Karolinska Institutet

Institutionen för Klinisk Neurovetenskap

Autism spectrum disorder in adults – biological dimensions

AKADEMISK AVHANDLING
som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i Föreläsningssalen Bryggarkungen, Westmanska Palatset, Holländargatan 17, Stockholm

Fredagen den 6 September, 2013, kl 13.00

av

Irina Manouilenko
Legitimerad läkare

Huvudhandledare:
Docent Susanne Bejerot
Karolinska Institutet
Institutionen för Klinisk Neurovetenskap

Bihandledare:
Professor Anna Åberg Wistedt
Karolinska Institutet
Institutionen för Klinisk Neurovetenskap

Marco Pagani, PhD
Institute of Cognitive Sciences and Technologies, CNR, Rome, Italy

Fakultetsopponent:
Professor emeritus Sten Levander
Malmö högskola
Institutionen för kriminologi

Betygsnämnd:
Professor Lisa Ekselius
Uppsala Universitet
Institutionen för Neurovetenskap

Professor Håkan Fischer
Stockholms Universitet
Psykologiska Institutionen

Professor Anne-Liis von Knorring
Uppsala Universitet
Institutionen för Neurovetenskap

Stockholm 2013

Abstract

Autism Spectrum Disorder (ASD) is a group of neurodevelopmental conditions characterized by difficulties in social interaction, communication and the presence of repetitive or stereotyped behaviors. Previous studies have demonstrated structural and functional abnormalities in different brain regions in ASD. Motor difficulties, unusual perception and minor physical anomalies have been reported but not systematically investigated in the adult population with ASD and normal intelligence.

In **Study I**, the internal consistency as well as diagnostic and concurrent validity of the Swedish version of the Ritvo Autism Asperger Diagnostic Scale - Revised (RAADS-R) were evaluated. The results imply that the Swedish version of the RAADS-R has good psychometric properties and is strongly correlated with the Autism Spectrum Quotient (AQ). The RAADS-R captures ASD symptoms and can be used for screening of ASD as well as in the assessment of ASD in adults with normal intelligence.

In **Studies II and III**, regional cerebral blood flow (rCBF) was assessed by positron emission tomography (PET) in thirteen adults with ASD and ten neurotypical controls after psychiatric and neurological assessments. In comparison with the neurotypical controls, individuals with ASD showed significantly increased cerebral blood flow bilaterally in large parts of cerebellum, occipital associative cortex and posterior parietal cortex. In Study III, principal components corresponding to "Autistic/ADHD symptoms", "Sensori-motor integration" and "Intelligence/motor sequencing" were identified by factor analysis based on the normalized scores of 13 neuropsychological measures. The positive correlation between ''Autistic/ADHD traits'' and rCBF in the caudate indicates a possible association of CBF changes with the executive impairments and ritualistic or stereotyped behaviors typical for ASD. Furthermore, "Sensorimotor integration" was correlated with rCBF in the occipital visual cortex, reflecting an atypical visual perception often reported in ASD. Cerebral blood flow in the left thalamus was negatively correlated with all three factors which supports the implication of this brain region in the pathophysiology of ASD. Autistic traits and ADHD symptoms were associated with shared neural substrates whereas sensory-motor deficits were grouped in another independent factor and correlated with rCBF in other regions.

In **Study IV**, minor physical anomalies (MPAs) were investigated in 53 individuals with ASD and 50 age- and gender matched controls. The ASD group showed significantly more MPAs in comparison to the control group. Moreover, MPAs were correlated with severity of symptoms and overall functioning according to the Global Assessment of Functioning (GAF).

On the whole, various behavioral, cognitive, neurological and morphological signs are suggested to converge into the ASD phenotype. Thus, in order to understand the complexity of ASD it seems meaningful to include assessment of ADHD symptoms, subtle neurological abnormalities and minor physical anomalies in the clinical evaluation of adults with ASD.

ISBN 978-91-7549-226-1