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

B.B. Quednow [1,2], I. Frommann [1], J. Berning [1], K.U. Kühn [1], W. Maier [1], M. Wagner [1]. [1] *Department of Psychiatry, University of Bonn, Bonn, Germany* [2] *Psychiatric University Hospital, University of Zurich, Zurich, Switzerland*

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

V. Kumari. *Department of Psychology, Institute of Psychiatry, Kings College London, London, UK*

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

S. De Santi. *NYU School of Medicine, Center for Brain Health, New York, NY, USA*

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

https://doi.org/10.1016/j.eurpsy.2008.01.255 Published online by Cambridge University Press

on gold standard paper and pencil tests. The computer version of the tests and touch screen make possible to examine patients with motor disabilities - such as patients with Parkinson's Disease. The specific data management system make possible to eliminate data with artifacts.

Selected tests from the system are used as a cognitive stimulation during neurophysilogical assessment (EEG, EMG, EOG) and during neuroimaging, especially with F-MRI.

S61.02

Neuromaging of cognitive impairment in schizophrenia and neurodegenerative disorders

T. Sharma. *The Cognition Group, Newark, DE, USA*

Cognitive dysfunction such as impairment of memory, attention, spatial and verbal functions plays important role in etiopathogenesis and clinical picture in neurodegenerative disorders. There are related with structural and functional abnormalities of different region of the brain connected with these cognitive processes. Cognitive dysfunctions caused severe functional and social disabilities of the patients. The neuroimaging methods such as F-MRI, or PET scan are very useful in diagnosis of structural and functional changes in the brain in neurodegeneration diseases, e.g. Parkinson's or Alzheimer's diseases. Neuroimaging during cognitive stimulations show different brain activation in patients with schizophrenia or neurodegenerative disorders in comparison to healthy subjects. F-MRI show increase of prefrontal cortex activation during n-Back test performance in healthy controls, while in patients with schizophrenia and Alzheimer disease this effect was not noted. In schizophrenia patients after treatment with risperidone (but not with haloperidol) the normalization of activation in different brain area was observed.

F-MRI assessment during N-back test (0 - back and 1-back tasks), encoding and recognition, visual discrimination performed in 9 patients with Alzheimer's Disease (AD) and 9 healthy subjects show abnormal activation in patients with AD. Among 9 patients with AD 5 were treated with rivastigmine, 4 received placebo. Cognitive improvement was observed after 3 months of treatment with rivastigmine - the same time fMRI showed an increase in brain activity in regions involved in attentional processes. This indicate that neuroimaging methods during cognitive stimulation may be useful in cognitive assessment in CNS disorders and in assessment of drug effect on cognition.

S61.03

Glutamatergic and dopaminergic system genes polymorphism in prefrontal tests performance in schizophrenia, bipolar disorders and in healthy subjects

A. Borkowska. *Clinical Neuropsychology Department, Nicolaus Copernicus University Torun, Collegium Medicum, Bydgoszcz, Poland*

Prefrontal functions impairment in schizophrenia and bipolar disorder are are markers of vulnerability to the diseases. Our previous data showed association between Wisconsin Card Sorting Test (WCST) performance in schizophrenia with the polymorphism of dopaminergic genes)COMT, DRD 1) and with polymorphism of Brain-derived neurotrophic factor (BDNF) in bipolar disorders. The Src-family tyrosine kinase Fyn plays important role in the interaction between BDNF and glutamatergic receptor NMDA in prefrontal cortex. The possible association between the polymorphisms of BDNF and Fyn genes and performance on WCST and N-back tests in healthy subjects were assessed in 200 healthy persons, genotyped for the two polymorphism of BDNF gene (C/T, Val66Met) and three polymorphisms of the Fyn gene (-93 A/G, IVS10+37T/C, Ex12+894T/G). In the whole group, the T/T genotype of C-270T BDNF polymorphism was associated with higher percentage of conceptual responses on WCST. Male subjects with C/T genotype obtained better results on percentage of correct reactions in N-back test. No significant differences between any of Fyn gene polymorphisms and WCST performance were found. Better results on percentage of correct reactions in N-back test were obtained by subjects with G/G genotype of 93A/G polymorphism and with G/G genotype of FYN T/G polymorphism. Female subjects having T/T polymorphism of T/C polymorphism performed better as to percentage of correct reactions in N-back test. The results obtained may suggest a contribution of BDNF and glutamatergic system genes to working memory efficiency in healthy subjects and bipolar disorder, while in schizophrenia with dopaminergic system genes.

S61.04

Neuropsychological prefrontal dysfunction in pathological obesity in the molecular genetics context

A. Tretyn. *Institute of Biology, Nicolaus Copernicus University, Torun, Poland*

Pathological obesity may be related with impairment of impulse control and cognitive disturbances. In this study the cognitive frontal functions in relation to the polymorphism of candidate genes in patients with pathological obesity were assessed. The prefrontal functions were evaluatedmusing Wisconsin Card Sorting Test. The polymorphisms of genes connected with serotoninergic and dopaminergic system : 5HT2A, 5HT2C, 5HTT, DAT1, and COMT, and also the polymorphism of BDNF - involved with modulation of nervous system development and neuroplasticity were assessed. Polymorphisms of the genes were detected by RFLP and VNTR PCR methods.

The 100 subjects with pathological obesity, BMI>40 operated with Mason method were enrolled. The results of WCST were compared with the results of healthy sex, age and education matched controls.

Subjects with pathological obesity show significant worse results on all domains of WCST, compared to controls. The frequencies of the polymorphisms in the obese group were: 5HT2A -1438A->G - A/A - 11%, A/G - 50%, G/G - 39%; DAT1 VNTR in 15th exon - short/short - 13%, short/long - 34%, long/long - 53%; BDNF Val66Met (G->A) - A/A - 3%, A/G - 24%, G/G - 73%. Interesting results were obtained in the case of 5HT2C: a known polymorphism (-759C->T) could not explain the banding pattern observed. It is possible that we have found a novel polymorphism that strongly correlates with obesity. The results obtained show significant prefrontal dysfunctions in patients with pathological obesity which may be related to the polymorphisms of serotonin and dopaminergic system genes and possible association of the obesity with the new polymorphism of 5HT2C gene.

Symposium: Family burden: Dimensions, determinants and interventions

S50.01

Caregiver burden during a 2-year follow-up period

A.M. Moeller-Leimkuehler. *Department of Psychiatry, Ludwig-Maximilians-University, Munich, Germany*

https://doi.org/10.1016/j.eurpsy.2008.01.255 Published online by Cambridge University Press