



Review article

A proposal for new neurorehabilitative intervention on Moebius Syndrome patients after ‘smile surgery’. Proof of concept based on mirror neuron system properties and hand-mouth synergistic activity



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ARTICLE INFO

Article history:

Received 29 August 2016

Received in revised form 26 January 2017

Accepted 27 January 2017

Keywords:

Imitation
Neurorehabilitation
Motor cortex
Facial mimicry
Kinematics

ABSTRACT

Studies of the last twenty years on the motor and premotor cortices of primates demonstrated that the motor system is involved in the control and initiation of movements, and in higher cognitive processes, such as action understanding, imitation, and empathy. Mirror neurons are only one example of such theoretical shift. Their properties demonstrate that motor and sensory processing are coupled in the brain. Such knowledge has been also central for designing new neurorehabilitative therapies for patients suffering from brain injuries and consequent motor deficits. Moebius Syndrome patients, for example, are incapable of moving their facial muscles, which are fundamental for affective communication. These patients face an important challenge after having undergone a corrective surgery: reanimating the transplanted muscles to achieve a voluntarily control of smiling. We propose two new complementary rehabilitative approaches on MBS patients based on observation/imitation therapy (Facial Imitation Therapy, FIT) and on hand-mouth motor synergies (Synergistic Activity Therapy, SAT). Preliminary results show that our intervention protocol is a promising approach for neurorehabilitation of patients with facial palsy.

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1. Introduction

The motor cortex of primates is located anterior to the central sulcus and is histologically characterized by the lack of the granular cell (agranular cortex). In humans, the classical Brodmann map distinguishes between two different areas: area 4, or primary motor cortex (M1), and area 6, the premotor cortex. A similar organization is present in other nonhuman primates (Rizzolatti and Luppino, 2001). The idea that the motor cortex is involved in the generation of movement derives not only from the seminal work on electrical stimulation conducted by the groups of Sherrington, Woolsey and Penfield, but also from the neurophysiological work, through single cell recordings, that were carried out in the monkeys starting from the 70's (Asanuma and Rosen, 1972; Cheney and Fetz, 1985; Kwan et al., 1978; Rizzolatti et al., 1987, 1988). These latter studies clearly provided a new picture of the functional role of the motor cortex. First, they showed that neurons in these areas do not only code simple movements, but are involved in the processing of sensory information aimed at supporting the execution of complex goal-directed movements (e.g. grasping, object manipulation, biting, etc.). Secondly, these studies showed that neurons in these areas are also involved in the decisional process related to movement initiation and execution (Rizzolatti and Craighero, 2004). Third, and most importantly for the current review, part of the brain circuits involving motor cortical areas are recruited for higher cognitive functions (e.g. such space coding, action recognition, imitation, etc) (Rizzolatti et al., 2014). For years, these functions have been considered anatomically located in associative cortex, but the neurophysiological work of the last twenty years has challenged such view. In particular, the discovery of mirror neurons (MNs) (di Pellegrino et al., 1992; Gallese et al., 1996) provided evidence that neurons in the premotor cortex could be involved in decoding others' behavior through a matching mechanism in which the visual description of an action activates a corresponding motor representation. The possibility of activating the motor cortex through the visual modality, has led some scientists to explore new potential neurorehabilitative interventions for patients who suffer from brain injuries with consequent motor deficits (Buccino, 2014).

In the current article, firstly, a description will be given of the studies on MNs and of the basic principles upon which such sensory-motor matching mechanism operates. Secondly, an account of how the mechanism responsible for behavioral phenomena such as facial mimicry and imitation will be provided. Thirdly, motor deficits involving facial muscles and their clinical implications will be examined. In particular, the main aim of this paper is to understand the consequences of motor impairments in Moebius Syndrome (MBS). In MBS, the lesion of the cranial nerve VII leads to a significant reduction, if not total absence, of the capacity to activate facial mimic muscles. A description will be given of the clinical aspects of MBS and of the surgical approach (named 'smile surgery'). Smile surgery is aimed at reanimating facial muscle in children, through muscle transplant and neuro-rehabilitation. Such surgical approach gives the patient the opportunity to produce smile, which is most critical for human social communication. MBS offers a unique opportunity to investigate the MN system under perturbed motor conditions. Lastly, in the current article, a description will be given of a new post-surgical neurorehabilitative intervention based on our knowledge of the link between perception and action, and on other specific properties of the motor cortex. In order to prove the concept and the potential benefits of such intervention, the smile movement kinematics of a MBS patient who underwent 'smile surgery' has been assessed.

1.1. The action-observation network in monkey

MNs are visuomotor neurons that fire both when a goal-directed action is performed and when the same action is passively observed (Rizzolatti and Craighero, 2004). MNs were first found through microelectrode recordings of single neurons in area F5, which occupies the most rostral part of the ventral premotor cortex in the macaque monkey (di Pellegrino et al., 1992; Gallese et al., 1996; Rizzolatti et al., 1996). Area F5 constitutes a fundamental region for coding the goal of hand motor acts such as grasping, manipulating, tearing, and holding (Rizzolatti et al., 1988), but also for mouth movements involved in ingestion (e.g. biting) and in communicative gestures (e.g. lipsmacking, a monkey affiliative gesture; Ferrari et al., 2003). Some MNs in F5 fire for both hand and mouth actions. This is not surprising since there is a considerable overlapping motor representation between the hand and the mouth cortical sectors, with the mouth more laterally represented with respect to the hand (Maranesi et al., 2012). Thus, it was observed that mouth actions could activate neurons involved in both the motor control of the hand and of the mouth. This aspect of the motor cortex organization will be further elaborated in the following sections as it has important implications for the proposed intervention strategy described below.

The majority of MNs discharge for only one type of action during execution and observation ("strictly congruent"; Gallese et al., 1996). Nevertheless, some MNs discharged for more than one, like grasping and holding ("broadly congruent"; di Pellegrino et al., 1992; Gallese et al., 1996; Rizzolatti et al., 1996). It is commonly accepted that the discharge of MNs represents the neuronal correlate of an internal representation of the observed action's goal. The functional significance of this representation is that the mapping of the observed action onto the observer's motor repertoire subserves action understanding purposes (Gallese et al., 1996; Rizzolatti and Fogassi, 2014).

Recent results support the notion that F5 MNs exhibit remarkable generalization properties (Casile et al., 2011; Ferrari et al., 2005). For example, after extensive monkey visual exposure to actions executed with a tool, a subset of MNs in the ventral part of area F5c started also to respond to such type of visual stimuli (Ferrari et al., 2005). In addition, an action can also be recognized when it is only acoustically presented (audio-visual MNs; Kohler et al., 2002) or even if it is partially occluded, demonstrating that the action goal can be inferred through different sensory modalities or even when the information related to the whole motor sequence is partly available (Umiltà et al., 2001).

Neurons responding to the observation of actions done by others are not only present in area F5. Indeed, the inferior parietal lobule (IPL) is critical for object grasping and it also responds during passive observation of grasping actions. Neurons present in the convexity of the IPL (prefrontal gyrus area, PFG; Fogassi et al., 2005), but also in the anterior intraparietal area (AIP), discharge during the observation of finger and hand movements. It has been demonstrated that these two parietal areas, PFG and AIP, are anatomically connected to F5c (Nelissen et al., 2011). Thus, the circuit connecting the IPL with F5 plays a fundamental role in controlling the organization of hand-object interactions and in decoding others' actions (Rizzolatti and Fogassi, 2014). More recent studies described the possible mechanism through which this parieto-premotor pathway operates a distinction between the visual representation of one's own and others' action (Bonini, 2016; Maeda et al., 2015). These studies demonstrated the involvement of this circuit in the understanding of the intention of others' action, that is, the final goal of a chain of sequential motor acts (Ferrari et al., 2005; Kaplan and Iacoboni, 2006).

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