Thesis notes:

# The ABCD study:

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* The current review will describe how the ABCD Study was designed to elucidate factors associated with the development of negative mental and physical health outcomes. This review will also provide a selective overview of results already emerging from the ABCD Study. This review will discuss the challenges and opportunities to understanding the development of risk using the ABCD Study. Lastly, we will discuss the future directions of this massive undertaking that will shape our understanding of the development of risk in adolescence.

The ABCD Study employs a robust, multi-stage probability sampling strategy to capture a diverse and representative cohort of youth in the U.S. It leverages stratified sampling within defined catchment areas to minimize selection biases and utilizes weighting methods to enhance representativeness. The inclusion of a unique twin sample further enriches the dataset, allowing for in-depth genetic and environmental analyses.

**Key References:**

1. [14] Specific reference to the ABCD Study’s sampling methods and site selection protocols.
2. [12] Details on the recruitment processes for the twin samples.
3. [15] Discussion on the use of weighting methods to ensure representativeness of the sample.

Substance use. For an overview of measures started at baseline and year 1 (youth = 10–11-years-old), please see ref. [7].

A variety of measures collected from youth are used to accomplish this goal, with a central one being the Timeline Followback interview [19, 20] designed to establish the specifics of substance use onset and timing.

Lastly, biospecimens (saliva and hair) are assessed for exposure to alcohol and substances.

Mental health. For an overview of all measures that started at baseline and year 1, please see ref. [1]. The goal of the mental health assessments is capturing categorical and dimensional assessments of current and past mental health from the parent and youth perspective, as well as teacher perspective, and assessing traits and characteristics relevant to understanding risk trajectories for mental health.

Categorical assessment: Kiddie-Structured Assessment for Affecitive Disorders and Schizophrenia (KSADS), used to assess parent-report of youth mental health as well as youth’s self-report [21–23].

dimensional assessments: is the Achenbach system of emprically based assessment (ASEBA) system [24, 25]

# The conception of the ABCD study

* Complexities of Substance Use and Neurodevelopment:
  + Advances in neuroimaging have provided insights into the impact of substances on the brain, but many questions remain about how substance use and other adolescent experiences influence brain development and later health outcomes like addiction and mental illness.
* Key Questions:
  + Substance Impact on Neurodevelopment:
  + Extent to which tobacco, alcohol, marijuana, and other drugs alter neurodevelopmental trajectories.
  + Impact on academic achievement, social and emotional development, and other life aspects.
* Neurodevelopmental Risk Factors:
  + Extent to which different neurodevelopmental trajectories increase the risk for substance use.
* Interactions and Specific Effects:
  + How different types of substance use interact.
  + Whether the effects of individual drugs can be disentangled in poly-substance users.
* Persistence of Substance Effects:
  + Whether the impacts of substance exposures are persistent or reversible after cessation.
* Understanding Healthy Neurodevelopment:
  + To answer these questions, understanding the normal trajectory of healthy human neurodevelopment is crucial.
  + Consideration of whether there is a single trajectory or multiple pathways of healthy neurodevelopment.
* Interconnected Nature of Substance Use and Neurodevelopment:
  + Substance use is intricately linked with mental and physical health, as well as social systems.
  + Neurodevelopment is similarly complex, influenced by both genetic and environmental factors.
* ABCD Study Goals:
  + Conceived to address a broad range of questions regarding genetic influences and environmental exposures on neurodevelopment during the second decade of life.
  + Collaboration with various NIH Institutes, Centers, and Offices to tackle their specific priority areas.
* NIMH Involvement:
  + Mental disorders often start in childhood or adolescence and frequently co-occur with substance use (Kessler, 2004).
  + NIMH aims to chart mental illness trajectories to identify optimal intervention points.
* Unique Opportunities Provided by the ABCD Study:
  + Delineates the relationship between brain development and the emergence/progression of psychopathology.
  + Identifies premorbid signs of illness and sensitive intervention periods.
  + Gathers data on low-incidence behaviors (e.g., suicide attempts) not possible in smaller studies.
  + Addresses interrelationships among substance use, psychopathology, and genetic vulnerabilities (e.g., marijuana use and schizophrenia).
    - The study will provide much-needed information on low-incidence behaviors (e.g., suicide attempts) that cannot be garnered from smaller studies and will be able to address critical, lingering questions about the bidirectional influences of substance use and psychopathology, such as the complex interrelationships among marijuana use, schizophrenia, and genetic vulnerabilities.
* Potential Impact on Public Health:
  + Informs policies and practices to improve public health in diverse ways.
  + Fills significant gaps in knowledge, laying the groundwork for altering risk trajectories and improving lives of those with substance use or mental disorders.
* NIMH Expertise Contribution:
  + Provides expertise in developing large-scale imaging databases (e.g., the HCP database) for widespread data sharing.

# Applications of MRI in schizophrenia

* Current Schizophrenia Diagnosis:
  + Historically relies on structured interviews, clinical observations, and psychopathologic ratings.
  + Diagnostic criteria are primarily outlined in the DSM-5.
  + Symptom-based and empirical, highly dependent on the psychiatrist's experience.
  + Results in approximately 25% misdiagnosis rate (Reference 3).
* Challenges in Treatment:
  + Time-consuming diagnosis impedes swift treatment initiation.
  + Treatment selection is challenging, with about 30% of patients with first-episode psychosis or schizophrenia not responding to standard antipsychotic medications (Reference 4).
* Need for Precision Medicine:
  + Urgent to identify and translate clinically useful biomarkers into clinical practice.
  + Neuroimaging, particularly MRI, has shown potential in identifying brain alterations associated with schizophrenia (Reference 5).
* Advances in Machine Learning (ML) and Deep Learning (DL):
  + ML and DL enable significant feature extraction from complex, high-dimensional data.
  + Traditional ML algorithms often require hand-crafted features and struggle with raw MRI data (Reference 49).
  + DL approaches can autonomously identify the best possible representation from raw data, reducing the need for prior feature selection (Reference 50).
  + ML and DL have expanded the possibilities of neuroimaging beyond traditional case–control group comparisons, improving diagnostic accuracy and patient care.
* Key Contributions:
  + Sadeghi et al reviewed and introduced significant ML and DL techniques and their applications to MRI, highlighting their potential in advancing schizophrenia diagnosis and treatment (Reference 51).

# An overview of artificial intelligence techniques for diagnosis of Schizophrenia

* Challenges in Diagnosing Schizophrenia (SZ):
  + Diagnosis is difficult due to the heterogeneity of SZ and the lack of specific effective biomarkers (Reference 8).
  + Clinical evaluation for SZ includes assessing physical, psychiatric, and psychological indicators (References 9–11).
* Clinical Examination:
  + Involves various tests, such as blood tests and medical imaging (References 12–13).
  + If no physical cause is found for the symptoms, patients are typically referred to a psychiatrist, psychologist, or other experts (References 14–15).
* Role of DSM-5 in SZ Diagnosis:
  + Introduced to assist with SZ diagnosis by standardizing the criteria (References 278–279).
  + Before DSM-5, SZ was often diagnosed based on a single symptom; now, an individual must exhibit at least two symptoms to be diagnosed with SZ (Reference 275).
  + DSM-5 provides a comprehensive list of symptoms, aiding specialists in determining the type and severity of SZ (Reference 275).