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Language lateralization and cognition: considerations on schizophrenia and autism

Estudiant: Amaia Oliden Manterola

Directora: Joana Rosselló Ximènes

Tutor: Xavier Laborda Gil

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Abstract

Language lateralization should be understood as the specialization of the hemispheres to carry out different linguistic functions each. It has been a common research topic that has attracted the attention of a wide range of researchers of different fields through history. Nonetheless, the matter is still not fully understood nowadays. The technological and technical advances have allowed to delve into human brain and investigate it more accurately, which has enabled current research to reveal significant findings about how language is organized in the human brain. Among the most relevant observations, we could name the role of the right hemisphere for language, anatomical asymmetries of the human brain, possible sexual dimorphism of language lateralization, and most importantly, the significance of the white matter pathways connecting cortical language areas, which entails a change of conception of the human brain, from a more localist view to a conception of the brain as a complex and highly interconnected structure. Moreover, new findings underpin the crucial role of language lateralization for human cognition, as it is supported by evidence of the relation between deviant patterns of lateralization and certain psychotic disorders, such as schizophrenia and autism. Overall, the main objective of the present paper is to provide an overview of the research on language lateralization, from classical studies until nowadays, focusing specially our attention on what is known about the lateralization patterns of autism spectrum disorder and schizophrenia. We will conclude stating that language lateralization seems to be a central factor for human cognition and condition, and try to propose prospects for future research.

Key words: language lateralization; brain asymmetry; cognition; autism; schizophrenia

Resum

La lateralització del llenguatge s'ha d'entendre com l'especialització dels hemisferis per dur a terme diferents funcions lingüístiques cadascú. Al llarg de la història ha sigut un tema que ha interessat a un gran nombre d'investigadors de diferents especialitats. Tot i així, encara avui no s'ha pogut arribar a comprendre la lateralització del llenguatge en la seva totalitat. Els avanços tecnològics i tècnics han fet possible un estudi més acurat del cervell humà, i per tant, ha facilitat que la investigació actual hagi pogut fer noves descobertes sobre com el llenguatge s'organitza al cervell humà. Entre les observacions més importants, podríem mencionar el paper de l'hemisferi dret en el llenguatge, asimetries anatòmiques del cervell humà, possible dimorfisme sexual de la lateralització del llenguatge, i més significativament, la importància de la matèria blanca, que connecta les àrees corticals del llenguatge. La descoberta de la rellevància de la matèria blanca, ha portat a la investigació a canviar la concepció sobre el cervell humà, des d'una perspectiva més localista a la concepció del cervell com una estructura complexa i considerablement interconnectada. Endemés, les noves descobertes donen suport al paper crucial que comporta la lateralització del llenguatge per a la cognició humana, com indiquen les evidències sobre la relació entre els patrons atípics de lateralització i certs desordres psicòtics, com ara l'autisme i l'esquizofrènia. Així doncs, el principal objectiu del present treball és exposar una visió general sobre la investigació en la lateralització del llenguatge, des d'estudis clàssics fins als més actuals, centrant-nos especialment en el que se sap sobre els patrons de lateralització de l'autisme i l'esquizofrènia. Conclourem defensant que la lateralització del llenguatge sembla ser un factor central per a la cognició i condició humanes, així com intentarem proposar perspectives per a la investigació futura.

Paraules clau: lateralització del llenguatge; asimetria cerebral; cognició; autisme; esquizofrenia

Laburpena

Hemisferio bakoitza funtzio linguistiko jakin batzuk burutzeko espezializatzean datza hizkuntzaren lateralizazioa. Historian zehar hainbat jakintza arlotako ikertzaileek sarri jorratutako gaia izanagatik, gaur egun oraindik ezin izan dugu hizkuntza giza burmuinean antolatzen den modua bere osotasunean ulertu. Alabaina, azken urteetan zientziak jasan duen iraultza teknologiko eta teknikoari esker, gaur egungo ikerkuntzak giza garuna sakontasun eta zehaztasun handiagoz ikertzeko aukera du, eta ondorioz, hizkuntzaren lateralizazioaren inguruan hainbat aurkikuntza egin ahal izan dira. Besteak beste honakoak aipa genitzake: eskuin hemisferioak hizkuntzaren prozesamenduan duen garrantzia, giza burmuinaren asimetria anatomikoak, ustezko sexu-dimorfismoa hizkuntzaren lateralizazioari dagokionez, eta adierazgarrienetarikoa, hizkuntzaren prozesamendurako esanguratsuak diren garun-azaleko areak lotzen dituen gai zuriaren garrantzia. Azken aurkikuntza honek giza burmuinaren ikuskeran ondorioak izan ditu; izan ere, garun-areetan oinarrituriko ikuspegia atzean utzita, gaur egun giza burmuina bere baitan biziki konektaturiko egitura konplexu gisa ulertzen da. Aitzitik, egungo ikerkuntzak mahai gainean jarritako egiaztapenak hizkuntzaren lateralizazioak giza kognizioan duen garrantziaren isla dira; garunean hizkuntzak izan dezaken ohiz kanpoko antolamenduak adimenaren nahasmendu psikotikoekin duen harreman estuak argi adierazten duen moduan, autismoa edo eskizofrenia kasu. Horrenbestez, hizkuntzaren lateralizazioaren inguruan egindako ikerkuntzen ikuspegi orokorra azaltzea da lan honen xede eta funts; ideia klasikoetatik abiatu eta gaur egungo pentsaerara iritsi arte, autismoaren eta eskizofreniaren inguruko ikerkuntza ardatz hartuz. Etorkizuneko ikerkuntzarako zenbait iradokizun eginez amaituko dugu lana, baita hainbat ondorio kritiko azalduaz ere, hala nola, itxuraz hizkuntzaren lateralizazioak giza kognizio eta izatean duen eragina azpimarratuko dugu.

Gako-hitzak: hizkuntzaren lateralizazioa; garunaren asimetria; kognizioa; autismoa; eskizofrenia

"*Man is, of all the animals, the one whose brain in the normal state is the most asymmetrical. He is also the one who possesses most acquired faculties. Among these the faculty of articulate language holds pride of place. It is this that distinguishes us the most clearly from the animals*"

Broca, 1877, translated in Harrington, 1987:65-66

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Introduction

The lateralization of human language is not a new research topic. In fact, Paul Pierre Broca is considered one of the first scientists to cast light on the matter in the 1860's. Thus, we could establish the beginning of the history of research on language lateralization with the french anatomist, yet it has still not arrived to its end, since, more than a century later, the organization of language in the brain and its contribution for human cognition are not fully understood.

During decades, several studies have contributed to clarify how human brain is constituted to support such a complex system as language is, and many of those reports have been determining to arrive to the point where we are nowadays. However, the great technological, and consequently technical, revolution implied a profound change for science in general, and for neuroscience in particular; which allowed to more accurate investigations of the linguistic function in the brain. Indeed, investigation is improving over time, enabling access to the brain areas that could not be investigated in the past. Thus, we could say that brain research in relation to language is increasingly active nowadays, resulting in a high number of research papers reporting new findings or confirming as well as refuting older ones each year. Considering the great variety of studies that one can find on the topic, our main objective was to provide the reader a general overview about the lateralization of language and the lines of investigation that science is following nowadays in order to shed light on the unclear issues. To do so, we carried out a selection of diverse bibliography which could account for what is known about language lateralization.

In this way, the present paper is divided in two parts. In the first part we try to make a general overview, starting with some basic concepts in the first section that are required in order to understand what language lateralization means. As we claimed in previous lines, the models proposed historically are determining to understand the current view about language lateralization, and therefore, in the second section we summarized the most influential classical proposals about how language is organized in human brains. The third and last section of the first part of this paper is an attempt to gather the contemporary findings of how the human brain is thought to operate in relation to language.

We saved the second part of our study to go in depth on brain disorders that have strong relation with language lateralization and can help us understand its relation to human cognition. Thus, in this part we focus our attention on psychotic disorders, namely, autism spectrum disorder and schizophrenia. Although more recent research topic, several studies account for the (dis-)organization of the brains with these disorders and seems to be a highly contributing line of investigation.

In summary, our aim is to describe what we know about language lateralization, emphasizing its role for human cognition. Remarking the issues that remain unclear and claiming an inter-disciplinary research, we will conclude the paper with a critical perspective and suggestions that we consider should be taken into account for the future research.

Part I. Language lateralization, an overview

1. Brain asymmetry, language lateralization and cognition

The asymmetry of the human brain has been a topic that has interested to neuroscientist, neuropsychologists and linguists, among others, for centuries; however, we still have not managed to comprise the matter in its entirety.

As far as we know, the asymmetry of the brain and behavior is not uniquely human, as Ocklenburg et al. (2014) assert, *"Hemispheric asymmetries are abundant in the anatomy, neurochemistry and cytoarchitecture of the vertebrate brain [...]"*. Nonetheless, and not forgetting that humans share this characteristic with the rest of vertebrates, we will concentrate here on the asymmetries of the human brain, focusing our attention on the lateralization of the language system.

Jonathan E. Peelle (2012) states two possible interpretations of the term lateralization:

1. *"One hemisphere performing a task and the other not being involved"*.
2. *"Both hemispheres being engaged in a task, but one hemisphere is doing more of the work or being slightly more efficient."*

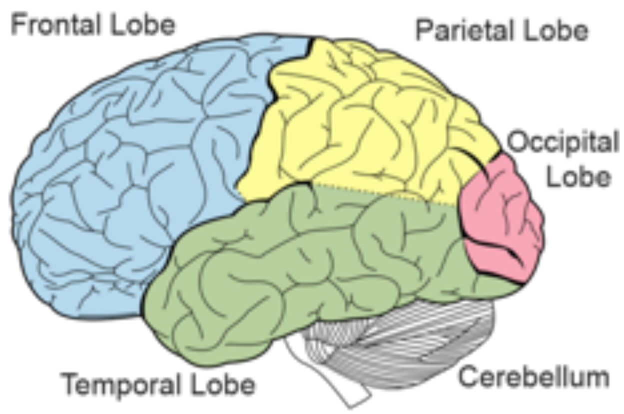
As we will show in this paper, the appropriate definition of lateralization, at least for language, is the second one. Therefore, we understand lateralization of language as the specialization of one hemisphere (usually the left) for some, probably most of the linguistic tasks, and the specialization of the other hemisphere (usually the right) for other linguistic tasks. Furthermore, *"mechanisms that enable the inter-hemispheric coordination [are] necessary for efficient processing"*(Hervé et al. 2013). Therefore, we assume that language lateralization implies the connections within and between the two hemispheres, performing different specialized tasks each.

There is no doubt that language is lateralized, in terms of hemispheric specialization. This fact is not that surprising considering that language is a highly complex system, yet it does not mean any effort for human beings to deal with it. In other words, inasmuch as language is a highly integrative system, and therefore the human brain needs to carry out different processes simultaneously and continually, it does not result shocking that each hemisphere specializes in some linguistic functions so as to be effective. Along these lines, some authors have stated that a lateralized brain may grant some advantages, namely:

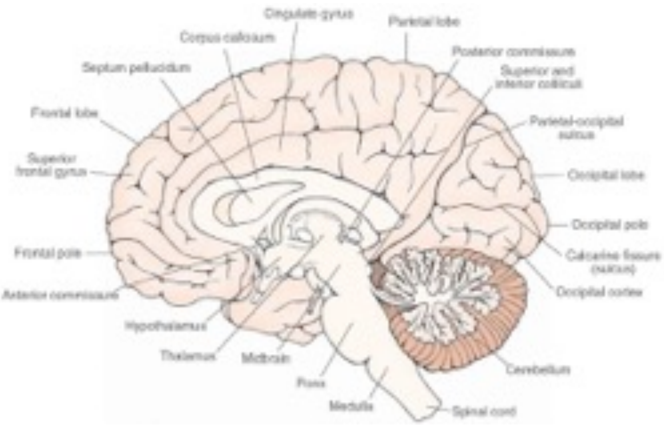
“[...] *sparing neural tissue by avoiding duplication of functions in the two hemispheres (Levy, 1977); processing information in parallel (Rogers, 2002; Rogers et al., 2004); and preventing the simultaneous initiation of incompatible responses by allowing one hemisphere to have control over actions (especially in animals with laterally placed sensory organs, Andrew, 1991; Vallortigara, 2000)”*(Frasnelli 2013)*,* among others.

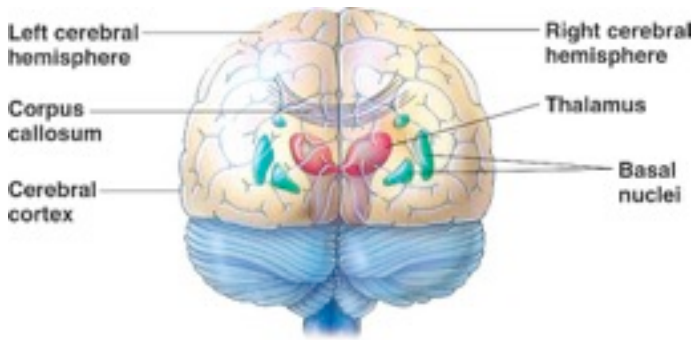
Thus, hemispheric specialization seems to be crucial for language as such, for its acquisition and functioning. However, its importance for cognition is still unclear, although the research is showing that language lateralization would play an important role in human cognition as we will see later on.

Before focusing our attention on how the brain is organized according to the functions that each area or structure carries out, we will introduce some basic concepts about the anatomy of the human brain. As it is well known, the human brain can be divided into two hemispheres, the left and the right hemispheres. In addition, two surfaces can be observed: cortical surface (80% of the brain) and medial surface. The cortex is divided into four lobes with a principal function each: frontal (function: motor), temporal (function: audition), parietal (function: somatosensory) and occipital (function: vision) lobes.



Moreover, the cortical surface consists of gyri (ridges) and sulci (grooves surrounding the gyri), the latter being either lateral or medial. It is in the medial surface that lie the connection fibers of white matter. These connections can be short (connecting gyri), long (connecting lobes) or inter-hemispheric (connecting hemispheres, the most important one being the corpus callosum).





We have seen by now that language lateralization has to be understood as the specialization of the hemispheres to carry out specific functions, that it may be an important factor for cognition and some basic information about the brain has also been presented. In the following section we will account for how the research started on language lateralization and what was thought to be the cerebral organization for language classically; we will mainly focus on two influential models, Broca's model and Wernicke-Lichtheim-Geschwind model.

2. Classical perspective

Probably, the lateralization of language has been the most widely investigated lateralized function in the human brain. It was first observed by Paul Pierre Broca (although, he did not use this term) and many scientist have investigated his discovery for decades until today. In 1861, Broca described a patient, Tan, who lost his capacity to articulate speech, supporting the view of Bouillaud that speech was localized in both frontal lobes. However, in 1865, Broca wrote a report where he upheld the localization of articulated speech in the third left frontal gyrus, which we name nowadays as Broca's area. It was the result of the description he carried out in 1863, of over 25 patients with *aphémie* (loss of articulate speech in Broca's terms), all with lesions in the left hemisphere including the third left frontal gyrus. (Berker et al. 1986)

In this description he started considering the localization of speech faculty in the third left frontal gyrus, and not in both frontal lobes, and despite the critiques of discussants as Laborde who stated that "*such an admission would imply a serious exception to the law of organic duality and functional unity*" (Berker el al. 1986), and therefore it was difficult to admit, Broca confirmed his findings in the 1865's report.

Thus, he defends that even if *"it is well known that the two hemispheres of the brain are perfectly similar[...], a great many mechanical actions are controlled mainly or even exclusively by the left hemisphere of the brain."* (Berker et al. 1986). At this point, the French anatomist tries to link the speech articulation in the left hemisphere with handedness, that is, "*almost all men are right-handed*" (Berker et al. 1986), and we know that the left hemisphere controls the right part of the body and vice-versa. Nonetheless, Broca surprisingly emphasizes the symmetry of the two halves of the brain, and following the physiological law that states that "*two organs that are equal and symmetrical have the same attributes*" (Berker et al. 1986), he affirms that it is not possible that the two hemispheres of the brain have different functions. Although it might seem at first that the influential anatomist is defending contradictory ideas, in fact, pointing out what his colleague Gratiolet found, he explains that:

"*in the development of the brain the convolutions of the left hemisphere are developed earlier than those of the right hemisphere.* [...] *The left hemisphere, which controls the movement of the right extremities, is therefore more precocious in its development than the opposite hemisphere.*" (Berker et al. 1986)

Thus, he attributes the preference for the right extremities, which results in that most people become right-handers, to this earlier development of the left hemisphere. When explaining the preference of the left hemisphere for the articulate speech he distinguishes between articulation as such, and articulated speech. According to Broca "*articulation depends on the two cerebral hemispheres, since it is brought out simultaneously and uniformly by the muscles of both sides, associated in their movements*". (Berker et al. 1986)

Articulated speech, instead, actually resides on the corpus striatum and,

"*this articulated speech depends on the part of the encephalon linked to intellectual phenomena and of which the cerebral motor organs are, as it were, just the agents. Now, this function of the intellectual order, which controls the dynamic element as well as the mechanical element of the articulation, seems to be the nearly constant privilege of the left hemisphere convolutions [...]*". (Berker et al. 1986)

The fact that "*we are left-brained with regard to language*" (Berker et al. 1986), could be explained by the same phenomenon, since:

"*This cerebral exercise [learning to articulate speech] is imposed on him [the child] at an age very close to these embryonic periods in which the development of the left hemisphere takes place before the right hemisphere.*" (Berker et al. 1986)

Hence, Broca affirms that speech articulation is specialized in one hemisphere, which almost always is the left one, but not always. Just as there can be people with preference for the left extremities, say, left-handers, there can also be people who articulate speech in the right hemisphere, that is, “right-brained” in Broca’s terms. That would explain the few cases that he described where *aphémie* results from lesions in the right hemisphere. According to the french expert, the cause of this exceptional cases of right-brained people, would be an atrophy of the third left frontal gyrus from birth, which would force these people to learn to speak with the third right frontal gyrus.

Moreover, the right hemisphere not only can assume the functions that in a typical brain acquires the left hemisphere, but it also collaborates in language in a healthy brain. “*[...] the general capacity of language, which consists of establishing a determined relationship between an idea and a sign”* (Berker et al. 1986) is carried out with both hemispheres. This bilateral “general language capacity” would explain why Broca’s *aphémic* patients lose just the articulation of speech but not comprehension; that is, according to the anatomist, a patient with a lesion in the left hemisphere “*continues to understand what one says to him, and consequently, he understands perfectly the connection between ideas and words*” (Berker et al. 1986).

Before moving to explain the other influential classical model, it is worth stressing that although Paul Broca tried at first to link the handedness with the dominance of one hemisphere for reasons of earlier development, he clearly states that it is not “*necessary that the motor part and the intellectual part of each hemisphere should be responsible for one another*” (Berker et al. 1986) . That is, even thought the two factors are related, it does not mean that leftward lateralization of language causes right-handedness, or vice-versa, they just co-occur.

To summarize, the Broca’s language model could be briefly explained as follows. Both hemispheres of the brain, which are symmetrical, take part in the “general language capacity”, say, the capacity to establish a relationship between an idea and a sign; which implies speech comprehension. However, due to the more precocious development of the left hemisphere which provokes that we execute the most complex manual and intellectual tasks with that side of the brain, we also specialize the articulation of speech, that is, according to Broca, the capacity to relate an idea with an articulated word, in the left hemisphere; specifically in the third left frontal gyrus (Broca’s area). In case that the Broca’s area is damaged from birth, its counterpart in the right hemisphere, that is, the third right frontal gyrus, assumes this function.

A decade after Broca's statements, Carl Wernicke (1874), following the ideas of his mentor Theodor Meynert, described patients with lesions in the posterior superior temporal lobe of the left hemisphere. These patients presented fluent speech, but apart from making paraphasic errors, had problems with naming, repetition and comprehension of speech. In his studies, he concluded that we can distinguish two language centers: the one described by Broca, "the cortex anterior to the Rolandic sulcus", which served motor functions, and "the cortex posterior to the Rolandic sulcus", which served sensory functions(Poeppel&Hickok 2004).

Just as Paul Broca localized the motor speech functions specifically in the third left frontal gyrus, Wernicke stated that, the superior temporal gyrus of the left hemisphere (Wernicke's area) was the responsible for the speech perception. Furthermore, the german anatomist believed that these regions not only are involved in respectively executing or perceiving speech, but also function as the "*memory storage of sensory and motor imagery*" (Poeppel&Hickok 2004). Thus, the Broca's area would deposit motor images for speech, and the Wernicke's area the acoustic images of words.

Before continuing to describe the classical language model, it is worth mention that the statements of Wernicke were systematized by Lichtheim in 1885, and afterwards restated by Geschwind in 1970, whence, the literature refers to it as the Wernicke-Lichtheim-Geschwind model (W-L-G model), and so will we from now on.

Coming back to the topic on discussion, Wernicke postulated that this two language regions (Broca's and Wernicke's areas), were subcortically connected. According to the W-L-G model, this connection was a consequence of the language acquisition process, since as a result of hearing a word, the child creates a sensory or acoustic word image in the Wernicke's area, and in a reflexive action the child mimics that word in speech, creating a motor word image and resulting in a simultaneous activation of sensory and motor images, provoking a direct association between the two linguistic areas by the subcortical arcuate fasciculus.

In addition, these sensory and motor images are associated to a concept, which "*is formed by the sum total of the memory images associated with, say, a particular object*" (Poeppel&Hickok 2004) or, in other words, the meaning of the concept relies on the "*various cortical connections emanating from the language centers*" (Poeppel&Hickok 2004). Therefore, there is a clear distinction between the sensory and motor images and the concept to which they are related, and

"*in order to comprehend the meaning, an association had to be made between the acoustic image [located just in the auditory cortex] and the various sensory memory images representing the concept itself.*" (Poeppel&Hickok 2004)

Thus, the connection is not only between the two language centers but also between the two centers and the representation of the concept distributed throughout the cortex. In this way, on the one hand comprehension of speech activates a sensory word image, which produces a consecutive activation of the memory images that form the concept. On the other hand, spontaneous production of speech implies the activation of the concept, which in parallel activates both the sensory and the motor images linked to that concept. The following figure summarizes the W-L-G model (Channg et al. 2015):

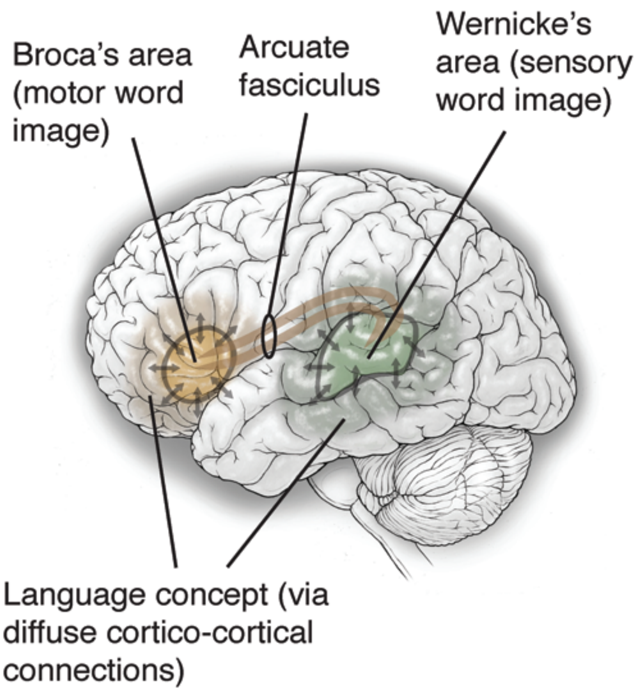


FIG. 1. Classical model of language organization in the left hemisphere of the brain. Broca's area *(gold)* is located in the inferior frontal lobe and Wernicke's area *(green)* in the posterior superior temporal lobe, connected by the arcuate fasciculus. Language concepts *(shaded)* surround each canonical language area. *Arrows* represent diffuse cortico-cortical connections between Broca's/Wernicke's area and the widely dispersed language concepts. Copyright Edward F. Chang. Published with permission.

Overall, we have seen the two most influential models of language lateralization that can be referred as classical. The great contribution that these models implied is undeniable, yet, although being crucial studies that have been accepted for many decades, they are being nowadays revisited and new findings, which we will present in the following section, are resulting in a change of perspective in relation to the classical models.

2. Present perspective

In this section we will account for the new findings that we consider crucial for understanding the present perspective about language lateralization. For the seek of brevity, we selected some aspects on which current research is implying important changes as compared to the classical perspective. Thus, it is not an exhaustive and deep explanation about the modern revealings. However, in the second part, we will introduce more details about what is being investigating nowadays, and for now, we will limit the section to provide a general overview of how the brain is thought to be organized nowadays.

2.1 Anatomic differences between the two hemispheres: structural and functional lateralization

We could affirm that the existence of functional specialization of the hemispheres for linguistic tasks is undeniable and accepted among the scientists of the field, yet, could we talk about structural lateralization of the brain? That is, not only functional but also structural asymmetries, or differences in terms of anatomy. If so, the following question comes up, that is, whether the functional lateralization for language, is due to the anatomical differences between the hemispheres; or the other way round, say, the lateralization of language is the reason why anatomical asymmetries between hemispheres are observable.

As we have explained above, Paul Broca postulated that a precocious development of the left hemisphere during the embryonic period results in a specialization of the left hemisphere (third left frontal gyrus) for speech production. Conversely, he upheld the idea that both hemispheres are perfectly similar. A century later, Yakovlev and Rakic (1966), following the statements of Gratiolet, pointed out that anatomical differences could be observed between the two hemispheres of the human brain. They named this anatomical difference as the 'torque', which is better known nowadays as the 'Yakovlevian torque'. As S. Chance and T. Crow (2007) explain , we can distinguish two aspects of the torque.

First of all, "*a horizontal shift of one hemisphere with respect to the other that we have found to be associated with petalia*"(Chance&Crow 2007). The word 'petalia' refers to the differences of the frontal and occipital lobes between hemispheres, that is, the right frontal lobe is bigger than the left one, and the left occipital lobe is bigger than the right one. The second aspect or component of the torque, according to Chance and Crow is what they refer to as "volume torque", *"a differential distribution of tissue within each hemisphere along the antero–posterior axis"* (Chance&Crow 2007).

Precisely, this differential distribution that they talk about can be interpreted as more tissue in the right anterior side of the antero-posterior axis than in the posterior side, and more tissue in the left posterior side of the antero-posterior axis than in the anterior side, as is observable in the following figures.

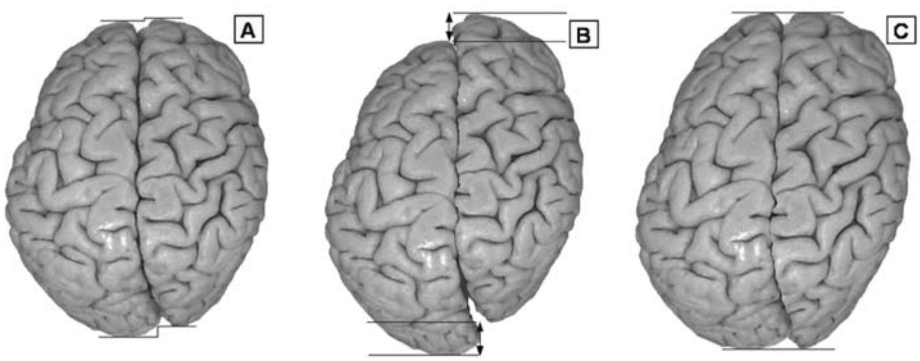


Fig. 3 - In its simplest definition petalia refers to the appearance of more tissue at the poles of the hemispheres on one side than the other. This usually takes the form of greater protrusion of the pole of one hemisphere in front or behind the other hemisphere. Definitions of petalia vary, and may take more or less account of the width of the polar regions. Figure A shows a human brain from above (front at top, posterior at bottom) with marginal rightwards frontal petalia and clear leftwards occipital (posterior) petalia. Hemisphere shift can be exaggerated, by shifting the hemisphere positions (B), or diminished, leaving only an asymmetry of tissue distribution (volume torque) augmented in this image for illustrative purposes (C).

Figure 1. (Chance&Crow 2007)

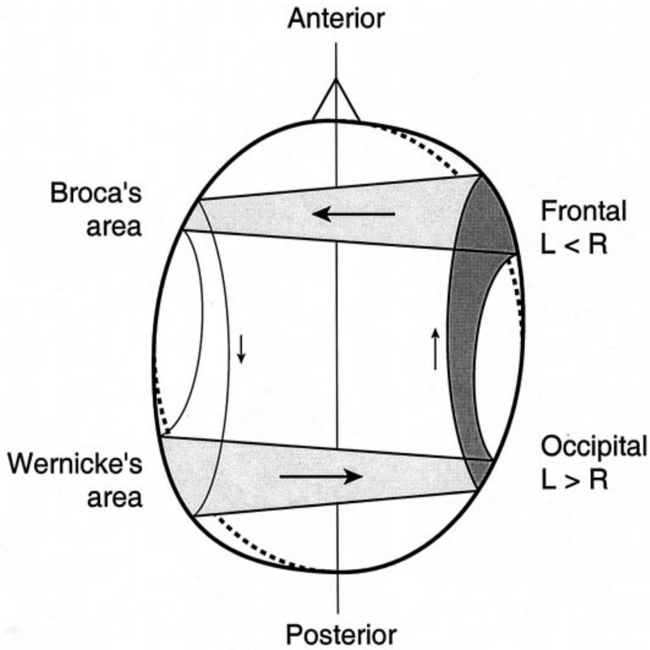


Fig. 2. The fronto-occipital axis of asymmetry in the human brain. A relative (but inter-individually variable) increase in the development of the right frontal 'hetero-modal' cortex relative to the left, and of the left occipito-parieto-temporal association cortex relative to the right implies a convergence of callosal fibres from left-to-right in sensory (posterior) association cortex and right-to-left in motor (anterior) association cortex. The intra-hemispheric antero-posterior commisural connections carry reciprocal convergences and divergences [35].

Figure 2. (Crow 2000)

According to Chance and Crow, the first component of the torque would not be related to language lateralization, since humans who have inverted asymmetry of the organs, "situs inversus", also show inverted petalia; whilst, normal language dominance is observed in these individuals. Contrarily, the second component of the torque, insofar as being "*correlated with the volume of the superior temporal gyrus (Chance et al., 2005) that forms the inferior boundary of the Sylvian fissure, containing auditory language cortex, including the planum temporale*" (Chance&Crow 2007), might have a relation with the lateralization of language.

Soon after, Geschwind and Levitsky observed an asymmetry of the planum temporale, which seems to be pertinent for speech processing. Studying post-mortem brains, they noted that the left planum temporale was bigger than the right one in most of the brains (Lyttelton et al. 2009). In the same report, the authors claim an asymmetry of the trajectory of the Silvian fissure, which "*curves upwards more anteriorly on the right than on the left hemisphere*" (Lyttelton et al. 2009).

Other important anatomical differences between hemispheres would include, namely, Heschl's gyrus, being greater on the left hemisphere, and the planum parietale, being larger in the right hemisphere, as well as the leftward arcuate fasciculus asymmetry.

Accordingly, it seems reasonable to state that human brain is characterized by both functional and structural lateralization, with a greater tendency for the dominance of the left hemisphere. Still, the question that we pointed out at the beginning of this section remains unclear. According to studies performed 'in utero' or in newborns, some asymmetries as the leftward planum temporale and arcuate fasciculus are established early in life; together with a deeper right superior temporal suclus. (Hervé et al. 2013) Therefore, we could state that some aspects of structural lateralization are placed from birth and may influence in some aspects of the development of the functional lateralization, which comes along with maturation and linguistic experience, as longitudinal studies have shown(Hervé et al. 2013, Bishop 2013). Moreover, some authors claim that "*development of lateralization with age may involve topographic as well as directional changes*"(Bishop 2013). Thus, further study of the topic is needed to resolve this question.

2.2 The right hemisphere

For more than one century, scientists of the field have focused their interest mainly investigating the function of the left hemisphere for language, as being the usually dominant one, and consequently, the right hemisphere has taken a back seat. However, from some decades ago on, a recovery of the importance of the right hemisphere is taking place, and the left-hemisphere 'imperialism', as Poeppel and Hickok (Poeppel&Hickok 2004) name it, is being modified. As we noted at the introduction of this paper, lateralization of language must be understood as both hemispheres being involved in language, yet with different tasks each. Thus, in this section we will try to account for what investigators found out about the functions of the right hemisphere for language, and we seek to show how the functional organization of the human brain is seen nowadays.

Some authors, based in data showing that intra-hemispheric connectivity is greater in the right hemisphere and more significant core regions are observed in the left hemisphere, state that the right hemisphere is specialized for broader processes and the left hemisphere for specific processes.(Hervé 2013) These statements are compatible with the claims of Poeppel (Poeppel 2003), among others, that left hemisphere is specialized for processing rapid changes of the input, whereas the right hemisphere is necessary for processing longer changes of the input. Contrarily to the canonical view that perception of speech is lateralized in the left hemisphere, they show that the analysis of the linguistic input is processed bilaterally, and that the acoustic signals are represented symmetrically in the superior temporal primary cortex of the two hemispheres.

However, they do not deny the lateralization of speech processing, yet they claim that this specialization remains on the non-primary auditory areas and that "[...] *the crucial hemispheric difference derives from the manner in which auditory signals in general are quantized in the time domain*" (Poeppel 2003). Thus, and taking into account that, "*the information contained in speech signals occurs on multiple time scales*" (Poeppel 2003) and following the hypothesis that there are different neuronal oscillations between the two hemispheres (gamma: short temporal integration in the left hemisphere, and theta: longer temporal integration in the right hemisphere), left hemisphere would be specialized in resolving "*the rapid frequency changes typical of the formant-transitions relevant to place-of-articulation distinctions*" (Poeppel 2003) and the right hemisphere would be involved in distinguishing "*among very small frequency changes, for example in context of prosodic information [and] music perception [...].*" (Poeppel 2003). Moreover, the right hemisphere might also analyze the syllables, suggesting that these segments could be basic for speech, in correspondence with recent works about the importance of these units.

Poeppel and Hickok are not the only authors that have established differences between the processing of smaller units in the left hemisphere and larger ones in the right. Some authors claim that, phonemic analysis is processed in the left hemisphere and prosody is lateralized rightwards; what is more, characteristics that are in most languages related to prosody, become to be processed in the left hemisphere when they are used as phonemically contrastive, like pitch in tone languages. (Bishop 2013) In addition, some studies with simultaneous electroencephalography and functional magnetic resonance imaging have backed up these hypotheses. (Giraud et al. 2007)

It is crucial here to stress that recent studies have shown that in those people whose dominant hemisphere is the right one, the distribution of language is "*quite similar to the configuration classically reported in the LH [left hemisphere] [...].*". (Duffau et al. 2008)

Although the topic of the right hemisphere's linguistic functions has been shortly addressed here, it is obvious that this hemisphere probably plays a quite important role for language and further investigation is necessary if we wish to cast light on the functional organization of the human brain for linguistic and, consequently, cognitive tasks.

Besides the role of the for so long neglected hemisphere, recent techniques have made possible to discover other brain regions involved in language, apart from the classical regions pointed out by Broca and Wernicke. Our aim here is not to provide a detailed review of the recent findings about the cerebral organization of language, but we try to give a general overview of the current lines of research on the field.

One of the contributions of the contemporary investigation is a strikingly increasing interest on other cortical regions besides the classical perisylvian zone (Broca's and Wernicke's areas). Different studies have demonstrated that out of these classical areas, there are more regions implied in language processing including parts of the temporal lobe, the temporoparietal region, the posterior middle temporal gyrus and even some equivalent areas in the right hemisphere. Furthermore, current investigations show that the location of language crucial areas can be variable across individuals, and taking into account that, thanks to the plasticity of the brain cortex, after a lesion or malady functional reorganization can take place, along with the findings that state a lack of both anatomical and functional homogeneity of the classical regions, it is obvious that Broca's and Wernicke's areas and their relevance for language must be revisited.

Moreover, it is nowadays widely accepted that subcortical regions, such as the basal ganglia and cerebellum, as well as the white matter play a decisive role in language. Along these lines, the function of many subcortical pathways is also being investigated. These pathways may include, the arcuate fasciculus, the superior longitudinal fasciculus[1] or dorsal and ventral pathways originated in the superior temporal gyrus. The discovery of such pathways leads us to think about the brain as a complex network in which not only specific regions play an important role for language processing, but the connectivity of neurons is also crucial. It seems that this connectivity is related to lateralization of language, since the pattern shows a trajectory from mainly inter-hemispheric functional and white matter connectivity in childhood towards a more intra-hemispheric connectivity in middle-age.

Thus, although, once again, further investigation is needed in order to clarify more questions about the cerebral organization of language, we could state that a deep change has taken place on how it is conceived. Nowadays, language is understood "*as an emergent property of a dynamic, plastic and highly interconnected system*"(Chang et al. 2015)

2.3 <u>More questions on language lateralization</u>

We would like to briefly treat some other issues about language lateralization which we consider relevant for the paper. Namely, we are talking about the relation between language lateralization and handedness on the one hand, and the sexual differences in language lateralization patterns on the other.

[1] More about arcuate fasciculus and SLF in following sections.

The topic of handedness has been a controversial topic throughout history of the investigation on the matter that concerns us. Starting with Broca, who tried to link language lateralization and handedness, suggesting that human brain is characterized by a dominant hemisphere for both motor and language tasks, most of the investigations have treated this research topic. Nowadays, although admitting some relating points such as that it seems that "*left-handed subjects present less asymmetrical language lateralization*" (Duffau et al. 2008), it is widely accepted that no direct relation exists between handedness and language lateralization. Indeed, left-handedness does not imply a dominant role of the right hemisphere for language. However, as left-handers present a more variable lateralization pattern for language, it is interesting to go deeper into this research topic since it may help to shed light on how language can be organized in human brains and why the general pattern follows a leftward lateralization along with a left hemisphere dominance for executive tasks.

As for the sexual dimorphism of language (as well as other cognitive behaviors) lateralization, the topic is not exempt from debate. In the following sections we will again mention sexual differences in the brain, specially when we treat the lateralization pattern in schizophrenia disease, yet we will introduce the affair here, providing a general overview about it.

Sex differences in the cognitive behavior have been widely pointed out by different authors, and one of the explanation hypothesis is that female brain may be more bilateral than male brain; in other words, according to this hypothesis, female brain would consist of more inter-hemispheric connectivity than male, and male brain would comprise more intra-hemispheric connectivity than female. According to some meta-analytic studies, not relevant difference on functional lateralization can be reported between male and female. (Sommer 2004)

However, different studies show that structural differences between sexes might be observed. Some of them account for a larger left planum temporale in males than in females (Sommer 2004), dissimilarities in cortical complexity and volume (Meyer et al. 2013) or even a deviation of the insula, thalamus and the posterior cingulate(Crow et al. 2013) in relation to sex.

Overall, it seems that the observed data are not concluding for now, which leads investigators of the field to extract unalike conclusions. While a few authors claim the importance of sex-related lateralization differences, others resort to other possible explanation to account for the gathered data, such as the individual variability of the brain volume.

Thus, as we have shown, the matter is still under discussion, and future detailed investigations are needed to resolve the affair of the sexual dimorphism of language, along with other cognitive behavior lateralization.

Part II. Disorganized brains: language lateralization in schizophrenia and autism

In the first part, we focused on how the brain is organized in relation to language, that is how different linguistic functions lateralize in the human brain. In the following section, we will see what happens when the typical organization of the brain is altered, resulting in an atypical brain pattern.

The claim that language lateralization is gradual among humans is quite accepted, that is, it may vary from a strongly left lateralization to a more bilateral pattern, and we could rarely find language lateralization towards the right hemisphere. However, a deviant language lateralization pattern could be related to some mental disorders, such as autism and schizophrenia.

These maladies can be classified as psychotic disorders, which are defined and explained through certain symptoms and/or behaviors, that is, in the interaction process between the individual and his/her environment. Indeed, it is undeniable that language is the mechanism that humans possess not only for the interaction with the external world, but also for the development of self-consciousness, identity, thought etc. Both schizophrenic and autistic individuals show certain deficiencies related to language, as a disorganized speech and deictic problems in schizophrenia, or misarticulated speech and deictic problems in autism. Therefore, in light of the linguistic problems they present, current investigation has given special value to the language processing in psychosis, which has showed that both autistic and schizophrenic individuals present a deviant pattern of language lateralization. Thus, in the following lines we will try to describe what it is by now known about the psychotic brains and their organization for language.

3. Autism spectrum disorder

Marjolein Verly and others provide a pretty clarifying definition of autism, or more frequently named in the available literature as autism spectrum disorder (ASD):

"a pervasive neuro-developmental disorder characterized by severe difficulties in reciprocal social interaction, stereotyped patterns of behavior, and profound impairments in verbal and non-verbal communication." (Verly et al. 2014)

Thus, ASD must be understood as a neurological disorder which arises during cognitive development and affects an average of 1% of the general population (Meng-Chuan et al. 2013).

Individuals with autism tend to show poor social skills, problems with language (although not always obvious) along with some atypical behaviors, such as repetitive behaviors and restricted interests (Cardinale et al. 2013). However, these characteristics of ASD must be conceived as general, since the spectrum is highly wide and heterogeneous; whats more, "*in autism, heterogeneity is the rule rather than the exception*" (Meng-Chuan et al. 2013). Patients within autism spectrum can be distinguished according to the current classification in three main types, taking mainly into account their linguistic behavior (which implies a cognitive factor); on the one hand, there is a group of non-verbal or low-functioning autism patients whose linguistic performance is absent or extremely low; and on the other hand, high-functioning and Asperger syndrome show subtle language impairments, the latest being identified for their use of idiosyncratic or pedantic language. Moreover, a delay in the development of language seems to be a significant factor in ASD since, although it is not exempt of heterogeneity and, therefore, is not common in all individual with autism, it seems that "*presence or absence of childhood language delay (irrespective of current language) modulates brain structure*" (Moseley et al. 2016).

In order to account for the so wide range of symptoms distinctive of ASD, scientists of the field try to find neural, both structural and functional, motives that trigger such a disorder we are treating here. Just like the disorder as such is characterized by heterogeneity, suggesting that we are facing a probably highly complex disorder, the literature available on the topic is remarkably diverse. Considering that neuroscience research has just undergone a determining technical and technological advance, it is not surprising that investigators put forward different and diverse proposals in an attempt to cast light on the matters that concern us here.

Nonetheless, in the last years, investigations have reported important findings about the cerebral organization of the ASD individuals, which has prompted scientists to postulate different hypotheses. In the following lines, we will summarize which we considered the most important discoveries.

3.1 Structural and functional asymmetries

Abnormalities in brain lateralization in autism spectrum disorder have been widely reported by several studies. Here we will explain the concluding findings about the asymmetries (both structural and functional) and specialization of hemispheres that literature reports.

As for the functional lateralization of the brain in autism, we could state that although not all the studies report concluding results, it is quite accepted that ASD shows a lack of typical left-lateralization and an atypical greater activation of the right hemisphere comparing to typically developing individuals. Although most of the literature focuses on the lateralization of language, several studies have tried to account for abnormalities in the lateralization of other networks out of the language domain.

Those networks might include "*auditory, visual, sensorimotor, executive, attentional, and visuospatial processing*" (Cardinale et al. 2013). However, a lack of agreement on this topic is observable in the literature, since, as we said, most of the literature gives distinctive value to the lateralization of language and, additionally, there are studies that, in an attempt to clarify the controversy, have reported most pronounced abnormalities for language lateralization than other networks in autism (Nielsen et al. 2014). Therefore, and stressing that further study is needed in order to resolve this disagreement, from now on we will focus our attention specifically on the lateralization of language.

Thus, as we mentioned above, a decreased activation of the cortical left core language classical areas (Left Inferior Frontal Gyrus and Left Superior Temporal Gyrus) and an atypically increased activation of the right homologue areas have been reported in language processing tasks for autism (Herringshaw et al. 2016), data consistent with the generally accepted atypical lateralization claim for autism. It must be taken into account that "*atypical lateralization does not always correlate with poorer language functioning*" (Herringshaw et al. 2016), which could be linked to the neural cortex plasticity allowing functional reorganization that we talked about before.

However, atypical increase of the right hemisphere activation (and not a decreased left hemisphere activation) in autism than in typical individuals, as well as a greater left inferior frontal and superior temporal gyrus activation within the ASD group, have been related to a worse linguistic performance in autism compared to typically developing individuals. (Herringshaw et al. 2016) Considering that some studies reported a relation between linguistic impairments, such as dyslexia, with a weaker cerebral lateralization (Bishop 2013), it seems plausible to hypothesize a weaker lateralization in ASD as well[2]. In accordance with the statement that atypical lateralization does not necessarily imply linguistic deficits, Herringshaw and others (Herringshaw et al. 2016) claim for a compensating tendency in autism cerebral organization. In other words, they argue that a lower activation of some regions in ASD, such as the bilateral middle temporal gyrus or the left core language areas, is compensated by an increasing activation of other areas, for instance the lingual gyrus in the left frontal lobe, resulting in an effective linguistic performance similar to those with typical development, which seems consistent with the possibility for functional reorganization thanks to cortical plasticity.

Furthermore, there are studies showing that a greater left superior temporal gyrus activation as compared to an atypical decreased left inferior frontal activation, alongside with a lower activation in the occipito-parietal area was observed in autistic individuals (Just et al. 2004).

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[2] It is important to state here that we are not suggesting a causal relation between weak lateralization and cognitive or linguistic deficits, since "*individuals with language and literacy impairments have weak cerebral lateralization, but those with weak cerebral lateralization usually have normal cognitive skills. It may be that atypical lateralization can take different forms, only some of which are associated with poor functioning*". Cause correlate.

These data, according to Just and others, seems to be in line with the statements that individuals with autism may show an unusual skill for processing single words for which the Wernicke's area is thought to be relevant, yet are deficient in processing whole sentence meaning which requires more integration and the involvement of the above mentioned decreased activated areas.

Regarding structural hemispheric asymmetries observed in ASD in contrast to typically developing individuals, Just and others (Just et al. 2004) report that in high-functioning autistic children, a rightward positive asymmetry can be observed for the inferior frontal and superior temporal gyrus; that is, these areas seem to be smaller in the left-hemisphere than in the right. These observations would account for the atypical greater activation of the mentioned areas in the right hemisphere for linguistic tasks. Moreover, probably one of the most important findings resides on the differences in the structural asymmetries of the arcuate fasciculus, a segment connecting posterior temporal and the frontal lobes.

Several studies have shown abnormalities on the structure of the arcuate fasciculus in ASD, reporting an absence of typical leftward lateralization in autism or even length differences between autism and typically developing along with language-impaired individuals. Furthermore, Verly and others (Verly et al. 2014) have observed that the absence of the right-hemispheric arcuate fasciculus was more frequent in ASD children than in typically developing children and claim that this lack of connection between frontal and temporal areas has a relation with a lower language function in children with autism.

In light of these statements, a recent study reports a volumetric difference of the arcuate fasciculus between high-functioning autistic individuals and those with a typical development (Moseley et al. 2016). It is important to emphasize that previous studies reported arcuate fasciculus abnormalities either for low-functioning individuals with autism or without considering the patient's linguistic skills as a differential factor. Focusing on high-functioning autism, may reveal whether this abnormalities are likely to be a general characteristic of ASD or they are subjected to age and developmental differences.

Before going in depth on the findings of these study in terms of volume differences of this segment, like the authors show in the paper, the notion of the arcuate fasciculus must be clarified. Although generally defined as a "*direct segment connecting Wernicke's area to Broca's area*" (Moseley et al. 2016), recent works have identified two more segments of the arcuate fasciculus: "*an anterior segment connecting Broca's territory to inferior parietal cortex, and a posterior indirect segment connecting Wernicke's territory to inferior parietal cortex*" (Moseley et al. 2016) dividing it in three segments. Conversely, some authors have claimed the arcuate fasciculus as being a part of a major key language tract connecting Broca's and Wernicke's areas, the Superior Longitudinal Fascicle (SLF). According to these view, SLF is divided into four tracts, the arcuate fasciculus being the fourth one and the "*direct frontotemporal segment of this pathway*" (Moseley et al. 2016).

Setting aside disagreements that require further study, and assuming the first definition of the arcuate fasciculus (including anterior and posterior segments), Moseley and others reveal that:

"*the volume of the arcuate fasciculus is not strongly left-lateralized. Although the direct long frontotemporal SLF segment has indeed been reported to be left-lateralized in FA and volume, the arcuate as a whole is slightly right-lateralised in volume and left-lateralized in FA [fractional anisotropy]*" (Moseley et al. 2016)

Although these statements are of great importance, the most interesting contribution of the study carried out by Moseley and others, is that they observed a "*significant volumetric reduction of the arcuate fasciculus, an effect strongest in the right hemisphere, in high-functioning individuals with ASC [Autism Spectrum Condition] as compared with typical controls*". Moreover, they show data suggesting that there might be a relation between the decreased right arcuate fasciculus volume and a greater number of present autistic characteristics; yet, this needs to be confirmed by further study.

Taking into account that the right hemisphere is thought to be responsible for processing emotional prosody (i.e. intonation etc.) and abilities related to theory of mind, that is, "*the ability to infer a speaker's or listener's intentions and current knowledge*" (Moseley et al. 2016), and that ASD is characterized, among other factors, by deficiencies of these abilities, the findings about the arcuate fasciculus are, not only consistent with, but also a supporting evidence for those assumptions. Moreover, in an attempt to link the functional data provided above with the reveals that we are dealing with now, it seems plausible to state a consistency between the data. In other words, the fact that a greater activation of the right hemisphere is observed in autistic-individuals when their linguistic performance is worse, might be related to the reduced volume of the arcuate fasciculus, specially in the right hemisphere explained here; clarifying probably why in these case atypical lateralization comes along with a worse linguistic performance, in contrast to other cases where the two factors are not related.

Finally, in light of a study carried out with low-functioning, non-verbal children that showed a greater volume of the right than the left arcuate, Moseley and others suggest that "*visual inspection of the figures suggests that there might be a difference in only the volume of the left arcuate fasciulus, which is larger in typically developing children than children with autism*" (Moseley et al. 2016). Again, this statement seems consistent with the functional data that reveals a relation between a worse linguistic performance and the greater activation of the linguistic areas on left hemisphere. That is, the reduced volume of the left arcuate fasciculus in children with autism as compared to typical developing children may account for the linguistic deficiencies when activation of the left hemisphere.

In fact, it is now known that the brain areas thought to be involved in language processing and other cognitive tasks do not work individually; that is, anatomical pathways communicating different brain areas are conceived as a crucial factor allowing for collaboration between areas, which is determining for language and cognitive parallel and integrative processing. Actually, the arcuate fasciculus is an instance of subcortical connection between intra-hemispheric areas, yet it is far from being the only one and, as we will see in the following section, neither is it the only connection pathway showing dysfunctions in ASD.

3.2 (Under)connectivity

As far as we know, human brain consists of anatomical pathways, such as corpus callosum, thalamus and many other connective segments for both intra- and inter-hemispheric transmission of information.

Autism spectrum disorder has been frequently reported as characterized by an atypical low connectivity between cortical areas. This hypothesis of an under-connected brain pattern for individuals with autism is gaining consistency due to the increasing empirical evidence supporting it. Indeed, the discoveries about the arcuate fasciculus pointed out in earlier lines constitute an anatomical evidence in favor of the under-connectivity hypothesis for ASD, since the absence, or more recently reported reduced volume of the arcuate fasciculus implies a lower connection between temporal and frontal lobes. Several studies (Meyer et al. 2013, Verly et al. 2014, Nielsen et al. 2014) account for the under-connectivity theory, providing general empirical data that corroborate it and even claiming that autism might be understood as "*marked and caused by underfunctioning integrative circuitry that results in a deficit of integration of information at the neural and cognitive levels*" (Meyer et al. 2013).

More specifically, Minzuno and others (Mizuno et al. 2011) describe deficiencies present in ASD in precise connecting networks, underpinning the theory. In an attempt to cast light on why children with autism show a longer presence of 'pronoun reversals' (confusing the referents of first and second person pronouns) in a basis of 'deictic-shifting' (shifting the relationship between the speaker and listener), they identify as the cause of this disruptions the dysfunctions on the connecting network between the right anterior insula and the precuneus[3] (areas that seem to be the neural substrate of self-awareness and involved in shifting attention between targets of attention, and thus may be related to deictic shifting).

[3] Precuneus: an area situated in the medial posterior region of the parietal cortex and adjoining the posterior cingulate cortex.

In other words, they observed a lower functional connectivity between the right anterior insula and the precuneus for autism in tasks requiring deictic shifting; suggesting that under-connectivity exists for this network in autism and it may be the reason why ASD children present problems with shifting a deictic centre form another person to oneself, or more generally "*representing the external world on the basis of understanding its relation to oneself*" (Mizuno et al. 2011), which could be related to the extreme self-focus that characterizes ASD individuals.

Nevertheless, there is opposite data that report not a decreased but an increased brain connectivity in ASD. Literature supporting the under-connectivity theory also mentions a possible higher functional connectivity in those individuals with autism presenting an excellent cognitive function. The observed over-connectivity in autistic individual's brains confirms the great heterogeneity in the autism spectrum disorder.

Considering the controversy of different studies, Hahamy and others (Hahamy et al. 2015) claim that heterogeneity should be understood in a basis of individually specific distinctions that the canonical connectivity pattern presents in ASD. They assume that functional connectivity is not homogeneous, nor among individuals neither within the same individual. In other words, they claim that while some regions might present a high level of connectivity, others could show connectivity to a lower degree, and the patterns can vary from one to another subject. In their study comparing ASD to typically developing individuals, they found that "*individual ASD participants tended to differ from each other in their functional [both intra- and inter-hemispheric] connectivity patterns to a greater degree than was true for the control participants*." (Hahamy et al. 2015). Moreover, they reported a correlation between the level of individual specificity and the degree of autism severity. Thus, to account for these findings, their suggestion, to our knowledge a truly interesting one, is that "*the reported functional idiosyncrasy in ASD may be an extreme end of dimensionally distributed functional patterns in the general population*" (Hahamy et al. 2015).

Although, as the same authors remark, further study is required to confirm or deny the hypotheses, it seems to be a plausible explanation for at least part of the great heterogeneity observed in ASD, namely the distinctions between low-functioning, high-functioning and Asperger syndrome autistic individuals, which differ in their language and cognitive abilities.

Another explanation for heterogeneity in autism is the biological sex differences, that despite having a smaller place in the literature, some studies have shown evidence in support. In the following section we will discuss the topic of biological sex differences in ASD.

3.3 Sex differences and the genetic factor

Considering that autism spectrum disorder is more prevalent in males, it is not surprising that most of the studies are characterized by an uneven number of male and female participants. In light of the heterogeneity that all of these studies need to deal with, some authors have claimed that sexual differences in ASD might be, at least partly, a cause of the spectrum variability. Meng-Chuan and others (Meng-Chuan et al. 2013) in a quite recent study tried to clarify how biological sex affects the neurobiology of autism. Their investigation of high-functioning autistic adults showed that, for individuals with those traits, males and females may have different structural neurophenotypes, since data suggested that "*some neuroanatomical features of autism manifest differently by sex*" (Meng-Chuan et al. 2013), and additionally, they observed "*minimal overlap between the neuroanatomical features of autism in males and females*" (Meng-Chuan et al. 2013). Actually, they report grey and white matter differences between females and males with autism, along with the more obvious behavioral divergences. In an attempt to find an explanation for these differences, Meng-Chuan and others argue the widely claimed statement that females with autism are more severely affected than males, defensing that it may be that they are simply different.

In fact, in their study the authors tried to confirm the theory of the 'extreme male brain' (EMB). The EMB theory suggests that the autistic brain might be an extremely 'masculinized' brain, both for males and females, understanding the disorder as a case of a extreme amplification of sexual factors that influence the typical sexual dimorphism in brain and cognition. Meng-Chuan and others report that the theory could be confirmed for females with autism, for whom they found to have "*neuro-anatomical features that overlapped substantially with sexually dimorphic structures in controls*" (Meng-Chuan et al. 2013), yet in the case of males with autism the theory could not be confirmed. Although they hypothesize different reasons for the results that could still support the EMB theory, they emphasize that alternative theories have been described for autism.

The 'gender incoherence' hypothesis proposes that females with autism might be 'masculinized' and males, instead, 'feminized'. In their study, Meng-Chuan and others found that in neuroanatomical terms, there was "*a non-random overlap between structures sensitive to autism diagnosis in males and sexually dimorphic structures in controls representing 'feminization'*" (Meng-Chuan et al. 2013). Therefore, the results of the study could fit both theories for sexual differences in autism.

Although the literature is not consistent about the topic, it is meaningful that the most recent study consulted (Moseley et al. 2016), also mentions sex as a possible factor affecting brain structure and function. Thus, overall it seems that sexual dimorphism should be taken into serious consideration, both for typical and disordered brains. Moreover, it should be noticed that, if confirmed, sexual neuroanatomical differences would imply a strong genetic factor for autism.

Overall, it is obvious that further study is needed in order to settle a language lateralization pattern for autism spectrum disorder. It seems, however, that the studies carried out by now, all point to the same direction. On the one hand, the evidence is concluding to state that language lateralization is deviant in autistic individuals and that these abnormalities can account for the origin of many autistic symptoms. On the other hand, the underconnectivity theory seems to be plausible, as evidence that support it are significantly increasing. Therefore, we suggest that future investigation should follow these research lines in autism, yet as it was observed in the literature, these studies should take into consideration the factors that generate heterogeneity within the spectrum, namely: the age of the participant, the type of syndrome they suffer, whether the participants' language development was delayed and their gender. In summary, the evidence suggest that language lateralization might be a determining factor for the development of autism, thus, it seems that further study on the lateralization pattern of autism spectrum disorder might shed light on the origin of this psychosis.

4. Schizophrenia

What we understand as schizophrenia, the most well-known psychotic disorder, is a complex and severe illness, difficult to define. Indeed, different psychiatric schools have not yet arrived to any consensus when defining the malady. Gianni Jervis provides the following definition, which to our knowledge is a pretty complete one:

"Schizophrenia is a grave mental disorder that designates a whole of, psychotic kind, psychological difficulties generated by a dissociation of the personality between thoughts, affections and wills [in other words, between thoughts, emotions, wishes and action]" (Jervis 1979)

Thus, individuals with schizophrenia present a severe distortion in thought, perception and emotions, and manifest a loss of contact with reality. Accordingly, the most common symptoms in schizophrenia are, as Jervis postulates, the isolation from reality, delusions, hallucinations; the latter being mainly verbal, and a conservation of a normal intelligence, along with a perfect state of spatial orientation. It is crucial to clarify here that, this paper assumes that thought and language are at the same level, we conceive them as an indivisible whole and therefore, distortion of thought is equivalent to say distortion of language[4].

Moreover, and setting apart diagnostic classifications of the patients, Timothy Crow (Crow 1980) described two types of syndromes within the general schizophrenia disease, discernible on their symptoms. On the one hand, the one equivalent to the 'acute schizophrenia', is characterized by what literature names as positive symptoms, namely, delusions, hallucinations and thought disorder, which are reversible, showing emanations and remissions.

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[4] See Hinzen&Rosselló 2015 for a detailed discussion.

On the other hand, the one equivalent to the 'defect state' exhibits negative symptoms, such as, affective flattering and poverty of speech, which are thought to be irreversible or chronic.

In this way, the origin of schizophrenia, which normally arises between the age of 20 and 30 years (despite sex differences that will be discussed later), remains still unclear. However, several factors, such as genetic or environmental ones, have been reported as influential for the development of the malady. Within those factors, lateralization of language is widely thought to play an important role on schizophrenia. Several studies have reported altered hemispheric asymmetry, both functional and structural, alongside with an abnormal connectivity pattern of the schizophrenic brain. The following lines will be an attempt to account for the most relevant findings on the topic, although disagreements are present in the consulted literature.

4.1 Structural and functional asymmetries

As for the functional asymmetries, practically all the literature consulted agreed that, overall, language lateralization is significantly decreased in schizophrenic patients as compared to typical individuals. Disagreements, yet not exclusive to one another, arise when establishing a pattern of functional asymmetry for schizophrenia. Several studies cited in the consulted literature (Mohr et al. 2000, Sommer 2004), report that activation of the left frontal areas is decreased in schizophrenic patients, suggesting a dysfunctional left hemisphere of the affected individuals. More specifically, Angrilli and others observed that "*The main deficit in schizophrenia was localized at the anterior left sites […], expressed as a significant inversion of asymmetry in the phonological component of words*." (Angrilli et al. 2009); in other words, they found that during word processing, left lateralization of the anterior areas was lost and inverted selectively for the phonological component, that is, recognition of words and its semantic interpretation; which is consistent with the difficulties that schizophrenic patients show to organize perceived information and to plan motor acts (Sommer 2004), as well as the disordered speech production characteristic of schizophrenia.

However, several other studies fail to demonstrate a decrease on the left hemisphere activation; disagreement that Sommer attributes to the differences on the patient's symptoms in different studies (Sommer 2004). These differences and the divergence of the result are hypothesized by the author as suggesting a correlation between different symptoms and the dissimilarity on brain activation, namely, the negative symptoms would be related to decreased activation of the left hemisphere, whereas positive symptoms could be linked to an increased activation of the right hemisphere. In fact, most of the studies are consistent with an increased activation of the right hemisphere during language processing in schizophrenia as compared to control individuals (Sommer 2004). Nevertheless, there are studies, as the one carried out by Catani and others, reporting a bilateral activation of the perisylvian language areas when schizophrenic patients are experiencing auditory verbal hallucinations (Catani et al. 2011).

Overall, the data presented until now is consistent with the statement that schizophrenic patients show a more bilateral brain pattern, lacking the dominance of one hemisphere for motor controls and a typical distribution of functions between hemispheres, that is, hemispheric specialization. Suggested supporting evidence include a higher frequency of ambidextrous in schizophrenic population and a possible correlation between hemispheric indecision and the development of the malady (Crow 2000, Sommer 2004, Mohr et al. 2000).

The findings about the abnormalities in the structural asymmetries in schizophrenia are actually consistent with what we exposed about the functional asymmetries. In a meta-analysis, Sommer found an agreement about the planum temporale. Contrarily to the leftward asymmetry observed in typical individuals, in schizophrenic patients it is significantly reduced (which means that it is similar in both hemispheres and not greater in the left hemisphere) (Sommer 2004). As this structure being included in Wernicke's area, these data is consistent with the higher activation of the right hemisphere that is observed in schizophrenic patients, as well as with the bilateral activation of the perisylvian areas during auditory verbal hallucinations reported before. Accordingly, the asymmetry of sylvian fissure typically favoring the left hemisphere is also reported decreased in schizophrenia. However, these would not account for a dysfunctional left hemisphere claimed by several studies.

In former sections, we have introduced the notion of the 'brain torque' (see Par I...). Interestingly, T.J Crow (Crow 2000) and Sommer (Sommer 2004), mention studies that report a loss of this fronto-occipital torque in schizophrenic patients. In addition, in the very same article, Crow cites evidences of other studies suggesting a loss of substance in the left temporal lobe for schizophrenia, along with the parahippocampal, fusiform and the superior temporal gyrus. In fact, these data would account for a dysfunctional left hemisphere.

In a more recent study, T.J Crow (Crow 2013) concludes that the centrally affected structures in schizophrenia disease are, the insula, the limbic system (anterior and posterior cingulate gyri and parahippocampal gyrus) and the thalamus. As for the insula, which, according to the author is the most affected in schizophrenia, the meta analysis concludes in a loss of volume of this structure, specially in the left hemisphere. However, Crow discusses that proportionally the loss that the studies report is too large, as the insula is a really small structure. Therefore, he suggests that although a substantial loss or destruction of the insula is implied, the change might not be on its volume but on its location: "*a primary shape change influences the location of the insula relative to other hemispheric landmarks*" (Crow 2013). Both the anterior cingualte gyrus and the parahippocampal/uncal complex are reported to show a deficit in the left hemisphere, that is, the leftward asymmetry is lost. Finally, the thalamus seems to lose its typical rightward asymmetry in schizophrenia. Once again, the data presented is consistent with the claim of a dysfunctional left hemisphere.

All the same, as Angrilli and others accurately claim, schizophrenia should be understood "*as a deficit of integrative cortical function and loss of neural interconnectivity rather than as a disorder due to a specific functional-anatomical or neurochemical impairmen*t" (Angrilli et al. 2009). In fact, several studies demonstrate alteration of the pathways linking cortical areas, suggesting that the connectivity pattern of the schizophrenic brain is abnormal as compared to typical individuals. It has to be taken into account that, although we establish a separate section for the brain connections, both structural and functional asymmetries are involved in it. It is in its importance that relies the reason why we treat it separately.

4.2 Connectivity

Considering that the literature is consistent about the issue, it is plausible to state that a deviant connectivity pattern is a central characteristic of the schizophrenic brain. Taking into account different researches (Angrilli et al. 2009, Catani et al. 2011, Mohr et al. 2000, Crow 2000, 2013), we could say that, for now, an altered connectivity has been observed for the arcuate fasciculus (the direct segment that links frontal and temporal lobes), the uncinate fasciculus (a bundle that connects the frontal cortex with the temporal pole) and, most importantly, for the corpus callosum (the largest white matter structure in the brain, that connects the right and left hemispheres).

The uncinate fasciculus seems to lose the typical asymmetry favoring the left hemisphere. Thus, the reported reduction of the uncinate fasciculus in schizophrenia would cause a loss of interconnectivity between frontal and temporal pole, which is consistent with the dysfunctional left hemisphere, specially for the phonological component (Angrilli et al. 2009). Regarding the arcuate fasciculus, M. Catani and others reported anatomical evidence for a bilateral reduction of the degree of connectivity of this segment in schizophrenia, specially in those psychotic patients with a history of auditory verbal hallucinations. They measured the microstructural integrity of the segment, which indeed schizophrenic patients with auditory verbal hallucinations seem to have lost or reduced bilaterally, while patients without these hallucinations show it only for the left segment, since the microstructural integrity of the right arcuate fasciculus was preserved. Therefore, they suggest that bilateral abnormalities of the white matter are required to experience auditory verbal hallucinations.

As we mentioned before, one of the most important findings is an altered connectivity of the corpus callosum. The structural differences on the corpus callosum between schizophrenic and typical brains are still unclear. However, the consulted literature mentions studies which report size and fiber composition differences, some of them claiming a reduction of the corpus callosum or some parts of it, and others defending an increased size in schizophrenia. Setting apart the anatomical differences that require more investigation, it seems that a deviant functioning of the corpus callosum in schizophrenia is widely accepted among the investigators.

Several studies (Mohr et al. 2000, Mohr et al. 2008) agree that the schizophrenic disorder is characterized by a deficit for the interaction of the hemispheres. In other words, schizophrenic patients show that lexico-semantic information is not correctly transmitted from one hemisphere to the other. Using visual stimulation for the hemispheres, the research reports that information is correctly processed when just one hemisphere is stimulated or simple identification is required, independently of being left or right hemisphere, whereas when the task requires a match of information or bilateral simultaneous stimulation is carried out, schizophrenic patients fail. More precisely, B. Mohr observed that the deficiency emerges when the information has to be transferred from the right hemisphere to the left, that is, the left hemisphere does not receive the activation related to the right hemisphere, which the authors conclude that implies a deficit processing of the left hemisphere for language.

According to I. Sommer , the corpus callosum consists of a great number of white matter fibers functioning as excitatory and inhibitory. In fact, the author describes that "*stimulation of the cortex or of the callosal fibers directly results in a brief excitation of the contralateral homologue area followed by a prolonged inhibition*" (Sommer 2004). Thus, it is thought that, in order to avoid unnecessary duplication of the activity of the brain, the hemisphere that is specialized in one function, inhibits the other hemisphere to carry out the same function. For language, according to the "callosal homotopic inhibition" theory (i.e. activation of one area supresses activity of the same contralateral area), left hemisphere would inhibit focal language processing, heightening a broader language processing (i.e. syllables, prosody etc.) in the right hemisphere. In other words, corpus callosum is thought to be an important, yet not the only, factor for language lateralization.
Actually, this explanations would account for an atypically higher right hemispheric activation for language processing in schizophrenia and the bilateral activation during auditory verbal hallucinations. Indeed, it seems coherent to hypothesize that the auditory verbal hallucinations come from a lack of inhibition of the right hemisphere for the phonological component, and a deficiency on transferring the information from the right to the left hemisphere. In this way, as I. Sommer describes:

"*Verbal thoughts originating from the non-dominant hemisphere may not be recognised as self-generated language. If it is not recognised as one's own thoughts, the subject consequently concludes that they must have an external origin, leading to the experience of verbal hallucinations*." (Sommer 2004)

Overall, in light of the deficient inter-hemispheric integration and cooperation, the studies conclude that schizophrenic patients would share some characteristics with split-brain patients (patients that have undergone corpus calloscotomy, which involves a severing of the corpus callosum in order to mitigate epileptic convulsions)[5], for the higher independence that their hemisphere present.

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[5] Michael Gazzaniga and Roger Sperry were the first who studied split-brain in humans.

4.3 Sex differences and the genetic factor

As we have seen in the first part of this paper, sexual differences in the neuroanatomical and brain functional level are not clear, and the literature is not consistent about whether they exist or not. However, it is known that gender plays an important role in schizophrenia. I. Sommer, summarizes the sexual differences in schizophrenia, mentioning first of all, the age of onset. It has been observed that in males the first appearance of psychotic symptoms is earlier than in females, the latter showing the first symptoms around 5 years later than males. Moreover, a difference in symptomatology can also be established, the negative symptoms being more observable in males and affective and paranoid psychotic symptoms in females. Accordingly, males seem to show poorer social competence as compared to females, and the response to treatment as well as the prognostic has been reported to be better in females (Sommer 2004). As the origins for these differences are not clear, it might be that language lateralization is a factor that could explain the divergence.

Based on the sexual dimorphism reported by several studies in typical individuals, some investigators have focused their attention in the sexual difference of brain lateralization pattern in schizophrenic patients. Similarly to what happens in studies that investigate typical individuals, literature is inconsistent as for the different lateralization patterns between schizophrenic males and females. Some of them, as is the case of I. Sommer and others, did not find significant group differences in schizophrenic patients, while other studies describe neuroanatomical evidence in support of the sexual dimorphism.

If we consider three of the many papers of Timothy J. Crow (Crow 2000, 2013, Chance&Crow 2007), we could state that he accepts the existence of sex differences for language lateralization. He mentions several evidence found in other studies that may support the claim of these differences, sexual dimorphism of the insula and the cingulate gyrus, being the most asymmetric structures and most severely affected in schizophrenia, among others. Moreover, the corpus callosum would also be sexually dimorphic, being proportionally larger in females than in males. Interestingly, we have described that the corpus callosum shows deficiencies in schizophrenia, accounting for the lack of inter-hemispheric communication. This suggests that it would be interesting to take the sexual factor into consideration for future studies about the corpus callosum and its deficiencies in schizophrenia, to test if it could be related to sexual differences in symptoms. Another significant finding that Crow mentions, is the differences of the lobular volume asymmetry in psychosis, which would suggest the torque to be an important factor in psychosis, and to show some differences between males and females.

Obviously, these issues require further deep study to be confirmed or not. However, in light of those evidence and emphasizing that language lateralization is a crucial factor for Homo sapiens, Chance and Crow propose that "*the presence of sex differences and their absence in chimpanzees provide a scope to suggest that sexual selection has played a role in the evolution of the lateralised human phenotype*" (Chance&Crow 2007).

It needs to be considered that T. J. Crow defends the brain torque as being a crucial change in our species, allowing a lateralized brain, and the predisposition to psychosis may rely on a failure to develop a lateralized brain. Thus, he understands "*schizophrenia as the price that Homo sapiens pays for language*" (Crow 2000).

Indeed, studies carried out with monozygotic twin pairs discordant for schizophrenia suggest that "*decreased language lateralization in the discordant twin pairs may be a functional substrate of their genetic predisposition to develop psychotic symptoms of schizophrenia*" (Sommer 2004). Moreover, some studies report that both the parents with schizophrenic children and the children of schizophrenic parents present a significant decrease on language lateralization, which suggests a strong genetic factor for language lateralization (Sommer 2004). Therefore, this findings are consistent with the view of T. J. Crow.

Overall, similarly to what we stated for autism, further investigation is required in order to clarify the inconsistencies of the literature and establish a full pattern of language lateralization for schizophrenic individuals, as well as to cast light on the origin of the disorder. It seems that future research should take into account the symptomatology factor and the gender factor.
Moreover, the evidence about the deviant connectivity pattern seem to be plausible and to be able to account for the main symptoms that the patients present. We suggest, however, that apart from the connections deficits of the corpus callosum described above, information about the intrahempispheric connections are also needed. For now, we can conclude that, basing on the evidence, schizophrenia seems to be a disassociation not only between thoughts, affections and wills, but more specifically, a disassociation of the hemispheres, with all the implications that it entails.

5. Conclusions

The present study has reviewed the most important findings on the topic of language lateralization reported by a great body of studies. All the same, the limitations of the paper need to be considered, since the literature about the topic is really large, and increasing over time. Thus, we made a selection of the bibliography that could allow us to fulfill our objective, and consequently the topic was not covered in all its extension, nor in all its depth. However, our paper provides an overview that enables to understand the point where the research is in the way to fully understand how the language works in the human brain. Indeed, we have much work to do; we do not know far more than what classical models reported, which suggests that we are still at the beginning of a long way to go through.

Nonetheless, current research seems to be on the right track. In the first part of this paper, we have shown that a profound change of perspective is in course in terms of neuroanatomy and the involvement of the right hemisphere in language, the still relatively unknown hemisphere.

Moreover, we consider of great relevance the way which the brain as a whole is conceived nowadays, say, as a highly interconnected structure. Therefore, white matter connections are thought nowadays to be crucial for the functioning of the brain, specially for language processing. Considering the whole paper, it seems that language lateralization might be not only important, but rather a determining factor for human cognition, and, as long as language is crucial in our species and relies on cerebral lateralization, it may also be a significant factor for human condition.

More specifically, the second part has focused on atypical language lateralization. And as we said before, autism and schizophrenia disorders are strongly related to a deviant pattern of language lateralization, specially to a deviant white matter connectivity. We have seen that investigation on these disorders suggests that sexual dimorphism in neuroanatomical and functional terms has to be taken into serious consideration, since, although they might be wrong, the evidence reported in these lines cannot be ignored. Taking into consideration the different studies carried out for schizophrenia and autism, we would suggest that future research should take into account what both disorders have in common. In other words, focusing on the connectivity pattern that seems to be crucial for these psychotic disorders, it seems that the investigations that have been carried out for autism, such as on the arcuate fasciculus and other intra-hemispheric pathways, should also be realized for schizophrenic patients, and vice-versa. That is, the largest white matter structure of the human brain, the corpus callosum, is acquiring special value on the research about schizophrenia, and probably, observing this structure in autistic patients would also be clarifying for the research. Accordingly, it seems plausible to claim a unified interdisciplinary approach on the research about language lateralization. Several scientific fields are involved in the investigation, namely, linguistics, psychology and psychiatry, and neurobiological sciences. It is obvious that a unified approach will not take place in the near future, yet an increasingly interdisciplinary scope should be considered if we wish to achieve a full understanding of the human brain and the organization of language in it some day. It is likely that in order to embrace the issue on its entire extension, all the domains of inquiry will have to carry out a conceptual restructuring, which, to our knowledge, is positive in all scientific domains.

To conclude, we would like to emphasize that the evidence described in the second part strongly suggest that language lateralization plays a crucial role in humans, as it may be a factor originating psychotic disorders, such as schizophrenia and autism. Therefore, although overall we can conclude that the issue still remains open, the claim that T. J Crow defends, say, "schizophrenia is the price that homo sapiens pays for language" (Crow 2000) seems to be plausible. What is more, in light of what we have learned on both schizophrenia and autism, we will dare to say that including the autism spectrum disorder in this statement should be considered. Therefore, adopting Crow's claim we would suggest that schizophrenia and autism might be the price that homo sapiens pays for language. Future research has the only key to either corroborate or refute it.

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