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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

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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?

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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