Research Interests:
My research area is examining how disruptions in brain connectivity may influence the pathophysiology, prognosis and treatment of neuropsychiatric disorders. To this end, my group has been focusing on the examination of white matter, whose axons form the anatomical basis of brain connectivity. Much of my work has focused on the use of a novel magnetic resonance neuroimaging method, diffusion tensor imaging (DTI) to quantitatively assess white matter microstructural status. Our group was one of the first to apply this methodology to the study of schizophrenia (Lim et al., 1999).

My research focus has been two-fold. The first has been to determine the specificity of white matter abnormalities in various neuropsychiatric disorders with known or suspected white matter involvement. To this end we have demonstrated that DTI changes are observed in schizophrenia, normal aging, HIV-1 infection and cocaine dependence. The second focus has been determining the functional consequences of altered white matter diffusion parameters. We have demonstrated significant correlations between white matter DTI measures and functional measures. For example in schizophrenia we have observed significant correlations on measures of impulsivity and aggression (Hoptman et al. 2002) and negative symptoms with orbitofrontal white matter. With regards to treatment response, we found that frontal white matter integrity predicted response to anti-depressant treatment in geriatric depression (Alexopoulos et al., in press).

Future directions are to elucidate the neurobiological underpinnings of the in vivo imaging findings. One strategy is the simultaneous study of fixed tissue (using DTI) and frozen tissue (using Western blot of myelin basic protein, neurofilaments) to uncover potential biochemical correlates of DTI measures. Other avenues we are exploring are the use of mutant (e.g. Shiverer) and transgenic mouse models with known biochemical deficits to tease apart the biochemical contributions to the DTI signal. Recent postmortem gene expression studies in
schizophrenia have found reductions in myelination related genes, providing potential genomic targets which may be relevant to the observed white matter imaging findings. For future human in vivo studies, we plan to supplement our imaging data with genomic information starting with the examination of single nucleotide polymorphisms of myelination related genes identified from post-mortem gene expression studies or from convergent loci and convergent functional genomics approaches. Additional magnetic resonance imaging methods are also being developed to provide more specific information about myelin status and neuroaxonal tissue.

Recent Publications:


Murphy CF, Gunning-Dixon FM, Hoptman MJ, **Lim KO, Ardekani B, Shields JK, Hrabe J,


(For a comprehensive list of recent publications, refer to PubMed, a service provided by the National Library of Medicine.)

Education:
- Massachusetts Institute of Technology, Cambridge, MA, 1976-78
- BA Psychology – Johns Hopkins University, Baltimore, MD, 1980
- MD – Johns Hopkins University School of Medicine, Baltimore, MD, 1983
- Internship and Residency in Psychiatry – Stanford University School of Medicine, Stanford, CA, 1984-88
- Fellow in Neuropsychiatric Imaging Laboratory of Physiological and Structural Brain Imaging – VA Medical Center, Palo Alto, CA, 1987-90
- Leadership Development for Physicians in Academic Health Centers – Harvard School of Public Health, Boston, MA, November, 2006

Board Certification:
- Diplomat of American Board of Psychiatry and Neurology in Psychiatry, 1990

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