IDENTIFYING IMAGING BIOMARKERS FOR MANGANESE TOXICITY IN OCCUPATIONALLY EXPOSED WELDERS

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Abstract:

Manganese (Mn) is a neurotoxin that many workers are exposed to daily. Increased Mn body burden due to occupational exposures can lead to a parkinsonian disorder that features symptoms such as mood disturbances, cognition deficits, and motor dysfunction. To understand an exposed worker’s risk, biomarkers of exposure have been developed using blood, hair, bone, and toenails. None of these biomarkers take into account how much Mn is in the brain, but instead rely on the assumption that Mn uptake in these materials is proportional and related to the levels in the brain. Neuroimaging, such as magnetic resonance imaging (MRI), spectroscopy (MRS), and positron emission tomography (PET) can be used to assess the effects of Mn accumulation in the brain. However, there remains a need to establish reliable neuroimaging biomarkers for Mn exposure and its toxicological effects. This thesis addresses this need using three methods. First, changes in MRI and MRS measures were assessed in a longitudinal cohort study to determine how changes in Mn exposure affect these measures over time. Second, PET with a pharmacological challenge was employed to measure the effect of Mn exposure on striatal dopamine release. Third, advanced data analysis methods using machine learning assessed how well MRI can predict Mn exposure and its biological effects. Collectively, this thesis is a successful step towards establishing neuroimaging biomarkers of effect from occupational exposure.