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Multiband fractional amplitude of low-frequency fluctuations predicts social functioning transdiagnostically in the clinical high-risk for psychosis state and recent-onset depression

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Background: Social functioning impairments are prevalent in psychotic and depressive disorders. However, to date, we lack a thorough understanding of the brain functional changes underlying these impairments and the extent to which brain-based biomarkers could help overcome the currently limited accuracy of practitioner-based risk-stratification of poor social outcomes. Specifically, functional brain imaging has not been investigated in this framework so far, despite existing evidence of transdiagnostic abnormalities in brain networks associated with socio-cognitive functions in the early stages of psychosis and depression.
Aims: To build and validate transdiagnostic and diagnostic-specific supervised machine learning models for the longitudinal prediction of social functioning outcomes based on multivariate patterns of resting-state fMRI in the clinical high-risk for psychosis (CHR) state and recent-onset depression (ROD).
Methods: A sample of 105 CHR individuals and 109 ROD patients (respectively 90 CHR, 72 ROD) drawn from the european multisite PRONIA study was used to train and respectively validate machine learning models for the prediction of one-year social functioning outcomes based on baseline multiband fractional amplitude of low-frequency fluctuations (fALFF). Differences in accuracy between transdiagnostic and diagnosis-specific models, and associations of the predictive models with clinical, cognitive, and demographic variables were evaluated. Additionally, we investigated the associations between the fALFF-based model's decision scores and those coming from previously published models of social functioning based on gray-matter volume (GMV) and clinical data [1], as well as the added value of the fALFF model to the performance of these previous classifiers.
Results: The transdiagnostic models trained on the slow-4 and slow-5 fALFF frequency sub-bands predicted social functioning outcomes above chance level, with the slow-4 sub-band (0.027 – 0.073 Hz) yielding the highest performance (BAC = 65%, Sensitivity = 65.3%, Specificity = 64.7%). Poor outcomes were predicted by distributed patterns of baseline fALFF increases and decreases, more prominent in posterior regions and the cerebellum. The transdiagnostic models had comparable performances for the CHR and ROD patients and partially generalized to an independent transdiagnostic sample (BACreplication = 56%), with higher performances for the ROD patients (BACreplication ROD = 61.8%, BACreplication CHR = 53.2%). Moreover, the model's decision scores were predicted by clinical, sociodemographic, and cognitive variables and correlated with those coming from the GMV- and clinical-based models of social functioning. At diagnostic-specific level, only the models trained on the slow-4 data of the CHR participants performed above-chance level (BAC = 64.2%) and partially generalized to the ROD patients (BAC = 57.1%), while none of the ROD-specific models predicted functioning above chance.
Conclusions: Evidence for the value of rs-fMRI data as a transdiagnostic prognostic biomarker of social functioning in early psychotic and affective stages is provided. Our results open the avenue for further investigation of the added value of this measure to previously established predictors of functioning and for the identification of specific patient subgroups for which it may prove especially valuable.
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Early-onset schizophrenia in Riga's Children's Clinical University Hospital 2012-2021 – epidemiology and associated factors

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Introduction: Schizophrenia is considered one of the most damaging mental disorders affecting children and adolescents. Early-onset schizophrenia (EOS) is a rare manifestation of the disorder, with the development of the first psychotic episode before 18 years. Very early-onset schizophrenia (VEOS) with symptoms occurring before the age of 13 is an infrequent condition with an estimated prevalence of less than 1:10000. EOS has probable rates of 1-2 per 1,000.[1] The exact mechanisms leading to manifestations of schizophrenia are still under investigation; however, numerous risk factors may potentially interact with the genetic predisposition to mediate the timing of onset. Patients with EOS and VEOS are more likely to have a history of social neglect, drug abuse, experienced emotional violence, and obstetric complications.[2], [3] A familial history of psychiatric diseases is a significant risk factor both for early onset and for the severity of the illness.[4]
Aims of the study: To collect epidemiological data of all cases of EOS/VEOS in Children's Clinical University Hospital from 2012 to 2021, evaluate the incidence, and identify factors associated with the age of onset of EOS.
Materials and Methods: A retrospective study that included patients admitted between January 2012 and December 2021 with a diagnosis of schizophrenia (ICD-10). The data were collected from medical records of Riga's Children's Clinical University Hospital, the largest Latvian hospital which covers a third of population; in-patient and out-patient contacts were explored. Data were analyzed with statistical software (IBM SPSS 23), χ^2 tests, t-test, ANOVA tests were used.
Results: During the analyzed period, 45 patients were diagnosed with EOS (18 females, 27 males), and 4 were diagnosed with VEOS (1 female, 3 males). The onset age was from 10 to 17, with a mean of 14.83 (+-1.74). No significant difference in the mean age was found between the sexes. 83.7% of subjects presented with nonspecific prodromal symptoms.
Several factors, that could potentially influence the age of onset, were detected in patients' medical records: emotional violence (in 42.8% of patients), obstetric complications (36.7%), a first-degree relative with psychotic-spectrum disorder (24.5%), or other mental disorder (34.7%), parents' divorce (42.8%), drug abuse (24.5%), traumatic childhood events (20.4%), premature birth (16.3%), birth by