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Institutionen för kvinnors och barns hälsa

AUTISM SPECTRUM DISORDERS – GENETIC AND NEURODEVELOPMENTAL ASPECTS IN CHILDREN WITH EARLY DIAGNOSIS

AKADEMISK AVHANDLING

som för avläggande av medicine doktorexamen vid Karolinska
Institutet offentligen försvaras i **Skandiasalen, Astrid Lindgrens
barnsjukhus**

Fredagen den 25 oktober 2013, kl. 09.00

av

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Stockholm 2013

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The overall aim of the thesis was to describe the broad variability in neurodevelopmental profiles in preschool children with autism spectrum disorders (ASD) and to relate these findings to co-existing genetic conditions and other medical disorders. Children in the study were assessed with regard to neurodevelopmental characteristics, before and after intervention, and were recommended genetic testing including chromosomal micro-array. Data concerning parental neuropsychiatric conditions were also collected.

The objective of the first study was to characterize ASD severity, general cognitive and language level and associated co-existing disorders in a population-based group of 208 preschool children (age 20-54 months at first assessment) with a clinical diagnosis of ASD, before the initiation of early intervention at the Autism Centre for Young Children, in Stockholm County. The study set up base-line data for a 2-year follow-up regarding outcome based on adaptive functions. Intellectual disability and developmental delay were found in a large proportion as well as hyperactivity. A regressive trajectory was found in one fifth and epilepsy in 6 %.

In the second study, certain prenatal risk factors were studied in the group of 208 preschool children with early-diagnosed ASD and the data were contrasted to the general population, using the Swedish Medical Birth register. Compared to the general population, fathers of children with ASD were older and parents more often of non-European origin. Mothers of children with ASD had an increased rate of antidepressant and psychoactive medication use, as well as of scheduled caesarean sections. At parental interview, information was also obtained regarding developmental and psychiatric disorders in the family. Fathers and brothers of children with ASD had high rates of ASD including the broader phenotype. Mothers of children with ASD had high rates of depression and other psychiatric disorders. The third study reports all available medical information regarding the 208 children with ASD and preliminary results from genetic analyses. All children had received early intervention, intensive or non-intensive. Outcome at the two-year follow up was measured as change in adaptive function, according to Vineland composite score. A significant genetic or other medical condition was found in 18%. Epilepsy prevalence was now 8.6%. Children with a medical/genetic condition, including epilepsy, had been diagnosed with ASD at an earlier age than those without such conditions and the presence of a medical disorder correlated negatively with adaptive functioning outcome.

In the fourth study, 162 of the 208 children with early-diagnosed ASD were analysed with chromosomal micro-array analysis to detect Copy Number Variants (CNVs) associated as risk factors for autism. Pathogenic aberrations were detected in 8.6 % of the patients, and in an additional 8,6 % variants of uncertain significance were present. CNVs were more frequent in children with congenital malformations or dysmorphic features as well as in children with intellectual disability in addition to ASD. Finally, we explored how parentally transmitted CNVs related to neurodevelopmental and psychiatric conditions in the parents. There was a trend towards increased rates of neurodevelopmental and psychiatric conditions in mothers transmitting a potentially pathogenic CNV as compared to the mothers of children where no CNV was detected.