Title

192. Different Age-Related Trajectories of Social Cognition in Youths at Clinical High Risk of Psychosis

Journal

Schizophrenia bulletin, 43(Suppl 1)

ISSN

1787-9965

Authors

Davidson, Charles
Piskulic, Danijela
Addington, Jean
et al.

Publication Date

2017-03-01

Peer reviewed

190. PARENTAL MUSCULOSKELETAL DISORDERS ASSOCIATE WITH CHILDREN'S PRODROMAL SYMPTOMS OF PSYCHOSIS: A POPULATION-BASED BIRTH COHORT STUDY WITH 8-YEAR FOLLOW-UP

Lotta Kinnunen*[,1], Tanja Nordström[1], Mika Niemelä[2], Sami Räsänen[2], Michael Sawyer[3], and Jouko Miettunen[1]
[1]University of Oulu, [2]Oulu University Hospital, [3]University of Adelaide

Background: The aim of this study is to find out whether the onset of parental somatic illnesses per se is associated with increased level of prodromal symptoms of psychosis when children's earlier symptoms are taken into account. And if so, which specific parental illnesses are most relevant in this respect.
Methods: This study is a prospective population-based survey. The Northern Finland Birth Cohort 1986 covers all children (6682 in total) born alive in Northern Finland during 1 year. At the age of 16, the cohort members completed the PROD-screen questionnaire, which is a screening instrument for prodromal symptoms of psychosis with 21 questions of which 12 questions are symptom specific for psychosis. Parental somatic illness diagnoses were collected from health registers between children's age 8–16. The illnesses were subsumed in 19 different categories according to the *International Classification of Diseases* (ICD) Coding. We compared children with and without each parental somatic illness and UNIANOVA were used to evaluate the impact of parental somatic illness on children's prodromal symptoms of psychosis at the age 16. Rutter problem behavioral questionnaire completed by teachers was a baseline at the age of 8. Adjusting factors were parental psychiatric diagnoses, socioeconomic status (SES), and gender.
Results: This study found that of the 19 different parental disease groups only children with parental musculoskeletal disorders had statistically significantly higher symptom specific PROD12-screen scores (PROD12 mean 2.1, SD 2.1) compared to their peers (mean 1.9, SD 2.0), $P = .001$. When adjusting with the sum of Rutter questionnaire, the results remained the same ($P = .001$). When adding other adjusting factors in the analyses, the results remained statistically significant ($P = .036$). A total score of the PROD21-screen showed the same difference: children with parental musculoskeletal disorders had statistically significantly higher PROD21-screen scores (PROD21 mean 3.8, SD 3.7) compared to other children (PROD21 mean 3.5, SD 3.4), $P = .002$. In comparison with girls, the relation was stronger with boys. In other disease groups, statistically significant differences were not found.
Conclusion: In this general population-based sample, only parental musculoskeletal disorders stand out as potential risk factors for children's prodromal symptoms of psychosis and especially boys seem more vulnerable. The finding of the parental musculoskeletal illnesses as a risk factor for children mental health symptoms could be explained by comorbidity of the musculoskeletal disorders with mental health problems. Musculoskeletal disorders are often considered as chronical illnesses with chronic pain and mental health problems. In this study, parental psychiatric diagnoses were taken into account; however, parental psychiatric symptoms can be elevated with a chronically ill parent without a psychiatric diagnose.

191. INDEPENDENT CONTRIBUTIONS OF EARLY ADOLESCENT DELUSION-LIKE EXPERIENCES AND HALLUCINATION-LIKE EXPERIENCES TO POORER PSYCHOLOGICAL OUTCOMES AND GLOBAL FUNCTIONING IN MID-ADOLESCENCE: LONGITUDINAL COHORT STUDY.

Colm Healy*, and Mary Cannon
Royal College of Surgeons in Ireland

Background: It is well established that young adolescents are particularly susceptible to subclinical psychotic-like experiences (PLEs). These experiences have been linked to an increased risk of lifetime development a mental health disorder. PLE's consist of a variety of experiences and there is little research investigating which subtype of PLEs contributes to the development of psychopathology and poorer global functioning.
Methods: We followed a cohort from early to mid-adolescence to investigate whether endorsing PLE symptoms in early adolescence is related to poorer psychosocial functioning in mid adolescence. At T1, 212 of the participants (mean age: 11.5 years) who participated in the "Adolescent Brain Development" study and completed the Adolescent Psychotic Symptoms Screener (APSS). Factor analysis was conducted on APSS scores and identified two clear independent factors; Hallucination-Like Experiences (HLEs) and Delusion-Like Experiences (DLEs). 86 took part in a second phase (T2) of the study (mean age: 15.7yrs). At T2, participants were administered the Youth Self Report questionnaire (YSR; Total score, internalized and externalized scores) and were assessed on the Global assessment of functioning scale (GAF-current and GAF-most severe past). Regression analysis was used to investigate the independent contributions of T1 factors (HLEs and DLEs) on participant's psychological well-being (YSR) and general functioning (GAF) at T2.
Results: The results indicated that HLEs, but not DLEs, contributed to T2 YSR Total Score ($r^2 = .219$, $P = .002$) and Internalizing Score ($r^2 = .113$, $P = .019$). HLEs contribute more than DLEs to Externalizing Score ($r^2 = .127$, $P = .002$ and $r^2 = .067$, $P = .047$, respectively). However, DLEs made a greater contribution to GAF current scores (DLEs: $r^2 = .146$, $P = .001$; and HLEs: $r^2 = .059$, $P = .028$) and DLE's were the only significant predictor of GAF most severe past scores ($r^2 = .113$, $P = .002$).
Conclusion: These results indicate divergent roles for HLE's and DLE's in the development of poor psychosocial functioning in mid-adolescence. Early adolescent HLEs increase vulnerability to mid-adolescent internalizing and externalizing behavioral problems. Interestingly, DLEs appear to contribute to poorer global functioning (e.g., distress at symptoms and poor social functioning). Therefore, these experiences should be considered as independent markers when evaluating risk of psychopathology in young people.

192. DIFFERENT AGE-RELATED TRAJECTORIES OF SOCIAL COGNITION IN YOUTHS AT CLINICAL HIGH RISK OF PSYCHOSIS

Charles Davidson*[,1], Danijela Piskulic[2], Jean Addington[2], Kristen Cadenhead[3], Tyrone Cannon[1], Barbara Cornblatt[4], Tom McGlashan[1], Diana Perkins[5], Larry J. Seidman[6], Ming Tsuang[3], Elaine Walker[7], Carrie Bearden[8], Daniel Mathalon[9], Scott Woods[1], and Jason Johannesen[1]
[1]Yale University; [2]University of Calgary; [3]University of California, San Diego; [4]Zucker Hillside Hospital; [5]University of North Carolina; [6]Harvard Medical School; [7]Emory; [8]University of California, Los Angeles; [9]University of California, San Francisco

Background: Social skills develop along with metacognitive abilities from early childhood through young adulthood. Impairment in metacognitive and other social cognitive abilities may contribute to poorer social function in clinical high risk for psychosis (CHR) adolescents. However, it is unclear whether social cognitive impairment represents developmental delay in skill acquisition or, rather, a consequence of emerging symptoms. Furthermore, it is unknown how early pharmacotherapy could influence this developmental trajectory. This study examined the hypotheses that (1) age-related trajectories of social cognition differ between CHR and normally developing youth and (2) age-related trajectories are partially explained by history of symptoms and psychotropic medication.
Methods: Emotion perception, social perception, and theory of mind abilities were assessed in 675 CHR and 264 age-matched healthy comparison

(HC) participants aged 12–35 (average = 19.0 ± 4.5 years). Linear and nonlinear curves were fit to relationships between social cognitive variables and age. Differences in age effects between CHR and HC were modeled as interaction terms. Duration of a prodromal syndrome prior to baseline and medication history were tested for interactions with age effects.
Results: Emotion perception and social perception age trajectories did not differ by group. Theory of mind age trajectory, particularly for sarcasm items, had a lower slope for CHR than HC. CHR diverged from HC from mid-adolescence onward (starting to differ between approximately ages 15 and 17.5), with a minimum observation window of 4 years required to detect correlations with age. Age trajectory for theory of mind was unrelated to the presence or duration of a prior prodromal syndrome but did interact with medication history, wherein participants with an antipsychotic or antidepressant medication history did not differ from HCs. Only antipsychotic- and antidepressant-naive CHR participants showed a smaller slope for theory of mind, with differences from HC increasing with advanced age.
Conclusion: In the current study, all social cognitive abilities increased during adolescence, but development of theory of mind appeared blunted for CHR participants starting in mid-adolescence. This difference, however, was only true for participants without an antipsychotic or antidepressant medication history, which could suggest benefits of early treatment or subgroups within CHR for whom social cognition is affected differently. These cross-sectional results require longitudinal replication and further inquiry into the relationships between treatment history and social cognitive development. Current results suggest that factors related to risk for psychosis may moderate adolescent social development, and that interventions targeting social cognition may be particularly helpful at this stage.

193. PROBABILISTIC MODELING OF TRANSITION TO PSYCHOSIS USING CLINICAL AND COGNITIVE VARIABLES IN THE PERSONAL ASSESSMENT AND CRISIS EVALUATION ("PACE 400") STUDY

Scott Clark*[,1], Paul Amminger[2], Ashleigh Lin[3], K, Oliver Schubert[1], Christos Pantelis[4], Alison Yung[5], Stephen Wood[6], Bernhard T Baune[1], Patrick D. McGorry[6], and Barnaby Nelson[6]
[1]University of Adelaide; [2]Orygen, The National Centre of Excellence in Youth Mental Health, [3]Telethon Kids Institute, [4]Melbourne Neuropsychiatry Centre; The University of Melbourne; [5]University of Manchester; [6]Orygen, The National Centre of Excellence in Youth Mental Health, The University of Melbourne

Background: Clinical criteria for Ultra-High Risk of psychosis (UHR) show moderate specificity for the prediction of the first psychotic episode (FEP), with an average true positive rate of approximately 30% at 3 years. We have recently developed a multimodal probabilistic model using the odds ratio form of Bayes' rule that achieved sensitivity=73% and specificity=96% for FEP combining clinical data and biological data in a small sample of UHR patients. To validate this approach, we built a similar model using cognitive and clinical data from the Personal Assessment and Crisis Evaluation ("PACE 400") study.
Methods: 430 UHR patients presenting to a specialist psychosis service in metropolitan Melbourne, Australia, were identified using the Comprehensive Assessment of At-Risk Mental State (CAARMS). Transition to FEP occurred in 114 within 13 years of presentation. Demographic and clinical data were available for the full cohort and cognitive data for 258 cases. Positive and negative likelihood ratios (LRs) for FEP were calculated for clinical and cognitive variables with statistically significant receiver–operating curves (ROCs). LRs were combined using the odds ratio form of Bayes' Rule to calculate probability of transition for 258 cases with complete data. ROC curves, positive, and negative predictive values for this model were calculated at yearly intervals of follow-up. Model accuracy was calculated for brief limited intermittent psychotic symptoms (BLIPS), attenuated symptoms, and vulnerability subgroups of CAARMS risk.
Results: Significant predictors of transition included global assessment of function, duration of symptoms prior to presentation, quality-of-life scale, CAARMS items (Disorders of thought content, Conceptual disorganisation), performance IQ, and Full Scale IQ. An odds ratio form of Bayes' rule model using these variables predicted transition with a sensitivity of 50%–64% and a specificity of 75%–92%(AUROC = 0.75–0.765) over 14 years post assessment. At 14 years, positive predictive value(PPV) = 50.7% and negative predictive value(NPV) = 86.4%. The model was more accurate in those presenting with BLIPS (PPV = 100%, NPV = 100%) in comparison to vulnerability criteria (PPV = 50%,NPV = 90.9%) or attenuated symptoms (PPV = 37.0%,NPV = 86.4%). Cases with overlapping symptoms were intermediate to these groups.
Conclusion: In a sample enriched by UHR criteria, multimodal modeling using simple Bayesian techniques can improve predictive power. Systematic use of clinical and cognitive assessment may facilitate personalized psychosis prevention strategies. The accuracy of UHR prediction may be improved by separate models for each UHR criteria subgroup. Further analysis should explore the value of additional modes of assessment such as imaging, electrophysiology, or other biomarkers, particularly in cases presenting with features other than BLIPS.

194. NEUROMELANIN-SENSITIVE MRI AS AN EARLY INDICATOR OF DOPAMINE DYSFUNCTION IN INDIVIDUALS AT RISK FOR PSYCHOSIS

Clifford Cassidy*[,1], Ragy Girgis[2], Caridad Benavides[2], Emanuele Ferrari[3], Fabio Zucca[3], David Sulzer[2], Anissa Abi-Dargham[4], Luigi Zecca[3], and Guillermo Horga[2]
[1]IMHR Royal Ottawa Hospital; [2]Columbia University; [3]Institute of Biomedical Technologies; [4]Stony Brook University

Background: The current study uses neuromelanin-sensitive MRI (NM-MRI), a brief, noninvasive, imaging technique that has widely been used in Parkinson's disease, to investigate signal changes in the substantial nigra of subjects at risk for psychosis which may reflect excess dopamine activity prior to the full onset of psychosis.
Methods: We performed NM-MRI scans on 20 healthy controls, 10 individuals at risk of schizophrenia, 20 patients with schizophrenia, and 3 postmortem sections of human midbrain. To validate NM-MRI as a neuromelanin-sensitive measure (not just a marker of dopamine cell loss as it has been used in Parkinson's disease), tissue concentrations of neuromelanin were estimated in postmortem samples using spectrophotometry (ex vivo study). We compared the signal intensity changes of NM-MRI across clinical groups using voxelwise analysis (in vivo study).
Results: NM-MRI signal variation in different regions of a post-mortem midbrain sample was highly correlated to neuromelanin concentration in the same regions (Pearson $r = .81$, $P = .0004$). Voxelwise analysis within the SN examining clinical groups, identified an SN cluster, where patients with schizophrenia had higher NM-MRI signal than matched controls ($P < .05$, uncorrected) and a partially overlapping cluster was observed to have higher signal in individuals at risk of schizophrenia compared to controls ($P < .05$, uncorrected).
Conclusion: These preliminary data indicate that NM-MRI indeed appears to be sensitive to neuromelanin content, even in the absence of neurodegeneration. The method shows promise as an imaging tool in neuropsychiatric illness, since it may be able to capture interindividual variability in dopamine system function and psychopathology. Indeed, we found that the signal may be altered in individuals at risk of psychosis. Further work is needed to confirm these results.