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Imaging and molecular biomarkers of redox dysregulation and oxidative stress: NAD^+ and NADH measurments *in vivo*

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Nicotinamide Adenine Dinucleotide *(oxidizing and reducing forms, i.e.* the redox pair NAD^+ and NADH) is crucial to life. Essentially, the redox ratio (RR=NAD^+/NADH) reflects the balance between oxidized NAD^+ and reduced NADH, and indexes the system's ability to carry out energy production via ATP synthesis (glycolysis and oxidative phosphorylation). During inflammatory states and intensive energy metabolism, reactive oxygen species (ROS) are also formed which leads to toxicity via oxidative stress, Accumulated evidence also indicate that NAD has emerged as a signaling molecule, which controls hundreds of key processing from energy metabolism to cell survival, inflammation, circadian rhythm, stress resistance as well as downstream effects on neuronal function and plasticity (1). NAD deficiency due to genetic and/or environmental issues is linked to many diseases (2). Also of interest, NAD can be modulated using interventions such as Nicotinamide Riboside (NR), a precursor of NAD^+, potentially opening a path to improving brain and peripheral function and metabolism. For instance, there has been reported rescued Alzheimer's disease (AD) (3) and recovered vascular vessels by NAD supplement (4) in animal models. Despite the strong theoretical rationale and preclinical evidences, clinical trials targeting redox NAD system associated with oxidative stress mechanisms have been started, no imaging measurements have been performed. This is likely due to the very challenging process required to measure NAD^+/NADH *in vivo* which needs dedicated state-of-the-art imaging. Recently we developed a novel 31P-MRS approach to measure NAD^+ and NADH and identified a striking reduction in RR in chronic (38%) and first episode schizophrenia (50%) and found RR is highly age-dependent (5). These findings were featured in *AAAS, Medical Daily, Neuroscience News, and Science Daily* in a report entitled "MRI scans detect 'brain rust' in schizophrenia". These methodological enhancements would broadly accelerate human diseases study such as mild cognitive impairment (MCI) subject at risk of Alzheimer's disease or dementia, a decline in capillary density and blood flow with aging is a major cause of mortality.

Biography

Fei Du is an MR biophysicist with a substantial background in magnetic resonance imaging/spectroscopy (MRI/MRS). After rigorous training in the technical aspects of this field, he has begun to use his expertise in the service of neurobiological research on neurodegeneration and psychiatric diseases. His career interests evolve to combine MRI/MRS technique developments with "translational imaging", from bench study to bedside. Current one of major projects focus on novel MRS technical development to measure redox state (NAD^+/NADH), antioxidant (GSH) and vascular perfusion, providing convergent evidence and imaging/molecular biomarkers on redox dysregulation, oxidative stress associated with various diseases such as aging, schizophrenia.

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