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2013 Global NeuroDiscovery Challenge

MIND THE DATA

Search for Gender Based Differences In Alzheimer's Disease

Round I: BEST HYPOTHESIS AWARDEE

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GENDER AND THE ALZHEIMER'S DISEASE PATHOLOGICAL CASCADE

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Although Alzheimer's disease (AD) is more prevalent in females, even accounting for life expectancy, recent biomarker studies of AD development have not addressed mechanisms that may underlie this heightened risk. For instance, the AD pathological cascade model suggests a long preclinical period that begins with aberrant accumulation of the beta-amyloid ($A\beta$) protein, downstream changes to neuronal integrity, and eventually, cognitive decline. However, the impact of gender on this cascade is unknown and understudied. It is possible that females may have an increased likelihood of entering the cascade if they are more prone to $A\beta$ accumulation (pathology-promoting mechanism). It is also possible that downstream responses to $A\beta$ differ, such that females are more negatively impacted by $A\beta$ and therefore have a shorter delay between initiating pathology and cognitive decline (heightened vulnerability mechanism). A major barrier in addressing differences across gender in previous studies are small sample sizes, which may be insufficient to model interactions between gender and AD biomarkers. Excitingly, the recent availability of imaging biomarkers collected in large cohorts will allow us to dissociate these potential mechanisms. These large datasets provide the opportunity to address how gender may influence the AD pathological cascade, which has important implications for upcoming secondary prevention trials using biomarker data to understand the impact of anti- $A\beta$ therapy in preclinical AD.



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