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Oxidative Stress and Cortical Thickness in the Psychosis Spectrum: Investigating Glutathione Metabolism and Antioxidant Defenses in Youth

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Introduction: Oxidative stress, particularly through disruptions in glutathione metabolism and Total Antioxidant Capacity (TAC), has been implicated in cortical thinning and other brain structural changes seen in psychosis. These changes may be more pronounced in the early psychosis spectrum, but this relationship remains underexplored.

Objectives: This study investigated the relationships between key oxidative stress markers—reduced glutathione (GSH), oxidized glutathione (GSSG), the GSH/GSSG ratio, and TAC—and cortical thickness in the cingulate, insula, and fronto-temporal brain regions.

Methods: A total of 57 youths on the early psychosis spectrum and 44 healthy controls participated, with a mean age of 15.51 years. There were no significant differences in age or sex between the groups. Cortical thickness was measured using MRI, and blood samples were analyzed for oxidative stress markers. Partial correlations were performed, controlling for total intracranial volume, age, and sex, to examine the relationships between oxidative stress markers and cortical thickness. A permutation analysis was then conducted to assess group differences in these associations.

Results: In healthy individuals, a higher GSH/GSSG ratio was significantly associated with increased cortical thickness in the right insula ($r = 0.50$, $p < 0.05$). Conversely, in the early psychosis spectrum group, there was a consistent trend of negative correlations between TAC and cortical thickness, particularly in the left frontal cortex. Permutation analysis revealed significant group differences in the association between GSH and cortical thickness in both the left insula and left temporal regions ($p < 0.05$). Additionally, TAC showed significant differences in its relationship with cortical thickness in the left and right frontal regions ($p = 0.01$ and $p < 0.05$), indicating asymmetrical oxidative stress involvement across hemispheres in the early psychosis spectrum group compared to healthy controls.

Conclusions: These findings suggest that oxidative stress markers, particularly related to glutathione metabolism and TAC, are linked to regional cortical thickness variations. The results highlight distinct oxidative stress effects in the early psychosis spectrum compared to healthy individuals, emphasizing the potential role of oxidative stress markers as early indicators of neuroanatomical changes in psychosis.

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EPV0365

A Multilevel Investigation of Conduct Problems in Adolescents: Insights from Neural, Cognitive, and Environmental Perspectives

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Introduction: Conduct problems (CP) in adolescents are associated not only with long-term personality and social development challenges, but also impose significant burdens on families, schools, and communities.

Objectives: While numerous risk factors for CP have been identified in prior research, a comprehensive understanding of the underlying deficit mechanisms remains incomplete.

Methods: Utilizing data from the Adolescent Brain Cognitive Development (ABCD) study ($N = 11,875$), the largest longitudinal investigation of brain development and child health in the United States, we conducted a systematic analysis of the neural, cognitive, and environmental features linked to CP. The findings were further tested for generalizability across diverse cross-cultural datasets.

Results: Our results propose a novel framework that accounts for cognitive deficits associated with CP, while also highlighting the interactions between biological and environmental factors in the development and potential remission of CP in adolescents.

Conclusions: These insights provide valuable directions for future research and intervention strategies targeting adolescent conduct problems.

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Focusing on ADHD: Analyzing Five-Year Search Trends

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Introduction: An estimated 10% of children in the United States carry a diagnosis of ADHD (Li *et al.* JAMA Netw Open 2023; 6). Parents, caregivers, and children themselves utilize search engines to better understand their diagnosis and treatment options as well as discover other resources such as finding providers or support groups. Furthermore, evaluating search trends may elucidate individual and societal barriers towards accessing treatment. (Zhao *et al.* Adm Policy Ment Health 2022; 49 357–373)