The Evolution of Diffusion Tensor Imaging in Parkinson's Disease Research

I read with great interest the thorough and well written review by Duncan and colleagues on magnetic resonance imaging (MRI) as a biomarker for cognitive impairment in Parkinson's disease (PD).[1] The authors accurately discuss the difficulties of direct comparison across MRI studies. These include patient heterogeneity, different neuropsychological tests and cutoff scores, widely differing definitions for PD with dementia (PDD) and PD with mild cognitive impairment (PD-MCI), as well as image analysis choices and the diversity of statistical methods used. I agree that the *Movement* Disorders Society PD-MCI criteria[2] are a positive step in the process toward standardization. The reviewed studies employing diffusion tensor imaging (DTI) illustrate another potential confound when comparing across studies—DTI data quality. In fact, the articles cited in the review provide a beautiful example of the evolution of DTI data in the field of PD research.

Early DTI studies (published in 2004[3] and 2007[4]) used what was then cutting-edge technology to investigate PD and produced informative findings. However, the quality of DTI data has improved substantially over the past decade. Multiple advances, including the increase in field strength to 3 Telsa, the use of multi-channel head coils, the increase in the number of diffusion-encoding directions, and improved postprocessing methods to minimize the effects of head motion and eddy current distortions, have combined to yield superior fractional anisotropy and mean diffusivity images. Figure 1 provides a visual example of the impressive increase in data quality over the lifetime of DTI studies in PD. Thus, raw DTI data quality also may contribute to the variability of findings that range from normal to highly abnormal in early PD and PD with normal cognition.

Although numerous MRI studies have increased our knowledge of the imaging signature of cognitive impairment in PD, Duncan and colleagues conclude that a validated MRI biomarker does not currently exist. Nevertheless, with continued refinement of DTI techniques and more novel methods of quantifying tissue microstructure, such as high angular resolution diffusion imaging (HARDI), Q-ball vector analysis, and diffusion kurtosis imaging, diffusion MRI may yet provide a key component in the armamentarium of a useful, multimodal biomarker of cognitive decline in PD. ■

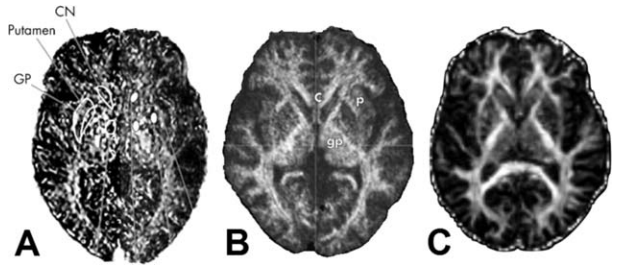

FIG. 1. These are examples of the quality of fractional anisotropy (FA) maps used for analysis in previous studies investigating Parkinson's disease (PD). From A through B to C, the quality of the images improves visually. (**A**) This image was acquired in 2001/2002[3] and displays the FA map at the level of the basal ganglia with regions of interest drawn over the caudate nucleus (CN), putamen, and globus pallidus (GP); white matter tracts appear noisy and ill defined (1.5 T; 6 noncollinear diffusion-encoding directions; voxel size, 1.8 × 3.1 × 3 mm^3). (**B**) This image was acquired in 2005/2006[4] and also displays the basal ganglia (c, caudate; p, putamen; gp, globus pallidus); white matter tracts are more recognizable (1.5 T; 12 noncollinear diffusion-encoding directions; voxel size, 1.2 × 1.2 × 4 mm^3). (**C**) This image was acquired in 2009 and provides an example of the data used in our recently published article[5]; white matter tracts are well defined and identifiable (3.0 T; 28 noncollinear diffusion-encoding directions; voxel size, 1.8 × 1.8 × 3 mm^3). Newer sequences with increased numbers of diffusion-encoding directions and optimized b values produce FA images of still higher quality than those displayed here. A and B were adapted with permission from BMJ Publishing Group Limited: A was provided courtesy of Yoshikawa et al.[3] (Yoshikawa K, Nakata Y, Yamada K, Nakagawa M. Early pathological changes in the parkinsonian brain demonstrated by diffusion tensor MRI. J Neurol Neurosurg Psychiatry 2004;75:481–484), and B was provided courtesy of Chan et al.[4] (Chan L-L, Rumpel H, Yap K, et al. Case control study of diffusion tensor imaging in Parkinson's disease. J Neurol Neurosurg Psychiatry 2007;78:1383–1386).

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Tracy R. Melzer, PhD[1,2]

[1]New Zealand Brain Research Institute, Christchurch, New Zealand; [2]Department of Medicine, University of Otago, Christchurch, New Zealand

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*Correspondence to: Dr. Tracy R. Melzer, 66 Stewart St, Christchurch 8011, New Zealand; tracy.melzer@nzbri.org

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