Study Examines Risk Factors for Executive Deficits Among Mothers who are Carriers of FMR1 Premutation

Dr. Jessica Klusek, an assistant professor in the Department of Communication Sciences and Disorders (University of South Carolina, Arnold School of Public Health), in collaboration with a team of scientists from the University of Wisconsin Waisman Center and Rush University Medical Center, has published a study on inhibition deficits among carriers of the FMR1 premutation allele who are mothers of children with fragile X syndrome. The resulting paper was published in Brain and Cognition.

“Individuals who carry a premutation allele on the FMR1 gene may experience executive limitations associated with their genetic status, including inhibition deficits,” says Dr. Klusek. “However, we currently have a poor understanding of individualized risk factors, which has limited clinical management of this group.”

With this study, Dr. Klusek and her team examined the CGG repeat length – a DNA segment on the FMR1 gene that is expanded among those with the premutation compared to those without – and age as factors that may account for variable expressivity of inhibition deficits. The participants included 134 mothers of children with fragile X syndrome who were carriers of the premutation allele.

The researchers measured inhibition skills, a component of executive functioning, using both self-report and direct behavioral assessments. They found increased vulnerability for inhibition deficits among the participants with mid-range CGG lengths (i.e., 80-100 repeats). They also observed some evidence of a second zone of vulnerability among the participants with higher CGG lengths (i.e., 130-140 repeats). Their analysis further revealed that the risk for inhibition deficits became pronounced with older age.

“This study identifies personalized risk factors that may be used to tailor the clinical management of executive deficits in carriers of the premutation allele,” says Dr. Klusek. “Inhibition deficits may contribute to poor outcomes in carriers of the premutation allele and their families, particularly in midlife and early old age, and clinical monitoring may be warranted. A future direction of this study is to determine whether similar patterns are observed among carriers of the premutation allele who do not have a child diagnosed with fragile X syndrome. This work could have significant implications for understanding genetic determinates of health in the general population. The premutation allele is actually a very common genetic mutation—population-based screening suggests that it affects about 1 in 150 women and 1 in 470 men in the United States.”

This research was funded by the National Institutes of Health (R01HD082110, P30 HD003100-S1, U54 HD090256).