

PLEASE JOIN US FOR TWO TALKS BY



David Eidelberg, MD

DIRECTOR AT THE CENTER FOR NEUROSCIENCES
FEINSTEIN INSTITUTES FOR MEDICAL RESEARCH

MONDAY, January 29th, 2024
3:00 PM
Keating 103

WEDNESDAY, January 31st, 2024
12:00 PM
College of Medicine Lecture Hall
Conference Room 2117

Bio: David Eidelberg, MD is the director of the Center for Neurosciences at the Feinstein Institutes for Medical Research. A neurologist and neuroscientist, he is widely regarded for his groundbreaking work on network dysfunction in Parkinson's disease, dystonia, and other brain disorders. Dr. Eidelberg has pioneered the use of functional brain imaging to identify disease-specific networks as quantitative biomarkers of underlying pathology in patients and persons at risk, and in experimental animal models. His methods are currently in use worldwide to assess disease progression, responses to new therapies, and as an aid to clinical diagnosis. Dr. Eidelberg received his medical degree from Harvard Medical School. He completed his residency in neurology there, followed by postdoctoral training in brain imaging in London and New York. Dr. Eidelberg has authored over 400 peer-reviewed research articles, reviews, and editorials (H-index 103), as well as a published volume (D. Eidelberg, *Imaging in Parkinson's Disease*, Oxford University Press, 2011). He serves on the editorial boards of several major journals and is editor-in-chief (Western Hemisphere) of *Current Opinion in Neurology*. Dr. Eidelberg has received numerous grants and awards, including the 2018 Bachmann Strauss Prize for his pioneering research in dystonia. He is a member of the Association of American Physicians.





Monday, January 29th, 2024
3-4 p.m.

Keating, Rm 103
1657 E. Helen St., Tucson, AZ



Speaker: David Eidelberg, M.D.

Adaptive and Pathological Connectivity Responses in Parkinson's Disease Brain Networks

Brain imaging has been used extensively to identify and validate disease-specific functional networks as biomarkers in neurodegenerative disorders [Perovnik et al. Nat Rev Neurol 2022]. Although disease networks are highly reproducible across patient populations, it is not known whether these topographies reflect pathological connectivity patterns that worsen with advancing disease, or beneficial adaptations that may be promoted by treatment. To distinguish between these possibilities, we used graph theory to study connectivity patterns in an extensively validated metabolic network termed the Parkinson's disease-related metabolic pattern (PDRP) [Schindlbeck and Eidelberg Lancet Neurol 2018; Ko et al. Cereb Cortex 2018; Perovnik et al. Nat Rev Neurol 2022; Barbero et al. Neurotherapeutics 2023]. In particular, we focused on assortativity, a metric that captures the tendency of connections to form between nodes with similar properties. In graph theory, assortativity has been linked to network stability. High values are associated with inefficient information flow through the network, and with increased susceptibility to fragmentation. Low assortativity, by contrast, is defined by greater diversity of connections, resulting in improved efficiency of information flow and greater network robustness [Noldus and Van Mieghem J Complex Networks 2015; Barabasi Network Science 2016].

Accordingly, PDRP assortativity increased with disease progression in multiple independent patient populations [Vo et al. Cereb Cortex 2023]. Moreover, this metric was elevated in clinically aggressive PD genotypes (GBA-1 variants) compared to sporadic disease, and was reduced in patients with slow progression mutations (LRRK2-G2019S). A similar dichotomy was seen in the response to PD treatment with levodopa infusion compared to subthalamic nucleus (STN) deep brain stimulation (DBS). Despite titration to the same degree of motor improvement, the two interventions had opposite effects on PDRP assortativity, with increasing values (i.e., network destabilization) during levodopa infusion, but with reductions to near normal levels (i.e., network stabilization) during STN stimulation. Notably, an analogous reduction in assortativity was observed in the PDRP space 12 months after STN AAV2-GAD gene therapy, an experimental surgical procedure that slowly remodels basal ganglia-cortical motor networks [Niethammer et al. Sci Transl Med 2018; Vo et al. Cereb Cortex 2023]. In aggregate, the findings suggest that stereotyped changes in network architecture underlie disease progression and the response to treatment in PD patients.

MEDICAL IMAGING GRAND ROUNDS PRESENTS



David Eidelberg, MD

Metabolic Networks as Functional Biomarkers of Parkinson's Disease

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Abstract: Network analysis of functional brain scans acquired with [18F]-fluorodeoxyglucose positron emission tomography (FDG PET, to map cerebral glucose metabolism), or resting-state functional magnetic resonance imaging (rs-fMRI, to map blood oxygen level-dependent brain activity) has increasingly been used to identify and validate reproducible circuit abnormalities associated with neurodegenerative disorders such as Parkinson's disease (PD). In addition to serving as imaging markers of the underlying disease process, these networks can be used singly or in combination as an adjunct to clinical diagnosis and as a screening tool for therapeutics trials. Disease-specific networks can also be used to measure rates of progression in natural history studies and to assess responses to symptomatic treatment or to potential disease modifying agents. Recent imaging studies in PD subjects scanned before and after treatment have revealed therapeutic effects beyond the modulation of established disease networks. Rather, other mechanisms of action may be at play, such as the induction of novel functional brain networks directly by treatment. To date, reproducible treatment-induced networks have been reported for established interventions such as deep brain stimulation (DBS) and novel therapeutic strategies such as subthalamic gene therapy and oral nicotinamide riboside (NR), and as a potential imaging marker of the placebo response. Indeed, changes in the expression of these networks with treatment have been found to correlate consistently with clinical outcome. Together, the data suggest a role for functional brain networks as treatment biomarkers in clinical trials for PD and other brain disorders.

