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Improving early identification of psychotic or bipolar disorders in adolescents based on the fusion of EEG and eye-tracking signals: a prospective longitudinal cohort study protocol

Zhiruo Zhou
Peking University Sixth Hospital
Yujia Qiu
Peking University Sixth Hospital
Shiyang Wang
Peking University Sixth Hospital
Yulu Wang
Peking University Sixth Hospital
Xiaozhen Lv
Peking University Sixth Hospital
Zhijiang Wang
Peking University Sixth Hospital
Xin Yu
Peking University Sixth Hospital
Jing Wang
Peking University Sixth Hospital
Chuan Shi
shichuan@bjmu.edu.cn

Peking University Sixth Hospital

Study protocol

Keywords: Bipolar disorder, psychotic disorders, adolescents, clinical high risk, elevated risk, electroencephalography, eye-tracking.

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Title

Improving early identification of psychotic or bipolar disorders in adolescents based on the fusion of EEG and eye-tracking signals: a prospective longitudinal cohort study protocol

Running title

EEG and eye-tracking markers of severe psychiatric risk in adolescents

Zhiruo Zhou[1#], Yujia Qiu[1#], Shiyang Wang[1], Yulu Wang[1], Xiaozhen Lv[1], Zhijiang Wang[1], Xin Yu[1], Jing Wang[1*], Chuan Shi[1*]

[1] Peking University Sixth Hospital, Peking University Institute of Mental Health, NHC Key Laboratory of Mental Health (Peking University), National Clinical Research Center for Mental Disorders (Peking University Sixth Hospital), Beijing, China

[#]Zhiruo Zhou (Email: zhouzhiruo0625@163.com) and Yujia Qiu (Email: amor6693@bjmu.edu.cn) contributed equally to this work as co-first authors

Correspondences: Jing Wang (Email: wangjing1796@bjmu.edu.cn) and Chuan Shi (Email: shichuan@bjmu.edu.cn) are co-corresponding authors for this manuscript.

Abstract

Background

Efficient early identification of individuals at risk of developing psychotic disorders or bipolar disorders is crucial and challenging to improving mental health outcomes in adolescents. Objective neurophysiological and neurobehavioral measures may provide information complementary to conventional symptom-based assessment. Electroencephalography (EEG) and eye-tracking offer non-invasive and relatively accessible measures of neural and behavioral function and may support longitudinal risk detection for psychotic disorders or bipolar disorders. This study aims to prospectively evaluate and develop early recognition models for adolescents at high risk for psychotic or bipolar disorders using EEG and eye-tracking features.

Methods

This is a prospective, observational, single-centre longitudinal cohort study conducted at Peking University Sixth Hospital. A total of 300 adolescents aged 12–19 years at elevated risk for psychotic or bipolar disorder (BD) will be recruited. Baseline assessments will include diagnostic interviews, clinician-rated and self-report symptom measures, psychosocial functioning assessments, cognitive tasks, and simultaneous EEG and eye-tracking recording. Participants will undergo clinical reassessments at 6, 12, 18, and 24 months. The primary objective is to identify the specific EEG and eye-tracking features associated with adverse clinical progression over 2 years in adolescents at elevated risk for psychotic disorders or bipolar disorder, and to develop and validate the risk-stratification prediction models based on synchronized EEG and eye-tracking data. Secondary objectives include estimating the rate and temporal pattern of diagnostic transition to psychotic disorder or BD, characterizing longitudinal trajectories of psychiatric symptoms and psychosocial functioning, and evaluating the incremental prognostic value of digital phenotype markers beyond conventional clinical assessment. Statistical analyses will include Cox proportional hazards models, linear mixed-effects models, and machine learning approaches with feature selection and internal validation.

Discussion

This study applies a longitudinal multimodal framework to investigate the developmental trajectories of adolescents at elevated risk for psychotic disorders or BD. By deriving EEG-eye-tracking fusion digital biomarkers, this study aims to clarify whether integrating objective neurophysiological and behavioral measures can improve individual-level prediction of adverse clinical progression beyond traditional clinical assessment. Findings from this cohort may provide preliminary evidence for precision risk monitoring and inform future preventive strategies for severe mental disorders in youth.

Trial registration

Chinese Clinical Trial Registry: ChiCTR2500099868 (Registered 31 March 2025); National Medical Research Registration and Filing Information System: MR-11-25-026715

Keywords

Bipolar disorder; psychotic disorders; adolescents; clinical high risk; elevated risk; electroencephalography; eye-tracking.

Background

Epidemiological evidence highlights that severe mental disorders, such as psychotic disorder and bipolar disorder, account for substantial impacts on the worldwide disease burden[1, 2]. The both disorders often emerge during the critical neurodevelopmental years of adolescence and early adulthood, often follow a persistent or recurrent course[3]. They are associated with elevated morbidity and mortality, including suicide, which reduces life expectancy[4]. These consequences underscore the urgent priority for earlier detection of the clinical high-risk for psychosis and bipolar states during adolescence, which may help reduce the incidence and burden of these disorders in young people.

Both psychotic disorders and bipolar disorders exhibit substantial overlap in etiology, onset pattern, symptom fields, and diagnostic criteria. Notably, a subset of clinical high-risk for psychosis (CHR-P) individuals (67.1%) additionally meet the clinical high-risk for bipolar disorder (CHR-BD) criteria, and a subset of CHR-BD individuals (59.2%) also met CHR-P criteria[5]. Furthermore, longitudinal studies have shown that clinical trajectories of the individuals with the high-risk mental state are often heterogeneous rather than disorder-specific[6]. Accordingly, current preventive guidelines recommend transdiagnostic early detection and care pathways for both conditions. Given these considerations, a precision medicine-based clinical prediction model for detecting bipolar and psychotic disorders would be necessary in preventive psychiatry.

To date, several models based on clinical symptoms and demographic data have been published for the prediction of risk for psychotic disorders or bipolar disorders[7, 8]. More recently, two transdiagnostic clinical prediction models extracted from electronic health records have been reported to detect risk for both disorders simultaneously[9, 10]. However, these models rely on phenomenological descriptions, including diagnoses, symptoms, substance use, trauma and family history and lack biological criteria, which are not objective validated and might be prone to perturbations and inaccuracies.

Electroencephalography (EEG) and eye-tracking technologies provide the noninvasive, clinically

accessible tools for capturing real-time synaptic activity and attentional allocation, visual scanning patterns in psychiatric disorders. Related findings have been reported in people at familial risk, suggesting that EEG alterations may reflect vulnerability-related characteristics[11, 12]. Besides, several prospective studies preliminarily revealed baseline reductions in mismatch negativity, P300, and N100 to subsequent psychosis conversion in individuals at CHR[13, 14]. While resting-state EEG may microstate temporal instability at baseline distinguishes future converters from non-converters and predicts earlier conversion[15]. Eye-tracking offers complementary information by capturing attentional allocation, inhibitory control, emotional bias, and reinforcement-related decision processes. In an exploratory study of CHR individuals, a logistic regression model using two eye-movement indices differentiated converters from non-converters with an AUC of 0.80 (95% CI: 0.724 to 0.904)[16]. In addition, previous studies in BD have reported abnormalities in saccadic control, emotional attention, and reward-related visual behavior, indicating that eye-tracking may serve as a behavioral marker of cognitive-affective dysfunction[17].

Despite these advances, important gaps exist. First, most previous cohort studies focused on EEG, or eye-tracking measures in isolation in CHR-P and CHR-BD separately, limiting integration of EEG and eye-tracking information in transdiagnostic clinical predictions. Evidence suggests that neuroimaging and neurobehavioral markers may complement symptom-based risk assessment among at-risk youth[11]. Second, although biological and neurobehavioral markers may supplement symptom-based assessment, their longitudinal utility within cohorts of the individuals with the high-risk mental states has yet to be firmly established. Third, substantial methodological heterogeneity persists: EEG studies vary widely in frequency bands, ERP components, and analytical parameters, while eye-tracking studies lack standardized paradigms, area-of-interest definitions, and feature extraction methods, hampering cross-study integration. Finally, no externally validated framework currently exists for integrating multimodal data to enable individual-level risk stratification.

Study objectives

The primary objective is to identify EEG and eye-tracking features associated with adverse clinical progression over 24 months in adolescents at elevated risk for psychotic disorders or bipolar disorder, and to develop internally validated risk-stratification prediction models based on these multimodal markers.

The secondary objectives are as follows: (1) To estimate the 24-month cumulative incidence and temporal pattern of diagnostic transition to psychotic disorder or bipolar disorder in this elevated-risk cohort; (2) To characterize longitudinal trajectories of affective symptoms, emotion regulation, and psychosocial functioning over the 24-month follow-up period; (3) To evaluate the incremental prognostic value of EEG- and eye-tracking-derived markers beyond conventional clinical assessment.

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Methods

Study Design and Setting

This is a prospective, observational, single-centre longitudinal cohort study, conducted at Peking University Sixth Hospital. Participants will be recruited through outpatient psychiatric clinics, clinician referral pathways, community-based recruitment, and social media, where applicable. Participants will undergo a comprehensive baseline assessment and will be reassessed every 6 months during follow-up. A schematic overview of recruitment, baseline assessment, follow-up, and study outcome is shown in **Figure 1**.

This study will be conducted in accordance with the Declaration of Helsinki and the relevant ethical guidelines of the National Health Commission of China. The protocol was approved by the Institutional Review Board of Peking University Sixth Hospital (IRB Approval No. (2025) Ethics Review (29) Chinese Clinical Trial Registry: ChiCTR2500099868; National Medical Research Registration and Filing Information System: MR-11-25-026715). Written informed consent will be obtained from participants aged 18 years or older, and from parents or legal guardians of participants younger than 18 years. Written assent will be obtained from all participants aged 12 to 19 years. Participation is voluntary, and withdrawal will not affect clinical care.

Study participants

The study population will consist of adolescents at elevated risk for psychotic disorders or bipolar disorder. Eligible participants must be able to complete study interviews, questionnaires, and neurobehavioral tasks independently.

Inclusion criteria are as follows: (1) age between 12 and 19 years at enrolment; (2) right-handed; (3) for the psychotic disorder risk group, meeting criteria for one of the three prodromal syndromes: Brief Intermittent Psychotic Syndrome (BIPS), Attenuated Psychosis Syndrome (APS), or Genetic

Risk and Deterioration Syndrome (GRDS), assessed by the Structured Interview for Prodromal Syndromes (SIPS); or (4) for the bipolar disorder risk group, presence of at least one of the following risk factors: (a) First-degree family history of bipolar disorder; (b) Subthreshold affective symptomatology, including depressive syndrome, hypomanic, or mood swings; (c) Circadian rhythm or sleep disturbances; (d) a depressed syndrome in the context of : Major depressive disorder, other Specified Bipolar and Related Disorders according to DSM-5 criteria [18-20] ; and (5) written informed consent provided by the participants and/or their legal guardians.

Exclusion criteria are: (1) current or past diagnosis of delirium, dementia or other cognitive disorders, intellectual developmental disorder, mental disorders due to a general medical condition or psychoactive substance use; (2) a history of significant head trauma or loss of consciousness exceeding 30 minutes; (3) a history of alcohol and/or drug abuse or dependence; (4) presence of severe or unstable somatic diseases; (5) an estimated IQ ≤ 70; and (6) visual or hearing impairments that would interfere with study procedures.

Clinical Assessment

The schedule of enrolment, assessments, and follow-up is summarized in **Table 1**. At baseline and each follow-up, trained raters will administer diagnostic and symptom assessments using standardized procedures. Diagnostic status will be established via the Mini-International Neuropsychiatric Interview (M.I.N.I.) with age-appropriate modules, supplemented by DSM-5 diagnostic criteria for psychotic disorders and bipolar disorder.

Clinical instruments for the psychotic disorder risk group, assessments will include the Structured Interview for Prodromal Syndromes (SIPS) for risk syndrome classification, the Positive and Negative Syndrome Scale (PANSS) for symptom severity, the Clinical Global Impression-Severity scale (CGI-S) for overall illness severity, and the Negative Symptom Assessment-16 (NSA-16) for negative symptoms. For the bipolar disorder risk group, the Bipolarity Index (BPx) will be completed by experienced clinicians to quantitatively assess multi-dimensional risk based on episode characteristics, age of onset, illness course, family history, and treatment response. Manic, depressive, and anxiety symptom severity will be rated with the Young Mania Rating Scale (YMRS), Hamilton Depression Rating Scale-17 (HAMD-17), and Hamilton Anxiety Rating Scale (HAMA), respectively. Global and social functioning will be assessed using the Global Assessment of Functioning (GAF) and the Social Disability Screening Schedule (SDSS).

Self-report instruments will capture affective and psychosocial dimensions: the Snaith-Hamilton Pleasure Scale (SHAPS) for anhedonia, the Affective Reactivity Index (ARI) for irritability, the Difficulties in Emotion Regulation Scale-16 (DERS-16) for emotion regulation, the Patient Health Questionnaire-9 (PHQ-9) for depressive symptoms, the Generalized Anxiety Disorder-7 (GAD-7) for anxiety, and the Sheehan Disability Scale (SDS) for functional impairment. Bipolar spectrum features will be assessed with the Mood Disorder Questionnaire (MDQ) and the Hypomania Checklist-32 (HCL-32), and affective temperament with the TEMPS-A.

Contextual and dimensional features, including sleep or circadian disturbance, irritability, childhood adversity, family functioning, academic stress, and major environmental stressors, will be documented to characterize clinical heterogeneity and support descriptive and exploratory analyses. Treatment exposure, including medication use, psychotherapy, hospitalization, emergency psychiatric evaluation, and other clinically relevant changes in care, will be recorded throughout follow-up. Self-harm or suicidality will be assessed at each visit, and participants identified as being at acute risk will be referred for appropriate clinical management according to institutional procedures.

Cognitive, EEG, and Eye-Tracking Assessment

Cognitive performance will be evaluated using a computerized neuropsychological battery assessing attention, processing speed, working memory, inhibitory control, and cognitive flexibility, including the Trail Making Test (TMT), Digit Symbol Substitution Test (DSST), Continuous Performance Test (CPT), Digit Span (forward and backward), and Stroop Color-Word Test.

EEG and eye-tracking data will be collected simultaneously during resting-state and task-related paradigms. Resting-state EEG will include eyes-closed and eyes-open conditions. Task-based paradigms will include: (1) an emotional film clip viewing task; (2) an emotional face-matching task using validated facial-expression stimuli; (3) a modified probabilistic reversal learning task; and (4) prosaccade and antisaccade tasks with gap, overlap, and step conditions, in which participants are instructed to look toward (prosaccade) or away from (antisaccade) a peripheral target appearing at 4°, 8°, or 12° eccentricity.

EEG will be recorded using using a 24-channel dry-electrode EEG acquisition system (DSI-24, Neuracle, Changzhou, China) at a sampling frequency of 300 Hz. Eye-tracking data will be simultaneously acquired using a Tobii Pro Fusion eye-tracking system at a sampling frequency of

240 Hz. EEG preprocessing will include band-pass filtering (0.5–45 Hz), notch filtering at 50 Hz, ocular and muscular artifact rejection via Independent Component Analysis (ICA), epoching time-locked to task events with baseline correction (–200 ms to 0 ms), average re-referencing, and bad-channel interpolation. Eye-tracking preprocessing will include calibration of eye-movement coordinates, removal of blinks and signal-loss segments, extraction of fixation duration, saccade amplitude, saccade latency, gain, and pupil diameter change rate, alignment with task events, and Z-score normalization to eliminate inter-individual baseline differences.

Study outcomes

The primary outcome is adverse clinical progression, defined as a binary composite endpoint comprising at least one of the following: transition to psychotic disorder or bipolar disorder based on DSM-5 diagnostic criteria; clinically significant worsening of psychiatric or affective symptoms requiring treatment escalation, urgent psychiatric reassessment, emergency evaluation, or hospitalization; or persistence of elevated risk accompanied by deterioration in psychosocial functioning.

Secondary outcomes include longitudinal changes in psychiatric and affective symptoms, emotion regulation, and psychosocial functioning, assessed by repeated measures of the PANSS, NSA-16, SIPS, HAMD-17, HAMA, YMRS, ARI, PHQ-9, GAD-7, DERS-16, GAF, SDSS, and SDS over the 24-month follow-up period. Additionally, changes in bipolar spectrum features will be evaluated using the MDQ and HCL-32, and treatment exposure, including medication use, psychotherapy, hospitalization, and emergency psychiatric evaluation will be documented throughout follow-up. Contextual and environmental factors, including childhood adversity, family functioning, academic stress, and major environmental stressors, will be assessed at baseline and selected follow-up time points.

Follow-up endpoint is defined as the time point at which a diagnostic transition to psychotic disorder or bipolar disorder is confirmed during any follow-up visit; for participants who do not transition, the endpoint is the completion of the 24-month follow-up.

Sample size

The total planned sample size is 300 participants, with 150 adolescents at risk for psychotic disorders and 150 at risk for bipolar disorder. For the psychotic disorder risk group, sample size was calculated using G Power ($\alpha = 0.05$, $1–\beta = 0.80$, two-group ratio 1:1) based on a reported effect size

of 0.64 for P3b between converters and non-converters, yielding a minimum of 40 evaluable participants. Assuming a 2-year conversion rate of approximately 33%, 120 evaluable individuals are required to ensure an adequate converter sample, which, after accounting for 20% attrition, corresponds to 150 enrollees. For the bipolar disorder risk group, using the same G Power parameters and a reported effect size of 0.63 for antisaccade indices between BD and control groups, a minimum of 41 evaluable participants is required. Based on reported 2-year conversion rates of 15–35%, and again allowing for 20% attrition, we plan to enroll 150 participants.

Thus, the total enrolment of 300 participants also satisfies the general recommendation of at least 50 outcome events for stable prediction model development and validation [21].

Statistical Analysis

Baseline demographic, clinical, cognitive, EEG, and eye-tracking characteristics will be summarized using descriptive statistics. Continuous variables will be presented as mean ± standard deviation or median with interquartile range depending on their distribution. Categorical variables will be reported as frequencies and percentages.

The primary analysis will examine predictive associations between prespecified EEG- and eye-tracking-derived digital phenotype markers and adverse clinical progression over 24 months. Adverse clinical progression will be analyzed as a time-to-event outcome using Cox proportional hazards models, with effect estimates reported as hazard ratios with 95% confidence intervals. Univariable models will first evaluate each candidate marker. Multivariable models will then be performed using a limited set of prespecified EEG and eye-tracking markers and clinical covariates, including age, sex, baseline depressive and manic symptom severity, family history, baseline treatment status, and the number or type of elevated-risk indicators, as appropriate. Given the expected number of outcome events, multivariable models will be kept parsimonious. Candidate markers will be selected a priori based on previous literature and theoretical relevance, and the final number of predictors will be guided by the observed event count. If event numbers are insufficient, analyses will be limited to univariable or minimally adjusted models and interpreted as exploratory.

Diagnostic transition to psychotic disorder or BD will be analyzed as a key secondary outcome, with 24-month cumulative incidence estimated alongside 95% confidence intervals. If sufficient transition events are observed, Cox regression analyses will assess predictive associations with selected clinical, EEG, and eye-tracking markers; otherwise, transition rates will be reported

descriptively. Longitudinal trajectories of depressive, manic, and anxiety symptoms, irritability, emotion regulation, and psychosocial functioning will be analyzed using linear mixed-effects models with participant-level random intercepts to account for within-subject correlation; fixed effects will include time, predictors of interest, and prespecified covariates where appropriate.

For the exploratory multimodal risk-stratification modeling, machine learning algorithms and representational similarity analysis will be employed to integrate high-dimensional clinical, EEG, and eye-tracking features. To mitigate the risk of overfitting inherent to the expected event-to-variable ratio, rigorous feature selection and dimensionality reduction techniques, including leave-one-subject-out cross validated principal component analysis (LOSO-PCA), will be applied prior to model training. Candidate algorithms encompass conditional variational autoencoder (CVAE), Logistic regression (LR), light gradient boosting machine, Support Vector Machines, and random forests. The developed models will undergo internal validation via 10-fold cross-validation to ensure robustness. The incremental prognostic value of the digital phenotype markers will be evaluated by comparing a base clinical model against expanded multimodal models. Model discrimination will be quantified using the area under the receiver operating characteristic curve (AUC-ROC), alongside sensitivity, specificity, and accuracy metrics. Calibration will be assessed visually through calibration plots and quantitatively using the Brier score. Ultimately, the optimal model will be selected based on the minimum information criterion to balance predictive accuracy with structural parsimony.

Missing data will be described by time point and variable. Mixed-effects models will accommodate incomplete repeated-measures data under a missing-at-random assumption. Binary-outcome regression analyses will primarily use complete cases, with multiple imputation considered in sensitivity analyses when appropriate. All tests will be two-sided with $P < 0.05$.

Data management and confidentiality

All participant data will be de-identified and assigned a unique study identification number. Personal identifiers and research data will be stored separately in secure, access-restricted files. Electronic data will be stored on password-protected institutional servers or approved secure data platforms, and only authorized study personnel will have access to identifiable information. Data entry and management procedures will include a range of checks, consistency checks, and periodic quality review. EEG and eye-tracking source files will be retained in their original

format together with processed analytic datasets. Results will be reported only in aggregate form to protect participants' confidentiality.

Discussion

This protocol describes a prospective, observational longitudinal cohort study of adolescents and early youth at elevated risk for psychotic disorders or bipolar disorder, integrating repeated clinical assessments with EEG- and eye-tracking-derived digital phenotype measures. The study is designed to characterize the 24-month clinical course of this elevated-risk cohort, estimate the rate of adverse clinical progression and diagnostic transition to psychotic disorders or BD, and examine whether prespecified neurophysiological and neurobehavioral markers are associated with longitudinal clinical outcomes.

A key feature of this protocol is its multimodal design. Conventional assessment of high-risk in adolescents relies largely on clinical history, symptom reports, and clinician judgment, whereas the current study combines these approaches with objective measures of neurophysiological and behavioral function. This approach is supported by recent reviews indicating that candidate risk biomarkers in at-risk youth span multiple biological and neurocognitive domains, including emotion and reward processing circuits[11]. EEG may provide information about neural activity and oscillatory abnormalities relevant to attention, emotional salience, cognitive flexibility and reward processing, while eye-tracking may capture gaze-based indices of attentional allocation, saccadic control, and cognitive-affective processing[17, 22].

The longitudinal follow-up is intended to move beyond cross-sectional risk characterization and expand to the transdiagnostic clinical predictions. Repeated assessments will allow evaluation of symptom trajectories, psychosocial functioning, treatment exposure, self-harm or suicidality, major environmental stressors, and adverse clinical progression. This is important because adolescent risk states are often clinically heterogeneous, and different risk indicators may reflect distinct developmental pathways rather than a single prodromal condition. If multimodal markers provide incremental information beyond conventional assessment, the findings may inform future approaches to closer monitoring and more individualized preventive care; however, any predictive models developed from this cohort should be regarded as

preliminary until externally validated.

Several limitations should be acknowledged. First, the sample size, while sufficient for the primary analyses, may limit the power of exploratory subgroup analyses, particularly when stratifying by specific risk indicators or clinical subtypes. Second, as a single-centre study conducted at a tertiary psychiatric hospital, the robustness of the findings should be verified on independent external datasets. Third, owing to the possible limited conversion rates during the follow-up, expanding the sample size and prolonging observation time will be necessary for subsequent verification. Finally, attrition is an inherent challenge in longitudinal adolescent research, and missing data will be reported transparently and addressed using prespecified statistical procedures.

Data availability

No datasets were generated or analyzed during the current study.

Competing interests

The authors declare that they have no competing interests.

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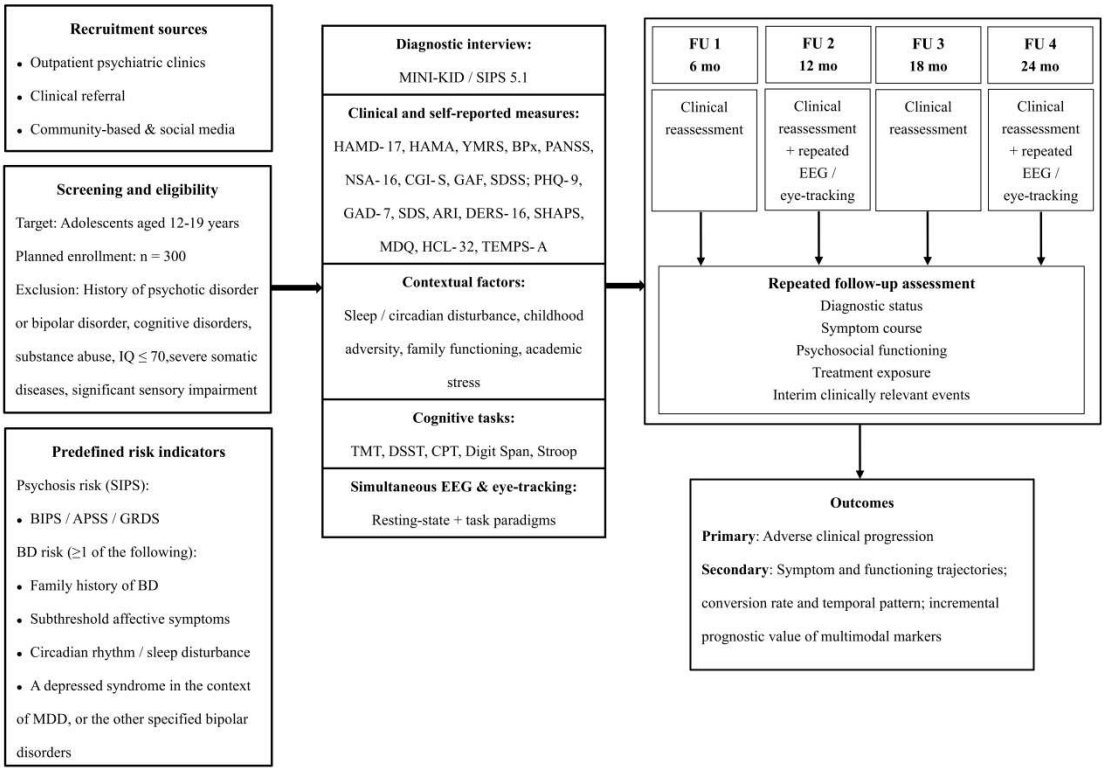


Figure 1. Overview of the study design. BD, bipolar disorder; BIPS, Brief Intermittent Psychotic Syndrome; APSS, Attenuated Psychotic Symptom Syndrome; GRDS, Genetic Risk and Deterioration Syndrome; SIPS, Structured Interview for Prodromal Syndromes; MINI-KID, Mini-International Neuropsychiatric Interview for Children and Adolescents; HAMD-17, Hamilton Depression Rating Scale-17; HAMA, Hamilton Anxiety Rating Scale; YMRS, Young Mania Rating Scale; BPx, Bipolarity Index; PANSS, Positive and Negative Syndrome Scale; NSA-16, Negative Symptom Assessment-16; CGI-S, Clinical Global Impression-Severity Scale; GAF, Global Assessment of Functioning; SDSS, Social Disability Screening Schedule; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder-7; SDS, Sheehan Disability Scale; ARI, Affective Reactivity Index; DERS-16, Difficulties in Emotion Regulation Scale-16; SHAPS, Snaith-Hamilton Pleasure Scale; MDQ, Mood Disorder Questionnaire; HCL-32, Hypomania Checklist-32; TEMPS-A, Temperament Evaluation of Memphis, Pisa, Paris and San Diego Autoquestionnaire; TMT, Trail Making Test; DSST, Digit Symbol Substitution Test; CPT, Continuous Performance Test; EEG, electroencephalography; FU, follow-up.

Table 1. Schedule of study procedures, assessments, and follow-up evaluations

Assessment	Screening	Baseline	6 months	12 months	18 months	24 months
Eligibility assessment	X					
Informed consent / assent	X					
Predefined risk indicators	X	X				
BPx		X				
Diagnostic interview		X	X	X	X	X
SIPS / PANSS / NSA-16 / CGI-S		X	X	X	X	X
HAMD-17 / HAMA / YMRS		X	X	X	X	X
GAF / SDSS		X	X	X	X	X
ARI / DERS-16		X	X	X	X	X
PHQ-9 / GAD-7 / SDS		X	X	X	X	X
SHAPS		X	X	X	X	X
MDQ / HCL-32 / TEMPS-A		X		X		X
Contextual features		X		X		X
Cognitive tasks / Stroop		X		X*		X*
Simultaneous EEG-eye-tracking		X		X*		X*
Medication exposure		X	X	X	X	X
Self-harm / suicidality		X	X	X	X	X
Major environmental stressors			X	X	X	X
Adverse clinical progression			X	X	X	X
Diagnostic transition to psychotic disorder or BD			X	X	X	X

X indicates that the assessment or procedure is scheduled at the corresponding time point. *Selected cognitive, EEG, and eye-tracking assessments may be repeated where feasible. ARI, Affective Reactivity Index; BD, bipolar disorder; BPx, Bipolarity Index; DERS-16, Difficulties in Emotion Regulation Scale-16; DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; EEG, electroencephalography; GAD-7, Generalized Anxiety Disorder-7; GAF, Global Assessment of Functioning; HAMA, Hamilton Anxiety Rating Scale; HAMD-17, Hamilton Depression Rating

Scale-17; HCL-32, Hypomania Checklist-32; MDQ, Mood Disorder Questionnaire; M.I.N.I., Mini-International Neuropsychiatric Interview; NSA-16, Negative Symptom Assessment-16; PANSS, Positive and Negative Syndrome Scale; PHQ-9, Patient Health Questionnaire-9; SDSS, Social Disability Screening Schedule; SDS, Sheehan Disability Scale; SHAPS, Snaith-Hamilton Pleasure Scale; SIPS, Structured Interview for Prodromal Syndromes; TEMPS-A, Temperament Evaluation of Memphis, Pisa, Paris and San Diego Autoquestionnaire; YMRS, Young Mania Rating Scale.

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