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Editorial

Decreased alpha2 connectivity in EEG is correlated with the cognitive and psychiatric manifestations of Parkinson's disease

See Article, pages 1748–1755

Parkinson's disease (PD) was traditionally thought of as a motor disorder induced by selective apoptosis of unknown cause affecting dopaminergic neurons in the pars compacta of the substantia nigra (SNpc), leading, in turn, to basal ganglionic dysfunction that manifests itself as bradykinesia, rigidity, and rest tremor. These features remain important elements of the current diagnostic criteria for PD, which, however, also give a prominent role to non-motor manifestations of the disease (Postuma et al., 2015). The progressive loss of SNpc neurons is insidious, with 60–80% already lost by the time PD is diagnosed. PD is among the neurodegenerative disorders that have now been shown to involve an intracellular accumulation of toxic proteins (Jucker and Walker, 2013). Intraneuronal alpha-synuclein accumulation is present in the vast majority of patients with PD (Walker and Jucker, 2015); this alpha-synucleinopathy represents the final common pathway of multiple environmental and genetic factors in the pathophysiology of PD (McNaught et al., 2001; Michel et al., 2016). Neurons containing toxic alpha-synuclein are found not only in the SNpc, but at many other sites as well, including the gut and the skin, accounting for the diversity of the clinical manifestations of PD, which are not only motor, but also olfactory, autonomic, neuropsychiatric, and cognitive. Because the medical and surgical treatments for PD have vastly improved in recent years (Schuepbach et al., 2013), it is now the mental disturbances rather than the motor dysfunction that limit the prognosis as to independence and lifespan of patients with PD (Forsaa et al., 2010). It follows that a reliable and valid quantitative measure of the non-motor, particularly cognitive and psychiatric, manifestations of the disease would be of both scientific and clinical importance. Quantitative measures of cognitive dysfunction and psychopathology in PD have been validated in multiple independent studies (Weintraub et al., 2004; Chaudhuri et al., 2007; Martinez-Martin et al., 2009; Litvan et al., 2012); an abbreviated test of mental functioning is part of the routine testing in PD recommended by the Movement Disorder Society (Goetz et al., 2008). While neuropsychiatric examination and quantitative neuropsychological testing are still the gold standard for assessing the patient's mental status, they are not always readily available and are susceptible to bias from practice effects if repeated.

Quantitative EEG (qEEG) offers reliably repeatable insight into the neuronal activity of the brain through the simultaneous measurement of rhythmic activity in multiple cortical areas. Many different test variables can be examined both at rest and during task performance. Cross-sectional studies have shown that a shift of the power spectrum in the resting state toward lower frequencies is correlated with cognitive deterioration in both demented and non-demented patients with PD (Caviness et al., 2007; Stoffers et al., 2007; Bousleiman et al., 2014). A background rhythm whose frequency is less than 8.5 Hz in a non-demented patient is associated with a hazard ratio of 13 for developing dementia within 5 years and can therefore be considered a prognostic biomarker (Klassen et al., 2011). Later, decreased functional connectedness of the left fronto-polar region has been shown to be associated with beginning apathy in PD (Hatz et al., 2017).

The article by Geraedts and colleagues in the current issue of *Clinical Neurophysiology* extends current knowledge by demonstrating that the resting-state functional connectivity specifically in the alpha2 band in patients with PD correlates with non-dopaminergic disease severity, in particular cognitive deficits and psychotic symptoms (Geraedts et al., 2018). Alpha2 power is linked to the local capacity to engage in new activity (Klimesch, 1999); thus, decreased functional alpha2 connectivity indicates a decline in the mutual accessibility of multiple cortical areas. While no correlation was found with motor signs, it seems plausible, as the authors suggest, that this decrease of alpha2 connectivity is not merely an epiphenomenon but actually reflects the mechanism underlying the cognitive and psychiatric manifestations of PD.

The study was performed with routine EEG recording, and its method presents no obstacle to general use beyond data processing and computation, which will be standardized and automatized in the future. An initiative toward this goal is now being supported by the International Federation of Clinical Neurophysiology (Babiloni, 2018). As these techniques come into wider use, both scientific and clinical benefits can be expected. A good step in this direction is the recent declaration of the BRAIN Initiative® that neurophysiological brain connectivity is now a priority subject for research (Koroshetz, 2018).

Conflict of interest

No conflict of interest.

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