Neurite Orientation Dispersion and Density Imaging in Psychiatric Disorders: A Systematic Literature Review and a Technical Note

Supplemental Information

Acquisition considerations for NODDI

NODDI makes use of standard diffusion-weighted MRI sequences based on pulsed gradient spin echo (PGSE) echo-planar imaging (EPI) which images the brain, a 3-D object, as a set of consecutive 2-D axial slices. The key acquisition factors to consider are acquisition time, spatial resolution, and microstructural resolution. The challenge is to design an imaging protocol with spatial and microstructural resolutions as high as possible while keeping the acquisition time at a minimum.

To minimize compromised image quality due to subject motion, it is important to keep the acquisition time at a minimum. On older systems without the recently developed simultaneous multi-slice (SMS) capability (also known as multi-band), typical acquisition times are about 15 minutes. On systems equipped with the SMS capability, with two or three slices being acquired at the same time, typical acquisition times may be halved or reduced to a third, while keeping spatial and microstructural resolutions constant. In practice, one may choose not to reduce the acquisition time so drastically but invest the efficiency gain offered by SMS to increase spatial and/or microstructural resolutions.

The choice of spatial resolution depends on the application and has a significant impact on the acquisition time. On older systems without the SMS capability, typical spatial resolution is either isotropic 3mm x 3mm x 3mm or 2.5mm x 2.5mm x 2.5mm. While this may be reasonable for studying the majority of white matter structures, it may be too low for examining cortical gray matter. With the introduction of the SMS capability, it is now practical to acquire data at an isotropic resolution of 2mm x 2mm x 2mm within a reasonable acquisition time, which should improve our characterization of cortical gray matter.

The choice of microstructural resolution is arguably the most important. There are two key considerations here. First is the choice of the diffusion-weighting factors, known as the b-values. They should be chosen to allow the respective contribution of each compartment to be differentiated. The recommended choice (1) is to use three non-zero b-values: 300 s/mm^2, 700 s/mm^2, and 2000 s/mm^2. Including multiple non-zero b-values is important for robustly estimating FWF and NDI (2). Second is the choice of the diffusion-sensitizing gradients, known as the b-vectors. While NODDI does not depend strongly on the number of b-vectors, the choice is important for resolving crossing fibers with techniques like constrained spherical deconvolution (CSD). The recommended choice (1) is to use progressively more b-vectors for the larger b-values: 8 for 300 s/mm^2, 32 for 700 s/mm^2, and 64 for 2000 s/mm^2. This ensures that the data acquired will be compatible with both NODDI and CSD. In addition, it is recommended that 1 b=0 image is acquired for every 8 non-zero b-values. Finally, it is presently essential to acquire different b-values all at the same echo time (TE) and repetition time (TR), as NDI and FWF are TE-dependent (3).

Finally, it is worth noting that NODDI is fairly robust to the choice of acquisitions. The original NODDI paper compared nine different protocols with varying numbers of shells, choices of b-values, and numbers of gradient directions (4). The results suggest for protocols of at least two shells, NODDI depends only weakly on the precise choice of b-values and number of gradient directions. Reduced number of gradient directions naturally reduces the overall signal-to-noise ratio of the data but the number required will depend on the effect size of the changes to be determined. For protocols with a single shell, while NDI cannot be determined accurately, ODI can.

Supplementary References

1. Slattery CF, Zhang J, Paterson RW, Foulkes AJM, Carton A, Macpherson K, et al. (2017): ApoE influences regional white-matter axonal density loss in Alzheimer's disease. *Neurobiol Aging*. 57:8-17.
2. Timmers I, Roebroeck A, Bastiani M, Jansma B, Rubio-Gozalbo E, Zhang H (2016): Assessing Microstructural Substrates of White Matter Abnormalities: A Comparative Study Using DTI and NODDI. *PLoS One*. 11:e0167884.
3. Gong T, Tong Q, He H, Sun Y, Zhong J, Zhang H (2020): MTE-NODDI: Multi-TE NODDI for disentangling non-T2-weighted signal fractions from compartment-specific T2 relaxation times. *Neuroimage*. 217:116906.
4. Zhang H, Schneider T, Wheeler-Kingshott CA, Alexander DC (2012): NODDI: practical in vivo neurite orientation dispersion and density imaging of the human brain. *Neuroimage*. 61:1000-1016.