Role of major long fiber tracts association in empathy

Javier Comes-Fayos, Ángel Romero-Martínez, Luis Moya-Albiol

Introduction. The empathic capacity is a field of research that has been studied from various disciplines such as psychology, philosophy, or ethology and recently the field of neuroscience has been added. Thus, there has been an increase in studies using structural and functional neuroimaging, which has allowed to establish the brain structures that underlie its functioning. On the other hand, the appearance of measurement instruments such as diffusion tensor, have allowed us to begin to understand the role of white matter and neural connectivity in empathy.

Aim. To review the results obtained from the relation of the long fiber tracts of association with the functions associated with the empathic capacity. Emphasis is placed on the division of empathy into its cognitive and affective components.

Development. The scientific literature has been revised using the Google Scholar, Science Research, Chemedia, PubMed, Dialnet and Teseo search engines.

Conclusions. Both the functions associated with empathic capacity and empathy itself appear to be related to white matter fascicles. Likewise, in disorders characterized by a deficit in empathy, a relationship is suggested between the white matter tracts and alterations in important functions so that the empathic capacity dies. In this sense, the white matter tracts most related to empathy are the fronto-occipital fasciculus, the inferior longitudinal fasciculus, the superior longitudinal fasciculus and the uncinate fasciculus. Considering these results, it could be argued that neuronal connectivity, independently of structural and functional aspects, could play an important role in empathic function.

Key words. Autism. Connectivity. Empathy. Long association fiber tracts. Psychopathy. Social cognition. White matter.

Psychobiology Department. University of València. Valencia, Spain.

Corresponding author:
Dr. Luis Moya Albiol. Departamento de Psicobiología. Universitat de València. Avda. Blasco Ibáñez, 21. E-46010 Valencia (Spain).

E-mail:
luis.moya@uv.es

Accepted:
12.04.18.

How to cite this paper:
Comes-Fayos J, Romero-Martínez A, Moya-Albiol L. Role of major long fiber tracts association in empathy. Rev Neurol 2018; 67: 263-72.

Versión española disponible en www.neurologia.com

Introduction

Empathy is a component of social cognition that has been defined as the act of perceiving, understanding, experiencing and responding to the emotional state and ideas of another person [1], being similar the emotion one feels to the one perceived (experiencing it directly or imaginatively), and recognizing that the source of that emotion is not its own [2]. In fact, empathic capacity is relevant for the proper functioning of social relations, since it favors prosocial behavior and inhibits antisocial behaviors [3]. Empathy is composed of an affective component (emotional empathy) and a cognitive component (cognitive empathy). Emotional empathy is a relatively automated capacity whose function is associated with the identification of an emotion observed in another person and a subsequent affective reaction similar to that observed [4-6]; while, on the other hand, cognitive empathy is a capacity focused on taking perspective of the situation of others and that makes use of cognitive functions of a higher order [5,7,8]. The relationship between these two components of empathy continues to be the subject of debate, although there is a certain consensus when it comes to understanding them as two systems composed of relatively differentiated brain circuits with independent functioning [7-9].

Research aimed at discovering the neuroanatomical bases of empathy has focused on demonstrating correlations between specific brain areas and various socio-cognitive variables associated with empathy [10-12]; as well as investigating possible alterations in people with disorders characterized by a lack of empathy [5,12,13]. These studies have indicated that the main cerebral structures involved in empathy include the ventromedial and dorsolateral prefrontal cortex, the anterior cingulate cortex, the superior and inferior left frontal gyrus, the frontopolar cortex, the temporoparietal junction, the amygdala and the insula [3,7,14]. More specifically, emotional empathy seems to be more associated with the putative system of mirror neurons, the inferior frontal gyrus, the inferior parietal gyrus, the posterior superior temporal sulcus, the insula, and the amygdala. Cognitive empathy is associated with regions of the medial prefrontal cortex, the temporoparietal junction, the posterior superior temporal sulcus, and the temporal poles [15].

While it is true that there have been many studies focused on cortical and subcortical structures involved in empathy, there are few who have analyzed the role of white matter. Thus, it has been relegated to a secondary level despite it seems to be an essential component of the central nervous system (CNS). White matter is composed of myelinated nerve fibers and its main task is to act as a connecting path between the different brain regions, establishing links that facilitate the optimal transmission of information between them [16].

White matter fibers are classified into three categories: association fibers that join the cortex of two nearby convolutions (short fibers) or more distant regions of the same hemisphere (long fibers); commissural fibers that unite both hemispheres; and projection fibers that unite the cortex with lower level formations such as the thalamus, brainstem or spinal cord [17].

The fundamental objective of this article is to analyze the relationship between the different long fascicles of white matter association and empathy. In addition, it is intended to establish a differentiation between these fascicles, the functions to which they are associated and the specific type of empathy (cognitive or emotional) with which they are related. Based on this, we hypothesized that an optimal functioning and structural integrity of the long fascicles of association of the white matter will be related to a better empathic capacity [18,19]. In addition, this relationship will be greater among the tracts of white matter that connect the fronto-temporo-parietal areas [19-21]. Finally, based on the deficits in empathy observed in certain mental disorders, it can be assumed that a deficient functioning of the frontal-temporal-parietal white matter will be related to alterations in important functions for empathy in disorders with a marked deficit in this component of social cognition [22-24].

Parameters of the bibliographic search

A literature review of articles focused on the relationship between white matter and empathy has been carried out. The articles provided evidence of this relationship through the establishment of associations with functions linked to empathic capacity or through the study of disorders characterized by a marked empathic deficit. This review has been done through the Chemedia, Science Research, PubMed, Google Academic, Dialnet and Teseo platforms. The terms used in the initial search were: 'affective empathy', 'cognitive empathy', 'social cognition', 'white matter fascicles', 'cognitive deficits', 'neuropsychological correlates', 'diffusion tensor', 'fractional anisotropy', 'autistic spectrum disorder', and 'psychopathy'. As for Boolean operators, the search has used the following: 'and', 'or' and 'not'.

Inclusion parameters have focused on articles that refer to long association fibers of white matter in relation to empathy, either by measuring empathy itself or its functions. Secondarily, research associated with the study of their neural structures, or alterations of important functions in empathy in various psychological disorders such as autism spectrum disorders (ASD), was also considered (characterized by deficits in processing and emotional regulation, perspective taking and the establishment of social concepts, among others).

Those articles that have referred to a disorder whose etiology, or symptomatic manifestation, were not associated with a deficit or alteration of empathy or social cognition were discarded; as well as those studies focused on short association fibers, commissural fibers or projection fibers, were dismissed.

White matter tracts and empathy

Higher socio-cognitive functions, such as emotional regulation or affective problem solving, could be the result of the connection between various specific functions at the neural level, giving great importance to both the gray matter and the white matter [25]. Most research that has studied the relationship of white matter with empathy has used the diffusion tensors image (DTI), an MRI instrument capable of determining the organization and integrity of the white matter. This instrument analyzes the degree of diffusion of the molecules, differentiating between isotropic (egalitarian diffusion) or anisotropic (diffusion oriented to a direction) [26]. Anisotropy is measured on a continuum from 0 to 1, with 0 being the isotropy and 1 the perfect anisotropy. Transferred to the measurement of white matter, the score closer to 1 would be related to better connectivity since it suggests that the direction of the molecules is perfect [27]. By means of this technique, anomalies in white matter tracts can be inferred, knowing which zones or regions have a connectivity failure between them as well as associating these deteriorated regions with specific functions and with the symptoms underlying these functions [17].

In this way, the main studies of long fiber association tracts have focused directly on empathy; on the specific functions associated with this capacity;

and on disorders characterized by suffering alterations in important functions for empathy.

In a first section, we are going to talk about different long association tracts that seem to be linked to empathy due to their relationship with various functions important for social cognition.

Inferior longitudinal fasciculus/ inferior fronto-occipital fasciculus

Two associative tracts of white matter that seem to be strongly linked with empathy are the inferior longitudinal fascicle (ILF) and the inferior fronto-occipital fascicle (IFOF). The first begins in the occipital cortex, continues through the medial temporal cortex and ends in the orbitofrontal cortex, while the second extends from the occipital cortex to the temporal lobes, (superior, middle and anterior), in the vicinity of the amygdala and the parahippocampal rotation.

Both fascicles seem to have an important role in an essential function for empathy, the visual recognition associated with an affective component [28-31]. Bauer related the deterioration of these tracts with a dampening of emotional responses to visual stimuli (hypoemotionality) [29]; whereas Philippi showed a causal relationship between the impaired functioning of these two tracts and worse facial recognition of emotions [30]. In addition, the specific damage of the right IFOF predicted a worse performance in the facial recognition of emotions, providing evidence of a specific correlation between the IFOF and the facial recognition of emotions. In short, a subsequent study revealed that a group of people with prosopagnosia showed a marked reduction in the integrity of both fascicles compared to a control group [32].

Thus, it seems that both ILF and IFOF could be of great importance for empathy through their participation in the visual recognition and processing of their affective component.

Superior longitudinal fasciculus

The superior longitudinal fascicle (SLF) is a white matter long-range associative tract that unites the temporoparietal areas associated with perception with inferior frontal areas involved in production [28]. While the left SLF has been closely related to language processing, the right SLF has been more related to the processing and reproduction of melodic patterns, linking the temporoparietal areas involved in the perception of tone with inferior frontal areas involved in its production [15].

Another system with which the SLF has been strongly linked is the mirror neuron system. The frontoparietal mirror neurons system seems to favor the low-level processes involved in affective empathy and the decoding of other people's intentions [33]. It has been suggested that this frontoparietal network would be interconnected through the lateral SLF [34] since it has cortical terminations in the anterior part of the mirror neuron system. A study focused on the theory of mind and white matter [35], analyzed the relationship between an alteration in the white matter tracts and the failures in the processes of low level mentalization (mirror neuron system). For this, 'Reading the Mind in the eyes' was used, an instrument that has been closely related to the functionality of the mirror neuron system [36]. Negative correlations were found between the performance of the questionnaire and the level of disruption of the bilateral SLF, providing evidence that the damage in this fascicle could account for the deficiencies in the correct functioning of the mirror neuron system.

Therefore, it is proposed that the SLF could be related to social cognition and empathy through the perception and production of auditory stimuli (mainly prosodic) and the emotional contagion underlying the mirror neuron system.

Uncinate fascicle

The uncinate fascicle (UF) unites the superior, medial and inferior structures of the temporal lobe, including the amygdala and the hippocampus, with the insular and orbitofrontal cortex. It is the most ambiguous tract of those indicated so far [6,15,37]. This fascicle facilitates the integration between structures that process emotional and cognitive information [37]. Specifically, it is believed that this section plays an important role in the processing of new stimuli, deciphering the emotional aspects of auditory information, visual learning, and self-regulation [38].

Within the main UF structures, the orbitofrontal cortex (OFC) and the ventromedial prefrontal cortex (vmPFC) have been considered of great importance for the social behavior and the identity of the individual [14]. The OFC is vital for the optimal functioning of inverse learning, a very important function for interpersonal relationships [39], while the vmPFC is more related to the monitoring of one's thoughts and emotions, as well as to the memorization of autobiographical events [7]. On the other hand, the amygdala is also an essential component in empathic capacity, since it is responsible for the modulation of the emotional valence of the received

stimuli [40]. Finally, another fundamental part of the empathic capacity is the right anterior temporal cortex, which seems to be associated with the integration of several components of affective empathy, and the representation of social concepts [41].

In this way, a good functioning of these structures and their optimal integration seem to be important for the empathic capacity. Thus, it can be suggested that the UF, which fulfills this integrating function, could be critical for the functioning of empathy.

White matter and empathy

In relation to research that has focused directly on the study of white matter and empathic capacity, one of the most significant works is that of Parkinson and Wheatley [15]. This study used the Interpersonal Reactivity Index (IRI) and the DTI to find direct relationships between the degree of integrity of white matter and the level of empathy in normative population. In this study, the empathic concern (the subcategory most related to affective empathy) correlated with a more robust white matter microstructure in the IFOF, in the ILF, in the SLF and in the UF suggesting that better connectivity in these fascicles could facilitate empathic capacity.

These results suggest that better connectivity in the aforementioned fascicles would be related to higher scores on the subscale 'empathic concern', being able to establish a relationship between these tracts and emotional empathy.

But these fascicles have not only been related to affective empathy. In another study focusing on sarcasm (a type of intellectual/attitudinal prosody) in patients with frontotemporal dementia, it was found that the rate of error in the recognition of sarcasm was mainly based on the degree of damage of the sagittal stratum (bundle of fibers of white matter in which the ILF and the IFOF are involved) [42]. According to the authors of this study, the understanding of sarcasm requires making inferences about the beliefs and intentions of another person, functions that are necessary for cognitive flexibility and perspective taking, that are essential in cognitive empathy. Thus, it could also be suggested that both the IFOF and the ILF could be related to this type of empathy.

In addition, in their research, Oishi et al [37] used an empathy measurement instrument and found that deterioration in the UF was negatively related to the results of the questionnaire. On the other hand, no relationship was found between UF deterioration and gray matter deterioration, suggesting that the specific damage of the UF could produce on its own a worsening in the emotional empathy of the subjects.

Finally, a recent study made use of the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT), a questionnaire that measures emotional intelligence, to know if there was any kind of relationship with the cerebral white matter. As a result of this research it was observed that the 'emotional understanding' was associated with a greater integrity of the left SLF and, on the other hand, it was observed that a greater integrity in the right UF resulted in a higher score of the category 'management of emotions' [19]. These findings suggest that specific components of emotional intelligence, which in turn are of great importance for a good empathic capacity, could be directly related to the microstructure of various axonal pathways, such as the UF and the SLF.

In summary, while it is true that it is necessary to continue with more projects focused directly on empathic capacity and fascicles of white matter, the studies shown in this section seem to suggest that the integrity of diverse tracts of white matter (eg IFOF, ILF, SLF and UF) could play an important role in the cognitive and socio-emotional functioning to which the empathic capacity is subordinated.

White matter deficits and its relation to social cognition and empathy in various disorders

The scientific literature suggests that people with a diagnosis of severe mental disorder present alterations in several underlying functions of social cognition, including empathy, which would have a negative impact on both occupational and social functions of the person and, of course, in their quality of life [43].

Therefore, within the construction of brain architecture in social cognition, one of the main fields of research has been the study of white matter associated with social cognition in psychopathological population, especially in those mental disorders where seems to exist a dysfunction of socio-affective and interpersonal functions.

For this reason, we proceed to present the scientific studies that have analyzed this relationship and the most significant results of each of them. For this we propose two categories: the first category with clinical disorders corresponding to axis I of DSM-IV, ASD and schizophrenia, and the second category with personality disorders corresponding to axis II of the DSM-IV, namely, psychopathy and borderline personality disorder.

However, it must be borne in mind that at the present time it is not sufficiently clear if the cause of the difficulties in social cognition in these disorders is due to alterations in empathic function. For this reason, empathic capacity will not be analyzed only, but social cognition, in general, will also be addressed.

Autism spectrum disorders and schizophrenia

The ASD is characterized by alterations in various areas such as interpersonal, affective and behavioral [44]. In relation to the topic that concerns us in this article, ASD has been related to a marked lack of empathy [45,46]. In fact, there are numerous structural alterations that overlap with those involved in empathic capacity [47].

However, at present, it has been growing the opinion that abnormalities in brain connectivity could also be related to the etiology of this disorder [48]. Thus, several investigations have focused on the study of the possible relationship between a deterioration of white matter and ASD.

As a consequence, many studies have been able to identify anomalies in the integrity of several fascicles of white matter from which the main affected fascicles are: ILF and IFOF [22,24,49-51], the SLF [21,24,51,52], the cingulate fascicle (CF) [52,53], and the UF [21,22,45,51] in the autistic population.

But given the nature of our study, we have focused on the search for associations between these impaired fascicles and the social and affective deficits associated with ASD.

Thus, the fascicle that has been most closely associated with the socio-affective deficit in ASD is the UF. It has been stated that macrostructural alterations of UF correlated directly with socio-affective deficiencies [51]. In addition, evidence has been provided of a specific relationship between an alteration in UF and socio-affective deficits of ASD [45]. Regarding the SLF, ILF and the IFOF, in a recent literature review these three fascicles were related to the socio-emotional processing of the autistic population arguing its importance in the mirror neuron system, by the SLF, and with the facial recognition system of emotions, on the part of the ILF and the IFOF [54].

On the other hand, another disorder of axis I that has been characterized by problems in social cognition is schizophrenia [44,55].

In this sense, as has been the case with ASD, several scientific studies have been carried out focused on the alterations of white matter as indicators of impaired functions of social cognition in schizophrenia. Specifically, it has been possible to provide evidence of disruptions in the white matter of the UF, the cingular tract (CT), SLF, ILF and IFOF [55]. In addition, this deficit in the connectivity has been able to directly relate to alterations in social cognition and empathy [55,56], stating that the mentioned fascicles seem to play a very important role for these functions.

Psychopathy and borderline personality disorder

On the other hand, within personality disorders, psychopathy is one of the most characterized by a malfunctioning in the socio-affective environment. In fact, it is a disorder very closely linked to difficulties in the capacity to empathize [44], there being similarities between those areas necessary for empathy to occur and those that are altered in psychopathy [57].

In recent years, it has been proposed that connectivity between these structures could also have a vital role in the etiological explanation of psychopathy [58].

Following this current of thought, interest in the study of white matter in psychopathy has increased and several investigations have been able to identify anomalies in the integrity of various fascicles of white matter in psychopathy, among which the main ones affected fascicles are: ILF and IFOF [59-61], SLF [62] and UF [63].

Several projects used the PCL-R, an instrument that divides psychopathic personality disorder into two main factors (e.g., the antisocial factor and the interpersonal-affective factor). As a result, they found that a deterioration in the connectivity of the mentioned white matter tracts was related to a greater alteration in the affective-interpersonal factor of the psychopathic subjects [58,60], thus supporting the theory of the role of cerebral connectivity in social cognition and evidencing the type of deficits that can cause a malfunction of it.

In relation to the borderline personality disorder, the studies allow hypothesis that different altered functions of social cognition could be partially explained by a specific alteration of the microstructure of white matter, more specifically the microstructure of the UF, the CT, the ILF, the IFOF, and the SLF [64-66].

In this way, evidence has been provided that specific alterations in UF, CT, ILF and IFOF could be involved in the processing and emotional regulation of borderline personality disorder [64,65]. Regarding the involvement of deficient parts of the SLF in patients diagnosed with borderline personality disorder, it could be of great importance in re-

Table. Functions and types of empathy related to the long fascicles of white matter,

	Uncinate fasciculus	Inferior longitudinal/inferior fronto-occipital fasciculus	Superior longitudinal fasciculus
Anatomical network	Longer fronto-temporal fascicle Connects ventral regions of the frontal and temporal lobes and lateral portions of the orbitofrontal cortex with the amygdala	It unites the occipital cortex, the medial temporal cortex and the orbitofrontal cortex It unites the occipital cortex with the temporal lobes, superior, middle and anterior, near the limbic area of the amygdala and the parahipocampal gyrus	Connects regions of the action-perception frontal cortex with areas of action-parietal perception
Main associated functions	Autobiographical memory Representation of social concepts Monitoring of own thoughts and emotions Reverse learning	Facial and object recognition Assignment of emotional valence to visual stimuli	Auditory emotional recognition Functions related to the mirror neuron system
Type of empathy with which it is mainly related	Emotional empathy and cognitive empathy	Emotional empathy and emotional contagion	Emotional empathy and emotional contagion

lation to the recognition of emotions and emotional contagion [66].

All these results reinforce the theory that confers a central role to the cerebral disconnection in psychological disorders, also providing evidence of a specific association between certain fascicles of white matter (namely, UF, SLF, ILF and IFOF) and socio-affective symptoms of these disorders, regardless of whether they are clinical disorders of axis I or personality disorders of axis II.

Thus, it has been proposed that an alteration in the connectivity between structures associated with the processing of emotions can be an important pathogenic factor that contributes to basic social deficiencies, among which a marked deficit in empathic capacity is included.

Conclusions

Traditionally, empathy has been associated with a large number of structures of the CNS, leaving the connectivity between them aside. From this review article, we present studies that have provided evidence of the importance that white matter also seems to have for empathic capacity.

These investigations have provided evidence of the existence of various types of relationship between the degree of integrity of the white matter and the functions underlying the empathic capacity. Thus, a positive correlation between better brain connectivity and empathic capacity has been described. Evidence has also been provided of negative correlations between the integrity of white matter tracts and the degree of impairment in functions that are deemed necessary for empathy in various mental disorders. These results propose the existence of an extensive disconnection in the cerebral modules, covering all the cortices, frontal, temporal, parietal and occipital in the disorders with affected empathy; showing that large sets of nerve fibers can be seen related to empathy.

An important fact is that, although all the fascicles influence on a certain extent the different forms of empathy, each tract seems to have a specific function mostly associated with it. This may be due to the fact that there are links between certain regions to which lie specific functions.

Therefore, empathy seems to be reflected through several tracts of white matter, connecting different neural regions and establishing a joint functioning of various defined capacities. This global performance is consistent with the multidimensional characteristics of empathic behavior that encompasses affective, cognitive, attentional and cerebral flexibility functions [67].

Hence, the adoption of an interconnected functions approaches through multiple fascicles of white matter is very useful because it helps to conceptualize empathy in a more complete way, explaining empathy as the consequence of various events occurring in multiple brain areas practically simultaneously.

With regard to the types of empathy (cognitive and affective), research has concluded that, although all the fascicles are involved in one degree or another in the two types of empathy [22,30,42,67], there are some capacities that could be seen specifically related to certain fiber tracts. Thus, the deterioration of a specific tract could condition a failure in a specific empathic capacity, causing a characteristic symptom of a disorder. But it is very unlikely

that these functions/symptoms are related to only one of the tracts. This may be due to the fact that they are anatomical networks that, although they are categorized differentially, are deeply linked to each other, and their interconnections can be affected by alterations in any of the brain regions.

As shown in the table, the main conclusions we obtain from this review article would be that the ILF and IFOF are related to areas involved in facial and object recognition, as well as the assignment of emotional valence to said visual stimuli [30]. This combination of primary visual information and affective responses allows facial recognition of emotions, a necessary function for empathy. Within the types of empathy, these fascicles have been mostly related with emotional empathy and emotional contagion [15]; although it is true that they have also been associated with cognitive empathy [42], due to the importance of visual stimuli for making inferences.

SLF, on the other hand, has been linked to language processing and reproduction (left SLF) and prosody detection (right SLF). One of the specific empathic functions of this fascicle is the auditory emotional recognition, although it is not the only function to which it is associated. It has been suggested that the SLF is intimately related to the mirror neurons system (since it connects regions such as the inferior frontal gyrus, the ventral prefrontal cortex, and the inferior parietal lobe) [35]. Thus, this fascicle would also be more closely related to emotional contagion and affective empathy [15,35], also relating to cognitive empathy through auditory stimuli, in the same way as IFOF and ILF [42].

Finally, UF has been associated with autobiographical memory and its emotional valence, the representation of social concepts, the monitoring of one's own thoughts and emotions and with inverse learning. This makes this fascicle of great importance for the evaluation of social stimuli, the assignment of emotional meaning and for the prediction of the results of actions. There is a debate regarding what kind of empathy can be linked more, emotional empathy [15,37] or cognitive empathy [5,6], and it is very possible that this tract is involved in both.

In sum, it has been possible to verify a relationship between a deficit in neural connectivity and an alteration in social cognition in several disorders (both clinical and personality disorders). It has been possible to establish a specific relationship between a failure in the white matter and socio-affective deficiencies in ASD [50], schizophrenia [55,56], psychopathy [58,60] and borderline personality disorder [64-66]. In addition, this has been the case even when other pathognomonic factors were excluded in ASD and psychopathy. This provides evidence to the theory of a specific relationship between white substance tracts and deficits in social cognition, thus reinforcing the hypothesis that good neural connectivity is of paramount importance for social cognition and, ultimately, for empathy.

The discovery that white matter dysfunction is a common factor in neurological and personality disorders is of great importance since it can help guide future research that enhances the emergence of interventions, both psychological and pharmacological. In fact, at a neurological level, studies begin to attribute pathology in the white matter to axonal lesions, myeloid damage, or both [68]. In this sense, pharmacology is focusing its efforts on the promotion of myelination, mainly in oligodendrocytes, obtaining very promising results through the activation of AMPA glutamate receptors [69], or through the administration of merosin, a substance that promotes differentiation in oligodendrocytes [70]. Although it is true that great advances are being made in the study of white matter, to the best of our knowledge there is still no study that has provided evidence of an improvement in social cognition in the white matter fascicles after a psychological intervention or after a treatment of the myelin of the white matter.

From this review, we propose a series of limitations, from the great heterogeneity of the samples used to carry out the studies to the variety of instruments used to measure empathy. Finally, another limitation has been the lack of consensus on the concept of empathy, emotional empathy, and cognitive empathy.

Hence, in view of future avenues of investigation, we recommend that efforts should be focused on clarifying the functioning of the types of empathy (in relation to their specific structures, linked white matter tracts, associated functions and the interaction they have between them). With regard to the white matter, the use of longitudinal studies could greatly benefit this field, as well as the use of more homogeneous samples and instruments.

To conclude, we can end by emphasizing the great importance of the study of connectivity in complex functions, such as empathy. Throughout the last decades, with the appearance of studies that have linked certain brain regions with specific functions, a localizationist vision of the brain has been formed, assuming the existence of a unidirectional role between the integrity of these structures and the correct functionality of our capabilities.

At present, it has been breaking with this localizationist belief to move to a vision in which diverse structures interact with each other in a bidirectional way to give rise to specific and complex functions. For this reason, the study of connectivity acquires great relevance, since this is the current of research that can provide us with information on how communication is made between the mentioned regions that are in interaction with each other, offering us the possibility of a more complete and holistic vision of the brain.

Finally, in relation to the study of the empathic function, the panorama presented to us is encouraging. Increasingly, more important leaps are being made in the study of empathy, gradually unraveling the unknowns underlying this capacity, which, in turn, enables a greater understanding of various disorders in which empathy can be compromised. Although, if it is true, there are still many questions to be investigated, thus opening a path of very stimulating study.

References

1. Pelligra V. Empathy, guilt-aversion, and patterns of reciprocity. J Neurosci Psychol Econ 2011; 4: 161.
2. Decety J, Michalska K. Neurodevelopmental changes in the circuits underlying empathy and sympathy from childhood to adulthood. Dev Sci 2010; 13: 886-99.
3. Moya-Albiol L. Neurocriminología. Psicobiología de la violencia. Madrid: Pirámide; 2015.
4. Decety J, Jackson P. The functional architecture of human empathy. Behav Cogn Neurosci Rev 2004; 3: 71-100.
5. Shamay-Tsoory S, Aharon-Peretz J, Perry D. Two systems for empathy: a double dissociation between emotional and cognitive empathy in inferior frontal gyrus versus ventromedial prefrontal lesions. Brain 2009; 132: 617-27.
6. Shamay-Tsoory S. The neural bases for empathy. Neuroscientist 2011; 17: 18-24.
7. Filippetti VA, López MB, Richaud de Minzi MC. Aproximación neuropsicológica al constructo de empatía: aspectos cognitivos y neuroanatómicos. Cuadernos de Neuropsicología 2012; 6: 63-83.
8. Smith A. Cognitive empathy and emotional empathy in human behavior and evolution. Psychological Record 2006; 56: 3-21.
9. Baron-Cohen S, Tager-Flusberg H, Lombardo M, eds. Understanding other minds: perspectives from developmental social neuroscience. Oxford: Oxford University Press; 2013.
10. lvaro-González LC. El cerebro social: bases neurobiológicas de interés clínico. Rev Neurol 2015; 61: 458-70.
11. Decety J, Lamm C. Human empathy through the lens of social neuroscience. Sci World J 2006; 6: 1146-63.
12. González-Liencres C, Shamay-Tsoory S, Brüne M. Towards a neuroscience of empathy: ontogeny, phylogeny, brain mechanisms, context and psychopathology. Neurosci Biobehav Rev 2013; 37: 1537-48.
13. Saxe R. Uniquely human social cognition. Curr Opin Neurol 2006; 16: 235-9.
14. Moya-Albiol L, Herrero N, Bernal MC. Bases neuronales de la empatía. Rev Neurol 2010; 50: 89-100.
15. Parkinson C, Wheatley T. Relating anatomical and social connectivity: white matter microstructure predicts emotional empathy. Cereb Cortex 2012; 24: 614-25.
16. Fields RD. White matter matters. Sci Am 2008; 298: 54-61.
17. Rodríguez MR, Aceituno DH, González LH, De Vega-Fernández VM, Carrascoso J. Imagen de tractografía 3T: anatomía y aplicaciones clínicas. Radiología 2013; 55: 57-68.
18. Koshino H, Kana RK, Keller TA, Cherkassky VL, Minshew NJ, Just MA. fMRI investigation of working memory for faces in autism: visual coding and underconnectivity with frontal areas. Cereb Cortex 2007; 18: 289-300.
19. Pisner DA, Smith R, Alkozei A, Klimova A, Killgore WD. Highways of the emotional intellect: white matter microstructural correlates of an ability-based measure of emotional intelligence. Soc Neurosci 2017; 12: 253-67.
20. Lo Y, Soong W, Gau S, Wu Y, Lai M, Yeh F, et al. The loss of asymmetry and reduced interhemispheric connectivity in adolescents with autism: a study using diffusion spectrum imaging tractography. Psychiatry Res 2011; 192: 60-6.
21. Poustka L, Jennen-Steinmetz C, Henze R, Stieltjes B. Fronto-temporal disconnectivity and symptom severity in autism spectrum disorders. Eur Psychiatry 2011; 26: 1838.
22. Ameis S, Fan J, Rockel C, Voineskos A, Lobaugh N, Soorya L, et al. Impaired structural connectivity of socio-emotional circuits in autism spectrum disorders: a diffusion tensor imaging study. PLoS One 2011; 6: e28044.
23. Craig M, Catani M, Deeley Q, Latham R, Daly E, Kanaan R, et al. Altered connections on the road to psychopathy. Mol Psychiatry 2009; 14: 946-53.
24. Shukla D, Keehn B, Müller R. Tract-specific analyses of diffusion tensor imaging show widespread white matter compromise in autism spectrum disorder. J Child Psychol Psychiatry 2011; 52: 286-95.
25. Luna FG, Marino J, García R, Jaldo R, Leaniz AF, Foa-Torres G, et al. Conectividad cerebral en la regulación emocional: la solución de problemas emocionales. Psicológica 2016; 37: 35-59.
26. Jones DK. The effect of gradient sampling schemes on measures derived from diffusion tensor MRI: a Monte Carlo study. Magn Reson Med 2004; 51: 807-15.
27. Basser PJ, Pierpaoli C. Microstructural and physiological features of tissues elucidated by quantitative-diffusion-tensor MRI. J Magn Reson Imaging 2011; 213: 560-70.
28. Wakana S, Jiang H, Nagae-Poetscher LM, Van Zijl PC, Mori S. Fiber tract-based atlas of human white matter anatomy. Radiology 2004; 230: 77-87.
29. Bauer RM. Visual hypoemotionality as a symptom of visual-limbic disconnection in man. Arch Neurol 1982; 39: 702-8.
30. Philippi C, Mehta S, Grabowski T, Adolphs R, Rudrauf D. Damage to association fiber tracts impairs recognition of the facial expression of emotion. J Neurosci 2009; 29: 15089-99.
31. Rudrauf D, David O, Lachaux JP, Kovach CK, Martinerie J, Renault B, et al. A. Rapid interactions between the ventral visual stream and emotion-related structures rely on a two-pathway architecture. J Neurosci 2008; 28: 2793-803.
32. Thomas C, Avidan G, Humphreys K, Jung K, Gao F, Behrmann M. Reduced structural connectivity in ventral visual cortex in congenital prosopagnosia. Nat Neurosci 2009; 12: 29-31.
33. Rizzolatti, G, Sinigaglia C. The functional role of the parieto-frontal mirror circuit: interpretations and misinterpretations. Nat Rev Neurosci 2010; 11: 264-74.
34. Iacoboni M, Dapretto M. The mirror neuron system and the consequences of its dysfunction. Nat Rev Neurosci 2006; 7: 942-51.
35. Herbet G, Lafarge G, Bonnetblanc F, Moritz-Gasser S, Menjot de Champfleur N, Duffau H. Inferring a dual-stream model of mentalizing from associative white matter fibres disconnection. Brain 2014; 137: 944-59.
36. Chapman E, Baron-Cohen S, Auyeung B, Knickmeyer R, Taylor K, Hackett G. Fetal testosterone, and empathy: evidence from the empathy quotient (EQ) and the 'reading the mind in the eyes' test. Soc Neurosci 2006; 1: 135-48.
37. Oishi K, Faria A, Hsu J, Tippett D, Mori S, Hillis A. Critical role of the right uncinate fasciculus in emotional empathy. Ann Neurol 2015; 77: 68-74.
38. Schmahmann JD, Pandya DN, Wang R, Dai G, D'Arceuil HE, De Crespigny, et al. Association fiber pathways of the brain:

parallel observations from diffusion spectrum imaging and autoradiography. Brain 2007; 130: 630-53.
39. Budhani S, Richell RA, Blair RJR. Impaired reversal but intact acquisition: probabilistic response reversal deficits in adult individuals with psychopathy. J Abnorm Psychol 2006; 115: 552
40. Critchley HD. Psychophysiology of neural, cognitive, and affective integration: fMRI and autonomic indicants. Int J Psychophysiol 2009; 73: 88-94.
41. Brambati SM, Rankin KP, Narvid J, Seeley WW, Dean D, Rosen HJ, et al. Atrophy progression in semantic dementia with asymmetric temporal involvement: a tensor-based morphometry study. Neurobiol Aging 2009; 30: 103-11.
42. Davis C, Oishi K, Faria A, Hsu J, Gomez Y, Mori S, et al. White matter tracts critical for recognition of sarcasm. Neurocase 2016; 22: 22-9.
43. Martín-Contero MC, Secades-Villa R, Aparicio-Migueza A, Tirapu-Ustárroz J. Empatía en el trastorno mental grave. Rev Neurol 2017; 64: 145-52.
44. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, fifth edition (DSM-5). Washington DC: APA Publishing; 2013.
45. Samson AC, Dougherty RF, Lee IA, Phillips JM, Gross JJ, Hardan AY. White matter structure in the uncinate fasciculus: implications for socio-affective deficits in autism spectrum disorder. Psychiatry Res 2016; 255: 66-74.
46. Bird G, Viding E. The self to other model of empathy: providing a new framework for understanding empathy impairments in psychopathy, autism, and alexithymia. Neurosci Biobehav Rev 2014; 47: 520-32.
47. Amaral DG, Schumann CM, Nordahl CW. Neuroanatomy of autism. Trends Neurosci 2008; 31: 137-45.
48. Courchesne E, Pierce K. Brain overgrowth in autism during a critical time in development: implications for frontal pyramidal neuron and interneuron development and connectivity. Int J Dev Neurosci 2005; 23: 153-70.
49. Bradstreet L, Hecho E, King T, Turner J, Robines D. Associations between autistic traits and fractional anisotropy values in white matter tracts in a nonclinical sample of young adults. Exp Brain Res 2017; 235: 259-67.
50. Koldewyn K, Yendiki A, Weigelt S, Gweon H, Julian J, Richardson H, et al. Differences in the right inferior longitudinal fasciculus but no general disruption of white matter tracts in children with autism spectrum disorder. Proc Natl Acad Sci U S A 2014; 111: 1981-6.
51. Kumar A, Sundaram S, Sivaswamy L, Behen M, Makki M, Ager J, et al. Alterations in frontal lobe tracts and corpus callosum in young children with autism spectrum disorder. Cereb Cortex 2009; 20: 2103-13.
52. Barnea-Goraly N, Lotspeich LJ, Reiss AL. Similar white matter aberrations in children with autism and their unaffected siblings: a diffusion tensor imaging study using tract-based spatial statistics. Arch Gen Psychiatry 2010; 67: 1052-60.
53. Ikuta T, Shafritz KM, Bregman J, Peters BD, Gruner P, Malhotra AK, et al. Abnormal cingulum bundle development in autism: a probabilistic tractography study. Psychiatry Res 2014; 221: 63-8.
54. Ameis SH, Catani M. Altered white matter connectivity as a neural substrate for social impairment in autism spectrum disorder. Cortex 2015; 62: 158-81.
55. Saito Y, Kubicki M, Koerte I, Otsuka T, Rathi Y, Pasternak O, et al. Impaired white matter connectivity between regions containing mirror neurons, and relationship to negative symptoms and social cognition, in patients with first-episode schizophrenia. Brain Imaging Behav 2018; 12: 229-37.
56. Fujino J, Takahashi H, Miyata J, Sugihara G, Kubota M, Sasamoto A, et al. Impaired empathic abilities and reduced white matter integrity in schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry 2014; 48: 117-23.
57. De Oliveira R, Hare RD, Bramati IE, Garrido GJ, Ignácio FA, Tovar-Moll F, et al. Psychopathy as a disorder of the moral brain: fronto-temporo-limbic grey matter reductions demonstrated by voxel-based morphometry. Neuroimage 2008; 40: 1202-13.
58. Wolf R, Pujara M, Motzkin J, Newman J, Kiehl K, Decety J, et al. Interpersonal traits of psychopathy linked to reduced integrity of the uncinate fasciculus. Hum Brain Mapp 2015; 36: 4202-9.
59. Sundram F, Deeley Q, Sarkar S, Daly E, Latham R, Craig M, et al. White matter microstructural abnormalities in the frontal lobe of adults with antisocial personality disorder. Cortex 2012; 48: 216-29.
60. Hoppenbrouwers SS, Nazeri A, De Jesus DR, Stirpe T, Felsky D, Schutter DJ, et al. White matter deficits in psychopathic offenders and correlation with factor structure. PLoS One 2013; 8: e72375.
61. Lindner P, Savic I, Sitnikov R, Budhiraja M, Liu Y, Jokinen J, et al. Conduct disorder in females is associated with reduced corpus callosum structural integrity independent of comorbid disorders and exposure to maltreatment. Transl Psychiatry 2016; 6: e714.
62. Karlsgodt KH, Bato AA, Blair MA, DeRosse P, Szeszko PR, Malhotra AK. White matter microstructure in the executive network associated with aggression in healthy adolescents and young adults. Soc Cogn Affect Neurosci 2015; 10: 1251-6.
63. Sobhani M, Baker L, Martins B, Tuvblad C, Aziz-Zadeh L. Psychopathic traits modulate microstructural integrity of right uncinate fasciculus in a community population. Neuroimage Clin 2015; 8: 32-8.
64. Lischke A, Domin M, Freyberger HJ, Grabe HJ, Mentel R, Bernheim D, et al. Structural alterations in white-matter tracts connecting (para-) limbic and prefrontal brain regions in borderline personality disorder. Psychol Med 2015; 45: 3171-80.
65. Ninomiya T, Oshita H, Kawano Y, Goto C, Matsuhashi M, Masuda K, et al. Reduced white matter integrity in borderline personality disorder: a diffusion tensor imaging study. J Affect Disord 2018; 225: 723-32.
66. Maier-Hein KH, Brunner R, Lutz K, Henze R, Parzer P, Feigl N, et al. Disorder-specific white matter alterations in adolescent borderline personality disorder. Biol Psychiatry 2014; 75: 81-8.
67. Waller R, Dotterer HL, Murray L, Maxwell AM, Hyde LW. White-matter tract abnormalities and antisocial behavior: a systematic review of diffusion tensor imaging studies across development. Neuroimage Clin 2017; 14: 201-15.
68. Budde MD, Kim JH, Liang HF, Schmidt RE, Russell JH, Cross AH, et al. Toward accurate diagnosis of white matter pathology using diffusion tensor imaging. Magn Reson Med 2007; 57: 688-95.
69. Kougioumtzidou E, Shimizu T, Hamilton NB, Tohyama K, Sprengel R, Monyer H, et al. Signalling through AMPA receptors on oligodendrocyte precursors promotes myelination by enhancing oligodendrocyte survival. Elife 2017; 6. pii: e28080.
70. Lourenço T, De Faria JP, Bippes CA, Maia J, Lopes-da-Silva JA, Relvas JB, et al. Modulation of oligodendrocyte differentiation and maturation by combined biochemical and mechanical cues. Sci Rep 2016; 6: 21563.

Papel de los tractos de fibras largas de asociación en la empatía

Introducción. La capacidad empática es un campo de investigación que se ha estudiado desde varias disciplinas, como la psicología, la filosofía o la etología y, recientemente, la neurociencia. Últimamente ha habido un incremento del interés en el estudio de la empatía, y el incremento de las investigaciones que hacen uso de la neuroimagen ha permitido establecer las estructuras cerebrales que subyacen a su funcionamiento. En suma, la aparición de instrumentos de medida *in*

vivo, como la imagen con tensores de difusión, ha permitido comenzar a comprender el papel de la sustancia blanca y la conectividad neuronal en la empatía.

Objetivo. Revisar los resultados obtenidos de la relación de los tractos de fibras largas de asociación con las funciones asociadas a la capacidad empática. Se enfatiza la división de la empatía en su componente cognitivo y afectivo.

Desarrollo. Se ha revisado la bibliografía científica usando los buscadores Google Scholar, Science Research, Chemedia, PubMed, Dialnet y Teseo.

Conclusiones. Tanto la capacidad empática como sus funciones asociadas parecen estar relacionadas con los fascículos de sustancia blanca. En los trastornos caracterizados por un déficit socioafectivo también parece existir una relación entre los tractos de sustancia blanca y las alteraciones en funciones importantes para que se dé la empatía. Los tractos más vinculados con la función empática son el fascículo frontooccipital, los fascículos longitudinales inferior y superior, y el fascículo uncinado. A la luz de estos resultados se podría argumentar que la conectividad neuronal, independientemente de aspectos estructurales y funcionales, podría desempeñar un papel importante en la función empática.

Palabras clave. Autismo. Cognición social. Conectividad. Empatía. Fascículos largos de asociación. Psicopatía. Sustancia blanca.