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Objective: Ventricular enlargement is one of the most consistent brain changes associated with schizophrenia. However, there are only few cross-sectional studies in genetic at risk individuals, and no studies in individuals meeting ultra high risk (UHR) criteria of developing frank psychosis. This study investigates the timing of ventricular volume changes across the different stages of emerging psychotic disorders.

Methods: We measured ventricular volumes in 473 subjects comparing 135 UHR subjects (of whom 39 subsequently developed a psychotic illness), 162 first-episode psychosis (FEP) subjects, 89 chronic schizophrenia (CS) subjects with 87 normal controls (NC). 29 UHR, 25 FEP, 13 CS, and 24 HV had longitudinal follow up scans.

Results: We found significant ventricular enlargement in FEP and CS, but not in UHR and NC. Longitudinal analysis confirmed ventricular enlargement in non-affective psychosis only. UHR patients had normal ventricular volumes regardless of whether they made transition to frank psychosis or not.

Conclusion: Our results are suggestive that ventricular enlargement is a consequence of transition and/or progression of illness rather than a risk marker in that it is apparent only after the onset of frank psychosis, with prominence in patients with schizophrenia-like psychoses. The results parallel our previous study in that hippocampal volumes were reduced in CS and normal in patients having non-schizophrenic psychoses as well in UHR individuals.

S18.05

Association of regional grey matter abnormalities with cognitive functions in the at risk mental state

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Objective: There is some evidence that psychosis and its prodrome are associated with neuroanatomical abnormalities and cognitive deficits. However, the brain structure - cognition associations in this disorder are less clear. The aim of the study was to investigate brain structure – cognition associations in individuals with an At Risk Mental State (ARMS) relative to patients with first-episode psychosis and healthy volunteers.

Methods: The subjects were recruited through a specialised clinic for the early detection of psychosis (FEPSY) at the Psychiatric Outpatient Department, University Hospital Basel. We examined structural brain abnormalities, identified using voxel-based morphometry (VBM), and cognitive function (general intelligence, attention, executive function, and working memory) in 32 individuals at high risk of developing psychosis (ARMS), 22 patients with a first-episode psychosis and 11 healthy volunteers.

Results: We expect that regional grey matter volume abnormalities are associated with specific cognitive deficits in people with an ARMS.

Conclusions: We predict that some associations are specific to individuals with an ARMS and may be a correlate of their increased vulnerability to psychosis. Furthermore, we expect structure – cognition associations within the high risk group to be associated with the subsequent onset of psychosis.

S19. Symposium: PSYCHIATRY AND THE CULTURES OF SUBJECTIVITY (Organised By The AEP Section on Philosophy And Psychiatry)

S19.01

On capturing subjectivity in narrative

T. Thornton. *Department of Philosophy and Mental Health, University of Central Lancashire, Preston, Lancashire, United Kingdom*

In this paper I distinguish between two claims. 1) That subjects or selves are constituted by narratives. 2) That narratives play an essential and irreducible role in capturing subjectivity. I will argue that whilst the reduction of selves to narratives - in claim 1 - fails, claim 2 helps highlight the essential role of normativity in characterising subjects' mental lives. But the irreducibility of normativity places principled limits on the range of phenomena on which psychiatry can aim to shed light.

S19.02

Subjectivity and cultures in psychiatry

D. Moussaoui. *Psychiatric Centre, Ibn Rushs University, Casablanca, Morocco*

Subjectivity is an essential part of psychiatry, often forgotten in daily clinical work, despite the remarkable demonstrations done by the German school of phenomenology in the 20th century concerning this aspect of our specialty.

As a matter of fact perception of internal and external time, social space, relationship to pleasure and religion are essentially linked to culture. One of the most important determinants of culture is economy, which is itself largely determined by geography and history of the region.

The author will present the intertwine existing between these variables, and its impact on the clinical picture and the subjective interpretation of the patient, taking depression as a model for this theoretical construction.

S19.03

Objective evidence and subjective narratives in medicine and psychiatry

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Evidence Based Medicine and Psychiatry has had a (controversial) success in the last years. Narrative Based Medicine and Psychiatry has emerged subsequently as a complementary (not an alternative) movement. The object of this presentation is the following question: To what extent are these movements something new for medical science? Or, to what extent are they simply the current expression of an age-old tradition in the history of medicine and psychiatry? Our objective here is to review a series of possible (and scantily commented) historical antecedents, not so much of Evidence- and Narrative-Based Medicine and Psychiatry in themselves, as of the scientific aspirations and the human needs that are behind them.

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S19.04

Psychiatric epistemology in Spain: ideas and models

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Keeping in mind the constrictions and limitations that have marked the development of Spanish psychiatry during a good part of the 20th century, it is not surprising that its contributions to the epistemological and methodological foundations of psychopathological knowledge have been relatively scarce if compared with other countries and national traditions. Nevertheless, the writings of some outstanding authors include valuable reflections and theoretical insights that go beyond the mere reception of foreign ideas. Apart from the intense concern for anthropological questions or for the problems of existential analysis which were so typical during the central decades of the century, there have been a series of notable contributions related to the concept of understanding in psychiatry, to the development of psychopathology as an objective hermeneutics, to the historical and empirical calibration of the mental symptom and to the theoretical implications stemming from the nature of the psychiatric experience which will be presented and reassessed in the course of this presentation.

S20. Symposium: THE PHENOTYPIC SPECTRUM OF AUTISM CHALLENGED BY GENETIC STUDIES

S20.01

Autism: a molecular plasticity disorder

N. Ramoz [1], A.M. Bestel-Lepagnol [1], G. Maussion [1], J.M. Moalic [1], J.D. Buxbaum [2], P. Gorwood [1], M. Simonneau [1]. [1] *INSERM U675, IFR02, Faculté de Médecine X Bichat, Paris, France* [2] *Laboratory of Molecular Neuropsychiatry, Department of Psychiatry, Mount Sinai School of Medicine, New York, NY, USA*

Background and Aims: Autism (MIM#209850) is a complex neurodevelopmental affection that is largely genetic psychiatric disorder. Several genes have been found associated with autism but their expression levels and neuropathological effects remain unknown in autistic brain.

Methods: We compare the level of expression of autism candidate genes in post-mortem brain region samples between controls and patients. We studied Brodmann area (BA) 46 and the granule cells of the cerebellum lobule 6, for which neuropathological findings and functional abnormalities have been reported in autism.

Results: Different levels of transcription for SLC25A12/AGC1, EN2 and Nr-CAM genes are observed in the cortex and granule cells. Difference of expression are observed between patients and controls. We focused on SLC25A12 for which polymorphisms have been associated to autism in various studies. SLC25A12 encodes the mitochondrial aspartate/glutamate carrier and its function is requested to produce energy in neurons. By hybridation in situ, we analysed the expression pattern of SLC25A12 in human development and we studied the effects of SLC25A12 over-expression on mouse embryonic cortical neurons.

Conclusions: Convergent evidence suggest that level of expression of candidate genes may be involved in autism pathophysiology by modifying neuronal networks and molecular plasticity in specific brain subregions at both pre- and postnatal stages.

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S20.02

From mental retardation to autism: common aspects, common genes

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Background and Aims: Autism and mental retardation (MR) represent an etiologic enigma for clinicians and scientists. It is however considered that these conditions are closely related and are also associated with genetic alterations. The aim of this presentation is to provide an update of findings indicating that MR and autism share some common genetic causes, and to address questions of the cognitive functions involved in these brain disorders.

Methods: Various genetic strategies have shown that autism and MR are associated with identical mutations, raising the hypothesis of common genetic causes. Particularly, the characterization of chromosomal abnormalities has led to define some genomic territories encompassing candidate genes. Furthermore, the study of individuals or families with X-linked MR indicated a significant number of patients with both MR and autism.

Results: Interestingly, many genes involved in autism and MR disorders encode proteins of the postsynaptic density proteome network. Mouse genomic studies have shown specific cognitive abnormalities indicating that the postsynaptic proteome seems to be crucial for the establishment and/or maintenance of the normal cognitive function.

Conclusions: A close relationship exists between MR and autism since 75% of people with autism suffer from MR of varying degree, and 20-30% of people with severe MR exhibit some autistic features. Accumulating data also provides evidence that similar neurobiological pathways would affect both MR and autism. The study of syndromic forms of autism associated with MR should provide a powerful basis for the identification and the understanding of the pathophysiological pathways underlying these two conditions.

S20.03

Do autism and ocd have shared genetic vulnerability?

J.D. Buxbaum [1], N. Ramoz [2], T. Sakurai [1], J. Silverman [1], E. Hollander [1]. [1] *Mount Sinai School of Medicine, New York, NY, USA* [2] *INSERM, Paris, France*

Obsessive compulsive disorder (OCD) is observed at increased rates in first-degree relatives of probands with autism spectrum disorders (ASDs). In addition, OCD-like traits are observed in autism, and in Asperger syndrome. Furthermore, subjects with OCD may have traits that overlap with some aspects of higher functioning ASDs. These observations suggest that OCD and ASDs may share some genetic risk factors. In support of this, it has recently been suggested that both common and rare functional variants in the serotonin transporter (SLC6A4) may increase risk for OCD and/or ASD. We will review our large-scale analysis of common and rare functional variants SLC6A4 in ASDs and relate these results to studies of OCD. In parallel studies, we have carried our linkage analysis in families with ASDs, focusing on those with more severe OCD-like traits. These families demonstrated increased