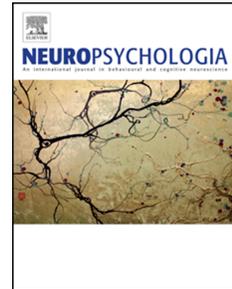


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Impaired emotional biases in visual attention after bilateral amygdala lesion

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**CRediT author statement**

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**Impaired emotional biases in visual attention after bilateral amygdala lesion**

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**Abstract**

It is debated whether the amygdala is critical for the emotional modulation of attention. While some studies show reduced attentional benefits for emotional stimuli in amygdala-damaged patients, others report preserved emotional effects. Various factors may account for these discrepant findings, including the temporal onset of the lesion, the completeness and severity of tissue damage, or the extent of neural plasticity and compensatory mechanisms, among others. Here, we investigated a rare patient with focal acute destruction of bilateral amygdala and adjacent hippocampal structures after late-onset herpetic encephalitis in adulthood. We compared her performance in two classic visual attention paradigms with that of healthy controls. First, we tested for any emotional advantage during an attentional blink task. Whereas controls showed better report of fearful and happy than neutral faces on trials with short lags between targets, the patient showed no emotional advantage, but also globally reduced report rates for all faces. Second, to ensure that memory disturbance due to hippocampal damage would not interfere with report performance, we also used a visual search task with either emotionally or visually salient face targets. Although the patient still exhibited efficient guided search for visually salient, non-emotional faces, her search slopes for emotional versus neutral faces showed no comparable benefit. In both tasks, however, changes in the patient predominated for happy more than fear stimuli, despite her normal explicit recognition of happy expressions. Our results provide new support for a causal role of the amygdala in emotional facilitation of visual attention, especially under conditions of increasing task-demands, and not limited to negative information. In addition, our data suggest that such deficits may not be amenable to plasticity and compensation, perhaps due to sudden and late-onset damage occurring in adulthood.

**Keywords:** emotion; attention; amygdala; attentional blink; visual search; medial temporal lobe

## 1. Introduction

Emotionally salient stimuli tend to enter, capture, or hold attention to a greater degree than non-emotional stimuli (Anderson, 2005; Arnell, Killman, & Fijavz, 2007; Barnard, Scott, Taylor, May, & Knightley, 2004; Pourtois, Schettino, & Vuilleumier, 2012; West, Anderson, & Pratt, 2009). This prioritization by emotion signals is believed to occur preattentively and involuntarily, allowing for rapid adaptive behavioral responses to take place (Schmidt-Daffy, 2011; see Dominguez-Borras, Saj, Armony, & Vuilleumier, 2012 and Vuilleumier, 2005 for reviews). It is still debated, however, whether the amygdala has a causal role in this phenomenon. This complex structure (with several nuclei) is richly connected to the sensory systems (see Abivardi & Bach, 2017; Amaral, Bauman, et al., 2003; Freese & Amaral, 2006; Tamietto, Pullens, de Gelder, Weiskrantz, & Goebel, 2012) and indirectly connected to the attention and arousal systems (Dringenberg, Saber, & Cahill, 2001; Sarter, Hasselmo, Bruno, & Givens, 2005; Vuilleumier, 2005), supporting the idea that it may act as a computational hub that rapidly allocates processing resources towards emotional information via multiple routes. Furthermore, amygdala dysfunction (Vuilleumier, Richardson, Armony, Driver, & Dolan, 2004) or deactivation (Hadj-Bouziane, et al., 2012) leads to reduced neural responses of visual cortex to emotionally significant stimuli. However, other cortico-subcortical pathways may also subserve such adaptive attentional effects of emotion, e.g., via thalamic or fronto-parietal networks, perhaps with a more indirect role of the amygdala (Pessoa & Adolphs, 2010; Vuilleumier, 2005).

To date, human lesion studies have provided conflicting evidence in this regard. On one hand, an early study (Anderson & Phelps, 2001) reported that patients with damage to the left amygdala after temporal-lobe resection did not show any affective prioritization when performing an attentional blink paradigm with emotional words, unlike healthy individuals. In attentional blink tasks, the detection of a visual target is impaired when presented shortly (i.e. with a short lag) after a first target appearing among distractors in a rapid serial visual presentation (RSVP; Raymond, Shapiro, & Arnell, 1992). However, it is believed that, during the “blink” effect, initial target processing and detection (possibly preconscious) may remain intact before information reaches awareness and memory processes, allowing for successful stimulus report (Bach, Schmidt-Daffy, & Dolan, 2014; Chun & Potter, 1995; Dux, Ivanoff, Asplund, & Marois, 2006). As a consequence, in healthy subjects, residual processing of sensory inputs prior to attentional selection may still extract their emotional value through rapid and coarse analysis in the amygdala and account for a reduction (or even suppression) of the attentional blink effect when the second target is emotional (Anderson, 2005; de Jong, Koster, van Wees, & Martens, 2009; De Martino, Kalisch, Rees, & Dolan, 2009; Fox, Russo, & Georgiou, 2005; Keil & Ihssen, 2004; Luo, Feng, He, Wang, & Luo, 2010; Maratos, Mogg, & Bradley, 2008; Milders, Sahraie, Logan, & Donnellon, 2006; Schwabe, et al., 2011); note, however, that evidence for emotionally positive targets is less clear than for emotionally negative targets (Bach, et al., 2014; de Jong, et al., 2009; Fox, et al., 2005; Mack, Pappas, Silverman, & Gay, 2002; Miyazawa & Iwasaki, 2010). Accordingly, this reduction of the blink effect by emotion was associated with increased response in the amygdala during this task (Schwabe, et al., 2011). Thus, emotion benefits on the attentional blink might be driven by modulatory influences from the amygdala on sensory areas dedicated to the

processing of visual inputs, through direct (e.g. feedback connections) and/or indirect (e.g. neuromodulatory) pathways (Hadj-Bouziane, Bell, Knusten, Ungerleider, & Tootell, 2008; Hadj-Bouziane, et al., 2012; Vuilleumier, Armony, Driver, & Dolan, 2001, 2003; Vuilleumier, et al., 2004).

In the seminal work by Anderson & Phelps (2001) reduced attentional blink for emotional compared to neutral words was not observed in patients with left amygdala damage, a lateralized deficit in affective prioritization possibly related to the use of linguistic stimuli (Strange, Henson, Friston, & Dolan, 2000). These authors concluded that the amygdala may play a causal role in boosting attention to emotional inputs and promoting better access to awareness. However, other lesion studies have challenged this idea, suggesting instead that the amygdala is not essential for such preattentive emotional enhancement of perception. For instance, Tsuchiya et al. (2009) reported that a patient with bilateral amygdala lesion, subsequent to progressive calcification (Urbach-Wiethe syndrome), still showed better detection of fearful than neutral (or happy) faces, not only in visual masking or (interocular) continuous flash suppression, but also in a visual search task with parametrically morphed neutral and fearful faces. In visual search paradigms, the detection of a visual target among an array of distractors is usually quicker for emotional than for neutral targets (Flykt & Caldara, 2006; Gerritsen, Frischen, Blake, Smilek, & Eastwood, 2008; Ohman, Flykt, & Esteves, 2001), a phenomenon also associated with increased amygdala response (Mohanty, Egnér, Monti, & Mesulam, 2009). These authors concluded that the amygdala might contribute to visual recognition of fear expressions in faces (Adolphs, Tranel, Damasio, & Damasio, 1994) and to oculomotor exploration of faces (Adolphs, et al., 2005) but not to preattentive processing and guidance (Tsuchiya, et al., 2009). Another study in two patients with bilateral amygdala lesions, again due to Urbach-Wiethe disease, also found an intact facilitation of detection for emotional versus neutral words during an attentional blink task (Bach, Talmi, Hurlmann, Patin, & Dolan, 2011). To reconcile discrepant findings, these authors speculated (among other potential factors, see below) that amygdala lesions occurring early in life or evolving progressively (as in Urbach-Wiethe disease) might lead to compensatory mechanisms and neural plasticity in alternative structures, whereas late-onset damage impairment (such as temporal lobe resection in adulthood) would abolish modulatory processes mediating automatic emotion prioritization (Bach, et al., 2011).

Nevertheless, other findings suggest that lesion-onset may not be sufficient to explain all divergent findings, or that it may be difficult to determine in some cases (e.g. sclerosis). For instance, epileptic patients with unilateral (right or left) amygdala dysfunction following temporal lobe resection (and therefore with presumably late damage-onset) may still exhibit intact attentional biases towards pictures with emotional content (spiders) during visual search (Piech, McHugo, Smith, Dukic, Van Der Meer, Abou-Khalil, & Zald, 2011), or towards pictures with aversive and erotic content during attentional blink conditions (Piech, McHugo, Smith, Dukic, Van Der Meer, Abou-Khalil, Most, et al., 2011). In patients with surgical removal or lobectomy for treatment of epilepsy, the causal link with acquired amygdala damage may be uncertain, given that amygdala lesions could have originated long before the time of surgery (Bach, et al., 2011). Therefore, further evidence in patients with more defined acute onset lesions is necessary to confirm this hypothesis.

Behavioral outcomes might also be conditioned by lesion extension (Bach, et al., 2011). Notably, those patients showing impaired emotional biases in attentional blink (Anderson & Phelps, 2001) had large temporal lobe damage that encompassed the inferior temporal cortex, including white matter in the ventral visual stream or the hippocampus, whereas those with intact emotional effects had no or more limited destruction of inferior temporal/hippocampal regions (Bach, et al., 2011; Piech, McHugo, Smith, Dukic, Van Der Meer, Abou-Khalil, Most, et al., 2011; Tsuchiya, et al., 2009). As regards hippocampal damage, because attentional blink performance depends on joint resources from attention and working-memory to report successive targets appearing in RSVP (Johnston, Linden, & Shapiro, 2012), and working memory depends on hippocampal function (Axmacher, et al., 2010; Axmacher, et al., 2007; Ben-Yakov, Rubinson, & Dudai, 2014; Fuentemilla, Penny, Cashdollar, Bunzeck, & Duzel, 2010; Poch, Fuentemilla, Barnes, & Duzel, 2011; Ranganath & D'Esposito, 2001), it is possible that patients studied by Anderson & Phelps (2001) partly owed their loss of attentional-blink effects to concomitant hippocampal lesion.

Finally, discrepancies among results may even occur within the same patients, further evidencing that factors other than lesion-onset or lesion extension, such as the task or stimuli used, may impact the findings. For instance, whereas early-onset damage patients in Bach, et al. (2011) showed intact emotional biases in attentional blink with words, these patients exhibited a significant emotional impairment in a face-in-the-crowd task with angry versus happy faces (Bach, Hurlemann, & Dolan, 2015). However, word stimuli (Anderson & Phelps, 2001; Bach, et al., 2011) may limit the efficacy of automatic emotional biases in attention, and/or increase its variability across patients, given that the perceptual analysis and emotional processing of these stimulus categories rely on complex, high-level cognitive functions. In contrast, facial expression might be better suited for limiting the role of high-level cognitive processes in extracting emotional meaning from stimuli. Moreover, given that the amygdala is highly sensitive to faces in general (Morris, et al., 1998; Vuilleumier & Pourtois, 2007), these stimuli may offer a reliable tool to test for emotional biases on attention, rather than sceneries or objects, whose emotional meaning derives from more complex, multi-element layouts (Piech, McHugo, Smith, Dukic, Van Der Meer, Abou-Khalil, Most, et al., 2011; Piech, McHugo, Smith, Dukic, Van Der Meer, Abou-Khalil, & Zald, 2011). In addition, recent intracranial EEG recordings from human amygdala indicate fast responses to emotional faces selectively, but more delayed responses to emotional scenes (Mendez-Bertolo, et al., 2016). Finally, it has been suggested that the role of the amygdala in preattentive emotion processing may be more critical for emotionally negative stimuli than for positive inputs (Bach, et al., 2015), given its pivotal function in fear or threat-related processing (LeDoux, 2000). Complying with this hypothesis, no clear evidence for impaired emotional biases after amygdala lesion has been provided in studies using positive emotional stimuli (Piech, McHugo, Smith, Dukic, Van Der Meer, Abou-Khalil, Most, et al., 2011; Bach, et al., 2015; Tsuchiya, et al., 2009).

To address these issues, we studied a rare patient (HE1) with severe lesions affecting the bilateral amygdala and right hippocampus after adult herpetic encephalitis. As damage occurred with sudden onset in late adulthood, neural compensatory mechanisms should be limited or absent in this patient. Given that previous literature suggests a possible role of the amygdala in perceptual

recognition of emotional expressions, particularly of fear (Adolphs, et al., 1994), unrelated to preattentive emotion detection (Tsuchiya, et al., 2009), we first examined our patient's recognition of facial expressions relative to healthy subjects. Then, we tested for attentional biases in her detection of emotional faces (fearful or happy), relative to neutral faces, in comparison with the performance of a group of healthy controls during two different paradigms. We employed both an attentional blink task (Raymond, et al., 1992) and a visual search paradigm (Wolfe, 1994; 1998), where emotional benefits have been consistently observed in studies with normal participants (Anderson, 2005; De Martino, et al., 2009; Eastwood, Smilek, & Merikle, 2001; Gerritsen, et al., 2008; Keil & Ihssen, 2004; Schwabe, et al., 2011). In visual search studies, attentional efficiency is often measured as the slope resulting from increasing response times as a function of the increasing number of visual items in the display. Thus, as an index of more efficient guided search towards the targets regardless of increasing task-demands, slopes are typically shallower for salient stimuli (both emotional [e.g. Eastwood, et al., 2001; Gerritsen, et al., 2008] and non-emotional [e.g. Wolfe, 1994; 1998]) than for non-salient stimuli. Importantly, by using this second task, we could ensure that any memory disturbance due to hippocampal damage would not be sufficient to account for impaired performance, since visual search is substantially less dependent on working memory than attentional blink (Woodman, Vogel, & Luck, 2001). Specifically, we assumed that, if the patient showed impaired emotional biases in visual search (in addition to attentional blink), such loss would be most likely to result from the amygdala lesion, despite concomitant damage to neighboring hippocampal structures. In turn, this would suggest that the amygdala plays a critical role in preattentive processing of emotion.

## **2. Methods**

### **2.1. Participants**

Our patient is a right-handed female (HE1), 53 year-old at the time of testing, who suffered bilateral lesions in the temporal lobe after an acute herpes simplex encephalitis, diagnosed 15 years prior to the current study. Structural MRI acquired at the time of testing showed bilateral focal damage in the temporal lobes, more extensive over the right side (Fig. 1), destroying the amygdala region totally in the right hemisphere, and almost totally in the left hemisphere (Fig. 1). Remaining tissue on the latter side corresponded to the ventral posterior basal amygdala, a subregion reportedly connected to the most rostral areas of the ventral visual cortex (but not directly to early visual areas; Amaral, Behniea, & Kelly, 2003). The exact functional role of this subregion is unknown in humans, but research in mice has suggested its involvement in triggering motoric defensive responses (Pardo-Bellver, Cadiz-Moretti, Novejarque, Martinez-Garcia, & Lanuza, 2012), or mediating anxiety behaviors (Adhikari, et al., 2015; Amano, Duvarci, Popa, & Pare, 2011). In the left hemisphere, the lesion also extended to the anterior part of the hippocampus and to the entorhinal and perirhinal cortices. In the right hemisphere, destruction was more extensive, reaching not only the hippocampus, parahippocampal gyrus,

entorhinal and perirhinal cortices, but also substantial cortical areas in the inferior temporal lobe and anterior pole. A small portion of the right anterior and ventral insula was also partially destroyed.

Residual clinical symptoms included occasional epileptic seizures that were stabilized with medication, discontinued after a few years, and severe memory disturbances predominating for non-verbal material (e.g. blocks) but extending to verbal material as well (single words, names; Table 1). The patient had no other major cognitive deficit and could work normally as a biology assistant and later teacher. She scored normally in tasks of Theory of Mind (Table 1), performed flawlessly on recognition of facial expressions across various categories (including happy) except for fearful expressions, for which recognition was significantly lower than controls (Table 2). Her response speed for correct emotion categorization in this task was similar to controls (or even numerally faster) for all emotion categories (see Table 2). All these deficits accord with those commonly observed in other encephalitic patients whose amygdala is affected (Broks, et al., 1998). In addition, our patient reported a subjective lack of bodily reactions in stressful conditions, and blunting of emotional feelings and motivation. However, her scores for the State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983) and the Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) showed relatively low state-anxiety levels (standard score: 40; centile 24 for standard population), but high trait-anxiety levels (standard score 85; centile 100 for standard population), as well as medium to moderate depression levels (score 12 of 39). The patient had a higher (university) education degree and showed very good understanding of instructions for all tasks given to her on the experiment session. As a control group to be compared with the patient, we recruited 20 healthy right-handed females (40-77 years, mean 62.3,  $\pm 10.7$ ) from the normal population, with a similar education level (12 with university degree and 8 with secondary education).

(Please insert Figure 1 about here)

(Please insert Table 1 about here)

(Please insert Table 2 about here)

## **2.2. Stimuli and procedure**

During both tasks, participants sat in a quiet dimly lit room, ~50 cm from the screen. The study procedure was approved by the local ethics committee and conducted according to the declaration of Helsinki. Before the experimental tasks, all subjects gave their informed consent to participate and completed the STAI (anxiety) and BDI (depression) questionnaires. Anxiety scores were within the normal range in most of the controls (STAI-state standard score:  $M=45.05$ ;  $SD=6.41$ ; mean centile 38.86; STAI-trait standard score:  $M=56.3$ ;  $SD=14.98$ ; mean centile 72.86), although 3 out of 20 showed high state-anxiety (over centile 65) and 11 out of 20 had relatively high trait-anxiety (over centile 65). On the BDI scale, 14 out of 20 subjects had no depression, while 3 had minimal depression and 3 mild to moderate depression (scores:  $M=2.85$ ;  $SD=3.66$ ; where 0 to 3 indicates no

depression). Finally, controls reported to have low stress levels at the moment of the experiment (mean 2.45,  $\pm 1.7$  on a scale from 1 to 10).

### **2.2.1. Attentional blink task**

The task was a modified version of the rapid serial visual presentation (RSVP) paradigm to examine the effects of emotional face expression on the attentional blink (Anderson, 2005; De Martino, et al., 2009; Keil & Ihssen, 2004; Schwabe, et al., 2011). Basic parameters of the paradigm were derived from previous studies testing the attentional blink with emotional words in amygdala patients (Anderson & Phelps, 2001; Bach, et al., 2011), and then adapted to the use of faces. Timing parameters and distractor stimuli were chosen through preliminary piloting in 24 healthy young students (details not shown). The task was controlled with the toolbox Cogent 2000 v1.32 (*Wellcome Department of Imaging Neuroscience*, London, UK) running on Matlab R2009b. All stimuli were pictures of faces selected from the NimStim (Tottenham, et al., 2009) and the Karolinska Directed Emotional Faces databases (Lundqvist, Flykt, & Öhman, 1998). Pictures had a resolution of 406 x 525 pixels and were presented in greyscale. They had similar luminance levels overall, as carefully controlled with Matlab, and similar feature position (eye-mouth) across all faces. The first target stimuli (T1) consisted of 24 different faces with a neutral expression (50% males). The second target (T2) stimuli consisted of 24 different faces (50% males) with either a neutral (Neutral condition), fearful (Fear condition), or happy (Happy condition) expression. All 3 emotional expressions shown in T2 faces were displayed by the same 24 actors, but these actors were different from those included in the set of T1 faces. Finally, distractor stimuli consisted of another 17 neutral faces that were either inverted or scrambled using Matlab. As pointed above, these 2 types of distractors were chosen based on pilot tests demonstrating that they were the most efficient in the elicitation of attentional blink. Again, these 17 faces depicted different actors in the T1 and the T2 target stimuli. On every trial, all faces were randomly selected within their corresponding stimulus category. Stimuli were always presented for 70 ms at the center of the screen, on a light grey background, with an interstimulus interval (ISI) of 30 ms (Fig. 2).

Each trial started with a central fixation cross presented for 950 ms on a light grey background; then, either 5, 10, or 15 (on a random basis) distractors appeared in rapid succession, followed by a T1 face. After the T1, a new series of distractors was displayed, consisting of either 1 or 2 stimuli (on a random basis; ShortLag condition), or 6 or 7 stimuli (on a random basis; LongLag condition). Then, the T2 face was presented, followed by 5 final distractors. At the end of the trial, subjects were presented with two response screens, one after the other, asking them to report whether they had seen the first and second upright faces in the distractor stream and their apparent sex (male or female). Subjects (patients or controls) were instructed to indicate if they saw a male or a female face by pressing a button with either their right index or middle finger, respectively (counterbalanced across subjects in the control group; Fig. 2) but to withhold responding when they failed to see the face (i.e., they were not required to guess the gender when missing a face target).

Each of the two questions remained on screen until the participant responded, or after a maximum of 1500 ms per question. Again, ShortLag and LongLag durations were determined through piloting. The scrambled and inverted distractor faces were presented in two different blocks, respectively, with the order of these two blocks counterbalanced across subjects.

The experimental conditions were determined by the amount of distractors in the lag between T1 and T2 (short or long), and the emotional content of T2 (neutral, fearful, happy), thus yielding 6 different trial types (2 lags x 3 emotion expressions). Each condition consisted of 16 trials, resulting into a total of 96 trials. Total experiment duration was of ~10 mins, with a short break after the first 5 mins.

(Please insert Figure 2 about here)

### **2.2.2. Visual Search task**

This task was adapted from a visual search paradigm with emotional and colored cues, previously described in detail in Lucas & Vuilleumier (2008). Stimuli were pictures of faces, selected from the Karolinska Directed Emotional Faces (Lundqvist, et al., 1998), comprising 16 different identities (50% males) presented with either a neutral, fearful, or happy expression. All emotional faces were shown in grayscale, while neutral faces were either in grayscale or slightly red-tinted to create a visually salient “pop-out” condition (see Lucas & Vuilleumier, 2008). Luminance and size were kept similar across all pictures. Stimulus delivery and response registration were controlled using the Eprime Software (Version 2.0).

Each trial started with a white central fixation cross on black background, shown for 800 ms. Next followed a search array where either 4, 6, or 8 faces were arranged around the central fixation cross, in a symmetric square (4stimuli condition) or circle configuration (6 and 8stimuli conditions; see Fig. 3). Each array comprised one target, that is, a single face, the identity of which was different from other faces in the display (face singleton), thus resulting in three conditions with either 3, 5, or 7 distractor faces. All distractors were always identical to each other (same identity), neutral, and grayscale. The target face could differ from the distractor faces by either identity alone (ID-only condition), by identity and expression (either fear: ID+FEAR condition; or happy: ID+HAPPY condition), or by identity and color (ID+COLOR condition). Hence, visual search for the identity singleton was guided by face features alone (ID-only) or cued by additional information (emotion expression or color), allowing us to probe for the effect of these different cues on attentional capture (Lucas & Vuilleumier, 2008; Wolfe, 1994; Wolfe & Horowitz, 2004). The target could occupy any of the eight possible positions in the array and position was unpredictable. Target type and position were randomly varied across successive trials, with an equal probability of all positions for the different target types. Participants were asked to detect the face singleton among the crowd of distractors, and to report its apparent sex category (male vs. female), as quickly as possible. The face array remained on the screen until a response key was pressed, or up to a maximum time-limit (15 s in healthy

subjects, 35 s in the patient). After an inter-trial interval of 1500 ms, the next trial started. If the subject did not respond within the time-limit, a warning message appeared on screen (for 1500 ms) and encouraged the subject to speed up in the next trial. This task design yielded 12 experimental conditions (4 target types and 3 distractor levels), each consisting of 32 trials, resulting into a total of 384 trials. Total experiment duration was of ~40 mins, with short breaks every 10 mins.

(Please insert Figure 3 about here)

## **2.3. Data analysis**

### **2.3.1. Attentional blink task**

We analyzed hit rate (HR) to second targets (T2) as the proportion of trials in which the face was detected and its gender correctly categorized, but importantly out of those trials where performance on the first target (T1) was also successful (Anderson & Phelps, 2001; De Martino, et al., 2009; Keil & Ihssen, 2004). However, for completeness, and because report failures could comprise both omissions (face not detected) and errors (face gender incorrectly categorized), we also report omission and error rates to T2 targets separately (again after T1 recall was successful).

HRs were then compared with a two-factor repeated-measure ANOVA using the factors Lag (ShortLag, LongLag) and Emotion (Neutral, Fear, Happy) with Greenhouse-Geisser adjustments to the degrees of freedom. Post-hoc comparisons were performed using the Bonferroni adjustment for multiple comparisons. For the patient, we performed individual analyses using single trial data for each condition (see below). For the control group (N=15), we computed the individual average HR over trials for each condition and each subject. For both the controls and the patient, we considered only experimental blocks where participants showed clear evidence for an attentional blink effect (that is, when target detection was lower in the ShortLag condition, compared to the LongLag condition) with Neutral face stimuli (see Chun & Potter, 1995 and Raymond, et al., 1992), and then probed for any emotional impact on the lag effect for these blocks only. This allows for taking into account the well-known variability in attentional blink between individuals and between tasks (Willems & Martens, 2016). More specifically, we computed the LongLag – ShortLag difference of average HRs for the Neutral condition (unbiased by any emotional influence), for each subject and each block (i.e. blocks with scrambled or inverted faces as distractors). Blocks were retained for analysis when this difference was positive and equal to or larger than 5% (i.e. when HR was better and at least 5% higher for Neutral-LongLag than Neutral-ShortLag). In turn, blocks falling below this cutoff value were excluded. Another five blocks were excluded due to technical problems during the recordings (2 out of 5 blocks) or misunderstanding of task instructions by the participant (3 out of 5 blocks). As a result, the average blink effect for Neutral faces in remaining blocks was 26% (i.e.

detection rate 26% better in long lag than short lag), ensuring a reliable assessment of any modulation by emotional cues without risks of floor or ceiling effects.

Overall, across all control participants, this selection procedure led to 19 blocks retained for analysis (from 15 subjects) and 19 blocks excluded (i.e. complete exclusion of 4 subjects and exclusion of one single block in 11 subjects). Thus, the control data corresponded to the block where distractors were scrambled faces for 4 subjects, to the block where distractors were inverted faces for 6 subjects, and to both blocks for 5 subjects. Both types of blocks / distractors were included in the patient data analysis, given that she showed attentional blink in both cases. To verify that the nature of distractors (scrambled or inverted) would not affect the results, we also included Block as a further factor in our ANOVA. Finally, to evaluate whether age, education level, anxiety or depression scores had any significant impact on the results, we computed an additional ANCOVA including education (secondary school or university level) as a between-subject factor and age, STAI-state, STAI-trait, and BDI scores as covariates.

For the patient, data were submitted to separate single-subject ANOVAs (again with Greenhouse-Geisser adjustments), in which each trial was entered as the random factor (Anderson & Phelps, 2001), using the same factors (Emotion and Lag) as those employed for the control group analysis, followed by pairwise t-tests (2-tailed, unless indicated otherwise) to examine differences between conditions. Critically, to compare the relative lag and emotion effects on performance across the patient and controls, we computed two additional ratios across all participants. First, we calculated the relative report rate for the ShortLag relative to the LongLag conditions (i.e. division ratio of ShortLag / LongLag accuracy), which indicates the sparing or survival from the attentional blink in short lag conditions, over and above any general variability in performance level. Larger values of this ratio reflect greater sparing of face detection on ShortLag trials, relative to LongLag trials. Second, we calculated the emotional benefit for this relative sparing index, by dividing the corresponding ratio value (ShortLag / LongLag) for emotional (Fear or Happy) conditions by the same value in the Neutral condition. Again, a larger value for this ratio indicates a larger benefit of emotional stimuli over neutral stimuli in the attentional blink, i.e., greater resistance to the attentional blink for emotional compared to neutral targets.

Finally, we compared the patient data with that of the control sample for each condition, and for the relative lag and emotion indices described above, by means of the Bayesian Monte Carlo statistical test (one-tailed probability; Crawford & Garthwaite, 2007). This test allows for evaluating whether a single patient's score is reliably out of the range of scores from controls, such that the null hypothesis (i.e. the patient data are observations drawn from the control population) can be rejected.

### **2.3.2. Visual Search task**

Our analysis for this task was two-fold. First, for the control group (N=18), response time was averaged across trials where the singleton face target was accurately detected (hit-RT), and separately for each condition. Outliers differing from the mean in more than 4 standard deviations

were removed (Smilek, Eastwood, & Merikle, 2000). Second, to explore cueing effects on search efficiency, similarly to previous studies (Smilek, et al., 2000; Wolfe, 1994; Eastwood, et al., 2001; Gerritsen, et al., 2008), we computed the search slopes for the relative variations of hit-RTs as a function of the number of stimuli in the face arrays (i.e. slope values were obtained from a regression analysis of hit-RT values over the 4, 6, and 8 stimuli conditions, calculated as the  $b$  parameter [in ms/item] in the linear function  $y=bx+a$ , where  $y$  is detection latency [hit-RT in ms],  $x$  is set size [item number], and  $a$  is a constant; see Horstmann, 2007). An assumption underlying visual search experiments is that differences in the slope of the search function (i.e. hit-RT over array sizes) reflect the speed at which items are scrutinized before the target is found, and hence the efficiency of preattentive processes that guide focused attention towards a potential target among the distractors (Wolfe, 1994). Therefore, conditions with a shallower search slope are those in which attention is more efficiently guided to the target. Importantly, emotionally salient cues have been repeatedly shown to reduce search slopes relative to non-emotional or less salient distractors (see Eastwood, et al., 2001; Gerritsen, et al., 2008; Piech, et al., 2010). Note that in the prototypical case of “pop-out” (e.g. with visually salient color singletons), the search slope should tend toward zero (indicating similar detection latencies regardless of distractor number; Wolfe, 1994).

The average hit-RT data were compared across conditions by means of a repeated-measure ANOVA with the factors Set Size (4, 6, or 8) and Cue Type (ID-only, ID+FEAR, ID+HAPPY, or ID+COLOR). A further selective ANOVA excluding the ID+COLOR conditions was performed, so as to specifically assess the emotion benefit on search. Greenhouse-Geisser adjustments to the degrees of freedom were applied to all ANOVAs. Post-hoc comparisons were performed using the Bonferroni adjustment for multiple comparisons. A further ANOVA also assessed whether the side of target presentation (left or right) impacted performance, using the additional factor Laterality. The slope data were analyzed with a similar approach but without the factor Set Size. To verify whether age, education level, and anxiety or depression scores in controls had any impact on performance, we computed an ANCOVA including education (secondary school or university level) as a between-subject factor, and age, STAI-state, STAI-trait, and BDI scores as covariates.

For the patient, hit-RT data were submitted to separate single-subject ANOVAs (with Greenhouse-Geisser adjustments), where each trial was entered as the random factor (Anderson & Phelps, 2001). Further pairwise t-tests (2-tailed, with Bonferroni adjustment) were also implemented to compare conditions with each other. Slopes were examined with regression analyses using hit-RT values from single trials in each condition. In addition, to better compare the relative cue and/or set size effects across patient and controls, we used a similar procedure as for the attentional blink task above, by computing a relative facilitation index on search slopes for each of the three cue conditions (color, fear and happy) relative to the “baseline” ID-only condition. Following a procedure used in previous work (Lucas & Vuilleumier, 2008), this facilitation index was calculated as the difference between search slopes for cued (ID+FEAR, ID+HAPPY, ID+COLOR) compared to uncued (ID-only) targets, divided by the slope values in the ID-only condition (i.e.  $[\text{slope}_{\text{ID-only}} - \text{slope}_{\text{cue}}] / \text{slope}_{\text{ID-only}}$ ). Larger values of this ratio indicate a larger emotion-driven facilitation on the target search slope across

increasing set sizes. Values computed from the patient were compared with those from the control sample by means of the Bayesian Monte Carlo statistical test (one-tailed probability; Crawford & Garthwaite, 2007), as described above.

### 3. Results

#### 3.1. Attentional blink task

##### 3.1.1. Healthy Controls

Overall, control subjects were more accurate at reporting the second target for the LongLag relative to the ShortLag condition (71.02% vs 56.18%; Fig. 4 and Table 3), reflecting typical attentional blink (Chun & Potter, 1995; Raymond, et al., 1992). This global effect was expected given that, by design, our analysis included only blocks where a Lag effect was apparent at the individual level (note that this selection was based on individual performance in the neutral condition), so as to ensure that emotional effects were probed for when attention was adequately engaged by the detection task<sup>1</sup> (see Methods). More critically, the emotional content of the T2 targets had a significant impact on the Lag effect in these blocks, specifically seen in the ShortLag condition (Table 3).

Thus, whereas HR for T2 faces in the LongLag trials was similar across emotion expressions, the ShortLag condition showed a reliable advantage in detection rates favoring the two emotional face categories (HRs for Fear 60.29%, Happy 61.82%, Neutral 46.42%; Table 3). Post-hoc t-tests revealed that fearful and happy faces were reported more often than neutral faces in the ShortLag condition, indicating that target detection was more resistant to the attentional blink when faces had an emotional expression. There were no significant HR differences between the ShortLag\_Fear and ShortLag\_Happy conditions (Table 3). Furthermore, paired tests comparing the LongLag and ShortLag conditions for each emotion category showed significant differences for the Neutral ( $T_{14}=-8.457$ ;  $p<0.0001$ ) and Fear expressions ( $T_{14}=-3.859$ ;  $p=0.002$ ), but not for Happy ( $p=0.22$ ).

We note that, in controls, HRs were determined by both omissions (failure to see the second face) and recognition errors (gender incorrectly categorized). Omission rates for T2 targets with ShortLag (when T1 was detected) were 17.14% for Neutral, 14.4% for Fear, 8.47% for Happy; and with LongLag, 9.7% for Neutral, 10.39% for Fear, 9.37% for Happy. In turn, gender error rates were 36.44% for Neutral, 25.31% for Fear, 29.71% for Happy with ShortLag; and 19.41% for Neutral, 15.24% for Fear, 22.86% for Happy with LongLag. We did not analyze these data separately, as these differences might be contaminated by individual guessing strategies, and given that our patient's performance was characterized by more frequent omissions than errors.

##### 3.1.2. Effects of distractor type, age, education, anxiety and depression in controls

In the healthy control group, there were no significant between-subject effects due to the distractor type (Blocks with scrambled vs. inverted faces vs. both distractor types,  $p=0.93$ ), but there was a significant Emotion x Block interaction ( $F_{(2,24)}=3.447$ ;  $p=0.026$ ). This effect stemmed from the fact that, for blocks including both distractor types (i.e. inverted and scrambled faces), detection of fearful and happy faces was overall higher than neutral faces, regardless of the Lag condition (Emotion:  $F_{(2,8)}=9.55$ ;  $p=0.022$ ; all neutral faces vs. all fearful faces:  $T_4=-3.26$ ;  $p=0.03$ ; all neutral faces vs. all happy:  $T_4=-3.37$ ;  $p=0.028$ ), with no differences between fearful and happy faces ( $p>0.1$ ). Importantly, there was no interaction of Block with our effect of interest (Emotion x Lag), indicating that the nature of distractors (scrambled or inverted faces, or both) did not impact our main results. Furthermore, an additional ANCOVA including education (secondary school or university level) as a between-subject factor, and age, STAI-state, STAI-trait, and BDI scores as covariates revealed no significant main effects for these factors, nor any interactions with other factors. Therefore, we disregarded them as potential confounds for the effects of interest.

### 3.1.3. Patient

Our patient HE1 also showed a strong Lag effect (Table 3), with lower accuracy for reporting T2 in the ShortLag than the LongLag condition (15.01% vs 91.92% respectively, Fig. 4, Table 3) but we observed neither a main effect of Emotion, nor an Emotion x Lag interaction (Table 3). Subsequent paired t-tests revealed no difference for Fear or Happy faces relative to Neutral faces, for any of the Lag conditions (Table 3). This suggests that emotion expression did not impact T2 face detection regardless of lag in this patient (although we note performance was generally low across conditions). Additional analyses examining any difference between Blocks (scrambled vs. inverted face distractors) revealed no main effect of Block ( $p>0.1$ ) but a Lag x Block interaction ( $F_{(1,9)}=13.91$ ;  $p=0.005$ ). This interaction stemmed from the fact that a Block effect was observed in the ShortLag condition only ( $F_{(1,15)}=14.273$ ;  $p=0.002$ ; LongLag:  $p=0.5$ ), reflecting that the patient never reported T2 faces among inverted distractors (0% HR) across all ShortLag conditions, compared to an average HR of 29% for T2 faces among scrambled distractors in the same Lag conditions. Nevertheless, neither Emotion nor Emotion x Lag effects were observed when considering scrambled faces alone.

We also note that HRs in our patient stemmed almost totally from misses (i.e., failure to see a second face after correctly reporting T1). For completeness, omission rates in the ShortLag condition were as follows: Neutral 87.5%, Fear 78.57%, Happy 83.3%; and in the LongLag condition: Neutral 12.69%, Fear 7.7%, Happy 3.85%. She made no or very few gender errors (all  $\leq 5.6\%$ ).

(Please insert Table 3 about here)

### 3.1.4. Patient vs. controls

Critically, a direct comparison between HE1 and controls with Bayesian Monte Carlo methods (Crawford & Garthwaite, 2007) showed that the patient's report rate for the ShortLag condition was significantly out of the normal range for the Fear ( $p=0.049$ ) and Happy ( $p=0.016$ ) conditions, but only marginally different for the Neutral condition ( $p=0.064$ ).

To allow further comparability of performance between the controls and the patient, while taking overall performance level into account, we also computed a relative sparing index for the ShortLag relative to the LongLag conditions (ShortLag/LongLag ratio), which indicates report survival from the attentional blink (see Methods). These values were then compared across Emotion conditions. In controls, this analysis revealed significant Emotion effects ( $F_{(2,28)}=6.363$ ;  $p=0.009$ ; Fig. 5), with paired t-tests showing differences between Neutral and Happy faces ( $T_{14}=-4.151$ ;  $p<0.001$ ), and between Neutral and Fear faces ( $T_{14}=-2.085$ ;  $p=0.028$ ). There was no difference between Fear and Happy faces ( $p>0.09$ , all one-tailed). This, again, supports the idea that reporting the T2 face target was facilitated for the ShortLag condition in controls when faces had an emotional expression. To compare this sparing index in the patient with the values observed in controls, we again used Bayesian tests (Crawford & Garthwaite, 2007), for each condition separately. These comparisons showed that the patient's sparing index was significantly lower than the range of values observed in the control population for all three emotion conditions (Neutral:  $p=0.004$ ; Fear:  $p=0.014$ ; Happy:  $p=0.004$ ). Scatterplots in Fig. 5 show individual data for this ratio in each emotion condition.

Finally, to further assess the relative emotion effects between the patient and the controls, we calculated an emotional benefit index for the sparing ratio in each condition. To this aim, we divided the sparing ratio from emotional trials (Fear or Happy) by the "baseline" value from Neutral trials (see Methods). Bayesian comparisons revealed a marginal difference between patient and controls for the happy/neutral ratio ( $p=0.071$ ) but no significant difference for the fear/neutral ratio ( $p=0.4$ ). However, the generally low report rates in the patient for the short lag condition (on average 15%) might create floor effects preventing a reliable measure of the relative emotional benefits. Nonetheless, low performance does not appear sufficient to fully account for a lack of emotional modulation on T2 report for patient HE1. In fact, when we examined a control participant with the poorest performance in ShortLag trials for the Neutral condition across the whole healthy group (18% of detection accuracy for this participant, relative to 56.2% for the whole control group and 12.5% in our patient), we could still observe a very clear enhancement of performance for emotional faces (i.e. increase in hit rates of 62% for Fearful faces and 36% for Happy faces, relative to Neutral), whereas such emotional benefit was practically absent in our patient (i.e. increase of 8% for Fear and decrease of 1.4% for Happy). Therefore, our patient showed substantially smaller emotion effects than the worst performer in our control sample (despite comparably low hit rate overall). Moreover, when comparing the emotional benefit in T2 detection (relative increase for fearful or happy faces, compared to neutral) between the 8 best performers and the 7 worst performers in the control group, we found no difference whatsoever between the two subgroups (independent-samples t-test, for Fear:  $T_{13}=1.1$ ,  $p=0.29$ ; for Happy:  $T_{13}=0.91$ ,  $p=0.38$ ). Taken together, these data strongly suggest that overall performance level does

not affect our sensitivity to assess the emotion effect observed in either the controls or the patient. In sum, we conclude that patient HE1 showed a loss of the emotional benefit in attentional blink, in contrast with the pattern observed in controls, combined with globally reduced detection rates at short lags (Figs. 4 and 5).

(Please insert Figure 4 about here)

(Please insert Figure 5 about here)

### **3.2. Visual Search**

#### **3.2.1. Correct target detection latencies**

##### **3.2.1.1. RT in controls**

In controls, hit-RT (i.e. response times for trials with correct target detection) was strongly influenced by the number of stimuli in the visual display (indicating recruitment of serial search processes, Fig. 6), as verified by the ANOVA showing a robust main effect of Set Size (Table 4). In addition, hit-RT was significantly affected by the cueing information that guided search (Table 4). Specifically, healthy participants were faster at reporting color-cued faces than all other face targets, but also faster to find the emotionally-cued faces as compared with the neutral faces (Table 4; Fig. 6). Furthermore, as predicted, the effect of Set Size was strongly modulated by the cueing conditions, as revealed by a highly significant Set Size x Cue Type interaction (Table 4).

In keeping with the above, follow-up ANOVAs, performed separately for each cue condition, showed that hit-RT was unaffected by the number of stimuli for the color-cued targets, consistent with perceptual “pop-out”, while it was significantly influenced by set size for both the emotionally-cued and the neutral faces (Table 4; see Fig. 6). A selective ANOVA excluding the ID+COLOR conditions, so as to specifically assess the emotion benefit on search efficiency, also revealed main effects of Set Size and of Cue Type, as well as a significant Set Size x Cue Type interaction (Table 4). Importantly, hit-RT was faster for emotional compared to neutral cues for each of the 3 stimulus-sets, as indicated by a main effect of (Expression) Cue Type in each of the one-way ANOVAs and in corresponding post-hoc t-tests (Table 4). Taken together, these data support the idea that controls were overall faster at detecting colored faces, relative to all other targets, but also faster for emotional faces relative to neutral. Moreover, search efficiency was affected to a lesser extent by distractor number when face targets were emotional, compared to neutral (see analysis of search slopes below).

##### **3.2.1.2. RT in patient**

In the patient, we found a marginal Set Size effect and a significant Cue Type effect, but no Set Size x Cue Type interaction (see Table 4 and Fig. 6). She responded consistently faster to colored compared to neutral faces and compared to happy faces, while the difference between colored and fearful faces did not reach significance (Table 4). A subsequent ANOVA excluding the ID+COLOR condition, similarly to that performed in controls, also revealed a significant effect of Set Size, but critically there was no effect of Expression Cue Type, and no interaction of Set Size x Expression Cue Type (Table 4), suggesting no reliable difference between emotional and neutral faces. Direct paired tests between conditions confirmed no difference for happy versus neutral faces, but somewhat faster responses to fearful than neutral faces, again when considering all array sizes together (Table 4). Thus, while the patient still showed a clear perceptual advantage for the “pop-out” color cues, emotional faces appeared to yield no or inconsistent advantages relative to neutral faces.

(Please insert Table 4 about here)

(Please insert Figure 6 about here)

### **3.2.1.3. Search slopes in patient vs. controls**

However, the critical prediction for emotional biases on search concerned the relative facilitation of target detection as a function of increases in the distractor array size as observed in previous studies (Eastwood, et al., 2001; Gerritsen, et al., 2008; Piech, et al., 2010; i.e. search slopes; Wolfe, 1994; Smilek, et al., 2000). In fact, search efficiency is best defined by the degree to which each additional distractor slows search for a target item (e.g. see Gerritsen, et al., 2008). Previous research on visual search with both emotional (Eastwood, et al., 2001; Gerritsen, et al., 2008; Piech, et al., 2010) and non-emotional stimuli (Smilek, et al., 2000; Wolfe, 1994; 1998) has shown that perceptual processes operating on preattentive visual information to draw attention towards relevant targets do not necessarily produce true “pop-out” effects independently of set size, but rather increase the gain of sensory signals competing for attention. This can thus reduce the slope (search cost) associated with increasing set size, rather than produce a flat slope (Eastwood, et al., 2001; Gerritsen, et al., 2008).

As can be seen in Fig. 7, color-cued targets produced the shallowest slopes (on average close to zero) in both healthy subjects and the patient. However, slopes for the emotional (relative to neutral) targets showed different patterns for the patient compared to controls. Whereas controls exhibited shallower slopes for the emotionally-cued (FEAR+ID and HAPPY+ID) than for the neutral targets (ID-only), patient HE1 showed similar (or even steeper) slopes for emotional faces compared to neutral (Fig. 7). Accordingly, for controls, an ANOVA on slope values revealed a significant effect of Cue Type ( $F_{(3,51)}=20.797$ ;  $p=0.00000004$ ), with pairwise comparisons confirming that search efficiency for the colored ( $T_{17}=7.339$ ;  $p=0.000001$ ), fearful ( $T_{17}=3.888$ ;  $p=0.001$ ), and happy ( $T_{17}=3.358$ ;  $p=0.004$ ) face targets produced significantly smaller slopes than neutral targets. Pairwise tests among cue-types also confirmed slope differences for the color condition compared to fearful ( $T_{17}=4.837$ ;  $p=0.00015$ ) and

happy ( $T_{17}=4.761$ ;  $p=0.00018$ ), but no difference between fearful and happy conditions ( $p=0.7$ ). These results indicate that the controls' attentional guidance was most efficient for colored-cued targets, followed by the emotionally-cued targets (equally so for fearful and happy faces), while it was the least efficient for neutral targets (see Fig. 7).

Absolute slope values were then compared between patient and controls across conditions with Bayesian Monte Carlo analysis, but showed no significant differences for any condition ( $p>0.1$ ). More critically, to probe for emotional effects, we compared the relative slope difference across conditions in the patient, relative to controls, by computing a cue facilitation ratio (see Methods) corresponding to the difference between conditions relative to the neutral ID-only (baseline) slope (i.e.  $[\text{slope}_{\text{ID-only}} - \text{slope}_{\text{cue}}] / \text{slope}_{\text{ID-only}}$ ; Lucas & Vuilleumier, 2008). Again these comparisons were performed with Bayesian Monte Carlo analysis. Results showed a significant decrease of the facilitation ratio for the happy face condition ( $p=0.038$ ; Fig. 8) and a marginal decrease for fearful faces ( $p=0.083$ ). Note that, when performing the same Bayesian test on the pooled data from fearful and happy faces  $[\text{slope}_{\text{ID-only}} - \text{slope}_{\text{fear and happy}}] / \text{slope}_{\text{ID-only}}$ , the difference between patient and controls was still significant ( $p=0.016$ ), suggesting that such abnormal cue benefits on search slopes in the patient may globally concern both emotion categories. Altogether, these data indicate that the patient's search slope for emotional faces (with a predominance for happy faces) was abnormally similar to that for neutral faces, unlike for healthy control participants, who showed shallower slopes for emotional than neutral faces.

(Please insert Figure 7 about here)

(Please insert Figure 8 about here)

#### **3.2.1.4. Effects of stimulus-laterality, age, education, anxiety and depression**

We also asked whether search efficiency might differ as a function of the side of the targets in the visual field. To this aim, we performed additional ANOVAs on hit-RTs with the factor Laterality (Left or Right). This revealed a significant Laterality x Set Size effect for controls ( $F_{(2,34)}=7.352$ ;  $p=0.002$ ), reflecting that Set Size effect was larger in the Right than the Left visual field ( $\eta_p^2$  for Left=0.563;  $\eta_p^2$  for Right=0.696), and thus suggesting more efficient search overall on the left side. No interaction of Laterality x Set Size x Cue Type was observed. Accordingly, the controls' search slope was also shallower for targets presented on the left compared to the right side (Laterality:  $F_{(1,14)}=10.416$ ;  $p=0.006$ ). This asymmetry accords with previous visual search work (Lucas & Vuilleumier, 2008), where the same face-stimuli were used, and may be due to a right-hemisphere dominance for face processing (Kanwisher, McDermott, & Chun, 1997; Kanwisher & Yovel, 2006). In contrast, the hit-RT

of patient HE1 did not show any main effect or interaction involving Laterality. Bayesian Monte Carlo tests comparing laterality biases (i.e. hit-RT for Left minus hit-RT for Right) between patient and controls showed that the patient's (seemingly abolished) laterality bias was significantly out of the normal range from the control population in all cueing conditions (ID-only:  $p < 0.00001$ ; ID+FEAR:  $p = 0.0001$ ; ID+HAPPY:  $p < 0.00001$ ; ID+COLOR:  $p < 0.00001$ ).

Finally, an additional ANCOVA including education (secondary school or university level) as a between-subject factor, and age, STAI-state, STAI-trait, and BDI scores as covariates revealed no main significant effects for any of these factors, nor any interaction with other search factors except for a Set Size x Cue Type x BDI-score effect ( $F_{(6,72)} = 2.554$ ;  $p = 0.049$ ). We therefore repeated an ANOVA on those controls who had a similar BDI score as the patient (scores 4 to 13, mild to moderate depression;  $N = 5$ ) but found the same main effects of Set Size ( $p = 0.024$ ), Cue Type ( $p = 0.008$ ), and Set Size x Cue Type ( $p = 0.009$ ) as observed for the whole group. These results indicate that all covariates above, including BDI scores, did not constitute potential confounds for the differential effects of interest observed in our patient and controls.

#### 4. Discussion

We probed for a causal role of the amygdala in the emotional guidance of attention, by testing a rare patient with bilateral damage to medial temporal lobe acutely acquired in adulthood. The patient was tested with two classic tasks, i.e., attentional blink and visual search, allowing us to probe for different facets of emotional attention effects, while accounting for possible confounds due to concomitant memory disturbance. In addition, we used face stimuli in these tasks, which should be optimal for assessing bottom-up emotional processing in the amygdala, given its high and rapid reactivity to such stimuli (e.g. Méndez-Bértolo, et al., 2016; Morris, et al., 1998). Importantly, the acute onset of our patient's lesion should limit the effects of compensatory mechanisms subsequent to amygdala damage. Compared to performance of a healthy control group, our patient showed consistent decreases in attentional benefits for emotional targets, as we discuss below in detail.

##### 4.1. Attentional blink

In the attentional blink task, controls showed enhanced detection of emotional faces among rapidly occurring targets, as expected (Anderson, 2005; de Jong, et al., 2009; De Martino, et al., 2009; Fox, et al., 2005; Keil & Ihssen, 2004; Luo, et al., 2010; Maratos, et al., 2008; Milders, et al., 2006; Schwabe, et al., 2011). When both targets were sufficiently separated in time by intervening distractors (i.e. long lag condition), the report rate for T2 targets was similarly high (above 65%) across neutral, fearful, and happy faces, whereas with a short time interval (short lag condition), correct reports declined to approximately 45% for neutral faces (Raymond, et al., 1992) but remained above 60% for emotional

faces, similarly to the long lag condition. Therefore, face report in controls appeared more resistant to the attentional blink when they had an emotional (fear or happy) expression. In contrast, patient HE1 showed a strong attentional blink effect, but the target report rate in the short lag condition was unaffected by the emotional expression of faces. Thus, face detection in conditions of attentional blink did not benefit from their emotional content.

These data seem to accord with the notion that the amygdala may play a causal role in involuntary emotional biases of attention, in line with previous observations of Anderson & Phelps (2001) where amygdala lesion led to impaired report of emotional words in an attentional blink paradigm (but see Bach, et al., 2011; Piech, McHugo, Smith, Dukic, Van Der Meer, Abou-Khalil, Most, et al., 2011; for conflicting results in other patients). The current data further suggest that an impairment in emotional biases after amygdala damage may be extended to emotional face processing. However, we note a possible floor effect in our patient's performance for this task (i.e. very low T2 report rates at short lags), which might seriously challenge the interpretation of her lack of relative emotional effects. However, please note that controls with globally poor performance still showed clear emotional benefits in detection rates. This low performance pattern in HE1 might at least partly be related to memory deficits associated with concomitant hippocampal damage, and is further discussed in the following sections.

#### **4.2. Visual search**

We also tested for emotional biases in a visual search task with face targets. Controls showed a clear facilitation by both emotional and color cues in faces, replicating previous studies with similar paradigms (Eastwood, Smilek, & Merikle, 2003; Lucas & Vuilleumier, 2008; Ohman, et al., 2001; Peelen, Lucas, Mayer, & Vuilleumier, 2009). Visual search is considered the most appropriate tool to test for preattentive access to stimulus features (Horstmann, 2007). It allows for measuring whether sensory cues are available for information processing independently of the current focus of visuo-spatial attention, and thus used for attention guidance (Horstmann, 2007). Moreover, search is less dependent on short-term working memory than other tasks examining preattentive emotion processing (Woodman, et al., 2001). As the latency to detect a target increases with the set size of a visual display, it is assumed that search operates through a serial deployment of focal attention on each stimulus until the target is detected. Search efficiency is therefore reflected by the speed of directing attention to the most salient or relevant stimuli among those present in the display, which can be quantified by the slope of RTs over set size (Wolfe, 1994). Accordingly, shallower slopes reflect more efficient search (even in the absence of a "pop-out" effect), whereas steeper slopes indicate inefficient search (Eastwood, et al., 2001; Gerritsen, et al., 2008; Horstmann, 2007; Smilek, et al., 2000; Wolfe, 1994). Importantly, this implies that even when targets are emotionally salient, detection latencies will still increase with the number of distractors, and thus be sensitive to serial search, but the RT slope will be shallower relative to less salient or neutral targets (Eastwood, et al., 2001; Fox, et al., 2000;

Smilek, Frischen, Reynolds, Gerritsen, & Eastwood, 2007; Vuilleumier, 2005). This indicates that attention has a higher probability to be guided to the former than to the latter type of stimuli.

In this task, both the controls and HE1 showed the shallowest RT search slopes for color-cued targets, as compared with all other cue conditions. This indicates that not only controls but also HE1 could benefit from a salient (non-emotional) physical feature in targets, and that HE1 had intact “parallel” processing of elementary sensory (color) cues at preattentive stages in the visual system. Importantly, even though the controls’ search slopes were steeper for the emotionally-cued faces (i.e. fearful and happy), compared to colored cues, slopes for emotional faces were shallower than those for neutral faces. This pattern fully replicates previous studies and accords with the notion that emotional biases in controls’ attention did not imply a “pop-out” effect, as observed for elementary visual features such as color, but still facilitated guided search (Domínguez-Borràs & Vuilleumier, 2013; Eastwood, et al., 2001; Fox, et al., 2000; Pourtois, et al., 2012; Smilek, et al., 2007; Vuilleumier, 2005).

In contrast, search slopes in patient HE1 did not show any systematic advantage for emotional over neutral face targets, even though she did show efficient search overall, and exhibited clearly shallower slopes for color-cued compared to neutral (ID-only) faces. If anything, her search slope was numerically steeper for emotional than for neutral faces (Fig. 7). Bayesian statistical tests confirmed such abnormal pattern, by showing that the relative cue benefits on the patient’s slopes were significantly outside the normal range for happy versus neutral face conditions, and marginally so for fearful versus neutral faces (Figs. 7 and 8). Moreover, when performing the same Bayesian test on the pooled data from fearful and happy faces [ $\text{slope}_{\text{ID-only}} - \text{slope}_{\text{fear and happy}} / \text{slope}_{\text{ID-only}}$ ], differences between the patient and controls were highly significant, suggesting that such abnormal cue benefits on search slopes in the patient concerned both emotion categories, despite a possible predominance for happy faces. Please note that the difference between the patient’s and controls’ slopes differed in the relative facilitation by emotion, and not when considering each condition separately. This deserves further investigation, but does not contradict our main conclusion. Altogether, these data indicate that guided search for emotional (particularly happy) faces was abnormally inefficient in the patient, compared to her search for neutral faces, unlike in control participants, in whom it showed a consistent relative facilitation.

The current data suggests that amygdala function in emotional guidance may be most apparent in conditions with perceptual competition and high attentional demands. This may partly explain why no visual search deficits were observed for patient SM in Tsuchiya et al. (2009). In fact, whereas their participants performed visual search with stimulus arrays of different set sizes (either with 4, 8, or 12 faces), their results focused on the average from all three array size conditions, and slopes were not considered. In this regard, our patient showed overall faster detection of fearful than neutral faces when pooling across array sizes (although effects were weak) and impairments became evident in search slopes. This may suggest, on one hand, that some attentional guidance may still operate for emotional faces regardless of amygdala function (Domínguez-Borràs & Vuilleumier, 2013), but also, and in line with previous work (e.g. Eastwood, et al., 2001), that slopes may be a critical

parameter for isolating amygdala function in emotion-guided search. In turn, this may also explain why other patients (AM and BG), with similar early-onset and bilateral lesions like those of SM, showed abnormal emotional biases when search slopes were examined (Bach, et al., 2015). In the latter study, however, the patients' slopes for angry faces were steeper than those for happy faces as set size increased (a pattern opposite to that found in controls), but no neutral faces were included. Thus, a direct comparison with our results seems difficult.

#### **4.3. Sensitivity to negative versus positive emotions**

Patient HE1 showed losses in emotional benefits for both fearful and happy faces, with even greater deficits for the latter than the former. It has often been suggested that the role of the amygdala in preattentive emotion processing may be more critical for threat-related cues than for positive information (Bach, et al., 2015), in keeping with influential theories of amygdala function focusing on fear (LeDoux, 2000). However, again search slopes in patient HE1 were predominantly abnormal for happy faces, relative to neutral, and to a lesser degree for fearful faces. Further, this pattern converged with results from attentional blink, where the relative sparing index (short/long lag ratio) differed weakly in the patient compared to controls for happy versus neutral face targets, but was far from significant in the same comparison for fear versus neutral faces. One explanation for this counterintuitive pattern with fearful faces could be the nature of these stimuli. Bach et al. (2015) suggested that fearful faces, such as those used here and in other studies where no abnormal visual search was observed in patients (Piech, McHugo, Smith, Dukic, Van Der Meer, Abou-Khalil, & Zald, 2011; Tsuchiya, et al., 2009), might not necessarily represent a threat to the observer, unlike angry faces that constitute a less ambiguous, more self-relevant threat signal directed toward the viewer (see also Cristinzio, N'Diaye, Seeck, Vuilleumier, & Sander, 2010; N'Diaye, Sander, & Vuilleumier, 2009). Thus, it is possible that fearful expressions in our task represented less salient or relevant threat signals, hence were less affected by amygdala damage, whereas happy faces were more clearly appraised as signals of reward. Accordingly, imaging studies in healthy individuals reported amygdala responses to both negative and positive emotions (e.g. see Domínguez-Borràs & Vuilleumier, 2013 and Phelps & LeDoux, 2005).

Another explanation for weaker differences with fearful faces might be the greater variability of performance in controls and the presence of two possible outliers among them who showed facilitation indices as low as patient HE1 in visual search (and likewise in attentional blink; see Figs. 5 and 8). At first sight, nothing distinguished these control participants from others, and Bayesian statistical tests indicated that the patient's performance still generally differed from normal when including these outlier data (see Results). In any case, our findings show that search impairment after amygdala lesion can be observed for emotionally positive stimuli (not only for negative stimuli). This suggests that the role of the amygdala in mediating preattentive search guidance may go beyond fear- or threat-related signals, contrarily to common assumptions (Bach, et al., 2015; LeDoux, 2000; Piech, McHugo, Smith,

Dukic, Van Der Meer, Abou-Khalil, & Zald, 2011), and instead may promote guided search for affective salience in general.

#### ***4.4. Facial expression recognition versus preattentive emotional processing***

Another important point concerns a possible dissociation between the role of the amygdala in perceptual recognition of emotional expressions and its role in preattentive emotion processing. As mentioned in the Introduction, an influential hypothesis regarding the role of the amygdala is that this structure mediates the perceptual recognition of emotional expressions (Adolphs, et al., 1994), in addition to or instead of their preattentive processing (Tsuchiya, et al., 2009). This leads to the question of whether abnormal biases in our patient were due solely to a deficit in emotion recognition. However, we also tested our patient for emotion recognition abilities with faces (see neuropsychological testing, Methods and Table 2) and found normal performance across all basic emotion categories except fear. In particular, her explicit recognition of happy expressions was fully normal in neuropsychological testing (both in terms of accuracy and response times), whereas she exhibited the strongest deficits in emotional biases for attention toward happy faces. At the same time, while the patient's explicit recognition of fearful faces was clearly abnormal, her deficits in emotional biases of attention were less severe for fear.

Thus, we conclude that the deficits observed in the attentional tasks in our patient were not secondary to difficulties, or delay, in the recognition of facial expressions, but more specifically linked to abnormal preattentive guidance by emotion. In other words, our findings suggest that amygdala lesion may impact emotional biases in attention regardless of (spared or impaired) emotion recognition abilities. The results have two additional implications. First, this dissociation suggests that both functions (i.e. explicit recognition and preattentive processing) are subserved by partly independent neural substrates, in line with previous assumptions (Tsuchiya, et al., 2009). Second, these findings do support a selective role of the amygdala in the recognition of fear expressions (Adolphs, et al., 1994), unlike a few other studies that reported normal fear recognition in faces after amygdala lesion (Koen, et al., 2016; Siebert, Markowitsch, & Bartel, 2003; Terburg, et al., 2012). Note, however, that patients in the latter studies suffered from Urbach-Wiethe disease, and therefore from early-onset and progressive amygdala damage.

#### ***4.5. Lesion-onset and lesion extension***

Our results seem consistent with the lesion-onset hypothesis (Bach, et al., 2011), given that brain damage in our patient occurred acutely and bilaterally in late adulthood, such that compensatory mechanisms may have been limited. Therefore, our findings may not necessarily contradict results from other amygdala-lesioned patients with earlier or more progressive onset (such as Urbach-Wiethe syndrome in Bach, et al., 2011; or Tsuchiya, et al., 2009), who showed intact emotional biases in various tasks. Unlike in our patient, these neurodegenerative lesions may have less impact on

attention due to compensatory mechanisms. This hypothesis may also apply to other amygdala patients with adult-onset lesions after surgical resection for treatment of epilepsy, who have been reported to exhibit normal emotional bias in attentional blink, using aversive or erotic pictures (Piech, McHugo, Smith, Dukic, Van Der Meer, Abou-Khalil, Most, et al., 2011), or normal slopes in visual search with aversive or neutral pictures (Piech, McHugo, Smith, Dukic, Van Der Meer, Abou-Khalil, & Zald, 2011). As mentioned above, the onset of amygdala damage in epileptic patients undergoing resection may be more uncertain compared to our patient, and may actually have already originated during the earliest years of life, long before the first symptoms (Bach, et al., 2011), allowing for extensive neuroplasticity. On the other hand, the findings of Bach, et al. (2015) suggest that prioritization of emotional cues in attention may also be impaired after early-onset amygdala lesions, despite possible compensatory neural mechanisms, again suggesting that lesion onset may not be the only factor to account for the variability of effects among patients.

On the other hand, our results may also support the notion that lesion extension could impact performance in specific tasks. In this vein, a plausible explanation for severe impairment of our patient in the attentional blink is that it may partly reflect additional damage to other temporal lobe structures adjacent to the amygdala. This is often the case after encephalitis, but also after temporal lobectomy. Accordingly, our patient suffered severe lesions to right hippocampal structures and, as a result, presented with important memory disturbance, including marked deficits in both verbal and non-verbal memory (see Methods and Table 1), even though she was not amnesic and could resume her professional activities normally. Thus, it is noticeable that her report rate in the attentional blink task was low in all of the short lag conditions (ranging from 11% to 21%; see Fig. 5). This then also raises the question of whether the patient's abnormal performance derived from a floor effect, due to a concomitant impairment in recall rather than just an impaired detection of targets in the visual stream.

As underscored above, attentional blink performance depends on joint resources from working-memory and attention (Johnston, et al., 2012), and working memory relies on hippocampal function (Axmacher, et al., 2010; Axmacher, et al., 2007; Ben-Yakov, et al., 2014; Fuentemilla, et al., 2010; Poch, et al., 2011; Ranganath & D'Esposito, 2001). Indeed, although traditional views assumed that the hippocampus plays a primary role in long-term episodic memory (Baddeley & Warrington, 1970; Cave & Squire, 1992; Drachman & Arbit, 1966; Milner, 1972; Wickelgren, 1968), recent research supports its important involvement in working memory processes that are also recruited in attentional tasks requiring the maintenance and report of target information in the presence of delays or competing distracters. Such memory effects might in part explain why patients tested in Anderson & Phelps (2001) who had hippocampal damage, but not those in Bach et al. (2011) and Piech, McHugo, Smith, Dukic, Van Der Meer, Abou-Khalil, Most et al. (2011), who had either absent or inconsistent hippocampal lesion, showed abnormal emotional biases during the attentional blink. Anderson & Phelps (2001) argued however that memory disturbances in their patient were not sufficient to explain the results, as she reported with high accuracy the first targets (i.e. T1 stimuli which, by definition, occur before the critical T2 targets), even in their long lag conditions. Similarly, our patient reported correctly the T1 targets (which were always neutral and not explicitly analyzed in our study) on about

80% of trials in the long lag conditions. However, missing T2 targets (and not T1 targets) during attentional blink has been linked to the fact that working memory and attention are sharing capacity-limited resources (Johnston, Linden, & Shapiro, 2012). Thus, despite the patient's correct performance for T1 targets, her poor working memory abilities might have intensified this competition for resources, and thus account for the high rate of misses on T2. In any case, emotion-memory interactions should not be underestimated in explaining our (and other) results in patients with medial temporal lobe pathology, given the strong links between these two processes (Cahill & McGaugh, 1998; Hamann, 2001; McGaugh, 2002). Further research in larger samples of patients with focal lesions and detailed anatomical analysis will be needed to definitely answer these questions. Nevertheless, despite memory difficulties and low detection performance overall, our patient still showed substantially smaller emotion benefits than the poorest performer in our control sample (see Results), suggesting that her deficits could not be solely accounted by memory dysfunction. Further, her emotion deficits were also evidenced in the search task where memory demands were not present.

In addition, lesion extension may also explain results in other studies (Piech, McHugo, Smith, Dukic, Van Der Meer, Abou-Khalil, Most, et al., 2011; Piech, McHugo, Smith, Dukic, Van Der Meer, Abou-Khalil, & Zald, 2011), where patients with unilateral (right or left) amygdala lesion due to temporal lobe resection showed normal emotion facilitation in attentional blink and visual search. It is remarkable that all lesions in the latter study were strictly unilateral (left or right), as opposed to our patient who had bilateral lesion, and they might thus have been able to compensate by recruiting their contralateral intact amygdala to perform the task (Piech, McHugo, Smith, Dukic, Van Der Meer, Abou-Khalil, & Zald, 2011).

Finally, it is worth noting two potential limitations for interpreting our results. First, our patient had a partial (although small) destruction of the right ventral insula. We can therefore not fully rule out that abnormal emotional biases in attentional blink and search were at least partly insula- (and not only amygdala-) dependent. In fact, the right anterior insula has been associated to the coordination and evaluation of attention-task performance with varying perceptual and response demands (Eckert, et al., 2009). However, other patients in Bach et al. (2015) who showed emotion deficits in search had no apparent damage in the insula. In addition, our patient also presented cortical damage in the right inferior temporal lobe, potentially including visual and object-selective areas, which could also have an impact on her perceptual performance in both tasks (Bach, et al., 2011; Vuilleumier & Pourtois, 2007). While this cannot be fully ruled out for the attentional blink results, it is unlikely that this was the case for visual search, given that her performance was normal and highly efficient for non-emotional targets. Another limitation concerns the use of face stimuli alone in both tasks. While this was intended to optimize the evaluation of emotional biases on attention (see Introduction), it may limit our main conclusions to only these type of stimuli. Therefore, it is unclear whether similar abnormal biases may be observed in our patient with other stimulus types. In fact, as stated above, the diversity of stimuli used in previous lesion studies (words, Anderson & Phelps, 2001; Bach, et al., 2011; faces, Bach, et al., 2015; Tsuchiya, et al., 2009, pictures of spiders, Piech, McHugo, Smith, Dukic, Van Der Meer, Abou-Khalil, & Zald, 2011, or images with aversive and erotic content, Piech, McHugo, Smith, Dukic,

Van Der Meer, Abou-Khalil, Most, et al., 2011), may also be a potential source of conflicting results. For instance, it is possible that previous reports of intact emotional biases for emotional pictures or sceneries (e.g. Piech, McHugo, Smith, Dukic, Van Der Meer, Abou-Khalil, Most, et al., 2011; Piech, McHugo, Smith, Dukic, Van Der Meer, Abou-Khalil, & Zald, 2011) were due to a stronger emotional impact elicited by sceneries (i.e. activating alternative circuits beyond amygdala) compared to faces (Bach, et al., 2015), or related to the fact that rapid pre-attentive emotion processing in the amygdala occurs only for specific emotional cues in single coherent stimuli, such as faces, but not for more complex, multi-element scenes (see iEEG from Méndez-Bértolo et al., 2016). Further research should elucidate the generalizability of amygdala function across stimuli.

## 5. Conclusions

Overall, our results suggest that amygdala lesion leads to deficits in the emotional biases guiding spatial attention to behaviorally relevant face stimuli, though it may not totally abolish such effects. These deficits might be caused by impaired amygdala inputs to several brain areas implicated in attentional selection and orienting, including orbitofrontal and anterior cingulate cortex, basal forebrain and upper brainstem (locus coeruleus), as well as sensory (visual) cortices (Domínguez-Borràs, et al., 2012; Domínguez-Borràs & Vuilleumier, 2013; Pourtois, et al., 2012; Vuilleumier, 2008; Vuilleumier & Pourtois, 2007). More research is needed to fully elucidate the various brain pathways through which emotions may impact on these processes, and their impairment in different pathologies (Dominguez-Borràs, et al., 2012).

In this vein, functional neuroimaging may yield valuable information that can add at least partial support to the current conclusions. For instance, a study using functional magnetic resonance imaging (fMRI; Mohanty, et al., 2009) showed that guided attention towards emotional (in this case threatening) targets in visual search was facilitated through connectivity between the amygdala and the spatial attention networks, even though the visual displays used in that study consisted of only 4 stimuli, with no variation of set size. Here we show that emotional deficits in visual search became more apparent with increases in stimulus set-size, suggesting that distinct mechanisms might exist and subservise different components responsible for these effects. Another study using visual search with 9-stimuli displays reported that amygdala activity correlated with target detection (Santos, Mier, Kirsch, & Meyer-Lindenberg, 2011), but this correlation was present for virtually all (emotional and non-emotional) targets, highlighting a more general role of the amygdala in signaling behavioral salience rather than emotional salience alone (Sander, Grafman, & Zalla, 2003). Moreover, still another fMRI study correlating amygdala response to masked emotional faces (inside the scanner) and target detection of emotional faces in visual search (outside the scanner), revealed that amygdala sensitivity predicted detection speed for faces in general, regardless of the emotional expression (Ohmann, et al., 2007). In contrast, our patient showed relatively good search abilities for non-emotionally (i.e. colored) salient targets, as compared with controls, suggesting a more prominent role

of the amygdala in guiding search based on affective salience rather than perceptual salience. However, the latter study reported that the observed correlations between amygdala responsivity to emotional (in this case fearful) faces and detection speed did not depend on the number of stimuli (2, 4 or 6 faces), and therefore did not predict search slopes. On the contrary, again our results suggest that the amygdala might play a greater role in search efficiency as a function of set size.

In sum, the present study extends previous findings pointing at a causal role of the amygdala on preattentive emotion processing, at least in particular tasks and specific attentional load conditions. We report a patient with extensive, almost complete, bilateral amygdala lesion, who showed impaired emotional biases during attentional blink and visual search for face targets. This deficit extended to (or even predominated for) happy faces, suggesting that amygdala functions are not restricted to negative, threat-related cues. We consider possible confounds regarding her lesion extension and conclude that her abnormal emotional biases of attention (particularly in visual search) are most likely to be due to amygdala destruction, rather than other neighboring structures, and to result from acute late-onset damage that does not allow full compensatory mechanisms to take place.

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**Footnotes**

<sup>1</sup>The Lag effect was nevertheless significant at the group level in controls, also when including all blocks in the analysis (i.e. blocks with inverted and blocks with scrambled faces as distractors;  $F_{(1,14)}=24.32$ ;  $p=0.0002$ ).

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### Figure captions

**Figure 1.** Structural MRI of patient HE1, MNI-normalized, showing bilateral temporal lesion including the amygdala and hippocampus. Top: with an overlaid probabilistic cytoarchitectonic map of the amygdala (Eickhoff, et al., 2005). Bottom: areas of lesion shown on coronal slices of the patient's MRI (native non-normalized image).

**Figure 2.** Attentional blink task, trial structure. Participants judged the gender of the two target faces, embedded within a series of distractors, all presented in rapid serial visual presentation (RSVP). First target faces (T1) were always neutral, whereas second targets (T2) were either neutral, fearful or happy faces. In the ShortLag condition T1 and T2 were separated by 1 or 2 distractors, whereas in the LongLag condition these were separated by 6 or 7 distractors.

**Figure 3.** Visual search task, illustration of the different conditions. The target face could differ from the distractors (all with same identity) either by identity alone, by identity+happy facial expression, identity+fearful facial expression, or by identity+red hue. Face arrays could consist of 4, 6 or 8 stimuli.

**Figure 4.** Attentional blink: results of patient HE1 and controls (N=15). Mean hit rates (%) for T2 in trials where T1 was correctly detected. Error bars indicate the standard error of the mean ( $\pm$ SEM). Patient HE1 showed a strong attentional blink effect but, contrarily to controls, failed to benefit from the emotional expression of T2 faces.

**Figure 5.** Attentional blink. Report sparing from the attentional blink (survival index, ShortLag / LongLag) for each emotion condition, for both controls and patient HE1, showing abnormally low values for T2 faces in HE1, compared to controls. Patient HE1 showed generally low sparing in all conditions, compared to healthy controls.

**Figure 6.** Visual search: results in controls (N=18) and patient HE1. Mean response latencies ( $\pm$ SEM) are plotted for each of the four cueing conditions and set size (4, 5 or 8 stimuli) of the visual display.

**Figure 7.** Visual search: search slopes (in ms/item) of both controls and patient HE1, as a result of increasing size of the visual display. Color-cued targets showed the shallowest slopes in both patient and controls. However, whereas controls exhibited shallower slopes for the emotionally-cued targets, in relation to the neutral (ID-only) targets, patient HE1 showed the opposite pattern, indicating that her

guided search for emotional faces (particularly happy faces) was comparably inefficient, relative to neutral faces, unlike in controls.

**Figure 8.** Visual search: emotion benefit for the happy and fearful faces, relative to neutral, on slope values ( $[\text{slope}_{\text{ID-only}} - \text{slope}_{\text{cue}}] / \text{slope}_{\text{ID-only}}$ ; Lucas & Vuilleumier, 2008). Scatterplots show abnormally low benefit for emotional (happy) faces on the patient's guided search, relative to controls. A similar difference, although non-significant, was observed for fearful faces.

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**Table 1.** Neuropsychological performance of patient HE1. Abnormal scores, relative to normative data, are indicated with \* (mildly abnormal) or \*\* (highly abnormal). %ile indicates percentile.

Function	Modality/ test		Scores
Memory	Verbal / Word Lists Test I and II (WMS-III)	Total recall	12**
		Learning curve (trial 4 - trial 1)	2*
		Delayed recall	0**
		Delayed recognition	5**
		Retention	0 %**
		Visual / Doors and People Test (part A)	5/12**
Short term and working memory	Verbal / WMS-III	Forward memory span	4**
		Backward memory span	2**
	Verbal paired associates (WMS-IV)	Recall	%ile >1**
		Spatial / WMS-III	Forward memory span
		Backward memory span	2**
	Attention	Color Trails Test 1	Seconds (errors)
Executive functions	Color Trails Test 2	Seconds	288" **
		Interference index	2.64 *
		Shifting errors	2 *
		Number sequence errors	2 *
Theory of mind	Task described in Corradi-Dell'Acqua, Hofstetter & Vuilleumier (2014)	Belief	Normal
		Emotion	Normal
		Pain	Normal
		Photo	Normal

**Table 2.** Patient HE1's performance (hit rate and response time for correct responses) in a dynamic facial expression recognition task (Cristinzio, et al., 2010; van Assche, et al., 2016). The control sample (N=10) was selected from van Assche et al. (2016). \* indicates significant difference ( $p=0.034$ ) between patient and controls in a Bayesian test (Crawford & Garthwaite, 2007).

Expression	Hit rate (%)		Response time (ms)	
	Patient HE1	Controls	Patient HE1	Controls
Neutral	100	86.7	3092	4441
Fear	62.5*	81.9	6419	7114
Happiness	100	98.6	2839	2574
Anger	87.5	76.2	4672	5668
Disgust	87.5	83.6	2872	4504
Sadness	75	76.6	8710	8702

**Table 3.** Data and main statistics, with corresponding F-values (F), T-values (T), and p-values (p-val), for the attentional blink task.

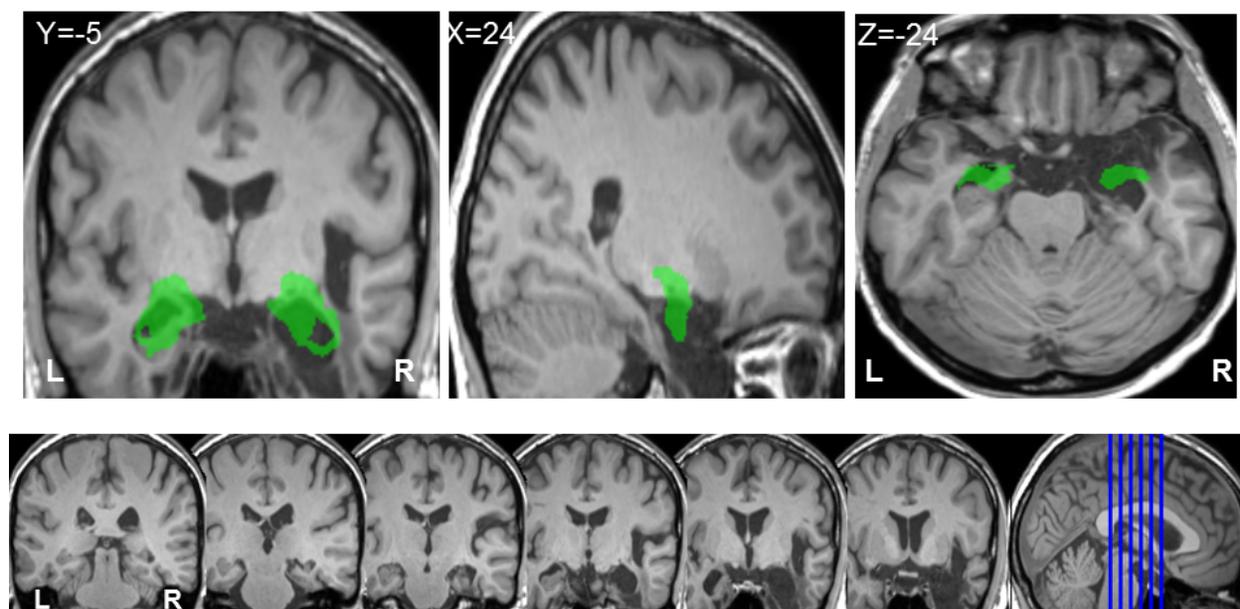
		CONTROLS (N=15)			PATIENT HE1		
		ShortLag	LongLag	Global	ShortLag	LongLag	Global
HR (%)	Neutral	46.42	70.89	58.66	12.5	87.31	49.91
	Fear	60.29	74.38	67.34	21.43	92.31	56.87
	Happy	61.82	67.78	64.8	11.11	96.15	53.63
	Total (mean)	56.18	71.02	63.6	15.01	91.92	53.47
ANOVA (F/p-val)	Emotion	6.79/0.005**	2.021/0.16	4.05/0.034*	1/0.37	0.49/0.6	0.58/0.57
	Lag			39.86/<0.0001****			91.91/<0.0001****
	Emotion x Lag			6.24/0.009**			0.1/0.86
t-test (T/p-val)	Fear > Neutral	-2.37/0.033*	-1.09/0.3		-0.44/0.67	-0.44/0.67	
	Happy > Neutral	-3.12/0.008**	0.75/0.47		0/1	-1/0.33	
	Fear > Happy	0.29/0.78	-1.78/0.1		-0.44/0.67	0.57/0.58	

**Table 4.** Response times (RT, on correct trials) and statistics, with corresponding F-values (F), T-values (T), and p-values (p-val), for the visual search task.

		CONTROLS (N=18)				PATIENT HE1					
		ID-only	ID+FEAR	ID+HAPPY	ID+COLOR	Global	ID-only	ID+FEAR	ID+HAPPY	ID+COLOR	Global
RT (ms)	4 stimuli	2127	1836	1858	1525	1837	1811	1527	1593	1674	1651
	6 stimuli	2325	1943	1969	1524	1940	1905	1675	1962	1545	1772
	8 stimuli	2580	2071	2111	1531	2073	2085	1844	1979	1594	1875
	Total (mean)	2344	1950	1979	1526	1950	1934	1682	1844	1604	1766
ANOVA (F/p-val)	Cue type					47.27/<0.0001****					3.75/0.02*
	Set size	15.24/ <0.0001****	15.24/ <0.0001****	11.94/ 0.001**	0.03/0.96	37.12/<0.0001****	0.74/0.46	1.77/0.18	2.98/0.08	0.45/0.63	3.32/0.052
	Cue type x Set size					11.44/<0.0001****					1.04/0.3
ANOVA excluding ID+COLOR (F/p-val)	Cue type					35.9/<0.0001****					2.5/0.095
	Cue type (4 stimuli)					14.95/0.00014***					2.51/0.11
	Cue type (6 stimuli)					32.12/<0.0001****					1.33/0.27
	Cue type (8 stimuli)					32.37/<0.0001****					0.38/0.68
	Set size					46.08/<0.0001****					4.33/0.024*
	Cue type x Set size					4.52/0.007**					0.45/0.74

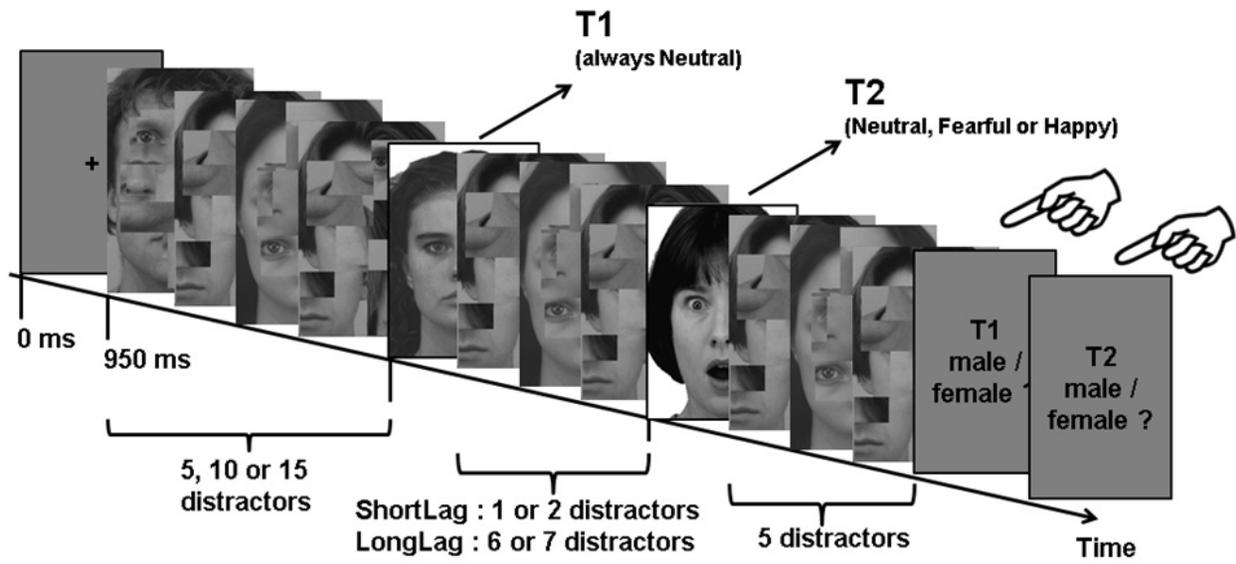
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<b>t-test</b>	<b>ID+COLOR &gt; ID-only</b>	<b>-7.46/&lt;0.0001****</b>	<b>-2.62/0.014*</b>
<b>(T/p-val)</b>	<b>ID+COLOR &gt; ID+FEAR</b>	<b>-6.78/&lt;0.0001****</b>	<b>-1.1/0.3</b>
	<b>ID+COLOR &gt; ID+HAPPY</b>	<b>-6.79/&lt;0.0001****</b>	<b>-2.69/0.012*</b>
	<b>ID+FEAR &gt; ID-only</b>	<b>-6.30/&lt;0.0001****</b>	<b>-2.16/0.039*</b>
	<b>ID+HAPPY &gt; ID-only</b>	<b>-6.12/&lt;0.0001****</b>	<b>-0.36/0.72</b>
	<b>ID+FEAR &gt; ID+HAPPY</b>	<b>1/1.2</b>	<b>-2.02/0.052</b>



Journal

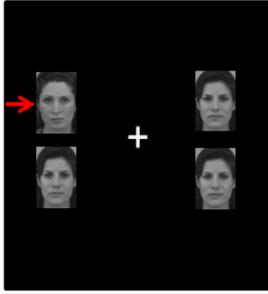
## Attentional blink



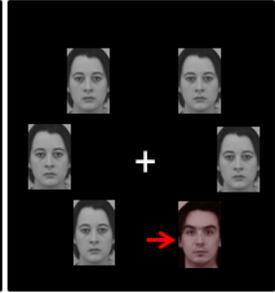
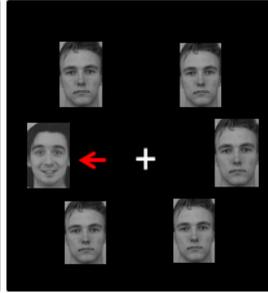
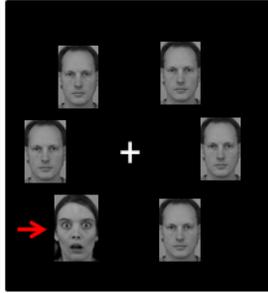
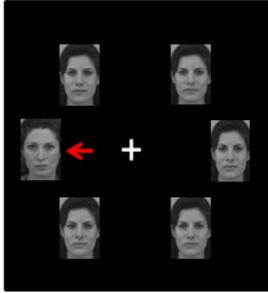
Stimulus duration: 70 ms (30-ms ISI)

### Visual Search

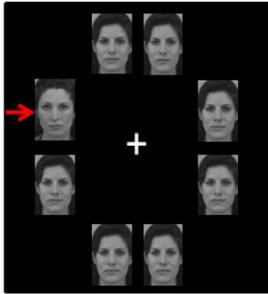
4 stimuli



6 stimuli



8 stimuli



ID only

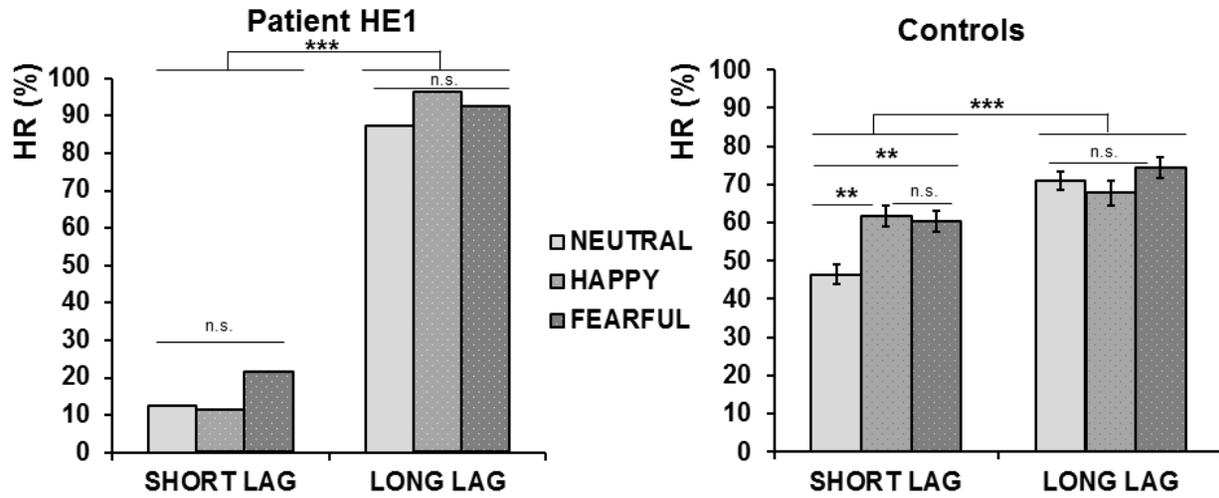
ID + FEAR

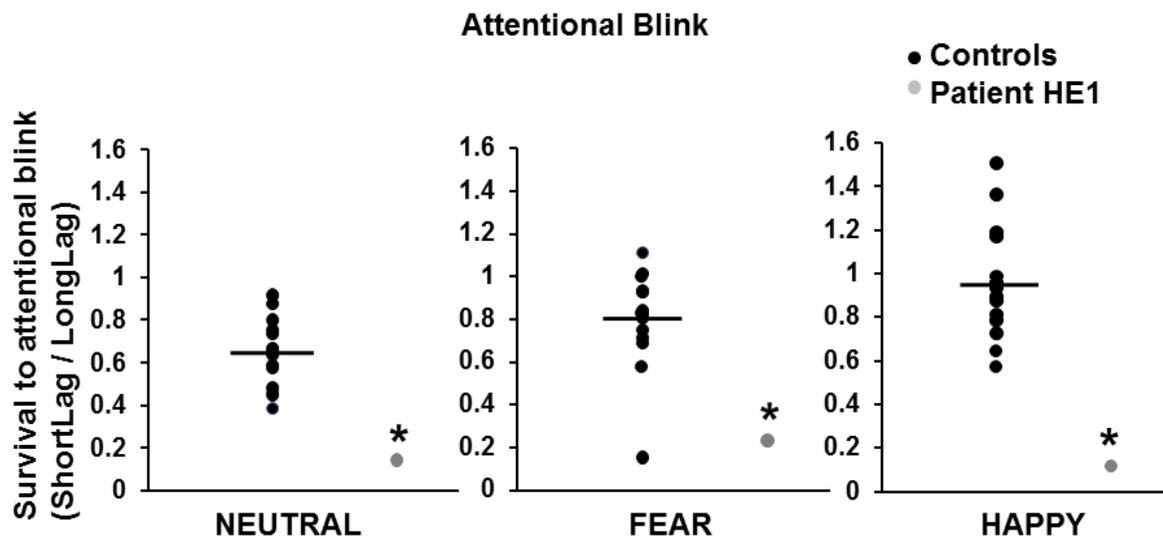
ID + HAPPY

ID + COLOR

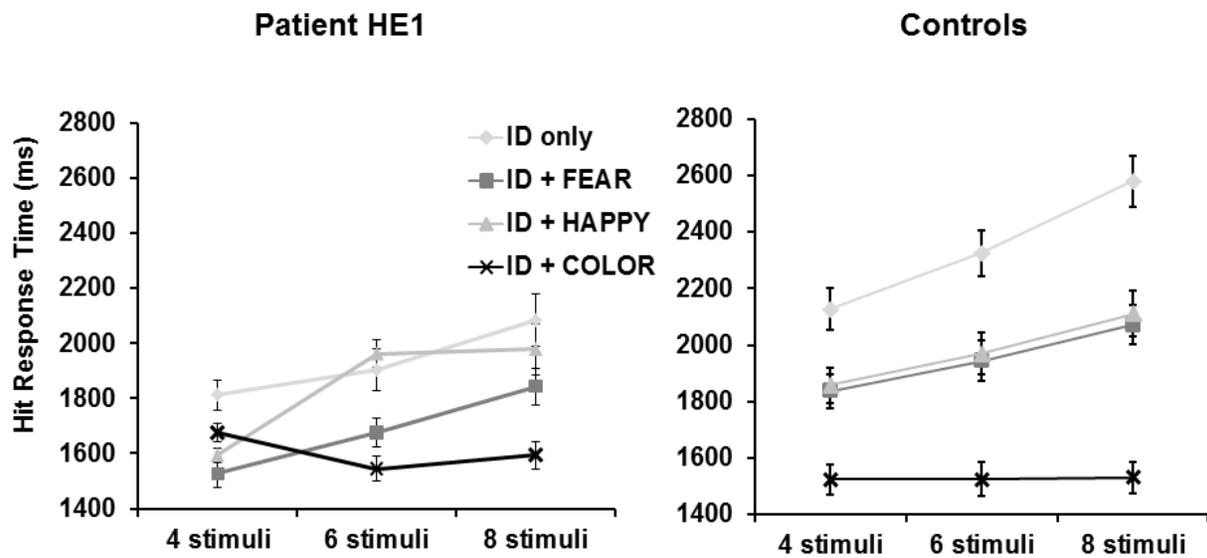
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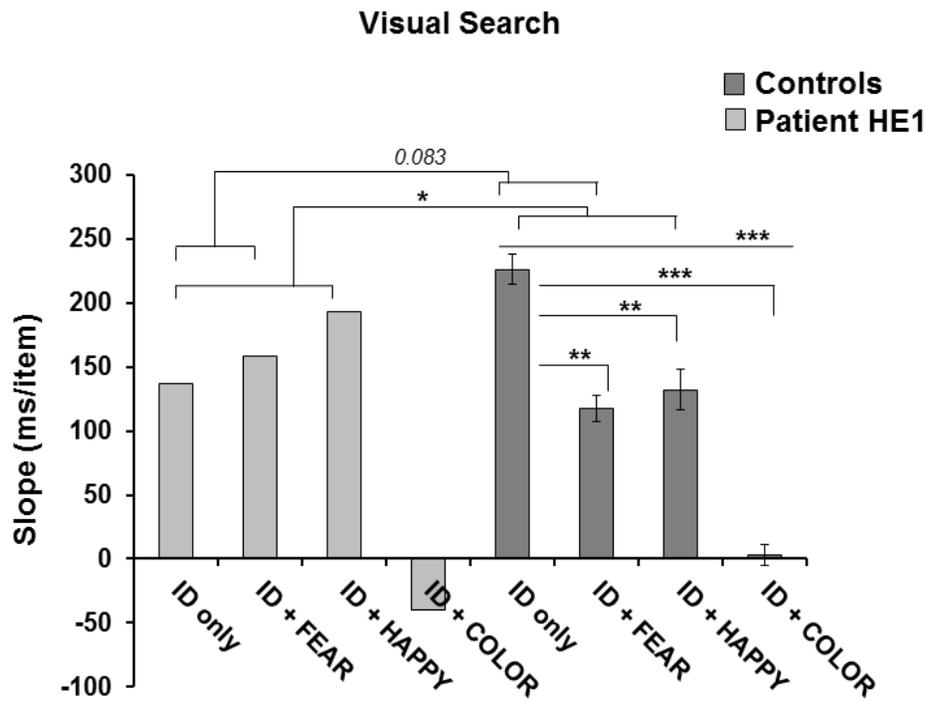
## Attentional Blink

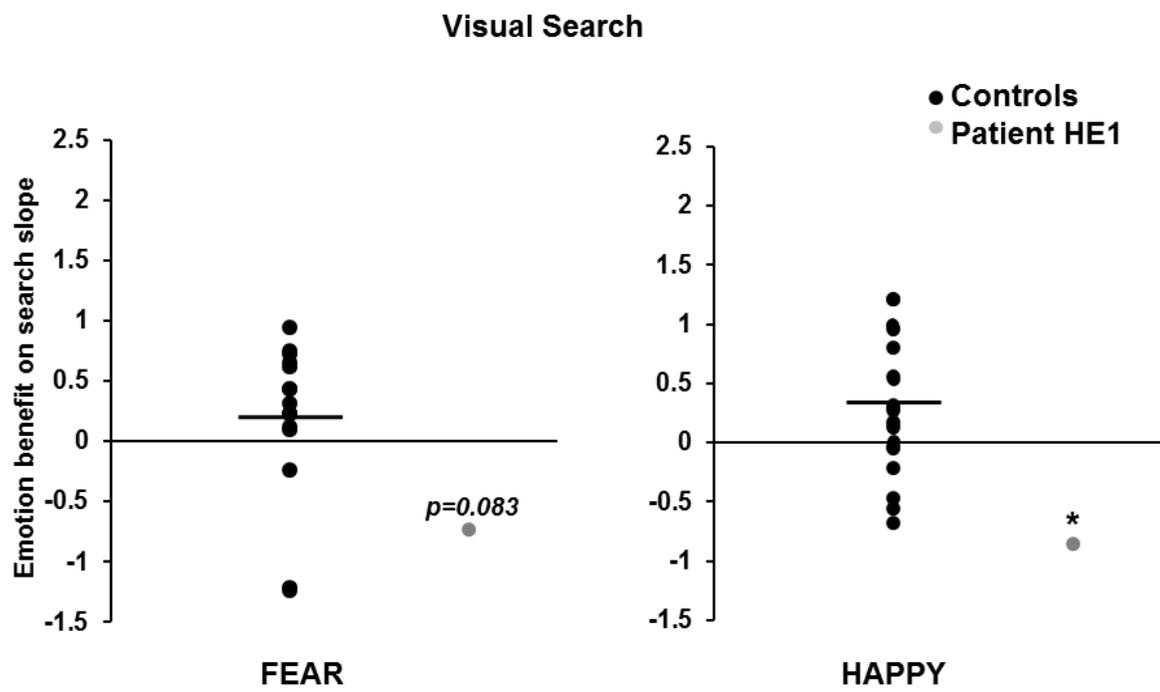




## Visual Search







## Highlights

- We investigated a patient with bilateral amygdala lesion after herpetic encephalitis
- Tests focused on emotional variants of attentional blink and visual search tasks
- Preattentive emotion detection was impaired in the patient compared to controls
- Deficits in attention and guided search were larger for happy than fear faces
- Results support a causal role of amygdala in emotional facilitation of attention

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