

Neurorehabilitation of Parkinson's disease: Is It Time for A New Approach??

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In the latest years a lot of studies have been published about neurorehabilitation of Parkinson's disease (PD). These studies have clearly demonstrated the efficacy of neurorehabilitation in all phases of the disease. In spite of various medical and surgical treatments for Parkinson's disease, infact, patients gradually develop significant physical problems (1). Physiotherapy aims to enable people with PD to maintain their maximum level of mobility, activity, and functional independence over time. A range of approaches to movement rehabilitation are used based on physical therapy. As recently demonstrated by a Cochrane review (1) benefit for physiotherapy was found in most outcomes over the short term (i.e. < 3 months) but was significant only for speed, two- or six-minute walk test, Freezing of Gait questionnaire, Timed Up & Go, Functional Reach Test, Berg Balance Scale, and clinician-rated UP. Moreover this review illustrates that a wide range of approaches are employed by physiotherapists to treat patients with PD. However no evidence of differences in treatment effect was noted between the different types of physiotherapy interventions being used, although this was based on indirect comparisons. Physiotherapy is currently considered as one of the tools in the treatment of the disease, in particular for the symptoms that are not controlled by the medical treatment such as fatigue, balance problems e falls (2). However it is clear that the physical approach is not completely able to control these symptoms. Therefore in recent years the neurorehabilitation has been directed towards cognitive neurorehabilitation (3-5). Infact we know that in early-stage non demented parkinson's disease patients there are a lot of cognitive deficit that may be linked with deambulation and equilibrium problems (6-10). Consequently, it could be useful to assess this cognitive problems since from the early stage of the disease and to treat them with a cognitive neurorehabilitative approach in order to maintain functional independence for a longer time. A lot of possible treatments are nowadays possible. From music therapy to formal cognitive neurorehabilitation: these tools are very useful to improve executive and visuospatial functions (11-13). Another recent type of possible cognitive approach is based on Action Observation therapy (AOT). It is based on observation of action performed by others. It is well-accepted that observation of the actions activates the same neural structures responsible of the actual execution of the same actions. These structures are defined as the Mirror Neuron Network. The first primate studies regarding the activation of mirror system was published in 1992 by Pellegrino et al and Galles et al 1996 (14-15). In these articles the authors showed that in nonhuman primates, neuron of the ventral premotor cortex (area f5) of the macaque monkey discharge when a monkey performs an action or, while at rest, observes a third person or another animal performing the same action. Different studies based on non invasive neuroelettrophysiological assessment of functional brain imaging techniques have demonstrated the presence of the mirror neuron system and their mechanism in humans (16-17).

These studies have demonstrated that in the human these networks are activated when individuals learn motor action via execution (as in traditional motor learning) or imitation, observation (as in observational learning). The brain areas are inferior parietal lobe, ventral premotor cortex caudal part of the inferior frontal gyrus. It is therefore believed that, in this way, individuals can relearn impaired motor function. This method has been used in stroke rehabilitation (18) More recently an interesting study published on Neurorehabilitation and neural repair 2010 (19) has demonstrated the utility of Action observation therapy in the treatment of freezing of gait (FOG) in patients with Parkinson's disease. The authors of the study explained that patients with PD and FOG do not lose the ability to generate a normal stepping pattern, but they experience difficulty in activating the motor control system and modulate gait parameters in response to environmental or task-dependent requirements (20). Infact freezing of gait typical occurs during shifting of attention or a circumstantial directional changes. FOG responds poorly to pharmacological treatment, but it's well known that focused attention and external stimuli can help these patients overcome the fog episodes. Previous studies suggested the effectiveness of sensory cues on the rehabilitation of gait disorders of parkinson's disease. This strategy is often used in clinical practise to improve fog episodes (21) However a recent review (22) pointed out that the scientific evidence of the effectiveness of cueing to alleviate FOG is still limited. So teaching motor strategy without cues to overcome or prevent FOG is an alternative rehabilitation approach, relying more on appropriate allocation of attention. The results of the study revealed a significant larger and longer lasting improvement in FOG for patients allocated in the group observation+physical training strategy (action group) compared with control patients allocated to a "physical training strategy" alone. The efficacy of this approach was demonstrated with fog – questionnaire and FOG diaries. According to this study the improvement was maintained for 4 weeks after the end of the treatment.

More recently our group published a study with the aim to demonstrate the modification of p300 pattern after a neurorehabilitation program based on action observation therapy (23). P300 is an event related potential (ERP) component elicited in the process of decision making. It is usually elicited using the oddball paradigm, in which low-probability target items are mixed with high-probability non-target (or "standard") items. The signal is typically measured most strongly by the electrodes covering the parietal lobe (24).

Infact a study published on *Noro Psikiyatr Ars.* (2017) detected cognitive changes by electrophysiological methods (p300) in PD patients who were indicated to be cognitively normal by neuropsychological tests (25). These findings suggest that cognitive changes in PD patients, which are not yet reflected in neuropsychological tests, may be detected by electrophysiological methods in earlier stages. Moreover previous studies showed a positive correlation between the prolongation of p300 latencies in PD and cognitive deficit in memory, attention, executive function domains and depression (26-27).

The aim of this study was to assess the role of Action Observation (AO) to improve balance, gait, reduce falls, and to investigate the changes in P300 pattern. Five cognitively intact (mmse>24) people with Parkinson's disease (PD) were enrolled in this prospective, quasi-experimental study to undergo a rehabilitation program of AO for gait and balance recovery of 60 min, three times a week for four weeks. The statistical analysis showed significant improvements for Unified Parkinson's Disease Rating Scale (UPDRS) motor section III $p=0.0082$, Shortform12-items Healthy Survey (SF-12), Mental Composite Score (MCS) $p=0.0007$, Freezing of gait Questionnaire (FOG-Q) $p=0.0030$, The 39-items Parkinson's Disease Questionnaire (PDQ-39) $p=0.100$, and for P300 $ld p=0.0077$.

The size of the patients sample enrolled in the study is small. So no definitive findings can be drawn. Nevertheless this study opens a very interesting pathway for further studies. Infact the suggestion is to use this cognitive approach since from the early stage of the disease in order to stimulate neural plasticity activity with a motor+cognitive approach. This could be useful, in particular, for patients with mild cognitive impairment detected with p300 (25).

Moreover another interesting study recently published on European journal of neurology demonstrated, with Mri scans, the long-term effect of the cognitive functionality and brain changes after attending a 3-month cognitive rehabilitation programme (28).

All These findings support the possibility that neurorehabilitation with a motor+cognitive approach since from the early stage of the disease may have a disease modifying effect and prolong functional independence of the patients.

In Conclusion, in our opinion, this new approach might be very useful at the early stage of the disease, together with lower doses of dopaminergic drugs, in order to prolong functional independence of PD patients.

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