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24.2 NEUROCOGNITIVE PROFILES IN THE PRODROME TO PSYCHOSIS IN NAPLS-1

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damage, is expressed at very low levels at birth but then increases significantly with age and is highest in adulthood, suggesting that significant changes in complement may occur after brain maturation is complete.

Discussion: Together these findings show very dynamic and complex patterns of expression from birth to adulthood, with the most active growth phase and dynamic changes occurring in the early years before adolescence. Thus, an insult during these early years could profoundly affect the developmental trajectory.

24. FROM DUSK TILL DAWN: LIFELONG TRAJECTORIES OF COGNITIVE FUNCTIONING IN PSYCHOTIC DISORDERS AND THEIR IMPLICATIONS FOR FUNCTIONAL RECOVERY AND TREATMENT DECISION

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Overall Abstract: This symposium will draw together state of the art findings on the lifelong cognitive trajectories, on key-predictors of cognitive functioning and the functional consequences of cognitive impairments in schizophrenia and related psychotic disorders from developmental epidemiological, prodromal, and clinical research. Four speakers will take the audience through new findings on the cognitive course of the lifespan, ranging from childhood to old age. Specifically, the talks will address four key-questions:

- 1) Which areas of cognitive functioning are impaired and when does this impairment start?
- 2) How well can cognitive functioning predict the development of a psychotic illness, as well as diagnostic and functional outcome?
- 3) Does cognitive functioning remain stable after illness onset or are psychotic disorders characterized by continuing decline? When does decline occur and is it possible to predict it?
- 4) And what is the functional sequelae of specific cognitive impairments in older adults with schizophrenia?

Specifically, Dr. Mollon will present new data examining the origin of cognitive impairment across the psychosis spectrum using a population-based cohort followed prospectively from birth. Her findings demonstrate that while individuals with affective psychosis, subthreshold psychotic experiences and even depression experience some degree of cognitive impairment across the first two decades of life, only those who go on to develop non-affective psychosis exhibit large, widespread and increasing deficits.

Most studies of neurocognitive functioning in Clinical High Risk (CHR) cohorts have examined group averages, likely concealing heterogeneous subgroups. The study of Dr. Velthorst therefore used two independent methods to identify neurocognitive subgroups in a large population at Clinical High Risk for developing psychosis. Her findings show that neurocognitive profiles vary substantially in their severity and are associated with diagnostic and functional outcome, underscoring neurocognition as a predictor of illness outcomes.

Dr. Fett will present recent research on cognitive functioning in a large sample of patients at first hospitalization for a psychotic disorder who have been followed 20-years into the illness. Her findings indicate that cognitive functioning in psychotic disorders continues to decline after illness onset, that this decline is not specific to schizophrenia but present across psychotic disorders, and that, relative to never-psychotic individuals, impairments on some key-cognitive domains worsen with age. Decline could not reliably be predicted by key patient characteristics at baseline.

Lastly, Dr. Harvey will share novel data on the course of cognitive functioning in middle aged and older patients with schizophrenia. His findings demonstrate that cognitive impairments are moderated in their impact on everyday outcomes by the presence of severe communication abnormalities.

Interestingly, verbal under-productivity and disconnected speech had different functional correlates, with under-productivity impacting clinician rated social outcomes and performance on measures of interpersonal social competence. A lifetime focus on cognition is paramount in order pinpoint critical periods for prevention and intervention. This symposium seeks to present a comprehensive overview of the cognitive landscape of psychotic disorders by integrating findings on predictors and consequences of lifelong cognitive functioning of individuals diagnosed with a psychotic disorder.

24.1 NEUROCOGNITIVE DEVELOPMENT FROM INFANCY TO EARLY ADULTHOOD IN THE PSYCHOSIS SPECTRUM

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Background: The majority of patients with psychotic disorders experience severe neuropsychological impairment. The onset and course of this impairment, however, is debated. Moreover, the course of neuropsychological functioning in other psychiatric conditions remains largely unexamined. This study used longitudinal data from infancy to early adulthood to chart the course of general and specific neuropsychological functions in individuals with psychotic disorders, psychotic experiences and depression.

Methods: Data were from the Avon Longitudinal Study of Parents and Children (ALSPAC), a prospective cohort study comprising all live births between 1991 and 1992 in Avon, UK. All participants who underwent cognitive testing at 18 months, 4, 8, 15 and 20 years, and psychiatric assessment at age 18 were included. Individuals with non-affective psychotic disorder, affective psychotic disorder, subclinical psychotic experiences and depression were compared to controls on full-scale, verbal and non-verbal IQ, and measures of processing speed, working memory, language, visuospatial ability and attention.

Results: Individuals with non-affective psychosis showed continually increasing deficits between infancy (18 months) and adulthood (20 years) in full-scale IQ (effect size of change (ESΔ) = -1.09, p=.02), and non-verbal IQ (ESΔ = -0.94, p=.008). The depression group showed a small, increasing deficit in non-verbal IQ (ESΔ = -0.29, p=.04) between infancy and adulthood. Between ages 8 and 20, the non-affective psychosis group exhibited developmental lags (i.e. slower growth) on measures of processing speed, working memory and attention (ESΔ = -0.68, p=.001; ESΔ = -0.59, p=.004; ESΔ = -0.44, p=.001), and large, static deficits on measures of language and visuospatial ability (ES = -0.87, p=.005; ES = -0.90, p=.001). There was only weak evidence for neuropsychological deficits in individuals with affective psychosis, depression, and subclinical psychotic experiences.

Discussion: These findings suggest that the origins of non-affective psychotic disorder involve dynamic neurodevelopmental processes, which affect both verbal and non-verbal abilities throughout the first two decades of life. These neurodevelopmental processes do not manifest in other psychiatric disorders, such as affective psychotic disorder and depression.

24.2 NEUROCOGNITIVE PROFILES IN THE PRODROME TO PSYCHOSIS IN NAPLS-1

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Background: The vast majority of studies of neuropsychological (NP) functioning in Clinical High Risk (CHR) cohorts have examined group averages, possibly concealing a range of subgroups ranging from very impaired to high functioning. Our objective was to assess NP profiles and to explore associations with conversion to psychosis, functional and diagnostic outcome.

Methods: Data were acquired from 324 participants (mean age 18.4) in the first phase of the North American Prodrome Longitudinal Study (NAPLS-1), a multi-site consortium following individuals for up to 2½ years. We applied Ward's method for hierarchical clustering data to 8 baseline neurocognitive measures, in 166 CHR individuals, 49 non-CHR youth with a family history of psychosis, and 109 healthy controls. We tested whether cluster membership was associated with conversion to psychosis, social and role functioning, and follow-up diagnosis. Analyses were repeated after data were clustered based on independently developed clinical decision rules.

Results: Four neurocognitive clusters were identified: Significantly Impaired (n=33); Mildly Impaired (n=82); Normal (n=145) and High (n=64). The Significantly Impaired subgroup demonstrated the largest deviations on processing speed and memory tasks and had a conversion rate of 58%, a 40% chance of developing a schizophrenia spectrum diagnosis (compared to 24.4% in the Mildly Impaired, and 10.3% in the other two groups combined), and significantly worse functioning at baseline and 12-months. Data clustered using clinical decision rules yielded similar results, pointing to high convergent validity.

Discussion: Despite extensive neuropsychological investigations within CHR cohorts, this is one of the first studies to investigate NP clustering profiles as a contributor to heterogeneity in outcome. Our results indicate that the four NP profiles vary substantially in their outcome, underscoring the relevance of cognitive functioning in the prediction of illness progression. Our findings tentatively suggest that individualized cognitive profiling should be explored in clinical settings.

24.3 EIGHTEEN-YEAR COURSE OF COGNITIVE FUNCTIONING IN PSYCHOTIC DISORDERS: FINDINGS FROM THE SUFFOLK COUNTY MENTAL HEALTH LONGITUDINAL STUDY

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Background: Knowledge about the long-term cognitive course in psychotic disorders is limited. In this 18-year follow-up of participants of the Suffolk County project we report on the longitudinal course of cognitive performance in individuals with schizophrenia spectrum disorders, affective psychoses and other psychoses. We investigate (i) change in functioning in 6 cognitive domains from 2-years to 20-years follow-up after first admission; (ii) 20-year performance and age-related differences in cognitive performance in patients relative to a never psychotic comparison group; and (iii) key predictors of clinically meaningful cognitive decline in patients.

Methods: Data came from the Suffolk County Mental Health Project, a prospective study of first-admission patients. Cognitive tests were administered 2 years (n = 399; schizophrenia spectrum: 285, affective psychoses: 226, other psychoses: 117) and 20 years (n = 240; 115, 92, and 34, respectively) after first admission, with 195 individuals completing cognitive tests

at both time points. A never psychotic comparison group (N=260) was assessed at year 20.

Results: Individuals with schizophrenia spectrum disorders showed lower cognitive functioning than those with affective and other psychoses. Over time, patients declined in cognitive performance on almost all tests (d = 0.24 (range 0.12- 0.44)) with comparable magnitude across diagnoses. Longer duration of untreated psychosis and low childhood IQ were significantly associated with clinically relevant decline (>0.5SD) in general verbal ability and processing speed, but there were no robust predictors of cognitive decline across tests. Cross-sectional comparisons of patients to controls showed increasing impairments with age for general verbal ability, verbal fluency, and executive functioning.

Discussion: Our findings indicate that cognitive functioning in psychotic disorders continues to decline after the illness onset, that this decline is not specific to schizophrenia but present across psychotic disorders, and that, relative to never-psychotic individuals, impairments on some key-cognitive domains worsen with age. These results imply that cognitive treatment should not only include cognitive remediation but also prevention of age-related cognitive stagnation and/or decline.

24.4 COGNITION AND COMMUNICATION AS DETERMINANTS OF ADAPTIVE DEFICITS IN LATE LIFE SCHIZOPHRENIA

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Background: Older adults with schizophrenia experience poor community integration and social functioning. These individuals are at elevated risk for functional decline and early institutionalization in long-term care facilities. Deficits in thought, language, and communication are core features of schizophrenia and may worsen with age; however, little research focuses on the functional sequelae of these impairments among older adults with schizophrenia.

Methods: The present study examined the relationships among age, TLC deficits, and functional outcomes in a sample of community-dwelling middle-aged and older adults with schizophrenia (N=245; ages 40–85). Participants completed assessments of symptoms, neurocognition, TLC deficits, and functional outcomes. Two different categories of TLC deficits were examined: verbal underproductivity (i.e., alogia) and disconnected speech.

Results: Regression analyses found that disconnected speech predicted impaired occupational functioning, while verbal under productivity predicted capacity to communicate skillfully in semi-structured social situations, as well as community functioning across interpersonal, occupational, and everyday living domains. Exploratory mediation analyses found that cognitive impairments were mediated by disconnected speed but not under productivity on certain functional outcomes.

Discussion: Targeted training to improve TLC deficits, especially verbal underproductivity, among older adults with schizophrenia could have downstream effects on community functioning, improving outcomes for a vulnerable group. It is likely that cognitive training interventions would also facilitate these interventions.

25. OLIGODENDROCYTE-BASED IMPAIRMENT OF BRAIN CONNECTIVITY AS TARGET FOR NEW TREATMENT STRATEGIES IN SCHIZOPHRENIA

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