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Functional MRI of impaired finger dexterity in Parkinson's disease

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The notion of limb kinetic apraxia is controversial. It has never been clear whether this term describes a type of clumsiness separate from other motor disorders such as bradykinesia, ataxia, and dysfunction of the corticospinal tract. Recently, there has been attention to the motor disorder of patients with Parkinson's disease (PD) where the possibility of limb kinetic apraxia has produced a spirited discussion (Gebhardt et al., 2008; Landau and Mink, 2007; Quencer et al., 2007). Evidence in favor of a disorder beyond bradykinesia has been the dissociation behaviorally and pharmacologically between simple finger tapping (FT) and the more complex task of coin rotation (CR). Additional evidence in the form of a separate physiology would help support the idea. The paper of Foki et al. (2010) which recently appeared in this journal attempts to do this with a functional MRI (fMRI) investigation. The authors compared fMRI activation during CR in patients with PD and matched healthy controls using FT with the index finger as a baseline task for bradykinesia. They found a trend to higher relative activations in PD patients during the CR task, notably in premotor and posterior parietal areas. Furthermore, based on a region of interest (ROI) approach, a "perirolandic index" was calculated that identified precentral overactivation and postcentral underactivation associated with deficient CR performance in PD. The authors proposed this index as a potential marker for limb kinetic apraxia. However, there are technical issues with this study limiting the ability to identify a new pathophysiological process that might underlie limb kinetic apraxia.

Neuroimaging studies on the neural basis of motor skill face the fundamental problem of how to dissect brain activation related to increased load of dexterity without being confounded with mere differences in sensory input or motor output. This has to be kept in mind when discussing the findings of the study by Foki et al. For instance, although contrasting CR and FT in an fMRI run attempted to control for the effects of PD-related bradykinesia, the tasks differ considerably in their kinematic requirements (i.e., coordinated

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three-finger movement versus isolated one-finger movement) and somato-sensory conditions (i.e., object interaction/perception versus simple movement perception). Moreover, FT speed was paced at 1 Hz, whereas CR speed could be freely chosen by the participant. Given these varied task features, differences in sensorimotor activations are not surprising. The authors partly overcame the issue as the same discrepancy in motor tasks existed within both patients and controls. However, a similar difficulty appeared in the between group comparisons as CR task performances were significantly different, healthy subjects being twice as fast as PD patients. The interpretation of findings may be further limited by the fact that imaging analysis was focused on the sensorimotor region. For instance, could the faster performance in healthy subjects have accounted for a stronger postcentral activation? The choice of using a motor task as baseline, rather than rest as is more usually done, is also somewhat problematic. How much of the difference is due to the baseline is unknown in this analysis.

Functional neuroimaging studies have demonstrated that movement frequency is likely encoded in primary motor cortex activation (Jenkins et al., 1997; Lehericy et al., 2006; Sadato et al., 1997) while increased complexity of movements additionally increases activation in premotor areas (Catalan et al., 1999; Lehericy et al., 2006). Furthermore, an fMRI study in patients with impaired motor skill due to stroke pointed to increased activity in premotor and posterior parietal areas when compared with healthy subjects (Schaechter and Perdue, 2008). The study used a paradigm for dexterity that controlled for kinematic differences (Ehrsson et al., 2002). In addition, patients were able to reach normal task performance which allowed to meaningfully interpret the findings (Price and Friston, 1999). Evidence from a combined fMRI and TMS study showed that premotor/parietal activations in stroke survivors are indeed functionally relevant and may reflect compensatory mechanisms (Lotze et al., 2006). Therefore, the trends to increased activations in several premotor and parietal areas in PD patients of the present study by Foki et al. merit further exploration. Indeed, structural MRI data from another recent study by Borroni et al. (2008) on patients with corticobasal degeneration (CBD) showed that limb kinetic deficits correlate with reduced gray and white matter integrity in premotor rather than primary sensorimotor areas.

The ability to selectively innervate and control individual finger muscles is particularly affected in PD (Agostino et al., 2003) and is considered the hallmark of limb kinetic praxis. It is believed that limb kinetic apraxia results from the impairment of the so called innervatory patterns in premotor cortex that mediate information from temporal-spatial plans of dexterous movements to appropriate motor areas (Denes et al., 1998). Therefore, future neuroimaging studies on dexterity in PD should particularly consider premotor regions and the study by Foki et al. represents a first step in that effort. Interestingly, in their study, CR did not correlate with parkinsonism as measured by the Unified Parkinson's Disease Rating Scale (UPDRS), pointing to the higher-order nature of the motor deficit, requiring further exploration.

Differences in global activations might also reasonably be taken into account. This is possible by determination of resting perfusion in each individual subject using the arterial

spin labeling (ASL) technique allowing to quantify the amount of fMRI signal changes (Federspiel et al., 2006).

The idea of a “perirolandic index” that defines a new pattern of pathophysiology, at least at this time, is difficult to interpret and appears to be a post hoc finding in a small number of subjects. The controversy about limb kinetic apraxia seems not yet settled, but this study takes the credit of pointing to a direction for further investigation.

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