Methods A graph theoretical approach was used to analyse the connectivity in networks centered on:
– Broca's area;
– Wernicke's area.
Connectivity information was acquired using diffusion tensor imaging (DTI).
Results Compared to healthy controls, adolescents with schizophrenia displayed a lower average degree of connectivity with the left inferior frontal gyrus (Broca's area). No significant differences were found in the degree of connectivity with the right inferior frontal gyrus and the superior temporal gyrus bilaterally (Wernicke's area).
Conclusions The results suggest a link between schizophrenia and impairment to areas where CDs associated with inner speech plausibly originate.
Disclosure of interest The authors have not supplied their declaration of competing interest.

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S03

GRIN2B mediates susceptibility to affective problems in children and adolescents

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Objectives Association studies have implicated the N-methyl-D-aspartate receptor 2B subunit gene (*GRIN2B*) as candidate for different brain illnesses, also including both internalizing and externalizing disorders. Here, we explored the association between selected SNPs of GRIN2B (rs5796555-/A; rs1012586C/G; rs2268119A/T; rs2216128A/G; rs11609779C/T; rs2192973G/A) and attention problems in children an adolescents as assessed by CBCL 6/18 (Achenbach and Rescorla, 2001).
Methods In a large cohort of 320 Italian nuclear families selected from an ongoing comprehensive project on child and adolescent psychopathology performed at two sites of our Institutes (BP and UD), we performed a family-based association study to determine whether the *GRIN2B* gene influence and/or mediates susceptibility to attention problems through time. Genetic association was investigated by the quantitative transmission disequilibrium test (QTDT, version 2.5.1; Abecasis et al., 2000). Quantitative traits were analyzed using the '-wega' and the '-ao' options. Empirical *P*-values were computed from 10,000 Monte-Carlo permutations, and the significance levels were adjusted by the false discovery rate method (Storey, 2002) applied to the tests performed for each marker (i.e., 8 phenotypes) at two different point times. Latent profile analysis was performed to assess the effect of gene on different trajectories over time. The effect of environmental determinants was also evaluated.
Results Evidence for significant association of GRIN2B-rs5796555-/A was found with attention problems both at first and second evaluation. Latent profile analysis suggested significant association with specific trajectories and specific environmental factors.
Conclusions These results provide preliminary evidence of an association between the GRIN2B polymorphism and continuity of attention problems throughout adolescence within an Italian population of referred children and adolescents, suggesting that the *GRIN2B* genes could play a role in susceptibility to attention problems during developmental age.
Disclosure of interest The author has not supplied his declaration of competing interest.

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Biological markers of short-term and long-term treatment outcome in mental disorders

S04

Brain glutamate levels and antipsychotic response in schizophrenia

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There is considerable interest in identifying biomarkers of antipsychotic response in schizophrenia. Glutamate is one key candidate. The development of brain imaging techniques for measuring brain glutamate levels has allowed this hypothesis to be tested directly in patients. This talk will present our ongoing research examining the relationship between brain glutamate levels and antipsychotic response in first-episode psychosis and in treatment-resistant schizophrenia. I will summarise our results from both our completed and ongoing studies, to consider whether glutamate imaging might be useful in the future to identify patients who would benefit from non-dopaminergic antipsychotic drugs and inform novel, glutamate-based, treatment strategies.
Disclosure of interest The author has not supplied his declaration of competing interest.

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S05

Biochemical and genetic markers in patients with alcohol dependence and affective disorders and their correlation with alcohol intake

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Rates of comorbid affective disorders in alcohol-dependent individuals are significant. Biomarkers of alcohol use may support the diagnosis of high and frequent alcohol use in these individuals. The aim of these analyses of the WHO-ISBRA Study on State and Trait Markers of Alcohol Use and Dependence is to compare biomarkers of alcohol use across individuals with and without comorbid alcohol dependence and affective disorders. Significantly, higher values of these biomarkers are hypothesized in individuals with comorbid disorders compared to alcohol dependence only. Assessment of Alcohol dependence and comorbid depression and bipolar disorders were conducted using an adapted version of the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS). Altogether, $n = 1863$ individuals were included into the analyses, of whom $n = 299$ had a lifetime history of depression and $n = 20$ a bipolar disorder. Clinical characteristics like mean alcohol intake last month and biomarkers including ASAT, GGT, CDT, 5-HTOL/5-HIAA ratio and MAO-Activity were included into the analyses. Results indicate that AD only subjects had higher measures of all biomarkers compared to comorbid bipolar and depression subjects, while the latter had a higher alcohol intake during last month.
Since this is a cross-sectional study, conducted in emergency rooms of several countries, this allegedly divergent result in alcohol intake in comorbid subjects compared to higher biomarkers in AD only subjects may indicate that drinking is more frequent in alcohol-dependent individuals while bipolar and depressed subjects may have more episodic pattern of alcohol intake. The latter may lead to shorter periods of intake compared to the chronic and frequent

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use of this substance in alcohol-dependent individuals and higher biomarkers of alcohol use.
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S06

Potential relationship between inflammatory markers, neuroimaging findings and treatment response in depression

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Pharmacological therapy in mental disorders is usually effective in 60–70%, the treatment reaction is worsening with the disease progression, and proper medication and early treatment regimen choice is crucial. Research showed that specific brain changes (structural and functional) are present in depressed patients. These abnormalities are probably linked to neurodegeneration. There is also an evidence that inflammation contributes to the depression pathophysiology, and both these processes – neurodegeneration and inflammation are related.
Novel biological markers allow us to better understand the individual mechanisms of treatment response in depression. Recently, several biological measures have been proposed, amongst them – neuropsychological dysfunction, decreased GABA level in proton magnetic resonance spectroscopy (^{1}H MRS), body weight, genetic factors and peripheral inflammatory markers. Latest research found that brain changes assessed with neuroimaging methods (including ^{1}H MRS, e.g. glutamatergic system abnormalities), correlate with peripheral inflammatory markers. Furthermore, both these factors taken together may serve as one integrated treatment prediction marker in depressed patients.
Disclosure of interest The author has not supplied his declaration of competing interest.

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Bipolar disorders: From detection to intervention

S07

Developmental trajectories to bipolar disorder

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Background Childhood subclinical phenotypes have been informative for etiological research and as a target for preventative interventions. Using a prospective longitudinal general population cohort we investigated whether childhood manic symptoms predicted a diagnosis of bipolar disorder (BD) or other psychiatric disorders by early adulthood.
Methods Subthreshold manic symptoms at age 11 years (n = 1907) and clinical outcomes by age 19 years (n = 1584) were ascertained in the TRacking Adolescents' Individual Lives Survey (TRAILS), a prospective Dutch community cohort. We used latent class analysis to stratify TRAILS participants at age 11 years into distinct classes based on the pattern and severity of childhood manic symptoms. We then determined the association between class membership and clinical diagnoses by age 19 years.
Results At age 11 years, we identified a normative class with negligible symptoms (n = 862), a mildly symptomatic (n = 846) and a highly symptomatic class (n = 199). The risk of BD was moderately increased in individuals in the mildly symptomatic class (OR = 2.65, 95% CI 1.41–5.01), and substantially increased in the highly symptomatic class (OR = 7.08, 95% CI = 3.32–15.11). Children in the highly symptomatic class were additionally characterized by lower IQ and socioeconomic status, greater family dysfunction and increased rates of parental psychiatric morbidity. Class membership did not show significant associations with depressive, anxiety and substance abuse disorders by age 19 years.
Conclusions The results provide support to developmental models of BD, and suggest that manic symptoms in childhood may be a marker for adult disorders and therefore potentially useful for early identification of at risk individuals.
Disclosure of interest The author has not supplied his declaration of competing interest.

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S08

Protecting the cardiometabolic health of young people experiencing psychosis

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This presentation will highlight how the early phase of major mental illness may provide a critical window of opportunity in which to prevent future life-restricting and life-shortening physical comorbidities.
Despite many recent advances in our understanding of severe mental illnesses, those affected still lose 15–20 years of life on average compared to the general population. Most premature deaths arise from the same common disorders that affect the general population such as cardiovascular disease, infections and cancers. Of these cardiovascular diseases is now the single biggest cause, far greater than suicide. Shockingly the mortality gap is still widening as the reduction in CVD morbidity and mortality seen in the general population over the last three decades continues to elude people with severe mental illnesses, for whom the prevalence of CVD, obesity and diabetes are now of epidemic proportion.
And yet, much of this epidemic can be predicted. High rates of tobacco use, physical inactivity and poor nutrition point to underlying health inequalities. Furthermore, initiation of antipsychotic treatment is associated with aggressive weight gain and metabolic disturbance from the early phase of psychosis, and yet often these adverse effects remain unmonitored and untreated.
This presentation will argue that these potentially modifiable risk factors provide natural targets for prevention from the onset of psychosis and its treatment. Extending the early intervention paradigm to embrace a far more holistic body & mind approach is overdue.
Disclosure of interest The author has not supplied his declaration of competing interest.

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S09

Implementing the clinical standards of the National Institute for Health and Care Excellence (NICE) bipolar clinical guideline

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In the UK, the National Institute for Health and Care Excellence (NICE) sets standards for interventions to drive improvement in the quality of services delivered. The actual update of clinical guidelines remains patchy and difficult to ascertain.