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The importance of visuo-motor coordination in upper limb rehabilitation after ischemic stroke by robotic therapy

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Abstract
Stroke is an acute hypoperfusion of cerebral parenchyma that most often leads to outstanding motor deficits that can last for the rest of the patient's life. The purpose of the neurorehabilitation process is to limit, as far is possible for the motor deficits and to bring the patient to an independent life. A modern method consists in robotic neurorehabilitation which is more and more used, associated with functional electrical stimulation (FES). At the lower limb, the use of robotic rehabilitation associated with FES is already considered a success due to relatively stereotypical movements of the lower limb. In opposition, the upper limb is more difficult to rehabilitate due to its more complex movements. Therefore, eye-hand coordination (EHC) constitutes an important factor that is conditioning the rehabilitation progress. The eye-hand coordination can be brutally disturbed by stroke with critical consequences on motor-executive component. The EHC development depends on the interaction between a feedback complex and the prediction of the upper limb motility in the space, and requires the association between visual system, oculomotor system and hand motor system. We analyzed the stroke impact on this sensorial-motor functional integration and looked for a possible solution for the interruption of coordination between eyes and the movements of the superior limb. We consider that our study can contribute to a better understanding and to a faster rehabilitation of the motor deficit in the upper limb after stroke.

Key words: *stroke, rehabilitation, eye-hand coordination, robotic neurorehabilitation*,

Introduction

Stroke is defined as a rapid onset of neurological focal deficit, symptoms caused by a vascular lesion of the cerebral parenchyma. The syndromes resulting are various and greatly depending on aetiology, severity, prognosis and recovery possibilities. Over the past 20 years an important changes in the early diagnosis, treatment and rehabilitation techniques were made (1-4). Stroke is the fourth killer and the first cause of adult long term disability in United States (US) (5). The worldwide impact of stroke seems to be more higher than it is in US (6). The rehabilitation interval has a window when the neuroplasticity is maximum, during which, the brain ability for rehabilitation is enhanced (5). In this context, robotic rehabilitation (RR), one of the most modern technique is intensively studied in this century along with using mechanotronics technologies and computer software development (7, 8). RR can facilitate and increase the efficiency of motor deficiency recovery therapies. It is currently one of essential therapeutic tools for restorative therapy of lost functions and return to functional independence in order to improve day by day activity for stroke survivors who experience limitation of mobility and communication (9). The results of a systematic review of studies that investigated the outcome after rehabilitation assisted by robotic therapy after stroke, compared with classical physical therapy was presented by Kwakkel et al (10). This study reveals a moderate but statistically significant better upper limb motor rehabilitation results for patients where robotic assisted therapy was used, compared with conventional therapy. In addition, computer assisted devices for regaining upper limb function can optimize the required movement pattern (10). By this technology, more personalized therapy, specific for

each patient needs, can be assigned better by robotics than by conventional rehabilitation methods. There are still more studies needed in order to differentiate the mechanism of rehabilitation in robotic assisted therapy, where is a recovery based on neuronal repair, and where is a recovery based on compensation strategies (11).
The functional outcome in stroke rehabilitation strategies has two targets: one dedicated to upper limb motor recovery, and one dedicated to lower limb motor recovery. Differentiation in applied rehabilitation strategies must take into account the spatial complexity of the upper limb movement, compared to the relatively stereotypic lower limb movement into environment. For the upper limb, movements are automatic or voluntary, goal oriented. For the lower limb there are rhythmic movements for the locomotion and gait (12). These differences are reflected in speed, amplitude and directions of movements for each part of the body, in a particular pattern, that can be controlled by robotic assisted therapy (12).
From a functional point of view, the robotic technique can be dedicated to mobilizing a limb with no function (type I) or mobilizing a limb with a partially lost function and still possessing a variable grade of muscle strength (13). Adding feed-back mechanisms can have a complementary role in improving rehabilitation, especially in prosthetic upper limb rehabilitation, due to empowering the users to correct their movements in order to get better results (14). Most of the clinical studies refer to the grasping force as a variable that can be controlled by feed-back when the patient vision is not able to evaluate it (15). Recent studies reported that it is possible to improve the efficiency of the feedback mechanism by introducing a somatosensory feedback and transferring the stimulus (without translation) directly to the peripheral nerve endings which are directly stimulated by this functional loop (16). An important conclusion regarding the sensiomotor assisted prosthesis with feedback function consists in ability of the patient to grade them the force of contraction, in order to execute a movement to a target, after the device is removed and after a proper training and a consistent quantitative acquisition of muscular force was made (17). The force generated after the device is removed is about 30-50% from the force generated with prosthesis (17). This aspect is important for self-training, because patient's satisfaction can increase the efficiency of rehabilitation therapy.
The aim of this paper is focused on analyzing the robotic rehabilitation therapy (type II technology), dedicated to upper limb rehabilitation, in order to improve its motor performances. The vault key of RR that offer flexibility to "human-robotic arm" interface is represented by biomimetics. We intend to create a basic framework and offer a new perspective, more advanced on human –technology integration, hopefully for improving therapeutic efficiency in stroke rehabilitation strategies.

Human-robotic interface – role in stroke rehabilitation

Engineering systems became more and more sophisticated and "intelligent". For a good functioning and respect for biomimetic principle, a robotic system must present three components: stimulating component, the possibility of recording the action potential and integration of the information (18). The training has to be gradual in amplitude and force in order to protect the joints (18). The Fugl-Meyer (FM) score at time of admission can be important for timing the rehabilitation procedures, shorter robotic training periods being helpful for patients with lower admission (FM) scores and greater upper extremity impairment, followed by longer training periods that can bring new improvements. Some of the patients can also improve their rehabilitation performances after the ending the robotic training (18).
Rehabilitation efficiency can be controlled by imagistic methods that can assess the progression of recovery of lost functions. Integration of robotic technology with brain imaging, especially those that are able to visualize the function of the brain could bring a real contribution to understand the rehabilitation process. One of the most used imaging technique is represented by positron emission tomography (PET) of the brain, that is able to visualise brain activity in different tasks that imply different brain areas functioning. For an adult subject (right handed) there are early learning process and late learning process each of these processes involving different cortical areas (13). Due to continued advancement of radioligands and due to recent integration of PET and magnetic resonance

imaging (MRI) a new window for exploration of brain function was opened. MRI having a better spatial and temporal resolution can substantial contribute to functional assessment of the brain during rehabilitation process, through functional MRI exploration variant (19). Both of techniques are able to capture a designed activity of the brain during learning process of manipulating objects by robotic devices and to observe the brain areas involved in these specific activities. There are reports which describes that PET assessment can be helpful for giving metabolic and blood flow information regarding the learning process due to rehabilitation, revealing that the cortico-striatal loop is important in early learning while the motor execution areas played a significant role during late motor learning (cortico-cerebellar loop) (20). As patients became more skilled at the motor tasks, the functional neural networks activity is commuted to the cortico-cerebellar loops, with a significant increased activity in left premotor, left primary motor, and sensory areas, and in the right cerebellar cortex. The same study conclude that patients with basal ganglia lesions would take longer to start the recovery process due to deficiency of early phase of learning process, and patients with lesions in motor-execution areas will slowly recover due to deficiency in the later phases of learning process (21). The smaller is the number and size of the lesions of those areas following stroke, the better outcome is expected (20). All of these data should be taken in consideration and they can't constitute a general rehabilitation pattern due to various co-morbidities associated with each patient that can limit the patient recovery (22).

The stimulating component of robotic rehabilitation technique must assure that the device is applying an adequate electrical stimulation at one motor point of muscle. This has to be assign in order to recreate a spatial model of neural activity in which the specialist wants to replace or improve. Lo Ac et all designed a protocol for active therapy with controlling the duration, the intensity, the methods, and the time applied of rehabilitation program, in order to improve the reproducibility of training for stroke survivors (taking into the study, moderate to severe affected patients) (23). But electrical stimulation presents a major inconvenience, related to multidirectional spread of electrical current into a tissue, resulting a global stimulation and loss of structure selectivity which must be stimulated (23). This inconvenience can be diminished by choosing a proper stimulation parameters, by using of an appropriate electrodes and by the the correct choice of stimulation (10, 23).

The recording of action potentials, for the robotic arm device, is also an important component of robotic rehabilitation process. The coordinated movement involves a two ways shifts (nervous command from the central nervous system to the muscles and a feed-back from the muscles to the central nervous system). This circuit allows continuously adjusting the muscles contractions to the required parameters (24). In the case of using a robotic arm, the feedback currents are very weak and is lost in background electric noise. This is the reason why the robotic rehabilitation device requires special sensors to appreciate the degree of muscle contraction produced by functional electrical stimulation (FES), or to appreciate the amplitude and the speed of the movements performed by robotic arm (18). A possible problem would be the increasing of the weight of the robotic arm by monitoring of too many sensors.

The integration of information play an essential role in robotic rehabilitation methods. Due to complexity of motility of the human body, the fine control is achieved through the integration of a lot of information from environment into the central nervous system (the information are intermediate by mechanoreceptors from muscles and joints, by visual system and vestibular system sensorial reception) (24). A self-organized and self-adaptive system of great complexity is achieved where the motor scheme is gradually composed due to the training process, a scheme by which the central nervous system is trying to compensate the motor disability thorough a force imposed by the environment (25). In order to be able to control the movements this system respects the following rules: finite state control, proportional control, compensated control, predictive control (24, 25). The models that incorporate and use these principles of feedback control, actually are represented in neurological terms by the plasticity of the central nervous system. Such a complex system gains the flexibility in performing motor task even after destructive lesion as are after stroke lesions, this process being named use-depend neuroplasticity, and is considered a basic goal in neuro- rehabilitation therapy (26). Mawase et al found that the action repetition while learning a motor task enhances use-dependent neuroplasticity (26).

The developing technique of the functional electrical stimulation is recorded in numerous studies. The development effort in this research field started 29 years ago and aimed to restore the motility in paraplegic patients (27). Rehabilitation of motor deficit in the upper limb represents a much greater challenge, considering the degree of kinetic complexity (28), but decoding the algorithms for the functioning of the neuromuscular unit remains an open challenge. In our opinion, the greatest problem of the using of functional electrical stimulation coupled with robotic arm is the lack of coherent and continuous feedback between amplitude of performed motion, and the algorithm of electrical stimulation applied to achieve optimal coordination during the movement of distal extremity of the robotic arm. We suggest there are three possible solutions. The first suggestion is the placement of contraction sensors or angular displacement sensors on the healthy contralateral upper limb. In this hypothesis, the coordination of the dysfunctional upper limb assisted by functional electrical stimulation is obtained by imitation movements performed by the healthy upper limb (which actually occurs within imitation synchinesis). This process is possible due to and mirror neurons functions first identified in the ventral premotor cortex (PMv; area F5) and later in the inferior parietal lobule (areas PF and PFG) of monkey brain, namely "mirror neuron" system and having an important role in motor rehabilitation and aphasia recovery after stroke (29). The second suggestion is the placement of some sensors on robotic rehabilitation device that can respond to a present voice command. A single voice command can, thus, increase and decrease the level of electrical stimulation applied to a muscle or more muscle units and resulting in increasing or decreasing the device power. Both first and specially the second method could have a strong therapeutically effect. Meanwhile both of them can lead to achieving an intense cognitive mobilisation and voluntary conceptual forming of the entire rehabilitation process, in order to control the desired voluntary movements. In this way, patient's involvement into the rehabilitation program, for developing a voluntary movement is greater, due to volitional component which is enhanced. The last suggested solution is the placement on the head and eye a position sensors which follows the distal extremity of the robotic arm, and modifies the functional electrical stimulation parameters. The last solution seems to be most suitable to physiological condition of adaptive process to the environmental stimulation. This solution restores visual control of the complex motor function of the upper limb into the space. The robotic-arm-eye connection via functional electrical stimulation actually reinforce the lost functional connection between eye and hand which is essential for movement coordination (30). If eye-hand coordination recovers through sensors and functional electrical stimulation, there is possibility for a more rapid progress in neurorehabilitation.

A more clear characterisation of eye-hand coordination regarding the connection between ocular motor control and manual motor control will improve the understanding of its role in upper limb motor rehabilitation after stroke (31). Therefore eye-hand coordination (also known as eye-hand coupling, visuo-manual coordination or oculo-manual synergy) physiology is defined as the coordinated control of eye movements associated with the fine movements of the hands toward a given target, reaching the target and performing the desired work (32). Good directed movements of the upper limb is provided by a large number of neural mechanisms: detection of the target in a three dimensional space (by visual perception), space assessment of the body and of the upper limbs, evaluation of the muscle tone (by proprioception) and execution on-line guidance of the hand trajectory (33-35). In fact, the essence of eye-hand coordination is the result of the very detailed coupling in space and time of kinetic learning mechanisms. An equivalent form of eye-hand coordination is found in all forms of life, being linked to the evolution of the visual system and its connections into the brain in order to assign species surviving (36,37). Evolutionary processes offers to the optic chiasm a particular importance due to crossing and non-crossing optic fibres structure that determines which hemisphere receives proprioceptive information about the ipsilateral hand (37). Multimodal neuron response to tactile as well as visual targets, and extensive use of multimodal sensory information supports the hypothesis that accurate upper limb control influenced the evolution of the primate visual system and consequently evolution of the brain. This hypothesis is named eye-forelimb hypothesis and consists in evolutionary change toward hemidecussation in the optic chiasm, providing the evolution of frontal vision and visually guided forelimbs (37, 38).

The afferent component of eye-hand coordination is important for the adequate function of this entity. The visual system is equipped with remarkable ability of detection and localization of the targeting objects (stationary or mobile). For mobile targets it is able to appreciate the speed, the trajectory, and can anticipate the position of the target in certain moment. There are currently an impressive numbers of researches that have as an objective the motor behaviour of the eyeballs when are pursuing an object and modern imagistic techniques for brain activity assessment, as is functional magnetic resonance imaging, can bring a new inside into this research field (39- 41). The line of sight follow the target and always keep it in the centre of visual field at the fovea level (35). At this level, the photoreceptors density ensure the best visual resolution for a 2-3 degree angle of the visual field. The foveation consists in centring of an object of interest onto fovea (35). This process is made by different mechanisms, depending to the distance to which the object is located. If the object is near the face, in the frontal plane, foveation is achieved by convergence phenomenon that is coordinated by the brain (42). But if the distance to the object is longer or if the object is moving fast, foveation is achieved by movements (possible rapid) of the head, in order to ensure the eye-hand coordination process or saccadic eye movements are onset (43). Both mechanisms contribute to the stabilisation of the line of sight on the target and to the target's projection on the fovea. Due to these mechanisms the eyes are able to pursue an object, and visual information is transmitted to the cortex, in order to guide the direction and the distance of movements for a specific action (35). The targeting time is variable. Sometimes the eyes remain fixed on the target until the motor action is finished, or, in other situations, the eyes are moving for pursuing another target, before the hand is reaching the object. Hand movement is performed in this case automatically in the absence of foveal control. This phenomenon is related to visual anticipation of the future kinetic plan and requiring the visual memory (44). In another circumstances, the line of sight returns to the original, due to the visual memory reinforcement (45). Sometimes, in the case of automatic movements with a well memorized kinetics, and when specific movements are frequently performed, the visual system offer a three dimensional support of the frame in which the movement is taking place. The kinetics of the hand can thus unfold at the periphery of visual field and fovealization is not necessary. By all of these mechanisms the human visual system is able to recognize different objects in different instances, and to transmit proper information to the brain in order to achieve an adequate decision regarding the future actions (46).

Eye-hand coordination abnormalities after stroke – importance for rehabilitation process

There are several abnormalities of eye-hand coordination that can occur in stroke survivor's patients. There can be a change in latency of saccades initialization for a target pursuing, comparing with control subjects (saccades occurs earlier). This can be due to upper-motor-neuron-like desinhibition phenomenon, in which, patients with cerebrovascular lesions anticipate the movement in spite of the instruction to the contrary (30).This phenomenon has as an explanation the inability to suppress saccades, that are maintained as a reflexively, in response to a target (initialization of saccades takes about 60 ms that are needed for the information to travel from the retina to brainstem where the command for extraocular muscle is made in order to initialize saccades ; the saccades are onset after 200 ms, the differences being attributed to the cognitive process to analyze these information and make a decision) (47). In stroke patients there is an anticipation of saccades which occur earlier than 60 ms (47). The motor control of the movements is more complex, because each movement imply visual contribution and saccades adjustment, in order to reach the targeting object, to touch it, to grip it, and eventually to lift it according with its size and weight. All of these action needs a modulation of saccades output (48). There are also different abnormalities regarding the eye-hand coordination, as are spatial errors leading to saccadic dysmetria associated with the lesions in cortex, pretectum, thalamus, superior colliculus, and cerebellum, where the patient can't predict the distance to the target or the size of the target (49, 50). There is also an alteration of predictive control which is essential for planning a visuomotor action. After stroke, the patients can experience the inability to program motor action sequences in space and time (51, 30).

Conclusions

The ocular motor system can constitute a sensitive marker, in ischemic stroke, for motor and cognitive recovery. The environmental perception with visual system has to be transposed in a precise motor action designed to a day by day living. Eye-hand coordination is an accurate circuit that serves to this goal. Understanding and improving eye-hand coordination can have an essential contribution role with clinical implication for a better and proper rehabilitation strategy post stroke. Despite the fact the brain lesions were considered mostly definitive, the neuroplasticity phenomenon proved that a proper training can recover partially lost or diminished functions. Future studies are needed for analyzing various techniques of rehabilitation, in order to organize a valuable scheme for the best outcome. There is a serious challenge to bring all the information in practice and offer to the patient a training model that can be comfortable and can bring real improvements for their disabilities. Informatics development and robotic techniques evolution, together with the possibility to make more and more brain functional mapping due to modern imagistic techniques, could bring for these patients, a new hope for improving their quality of life.

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