Title: Exploring the Developmental Roots of Schizophrenia: A Multifactorial Approach Using the Adolescent Brain Cognitive Development (ABCD) Study Dataset

Background: Schizophrenia is a complex disorder that often originates during adolescence, a critical period marked by significant changes in brain structure and function, hormonal fluctuations, and psychosocial environments (Gilmore et al., 2018; Patel et al., 2021). Schizophrenia is potentially fatal, therefore identifying at-risk individuals in the population efficiently and cost-effectively is crucial (Harkavy-Friedman, 2006). Assessing mental health conditions can be approached through various methods, each with its own strengths and limitations. This thesis aims to use extensive longitudinal data from the Adolescent Brain Cognitive Development (ABCD) study to investigate how increasing the complexity of assessment methods influences the accuracy of predicting the development of schizophrenia symptoms in adolescence. By focusing on various contributing factors and their interactions, our goal is to predict responses on the Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS) questionnaire. Specifically, we will assess how the inclusion of additional data—such as MRI scans, hormonal information, and cognitive assessments—affects the accuracy of predicting psychotic symptomatology on the KSADS.

Existing research highlights the role of psychosocial stressors, hormonal influences during puberty, and biological mechanisms in the development of schizophrenia. Psychosocial stressors such as social adversity and stress during adolescence, including experiences of isolation and bullying is associated to schizophrenia and can disrupt brain development (Lay et al., 2000; Makinodan et al., 2012). Hormonal influences during puberty, involving shifts in gonadal hormones (testosterone and estrogen) and stress hormones (cortisol), play a crucial role in neurodevelopment (Peper & Dahl, 2013). Additionally, biological mechanisms such as accelerated synaptic pruning and impaired myelination significantly affect brain structure and function (Caballero et al., 2016; Paus, 2010). Together, these factors illustrate the complexity of schizophrenia's developmental origins and highlight the importance of understanding the multifaceted influences on its onset. While traditional statistical techniques primarily detect group-level effects, machine learning (ML) offers promise in creating individualized predictions by integrating diverse data types and optimizing multivariate brain patterns (Abi-Dargham & Horga, 2016). This approach aims to transform group-level findings into clinically relevant individual predictions, ultimately improving prediction accuracy and possibly informing effective intervention strategies for schizophrenia.

Methodology: The ABCD study provides a rich dataset, including neuroimaging, cognitive assessments, psychosocial surveys, and hormonal measures from a diverse adolescent cohort. Our project will involve (1) a longitudinal analysis: Predict responses on KSADS by training a model on T1 and T2 measurements to predict outcomes at T3. This approach will help us track developmental changes and their cumulative effects on schizophrenia risk. And (2) a complexity analysis: Assess the impact of adding detailed biological and psychosocial assessments on predictive accuracy and cost-effectiveness. This will involve evaluating the marginal benefits of incorporating each additional layer of complexity into standard evaluation protocols.

Research Question: What is the optimal assessment required to detect phenotype symptom severity in a developmental community sample????

Planning and organization of the work (i.e. who does what and when):  
Ethical considerations and applications:  
Economics / resources needed:  
Timetable with deliverables / milestones (i.e. data collection, finishing data analyses, writing of article):

**NOTES?:**

Variables:

|  |  |  |
| --- | --- | --- |
|  | Schizophrenia | Depression |
| Basic Model: | Target outcome: KSADS - Psychotic Disorders (Indiv. Questions) [Parent]  Prodromal Psychosis Scale [Youth]  (items on positive symptoms, negative symptoms, cognitive symptoms)  Diagnosis?  scrn\_schiz,  ksads2\_4\_805\_p, ksads2\_4\_806\_p, ksads2\_4\_807\_p, | Target outcome: KSADS - Depressive Disorders (Indiv. Questions) [Parent]  KSADS - Depressive Disorders (Indiv. Questions) [Youth]  (items on depressive symptoms, cognitive symptoms, physical/somatic symptoms, psychomotor symptoms) |
| Psychosocial Surveys:  Data on environmental factors, social stressors, family dynamics and peer relationships | KSADS - Background Items [Youth]  KSADS - Background Items [Youth]  KSADS - Sleep Problems (Indiv. Questions) [Youth  Short Social Responsiveness Scale [Parent  Cyberbullying [Yout  KSADS - Post-Traumatic Stress Disorder (Indiv. Questions) [Parent]Life Events [Parent]Perceived Stress Scale [Pare  Life events [Youth  Personality | Family History:  fam\_history\_q6a\_depression |
| Cognitive Assessments: |  |  |
| Hormonal Measures: | Gonadal Hormones (testosterone, estrogen)  hormone\_scr\_ert\_mean  and stress hormones (cortisol, cannot find the variable?) |  |
| Neuroimaging data: | Cortical thickness in specific regions such as the prefrontal cortex  mrisdp\_1…  Fractional anisotropy, indicating white matter integrity in prefrontal regions  dmdtifp1\_38…  Mean diffusivity, another measure of white matter integrity  ddtifp\_1057… |  |

References:

Abi-Dargham, A., & Horga, G. (2016). The search for imaging biomarkers in psychiatric disorders. *Nat Med*, *22*(11), 1248–1255. https://doi.org/10.1038/nm.4190

Caballero, A., Granberg, R., & Tseng, K. Y. (2016). Mechanisms contributing to prefrontal cortex maturation during adolescence. *Neuroscience & Biobehavioral Reviews*, *70*, 4–12.

Gilmore, J. H., Knickmeyer, R. C., & Gao, W. (2018). Imaging structural and functional brain development in early childhood. *Nat Rev Neurosci*, *19*(3), 123–137. https://doi.org/10.1038/nrn.2018.1

Harkavy-Friedman, J. M. (2006). Can Early Detection of Psychosis Prevent Suicidal Behavior? *Am J Psychiatry*, *163*(5), 768–770. https://doi.org/10.1176/ajp.2006.163.5.768

Lay, B., Blanz, B., Hartmann, M., & Schmidt, M. H. (2000). The Psychosocial Outcome of Adolescent-Onset Schizophrenia: A 12-Year Followup. *Schizophr Bull*, *26*(4), 801–816. https://doi.org/10.1093/oxfordjournals.schbul.a033495

Makinodan, M., Rosen, K. M., Ito, S., & Corfas, G. (2012). A critical period for social experience–dependent oligodendrocyte maturation and myelination. *Science*, *337*(6100), 1357–1360.

Patel, P. K., Leathem, L. D., Currin, D. L., & Karlsgodt, K. H. (2021). Adolescent Neurodevelopment and Vulnerability to Psychosis. *Biological Psychiatry*, *89*(2), 184–193. https://doi.org/10.1016/j.biopsych.2020.06.028

Paus, T. (2010). Growth of white matter in the adolescent brain: Myelin or axon? *Brain and Cognition*, *72*(1), 26–35.

Peper, J. S., & Dahl, R. E. (2013). The Teenage Brain: Surging Hormones—Brain-Behavior Interactions During Puberty. *Curr Dir Psychol Sci*, *22*(2), 134–139. https://doi.org/10.1177/0963721412473755