who do not make the transition to psychosis. Verbal fluency may contribute to an improved prediction of psychosis in UHR patients. Follow up results will also be presented.

S55.04

The perception of expressed emotion in young people at high-risk of psychosis

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Objectives: The European Prediction of Psychosis Study (EPOS) involved a large (n=245) sample of young individuals at high-risk of developing psychosis. Participants appraisals of criticism and emotional over-involvement were described employing the Level of Expressed Emotion (LEE) measure. This presentation explores results and implications over an 18 month follow-up period.

Methods: Across six European centres, n=245 patients aged 16 – 35 years and ascertained to be at high-risk of developing psychosis were assessed over a period of eighteen months. Risk of psychosis was defined by occurrence of basic symptoms, attenuated psychotic symptoms, brief, limited or intermittent psychotic symptoms or familial risk plus reduced functioning. Appraisals of familial expressed emotion from participants towards key family members were examined for relationships to risk of transition to psychosis, psychotic symptomatology and demographical data.

Results: Individuals at high-risk of psychosis were included and compared on the five sub-scales of LEE. Levels of Criticism, Irritability, Intrusiveness and Lack of emotional support were examined with significant correlations found between patient-perceived intrusive over-involvement and depression as well as between sub-scales of LEE and positive symptoms of psychosis. Transition to psychosis was not predicted by LEE in participants.

Conclusions: Perceived LEE of significant others by individuals at high-risk of developing psychosis may have a role in the maintenance of both affective and positive psychotic symptoms prior to the onset of full psychosis. Further explorations of the impact of EE appraisal on developing psychotic symptoms may inform potential targets for therapeutic intervention in both at-risk individuals and family members.

Symposium: Neuropsychobiology of inhibitory deficits in schizophrenia: An update

S57.01

Antisaccade deficits in subjects either genetically or clinically at risk for schizophrenia

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Background and Aims: Disturbances of the oculomotor system are promising endophenotypes for schizophrenia. In two separate studies, we examined antisaccade task performance, a measure of inhibitory control, in first degree relatives of schizophrenic patients (genetic risk without manifest disorder) and in clinical high risk subjects with symptoms suggestive of a prodromal phase of schizophrenia.

Methods: In the first study, 41 parents of schizophrenia patients and 22 controls were tested with with a prosaccade task and an antisaccade task. Parents were grouped into more likely, less likely, and indeterminate risk carriers. The second study involved 160 subjects clinically at risk for schizophrenia, 32 first episode schizophrenic patients, and 76 healthy controls.

Results: In study 1 we found an increase of antisaccade latencies and error rates in parents of schizophrenics which varied with inferred genetic load, more likely gene carriers performing worst. In study 2, antisaccade performance varied with symptom load: subjects at risk with basic symptoms only were unimpaired, while at-risk subjects who had experienced brief psychotic episodes (BLIPS) showed deficits similar to first episode patients.

Conclusions: Reduced inhibitory control of oculomotor performance is associated with genetic loading for schizophrenia, and also with symptoms placing subjects at imminent risk of psychosis.

S57.02

Imaging and pharmacological studies of oculomotor inhibition

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The antisaccade task is a model of the conflict between an unwanted reflexive response (which must be inhibited) and an appropriate volitional response (which must be generated). In this talk I will present a study of the neural correlates of these cognitive components separately using a delayed saccade paradigm to dissociate saccade inhibition from generation. Event-related functional magnetic resonance imaging (fMRI) was carried out in healthy human volunteers. It was found that the right supramarginal gyrus showed significantly greater activation during response inhibition compared to response generation, suggesting a role in saccade inhibition or stimulus detection. The right lateral frontal eye field and bilateral intraparietal sulcus showed evidence of selective involvement in antisaccade generation. Ventrolateral and dorsolateral prefrontal cortices showed comparable levels of activation in both phases of the task. These areas likely fulfil a more general supervisory role in the volitional control of eye movements, such as stimulus appraisal, task set, and decision making. The findings will be discussed in relation to data suggesting that antisaccade deficits constitute an endophenotype for schizophrenia and in relation to pharmacological studies of brain function during antisaccade eye movements.

S57.03

Prepulse inhibition as a marker of prefrontal function: Studies in healthy individuals

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Prepulse inhibition (PPI) refers to the attenuation of the amplitude of the startle reflex in response to sudden intense stimuli (pulse) if preceded by a weaker sensory stimulus (prepulse). PPI reflects sensorimotor gating i.e. the ability to filter out irrelevant information in the early stages of processing so that attention can be directed to more salient environmental features. Recent neuropsychological studies show greater PPI in healthy individuals with superior performance on tasks that rely on the integrity and efficiency of prefrontal cortical (PFC) function. The PFC is an important node in the cortico-striato-pallido-thalamic circuitry, which modulates PPI. PFC function has been examined in relation to the COMT Val158Met polymorphism, which determines basal PFC dopamine (DA) neurotransmission levels and consequently, performance on PFC DA-dependent cognitive tasks. Met/Met individuals have the best PFC performance or greater ''efficiency'' and the highest PPI, Val/Val the worst performance and the lowest PPI, and Val/Met intermediate performance and PPI. Consistent with the increasingly accepted model of an inverted U-shape relationship between PFC DA levels and PFC function, the COMT inhibitor tolcapone as well as attention-to-prepulse, increase PPI in Val/Val individuals, while Met/Met individuals are unaffected or get worse. These findings strongly suggest that inhibition at the early stage of information processing is modulated by the PFC DA activity in a ''top-down'' fashion and this may account for the normal inter-individual variability in PPI and in cognitive performance.

S57.04

Impaired sensorimotor gating of the acoustic startle response in the prodrome of schizophrenia

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Schizophrenia patients exhibit impairments in prepulse inhibition (PPI) of the acoustic startle response (ASR). PPI is commonly used as an index of sensorimotor gating. Results of animal studies and some human data suggest that PPI deficits are in part genetically determined, such that PPI could be an endophenotypic indicator of risk for schizophrenia, Thus, PPI deficits should already be present prior to onset of psychosis. To test this assumption, we investigated PPI in individuals with prodromal symptoms of schizophrenia and patients with first-episode schizophrenia.

Startle reactivity, habituation, and PPI of ASR were assessed in 54 subjects with prodromal symptoms of schizophrenia (35 at an early prodromal stage, 19 at a late prodromal stage), 31 first episode schizophrenic patients (14 unmedicated, 17 medicated), and 28 healthy controls. Patients were also examined with the Positive and Negative Symptom Scale and the Global Assessment of Functioning Scale.

Prodromal subjects and unmedicated patients with first episode schizophrenia showed significant PPI deficits, whereas schizophrenic patients treated with risperidone had almost normal PPI. In contrast, startle reactivity decreased with severity of symptoms but was relatively unimpaired in the medicated patients. With respect to habituation, prodromal subjects and schizophrenic patients did not differ from healthy controls.

PPI disruption is present in subjects in a prodromal state likely to proceed to schizophrenia, supporting the hypothesis that PPI disruption is an endophenotype of schizophrenia. In contrast, startle reactivity and habituation deficits were not evident in the prodromal subjects, but only in unmedicated patients with diagnosis of schizophrenia.

S57.05

Imaging and pharmacological studies of prepulse inhibition in schizophrenia

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A key feature of schizophrenia is the inability to screen out irrelevant sensory input. Prepulse inhibition (PPI) of the startle response, a cross-species measure of sensorimotor gating, provides a valuable opportunity to study this feature. Patients with schizophrenia, first-degree relatives of patients with schizophrenia, patients with schizotypal personality disorder and healthy individuals scoring high on psychometric measures of psychosis-proneness display reduced PPI. Animal models of disrupted PPI have proved valuable for the evaluation of existing and potential new treatments for schizophrenia. Animal studies have also shown that PPI is modulated by the cortico-striatal-pallido-thalamic circuitry involving the prefrontal cortex, thalamus, hippocampus, amygdala, nucleus accumbens, striatum, ventral pallidum, globus pallidus, and subpallidal efferents to the pedunculopontine nucleus. Recent neuroimaging data from our and other laboratories confirm the involvement of this circuitry in (a) normal PPI in healthy people, (b) deficient PPI in patients with schizophrenia and related conditions, and (c) the effects of pharmacological agents relevant to the treatment of schizophrenic illness.

Symposium: The cognitive abnormalities as markers of abnormal brain activation

S61.01

Cognitive assessment using cog-test battery of abnormal brain activation

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Cognitive impairment is a core deficits in schizophrenia and in bipolar disorders. The cognitive dysfunctions are related to the abnormal brain activation in these illnesses. Working memory and executive dysfunctions associated with prefrontal cortex abnormalities in these illnesses are known as an neuropsychological marker of vulnerability to the diseases.

The most important methods used in assessment of abnormal brain activation are neuroimaging methods and neuropsychologial tests. Current data show high coincidence between the level of performance on cognitive tests and activation of the brain. The data obtained in patients with schizophrenia and bipolar disorder show the significant association between level of hypofrontality (decrease of blood flow and intensity of glucose metabolism) and the level of impairment of the performance of prefrontal tests.

The Cogtest Battery it the novel computerized neuropsychological battery used for cognitive screening in different mental and neurological diseases. This battery consisted with tests for evaluation different domains of cognition, such as frontal functions (working memory and executive functions), verbal abilities (connected mostly with left hemisphere activation), attention, psychomotor speed, spatial and motor performance, memory and learning (associated with temporal lobe activation). Based

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