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**The Consequences of Stroke on Mechanisms for Emotions and Empathy**

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**Summary**

Stroke is a promising 'pathophysiological' model for the study of emotions in man. Local cerebral lesions affect not only those functions directly controlled by the infarcted and peri-infarcted areas, but also impair functions controlled by other intact regions, anatomically distant, but functionally connected with the infarcted areas. An isolated lesion may affect the more widespread neuronal circuitries involved in the analysis and processing of new emotional inputs. In this context, the mirror system, initially described for observation and imitation of pure motor activities in man , may be relevant in the production of post-stroke emotional changes.

**Key words :** Post-stroke, Emotions, Mirror system.

For almost three millennia, the Aristotelian orthodoxy gave the concepts of 'feelings' and 'emotions' an alternating relevance, sometimes depicting them as the 'enemy' of all objective things, and sometimes considering them as the very 'centre' of human beings. Nonetheless, it was quite difficult to comprehend the real mechanisms subserving 'emotions', because the role of brain in their generation was still undefined, and the heart was instead considered the centre of the soul.1 In the last 100 years the entire scenario has changed.

The role of the diencephalon in the regulation of the vegetative reactions has been discovered and deeply investigated. However, little was known about the generation of the many different emotional reactions within the main stream of the vegetative nervous system. It was, Italian physiologist Giuseppe Moruzzi, in 1958,2 who for the first time suggested that the ascending reticular formation was by no means homogeneous and unspecific, so that different and opposite emotional states could result from its fractionated and differentiated activation.

In the following decades, the identification of the several different neurotransmitters and neuromodulators in brain stem structures has provided the physiological basis for understanding the neurobiology of emotions. However, with respect to interpersonal and social emotions, i.e. empathy, the new millennium was needed.

Nowadays, interpersonal relationships and how people of different origin and culture interact with each other are themes of highly crucial relevance, especially in this historical moment, when recent tragic events have re-evoked, after thousands of years, the forgotten ancient fear of the 'end of the millennium'. Besides emphasizing the importance of turning competition and antagonism between national cultures into solidarity, understanding and cooperation from these very tragedies and difficulties, the human kind may find the opportunity to adopt a more positive approach. However, the attention should be focused back on man himself, on his inherent values, on his feelings and emotions, not in the view of a simple introspective behaviour, but for an increased social participation, co-operation and care for each others. In this respect, a better understanding of which brain areas control empathy and social-racial interactions - the so-called 'social brain'3 and how they interact and work, may provide some cues towards the achievement of these positive perspectives, smoothing the present nearly unbearable social and ethnic tensions.

In a recent fMRI study on visual emotion recognition/imitation by our group, we observed that motor, premotor, inferior frontal; insula and amygdala areas are activated during the observation as well as during the imitation of visual 'emotional' expressions.

In regards to the observation/imitation of fMRI studies, Iacoboni et al4 had previously observed that the left inferior frontal cortex and the rostral region of the right superior parietal lobe were activated during a finger movement, as well as during the simple finger movement observation, without any active and/or positive movement. This neuronal population was initially identified in monkeys by Rizzolatti's group, and it has been defined as the 'mirror system'. This has been considered as the 'internal representation' of every single finalistic motor action.5

The activation of the mirror system after the presentation of several kinds of stimuli, i.e. visual, motor and emotional, suggests that this peculiar neuronal population plays a crucial role in the processes of imitation and, therefore, in the neurobiology of learning. As a matter of fact, the mirror system appears to be involved in the real 'comprehension' of actions. Since the comprehension of an action subserves the comprehension of the feelings and the empathy surrounding the action itself and the emotional context in which the action is represented,3 the hypothesis follows of the existence of a link between the 'mirror system' - consisting of the internal representation of motor actions - and the limbic system - devoted to the processing of emotions - probably through the Insula.6

In view of understanding the mechanisms underlying emotion generation, there is no doubt that stroke may represent a model. In fact, in the old classical experimental neurophysiological model, a lesion was provoked in the brain of an animal, and the analysis was then performed on the ensuing consequences. The study of experimental emotional reactions has been performed in the same manner.7

In human stroke survivors, emotional changes are highly frequent. It is now generally accepted that emotional changes and stroke bear a causal relation. Furthermore, the significantly decreased stroke mortality has lead to an increase of stroke survivors who present with several related clinical disabilities, including emotional changes. Consequently, researchers are focusing their attention on the chronic phase of stroke, emphasizing on continuing rehabilitation, long term support and emotional corrections through psychoactive drugs, in order to improve the quality of life after stroke.8,9 Different approaches and methodologies have been adopted. The results obtained seem to be encouraging: if we consider that only ten years ago,10 less than 50% of stroke survivors evaluated 1 to 3 years after the acute event were able to drive a car, walk outdoors or clean the house. In a recent study,11 a generally good healthrelated quality of life, including mood and emotions, was observed in stroke patients surviving up to 6 years after stroke.

Since 1981, 53 indexed peer-reviewed original articles have been published on the topic 'mood changes' and 'stroke', mainly referring to the 'post-stroke depression', which confirms the growing interest in emotional disturbances. Despite the large amount of clinical data collected, a true comprehension of the underlying pathophysiological mechanism as well as a consistent set of definite results on the relationships between emotional changes and stroke is still lacking. We may therefore assume that stroke is a promising "pathophysiological" model for the study of emotions in man, but by no means we can consider it as an easy one to manage! As a matter of fact, we acknowledge the influence of premorbid personality, the importance of the family history and the effects (direct and remote) of the lesion location that - despite the very accurate neuroradiological techniques presently available - are still largely undefined.11-13 The clinical observation that mood disorders often occur in stereotyped manners seems to suggest that there is an involvement of specific neuronal relays rather than the combination of a psychological reaction in patients with particular personality traits. Clear examples are represented by the catastrophic reaction described by Carota et al,14 the pathological laughter and crying described by Parvizi et al15 or the critical role of the left anterior hemisphere in depression and of the right hemisphere in secondary mania. However, although the accuracy of our knowledge of the limbic system organization is increasing, it is not yet possible to correlate specific cerebral lesions to each individual emotional poststroke disturbance.

It also may be worth bearing in mind that local cerebral lesions affect not only those functions directly controlled by the infarcted and peri-infarcted areas, but also impair functions controlled by other intact regions, anatomically distant, but functionally connected with the infarcted areas. In terms of cognitive neurology, vascular dementia due to strategically located lesions is an example.16 In a similar way, an isolated lesion may affect the more widespread neuronal circuitries involved in the analysis and processing of new emotional inputs. This impairment would interfere with the recall of the life long storage of similar or different emotional events, reflecting on emotional perception and response to emotional stimuli. In this context, the mirror system, initially described for observation and imitation of pure motor activities in man,3,4 recently shown to play a similar role in the elaboration-comprehension of emotional inputs,17 may be relevant (when affected by a lesion) in the production of post-stroke emotional changes. Initial clinical data in stroke patients seem to confirm this hypothesis.18 It is possible that other kind of cerebral pathologies impair the mirror system and thus impair emotional behaviours.

In conclusion, the 'mirror system' appears to be heavily involved in the physiology of the emotional reactions and empathy, described in the more recent literature as the 'social brain'. In this perspective, we may speculate that the 'social brain' should confront its approaches with the 'theory of mind': if a man was able to make attributions and reason about mental status of men standing in front of him, this would allow individuals to cope with other's individual behaviour, and groups with other groups.19

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