FNIRS application in Parkinson’s Disease

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Contributor: Augusto Bonilauri , Francesca Sangiuliano Intra , Luigi Pugnetti , Giuseppe Baselli , Francesca Baglio

The management of people affected by neurological disorders, such as Parkinson's disease, requires the adoption of targeted and cost-effective interventions to cope with chronicity. Although therapy adaptation and rehabilitation represent major targets, affordable and reliable neurophysiological correlates of cerebral activity to be used throughout treatment stages are often lacking. The functional Near-Infrared Spectroscopy (fNIRS) represents a versatile optical neuroimaging technology for investigating cortical hemodynamic activity in the most common chronic neurological conditions, including Parkinson's disease, with the advantages of non-invasiveness and portability which make fNIRS suitable for carrying out multiple measurements in rehabilitation settings.

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1. Introduction

The management of people affected by age-related neurological disorders requires the adoption of targeted and cost-effective interventions to cope with chronicity [1][2]. Therapy adaptation and rehabilitation represent major targets requiring long-term follow-up of neurodegeneration or, conversely, the promotion of neuroplasticity mechanisms [3]. However, affordable and reliable neurophysiological correlates of cerebral activity to be used throughout treatment stages are often lacking [4][5]. The application of functional neuroimaging methods, including functional Magnetic Resonance Imaging widely accepted as gold standard modality [6], is often limited either by high costs, long scan times, poor temporal resolution and sensitivity to motion that reduce patient compliance and the possibility to assess responses evoked by complex stimuli. Functional Near-infrared Spectroscopy (fNIRS) [7] is gaining an increasing relevance as a more versatile solution to investigate cerebral activity based on the principle of neurovascular coupling. It is a non-invasive optical imaging technique that employs near-infrared (NIR) light to measure cortical oxygenation and consequently cortical activation. This technique employs pairs of NIR sources and detectors placed over predefined scalp locations to estimate light intensity attenuations, next converted to oxygenated (HbO2) and deoxygenated hemoglobin (HbR) concentration changes according to the modified Beer-Lambert law [8]. Other chromophores are essentially stationary and allow sufficient transmittance in the NIR region. fNIRS is better suited to perform low-cost and multiple acquisitions in the rehabilitation context during the execution of a wide variety of tasks: motor, cognitive and somatosensory [9], as well as postural control and free-walking conditions [10][11].

2. fNIRS in Parkinson’s Disease

Parkinson's Disease (PD) is a slowly progressive neurodegenerative disorder and represents one of the most common pathologies related to ageing, involving about 6.1 million individuals worldwide and presenting considerable implications on national healthcare systems [12][13]. This pathology is characterized by a prominent impairment of motor functions (bradykinesia, muscular rigidity, rest tremor, postural and gait impairment) together with non-motor features (olfactory and autonomic dysfunction, cognitive impairment, psychiatric symptoms, sleep disorders, pain and fatigue) [14][15]. As a consequence, complex clinical pictures lead to numerous PD subtypes which can show different clinical profiles and disease progression [16]. This paragraph provides a review of actual fNIRS applications either to assess the effects of interventional procedures referred to Deep Brain Stimulation (DBS) [17][18][19][20] or to investigate clinical phenotypes associated to PD during usual and dual task (DT) walking [21][22][23][24][25][26][27][28]. Most of available articles investigated the cortical activity of the prefrontal cortex (PFC), while only a single study considered the primary motor cortex (PMC) as the region of interest [18]. Finally, one article employed a high-density probe configuration to simultaneously investigate brain activity associated to temporal and occipital cortices [20].

2.1. Deep Brain Stimulation

The use of fNIRS and NIRS in the context of DBS is based on the underlying hypothesis that the stimulation delivered at basal ganglia level can modulate the global cortical activity, which in turn is reflected by the neurovascular activity [18]. Sakatani et al. [17] were the first to employ NIRS for assessing changes in PFC oxygenation induced by frequency- and intensity-varying stimulation of the thalamic nucleus ventralis intermedius and globus pallidus internus. They observed HbO2 and HbR changes that were comparable to those induced by cognitive tasks, thus suggesting a possible interaction between the frontal lobes and the stimulated deep brain stuctures. More recently, Morishita et al. [18] investigated PMC cortical activity pre-operatively and at 1-month follow-up, while motor scores were assessed by means of the Unified Parkinson's Disease Rating Scale (UPRS). Results show pre- to post-operative improvement of the UPRS motor score and the group analysis of fNIRS revealed a post-operative cortical activity comparable to the pre-operative one though more confined to the motor cortex for HbO2. Mayer et al. [19]studied the effects of bilateral subthalamic nucleus stimulation on working memory functions. Early PD patients showed a reduced frontal activation with respect to the control group. Overall worsening of working memory performance was accompanied by an increased frontal activation under DBS and on-medication, while no modifications were observed with respect to medication states, thus suggesting a DBS-induced compensatory mechanism operating within the basal ganglia-prefrontal network. Finally, Eggebrecht et al. [20] utilized a new High-Density Diffuse Optical Tomography (HD-DOT) probe array to map distributed brain functions and resting-state networks in 3 patients undergoing subthalamic nucleus DBS. This study demonstrated that HD-DOT showed a reliable overlap with fMRI, thus suggesting that it can be used to provide individualized functional images when other traditional functional imaging modalities are unavailable.

2.2. Walking and Dual Walking Task

Most of reviewed studies in PD were focused on walking and DT conditions to investigate the extent of PFC motor vs. executive and cognitive dysfunction. The underlying hypothesis is that PFC compensates for the motor

impairment, hence cortical activation can be considered as an overall index of cognitive load. Within the context of rehabilitation, the promotion of more localized cortical activation associated with executive-attentional functions could be a viable way to activate this compensatory mechanism [24]. Mahoney et al. [21] reported that PD patients showed greater PFC activation in order to successfully achieve the same level of postural stability with respect to age-matched HCs and other mild PD patients. Nieuwhof et al. [22] observed overall increases of HbO2 levels in the PFC during three dual walking tasks (walking while counting forward, serially subtracting, reciting digit spans) compared to a rest condition (standing still). Another study by Cornejo et al. [23] found that both gait stability and PFC activation were enhanced when walking on a treadmill at a self-selected pace with respect to usual walking, suggesting that an external rhythmic pacing may reduce the cognitive mediation on gait. Stuart et al. [24] also found that ageing and pathology affect the PFC compensatory mechanism due to the cognitive control required to perform turning-in-place and walking tasks, while this effect is reduced once the action has begun.

Maidan et al. [25][26][27][28]carried out an extensive work to investigate the relationship between this compensation mechanism and PFC activation and promote strategies to reduce cognitive load. In 2015 the authors studied the interplay of PFC activation during freezing of gait (FOG), a common disturbance among PD patients, associated with anticipated and unanticipated turns, in order to distinguish opposite cognitive requests such as motor planning and reflexive responses [26]. Results revealed that frontal activation levels can be associated to different typologies of FOG. Successively, they studied PD patients without FOG and noticed increased activation during usual walking and a decrease during turning in the absence of cognitive load [25]. Increased activation was also found in a sub-group of patients with impaired ambulation, which further supports the role of PFC in motor-cognitive compensation. Yet another study suggested that a combination of motor and cognitive tasks - namely obstacle negotiation, usual, and DT walking—determined different involvements of PFC activity during gait in HCs and PD patients [28]. Finally, the same research group carried out a longitudinal randomized controlled trial to assess the effects of treadmill training (TT) alone or combined with virtual reality (VR) [27]. PFC activation during obstacle negotiation and DT walking was reduced in the combined TT-VR program condition. However, both experimental conditions induced an overall reduction in the rate of post-intervention falls and an improvement in gait performances, suggesting that simultaneous motor and cognitive training promotes the recruitment of more specific PFC areas.

3. Conclusion

In conclusion, the available literature supports the idea that fNIRS can be a viable tool to detect functional differences between normal ageing and people affected by the most common chronic neurological disorders, including PD. We found that this technology is mainly employed for the characterization of the patients' clinical phenotype, whereas a systematic adoption of intervention-based monitoring still remains to be seen. Overall results open the scenario of fNIRS as low-cost and portable tool to monitor cerebral plasticity during disease progression in order to promote subject-specific intervention strategies.

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