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387. Prenatal Maternal Inflammation is Associated With Offspring Sensory Gating in Late Midlife

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Background: Although sensory gating (SG; ability to filter irrelevant input) naturally declines with age, accelerated SG deficits are a transdiagnostic risk factor for psychopathology. Animal studies suggest these deficits originate in-utero, with prenatal maternal inflammation (PNMI) increasing the risk of neurodevelopmental disorders, particularly in females. As no human studies have examined PNMI's impact on adult SG, this study investigated the potentially sexually dimorphic effects of PNMI on offspring SG in late midlife.
Methods: Dataset included 128 mother-offspring dyads from the Child Health and Development Studies (CHDS) cohort with PNMI biomarkers [IL-6, IL-8, IL-1 receptor antagonist (IL-1RA) and soluble TNF receptor-II] from first (T1) and second trimester (T2) sera. Offspring SG was assessed at late midlife (ages 57-63) via the Sensory Gating Inventory (SGI)-16, which includes a total score and 4 dimensions: perceptual modulation, over-inclusion, distractibility, and fatigue−stress modulation. Higher SGI-16 scores indicate greater SG deficits.
Results: Higher T1 IL-8 was associated with greater offspring SGI total scores ($p = 0.05$), distractibility ($p = 0.006$), and fatigue−stress modulation ($p = 0.02$), and higher T2 IL-8 and IL-6 were associated with greater over-inclusion (both $p = 0.04$). When the cross-product of PNMI and sex was added to respective models, only T2 sTNF-RII interacted with sex to predict fatigue−stress modulation [$b = -13.04$ ($SE = 6.39$), $p = 0.043$]. However, when probing this interaction, neither simple slope for female nor male individuals was statistically significant.
Conclusions: Exposure to higher PNMI is associated with negative offspring SG outcomes in late midlife. More research is needed into sex-specific effects.
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Keywords: Inflammation, Pregnancy, Sensory Gating, Sex differences

388. Cortical Targets for iTBS Modulation of Autonomic Response in Impulsivity-Related Neuropsychiatric Disorders

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Background: Impulsivity via impaired inhibitory control is a shared feature of many neuropsychiatric disorders. Impulsivity is associated with impaired autonomic responses, typically increased sympathetic activity and reduced vagal response, which provides a potential mechanism to query the effectiveness of different potential treatment targets with non-invasive brain stimulation. To this end, we conducted a pilot study assessing the two most common targets for non-invasive brain stimulation, the right inferior frontal gyrus (rIFG) and left dorsolateral prefrontal cortex (lDLPFC), and evaluate whether stimulation could modulate autonomic activity.
Methods: Intermittent theta burst TMS (90%MT, 1,800 pulses, 9.5min) was applied over rIFG and lDLPFC in nine Veterans with impulsive behaviors, in a crossover trial with one-week washout. Five minutes of ECG was recorded before and after each session, and autonomic responses in time- and frequency-domains were evaluated.
Results: A mixed-effects model was fitted with target (lDLPFC vs. rIFG), time (pre vs. post-iTBS), and their interaction as fixed effects. Significant time effect showed reduction in mean HR (coefficient = -3.56, $p=0.036$), suggesting enhanced vagal activity across both targets. Higher RMSSD and lower LF, suggesting increased vagal activity and reduced sympathetic response after rIFG stimulation, were observed; however, without significance ($p = 0.434$, $p = 0.205$, respectively).
Conclusions: Both targets demonstrated potential for modulating autonomic responses. Although rIFG stimulation may yield increased vagal activity and reduced sympathetic response, results were nonsignificant. This demonstrates early promise for this approach and will inform future studies that can facilitate target engagement with objective and scalable biomarkers.
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Keywords: Impulsivity, Intermittent theta-burst stimulation (iTBS), Inhibitory Control, Heart Rate Varialbility, Neuromodulation