moderate quality because the highest rating is only given for randomized controlled and controlled clinical trials. In most studies the assessment and control of confounders is good, but some studies did not assess or report important confounding factors such as nutritional status of participants (Babiloni, Del Percio, Triggiani, Marzano, Valenzano, De Rosas, et al., 2011; Babiloni, Del Percio, Triggiani, Marzano, Valenzano, Petito, et al., 2011; Babiloni, Del Percio, Valenzano, et al., 2009). In none of the studies a procedure of blinding was described, but this most likely has no crucial influence on electrophysiological outcomes. Data collection methods and statistical testing were generally appraised as valid, reliable and appropriate. Still, the mostly small sample sizes lead to low sensitivity and thus the probability that small effects are not detected is relatively high. Furthermore, selective reporting and missing data is not unlikely: electrophysiological data contains a great deal of possibilities regarding data analysis, which opens to the risk of reporting only significant and coherent results. In some cases, studies did not report data on early potentials even though time intervals of electrophysiological data would have admitted this kind of analysis. Other cases lack statistical comparisons of picture categories or there was no reporting of statistical parameters. Future studies should also more frequently include results on lateral differences and structural results of source localization.

Altogether, electrophysiological research in ED and food processing has advanced a lot in the last decade. The current review on EEG-studies in ED and related eating traits adds information about the timing of attentional food processing to reviews using behavioral designs (Brooks et al., 2011; Giel et al., 2011; Nijs & Franken, 2012). There is promise that this research field leads to a better understanding of how people with different forms of maladaptive food intake differ in the processing of food stimuli and how they use cognitive strategies to cope with the incessant exposure to food cues in their surroundings.

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Conflict of Interest

None

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Study 6: Craving and brain response of binge-eating patients to visual and olfactory chocolate cues

Objectives: External cues such as the sight and smell of food can trigger binge-eating, and might be related to incentive sensitization. Furthermore, low inhibitory control can lead to an increased susceptibility to food cues and to loss of control over food-intake. Therefore, this study aimed to compare binge-eating and healthy individuals regarding self-report and neurophysiologic measures of craving, cognitive control and motivated attention towards visual and olfactory chocolate stimuli and to explore the interaction between the two sensory modalities (olfactive and visual) in craving induction.

Results: While both groups experienced a significant increase in craving throughout the experiment, patients reported higher craving than controls. Chocolate pictures primed by chocolate odour compared to neutral odour led to a slightly increased craving response and to increased inhibitory control in binge-eating patients. N2 and LPP amplitudes were higher for chocolate than for neutral pictures. The LPP as measure of motivated attention did not differ between groups. Patients compared to HC had lower baseline amplitudes of the N2 in neutral trials but showed a higher relative increase in N2 amplitudes related to chocolate versus neutral pictures than HC. Patients with higher craving levels tended to have lower N2 amplitudes while in healthy individuals this relation was inverted.

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Smells like chocolate: effects of olfaction on electrophysiological processing of visual food stimuli and craving in binge-eating and healthy individuals.

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Abstract

High-sugar/high-fat foods are related to binge-eating; especially people with low inhibitory control may encounter difficulties to resist. Incentive sensitization of food related stimuli might lead to increased motivated attention. To investigate the combined influence of olfactory and visual stimuli on craving, inhibitory control and motivated attention, 20 healthy and 19 binge-eating individuals viewed chocolate and neutral pictures, primed by chocolate or neutral odours. Subjective craving and electroencephalogram were recorded during the task, N2 and Late Positive Potential amplitudes were analyzed.

Patients reported higher craving than controls. Subjective craving, N2 and Late Positive Potential amplitudes were higher for chocolate versus neutral pictures. Patients showed a higher relative increase in N2 amplitudes to chocolate versus neutral pictures than controls. Patients with higher craving tended to have lower N2 amplitudes; in controls this relation was inverted. Chocolate images induce significant increases in craving, motivated attention and inhibitory control; chocolate odour might potentiate the craving response to visual stimuli.

Keywords: craving; binge-eating; neurophysiology; motivated attention; cognitive control; self-regulation.

1 Introduction

In our modern society, food is omnipresent; it can be easily purchased and rapidly consumed, without the need of further processing steps. The ubiquity of food in our environment may be highly problematic for some individuals, leading to obesity or even eating disorders. Binge eating disorder (BED) and bulimia nervosa (BN) are both marked by recurrent binges and high experienced craving [1]. Craving is defined as a strong and irresistible desire to consume a specific substance and often leads to loss of control over food intake [2]. External cues

such as the sight or smell of food are known to trigger craving and overeating [3]. The purpose of this study was to look at differences in the processing of and reaction to high-palatable food stimuli in patients with BE when compared to healthy adults. This could help to better understand the susceptibility to BE and cognitive processes which may protect from this kind of behaviour.

Chocolate is one of the most heavily craved foods and perceived as highly problematic with regard to the controllability of its intake [4]. However, it is not yet clear how exactly chocolate consumption influences physiological, psychological and biological functioning. There is some evidence suggesting that it is not the pharmacological effect of chocolate alone, nor its high sugar content, which produce these strong cravings in humans, but rather the sensory experience, a combination of different factors such as aroma, caloric content, and texture [5]. So far, little attention has been paid to the role of odour perception in the generation of craving. There is one study showing that the smell of food leads to increased craving and intake of food in restrained and normal eaters [6]. Basic studies in humans have reported a reduction of low frequency electroencephalogram (EEG) activity in response to different odours [7,8]; for chocolate odour in specific there was reduced frontal theta (4-7 Hz) activity in comparison to other odours or to neutral olfactory stimulation [9]. The authors explained this to be due to a more relaxed state when exposed to chocolate odour; it is however unclear how this reduction in theta frequency may relate to chocolate craving. Other studies indicate that the combination of odour and taste together create flavour and thus influence the reward value of food [10–12]. There is evidence to suggest that a combination of olfactory and visual stimuli lead to a more powerful craving response than visual stimuli alone [13]. In line with this, a study on reward processing found that a combination of viewing and tasting chocolate led to greater activation in the orbito-frontal cortex than the sum of these two modalities when presented separately, which was denominated as "supralinearity" [14].

The incentive salience of visual food stimuli, which corresponds to the craving or "wanting" for these stimuli [15], has been studied using event-related potentials (ERP) of EEG. The Late Positive Potential (LPP) is an ERP scaling the motivational value of pictures in that more arousing or emotional stimuli lead to higher amplitudes [16]. It is enhanced for substance-related stimuli in people with substance use disorder [17] and can be seen as an indicator of "motivated attention" towards salient stimuli [18]. In a similar way, food stimuli compared to neutral stimuli in general lead to higher LPP amplitudes [19,20], which illustrates their high incentive salience in healthy, normal-weight individuals. A much debated question is therefore, how motivated attention towards food relates to craving or BE. Contradictory results regarding processing of food stimuli in disordered eating were reported in studies using behavioural measures of attentional bias [21]. ERPs have the potential of a more exact timing and it seems that people with overeating or BE compared to normal-eating individuals have enhanced attention to food in early ERPs, but there is inconsistency regarding later components, such as the LPP (for a review see Wolz et al., 2015b). Another component important for the understanding of food processing is the N2, an early anterior-frontal ERP. It has been related to the dorsal anterior cingulate cortex and its conflict monitoring function [22,23] and was supposed to be related to top-down cognitive control mechanisms over the desire to consume chocolate [24].

The main aim of this study was to compare BEP to HC with regard to their craving and neurophysiologic response towards visual chocolate stimuli, whereby it was hypothesized that BEP compared to HC would have more craving (self-report), more motivated attention (LPP) and less inhibitory control (N2) and that chocolate pictures would evoke higher LPP and N2 amplitudes than neutral pictures. Moreover, we expected an increase of state chocolate craving throughout the experiment and a positive relation between self-reported craving and LPP and N2 amplitudes. Trait chocolate craving, difficulties in emotion regulation and eating pathology were expected to be positively related to self-report measures of state chocolate craving and to motivated attention (LPP), and negatively to inhibitory control (N2). A second aim was to explore the influence of chocolate odour on the processing of visual chocolate stimuli; we hypothesized that olfactory and visual stimuli would have an additive effect, leading to a potentiated response. The third aim was to test if there are differences between BEP and HC in the response to chocolate odour alone. We expected a higher subjective craving reaction towards odour stimuli in BEP than in HC; regarding theta frequency, due to the explorative nature of this aim, no directional hypothesis was put forward.

2 Materials and methods

2.1 Participants

The HC group (*n*=20, age 20-56 years, see Table S5.1 for *means (M)* and *standard deviations (SD)*) was recruited from students of the University of Barcelona and through a snowball system from hospital staff. The BEP group (*n*=19, age 19-56 years) was recruited from consecutive referrals to the ED unit of Bellvitge Hospital and diagnosed by means of semi-structured face-to-face interviews to either BN (*n*=12) or BED (*n*=7) according to the criteria of the fifth edition of the Diagnostic and Statistical Manual (DSM; American Psychiatric Association 2013). See Tables S5.1 and S5.2 for a description and comparison of socio-demographic and clinical variables.

Exclusion criteria for all participants were: being male, younger than 18 years, current or life-time history of chronic illness (which could influence electrophysiology) or neurological condition (abnormal EEG activity), having used in the last 24 hours psychoactive medication or drugs that may interfere with smell-taste capacity or cortical activity, current substance dependence, lifetime diagnosis of psychotic disorder, functional anosmia (value <16.5 in "Sniffin' Test"), and pregnancy. Additionally, in the HC group, an exclusion criteria was a lifetime diagnosis of ED, assessed by means of Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First *et al.* 1997) or being obese (BMI ≥ 30) or underweight (BMI < 18.5).

2.2 Procedure

The study was conducted in compliance with the Declaration of Helsinki 1975 and the Spanish legislation and norms, after revision and approval by the local ethics committee (CEIC Ciutat Sanitària i Universitària de Bellvitge). All participants signed informed consent. The study participation consisted of two parts of approximately one hour each, which were realized either in one or in two separate sessions (50% of HC and 63% of BEP did two sessions). The first part was to check inclusion criteria, participants were weighed and measured (height and head circumference), and were tested regarding their olfactory capacity. In the second part participants filled in a laboratory questionnaire (momentary mood and hunger (1-item Likert scale from 1 to 9), food eaten this day, menstrual cycle, and intake of coffee, alcohol and drugs in the last 24 hours), then the EEG electrodes were placed and participants did the

experimental testing with a duration of 26 minutes. Participants were instructed to have a normal meal two hours before doing the second session and then to refrain from eating until completion of the experiment.

2.3 Study design and experimental task

Hypotheses were tested in a controlled mixed study design. The intra-factors "odour type" and "picture type" were presented at random and counter-balanced order, with 4 combinations of chocolate versus neutral valence in the two sensory modalities (neutral-neutral, neutral-chocolate, chocolate-neutral and chocolate-chocolate).

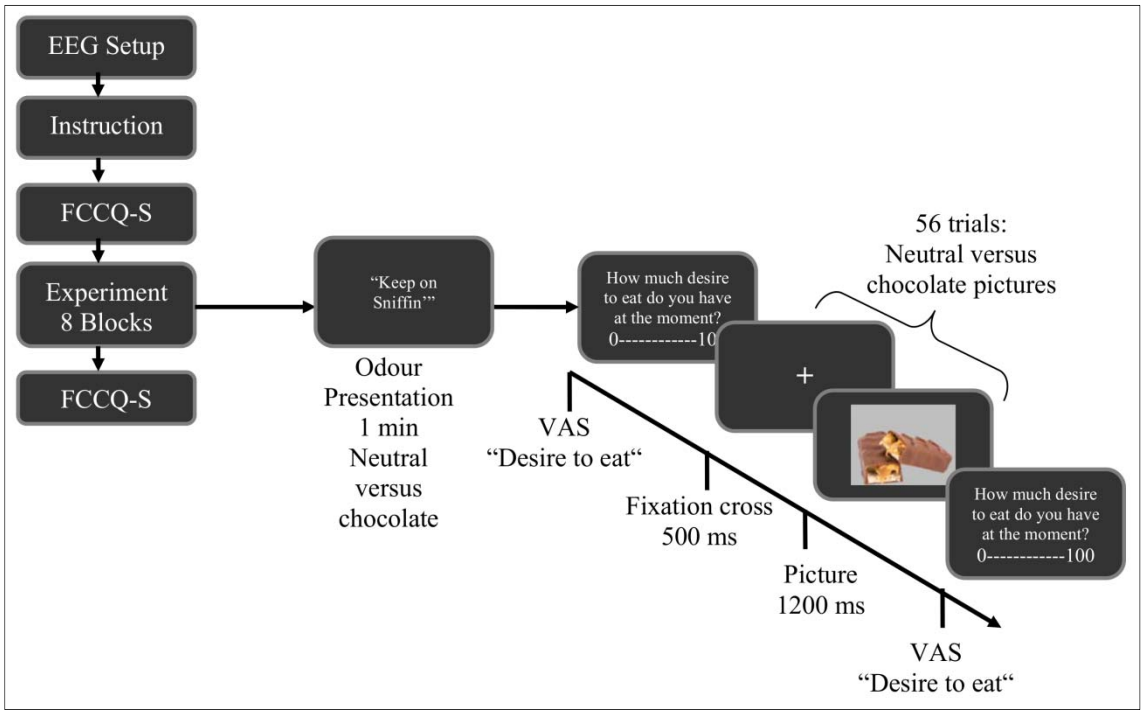

Figure 1. Experimental task and conditions.
EEG = Electroencephalogram; FCCQ-S = Food Chocolate Craving Questionnaire; VAS = visual analogue scale.

Each condition was done twice, in two consecutive blocks (see Figure 1). Visual stimuli consisted of 56 pictures each of chocolate products and neutral office items, used and kindly placed at our disposal by Frankort and colleagues (2014). Pictures were presented in random order on a gray computer screen using the stimulus delivery software Presentation (Neurobehavioral Systems); one block consisted of 56 trials, each starting with a fixation cross (500ms), followed by the picture (1200ms). Each visual block was preceded by a 1 min olfactory exposure to either chocolate or neutral odour, presented by a laboratory assistant, the participant had her eyes closed during this exposure. Olfactory stimuli were a piece of chocolate and a pencil (as in Frankort et al., 2014). For a graphical description of the task see Figure 1.

2.4 Assessment

2.4.1 Self-report measures

Subjective chocolate craving was assessed on three different levels: trait craving was assessed before the experiment, state craving was assessed before and after the experimental manipulation, and the momentary craving reaction was assessed

through a *visual analogue scale* (VAS) scaling from 0 (very little) to 100 (very strong) asking "At this moment, how much desire to eat do you have?" at 17 time points throughout the experiment, once at baseline and then after each the odour and visual presentations in the eight blocks.

State and trait craving for chocolate were assessed through the *Food Chocolate-Craving Questionnaire* (FCCQ) – State and Trait Version [25,26]. See section S5.1.2. for a more detailed description and psychometrical evaluation. Additional psychometric questionnaires were used in order to assess difficulties in emotion regulation, food addiction, eating disorder pathology and general psychopathology; olfactory capacity was assessed using "Sniffin' Sticks" (for a description and reliability measures see supplementary material, section S5.1).

2.4.2 Electrophysiology

EEG was recorded continuously throughout the experimental task using PyCorder (BrainVision). 60 active Ag/AgCI electrodes were inserted into an EEG recording cap (EASYCAP GmbH), distributed after the 10-20 system, the Cz electrode was used as online reference. Four electrodes were placed next to the eyes in order to control for eye movements. Impedances were reduced to be smaller than 20KOhm using the SuperVisc high-viscosity electrolyte gel for active electrodes. A sampling rate of 500Hz and an online filter between 0.1 and 100Hz were used.

The N2 was measured at electrodes AFz (central N2), AF3, F1, F3 (left N2) and AF4, F2, F4 (right N2) as the amplitude and latency of the maximum negative peak in the time window 180-350 ms after visual stimulus onset. The time window for the LPP was set to 300-1000 ms after visual stimulus onset and measured as the maximum positive peak at centro-parietal electrode sites: Pz (central LPP), CP1, CP3, P1, P3, P5 (left LPP) and CP2, CP4, P2, P4, P6 (right LPP). See section S5.2 of supplementary material for a more detailed description of EEG analysis steps.

2.5 Statistical analysis

Statistical analyses were conducted with SPSS20 for Windows. Socio-demographic and clinical variables were compared between the two groups using analysis of variance (ANOVA). State chocolate craving (FCCQ-S) before and after the experimental task was compared using repeated measures ("time" pre/post) ANOVA with the between subjects factor "group" (BEP/HC).

For momentary craving in response to picture stimuli, the mean VAS value of the two blocks for each condition was used in an analysis of covariance (ANCOVA) adjusted for baseline momentary craving, with the repeated factors "odour prime" (chocolate/neutral) and "picture type" (chocolate/neutral) and the between subjects factor "group" (HC/BEP). For each of the ERPs (N2 and LPP) the additional factor "localization" was added, wherefore a 2("odour prime" chocolate/neutral) x 2("picture type" chocolate/neutral) x 3("localization" central, right, left) x 2("group" BEP/HC) ANOVA was calculated for main and interaction effects. Pairwise comparisons were used to follow up main and interaction effects.

For momentary craving in response to odour stimuli, an ANCOVA adjusted for baseline momentary craving, with the repeated factor "odour type" (chocolate/neutral) and the between subjects factor "group" (HC/BEP) was calculated using the mean of the four VAS ratings assessed after odour presentation. For the QEEG data, theta frequency was compared by use of a 2("odour type" neutral/chocolate odour) x 2("group" BEP/HC) ANOVA to test for main and interaction effects.

Comparisons were considered significant with $p<.05$ after Bonferroni-Finner correction to avoid Type-I errors. Mauchley's Test was used to test for sphericity and if the assumption was not met ($p<.05$) Greenhouse-Geisser corrected values were used. Effect sizes were calculated as partial Eta squared (η_p^2) for ANOVA or Cohen's *d* for *mean differences (MD),* while $\eta_p^2>.01$ or $d>.2$ are considered as small, $\eta_p^2>.06$ or $d>.5$ as moderate and $\eta_p^2>.14$ or $d>.8$ as large [27].

Partial correlations including the covariates age and baseline-mood were calculated for each group to look at the influence of clinical variables on the dependent measures. Correlations were considered as moderate for $r>.24$ (corresponds to $d>.5$) and large for $r>.3$ (corresponds to $d>.8$) [27,28].

3 Results

3.1 Baseline measures

Groups did not differ in their olfactory capacity and all of the participants had values within the normal range (TDI>30 points, see Table S1). As expected, BMI was significantly different between groups; it was however not included as a covariate since it is a characteristic of the patient group and therefore is taken into account when comparing the two groups. BEP had higher values in trait craving, more difficulties in emotion regulation, higher food addiction, eating and general psychopathology than HC (see Table S2). BEP reported lower mood (*MD*=-1.46, $p<.01$) and more hunger (*MD*=1.83, $p<.01$) than HC at baseline before doing the experimental task. However, the time since they had their last meal did not differ between the two groups ($p=.13$) and baseline-hunger correlations with the subjective (VAS, FCCQ-S total) and electrophysiological (theta power, N2 peak and LPP peak) dependent variables were low ($rs\leq.3$). Age and baseline-mood were both found to have an influence on the correlations between dependent variables, but since the estimated means were very similar (variation of <10%) when adjusting the models by age and baseline-mood into ANCOVAS, in order to simplify the models and to maintain statistical power, it was decided to calculate ANOVAS without adjustments referring to the principle of parsimonia [29].

Table 1. State craving for chocolate measured by the FCCQ-S directly before and after the experimental manipulation in the two study groups.

	Mean				Group Effect		Time Effect		Group*Time Interaction	
	HC; *n*=20		BEP; *n*=19							
	Pre	post	Pre	Post	$F_{1,37}$	*p*	$F_{1,37}$	*p*	$F_{1,37}$	*p*
Desire	4.60	8.95	6.16	10.16	2.27	.140	66.05	<.001	1.99	.735
Positive reinforcement	6.15	7.35	6.83	9.06	1.58	.217	22.04	<.001	1.12	.166
Negative reinforcement	4.90	6.30	8.47	9.00	10.90	.002	5.49	.025	1.13	.295
Lack of control	4.40	4.90	8.32	9.42	21.14	<.001	5.14	.029	.73	.398
Hunger	6.20	8.40	8.63	10.42	5.17	.029	28.63	<.001	.30	.585
Total score	26.30	35.90	38.58	48.37	12.70	.001	56.71	<.001	.01	.942

BEP = binge-eating patients; BMI = body mass index; HC = healthy controls; MD = mean difference.
Significant comparisons are marked in bold.

3.2 Subjective craving

An ANOVA to compare effects of time and group on state craving showed a significant increase in the FCCQ-S through the experiment, as seen in a significant

main effect of time. A significant main effect of group showed that BEP patients reported higher craving than HC at both time points. Apart from the desire and positive reinforcement subscales which did not differ significantly between groups these results were mirrored by all subscales. There were no significant interactions (see Table 1).

For momentary craving towards visual stimuli, results showed a significant main effect for "picture type" ($F_{1,36}$=8.27, p<.01, η_p^2=.19). Chocolate pictures induced higher momentary craving than neutral pictures. A significant main effect of "odour prime" ($F_{1,36}$=8.34, p<.01, η_p^2=.19) showed that a preceding chocolate odour let to higher momentary craving than a preceding neutral odour. Pairwise comparisons showed that chocolate compared to neutral odour did not have a significant effect on the rating towards neutral pictures (*MD*=2.26; p=.21) but it did affect the rating towards chocolate. pictures (*MD*=5.26; p<.001). There was no main effect for "group", or significant interaction (all F<1.0 and p>.32). See Table S5.3 for *M* and *SD* of momentary craving ratings towards picture stimuli.

Similar to the results for visual stimuli, for the reaction towards odour stimuli a significant main effect of "odour type" ($F_{1,36}$=8.34, p<.01, η_p^2=.19) showed more craving in response to chocolate odour than neutral odour, but no main effect of "group" nor an interaction between "group" and "odour type" (F=2.18 and p=.15) was found

3.3 Electrophysiological data

Two patient data sets had to be excluded from the electrophysiological analyses because of poor data quality. The mean number of segments per condition for the whole sample was between 100 and 102 for all conditions. N2 and LPP mean amplitudes and latencies according to conditions and groups are shown in Table 2 and Figure 2.

Table 2. N2 amplitudes and latencies at central anterior electrodes and LPP amplitudes and latencies at right posterior electrodes for binge-eating patients (BEP) and healthy controls (HC).

			Peak amplitude (μV)				Latency (ms)			
			HC (*n* = 20)		BEP (n = 17)		HC (*n* = 20)		BEP (n = 17)	
	Odour Prime	Picture Type	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
N2	Neutral	Neutral	-4.28	2.30	-2.86	2.09	246.09	29.61	246.55	27.51
		Chocolate	-5.23	2.42	-4.13	2.14	251.37	44.38	248.85	32.62
	Chocolate	Neutral	-4.22	2.17	-2.76	2.02	241.21	31.17	241.27	22.08
		Chocolate	-5.01	2.36	-4.60	2.28	241.41	29.47	250.69	35.67
LPP	Neutral	Neutral	3.65	2.30	2.46	1.71	509.27	81.35	507.49	84.23
		Chocolate	4.88	2.85	3.80	1.79	447.90	58.53	494.44	126.36
	Chocolate	Neutral	3.40	1.87	2.42	1.53	479.14	73.56	539.11	116.71
		Chocolate	4.96	2.99	3.80	1.56	463.33	64.16	492.10	119.63

MD = mean difference; SD = Standard deviation.

3.3.1 N2 peak amplitudes and latencies

For N2 peak amplitudes, there was a significant main effect for "picture type" and "localization" and a significant interaction effect between "odour prime",

"picture type" and "group"; an interaction between "picture type" and "group" was marginally significant (See Table 3 for *F*- and *p*-values). No further main or interaction effects were found (all $F<2.86$ and $p>.10$).

The main effect of "picture type" was due to higher negative activity in response to chocolate pictures than to neutral pictures in the whole sample, which was expected. Highest N2 amplitudes were found at the central localization compared to left and right lateralized electrodes. Left and right hemispheres did not differ. The interaction effect between "odour prime", "picture type" and "group" was explained by BEP having significantly higher amplitudes for chocolate pictures primed by chocolate compared to neutral odour, which was not found for neutral pictures. No such effect was found in HC. Another single effect pointed out by this interaction was seen in higher N2 amplitudes in HC versus BEP for neutral but not for chocolate pictures (see Table 3).

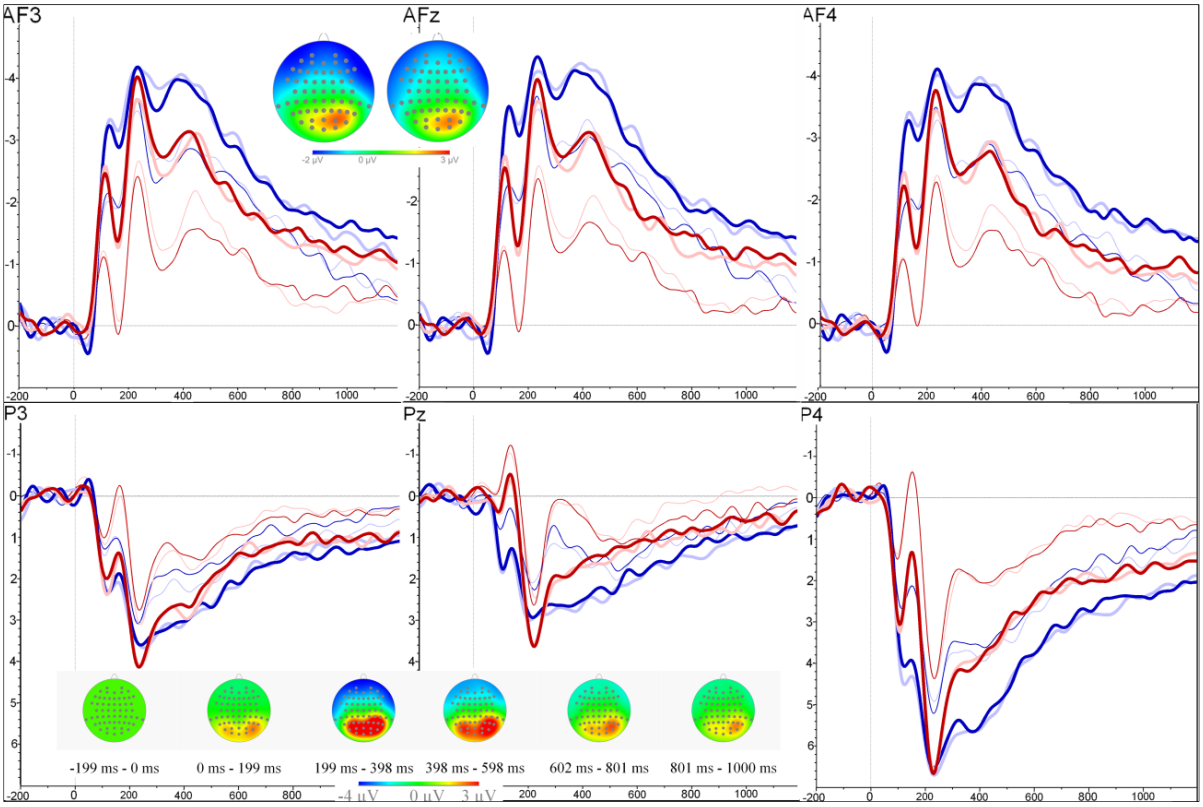

Figure 2. Event-related potentials in response to food and neutral pictures. a) N2 amplitudes (µV) at left (AF3), central (AFz) and right (AF4) anterior-frontal electrode sites. **b)** Difference maps of brain activity towards chocolate minus neutral pictures in the N2 time window (180-350 ms after stimulus onset) for BEP (left) and HC (right). **c)** LPP amplitudes (µV) at left (P3), central (Pz) and right (P4) posterior electrode sites. **d)** Temporal and spatial distribution of brain activity of BEP while viewing chocolate pictures for six time windows before and during stimulus presentation. HC are depicted in blue. BEP are depicted in red. Thick lines are for chocolate images; thin lines refer to neutral images. Images preceded by chocolate odour are depicted in the darker red/blue; images preceded by neutral odour are depicted in the lighter red/blue.

The marginally significant interaction between "picture type" and "group" was explained through lower amplitudes towards neutral stimuli in BEP than in HC.

This led to the conclusion, that BEP have a higher difference in activation when comparing neutral to chocolate stimuli than HC, wherefore a difference wave subtracting the activation during neutral stimuli from the activation during chocolate stimuli was calculated. An ANOVA including "group" as between subjects factor showed a significant effect of "group" ($F_{1,35}$=4.95, p<.05, η_p^2=.12), characterized by higher relative N2 amplitudes in BEP (M=-1.56, SD=.88) than in HC (M=-.87, SD=.98). See Figure 2 for activation difference maps.

For N2 latency the only significant effect was a main effect of "localization" (see Table 3, all other F<2.5 and p>.09), explained through shorter latencies for the central N2 compared to the left and right lateralized N2 (see Table 3).

3.3.2 LPP peak amplitudes and latencies

For LPP peak values, there was a significant main effect of "picture type" and "localization" and a significant interaction between "picture type" and "localization" (see Table 3 for F- and p-values). There were no further main or interaction effects (all F<2.1 and p>.16). As expected, chocolate pictures let to significantly higher amplitudes than neutral pictures, but contrary to hypotheses there were no differences between HC and BEP. Highest LPP amplitudes were found at right parietal electrode sites compared to left and central sites, activation at central sites was higher than at left parietal sites (this difference was not significant for neutral pictures) (see Table 3 for MD and p-values).

Regarding LPP latencies, results showed significant main effects for "picture type" and "localization" (see Table 3). No further main or interaction effects were found for LPP latency (all F<2.1 and p>.16). The LPP peaks for chocolate pictures were earlier in latency than those for neutral pictures. An earlier latency was found for the right LPP compared to central and left LPPs. Latencies did not differ between left and central localization (see Table 3).

3.3.3 Differences in theta frequency

Contrary to expectations, there were no significant effects for "group" or "odour type" in theta frequency (all F<2.1 and p>.12).

3.4 Correlation analyses

For BEP, momentary craving was highly correlated with trait craving for ratings in olfactory and visual chocolate blocks (rs>.4 for FCCQ-T-total), but not for neutral blocks (rs=.07 to -.22 for FCCQ-T-total). For HC, some of the FCCQ-T subscales were highly correlated with some of the VAS ratings, but this was not necessarily dependent on whether the rating referred to chocolate or neutral blocks.

More difficulties in emotion regulation in general were associated with higher self-reported craving in both groups (rs=.22 to .41 for DERS total). Higher eating pathology (EDI-2 total) was associated with higher momentary craving throughout the experiment for BEP (rs=.25 to .51) but not for HC (rs=.10 to .32). See tables S5.4a and S5.4b.

For HC, momentary craving was positively correlated with N2 and LPP amplitudes, high correlations were found for chocolate pictures primed by chocolate odour. Higher state chocolate craving at baseline went along with higher N2 (rs=.41 to .76) and higher LPP amplitudes (rs=.12 to .48). Surprisingly, for BEP this pattern was different: higher momentary craving predicted smaller N2 (rs -.02 to -.41) and LPP amplitudes (rs=.06 to -.41), high correlations were found for chocolate pictures (see Table S5.5 for r-values).

ERP amplitudes were highly correlated with some of the clinical trait measures; as expected, emotion regulation difficulties

and eating disorder pathology were positively related to ERP amplitudes in both groups. One surprising aspect of this data is the negative correlations of trait craving with N2 amplitudes in BEP, while positive relations were found for HC. LPP amplitudes were not clearly and highly related to trait craving in both groups (see Tables S4a, S4b and S5 for *r*-values).

Table 3. Statistical parameters of significant main and interaction effects and pairwise comparisons for N2 and LPP peak amplitudes (µV) and latencies.

	Factor	$F_{(df)}$	*p*	η_p^2	Pairwise comparison	*MD*	*p*
N2 peak amplitudes	"Picture type"	$_{(1,35)}$ 63.31	<.001	0.64	Chocolate - neutral	-1.13	<.001
	"Localization"	$_{(1.5,51.9)}$ 17.73	<.001	0.34	Central -left	-0.37	<.001
					Central - right	-0.54	<.001
					Right - left	0.17	.137
	"Group"/"Odour prime"/"Picture type" comparing "Odour prime"*	$_{(1,35)}$ 5.51	<.05	0.17	HC/Neut/Neut-	-0.05	.824
					BEP/Neut/Neut-	-0.16	.490
					HC/Neut/Choc-	-0.21	.119
					BEP/Neut/Choc-	0.45	.004
	"Group"/"Odour prime"/"Picture type" comparing "Group"*				HC/Neut/Neut-	-1.40	.056
					HC/Neut/Choc-	-1.22	.096
					HC/Choc/Neut-	-1.51	.034
					HC/Choc/Choc-	-0.56	.470
	"Picture type"/"Group" comparing "Group"*	$_{(1,35)}$ 4.05	.052	0.1	Neut/HC-Neut/BEP	-1.46	.039
					Choc/HC-Choc/BEP	-0.89	.234
N2 peak latency	"Localization"	$_{(2,70)}$ 6.21	<.01	0.15	Central -left	-4.52	.009
					Central - right	-6.54	.003
					Right - left	2.02	.332
LPP peak amplitudes	"Picture type"	$_{(1,35)}$ 61.23	<.001	0.64	Chocolate - neutral	0.95	<.001
	"Localization"	$_{(2,70)}$ 24.19	<.001	0.41	Central -left	0.38	.026
					Central - right	-0.99	<.001
					Right - left	1.37	<.001
	"Picture type"/"Localization" comparing "Localization"*	$_{(2,70)}$ 15.11	<.001	0.3	Neut /central-Neut/left	0.31	.057
					Neut/central-Neut/right	-0.70	<.001
					Neut/Right-Neut/left	1.01	<.001
					Choc/central-Choc/left	0.46	.024
					Choc/central-Choc/right	-1.27	<.001
					Choc/Right-Choc/left	1.73	<.001
LPP peak latency	"Picture type"	$_{(1,35)}$ 20.63	<.001	0.37	Chocolate - neutral	-46.49	<.001
	"Localization"	$_{(2,70)}$ 5.26	<.01	0.13	Central -left	12.84	.436
					Central - right	48.24	.003
					Right - left	-35.40	.025

BEP = binge eating patients; Choc = chocolate; HC = healthy controls; MD = mean difference; Neut = neutral.
Statistically significant pairwise comparisons (p <.05) are marked in bold.
*Pairwise comparisons for "picture type" are not listed because the difference between chocolate and neutral pictures was significant on all levels of this interaction (all p <.001).

4 Discussion

The current study aimed to compare the craving, cognitive inhibitory control and motivated attention of BE and healthy individuals towards visual and olfactory chocolate stimuli, when considering self-report and electrophysiological data, and its association with clinical variables. Additionally, we wanted to explore the additive effect of olfactory and visual stimuli on craving induction.

The first set of analyses referred to subjective data, showing that both groups had an increase in craving through the experimental manipulation, BEP reported more craving at baseline and after the experiment than HC. When controlling for baseline craving, chocolate pictures evoked a higher momentary craving response than neutral pictures in participants as a whole, but there were no differences between the two groups. Trait craving predicted higher self-reported momentary craving; while in BEP this was specific for craving towards chocolate stimuli and was not seen in general craving levels (neutral stimuli), in HC this distinction was not visible in the exact same manner. More difficulties in emotion regulation were associated with more self-reported craving.

These results were mirrored by ERP amplitudes, with higher amplitudes for chocolate than for neutral pictures in both groups. As expected, there was a significantly higher central N2 for chocolate than for neutral stimuli. There were no group differences in the absolute amplitude towards chocolate pictures, but the difference in activation between chocolate minus neutral stimuli was higher for BEP than for HC. The N2 has been related to response conflict and cognitive inhibitory control in basic research [22,23]. More recent studies found that N2 amplitudes were associated with emotion suppression [30], but also with a lack of inhibitory control in smokers [31]. Low inhibitory control is an important aspect of addictive behaviours [32], compulsive food intake may be included therein. A study comparing restrained and unrestrained eaters reported a comparable increased frontal negativity in restrained eaters in response to available food, which was not found in unrestrained eaters [33]. Asmaro and colleagues (2012) found an increased N2 (labeled as "Anterior Negativity") for chocolate versus neutral pictures in non-chocolate cravers, which was significantly reduced after chocolate intake. The authors interpreted this effect as top-down cognitive control in non-cravers; they did however not find this effect in chocolate cravers, which seems somehow counter-intuitive. In our study, although in the absolute amplitudes there were no differences between groups for N2 amplitudes towards chocolate stimuli, BEP had lower amplitudes towards neutral stimuli. This interaction effect highlights a higher difference between chocolate and neutral images in patients than in healthy individuals, indicating that the relative increase in cognitive control was higher in the patient group. However, in the patient group there was a tendency to negative relations between self-reported measures of cravings and N2 amplitudes. Although these results have to be regarded with care and replications are needed, these findings point out that those patients with less inhibitory control experience more craving. A possible explanation for the N2 results might be that there are two subgroups of patients: those who have a high increase in cognitive control (seen in high N2 amplitudes) and experience lower craving (seen in VAS ratings), and those who have little cognitive control mechanisms (lower N2 amplitudes) and experience a strong craving for chocolate (higher ratings in VAS). Restrained eating and control over food intake may thereby play a decisive role [33]. In HC, self-reported

state craving for chocolate at baseline was a strong predictor of N2 amplitudes, ratings of momentary craving were also positively related to N2 amplitudes for HC. This shows that the more craving healthy individuals experience the more inhibitory control they have in response to a craving induction task.

Regarding motivated attention, a late, right lateralized, posterior component consistent with the LPP was higher in amplitude for chocolate than for neutral pictures. The hypothesis of BEP having more motivated attention towards chocolate stimuli than HC was however not supported by our data. In contrast to earlier findings [34], no group effects for peak amplitudes towards chocolate pictures were found. However, this former study used a mix of high-caloric food pictures in contrast to chocolate pictures only in our study. Furthermore, the sample was a mere BED sample, while our sample was a mixed sample of patients with BE symptomatology, including BED and BN. Until now, there is no published data looking at motivated attention towards food in BN by use of EEG, and it is possible that they regulate their attention towards food stimuli in a similar way as it was proposed for obese adults [35]. This is supported by the correlations between self-reported momentary craving and LPP amplitudes, which pointed towards a positive association between craving and motivated attention in HC, but a negative association in BEP.

The second aim referred to a potential "supralinearity" or additive effect of olfactory and visual stimuli on craving induction. Results of subjective data partly support this hypothesis, by showing an increased craving response towards chocolate pictures primed by chocolate odour, while chocolate versus neutral odour did not modulate the self-reported craving towards neutral stimuli. The influence of a preceding odour stimulus was not visible in the amplitudes of the visually evoked ERPs (N2 and LPP) in the whole sample. Having said that, there was however a higher N2 amplitude for BEP towards chocolate pictures preceded by chocolate odour than chocolate pictures preceded by neutral odour, which was not found in HC. This might point out that BEP react more sensibly to the odour of food stimuli, which potentiates their craving response to visual cues.

The third study aim was to look at the effect of olfactory stimulation on electrophysiological activity. Similar to the results for visual stimuli, participants reported more craving after smelling chocolate than neutral odour. Contrary to our hypotheses no differences between groups were found. Furthermore, theta power density was analyzed during neutral and chocolate odour presentation, but this study did not find any differences between odour types or groups regarding this measure.

Although this study has many strengths, such as a sample of individuals with BE psychopathology, an experimental design and the comparison of subjective and electrophysiological measures, there are some limitations which have to be considered. First of all, the total sample was too small to have enough power to discover complex interactions with small effect sizes, wherefore some group differences may not have been detected. Second, the patient sample was a mixed sample of BN and BED patients; although both patient groups struggle with BE, there may be other processes underlying each one of these disorders which differ between the two diagnostic categories. Future studies should compare these two groups with larger samples in order to see if there are differences in craving induction depending on diagnosis. Regarding the experimental manipulation, two limitations have to be mentioned: first, the lack of differences in theta

activity may be due to the participants having their eyes closed during the presentation of the olfactory stimuli, wherefore the increase in alpha activity may disguise the underlying theta activity. Furthermore, in order to look at each sensory modality separately, olfactory and visual stimuli were not presented simultaneously in this experiment, wherefore the real "supralinearity" effect may be underestimated by the results of this study.

This is an important issue for future research. An olfactometer could be used for a simultaneous and precise, event-related presentation of odour stimuli, which may allow a better understanding of the interaction between olfaction and vision in stimulus induced craving. To better understand the meaning of enhanced ERPs in food processing, future studies should also look at neural generators of these potentials. This could also be helpful to inform about possible targets to reduce craving through neuromodulation, as proposed in recent research [36–38].

The main conclusions of the current study are that chocolate pictures are related to higher inhibitory control and motivated attention than neutral pictures; while BEP might have lower absolute inhibitory control, they showed a higher relative increase in response to chocolate cues than HC. When considering self-report, although BEP reported more craving than HC at baseline and after the experiment, when controlling for that variable, there were no differences between the two groups in the craving reaction towards chocolate stimuli (visual and olfactory). Patients experiencing higher chocolate craving may have lower inhibitory control and reduced motivated attention towards chocolate pictures. In HC on the other hand, higher craving relates to more inhibitory control but also higher motivated attention. Furthermore, the additive effect of olfactory and visual stimuli on craving induction was partially supported. Chocolate odour to some extend increased the incentive value and craving reaction towards visual chocolate images in both healthy and BEP, but BEP seem to be more susceptible to this effect.

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Author contribution statement

IW, AS, SJM and FFA conceptualized and designed the study. IW, AR, AJ and FFA wrote the main manuscript text. GMB and MB contributed during the data collection process and to the design of the study. RG, VMR and IW did the statistical analysis of the data. MVH screened participants for neurological disorders. All authors reviewed the final version of the manuscript.

Conflict of interests

None.

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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Discussion

6 Discussion

Eating disorders are mental disorders associated with a range of biopsychosocial risk factors (Culbert et al., 2015); in spite of the severe consequences EDs have on well-being and health, many aspects of the processes underlying development, maintenance and treatment of these disorders are not yet understood. Research on factors which precede and maintain disordered eating and of active factors in treatment will be helpful to create better and specific therapies for people suffering from an ED. It is known from former studies that emotions and their regulation are crucial to ED symptomatology (Macht, 2008; Fox and Power, 2009) and that these difficulties contribute to the maintenance of the disorder (Stroe-Kunold et al., 2016; Racine and Wildes, 2015). Furthermore, attentional biases (Brooks et al., 2011; Veenstra and Jong, 2012; Giel et al., 2011), incentive sensitization (Berridge, 2009), and compulsive behaviour towards food and associated cues (Banca et al., 2016) are implied in explanative models of the pathogenesis of EDs. Nevertheless, until now some aspects specifically in the interaction between emotional and cognitive factors in the psychopathology of EDs are still unclear. Therefore, this thesis aimed at improving the understanding of difficulties in emotion regulation in patients with EDs. Furthermore, an effort was made to build a bridge from emotion regulation difficulties, to addictive eating patterns and alterations in the attentional processing of food stimuli.

6.1 Summary of study findings

The research questions addressed in this thesis were focused on open questions regarding emotional and cognitive aspects of disordered eating behaviour. The first two studies show that ED patients have more difficulties to regulate and express their emotions. The third and fourth study were focused on addictive eating patterns and show the interrelation between emotion regulation, negative urgency and eating behaviour; while difficulties in emotion regulation are more strongly related to EDs in general, negative urgency seems to be more closely linked to FA. Two further studies were directed at cognitive aspects of disordered eating, i.e. attentional biases related to food processing and inhibitory control in stimulus-induced craving.

6.1.1 Discussion of hypothesis I: *Patients with an ED have more difficulties to show and regulate emotions than HC; this is seen in alterations in facial emotional expressions in response to emotional stimuli and in self-reported difficulties in emotion regulation*.

The data of study 1 indicates decreased facial emotional expressivity in individuals with different non-psychotic disorders, which supported hypothesis I. Medium to large summary effects were found for decreased facial expressivity of positive and negative emotions in patients with AN. There were less studies looking at patients with BN; the integrated evidence points towards decreased expression of negative emotions, while for positive emotions study results were inconsistent: some studies report increased and others decreased facial expression of positive emotions in BN. These results provide support for hypothesis I of this thesis that patients with an ED have difficulties to show and regulate emotions. Alterations in facial expressivity may at least partly explain ED patients' difficulties in social cognition (Caglar-Nazali et al., 2014), bringing along problems to recognize own and others' emotions (Kret and Ploeger, 2015). This may lead to reduced empathy, misunderstandings in social interactions, unsatisfactory social relations and loneliness (Tchanturia et al., 2015a; Tárrega et al., 2014), which has a strong influence on psychosomatic well-being and mental health in general (Cacioppo and Cacioppo, 2014).

Further support for hypothesis I was found in study 2 which shows that patients with AN, BN, BED and OSFED have more difficulties than HC to recognize and accept their own emotions, to control their impulses and to engage in goal-directed behaviour when experiencing strong emotions, and that ED patients are less aware of their emotions. Large effect sizes were found for non-acceptance of emotions, impulse control difficulties, lack of emotion regulation strategies and lack of emotional clarity.

6.1.2 Discussion of hypothesis II: *The established relationship between specific personality traits known to predispose ED, namely harm avoidance and self-directedness, is partly mediated by difficulties in emotion regulation*.

Study 2 further demonstrates that higher individual difficulties in emotion regulation are predicted by lower self-directedness and higher harm avoidance. As expected by hypothesis II, the well-documented relation between personality traits and EDs (Atiye et al., 2015) was mediated by difficulties in emotion regulation. These results indicate that individuals who have an avoidant, inhibited and reactive personality profile are

likely to have more problems to learn sufficient emotion regulation and therefore develop inadequate strategies to handle negative affect. Neuroticism is a personality concept describing this kind of inhibited and emotionally instable temperament and is strongly related to psychopathology in general (Jeronimus et al., 2016). It is formed by both trait and state influences and gets more and more stable with increasing age (Laceulle et al., 2013; Caspi et al., 2005). While at younger ages genetic influences are more important, with growing age the environment is more strongly associated with the consolidation of neuroticism (Laceulle et al., 2013); this may be at least partly attributable to differences in acquired emotion regulation strategies. A relation between personality traits and alterations in emotional regulation in ED psychopathology has been corroborated by a recent study showing that ED patients with low self-directedness have less facial expression of anger, and that the facial expression of joy was related to higher scores in reward dependence, novelty seeking and self-directedness (Giner-Bartolomé et al., 2016). Furthermore, emotion regulation capacities together with an outgoing personality style and secure attachment have been shown protecting factors against the development of psychopathology in individuals with early-life maltreatment (Hillmann et al., 2016). Altogether, this indicates that the acquisition of adequate emotion regulation strategies could be helpful to counterbalance dysfunctional personality traits and thus protect from psychopathology.

6.1.3 Discussion of hypothesis III: *FA in ED patients is related to a distinguishable personality profile, which is similar to other addiction disorders*.

The second set of studies aimed at investigating addiction-like eating patterns and its behavioural, cognitive and emotional correlates. Study 3 showed that ED patients fulfilling the criteria for FA as assessed by the YFAS have relatively more problems to pursue tasks to the end and to focus on long-term goals and that they are more likely to engage in rash action when having negative emotions than ED patients who do not report problems with addiction-like eating. Therefore, this patient group is likely to engage in impulsive behaviour such as loss of control over food intake, especially when they are in a negative mood. Hypothesis III of this thesis was however only partially supported: although patients with high FA differed in self-directedness and negative urgency from patients low in FA, there were no differences in novelty seeking, which would have been expected from the literature on “addictive personality” traits. A

possible explanation for this might be that FA in ED patients is more strongly related to *negative reinforcement* (as in negative urgency) than to *positive* reinforcement, which is rather the mode of action in novelty seeking.

6.1.4 Discussion of hypothesis IV: *Self-directedness, emotion regulation and negative urgency interact in their shared explanation of FA and explain variance over and above ED severity.*

Hypothesis IV predicted that self-directedness, emotion regulation and negative urgency interact in their shared influence on FA and explain variance in FA over and above ED severity; this hypothesis was only partly supported by the study's results. A comprehensive model of FA and EDs tested in study 4 suggests that low self-directedness and difficulties in emotion regulation are mainly related to higher ED psychopathology in general. Negative urgency however seems to be specifically related to FA in ED patients: a subgroup of patients, who in addition to low self-directedness and difficulties in emotion regulation tend to act impulsively when in negative mood states, are at risk to develop eating patterns analogue to addictive behaviour. A recent study shows that patients with borderline personality disorder, who also suffer from binge-eating and received a diagnosis of BN, have higher levels of negative urgency than those who do not have a comorbid BN (Reas et al., 2016). This study however did not measure FA, wherefore it is impossible to conclude whether elevated levels of negative urgency in the BN group can be mainly explained by FA or by BN in general. Still, negative urgency is also related to many other addictions including alcohol, nicotine, gambling and cannabis addiction (Torres et al., 2013; Verdejo-García et al., 2007; Roys et al., 2016; Wardell et al., 2016). One of these studies found negative urgency to be a unique predictor of alcohol and cannabis addiction in a sample of individuals with childhood maltreatment, while other forms of impulsivity were not associated with substance use (Wardell et al., 2016). Negative urgency also relates to PFC brain response to olfactory alcohol cues and craving in social drinkers (Cyders et al., 2014). These results emphasize the conclusions drawn from the studies of this thesis that show that negative urgency is an impulsivity trait specifically and strongly related to addictive behaviours.

6.1.5 Discussion of hypothesis V: *Food stimuli are processed with more motivated attention than neutral stimuli,* and hypothesis VI*: There are differences in motivated*

attention to food depending on eating behaviour; patients with binge-eating show higher motivated attention to food than HC.

The third set of studies examined attentional processes related to incentive sensitization of food stimuli. Results of the systematic review undertaken in study 5 provide strong support for hypothesis V and partly support hypothesis VI: food pictures were shown to generally lead to more motivated attention than neutral stimuli (hypothesis V), but the evidence regarding differences in motivated attention dependent on eating behaviour is inconsistent (hypothesis VI). Altogether, the analysed data suggests that individuals with abnormal eating behaviour have a strong orienting bias in response to food stimuli when compared to normal eaters. Regarding attentional maintenance, however, the evidence is less clear. It seems likely that individuals with binge-eating, emotional or external eating have increased and maintained motivated attention towards food which is in line with incentive sensitization processes. Study 6 did however not support this notion of an increased attentional maintenance in patients with binge-eating. There is a lack of electrophysiological studies in patients with an ED diagnosis. Recent studies using different measures of attention have replicated results regarding biases to food in *attentional orienting* as well in patients with AN (Godier et al., 2016) as in patients with BN (Albery et al., 2016) and BED (Schmitz et al., 2015; Schmidt et al., 2016; Popien et al., 2015; Svaldi et al., 2015a); only some of these studies reported increased *attentional maintenance* in patients with an ED compared to HC (Schmidt et al., 2016; Popien et al., 2015). Inconsistencies in study results show that the mechanisms underlying attentional biases to food are not yet totally understood and that there might be influencing factors which are unknown until now; it has been recently shown for example, that holding food-related cues in working memory increases attentional biases to food (Rutters et al., 2014). Furthermore, cognitive strategies are also known to have an influence on attentional processing of food cues (Svaldi et al., 2015b). It is however unclear, how different attitudes towards food leading to appetitive, aversive or ambivalent feelings related to food influence attentional processing (Field et al., 2016) or how differences in inhibitory control capacities or difficulties in emotion regulation might influence attentional biases to food.

In study 6, the question of a possible incentive sensitization of food cues in patients with binge-eating was further investigated. Results show that images of chocolate compared to neutral images induced a significant increase in craving, motivated attention and cognitive control in both healthy and binge-eating individuals. The evidence of this study did not support hypothesis VI, which predicted that patients with binge-eating have more motivated attention towards food than HC due to increased incentive sensitization. However, FA scores in the patient sample (and less clearly also in the HC group) were positively related to motivated attention to food, which may suggest that incentive sensitization is more strongly associated to addictive eating patterns than to binge-eating psychopathology in general.

6.1.6 Discussion of hypothesis VII: *Patients with binge-eating dispose of less inhibitory control when presented with visual food stimuli than HC participants*.

With regard to inhibitory control, there were no differences between the study groups in N2 amplitudes in response to chocolate, but binge-eating patients had lower amplitudes during the control condition (neutral pictures). A non-linear relationship between self-reported craving and N2 amplitudes further suggests that patients with higher craving had *lower* levels of cognitive control in response to cue-induced craving while HC with higher craving activate *more* inhibitory control resources. This underpins the suggestions brought forth in hypothesis VII that patients with binge-eating have less inhibitory control. However, the patient group as a whole had a stronger increase in inhibitory control in response to chocolate compared to neutral stimuli than. This *increase in inhibitory control* when exposed to chocolate stimuli speaks against hypothesis VII. However, the N2 has also been described as an indicator of *response conflict* (Nieuwenhuis et al., 2003) and neurostimulation of the DLPFC through active transcranial Direct Current-Stimulation (tDCS) has been shown to reduce craving, food intake and N2 amplitudes, which the authors interpret as facilitated response inhibition due to less conflict through DLPFC activation (Lapenta et al., 2014). Seen like this, the binge-eating group would experience a stronger increase of response conflict than HC in view of chocolate stimuli, but patients with higher craving would experience less response conflict, which then might lead to loss of control over food intake. This shows that there are several possible explanations for these results and that future studies are needed to better understand the dynamics underlying inhibitory control in binge-eating

and the neural mechanisms underlying the N2 response of ED patients to chocolate and neutral stimuli. Furthermore, a recent study points out that negative urgency and negative affect are likely to draw on inhibitory control resources (Chester et al., 2016) and emotion regulation difficulties could be a mediating factor between craving, the activation of inhibitory control resources and loss of control over eating. It would be important to also look at behavioural measures of inhibitory control in response to olfactory and visual food cues; for instance, a recent study has found that in social drinkers the *smell of alcohol decreases their inhibitory control* capacity in a Go/No-Go-Task in general (Monk et al., 2016).

6.1.7 Discussion of hypothesis VIII: *Cue-induced chocolate craving, motivated attention and inhibitory control induced through visual stimuli are potentiated when primed by a chocolate odour as compared to a neutral odour*.

In study 6 of this thesis, chocolate odour has been shown to be a potent stimulus to induce craving and might increase the inhibitory control response to visual stimuli, which partly supports the assumptions of hypothesis VIII that cue-induced craving is potentiated through the combination of visual and olfactory chocolate stimuli.

6.2 Integrating findings into a common model

A schematic model integrating study findings into a global model is depicted in Figure 3 (*p*. 187). As shown in this model, it is concluded from the theoretic background that temperament and character traits are highly influenced by both genetic predisposition and environmental factors. These temperamental traits affect an individual's capacity of learning how to adequately regulate emotions and are related to negative-emotion-based impulsivity (negative urgency), as has been shown by the studies presented in this thesis. Different measures of emotion regulation such as facial expressivity and self-reported measures of difficulties in emotion regulation have been shown to be related to several types of EDs, including AN, BN and BED. Measures of impulsivity such as negative urgency and inhibitory control have been shown to be related especially to binge-eating, including BN, BED and OSFED. Negative urgency is a strong predictor of FA, which on the other hand is related to increased craving; craving levels are supposed to moderate the influence of inhibitory control on the appetite regulation system and on food intake. In other words, low inhibitory control capacities together with strong craving may then lead to loss of control over food intake. The third domain of measures

relates to attentional processing of food stimuli and incentive sensitization. Since food is a salient stimulus also for healthy normal eating individuals, it is difficult to disentangle effects of disordered eating. More research is needed in order to fully understand processes of incentive sensitization in disordered eating, especially with regard to attentional maintenance, a lack of studies including patients with an ED and with regard to addictive eating behaviour.

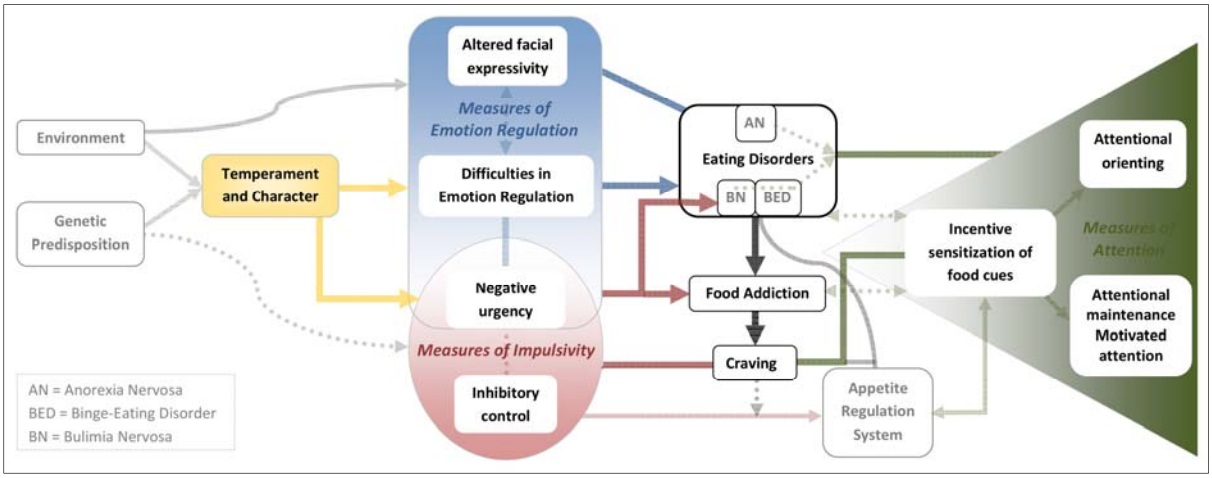

Figure 3. Integration of study findings into a common model. Findings of studies presented in this thesis are shown by thick arrows, thinner arrows indicate relations found in earlier studies and described in the introduction and discussion of this work. Dotted arrows are theoretically proposed relations which have not been proven yet or are unclear and stay open for future research. Relations where the direction of cause and effect is unclear are depicted without arrowhead. This model does not claim to be an exhaustive model of eating disorder psychopathology, but it represents the main findings of this thesis and some important aspects from the scientific background.

To put the model in a nutshell, it may be said that problems to regulate negative emotions lead to increased and undifferentiated negative affect, which is associated to disordered eating behaviour. The abuse of properties intrinsic to specific foods in order to attain an associated brain reward response and the repeated intake of food can lead to incentive sensitization of food cues and stimuli associated with the consumption and consecutive reward response, such as the smell or sight of food (e.g. pictures, commercials), a specific environment (e.g. the kitchen, bakery, supermarket) or situation (e.g. coming home after work, watching television, being in a sad mood). Incentive sensitization supposedly increases compulsive food intake, which results in behaviour similar to SUD and behavioural addictions.

With regard to the debate on FA, in view of all that has been mentioned so far, similarities between drug addiction and some specific patterns of disturbed food intake are apparent; the evidence is however insufficient to close the subject and to decide whether addictive eating is better described as a SUD or behavioural addiction. It seems reasonable to act on the assumption that changes in brain reward functioning and appetite regulation alone do not explain overeating and that the behavioural and emotional aspects underlying these disorders should be taken into account too (Treasure and Schmidt, 2013). There is an evolutionary dependence on food (Krashes and Kravitz, 2014), wherefore total abstinence from food is impossible. The brain is *evolutionarily prepared* to be "addicted" to food in order to assure survival, and drugs can mimic these rewarding effects through their chemic properties. Drugs thus exploit neural circuits developed for the rewarding properties of food, wherefore similarities in neural processing and neurobiology between drug addiction and food processing are *not surprising*. Nevertheless, food products have become quite artificial and strongly processed, high in sugar and high in fat, which apparently is not necessary in such quantities for survival. Therefore, it is suggested that the brain is not prepared for this amount of rewarding stimuli in the environment and individuals sensitive to reward may get caught in this trap and develop eating patterns which remind on substance addictions. Emotional eating or overeating could be a way to *abuse* reward pathways of the brain in a similar manner as seen in drug addiction, finally leading to compulsive eating or FA; the substance is different but the rewarding and self-medicating effect is the same, and it may be difficult for individuals to refrain from this kind of behaviour, in spite of negative consequences. A recent study supports the hypothesis of selective attention towards unhealthy food due to negative mood states in people with FA (Frayn et al., 2016); however, another study did not find increased attention to food in emotional eaters after the induction of negative mood (Werthmann et al., 2014c). Research is not yet clear about relations of cause and effect regarding eating patterns and alterations in the brain reward system, and the link between emotions, brain functioning and eating behaviour may significantly vary depending on ED diagnostic subcategories and inter-individual differences in functionality and pathogenesis of the disordered eating behaviour (García-García et al., 2013).

6.3 Strengths and Limitations

Specific strengths and limitations of each study are discussed in the respective articles. The key strength of this thesis as a whole is that it looks at emotional and cognitive aspects of EDs from different perspectives, using multiple traits and assessment methods in order to combine and integrate different aspects of disordered eating behaviour into one model. At the same time, one source of weakness of this thesis is that most of the studies were cross-sectional, relying on (retrospective) self-report, and although statistical modelling allows for preliminary conclusions, inferences on cause-effect-relations are limited. Longitudinal studies, momentary assessment and experimental studies are needed to strengthen this aspect. Furthermore, regarding the regulation of appetite, a strength of this thesis is to have integrated the research into a theoretical background arising from multidisciplinary research including biology, psychiatry and psychology. This thesis did however not directly measure biological substrates of the appetite regulation system, which limits the possibilities to conclude on the effects of emotion regulation and inhibitory control on neurobiological functions in the appetite regulation circuit.

One more specific limitation related to this thesis and research in EDs in general is a lack of studies on BED, due to the rather recent inclusion of this diagnostic category into the new edition of the DSM. For example, in the first study of this thesis looking at facial emotional expressivity in patients with ED, no studies on BED were found; therefore, no conclusions on facial expression in BED could be drawn. Another open question remaining regarding BED is whether the basic processes of binge-eating and stimulus-induced craving are comparable between BN and BED patients. For studies regarding binge-eating it may be important to pre-select stimuli according to individual preferences. As some of the patients participating in study 6 indicated, they may really like chocolate, have high craving for it and even eat it on a daily basis, but in some cases their most feared or most problematic food would rather be savoury products. Furthermore, the causal and preceding factors of binges may be differing between BN and BED patients or even between patients within a diagnostic category; for example, it may be important to distinguish between patients having binges mainly for physiological in contrast to emotional reasons.

6.4 Implications for prevention and treatment of eating disorders

The presented results have implications for prevention and treatment of EDs and FA. Future treatments have to focus on areas related to both *emotional* and *cognitive* deficits; on the one hand, in the emotional domain, difficulties in emotion regulation and the expression of emotions have to be addressed. On the other hand, difficulties in the cognitive domain including inhibitory control and attentional biases have to be taken into account in treatment especially for patients with binge-eating and addictive eating behaviour.

Training in emotion regulation is likely to be helpful to counterbalance susceptibility to EDs due to a dysfunctional personality profile. Emotion-based treatments should focus on helping patients to be able to better distinguish between different emotions (emotional clarity), to accept varying emotional states, to learn and to train specific emotion regulation strategies patients can apply in their daily lives and to increase impulse regulation abilities. Third generation therapies can help patients to learn how to manage dysfunctional emotional expression and regulation (e.g. DBT, (Wisniewski and Ben-Porath, 2015), CREST (Davies et al., 2012a)). Regarding social cognition, treatments with oxytocin as a supplement to psychotherapy seem promising (Maguire et al., 2013; Kim et al., 2014; Treasure, 2014). The use of EEG neurofeedback (Lackner et al., 2016) or video games with biofeedback (Fernandez-Aranda et al., 2015) are other complementary therapy tools which have shown useful for the treatment of emotion regulation and impulse control difficulties. Furthermore, positive psychology should be introduced to a greater extend into ED therapy (Tchanturia et al., 2015a), focusing on increasing positive emotions instead of just decreasing negative emotions. For instance, it has been shown in a recent experimental study that the induction of positive mood can have favourable consequences on eating behaviour in patients with BN and AN (Cardi et al., 2015a).

With regard to the cognitive domain, attentional bias modification training (Renwick et al., 2013) and brain-based treatments such as *non-invasive neurostimulation* (e.g. tDCS, repetitive Transcranial Magnetic Stimulation, (Sauvaget et al., 2015; Jansen et al., 2013; Val-Laillet et al., 2015)) or fMRI neurofeedback (Ihssen et al., 2016) targeting response inhibition and craving regulation are also promising as an addition to psychotherapy.

Furthermore, an effort should be made to prevent emotional and external food intake. There are two promising starting points regarding prevention of emotional eating: on the one hand, there is the modern food environment which drives people with low inhibitory control resources into overeating. More education in schools about healthy eating habits and addictive properties and consequent risks of specific foods are needed. The changing food environment should be regarded from a critical perspective and governmental regulations may be due if FA gets further scientific support. Research shows that evidence for the existence of FA would increase public support for new policies related to the regulation of our *highly-palatable food environment* (Schulte et al., 2016; Moran et al., 2016). On the other hand, there is the question of how emotional well-being can be improved in the general population in order to prevent a range of disorders related to emotional problems and difficulties in emotion regulation. "*Emotional hygiene*" (Winch, 2014) seems to be an important domain to target in prevention. Making people aware of the fact that emotional problems can abate when looking after one's own emotional well-being and that emotion regulation skills can be learned may help people to find more adequate ways to handle negative emotions. Research with regard to new interventions in the sense of "*emotional education*" will be helpful for the prevention of disorders related to difficulties in emotion regulation and negative urgency.

6.5 Future directions

As shown in Figure 3 and pointed out in the limitations section, there are some open questions linked to the results of the included studies and to this thesis as a whole. Regarding the effect of emotion regulation on ED symptomatology, longitudinal studies measuring emotion regulation in everyday life are needed to understand the cause and effect relations and the dynamical interaction between both over time. A study looking at the covariance of emotion regulation, mindfulness and binge-/purging symptomatology in patients with BN over a six-week period is now under preparation. Preliminary results corroborate the relation between emotion regulation and symptomatology, showing their interdependency over time (Wolz et al., in preparation). The study further suggests that a psychoeducative intervention not only reduces binge- and purge- frequencies, but also decreases the use of suppression and increases the use of mindfulness and reappraisal as emotion regulation strategies. An interesting

approach for future research would be to investigate if some type of mini-intervention (possibly provided by a Smartphone-App) could be helpful in everyday life for patients to find better ways to regulate their emotions on-site and thus reduce negative emotionality and binge-purging symptomatology.

Furthermore, the exact relations between difficulties in emotion regulation, negative urgency and inhibitory control are unclear. A recent study on negative urgency and self-control proposes that self-control failure under negative affect may not be due to a *failure to activate* cognitive top-down control in the PFC, but that it may rather be explained by an *overactivation* of these brain regions during negative affect (Chester et al., 2016). A possible explanation for these results is that the study group with high negative urgency used emotional suppression to regulate their negative emotions. This notion is underpinned by neuroimaging results which have shown that the use of suppression as emotion regulation strategy is related to increased PFC activity (Siep et al., 2012). The habitual use of suppression may thus consume resources necessary for inhibitory control and undermine successful control of impulses under negative affect. This assumption shows that the relation between negative urgency, inhibitory control and the use of suppression as emotion regulation strategy should be further investigated in future studies. In addition, not everybody with low inhibitory control has problems with addictive food intake, but some people have; a possible moderator in this relation is craving, and a suggested cause of increased craving is incentive sensitization and/or negative urgency. The exact manner in which increased craving influences the relation between low inhibitory control and food intake is however unclear.

Regarding incentive sensitization, further studies using different methods are needed including patient samples of AN, BN and BED to compare attentional processes underlying each of these disorders. Future research should focus on differences in attentional processing depending on different time windows and the availability and caloric content of food; furthermore, effects of positive and negative mood states and the use of top-down regulation strategies should be investigated. To give an example, in smokers it has been found that attentional bias is not homogenous for all smokers and that it depends on different factors: for instance those smokers who had made more than two attempts to quit smoking had a stronger attentional orienting bias towards

smoking-related stimuli than smokers who had not tried to quit (Bradley et al., 2003). In ED patients, factors such as duration of illness, treatment stage, and functionality of the disorder potentially influence attentional processes. Studies comparing binge symptomatology in BED compared to BN will help to understand similarities and differences in the pathology underlying these disorders. Furthermore, studies on incentive sensitization of food stimuli in people with FA are promising to understand whether or not these eating patterns are comparable to other SUD. Moreover, considering that there are far less men than women having problems with chocolate craving and binge-eating, another interesting approach for future research would be to compare the response towards chocolate in a male sample to that in a female sample. From this kind of comparison, it might be possible to deduce whether there are differences in the attentional processing properties of people at risk for increased craving compared to those who are not.

Regarding the discussion around FA, future investigations should try to find an answer on how to treat this group of individuals. There is preliminary evidence showing that through a psychoeducative group targeting BN, symptoms of FA decrease over a six-week period (Hilker et al., 2016). The results of this thesis however suggest that these patients may have a higher benefit from treatments tailored to their specific pathology related to strong negative urgency; in addition to emotion regulation training and usual CBT, skills to confront negative urgency should be included. Still, there are many open questions remaining with regard to FA. In contrast to other SUD, total abstinence from food is not possible and it is also known that dieting and "forbidden foods" are a risk factor for the development of EDs (Neumark-Sztainer et al., 2007; Stice et al., 2008; Burton et al., 2007) and restrained eating has been related to increased attentional biases to high-caloric food (Meule et al., 2012). A recent overview shows how food restriction provokes cerebral neuroadaptations which increase the risk of both reward driven food intake and drug abuse (Carr, 2016). Especially in an environment were highly palatable food is omnipresent the reward value of these foods gets potentiated through restriction of food intake. Therefore, treatments should focus on fostering healthy eating habits which can integrate hedonic food intake in the sense of "liking" into a normalized eating, where food can be enjoyed. Patients with FA should learn to realize at what point "liking" changes into "wanting" without "liking" or gets unnaturally high as in BED (Robinson et al., 2016) and food intake gets compulsory, which is the

moment where they have to stop themselves. Developing strategies people can use to obtain this objective is one of the big challenges for future research on the therapy of addictive eating (Ruddock et al., 2016).

Last but not least, as already mentioned in the preceding paragraph on clinical implications, studies on prevention of emotion-based and addictive eating should be another focus of future research. Increasing the awareness of psychological health, emotional problems and the importance of emotional care in everyday life may help to *improve people's well-being before they develop disorders* related to difficulties in emotion regulation. Interventions targeting deficits in social cognition with the aim of improving social relations should be developed not only for ED patients but also for pre-clinical populations. Since loneliness is strongly related to general psychological health (Cacioppo and Cacioppo, 2014), interventions focused on social and emotional skills could be helpful to improve mental health and well-being and to prevent the development of a range of psychological disorders, including EDs.

Conclusions

7 Summary of main findings and conclusions

After considering the findings obtained in the above mentioned studies which are part of this dissertation, the following conclusions were obtained:

1. Alterations in facial emotional expressivity in individuals with different non-psychotic disorders including eating disorders point towards underlying emotional problems. Decreased facial expressivity constrains satisfactory social interaction and might also explain difficulties to recognize own and other's emotions.
2. Patients with an eating disorder have more difficulties in emotion regulation than healthy individuals. Difficulties in emotion regulation furthermore mediate the relation between high harm avoidance/low self-directedness personality profiles and disordered eating. Training in emotion regulation may be helpful to counterbalance susceptibility to eating disorders due to dysfunctional personality traits.
3. Patients with an eating disorder with addiction-like eating patterns have relatively more problems to pursue tasks to the end and to focus on long-term goals, than patients who report fewer problems with addiction-like eating. Especially when in a negative mood, this patient group is likely to find difficulties to refrain from food intake.
4. While low self-directedness and difficulties in emotion regulation are mainly related to general eating disorder symptomatology, negative urgency seems to be specifically related to addictive eating patterns in patients with eating disorders. Therefore, patients who in addition to low self-directedness and difficulties in emotion regulation tend to act impulsively when in negative mood states are at risk to develop eating patterns analogue to addictive behaviour. Urgency-based treatments are recommended for this subgroup of patients.
5. Visual food stimuli lead to more motivated attention than neutral stimuli, but results regarding differences related to eating behaviour are inconsistent. Attentional biases to food stimuli depend on processing time; while early time windows reflect automatic attentional biases, later time windows seem to be

affected by cognitive strategies individuals use in order to control their eating behaviour.

6. Images of chocolate compared to neutral images induce a significant increase in craving, motivated attention and cognitive control in both healthy and binge-eating individuals.
7. Patients with binge-eating do not seem to have more motivated attention towards chocolate than healthy controls.
8. Binge-eating patients seem to be lower in baseline cognitive control, but may make a stronger effort to increase control when confronted with chocolate images. A non-linear relationship between self-reported craving and N2 amplitudes suggests that patients with higher craving have lower levels of cognitive control, while healthy individuals with higher craving have higher cognitive control.
9. Chocolate odour is a potent stimulus to induce craving and might increase craving and brain response to visual stimuli.

Index of Abbreviations

ACC: Anterior Cingulate Cortex

AN: Anorexia Nervosa

ANOVA: Analysis Of Variance

BED: Binge-Eating Disorder

BMI: Body Mass Index

BN: Bulimia Nervosa

CBT: Cognitive Behavioural Therapy

CNS: Central Nervous System

CPR: Cephalic Phase Response

CREST: Cognitive Remediation and Emotion Skills Training

DBT: Dialectical Behaviour Therapy

DERS: Difficulties in Emotion Regulation Scale

DLPFC: Dorsolateral Prefrontal Cortex

DSM: Diagnostic and Statistical Manual of Mental Disorders

ED: Eating Disorder

EDI-2: Eating Disorder Inventory-2

EDNOS: Eating Disorders Not Otherwise Specified

EEG: Electroencephalogram

EMA: Ecological Momentary Assessment

ERP: Event-Related Potential

FA: Food Addiction

fMRI: functional Magnetic Resonance Imaging

HC: Healthy Controls

HPA: Hypothalamic- Pituitary- Adrenal axis

Hz: Hertz

LPP: Late Positive Potential

NAc: Nucleus Accumbens

NPY: Neuropeptide Y

OFC: Orbitofrontal Cortex

OSFED: Other Specified Feeding or Eating Disorders

μV: Microvolt

ms: Millisecond

QEEG: Quantitative Electroencephalogram

PFC: Pre-Frontal Cortex

PRISMA: Preferred Reporting Items for Systematic reviews and Meta-Analyses

QEEG: Quantitative Electroencephalogram

SCL-90-R: Symptom Check List-90-Revised

SUS: Substance Use Disorder

tDCS: transcranial Direct-Current Stimulation

TCI-R: Temperament and Character Inventory-Revised

UFED: Unspecified Feeding or Eating Disorders

UPPS-P: Urgency, Premeditation, Perseverance, Sensation seeking - Positive urgency

VTA: Ventral Tegmental Area

WHO: World Health Organization

YFAS: Yale Food Addiction Scale

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Appendix

Appendix

Supplement 1. Supplementary material for Study 2

Emotion regulation difficulties in disordered eating: Examining the psychometric properties of the Difficulties in Emotion Regulation Scale among Spanish adults and its interrelations with personality and eating disorder severity

Table S1.1. Results of the exploratory factor analysis (EFA) and the confirmatory factor analysis (CFA) for the Spanish version of the DERS (total sample, n=208).

		EFA	EFA: rotated factor matrix						CFA	
		F1	F1	F2	F3	F4	F5	F6	Coef.	Scale
11	Angry with myself for feeling that way	**.739**	**.797**	.239	.073	.182	.106	-.130	.805	Non-acceptance
12	Embarrassed for feeling that way	**.716**	**.714**	.075	.100	.267	.189	.082	.772	
21	Ashamed with myself for feeling that way	**.796**	**.772**	.084	.148	.283	.142	.151	.840	
23	I feel like I am weak	**.713**	**.562**	.398	.158	.116	.280	.289	.733	
25	I feel guilty for feeling that way	**.771**	**.758**	.349	.068	.119	.122	.136	.862	
29	Irritated with myself for feeling that way	**.790**	**.742**	.264	.136	.170	.152	.187	.857	
13	I have difficulty getting work done	**.671**	.281	**.679**	-.042	.211	.015	.121	.737	Goals
18	I have difficulty focusing on other things	**.768**	.241	**.768**	-.053	.238	.100	.132	.879	
20	I can still get things done	**.534**	.001	**.454**	.313	.209	.102	-.085	.425	
26	I have difficulty concentrating	**.761**	.292	**.766**	.024	.185	.199	.011	.852	
33	I have difficulty thinking about anything else	**.733**	.159	**.696**	.002	.271	.249	.174	.833	
3	I experience emotions out of control	**.466**	.098	.133	-.005	**.409**	.296	.065	.474	Impulse
14	I become out of control	**.823**	.371	.350	.114	**.680**	.125	.133	.876	
19	I feel out of control	**.844**	.342	.376	.112	**.739**	.162	.132	.849	
24	I can remain in control of my behaviour	**.556**	.177	.212	.414	**.513**	.122	.077	.631	
27	I have difficulty controlling my behaviours	**.754**	.335	.395	.048	**.609**	.224	.164	.848	
32	I lose control over my behaviours	**.751**	.278	.321	.160	**.723**	.168	.101	.863	
2	I pay attention to how I feel	**.749**	.082	.055	**.801**	.104	.182	.104	.853	Awareness
6	I am attentive to my feelings	**.685**	.172	-.040	**.771**	.072	.001	.060	.824	
8	I care about what I am feeling	**.660**	.113	-.095	**.777**	-.038	.025	.061	.782	
10	I acknowledge my emotions	**.557**	.005	.065	**.654**	.108	.232	.006	.607	
17	My feelings are valid and important	**.531**	-.197	-.065	**.438**	-.197	-.003	-.382	.307	
34	I take time to figure out what I'm feeling	**.368**	.083	.101	**.416**	.053	.159	-.214	.429	
15	I will remain that way for a long time	**.779**	.373	.448	.088	.290	.172	**.458**	.801	Strategies
16	I'll end up feeling very depressed	**.750**	.396	.409	.121	.299	.253	**.425**	.817	
22	I know that I can find a way to feel better	**.543**	.054	**.325**	.497	.197	.051	**.224**	.517	
28	I believe nothing make myself feel better	**.719**	.284	**.389**	.285	.433	.220	**.342**	.799	
30	I start to feel very bad about myself	**.829**	**.581**	.346	.196	.305	.262	**.352**	.863	
31	I believe that wallowing in it is all I can do	**.526**	.273	**.409**	.178	.282	.166	**.291**	.678	
35	It takes me a long time to feel better	**.726**	.247	.407	.118	.246	.214	**.583**	.738	
36	My emotions feel overwhelming	**.748**	.323	**.481**	.143	.434	.219	**.295**	.805	
1	I am clear about my feelings	**.705**	.143	.129	**.571**	.182	**.467**	.099	.732	Clarity
4	I have no idea how I am feeling	**.764**	.242	.168	.301	.209	**.706**	.079	.850	
5	Difficulties making sense out of my feelings	**.790**	.251	.279	.329	.198	**.709**	.077	.881	
7	I know exactly how I am feeling	**.660**	.192	.044	**.529**	.166	**.489**	.082	.728	
9	I am confused about how I feel	**.691**	.252	.233	.225	.232	**.696**	.108	.815	
	Cronbach's alpha (α)	.956	.922	.864	.898	.807	.916	.901	SRMR=.088	
	Correlation between factors	F2	.550							
		F3	.631	.676						
		F4	.189	.127	.236					
		F5	.713	.743	.775	.264				
		F6	.557	.492	.606	.532	.653			

Table S1.2. Discriminative capacity of the DERS-scores to differentiate between controls and ED patients without controlling for socio-demographic variables age, sex and education.

	Control (*n*=74)		ED (*n*=134)		Means comparison: T-TEST			
DERS-scale	Mean	SD	Mean	SD	MD	t-stat	[1]p	|d|
Non-acceptance of emotional responses	11.81	5.01	18.69	6.84	6.88	7.55	<0.001	1.15**
Difficulties engaging in goal directed behaviour	13.59	4.42	16.43	4.95	2.84	4.09	<0.001	0.60*
Impulse control difficulties	10.53	3.63	16.03	6.14	5.50	7.00	<0.001	1.09**
Lack of emotional awareness	15.10	4.44	18.16	5.06	3.07	4.35	<0.001	0.64*
Limited access to emotion regulation strategies	15.48	5.88	23.83	8.27	8.35	7.63	<0.001	1.16**
Lack of emotional clarity	10.12	3.91	14.95	5.02	4.82	7.12	<0.001	1.07**
Total score	76.63	18.4	108.1	27.7	31.45	8.71	<.001	1.34**

Note. ED = eating disorder; HC = Healthy Control; MD = mean difference; SD = standard deviation; |d| = Cohen's d.
[1]p-values include Holm-correction for multiple statistical tests.
*Medium effect size for d>0.50 and **large effect size for d>0.80.

Table S1.3. Comparison of the DERS-scores between ED subtypes without controlling for socio-demographic variables sex, age and education.

	AN; *n*=30		BN; *n*=54		BED; *n*=20		OSFED; *n*=30		ANOVA and significant pairwise comparison					
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F	p	Contrast	MD	*p*	|d|
Non-accept.	16.60	7.52	19.67	6.00	17.90	6.46	19.53	7.59	1.56	.202	AN<BN	3.07	.050	0.45
Goals	14.53	4.81	17.30	5.11	15.40	3.80	17.43	4.99	2.84	.041	AN<BN	2.76	.014	0.56*
											AN<OSFED	2.90	.022	0.59*
Impulse	14.13	5.58	16.63	5.49	15.35	6.64	17.30	7.18	1.66	.179	AN<OSFED	3.17	.046	0.50*
Aware	17.87	5.43	18.11	4.86	19.20	5.46	17.87	4.95	0.34	.793	---	---	---	---
Strategy	19.87	7.52	25.50	7.91	23.75	7.52	24.83	9.14	3.34	.021	AN<BN	5.63	.003	0.73*
											AN<OSFED	4.97	.018	0.59*
Clarity	14.07	5.45	15.07	4.86	14.80	4.69	15.70	5.19	0.54	.653	---	---	---	---
Total	97.07	30.08	112.3	24.91	106.4	23.19	112.7	30.72	2.64	.074	AN<BN	15.21	.016	0.55*
											AN<OSFED	15.60	.028	0.51*

Note. HC = healthy controls; AN = anorexia; BN = bulimia; BED = binge eating disorder; OSFED = other specified eating and feeding disorders; MD = mean difference; |d| = Cohen's d. Bolded text indicates significant pairwise comparisons. *Medium (d>0.50) and large (d>0.80) effect sizes.

Table S1.4. Discriminative capacity of the DERS scores for the different ED subtypes: ANOVA adjusted by sex, age and studies levels.

	Descriptives: adjusted means and SD										Factor Group		Pairwise comparisons. HC = reference group							
	HC; *n=74*		AN; *n=30*		BN; *n=54*		BED; *n=20*		OSF; *n=30*				AN vs HC		BN vs HC		BED vs HC		OSF. vs HC	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F	[1]p	MD	|*d*|	MD	|*d*|	MD	|*d*|	MD	|*d*|
Non-acceptance	12.2	5.0	16.2	7.5	19.3	6.0	18.0	6.5	19.0	7.6	9.09	<.001	3.99	0.62*	7.11	1.29*	5.78	1.00*	6.77	1.05*
Goals	13.7	4.4	14.4	4.8	17.1	5.1	15.6	3.8	17.1	5.0	3.93	.004	0.68	0.15	3.36	0.70*	1.85	0.45	3.35	0.71*
Impulse	10.6	3.6	14.1	5.6	16.5	5.5	15.6	6.6	17.0	7.2	8.99	<.001	3.42	0.73*	5.87	1.26*	4.92	0.92*	6.41	1.13*
Aware	14.8	4.4	18.2	5.4	18.2	4.9	19.9	5.5	17.8	4.9	4.77	.001	3.43	0.69*	3.34	0.72*	5.11	1.03*	2.99	0.64*
Strategy	15.7	5.9	19.8	7.5	25.2	7.9	24.2	7.5	24.3	9.1	11.40	<.001	4.08	0.60*	9.48	1.36*	8.44	1.25*	8.57	1.12*
Clarity	10.3	3.9	14.3	5.4	14.9	4.9	15.2	4.7	15.3	5.2	8.04	<.001	4.01	0.85*	4.59	1.04*	4.90	1.14*	5.04	1.10*
Total score	77.5	18.4	97.1	30.1	111.2	24.9	108.5	23.2	110.6	30.7	13.51	<.001	19.6	0.79*	33.8	1.54*	31.0	1.48*	33.1	1.31*

[1]p-values include Holm-correction for multiple statistical tests. Bold: significant pairwise comparison. *Moderate (d>0.50) and large (d>0.80) effect size.
MD: mean difference. |d|: Cohen's d.
HC: healthy controls. AN: anorexia. BN: bulimia. BED: binge eating disorder. OSF.: other specified eating and feeding disorders.

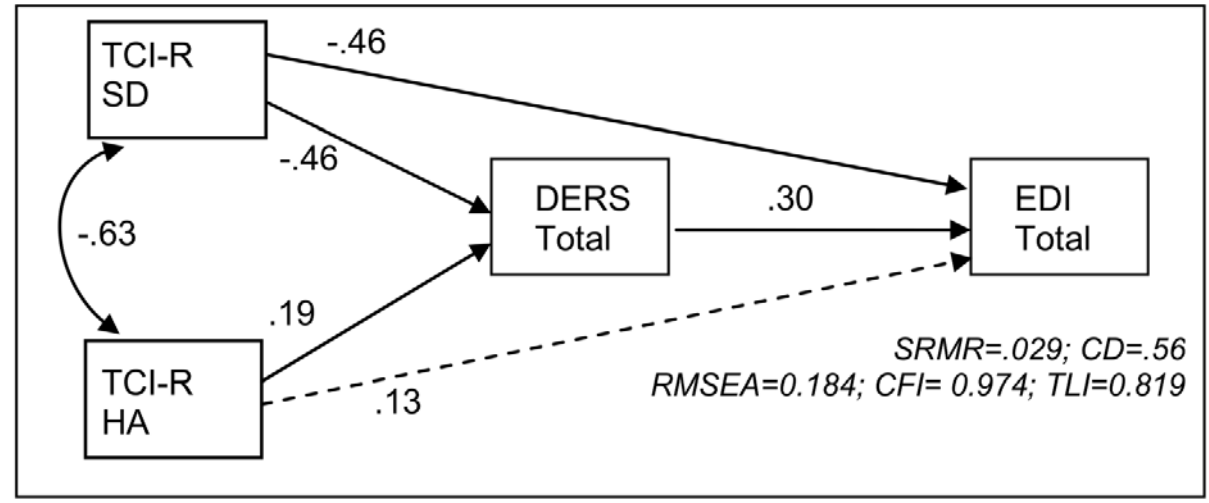

Figure S1.1. SEM of the proposed mediation model of emotion regulation difficulties mediating the relation of personality traits and eating disorder severity, without controlling for participants' age and sex.

Supplement 2. Supplementary material for Study 3

"Food addiction" in patients with eating disorders is associated with negative urgency and difficulties to focus on long-term goals

Table S2.1: Differences in ED severity and general psychopathology for patients with negative versus positive screening for food addiction: ANOVA adjusted by age and ED subtype.

	Adjusted means; SD				ANOVA (adjusted by age and ED subtype)				
	FA=negative *n*=70		FA=positive *n*=208		$F_{df=1;275}$	^1p	eta^2	MD	|*d*|
EDI-2: Drive for thinness	10.43	6.88	14.46	5.14	27.96	<.001	.093	4.02	0.66*
EDI-2: Body dissatisfaction	14.14	8.18	18.17	7.62	13.86	<.001	.048	4.03	0.51*
EDI-2: Interoceptive awar.	7.48	5.76	12.37	6.66	27.50	<.001	.092	4.90	0.79*
EDI-2: Bulimia	4.37	3.68	7.57	5.30	29.14	<.001	.097	3.20	0.70*
EDI-2: Interpers. distrust	5.93	4.64	6.14	5.02	0.08	.777	.000	0.21	0.04
EDI-2: Ineffectiveness	8.96	6.60	12.04	7.87	7.74	.009	.028	3.08	0.42
EDI-2: Maturity fears	8.78	5.87	8.34	5.82	0.26	.664	.001	-0.44	0.08
EDI-2: Perfectionism	4.49	3.63	5.86	4.43	4.80	.039	.017	1.37	0.34
EDI-2: Impulse regulation	4.36	4.94	7.18	6.21	10.72	.002	.038	2.82	0.50*
EDI-2: Ascetism	4.90	3.84	7.60	4.17	20.29	<.001	.069	2.71	0.68*
EDI-2: Social insecurity	6.67	4.70	8.13	5.72	3.30	.085	.012	1.45	0.28
EDI-2: Total score	80.52	42.94	107.86	42.99	20.24	<.001	.069	27.34	0.64*
SCL-90R: Somatization	1.49	1.00	1.93	0.90	10.42	.002	.037	0.44	0.46
SCL-90R: Obsess./comp.	1.51	0.85	1.99	0.81	16.58	<.001	.058	0.49	0.59*
SCL-90R: Interperson.	1.68	0.91	2.18	0.92	14.27	<.001	.050	0.50	0.55*
SCL-90R: Depressive	1.84	0.95	2.34	0.90	13.90	<.001	.049	0.50	0.54*
SCL-90R: Anxiety	1.22	0.79	1.74	0.87	16.91	<.001	.059	0.52	0.62*
SCL-90R: Hostility	1.09	0.87	1.46	0.98	7.01	.009	.025	0.37	0.40
SCL-90R: Phobic anxiety	0.77	0.73	1.09	0.90	6.40	.012	.023	0.32	0.39
SCL-90R: Paran. Ideation	1.10	0.69	1.57	0.81	18.38	<.001	.064	0.48	0.63*
SCL-90R: Psychotic	1.01	0.67	1.42	0.79	13.42	<.001	.047	0.41	0.56*
SCL-90R: GSI score	1.38	0.72	1.85	0.72	19.83	<.001	.068	0.47	0.65*
SCL-90R: PST score	57.11	22.89	66.28	15.34	12.79	.001	.045	9.16	0.47
SCL-90R: PSDI score	2.04	0.55	2.42	0.58	21.08	<.001	.072	0.38	0.67*

FA: food addiction diagnosis. ED: eating disorder. MD: mean difference. eta^2: Partial eta^2.

^1p: includes Bonferroni-Finner correction for multiple statistical comparisons.

Bold: significant comparison (.05 level). *Bold: moderate (|*d*|>0.50) to high ((|*d*|>0.80) effect size.

Table S2.2. Differences on behavioral addictions for patients with negative versus positive screening for food addiction: logistic regression adjusted by age and ED subtype.

	FA=negative	FA=positive	Logistic adjusted by patients' age and ED subtype					
	n=70	*n*=208	$Wald_{df=1}$	^1p	OR	95% CI		|*d*|
Gambling behavior	0.0%	3.0%	---	---	---	---	---	---
Kleptomania behavior	4.8%	7.5%	0.60	.500	1.69	0.45	6.42	0.60
Stealing behavior	20.6%	39.2%	7.66	**.033**	2.76	1.34	5.67	7.66
Compulsive buying behavior	6.2%	14.3%	2.84	.175	2.63	0.85	8.07	2.84
Alcohol use	33.1%	29.7%	0.24	.623	0.86	0.46	1.59	0.24
Tobacco use	3.9%	12.1%	3.53	.170	4.25	0.94	19.26	3.53
Other drugs use	8.3%	14.5%	1.73	.269	2.01	0.71	5.66	1.73

FA: food addiction screening. ED: eating disorder. MD: mean difference. --- Not estimable due to the extreme low prevalence.

^1p: includes Bonferroni-Finner correction for multiple statistical comparisons.

Bold: significant comparison (.05 level). *Bold: moderate (|*d*|>0.50) to high ((|*d*|>0.80) effect size.

Table S2.3. Comparison between diagnostic subtypes for the subscales of the Yale Food Addiction Scale.

	Total	AN	BN	OSFED	BED			
	n=278	*n*=68	*n*=110	*n*=61	*n*=39	χ^2	df	*p*
Consumed more than planned	54.3%	22.1%	79.1%	31.1%	76.9%	76.95	3	<.001
Unable to cut down or stop	95.7%	89.7%	99.1%	93.4%	100.0%	11.48	3	.009
Great deal of time spent	68.3%	42.6%	83.6%	59.0%	84.6%	39.87	3	<.001
Important activities given up	72.7%	60.3%	86.4%	57.4%	79.5%	23.72	3	<.001
Use despite consequences	56.8%	54.4%	63.6%	31.1%	82.1%	28.75	3	<.001
Tolerance	65.1%	45.6%	79.1%	45.9%	89.7%	41.20	3	<.001
Withdrawal	63.3%	36.8%	78.2%	55.7%	79.5%	37.00	3	<.001
Impairment or distress	82.0%	73.5%	91.8%	70.5%	87.2%	16.68	3	.001
Food addiction: screening positive	74.8%	55.9%	89.1%	62.3%	87.2%	33.08	3	<.001
	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	*F*	df	*p*
Food addiction: total criteria	4.76 1.89	3.51 1.71	5.69 1.46	3.74 1.72	5.92 1.36	42.93	3; 274	<.001

AN: anorexia. BED: binge eating disorder. BN: bulimia. ED: eating disorder. OSFED: Other Specified Feeding or Eating Disorders. SD: standard deviation.

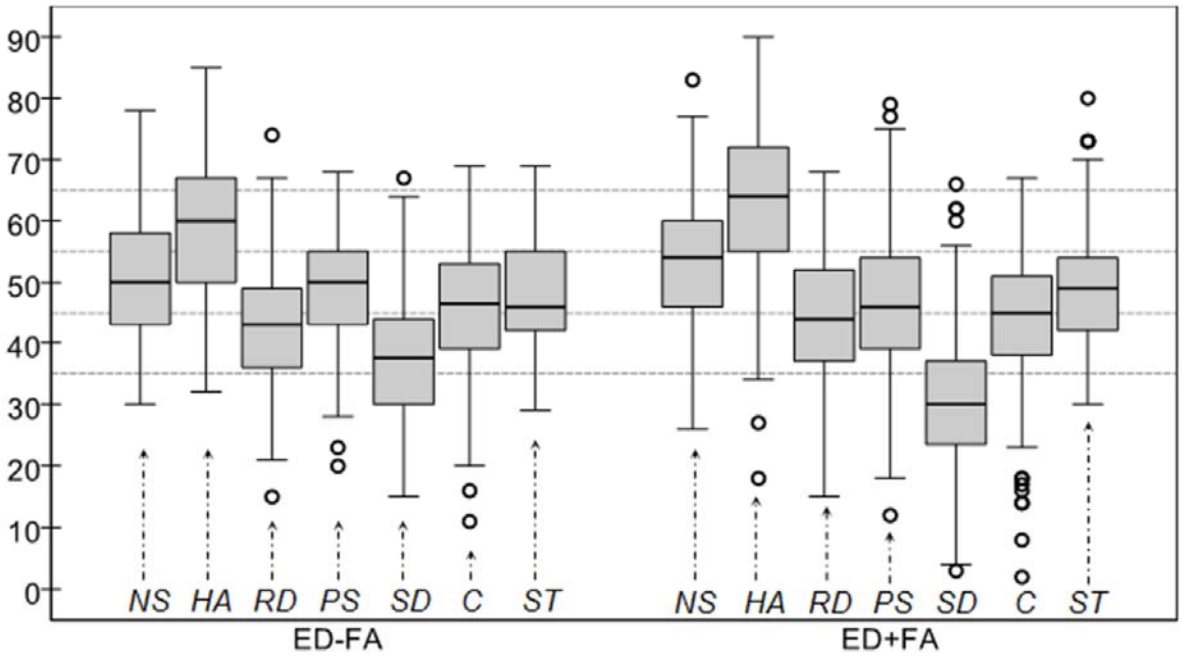

Figure S2.1. Box-plot of TCI-R T-scores. This figure shows the clinical interpretation of temperament and character traits for eating disorder patients with (ED+FA) and without (ED-FA) food addiction. Dashed lines indicate norm distributions: values between 55 and 65 or 35 and 45 are considered as subclinical, values higher than 65 or lower than 35 are considered as clinical. Comparisons are adjusted for age and ED subtype. Means in Self-Directedness were significantly different between groups, most patients with food addiction having clinically low values.

ED-FA = eating disorder patients without food addiction; ED+FA = eating disorder patients with food addiction; TCI-R: Temperament and Character Inventory- Revised; NS = Novelty Seeking; HA = Harm Avoidance; RD = Reward Dependence; P = Perseverance; SD = Self-Directedness; C = Cooperativeness; ST = Self-Transcendence

Supplement 3. Supplementary material for Study 4

Predictors of addictive eating in patients with binge-eating symptomatology: A comprehensive path model

Table S3.1. Descriptive statistics for the whole sample and for subgroups.

		Total		BN		BED		OSFED	
	α	(*n=315*)		(*n=176*)		(*n=61*)		(*n=78*)	
Gender: Females; *n-%*		292	92.7%	169	96.0%	53	86.9%	70	89.7%
Quantitative variables; mean-SD									
Age (years-old)		30.50	10.79	29.27	9.60	37.89	11.17	27.47	10.57
Onset (years-old)		20.18	8.74	18.97	6.65	23.67	11.35	20.21	9.89
Evolution-duration		10.29	9.03	10.34	9.03	13.57	10.12	7.62	7.17
TCI-R: Self-directedness	.854	114.31	20.42	114.01	20.23	110.67	18.60	117.83	21.86
Food addiction: total criteria	.880	5.36	1.67	5.77	1.39	5.89	1.32	4.03	1.80
UPPS-P: Negative UR	.810	34.78	6.30	35.48	6.32	34.89	5.29	33.13	6.74
DERS: total score	.939	113.5	22.37	114.4	23.79	111.9	21.27	112.6	19.91
EDI: Total score	.946	111.1	40.79	116.3	40.01	110.2	38.83	100.0	42.27

Note. SD: Standard Deviation; TCI-R: Temperament and Character Inventory-Revised; UPPS-P: negative Urgency, Premeditation, Perseverance, Sensation seeking – Positive urgency; DERS: Difficulties in Emotion Regulation Scale; EDI-2: Eating Disorders Inventory-2; BED: binge eating disorder; BN: Bulimia Nervosa; OSFED: other specified feeding or eating disorder.

Table S3.2. Correlation matrix for relations between dependent variables and covariates.

	Age of onset	Duration evolution	TCI-R: Self-D.	Food addiction	UPPS-P: Negative urgency	DERS: total score	EDI: total score
Age (years-old)	**.545**	**.572**	.046	.142	-.095	-.064	-.146
Age of onset (years-old)	---	**-.293**	.072	.004	-.031	-.060	-.174
Duration-evolution (years)		---	-.027	.147	-.069	-.012	-.016
TCI-R: Self-Directedness			---	-.229	**-.492**	**-.474**	**-.638**
Food addiction				---	**.289**	.207	**.282**
UPPS-P: Negative urgency					---	**.447**	**.470**
DERS: total score						---	**.561**

Bold: moderate ($|r|>0.24$) to high effect size ($|r|>0.30$).
Note. TCI-R: Temperament and Character Inventory-Revised; Self-D.: Self-directedness; UPPS-P: negative Urgency, Premeditation, Perseverance, Sensation seeking – Positive urgency; DERS: Difficulties in Emotion Regulation Scale; EDI-2: Eating Disorders Inventory-2.

Table S3.3. Results of the structural equation modelling (standardized coefficients)

	B	SE	z	p	95%CI B	
UPPS-P: negative UR						
TCI-R: Self-directedness	-0.492	0.043	-11.53	<.001	-0.576	-0.409
Constant	*8.287*	*0.277*	*29.86*	*<.001*	*7.743*	*8.831*
DERS: total score						
TCI-R: Self-directedness	-0.474	0.044	-10.86	<.001	-0.560	-0.389
Constant	*7.741*	*0.271*	*28.52*	*<.001*	*7.209*	*8.272*
EDI-2: total score						
UPPS-P: negative UR	0.111	0.047	2.39	.017	0.020	0.203
DERS: total score	0.296	0.045	6.55	<.001	0.208	0.385
TCI-R: Self-directedness	-0.436	0.045	-9.73	<.001	-0.523	-0.348
Sex (0=women; 1=men)	-0.150	0.039	-3.84	<.001	-0.227	-0.074
Constant	*3.097*	*0.510*	*6.08*	*<.001*	*2.098*	*4.096*
Food addiction						
UPPS-P: negative UR	0.207	0.062	3.36	.001	0.086	0.327
DERS: total score	0.016	0.065	0.25	.806	-0.111	0.143
EDI: total score	0.183	0.074	2.46	.014	0.037	0.328
TCI-R: Self-directedness	-0.003	0.071	-0.05	.964	-0.142	0.135
Age (years-old)	0.167	0.066	2.54	.011	0.038	0.295
Sex (0=women; 1=men)	-0.072	0.055	-1.30	.194	-0.179	0.036
Evolution (years)	0.064	0.065	1.00	.318	-0.062	0.191
Constant	*0.961*	*0.738*	*1.30*	*.193*	*-0.485*	*2.408*
Covariances						
UPPS-P: negative; DERS: total	0.278	0.052	5.35	<.001	0.176	0.380
TCI-R: self-directedness; Age	0.046	0.056	0.82	.411	-0.064	0.156
TCI-R: self-directedness; Sex	0.058	0.056	1.03	.302	-0.052	0.168
TCI-R: self-directedness; Evolution	-0.027	0.056	-0.48	.632	-0.137	0.083
Age; Sex	0.214	0.054	3.97	<.001	0.108	0.319
Age; Evolution	0.572	0.038	15.08	<.001	0.498	0.646
Sex; Evolution	-0.054	0.056	-0.95	.341	-0.164	0.057
Fit statistics: χ_2=8.137 (*p*=.420); RMSEA=.007; CFI=1.000; TLI=.999; SRMR=.026; CD=.516						

Note. DERS: Difficulties in Emotion Regulation Scale; EDI-2: Eating Disorders Inventory-2; UPPS-P: negative Urgency, Premeditation, Perseverance, Sensation seeking – Positive urgency; TCI-R: Temperament and Character Inventory-Revised. CD = Coefficient of Determination; CFI = Comparative Fit Index; CI = Confidence Interval; RMSEA = Root Mean Square Error of Approximation; SE= Standard Error; SRMR = Standardized Root Mean Square Residual; TLI = Tucker-Lewis Index

Supplement 4. Supplementary material for Study 5

The processing of food stimuli in abnormal eating: a systematic review of electrophysiology

Table S4.1. Summary of electrophysiological studies on attentional bias to food stimuli.

Authors	Participants				Methods		Outcomes		Comment
	*N** EG (f)/CG (f)	Age EG/ CG	EG	CG	Paradigm and stimuli	Type of measure	Main and interaction effects	Correlations with behavioral measures	
Asmaro et al., 2012	14 (14)/ 12 (12)	21.9 (3.9)/ 20.5 (2.9)	High in chocolate craving (Chocolate craving questionnaire; (Rodriguez et al., 2007))	Low in chocolate craving (Chocolate craving questionnaire)	Presentation of chocolate and bland food pictures (500 ms), reaction to target (chairs). 2 sessions: 1. anticipation to eat chocolate after first session of picture viewing, 2. after chocolate satiety	Mean amplitudes of AP (250-350 ms). AN (100-250 ms).	AP: EG: chocolate > bland food, CG: chocolate = bland food. AN:CG > EG to chocolate stimuli in session 1, no effect in session 2.		
(Babiloni, Del Percio, De Rosas, et al., 2009)	15 (9)	24.2 (0.2)	HNW		Oddball paradigm (presentation 1 s): Pictures of faces, food, control (flowers, landscapes, animals, objects). Reaction to rare stimuli (same pictures, graphically dilated by 25%).	Maximum peak latency and amplitude difference rare minus frequent of P300 (200-600 ms).		Positive correlation between body fat and difference measure. Significant correlation in FACE condition. FOOD and CONTROL condition non-significant correlation.	
(Babiloni, Del Percio, Valenzano, et al., 2009)	19 (15)/ 15 (9)	32.5 (2.6)/ 24.2 (0.9)	OB	HNW	See above	As above	FACE and FOOD condition: OB < HNW; CONTROL: OB = HNW.		Missing statistical parameters for main results
(Babiloni, Del Percio, Triggiani, Marzano, Valenzano, Petito, et al., 2011)	16 (11)/ 16 (13)	25.3 (1.4)/ 23.6 (1.4)	Healthy underweight	HNW	See above	As above	FACE and CONTROL condition: underweight < HNW, FOOD condition: underweight = HNW.		
(Babiloni, Del Percio, Triggiani, Marzano, Valenzano, De Rosas, et	18 (5)/ 24 (9)	23.8 (0.6)/ 21.9 (1.4)	HNW successful dieters (Karate athletes)	HNW non-dieting subjects	See above	As above	FACE condition: successful dieters > non-dieters, CONTROL: successful dieters < non-		Missing statistical parameters for main results

Authors	Participants				Methods		Outcomes		Comment
	*N** EG (f)/CG (f)	Age EG/ CG	EG	CG	Paradigm and stimuli	Type of measure	Main and interaction effects	Correlations with behavioral measures	
al., 2011)							dieters, FOOD: successful dieters = non-dieters.		
Blechert et al., 2010	18 (18)/ 21 (21)	22.6 (3.3)/ 23.6 (5.0)	HR (16-23 on Restraint Scale; (C. Herman & Polivy, 1980))	LR (1-10 on Restraint Scale)	Presentation (1 s) of binge-food and pleasant, neutral and unpleasant non-food pictures. Two blocks: 1. viewing only, 2. availability: some of the pictures presented were announced for a taste test to be done afterwards	LPP mean amplitude (300-700 ms)	First block: HR = LR, neutral = food < emotional. Second block: HR available < unavailable, LR available = unavailable.		
Blechert et al., 2011	21 (21)/ 22 (22)	AN = 26.1 (7.5) BN = 23.2 (4.6)/ 26.2 (5.0)	AN, BN (DSM-IV)	HNW	Rapid serial visual presentation (333 ms) of high- and low-cal food and pleasant, neutral and unpleasant non-food pictures	EPN mean amplitude (220-310 ms).	BN: high- = low-cal > neutral. AN: high- > low-cal > neutral. CG: high- > low-cal = neutral. ERPs for emotional pictures no differences.		Non-significant analysis of earlier time-intervals (100-120 ms), frontal electrode sites and laterality effects were not reported because not significant
Blechert et al., 2014	25 (25)/ 20 (20)	22.8 (2.8)/ 24.5 (6.0)	HEE (2.4-4.9 on Emotionality Scale of DEBQ, (Van Strien, Fritjers, Bergers, & Defares, 1986))	LEE (1.1-2.3 on Emotionality Scale of DEBQ)	Presentation (500 ms) of high-calorie food pictures. Idiosyncratic emotion elicitation technique, negative vs. neutral mood.	Peak of LPP (300-800 ms).	HEE > LEE under both conditions.		In a frontal negativity in the same time-range, HEE showed a higher relative positivity in the negative condition than in the neutral, in LEE negative = neutral.
Hachl et al., 2003	20 (20)/ 20 (20)	24.9/ 24.5	HR (score >9 on Cognitive restraint of eating-	LR (score <7 on Cognitive restraint of eating-	Tachistoscopic presentation (means 1 ms) of food-related, erotic and neutral words.	Peak latencies and peak to baseline amplitudes	P2: HR: preload < no-preload; LR: preload > no-preload.		Subliminal presentation.

Authors	Participants				Methods		Outcomes		Comment
	*N** EG (f)/CG (f)	Age EG/ CG	EG	CG	Paradigm and stimuli	Type of measure	Main and interaction effects	Correlations with behavioral measures	
			scale of Frageboge n zum Essverhalt en; (Pudel & Westenhöf er, 1989))	scale of Frageboge n zum Essverhalt en)	Identification task.	of P2 (125-175 ms) Area under the curve (AUC) for P3 (200-650 ms).	P3: HR < LR independent of stimulus category or condition.		
			Half of participants had a preload (2 muffins), half no preload						
Hanlon et al., 2012	17 (17)/ 18 (18)	32.9 (9.1)/ 31.9 (9.3)	OB	HNW	Presentation (2000 ms) of food and flowers pictures.	Mean amplitude of LPP (450-600 ms).	Food minus flower difference: exercise < non-exercise. OB = HNW.	LPP wasn't associated with food-intake during the rest of the day.	
			Crossover: one exercise (45 min walking) and one non-exercise (body-composition assessment) day (24h), counterbalanced.						
Hill et al., 2013	36 (18)	9.42 (1.1)	Healthy children, normal- and OW		Oddball paradigm (presentation 500 ms): Pictures of high-cal food (rare target, 25%) and of guinea pigs (frequent non-target).	Mean 50 ms on either side of the third positive peak 250-650 ms after stimulus onset and amplitude difference (food – non-food) of P3b	Food > neutral.	Negative correlation between BMI and difference score, positive with restriction when controlling for BMI (not significant in age and sex adjusted models).	
Meule et al., 2013	26 (26)	23.0 (2.2)	HNW		Instruction to think about immediate (NOW) vs. long-term (LATER) consequences of eating the food (3000 ms). Presentation (3000 ms) of high-calorie and low-calorie food pictures. Indication of craving	Mean amplitudes of N100 (150-200 ms) Early LPP (350–550 ms) SW (550-3000 ms).	N100: low-cal > high-cal pictures, no main effect of perspective, no interaction. Early LPP: No main effect of picture type (only in left-hemisphere high-cal > low-cal), but interaction picture type – perspective: high-cal-LATER > high-cal-NOW = low-cal-LATER = low-cal NOW. SW: high-cal-	No correlations of N100 with any of the self-report measures (food cravings, restrained eating, external eating, emotional eating, and eating disorder symptomatology). LPP amplitude (pooled across conditions) was positively correlated to emotional eating (DEBQ) in all conditions.	Comparing all conditions, lowest craving ratings were found in high-cal-LATER, but enlarged amplitudes . This was explained by higher arousal due to negative thoughts about the food.

Authors	Participants				Methods	Outcomes			Comment
	*N** EG (f)/CG (f)	Age EG/ CG	EG	CG	Paradigm and stimuli	Type of measure	Main and interaction effects	Correlations with behavioral measures	
							NOW < high-cal-LATER = low-cal-LATER = low-cal NOW.	Positive correlation between LPP and craving ratings only in high-cal-LATER condition SW amplitudes correlated with Restrained Scale in high-cal-NOW, with craving in high-cal-LATER and low-cal-NOW.	
Nijs et al., 2008	20 (16)/ 20 (16)	28.7 (6.6)/ 28.7 (6.1)	OB	HNW	Presentation (2000 ms) of high-cal food and office pictures.	Mean amplitudes of P300 (300-400 ms) LPP (400-800 ms)	No significant main effects for group. P3 and LPP larger for food than for office.	Positive correlation between self-reported increase of hunger (but not subjective craving) and posterior P3 and LPP amplitude (for food and office items). No correlation between valence/arousability ratings and P300/LPP.	No significant differences in valence and arousability ratings between obese and normal weight groups
Nijs et al., 2009	25 (25) 24 (24)	20.2 (1.9)/ 22.0 (5.2)	HEX (≥ 3.5 on DEBQ; (Van Strien et al., 1986))	LEX (<2.7 on DEBQ)	See above	Mean amplitude of P300 (300-500 ms).	Different patterns depending on electrode position, trending towards: HEX: babies = food > office; LEX: babies > food = office. Baby HEX = LEX; food: HEX > LEX.	Positive correlation between desire to eat and P300 amplitude.	Significantly higher food craving reported by HEX compared to LEX after the pictures presentation. No significant differences in valence and arousability ratings between groups
Nijs, Muris et al., 2010	26 (26)/ 40 (40)	EG1: 20.9 (3.7) EG2:	OW/OB EG1 = hungry (*n*=13)	HNW CG1 = hungry (*n*=20)	Presentation of high-cal food, emotionally pleasant (babies) and neutral (office)	Mean amplitude of P300 (300-	Food > office in all groups (not significant in obese hungry).	CG: strong positive correlations between P300	OW/OB consumed more snack-food

Authors	Participants				Methods		Outcomes		Comment
	*N** EG (f)/CG (f)	Age EG/ CG	EG	CG	Paradigm and stimuli	Type of measure	Main and interaction effects	Correlations with behavioral measures	
		22.1 (3.0)/ CG1: 22.2 (1.5) CG2: 20.6 (1.6)	EG2 = satiated (*n*=13)	CG2 = satiated (*n*=20)	pictures. Counting task.	450 ms).	Only in normal weight: hunger > satiety. Hungry condition: HNW > OB. In satiated condition trend towards higher bias in obese.	index of attention bias, subjective hunger level, food intake, and external eating. No significant correlation with P300 in OW/OB.	in a bogus taste test, but only in the hunger condition -> non-significant correlations may be due to socially desired self-report of hunger (under-report).
Nijs, Franken et al., 2010	Same sample as (Nijs et al., 2008)				Food-modified Stroop task (presentation 2000 ms) with high-cal and neutral words (office).	Mean amplitude of P2 (185-300 ms) P3 (300-550 ms).	P2: Anterior and central amplitudes to food OB > HNW P300: food > neutral; OB = HNW	Positive correlation between ERPs and food-craving in normal-weight but not in obese subjects.	
Nikendei et al., 2012	16 (16)/ CG1: 16 (16) CG2: 16 (16)	22.8 (5.2) CG1: 23.6 (5.2) CG2: 23.1 (4.2)	AN, 13 restricting, 3 purging subtype (DSM-IV)	CG1: HNW satiated CG2: HNW hungry (12 hrs without food intake)	Presentation (200 ms) of food-related and neutral words (nouns), food and neutral pictures, distracters (geometric shapes). Recognition test (half of stimuli new).	Mean amplitude of P3b (450-650ms).	P3b of correct old: food > neutral, pictures > words. AN = HNW. P3b of old/new difference: food > neutral. Main effect of group only for pictorial stimuli: AN < HNW. CG2 food > neutral; AN and CG1: food = neutral.	No correlation between ERPs and illness duration or leptin, estradiol, and cortisol serum levels, or comorbidity (anxiety, depression), nor significant differences depending on medication.	
Novosel et al., 2014	11 (11)/ 11 (11)	15.78 (1.67) / 15.7 (1.65)	AN (ICD-10)	HNW	Presentation (1-2 s) of pleasant, unpleasant, high-calorie, low-calorie and neutral pictures.	Mean amplitudes of P300 (240-380 ms) LPP (400-700 ms)	P300 high-calorie < low-calorie high-cal pictures: AN = HC low-cal pictures: AN > HC emotional pictures: AN = HC LPP high-cal < low-cal pictures high-cal		

Authors	Participants				Methods		Outcomes		Comment
	*N** EG (f)/CG (f)	Age EG/ CG	EG	CG	Paradigm and stimuli	Type of measure	Main and interaction effects	Correlations with behavioral measures	
							pictures: AN = HC low-cal pictures: AN > HC emotional pictures: AN = HC		
Sarlo et al., 2013]	33 (33)	22.5, (3.2)	HNW		Instruction word 4.5 s. Presentation (4 s) of neutral and high-cal pictures. 4 conditions: watch (neutral or food), increase and decrease (only food).	Mean amplitudes of P300 (280-400 ms) Early LPP (500-1000 ms) Late LPP (1000-1500 ms)	Food > neutral. P300: Decrease > watch food (left fronto-central). Increase > watch food (Left centro-parietal and right centro-parietal). Early LPP: larger for increase than for decrease and watch food. Late LPP: increase > watch neutral (left fronto-central); increase > decrease and watch neutral (right fronto-central, left and right parietal regions).	Pos. Correlations between Eating Disorders Inventory (Garner, Olmstead, & Polivy, 1983) subscales (fear of weight gain, binge eating and purging) and ERPs in all regions and time windows in decrease condition, but not in the other conditions. No association between BMI and ERPs.	Results for N100 and EPN were not significant, thus not reported in the article.
Svaldi et al., 2010	22 (22)/ 22 (22)	41.9 (13.9) 37.5 (13.6)	BED (DSM-IV)	OW	Presentation (6 s) of high- and low-cal food pictures. Two blocks: 1. viewing only, 2. availability: some of the pictures presented were announced for a taste test to be done afterwards.	Mean amplitude of LPP (500-800 ms) SWP (1000-6000 ms).	LPP: available > unavailable. High-cal pictures: BED > CG, low-cal BED = CG. SWP: available = unavailable. High-cal pictures: BED > CG, low-cal BED = CG.	Correlation with subjective feeling of craving/hunger not significant.	High-calorie pictures were rated more palatable than low-caloric pictures, no between group differences on this rating. BED rated high-caloric pictures more often as

Authors	Participants				Methods		Outcomes		Comment
	*N** EG (f)/CG (f)	Age EG/ CG	EG	CG	Paradigm and stimuli	Type of measure	Main and interaction effects	Correlations with behavioral measures	
									forbidden than OW.
Watson & Garvey, 2013	48 (32)	21.6 (2.3)	HNW		Go/No-Go paradigm (presentation 500 ms). Go: large green triangle, No-Go: vegetarian high-cal food and non-food (natural scenes) pictures.	Peak amplitudes of N2 (180-280 ms) P3b (280-450 ms). Mean amplitude of SW (450-800 ms). Only ERPs elicited by No-Go stimuli are reported. Difference score NoGo food – non-food.	N2: no main effect of picture stimuli, only in women higher N2 for food stimuli. P3: food > non-food and men > women. SW: food > non-food.	N2 difference score correlates positively with BMI (primarily driven by females). Positive correlation between SW and Stroop interference score (higher = more successful inhibition). No correlations between ERPs and external, emotional, restrained eating, impulsivity or behavioral activation, only for females: positive correlation between N2 and external eating and BMI.	

AN = Anorexia Nervosa; AP = Anterior Positivity; AN = Anterior Negativity; BED = Binge Eating Disorder; BMI = Body Mass Index; BN = Bulimia Nervosa; CG = Control Group; EG = Experimental Group; EPN = Early Posterior Negativity; HEE = High Emotional Eaters; HEX = High External Eaters; HNW = Healthy Normal Weight; HR = High Restrained Eaters; LEE = Low Emotional Eaters; LEX = Low External Eaters; LPP = Late Positive Potential (associated to motivational attention); LR = Low Restrained Eaters; OW/OB = Overweight/Obese; SPW = Slow Positive Wave; SW = Slow Wave

* Final sample size for EEG analysis

Supplement 5. Supplementary material for Study 6

Smells like chocolate: effects of olfaction on electrophysiological processing of visual food stimuli and craving in binge-eating and healthy individuals

S5.1 Assessment of baseline measures

S5.1.1 Olfactory capacity: The olfactory capacity of participants was measured by use of "Sniffin' Sticks" (Kobal et al., 1996; Hummel et al., 1997), a test of nasal chemosensory performance through pen-like odour dispensers. The sum of the scores from the three subtests assessing odour threshold, discrimination, and identification results in a total score, the TDI-score with a maximum of 48 points. As defined in Kobal et al., 2000 a TDI-score of 30.5 points or more indicates normosmia, a score between 16.5 and 30 points indicates reduced olfactory function termed hyposmia, and less than 16.5 points indicates functional anosmia.

S5.1.2. Chocolate craving: The *Food Chocolate-Craving Questionnaire* (FCCQ) – State and Trait Version (Rodríguez et al., 2007; Meule and Hormes, 2015) is an adaptation of the Food Cravings Questionnaire, which has been validated in English and Spanish, showing good internal consistency and excellent test-retest reliability (Cepeda-Benito et al., 2000b, 2000a). The FCCQ-T is a multidimensional measure of chocolate craving measuring on a 1-6 Likert-scale intentions to eat chocolate, positive and negative reinforcement, poor control over chocolate, preoccupation with chocolate, craving as a physiological state, emotion-dependent craving, environment-dependent craving, and guilt-loaded chocolate craving. These nine subscales result in a total score for trait chocolate craving. The state version measures momentary desire to eat chocolate, expected positive and negative reinforcement of eating chocolate, expected loss of control and hunger on a 1-5 Likert-scale.

Cronbach's alpha values for the FCCQ-T in the current sample were excellent for the total score (α =.989) and ranged from good (α =.879, positive reinforcement) to excellent (α =.970, control over chocolate) for the subscales. Internal consistency for the FCCQ-S ranged from acceptable (α =.700, positive reinforcement subscale) to excellent (α =.917, desire subscale) for the baseline assessment and from good (α =.814, positive reinforcement subscale) to excellent (α =.913, control subscale) for the post assessment.

S5.1.3. Emotion regulation: The *Difficulties in Emotion Regulation Scale* (DERS; Gratz & Roemer, 2004) is a 36-item self-report measure that assesses the individuals' typical

levels of emotion dysregulation across six domains: nonacceptance of emotional responses; difficulties pursuing goal-directed behaviours when experiencing negative emotions; difficulties controlling impulsive behaviours when experiencing negative emotions; lack of emotional awareness; limited access to emotion regulation strategies; and lack of emotional clarity. Higher values indicate greater difficulties in emotion regulation. The DERS has been found to demonstrate good reliability (Cronbach's α =.93; test–retest reliability over a period ranging from 4 to 8 weeks = .88) and adequate construct and predictive validity and is significantly associated with objective (i.e., behavioural, physiological, and neurological) measures of emotion regulation (Gratz and Roemer, 2004; Gratz et al., 2006). A Spanish version of the DERS is validated in the Spanish general adolescent population (Gómez-Simón, Penelo, & de la Osa, 2014), and in healthy and ED adults (Wolz et al., 2015). Internal consistency in the current sample for the DERS total score was α = .947 and ranged from good (α = .860, awareness) to excellent (α = .943, non-acceptance) for the subscales.

S5.1.4. Addictive eating: The *Yale Food Addiction Scale*-Spanish Version (YFAS-S; (Gearhardt et al., 2009b; Granero et al., 2014)) was used to measure addictive eating patterns using 25 items which are assigned to seven scales, referring to the seven criteria for substance dependence defined by DSM-IV (American Psychiatric Association, 2000). The diagnosis of food addiction is given when at least three of the seven criteria are fulfilled for a period of the last 12 month and the person feels significantly impaired and/or suffers due to the described behaviour. The YFAS was translated into Spanish and validated in the Spanish adult and ED population, with good validity and reliability scores (Granero et al., 2014). Internal consistency for the YFAS in the current sample was excellent (α = .968).

S5.1.5. Eating disorder pathology: The *Eating Disorders Inventory-2* (EDI-2; Garner et al., 1983) is a 91-item self-report questionnaire that assesses characteristics of ED on the dimensions drive for thinness, bulimia, body dissatisfaction, ineffectiveness, perfectionism, interpersonal distrust, interoceptive awareness, maturity fears, asceticism, impulse regulation, and social insecurity. This scale has been validated in the Spanish population (Garner, 1998), obtaining a mean internal consistency of α =.63. In the current sample, internal consistency values of the total score was excellent (α = .979).

S5.1.6. General psychopathology: The *Symptom Check-List 90 revised* (SCL-90-R; Derogatis, 1994) is a 90-item self-report questionnaire measuring psychological distress and psychopathology. The items load on nine symptom dimensions: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. The "Global Severity Index" (GSI) is a widely used index of psychopathological distress. The SCL has been validated in the Spanish population obtaining a mean internal consistency of α =.75 (Derogatis, 2002). In this sample, Cronbach's alpha for the total score (GSI) was excellent (α = .988).

S5.2. Electrophysiological Analysis

All EEG data sets were reviewed by a trained neurologist for any abnormality in the standard EEG recording. The background EEG activity and the response to eye opening were normal. No abnormal EEG activity was detected. After inspection, data was prepared for analysis using the BrainVision Analyzer software (Brain Products GmbH). First, the sampling rate was reduced to 256Hz, whereupon data was re-referenced to an average reference and filtered using a high pass cut-off of 0.1Hz (slope 24dB/oct), a low pass cut-off of 30Hz (slope 24dB/oct) and a notch-filter of 50Hz. After this, each individual data set was searched for artefacts, eye movements were corrected by help of an ocular correction independent component analysis. Two patient data sets had to be excluded from the electrophysiological analysis because of low data quality.

For ERP analyses, data sets were cut into equal epochs starting 200ms before visual stimulus onset until 1200 ms after stimulus onset and baseline corrected (-200 to 0ms). For data sets with at least 40 epochs per condition, epochs were averaged according to the four conditions, and the maximum peak amplitudes and latencies were searched using the semi-automatic mode. The N2 was measured at electrodes AFz (central N2), AF3, F1, F3 (left N2) and AF4, F2, F4 (right N2) as the amplitude and latency of the maximum negative peak in the time window 180-350 ms after stimulus onset. The time window for the LPP was set to 300-1000 ms after stimulus onset (as in (Schupp et al., 2004)) and measured as the maximum positive peak at centro-parietal electrode sites: Pz (central LPP), CP1, CP3, P1, P3, P5 (left LPP) and CP2, CP4, P2, P4, P6 (right LPP). Mean values for the respective electrodes at anterior-frontal and centro-parietal

electrode sides for each of the left and right clusters were calculated to compare lateralization effects of the N2 and LPP, respectively.

For the quantitative analysis of the electrophysiological data during odour presentation, the four 1-minute epochs of each condition (neutral and chocolate) were cut into segments of 2 seconds. The power density at frontal electrodes (Fz, FCz, F1, F2) in the frequency range of 4-8 Hz (theta) was extracted using Fast Fourier Transformation (FFT) with a Hanning Window of 10% and a resolution of 0.5Hz. The segments were then averaged for each condition separately, whereupon a mean value of the four frontal electrodes was calculated.

Table S5.1. Sample characteristics.

		HC; *n*=20		BEP; *n*=19		*p*
Age (in years)	*Mean, SD*	30.00	9.01	35.00	9.57	.101
BMI (kg/m^2)	*Mean, SD*	21.99	2.81	31.19	10.51	.001
Civil status	*Single*	16	80.0%	13	68.4%	.319
	Married	3	15.0%	6	31.6%	
	Divorced	1	5.0%	0	0.0%	
Olfactory capacity (TDI)	*Mean, SD*	34.99	2.88	33.72	1.70	.105

BEP = binge-eating patients; BMI = body mass index; HC = healthy controls; SD = standard deviation; TDI = Threshold Discrimination and Identification Score of the "Sniffin' Stick" Test.

Table S5.2. Comparison of clinical variables between groups.

	HC		BEP		
	Mean	SD	Mean	SD	p
Trait Chocolate Craving (FCCQ-T total)	68.15	25.27	132.38	55.50	<.001
Intentions to eat chocolate	4.95	2.33	9.75	4.30	<.001
Positive reinforcement	11.75	5.00	15.88	6.76	.043
Negative reinforcement	5.40	3.00	9.94	5.18	.002
Poor control over chocolate	10.00	5.22	21.94	9.35	<.001
Preoccupation with chocolate	8.63	2.09	19.63	11.06	<.001
Craving as a physiological state	7.25	2.57	13.13	6.17	<.001
Emotion-dependent craving	7.63	3.56	14.81	6.40	<.001
Environment-dependent craving	8.58	4.17	15.38	6.79	.001
Guilt-loaded chocolate cravings	4.35	2.21	11.94	4.33	<.001
Emotion regulation (DERS total)	64.47	20.49	117.59	22.47	<.001
Non-acceptance of emotions	10.79	5.49	19.29	5.58	<.001
Goal-directed behaviour	11.11	3.14	17.94	5.45	<.001
Impulse control	8.89	3.07	18.24	6.36	<.001
Awareness of emotions	12.11	3.97	19.29	4.51	<.001
Emotion regulation strategies	12.68	5.45	27.76	7.11	<.001
Emotional clarity	8.89	3.49	15.06	3.82	<.001
Food Addiction (YFAS criteria fulfilled)	1.45	0.60	5.94	1.26	<.001
Eating pathology (EDI-2 total)	24.11	22.24	115.26	38.77	<.001
General Psychopathology (SCL-90R: GSI)	0.37	0.26	1.89	0.67	<.001

BEP = binge-eating patients; DERS = Difficulties in Emotion Regulation Questionnaire; EDI-2 = Eating Disorders Inventory-2; FCCQ-T = Food Chocolate Craving Questionnaire- T; HC = healthy controls; SCL-90R = Symptom Check List – Revised; SD = standard deviation; YFAS = Yale Food Addiction Scale

Table S5.3. Means (M) and standard deviations (SD) for self-reported momentary craving (visual analogue scale from 0-100) in response to picture stimuli preceded by either neutral or chocolate odour in healthy controls (HC) and binge-eating patients (BEP).

Odour prime	Picture type	HC		BEP	
		M	SD	M	SD
Neutral	Neutral	29.70	22.38	36.39	27.75
	Chocolate	44.50	27.42	57.08	33.30
Chocolate	Neutral	33.60	22.26	37.00	27.90
	Chocolate	49.43	27.67	62.66	31.52

* Mean values for each condition averaged over the two blocks are shown.

Table S5.4a. Matrix for correlations of clinical variables with subjective and electrophysiological dependent variables in HC.

	VAS Rating 1 (Odour)				VAS Rating 2 (Pictures)				LPP amplitude (μV)				N2 amplitude (μV)			
	NN	NC	CN	CC	NN	NC	CN	CC	NN	NC	CN	CC	NN	NC	CN	CC
Trait Chocolate Craving (FCCQ-T total)	.22	.24	.40	.31	.24	.23	.38	.29	.15	-.10	-.11	.07	.22	.08	.21	.10
Intentions to eat chocolate	.19	.07	.30	.15	.23	.18	.23	.08	.02	-.16	-.19	-.06	.20	.11	.22	.15
Positive reinforcement	.21	.27	.27	.28	.10	.14	.39	.22	-.03	-.11	-.08	-.12	-.08	.00	.04	-.03
Negative reinforcement	.33	.30	***.48***	.37	***.41***	.39	***.43***	.33	-.12	-.18	-.32	-.13	-.12	-.05	.04	.05
Poor control over chocolate	.10	.13	.30	.25	.13	.11	.27	.25	.32	-.01	.03	.23	***.44***	.24	.35	.22
Preoccupation with Chocol.	.11	.23	.39	.36	.12	.27	.38	.36	.14	-.16	-.05	.08	.30	.27	.28	.20
Craving as a physiological state	.00	.11	.22	.20	.07	.09	.24	.15	.35	.01	.09	.23	.38	.22	.33	.16
Emotion-dependent craving	.40	.33	***.46***	.30	.35	.25	.40	.32	-.03	-.15	-.28	-.06	.01	-.11	.02	-.02
Environment-dependent craving	.10	.12	.30	.21	.18	.18	.26	.24	.24	-.12	-.09	.15	.28	.03	.18	.05
Guilt-loaded chocolate cravings	.13	.11	.29	.24	.19	.17	.23	.22	.14	-.11	-.13	.10	.35	.16	.29	.22
Emotion regulation (DERS total)	.26	.27	.40	.39	.28	***.41***	.33	.36	.23	.11	.10	.28	***.40***	.22	.29	.26
Non-acceptance of emotions	.17	.17	.34	.32	.26	.37	.29	.31	.22	.00	.05	.21	***.48***	.31	.36	.34
Goal-directed behaviour	***.56***	***.46***	***.55***	***.48***	***.55***	***.68***	***.54***	***.41***	-.02	.00	.03	.03	.06	.12	.09	.19
Impulse control	.14	.23	.29	.37	.15	.27	.25	.32	.21	.07	.07	.26	***.41***	.30	.34	.29
Awareness of emotions	-.04	.07	.12	.16	-.06	.09	.03	.15	.08	.20	.07	.22	.09	-.07	.05	.00
Emotion regulation strategies	.29	.30	***.42***	.35	.35	.39	.34	.35	***.48***	.18	.20	***.48***	***.59***	.24	.38	.28
Emotional clarity	.20	.16	.25	.25	.14	.28	.22	.23	.01	.06	.03	.05	.18	.13	.16	.16
Food Addiction (YFAS)	.21	.16	.23	.13	.24	.20	.14	.22	.12	***.54***	.23	.19	.23	.31	.38	***.41***
Eating pathology (EDI-2)	.13	.22	.28	.27	.10	.11	.15	.32	***.42***	.30	.24	***.48***	.39	.14	.17	.11
General Psychopathology (SCL-90R: GSI)	.31	.24	***.44***	.38	.31	***.52***	.35	.38	-.03	.10	.07	.06	.29	.37	.24	***.40***

NN: neutral odour prime –neutral pictures, NC: neutral odour prime –chocolate pictures, CN: chocolate odour prime - neutral pictures, CC: chocolate odour prime –chocolate pictures.

High correlation coefficients (r >.3) are indicated in bold, very high coefficients are indicated in bold italic (r >.4).

Table S5.4b. Matrix for correlations of clinical variables with subjective and electrophysiological dependent variables in BEP.

	VAS Rating 1 (Odour)				VAS Rating 2 (Pictures)				LPP amplitude (μV)				N2 amplitude (μV)			
	NN	NC	CN	CC	NN	NC	CN	CC	NN	NC	CN	CC	NN	NC	CN	CC
Trait Chocolate Craving (FCCQ-T total)	.07	-.11	***.57***	***.42***	-.22	***.55***	-.09	***.48***	.09	.04	.29	.21	-.11	-.29	-.06	-.08
Intentions to eat chocolate	.06	-.03	***.63***	***.46***	-.17	***.58***	-.02	***.54***	.10	.07	.30	.24	-.02	-.16	.07	.03
Positive reinforcement	-.07	-.23	***.48***	.31	-.33	***.48***	-.23	***.43***	-.10	-.14	.10	.01	-.27	***-.44***	-.27	-.23
Negative reinforcement	.02	-.11	***.50***	.39	-.23	***.49***	-.20	***.49***	-.14	-.33	.00	-.21	-.31	***-.48***	-.23	-.30
Poor control over chocolate	.10	-.04	***.60***	***.45***	-.12	***.56***	.00	***.47***	.09	.12	.32	.25	-.09	-.29	-.02	-.07
Preoccupation with chocolate	.17	.01	***.52***	***.40***	-.15	***.48***	.00	***.42***	.18	.09	.35	.29	-.03	-.17	.01	.01
Craving as a physiological state	.06	-.13	***.50***	.39	-.28	***.46***	-.12	.39	.09	.05	.33	.31	-.01	-.23	-.09	-.05
Emotion-dependent craving	.01	-.19	***.47***	.34	-.20	***.50***	-.14	***.44***	.25	.20	.35	.30	-.02	-.17	.09	.05
Environment-dependent craving	-.01	-.19	***.53***	.39	-.27	***.53***	-.13	***.46***	.07	.11	.31	.27	-.06	-.29	-.04	-.05
Guilt-loaded chocolate cravings	.17	-.07	***.59***	.43	-.13	***.61***	.02	***.50***	.03	-.02	.14	.05	-.26	-.40	-.19	-.21
Emotion regulation (DERS total)	.36	***.41***	***.40***	.22	.31	.25	***.40***	.34	***.49***	.33	***.49***	***.40***	.29	.37	.39	***.46***
Non-acceptance of emotions	.26	.32	.30	.16	.17	.13	.28	.24	.30	.20	.36	.35	.38	.37	.25	***.42***
Goal-directed behaviour	.34	.31	.35	.25	.21	.21	.28	.31	***.42***	.16	.37	.33	.39	***.41***	***.46***	***.47***
Impulse control	.17	.28	.08	-.03	.28	-.03	.27	.00	***.52***	.30	***.44***	.37	.10	.11	.08	.19
Awareness of emotions	-.22	-.13	.04	-.06	-.06	.05	-.15	.08	.23	***.45***	***.41***	.40	.10	.11	.30	.18
Emotion regulation strategies	***.41***	***.46***	.39	.21	.37	.29	***.50***	.33	.22	.02	.05	-.07	-.01	.22	.28	.29
Emotional clarity	***.51***	.39	***.60***	***.49***	.23	***.51***	***.41***	***.53***	.19	.24	.35	.28	.24	.24	.21	.25
Food Addiction (YFAS criteria fulfilled)	.14	.04	.17	.17	-.07	.18	***.00***	.18	***.41***	.26	***.48***	.39	.09	-.03	-.10	-.04
Eating pathology (EDI-2 total)	***.51***	***.47***	.33	.25	.32	.25	***.42***	.28	.37	.15	***.42***	.28	.03	.08	-.05	.03
General Psychopathology (SCL-90R: GSI)	.33	***.44***	***.50***	.22	.30	.36	***.44***	***.42***	.15	.07	.17	.04	-.06	.11	.11	.18

NN: neutral odour prime –neutral pictures. NC: neutral odour prime –chocolate pictures. CN: chocolate odour prime - neutral pictures. CC: chocolate odour prime –chocolate pictures.

High correlation coefficients (r >.3) are indicated in bold. Very high coefficients are indicated in bold italic (r >.4).

Table S5.5. Matrix of correlations for ERP amplitudes with VAS ratings of momentary craving and state craving (FCCQ-S) measured at pre-experiment baseline.

			VAS Rating 2 (Pictures)				FCCQ-S					
		Condition	NN	NC	CN	CC	Negative reinforcement	Desire	Positive reinforcement	Lack of control	Hunger	Total score
HC	LPP	NN	.23	.29	.30	.24	***.43***	.38	.39	.38	.38	***.48***
		NC	.25	.32	.27	.26	.34	.29	.26	.12	***.40***	.35
		CN	.23	.30	.23	.26	.36	.27	.37	.22	.36	.39
		CC	.29	***.41***	.38	.37	***.40***	.34	.30	.28	.35	***.41***
	N2	NN	.12	.12	.21	.18	***.65***	***.63***	***.55***	***.57***	***.55***	***.72***
		NC	.19	.21	.23	.32	***.56***	***.56***	***.60***	***.45***	***.63***	***.69***
		CN	.13	.14	.20	.22	***.63***	***.66***	***.64***	***.52***	***.67***	***.76***
		CC	.31	.31	.34	***.40***	***.62***	***.66***	***.63***	***.41***	***.70***	***.74***
BEP	LPP	NN	-.02	-.39	-.15	-.33	.19	-.33	-.05	-.07	.16	-.09
		NC	-.14	***-.41***	-.26	-.35	.26	-.25	-.14	-.06	.19	-.03
		CN	-.13	-.28	-.24	-.21	.28	-.24	-.12	.19	.14	.03
		CC	-.22	-.32	-.31	-.29	.25	-.30	-.21	.13	.28	.00
	N2	NN	-.22	-.24	-.29	-.09	.06	-.27	***-.41***	.02	.33	-.12
		NC	-.19	***-.41***	-.21	-.25	.09	-.17	-.32	-.20	.22	-.15
		CN	.06	-.04	-.05	.13	.12	.15	-.10	.02	.28	.15
		CC	-.21	-.32	-.21	-.19	.04	-.01	-.25	-.14	.16	-.07

BEP = binge-eating patients; HC = healthy controls;

NN: neutral odour prime – neutral pictures. NC: neutral odour prime – chocolate pictures. CN: chocolate odour prime - neutral pictures. CC: chocolate odour prime – chocolate pictures.

High correlation coefficients (r >.3) are indicated in bold. Very high coefficients are indicated in bold italic (r >.4).

Curriculum Vitae

Barcelona, 21st of September 2016

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Personal Information

Date of birth:	28th of October, 1986
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Education

Since 09/2013:	**PhD student** in Clinical and Experimental Neurosciences, Faculty of Medicine, University of Barcelona (Title: *"Emotions in eating disorders: The interplay of emotion regulation and inhibitory control in appetite and eating behaviour";* Supervisor: Dr. Fernando Fernández-Aranda).
11/2015-07/2016:	Postgraduate course in Group dynamics and Leadership (University of Barcelona)
10/2010- 07/2013:	**Master of Science** in Clinical Psychology, Neuroscience and Rehabilitation at Albert-Ludwigs-University in Freiburg (overall average grade: 1.2 equates to UK first class). Master thesis on "*The Effects of Emotion Regulation on Information Processing in High Restraint Eaters".*
09/2011- 06/2012:	**Erasmus** studies at Université de Toulouse II, Le Mirail (France).
10/2007- 08/2010:	**Bachelor of Science** in Psychology at University of Cologne (overall average grade: 1.3 equates to UK first class). Bachelor thesis on "*Behavioural Adjustments Guided by Information Content of Action Outcomes*".
27.06.2006:	Abitur (German diploma from secondary school, overall average grade: 1.2 equates to UK A level)
1993- 2006:	Primary and secondary school at Freie Georgenschule Reutlingen.

Relevant Research Experience

Since 09/2013: Doctoral researcher, **Eating Disorders Unit of Bellvitge University Hospital, Institut d'Investigació Biomèdica de Bellvitge (IDIBELL),** L'Hospitalet de Llobregat, Barcelona (Spain).

09/2015-11/2015: Research stay with Dr. Kate Tchanturia, Eating Disorders Unit, Psychological Medicine, **Kings College London**.

05/2013- 07/2013: **Tutor in psychological counselling for medical students,** University Hospital Freiburg (Germany), Department for Psychosomatic Medicine and Psychotherapy.

01/2013- 08/2013: **Student Assistant, Department for Psychosomatic Medicine and Psychotherapy** at the University Hospital of Freiburg (Germany).

07/2012- 08/2012: Internship in Psychotherapy, **Rehabilitation Clinic for Internal Medicine and Psychosomatics, Glottertal** (Germany).

02/2011- 04/2011: **Internship in clinical child psychology,** University Hospital of Cologne (Germany) at the **Department for Paediatrics**.

03/2009- 09/2010: Student assistant, **Max-Planck-Institute for Neurological Research**, Cologne (Germany).

03/2010- 04/2010: Internship in research, **Victoria University of Wellington** (New Zealand), laboratory for cognitive and behavioural neuroscience research mainly in aphasia.

11/2008- 02/2009: Internship, **University Hospital of Cologne** (Germany), **Department for Neurological Psychology.**

Publications

Jiménez-Murcia, S., Granero, R., **Wolz, I.**, Baño Alcazar, M., Mestre-Bach, G., Steward, T., … & Fernandez-Aranda, F. (Submitted). Food Addiction in Gambling Disorder: Frequency and Clinical Outcomes. *Special Issue Frontiers in Psychology*, 2017.

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Research Projects

Collaboration in **research project** granted by Ministerio de Sanidad y Consumo (**FIS**). Title: "Neurocognition and emotional regulation in Extreme Weight Conditions: A study of Brain Activity and cognitive changes associated with serios video game intervention" (PI14/ 290). Principal investigator: F. Fernández-Aranda, Servicio de Psiquiatría, Hospital Univ. de Bellvitge, Barcelona. Date: 01/2015-12/2017.

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Scholarships

Pre-doctoral scholarship "Grants for the recruitment of early-stage research staff (FI)", Secretariat of Universities and Research, Ministry of Economy and Knowledge, of the Catalonian Government „**Agència de Gestió d'Ajuts Universitaris i de Recerca**" (2014FI_B 00372).