Neural bases of empathy

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Introduction. Empathy is understood to refer to the capacity to vicariously experience the emotional states of others, and is considered to play a crucial role in many forms of adaptive social interaction. It has two components, one of which is cognitive and strongly related to the capacity to abstract the mental processes of other people, while the other is emotional and would be the reaction to the emotional state of another person. The development of neuroimaging techniques has made it possible to further our knowledge of the neuronal circuits involved in empathy by using a variety of strategies in the laboratory. The main studies in this field have focused on the presentation of stimuli. Thus, we have distinguished between those that involve emotions or expressing disgust, somatosensory and painful stimuli, and also those that analyse the relationship between empathy and forgiveness.

Aims and development. Our aim in this study was to offer an updated view of the brain structures involved in empathy by analysing the different methodological strategies used in the scientific literature on this topic. Furthermore, we also sought to show the behavioural and neuroanatomical dissociation that exists between the cognitive and emotional components of empathy, as well as the fact that the majority of neural circuits regulating empathy are similar to those related to aggression and violence.

Key words. Empathy. Limbic system. Mirror neurons. Neuroimaging. Prefrontal cortex. Temporal cortex.

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Sponsorship:
This work has been possible, in part, thanks to the financing of the General Direction of Scientific Policy and of the Direction of Conselleria d'Educació of the Generalitat Valenciana (projects GVPRE/2008/260 and GVACOMP2010-250) and the General Direction of Programmes and Transference of Knowledge of the Ministry of Science and Innovation (project PSI2008-0448/PSIC).

Accepted:
08.10.09.

How to cite this article:
Moya-Albiol L, Herrero N, Bernal MC. Neural bases of empathy. Rev Neurol 2010; 50: 89-100.

Spanish version available in www.neurologia.com

Introduction: the origin of empathy

The concept of empathy has a difficult history, marked by disagreement and discrepancy. It has been studied for many years by disciplines such as philosophy, theology, psychology and etiology, and recently the contributions of neuroscience have been added. However, there has been, and still is, a lack of consensus with regards the nature of the concept. In spite of this disagreement, empirical data are very consistent along a wide range of species. Individuals of many species are afflicted by the pain of a co-specific and attempt to do away with the object causing the pain, including when it means putting themselves in danger [1].

When Theodore Lipps introduced the concept of empathy (*Einfühlung*), he emphasized the critical role of 'interior imitation' of the actions of others. Compared to non empathetic individuals, empathic individuals show a greater unconscious imitation of the postures, mannerisms and facial expressions of other people [2,3]. This representation of the action of others modulates and forms the emotional contents of empathy. Preston and de Waal [1], influenced by the models of perception-action of motor behavior and imitation, proposed a model which incorporated theoretic explanations and empiric discoveries about empathy. According to this model, the observation or imagination of another person in a particular emotional state automatically triggers a representation of this state in the observer, together with the associated physiological responses. As this is automatic, it is a process which does not require conscience or processing effort, and cannot be inhibited or controlled. This model of perception-action includes two basic categories: motor behavior and emotional behavior, which in turn contain subordinate categories. Therefore, in agreement with the model, various phenomena such as emotional 'contagion', cognitive empathy, guilt, and helping behavior would depend on the mechanism of perception and action.

Empathy as a component of social cognition

In the last decades, the relevance of empathy in the prosocial disposition of people and its function of inhibiting aggression has been emphasized. Eisenberg [4] suggested the importance of empathy in the moral development of people, this being understood as an emotional response resulting from the comprehension of the state or situation of others and which is 'similar' to that which the other person is feeling. Empathetic response includes the capacity to understand the other person and put oneself in their place due to what they observe, verbal information or information accessible from the memory (perspective taking), and the affective reaction to share their emotional state, which could produce sadness, discomfort or anxiety. Thus, empathy would favour the perception of not only emotions (happiness, sadness, surprise) but also sensations (touch, pain) of other people. Therefore, empathy would take a central role in the prosocial disposition of people and in their survival [5], since this depends on the ability to optimally function in a social context, it being fundamental to understand how others feel [6]. Consequently, this has to do with a form of social cognition.

Social cognition is a concept that refers to an array of mental operations that underlie social interactions and which include the processes involved in perception, interpretation and generation of responses to the intentions, dispositions and behavior of others [7]. It deals, therefore, with the process of understanding the interdependence between cognition and social behaviour, and would refer to 'people thinking about other people'. Cognitive and social processes would refer to how we extract inferences about the beliefs and intentions of others and how we weigh up social and situational factors so as to carry them out. Social cognition includes the areas of processing of emotions, social perception, knowledge of social rules, attributional style and the theory of the mind (ToM) [8]. We could also include the concept of empathy; however, as we will point out, the limits between the different types of social cognition are not completely defined.

It has been suggested that cognitive and social abilities enable individuals to interact effectively with their social environment, and that a failure in certain aspects of social cognition would lead the individual to have less social perception, unexpected reactions towards others and, in time, social retreat [9]. Social cognition, therefore, seems to be critical for functioning in a community. For this reason, there is an increasing interest in identifying neuronal substrates that underlie social cognition (or the lack of it) and its components, such as empathy.

Emotional processing refers to the form in which we perceive and use the emotions and is based on different necessary abilities that occur in the process to be identified. It has been studied within the field of emotional intelligence [10], understood as a group of abilities which combine emotions and cognition. This model includes four components of emotional processing: identification, facilitation, understanding, and management of emotions [11]. One point to keep in mind is that emotions can have positive or negative aspects. In a recent study it has been postulated that the addiction to substances of abuse is a negative part of emotions [12].

Social perception is similar to the perception of emotions but differs in the type of assessment needed. Studies on social perception typically evaluate the ability to judge social roles and norms and the social context. Tasks of social perception require the individual to use social signals to deduce the situational events that have generated such signs. That is, for a given situation, individuals have to recognize interpersonal features or characteristics such as intimacy, social status, emotional state and veracity. Accordingly, social perception can also refer to the perception that one has about the relations between others, and not only to the perception of signs generated by just one person [13].

Social knowledge, also called social schemata, makes reference to the consciousness of the roles, norms and goals which characterize social situations and guide social interactions [14]. Social awareness is closely related to social perception due to the fact that the identification of social signs frequently requires one to know what is typical in a determined social situation.

Attribution refers to how one explains the causes of both positive and negative results and how the meaning of the events is based on the attribution one makes of the possible causes. They could be internal (caused by oneself) or external, both personal (causes attributed to others) and situational (attributed to situational factors) [15].

ToM, also known as social intelligence, involves the ability to deduce the intentions and beliefs of others, and was defined by Premack and Woodruff as the ability to conceptualize the mental state of other people (metarepresentations) in order to explain and predict a great part of their behaviour [16]. In fact, ToM has been, and currently is, one of the main models which explains the deficits that appear in different disorders such as autism and schizophrenia [17-19]. However, it is not the aim of this review to go into the description and analysis of the pathological side of empathy, since this embraces very diverse studies on a great number of pathologies such as those previously mentioned or others as could be the apathetic syndrome or the difficulty of relationships in patients with frontal cortex lesions. The extensive literature on this subject would make it necessary to carry out another review to cover the pathological aspect.

Empathy refers to the tendency to explicitly experience the emotional states of others and is crucial in many forms of adaptative social interaction. It deals with a complex form of psychological deduction in which observation, memory, knowledge and reasoning combine so as to understand the thoughts and feelings of others. It has two components: one cognitive and the other emotional. The cognitive component is closely related to ToM or the capacity to deduce the mental processes of other people. As this entails understanding and putting oneself in the other person's place, one would react to their emotional state. This reaction would be the emotional component of empathy [20]. Moreover, in a recent article two types of 'emotional empathy' have been differentiated: one more related to the emotional expression of anger and rage, and the other more associated with expressions of fear and sadness [21]. Probably, the best psychometrically developed scale to measure empathy, which has been used in the majority of studies cited in this review, is the Interpersonal Reactivity Index (IRI) [22,23]. The IRI evaluates empathy from a multidimensional perspective and includes both cognitive (perspective taking and fantasy) and emotional (empathetic preoccupation and personal discomfort).

Cerebral correlations of empathy

The present neuroscientific models of empathy postulate that a determined motor, perceptive or emotional state of an individual activates the corresponding representations and neuronal processes in another individual who observes this state [1]. The studies in this field have been carried out both in non-human primates and in humans. The discovery of the mirror neurons in the premotor and parietal cortex of non-human primates that are activated during the execution of a certain action and during the observation of the same action carried out by a co-specific (non-human primates or humans) suggests that their nervous system is capable of representing the actions observed in others in their own motor system [24]. More recently, another study [25] has shown that these mirror neurons of the inferior parietal lobe not only encode the motor actions observed but also permit the observer to understand the intentions of the other. Many of these neurons respond in a different form when the same behaviour (e.g. pick something up), which could form part of different actions, forms part of a specific action (e.g. eating). In fact, they even activate before the later behaviour that specifies the action. In another investigation, it has been shown that a part of the mirror neurons of the premotor cortex were not only activated during the presentation of an action but also when the final part of the action was hidden and thus could only be deduced [26]. This implies that the motor representation of an action carried out by others can generate internally in the premotor cortex of the observer, including when the visual description of the action is not complete. These recent findings in non-human primates show that mirror neurons are not only related to the representation of the action but also facilitate the comprehension of others and their intentions, which would be closely related to the cognitive component of empathy and ToM.

In humans, the evidence of neuronal representations shared between oneself and others was first described in the field of action [27] and emotion [3,28]. More recently, investigation has demonstrated the role of shared representations in the dominions of pain processing [29-32] and touch [31,33]. The mirror neurons in the premotor areas, which were thought to be only involved in the recognition of a determined action, are also implicated in the comprehension of the behaviour of others [34,35]. Understanding an intention means deducing an on-coming aim, a process which the motor system automatically carries out [36]. Furthermore, the mirror neuron system is not limited to a specific zone of the premotor cortex, but includes other motor circuits [37]. Individuals with greater empathy have been shown to have a greater activation of the motor system of the mirror neurons than those who have a low score [38]. Just as has been recently suggested [39], the mirror neurons would explain how we can accede to and understand the mind of others, thus making inter subjectivity possible and in this way facilitate social behaviour.

Social psychology has made manifest that imitation and mimic facilitate empathy and prosocial behaviour [40], while neuroscientific investigation has demonstrated the existence of physiological mechanisms implicated in these processes both at the level of specific neurons and at the level of neuronal systems which sustain cognitive and social constructs. When comparing gender, women have shown a greater suppression of the rhythm mu (a valid indicator of activity of the mirror neuron system in humans) than men when observing manual actions carried out by others through video clips. This suppression correlated positively with the subscale of personal distress of IRI [41].

There is not enough scientific evidence to determine whether both components of empathy (cognitive and emotional) are parts which interact in a sole system or whether they are independent, although recently it has been shown that the neuronal circuits which regulate them are different [42]. The area corresponding to the opercular parts of the inferior frontal gyrus (area 44 of Brodmann) was shown to be essential for emotional empathy, while the areas that form the anterior parts of the superior and middle frontal gyrus, and the orbital gyrus, the rectum, and the most anterior zone of the frontal superior gyrus (areas 10 and 11 of Brodmann, respectively) were for cognitive empathy. In another study, it has been observed that the neuronal substrates of cognitive empathy overlapped those which regulate the emotional states related to the state or situation of another person [43].

The development of neuroimaging techniques has allowed a considerable advance in the knowledge of the neuronal circuits involved in empathy. In continuation, the principle results reported in studies in which diverse laboratory strategies and functional measures of the brain have been used are presented.

Studies on the presentation of stimuli

To organize information from the studies which have analyzed the neuronal bases of empathy by means of the strategy of the presentation of stimuli, a division has been made in accord with the type of stimulus used, differentiating between emotional stimuli in general, the expression of disgust, somatosensory stimuli, and pain.

Emotional stimuli

One of the strategies frequently used to induce empathetic behaviour and to analyze the related neuronal structures is the presentation of images with an emotional content or situations in which one has to adopt the perspective of the other person. In the majority of studies an increase in activity in the occipital and limbic cortices has been observed, although the results do not always concur and include the activation of a multitude of neuronal substrates.

Geday et al [44] analyzed the empathetic reactions induced by the presentation of photographs of emotionally neutral images, positive or negative, both of low (facial expressions) and high (emotional situations) social complexity. A significant increase in the regional cerebral blood flow in the right posterior fusiform gyrus was observed during the presentation of emotive photographs. The cerebral activity in the left inferior occipital circumvolution was greater for the more complex emotional situations than for facial expressions. Unlike other studies [44-46], they found no changes in the amygdala or in other parts of the limbic system. Similarly, on the contrary to other previous reports [46,47], a decrease in the regional cerebral blood flow in the right inferior medial prefrontal cortex was observed during the presentation of emotional images in comparison to the presentation of neutral images. It was concluded that the posterior fusiform area would be implicated in the identification of many signs emotionally important in social perception. In fact, the messages from the fusiform area and from other areas converge in the right inferior prefrontal cortex, forming a neuronal network that is crucial for empathetic reactions and social interactions.

Empathy and imitation are two automatic processes which depend on the internal representation of oneself and of the other person. According to the motor theory of empathy, an individual recognizes the emotions of others, usually expressed through corporal and/or facial gestures, by means of the internal representation of said emotions and imitation. In this way we empathize with others because a mechanism exists through which the representation of the action modulates the emotional activity and provides a working base essential for empathy [3,48]. The superior temporal cortex and the inferior frontal cortex are areas which are vital for the representation of the action and are connected to the limbic system through the insula, which could constitute a critical via of transmission between the representation of the action and the emotion. The neurons of the inferior frontal cortex are activated during the execution and observation of an action (mirror neurons), while the neurons of the superior temporal cortex are only triggered during the observation of an action. Both the imitation and observation of facial expressions of sadness, happiness, anger, surprise, disgust and fear activated a network of very similar cerebral areas, although the activity was greater during imitation than during observation in premotor areas, which include the inferior frontal cortex, superior temporal cortex, the insula and amygdala. It was concluded that we understand what others feel thanks to a mechanism of representation of the action, which allows empathy and modulates the emotional content, a mechanism in which the insula plays a fundamental role [3].

In order to analyze the interaction between emotional and cognitive components of empathy a group of subjects was asked to adopt their own perspective or that of others in neutral daily (cognitive empathy) or socially emotive (emotional empathy) situations [49,50]. The clearest effect of putting themselves in someone else's place was an increase in cerebral activity of the limbic areas involved in emotional processing (like the thalamus), of the cortical areas implied in corporal and facial perception (e.g. fusiform gyrus), as well as the neuronal networks associated with the representation or identification of the actions of others (e.g. inferior parietal lobe). Ruby and Decety [49] also observed that the amygdala was activated only when subjects processed emotions related to social interactions. Their results, together with those of Nummenmaa et al [50] supported the theory that the frontopolar and somatosensory cortex in conjunction with the inferior parietal lobe are essential in the processing involved in the adoption of one's own perspective or of that of others. Furthermore, emotional empathy would facilitate the somatic, sensorial and motor representation of the mental states of others, and would lead to a more vigorous identification of the physical and mental states observed than that which appears in cognitive empathy.

Another aspect evaluated in some studies on the presentation of emotional stimuli is the role of gender differences in the regulation, experience and expression of empathy. Women frequently show higher scores in questionnaires on empathy, social sensibility and recognition of emotions than men. Recently, a study has been carried out to analyze whether these gender differences are associated with specific neuronal mechanisms implicated in social emotional cognition. To this end, a task of attribution of emotions was used in which the participants centered on their own emotional responses to the presentation of faces which expressed a concrete emotion, or evaluated the emotional state expressed by other faces [51]. In the two genders, both the emotional expression centered on themselves and on others activated the neural circuit formed by lateral and medial prefrontal cortex, temporal cortex and parietal regions involved in taking an emotional perspective. During the processing of their own emotions, the women showed a greater activation in the right inferior frontal cortex and in the superior temporal circumvolution, while in the men the activation was greater in the left temporoparietal intersection. When they evaluated the emotional state of others, the women showed an increased activation in the right inferior frontal cortex, while no increase in activity was registered in any cerebral structure in men. These findings have been interpreted to signify that women utilize, to a greater extent than men, cerebral areas that contain mirror neurons in face-to-face empathetic interactions, which could explain the underlying neurobiological mechanisms that facilitate 'emotional contagion'. On the other hand, an activation of the right hemisphere has been found both in men and in women when carrying out a task of recognition of faces, but there was a positive correlation between this activation and scores of the empathy questionnaire only in the case of women. This could indicate the existence of gender differences in the neuronal substrates that regulate empathy, which would be fundamentally linked to the right hemisphere [52].

Somatosensory stimuli

Another group of studies has analyzed empathetic capacity facing certain somatosensory stimuli. In one of them, the participants' legs were touched and/or they watched films in which other people or objects were touched [33]. The purpose of the investigation was to determine whether watching films that represented various types of touch, and not only the mere fact of being touched, activated the somatosensory cortex of the observer. The results made manifest that the cerebral structure which activates when the participant is being touched (experienced in first person) also does so when participants see someone else or something which is being touched (experience in third person). Therefore, the secondary somatosensory cortex would form part of a circuit shared by experiences in the first and third person.

Expression of disgust

One of the methodological strategies most frequently used in studies on the presentation of emotional stimuli is that related to the expression of disgust, a basic negative emotion essential in human behaviour. Both the observation of facial expressions of disgust or pain and the experience of disgust in itself activate the anterior insula and the adjacent frontal opercula, together with structures denominated IFO [53]. Lesions in this structure modify not only the experience of disgust [54] but also the interpretation of disgust in other people [55], subsequently, a fundamental role could be attributed to it in the network of cerebral areas implicated in the process of simulation of the states observed in others, making the insula a fundamental neuronal structure both for 'emotional contagion' and for empathetic comprehension. The IFO would be responsible, therefore, for the two key aspects of simulation: the activation of simulated states and feeling one's own states, be they simulated or experienced [56].

The hypothesis has been posed of whether the IFO is only limited to the processing of negative states like pain or disgust or whether it would also process positive states. The ingestion of enjoyable food or drink associated with positive corporal states provides a way of testing this prediction. Following this procedure, it has been observed that the regions of the IFO involved in the processing of our own sensation of taste when drinking would also activate when participants see others drinking both agreeable and disagreeable drinks. These findings would support the role of the IFO in the representation of the corporal states of others and would extend its implication to empathy for positive emotions or sensations [57]. The human bilateral IFO could, therefore, constitute a critical component of the neuronal mechanism which would permit the incorporation of the corporal states of others in our own internal states, thus facilitating our comprehension of our social surroundings and, hence, survival.

Studies on pain

Pain is a special psychological state with great evolutive importance, which could be experienced oneself but also perceived in others. The perception and processing of a painful stimulation are the product of a combination of perceptive, sensorial and emotional or affective components [58]. While the primary and secondary sensory cortices are principally involved in the discriminative sensorial aspects [59], the anterior cingulate cortex (ACC) and the insula are implicated in the affective-motivational component of pain [60]. However, both components are closely related and it is difficult to differentiate them [61], denominating the network of neuronal circuits related to pain as 'the pain matrix'. Numerous neuroimaging studies indicate that only the affective component of the pain matrix would be implicated in empathy to pain. Nevertheless, empathy is a complex construct which not only contains an emotional component but also cognitive and somatomotor factors. Therefore, it is possible that empathy could also be based on fundamental mechanisms that permit the representation of the sensations of others in one's own sensoriomotor system.

To confirm the hypothesis that the primary somatosensory cortex could be implicated in the shared representations of pain and touch, a group of subjects observed by means of a recording of somatosensory-evoked potentials the application of painful and non-painful stimuli to someone else's hands [62]. The observation of painful stimuli in an unknown person caused an increase in the amplitude of component P45, which correlated positively with the intensity of pain. However, this amplitude was reduced by the observation of harmless stimuli in another person. These findings coincide with those described in a previous study [31], and indicate a specific relationship between the codification of the sensory qualities of the painful and non painful corporal sensations of others and the modulations of the component P45. It also suggests that observing the corporal sensation of others could influence the way in which we process our own somatic sensations. That is to say, the primary somatosensory cortex not only would be involved in the real perception of pain and touch but would also play an outstanding role in the observation of somatic characteristics in social interaction. Jackson et al [30] obtained similar results, since in their investigation the fact of watching other individuals in situations which provoked pain activated a specific part of the neural network implicated in the processing of pain in oneself. Nevertheless, the same as in other studies [6,32] no changes in activation were produced in somatosensory cortex.

Recently, the hypothesis that empathy produces an activation of the neuronal networks of pain, which causes an increase in its perception, has been analysed. To this end, the sensibility of persons who observed an actor that supposedly was exposed to hot stimuli of different intensity was evaluated. The group of subjects categorized as highly empathetic considered the painful stimuli more intense and disagreeable than the group with low empathy [63]. Another study explored cerebral circuits implicated in pain that is felt when observing a person with whom there is an affective link (in this case, sentimental partners) experience it [6]. The cerebral activity of women was analyzed when a painful stimuli was applied to their right hands or to those of their sentimental partners. Results showed that the bilateral anterior insula, facial ACC, troncoencephalon and cerebellum were activated when the subjects received pain themselves and also when it was applied to their sentimental partner. However, the activation of the posterior insula, secondary somatosensory cortex, sensoriomotor cortex and in the ACC volume was specific for their own pain. Furthermore, there was a higher score in empathic worry (more feelings of compassion and affect due to the discomfort of others) greater activity in the anterior insula and facial ACC (areas which are significantly active when seeing the suffering of their companions). Thus, only cerebral response of activation in the anterior insula and ACC would be common for their own pain and that experienced by other people with whom there existed an emotional tie. This suggests that the neuronal substrate for empathetic experience would not involve the 'pain matrix' completely, so the authors concluded that only the part of the network of pain associated with affective qualities (and not sensitive qualities) would mediate empathy. These results coincide with those later obtained by Morrison et al [32].

Facial expressions of pain play a fundamental role in social communication. Right from an early age the human being shows both a special sensitivity to the detection of the pain of another person and a capacity to evaluate pain in facial expressions [64]. The basic neuronal substrates of the processing of facial expressions of pain were first studied by Botvinick et al [29], using a group of young women that watched sequences in which neutral facial expressions (without pain) or moderate pain were shown. To identify the areas which activated during their own experience of pain they also received painful and non-painful thermal cutaneous stimulation. The results of the study showed that during the visioning of facial expressions of pain, in contraposition to the neutral expressions, the ACC and the insula activated in a bilateral form. Moreover, an increase was observed in the activity of the thalamus, cerebellum, medial frontal cortex (three areas which usually activate with one's own pain) and the orbitofrontal cortex, besides the left amygdala. At the same time, the activation of diverse areas related to vision in the occipital cortex was registered, and also areas of the inferior parietal lobe, superior temporal cortex and the right fusiform gyrus. Some of the areas mentioned also activated during painful cutaneous stimulation in comparison to the non-painful, concretely, the ACC and the insula in a bilateral form, the cerebellum, thalamus and the medial frontal cortex. Nevertheless, and coinciding with previous studies [65] there were two other areas which activated only during the analysis of thermal pain: the right dorsolateral prefrontal cortex and the posterior cingulate cortex. The authors concluded that both the experience of their own pain and its identification in other people by means of their facial expressions would activate a group of intersection of areas implicated in both the representation of their own affective state and that of others. The areas which activated in common due to pain (especially the ACC, although also the insula, amygdala, and the orbitofrontal cortex) would also be involved in the processing of other affective and somatic states. Various previous studies have already described an activation of structures sensitive to pain, such as the ACC and the insula, in situations in which the subjects did not directly see the expression of pain but observed how harmful stimuli were applied to another unknown individual [66] or as has been previously mentioned, to their own sentimental partner [6]. This study is in agreement with the previous ones and also shows that the mere observation of the behaviour and/or facial expressions related to pain is sufficient to activate these neuronal structures of pain.

The main finding of Jackson et al [30], previously mentioned, is the activation in the ACC and in the anterior insula during the perception and evaluation of pain in another person. This is consistent with prior studies using neuroimaging, which showed its role in the affective aspect of the processing of pain [67], and in empathy for pain [6]. These regions are considered to be key cortical areas involved in the regulation of subjective feelings of a disagreeable nature related to pain in humans. The strong correlation between the activity of the ACC and the valuation of the participants of the pain of others support the fundamental role of this region which controls attention and evaluation associated with the situations which evoke pain [68]. Similarly, this mechanism would also be implicated in the evaluation of pain in others. This supports the discovery of Hutchison et al [66] who identified neurons in the ACC of neurological patients that responded to both painful stimulation and the anticipation or observation of the same stimulation applied to another person. However, in contraposition to the study of Singer et al [6], these authors did not find any significant correlation between the questionnaire of empathy and hemodynamic changes observed.

In another investigation a recording was shown in which a harmful instrument was portrayed (e.g. a sharp knife) or a harmless instrument (a butter knife) nearing a person's hand, participants had to press, or not, a button which emitted a response depending on whether the instrument hurt the hand or not. The fastest responses were with instruments which produced wounds, thus, the combination of stimuli and action affected the time of reaction. Cerebral activity increased during the combination of harmful instruments and the presence of wounds only in the regions of the medial, anterior dorsal and posterior dorsal of the cingulate cortex. This activation depended on whether the subject showed motor activity response to the presentation of the stimuli, which related the observation of pain with its motor processing. The study suggests that the functional representation in the medial premotor regions of the cortex would be implicated in 'empathic pain' [32]. Taking into account the studies reviewed, it could be concluded that the ACC also plays a central role in aversive learning [69]. Accordingly, the response of this cerebral structure when witnessing pain would be related to the learning of observational avoidance, which would permit the learning of pain avoidance without the necessity of experiencing it personally. With relation to this, it has been pointed out that the activation of the amygdala would indicate that the conditioning to fear could also be introduced by means of the observation of expressions of pain [29].

Recent investigation has made manifest that empathy can be increased by the administration of oxytocin and that individual differences in prosocial behaviour play a fundamental role in empathic cerebral responses [70]. After administering oxytocin to a group of men and inflicting painful stimulation on their own hand or on that of their partner, no changes in the activation of the anterior insula was observed. However, oxytocin reduced the activation of the amygdala when participants received the painful stimulation on their own hand, an effect which only appeared in the most egoistic. This was interpreted by the authors as that, on the contrary to what they had hypothesized, egoistic individuals could be less rational and more emotional, since their actions would be determined more by their state of anxiety than by reasoning. The intranasal administration of oxytocin facilitated the execution of a task (the more, the more difficult it was) of recognition of emotions in a look, a task in which only the photographs of eyes of people were presented and participants had to indicate to which emotion they corresponded [71].

According to Lamm et al [72], the altruist-empathetic or individualist-egoistic response to the observation of pain in others would depend on the capacity of differentiation between oneself and others, and the cognitive evaluation that is made of the situation. To test this hypothesis, measures of behaviour and cerebral activation were obtained while participants observed the facial expressions of pain resulting from medical treatment. A sequence of patients' faces was presented, and the instructions were given to imagine the feelings of the patient or imagine oneself in the same situation. Furthermore, the cognitive evaluation of the situation was manipulated, giving patients information about whether the medical treatment had been satisfactory or not. Taking a perspective and the knowledge of the efficacy of the treatment produced changes in the cerebral activation of the insula, medial ACC, amygdala and diverse visual areas, including the fusiform gyrus. Imagining oneself in this situation increased cerebral activation (although in a more gradual form) in the insula media, medial ACC, medial and lateral premotor areas as well as the parietal lobes. Moreover, the knowledge of the efficacy of the treatment increased the signals in the ACC, ventromedial orbitofrontal cortex, in the right lateralmedial frontal circumvolution and in the cerebellum. The results were interpreted as that human response to the pain of others would be modulated by motivational and cognitive processes, which could be extrapolated to the observation of other people in need of help and the empathetic reaction towards them.

The perception of pain in other people is also modulated by different factors such as the experience of the individual who observes [73]. Doctors expert in acupuncture were compared with participants who had never carried out this type of practise while they observed sequences in which needles were inserted into different parts of the body, including the mouth, hands and feet. In the group without experience, the anterior insula, somatosensory cortex, periaqueductal grey substance and the ACC showed a great activation, but not in the case of the doctors with experience who, instead, increased cerebral activation in the medial and superior prefrontal cortex and in the temporo-parietal intersection, structures more implicated in the regulation of emotions.

Recently, it has been demonstrated that women could be more reactive than men to the observation of painful stimuli (reflecting the vicarious response to pain), and thus, are more empathetic [74]. A possible difference between genders in cerebral response to the presentation of emotional photographs in which people appear in diverse contexts (positive or negative) or rural and urban scenes has been analyzed [75]. In both genders, the contrast between suffering and happiness in the presentation of the photographs was related to differences in the activation of areas of the temporal-occipital, right occipital cortex, parahippocampus region (bilateral level), the left dorsal prefrontal cortex and the left amygdala, however, the increase in activity in the right amygdala and in the right frontal area was observed only in women. The contrast between the presentation of photographs of people and of countryside showed differences in the activation of the medial occipital circumvolution in men and the inferior parietal and left superior temporal and right cingulate in women.

Empathy and forgiveness

A series of studies have evaluated empathy together with the behaviour of forgiving a person. The first investigation in this field was carried out by Farrow et al [76], who found that both empathetic judgment and forgiveness activated the left superior frontal circumvolution and the orbitofrontal cortex. Empathetic attitudes activated the left anterior temporal medial and left inferior frontal regions, while forgiveness activated the dorsal cingulate gyrus. A later study by the same authors confirmed the implication of these neuronal structures in empathy and forgiveness [77]. Patients of both genders with posttraumatic stress disorder carried out a task in which they read a story and, afterwards, they emitted a judgment on it, which involved three basic aspects: speculate on the intentions of others, evoke empathy and make forgivability judgments on the actions. Afterwards, subjects were submitted to a therapy of cognitive-behavioural modification, after which an increase in the activation of the cerebral regions described in their previous work in healthy subjects was observed. In concrete, a significant activation was produced in the left temporal medial in the post-therapy response to empathy and the activation of the posterior cingulate gyrus in the post-therapy response to forgiveness. These specific regions of the brain activated by empathy and forgiveness changed with the resolution of the symptoms of the posttraumatic stress disorder, which suggests that both the passing of time and the therapy itself could contribute to reach a 'normal' level of neuronal response in these cognitive social tasks.

Conclusions

The development of neuroimaging techniques has led to a spectacular advance in the knowledge of the neuronal structures involved in diverse complex psychological and behavioural processes. In the last years there has been a notable increase in the number of studies focused on analyzing and understanding the functioning of cerebral circuits involved in empathy. Different experimental strategies have been carried out in an attempt to reproduce in the laboratory situations which could create empathy in a similar way to which occurs in everyday life.

The main experimental designs centre on the presentation of stimuli with an emotional content: images or situations, painful stimuli, somatosensory stimuli, or the analysis of the relation between empathy and forgiveness. These studies have made manifest that, together with other structures, the prefrontal and temporal cortex, the amygdala and other limbic structures such as the insula and the cingulate cortex play a fundamental role in empathy. These cerebral structures are similar to those related to aggression and violence [78], thus, the neuronal circuits implicated in empathy and violence could be somewhat similar.

A large number of these studies have been criticized since the deficiency in some methodological aspects of the realization of the published works has been pointed out [79]. For instance, it was observed that numerous investigators selected the results which indicated significant levels of activity in certain cerebral structures, ignoring the others, and from them construct the measure of cerebral activity. All this contributes, ultimately, to increase the correlations and show results that lack absolute reliability.

The great complexity of this subject, together with the results obtained until now, makes it necessary to plan future studies in which there is a maximum control over numerous variables such as the theoretic model from which they part, the methodological strategy used, the type of technique, individual differences in empathy, differences in gender, and the personality of the subjects. Furthermore, it is fundamental to incorporate all this information into that proceeding from other studies centred on the pathological aspect of empathy, such as those carried out in autism, schizophrenia, frontal injury or apathetic syndrome among others.

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Bases neuronales de la empatía

Introducción. Entendemos por empatía la capacidad para experimentar de forma vicaria los estados emocionales de otros, siendo crucial en muchas formas de interacción social adaptativa. Tiene dos componentes: uno cognitivo, muy relacionado con la capacidad para abstraer los procesos mentales de otras personas, y otro emocional, que sería la reacción ante el estado emocional de otra persona. El desarrollo de las técnicas de neuroimagen ha hecho posible que se avance en el conocimiento de los circuitos neuronales implicados en la empatía mediante la utilización de diversas estrategias en el laboratorio. Los principales estudios se han centrado en la presentación de estímulos, entre los que hemos diferenciado los emocionales, los de expresión de asco, los somatosensoriales y los dolorosos, así como en el análisis de la relación entre empatía y perdón.

Objetivo y desarrollo. Con este trabajo hemos pretendido ofrecer una visión actualizada de las estructuras cerebrales implicadas en la empatía, analizando para ello las diversas estrategias metodológicas empleadas en la literatura científica sobre el tema. Además, se ha pretendido poner de manifiesto la disociación conductual y neuroanatómica existente entre los componentes cognitivo y emocional de la empatía, así como el hecho de que los circuitos neuronales que la regulan coinciden en gran parte con aquéllos relacionados con la agresión y la violencia.

Palabras clave. Corteza prefrontal. Corteza temporal. Empatía. Neuroimagen. Neuronas espejo. Sistema límbico.