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Metabolic Health Screening Using Compact NMR

Abstract:

The worldwide diabetes pandemic continues to worsen, and there is an urgent need for improved prevention strategies. The metabolic abnormalities that precede type 2 diabetes include early components of metabolic syndrome, such as, insulin resistance with compensatory hyperinsulinemia, dyslipidemia and subclinical inflammation. By the time glucose tolerance is impaired (prediabetes), a 50-70% decline in pancreatic insulin secretion has occurred. Therefore, it is imperative to identify early metabolic syndrome in order to preserve pancreatic β-cell function and prevent diabetes. Insulin resistance is the hallmark early abnormality in the progression towards prediabetes and type 2 diabetes, but is difficult to measure. There is an unmet need for new screening tools for metabolic health.

This work describes the discovery and characterization of a new biomarker for early metabolic syndrome, measured using benchtop nuclear magnetic resonance relaxometry. This biomarker is based on the transverse relaxation time (T_2) for proton-water in human plasma and serum, which is affected by the dynamic motions of water molecules as they interact with proteins and lipoproteins. Water T_2 values were measured in an observational cross-sectional study of 72 human subjects without acute or chronic disease. Water T_2 exhibited strong correlations with markers of insulin, lipids, inflammation, coagulation and electrolyte balance. After correcting for confounders, low water T_2 values were independently and additively associated with hyperinsulinemia, dyslipidemia and subclinical inflammation. Using water T_2, 16 individuals with early metabolic abnormalities (22% of the study population) were identified. Thirteen of the 16 did not meet the criteria for metabolic syndrome and would have been missed by conventional screening for diabetes risk. The contributions of individual proteins to the lowering of water T_2 were also quantified and the largest contributions were made by apolipoprotein B, complement C3, haptoglobin, fibrinogen, α-1 acid glycoprotein and complement C4. Water T_2 detects early abnormalities associated with metabolic syndrome, providing a global view of an individual's metabolic health. It shows promise as an early, global and practical screening tool for the identification of individuals at risk for type 2 diabetes and atherosclerosis.

Biography:

Dr. Ina Mishra is currently working as a postdoctoral research associate at the University of North Texas System College of Pharmacy, Fort Worth, Texas. She earned her doctorate in Biomedical Sciences from University of North Texas Health Science Center, Fort Worth, Texas and bachelor in pharmacy from University of Delhi, India. She has worked in applications of biophysical techniques for early identification of metabolic disorders. Her work has focused on nanoparticles and their biophysical properties, interactions of human protein and lipid complexes and development of methods for identification of individuals at-risk for diabetes and liver disorders, using time domain NMR (relaxometry) and dynamic light scattering. She is a current member of Sigma XI, The Scientific Research Honor Society and has been a past member of the Biophysical Society, American Society for Biochemistry and Molecular Biology and has presented her work at several conferences and meetings.