Eye Movement Metrics in the Differentiation of Parkinsonian Syndromes

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In this thesis we investigated conjugate and dis-conjugate eye movements (EM) in Parkinson's disease (PD) and other parkinsonian syndromes aiming to characterize and differentiate some aspects of their oculomotricity using infrared video-oculography.

First of all we published a practical review for medical students and clinicians describing clinical examination of eye movements, and interpretation of principal findings. Then we examined principal saccadic eye movements and smooth pursuit in the horizontal and vertical directions with video-oculography in a large group of healthy subjects, aiming to help new oculomotor laboratories in the constitution of their own norms. We conclude that age influence EM metrics but not gender or education level. The latency of saccades and the error rate of antisaccaes increases, while the velocity and gain diminishes with age. Saccades should be investigated in the horizontal and vertical plane because they are influenced by the direction of the target, resulting in a right/left and up/down asymmetry.

In a third project we focused on a frequent complain of PD patients, namely blurred near vision and visual discomfort during reading. We objectively assess for the first time vergence eye movements (VEM) in PD patients using VOG. Patients show increased latency of VEM and the divergence is slow and hypometric.

Rapid eye movement sleep behaviour disorder (RBD) is by far the strongest clinical marker of prodromal PD. We investigate EM a group of patients diagnosed as idiopathic RBD (iRBD), aiming to detect prodromal PD. We found two groups of patients: i) iRBD composed of patients, free from any parkinsonian sign with EM similar to controls; and ii) RBD with possible PD, composed of patients with disrupted EM. We concluded that EM abnormalities could be considered as an additional early diagnostic marker of PD.

Intraoperative microelectrode recording of single neuronal activity at the basal ganglia, in PD patients, was used to identify neurons participating in scanning eye movements based on specific electrophysiological pattern. We found that twenty percent of the neurons of the subthalamic nucleus, substantia nigra pars reticulata and globus pallidus showed eye movement related activity. Neurons related to scanning eye movements differ from neurons related to saccades, suggesting a functional specialization and segregation of both systems of eye movement control.

A recently described secondary toxic parkinsonian syndrome due to Ephedrone abuse draws the attention of the eye movement disorders community, because of its particular rapid onset and severe evolution. Horizontal and vertical eye movements were recorded in EP patients. We found slow and hypometric horizontal saccades, an increased occurrence of square wave jerks, long latencies of vertical antisaccades and high error rate in the antisaccade task. Patients make more errors than controls when pro- and antisaccades are mixed. Based on oculomotor performance, a direct differentiation between EP and PD was possible, EP patients presenting extensive oculomotor disturbances probably due to the manganese induced damage to the basal ganglia.

Finally we were interested in the relationship between eye movement disorders in PSP patients and gamma-aminobutyric acid (GABA) levels in the brain. GABA levels were measured with MRI spectroscopy and correlated to an eye movement paradigm, the remote distractor effect (RDE). We did not find any significant difference in GABA level at the frontal cortex, or an increased RDE in our patients compared to controls.

In this thesis we provide additional evidence about the importance and clinical utility of EM examination in the differentiation of PD and other parkisnonian syndromes, gaining insights into the physiology of the basal ganglia.