


MIND*lab*, Interacting Minds, Autism@Aarhus, DNC Seminar:

Autism@Aarhus 2013 Symposium: 3rd Anniversary Meeting
Tuesday 27 August 2013
13.30-16:50
DNC Auditorium, Building 10G
Aarhus University Hospital, Nørrebrogade 44, 8000 Aarhus C.

Please come to the third Autism@Aarhus Anniversary meeting. You will hear what is happening now in autism research within, as well as outside, Aarhus University.

ALL INTERESTED ARE WELCOME. We look forward to seeing you!

PROGRAMME:

13.30-13.35
Uta Frith & Raffaele Rodogno
Welcome & Introduction

13.35-14.05 + 5 mins Q&A
1. **Kai Vogeley** (University of Cologne)
   Nonverbal communication and interaction in high-functioning autism

14.10-14.25 + 5 mins Q&A
2. **Jakob Hohwy** (Monash University)
   Movement under uncertainty: differences in free energy minimization along the autism spectrum

14.30-14.55
3. **Joshua Skewes & Line Gebauer** (Aarhus University)
   Enhanced perception in autism: discrimination, bias, and learning

14.55-15.05
4. **Felix Munch** (Hinnerup Kollegiet)
   Autism advocacy: "Informatør"

15.05-15.30
Break with Refreshments and Poster Session

15.30-15.55
5. **Riccardo Fusaroli & Ethan Weed** (Aarhus University)
   Clinical voices: an update

15.55-16.05
6. **Jakob Christensen** (Aarhus University)
   Prenatal Valproate Exposure and Risk of Autism

16.05-16.35 + 5 mins Q&A
7. **Jørgen Scheel-Krüger** (Aarhus University)
   How animal models can reveal the biological basis of autism: current and future directions

16.40-16.50
Uta Frith
Concluding Remarks

Nonverbal communication and interaction in high-functioning autism

Kai Vogeley (Cologne University)

Social cognition as the capacity to process socially relevant information is an essential component of the human cognitive equipment that allows us to communicate and interact with others and to adapt to complex affordances created by our social environment; seemingly effortlessly we are able to generate impressions and make inferences about the inner experience of others in everyday life. Recent research findings suggest that autistic persons suffer from a specific deficit in the implicit component of social information processing essentially comprising nonverbal communication in contrast to the rule-based explicit component of social cognition. I will focus in my talk on deficits in understanding nonverbal communication cues with a focus on social gaze and their neural correlates in high-functioning autism in adulthood. More recent research endeavours in the field of social neuroscience have started to take true interaction into account. The future outlook will focus on the study of true ongoing interaction and its potential for the understanding of high-functioning autism.

Movement under uncertainty: differences in free energy minimisation along the autism spectrum
Jakob Hohwy (Monash University)

Abstract: Action may be a matter of minimising proprioceptive prediction error, where uncertainty about limb position translates to imprecise proprioceptive predictions. Increased uncertainty should then give rise to less smooth movement. We induced uncertainty about hand position by exposing participants to the rubber hand illusion and observed the smoothness of subsequent reach movements. Based on previous studies, we expected participants with many autism-like traits to have less top-down modulation in uncertain contexts (such as induced by the rubber hand illusion) than participants with fewer autism-like traits. In other words, there should be less smoothness in the reach movements of the less autism-like group than in the more autism-like group; this hypothesis was confirmed. This provides evidence that there are differences in free energy minimisation along the autism spectrum in the healthy population, which pertain specifically to the expected precisions of prediction errors; or in other words to how cues about uncertainty in the context are able to play a role in sensorimotor processing. I discuss how such differences may relate to social cognition in autism spectrum disorder.

Enhanced perception in autism: discrimination, bias, and learning

Joshua Skewes & Line Gebauer (Interacting Minds, Aarhus University)

Scientists have shown that people with autism are better at perceiving fine detail, but that they also have difficulties interpreting contextual meaning. For instance, people with autism are better at recognising pitch, but have trouble using it to interpret emotion in speech. Scientists have started

thinking of these differences in terms of perceptual inference. Look at the picture below. Notice the large, non-existent triangle dominating it? You only see this triangle because the visual system automatically infers it must be there, to account for an arrangement of objects that it would not expect otherwise. This always happens in perception – our perceptual systems use sensory information, but integrate it with prior experience, to represent the world. We will present ongoing research testing a new theory that in autism, prior expectations play a smaller role in perceptual inference, while sensory information plays a correspondingly larger role. We will discuss research examining whether autistic people are better at perceiving detail because sensory information is processed more thoroughly, whether autistic people have difficulties interpreting context because the prior knowledge that is essential for linking sensory information to context is underweighted, as well as investigating the consequences of these phenomena for individual differences in learning style.

Clinical voices: an update

Riccardo Fusaroli & Ethan Weed (Interacting Minds, Aarhus University)

Anomalous aspects of speech and voice, including pitch, fluency, and voice quality, are reported to characterise many mental disorders. However, it has proven difficult to quantify and explain this oddness of speech by employing traditional statistical methods. In this talk we will show how the temporal dynamics of the voice in Asperger's patients enable us to automatically reconstruct the diagnosis, and assess the Autism quotient score. We then generalise the findings to Danish and American children with autism.

Prenatal valproate exposure and risk of autism spectrum disorders and childhood autism.

Christensen J, Grønborg TK, Sørensen MJ, Schendel D, Parner ET, Pedersen LH, Vestergaard M.

BACKGROUND:

Valproate is used for the treatment of epilepsy and other neuropsychological disorders and may be the only treatment option for women of childbearing potential. However, prenatal exposure to valproate may increase the risk of autism.

OBJECTIVE:

To determine whether prenatal exposure to valproate is associated with an increased risk of autism in offspring.

DESIGN, SETTING, AND PARTICIPANTS:

Population-based study of all children born alive in Denmark from 1996 to 2006. National registers were used to identify children exposed to valproate during pregnancy and diagnosed with autism spectrum disorders (childhood autism [autistic disorder], Asperger syndrome, atypical autism, and other or unspecified pervasive developmental disorders). We analyzed the risks associated with all autism spectrum disorders as well as childhood autism. Data were analyzed by Cox regression adjusting for potential confounders (maternal age at conception, paternal age at conception, parental psychiatric history, gestational age, birth weight, sex, congenital malformations, and parity). Children were followed up from birth until the day of autism spectrum disorder diagnosis, death, emigration, or December 31, 2010, whichever came first.

MAIN OUTCOMES AND MEASURES:

Absolute risk (cumulative incidence) and the hazard ratio (HR) of autism spectrum disorder and childhood autism in children after exposure to valproate in pregnancy.

RESULTS:

Of 655,615 children born from 1996 through 2006, 5437 were identified with autism spectrum disorder, including 2067 with childhood autism. The mean age of the children at end of follow-up was 8.84 years (range, 4-14; median, 8.85). The estimated absolute risk after 14 years of follow-up was 1.53% (95% CI, 1.47%-1.58%) for autism spectrum disorder and 0.48% (95% CI, 0.46%-0.51%) for childhood autism. Overall, the 508 children exposed to valproate had an absolute risk of 4.42% (95% CI, 2.59%-7.46%) for autism spectrum disorder (adjusted HR, 2.9 [95% CI, 1.7-4.9]) and an absolute risk of 2.50% (95% CI, 1.30%-4.81%) for childhood autism (adjusted HR, 5.2 [95% CI, 2.7-10.0]). When restricting the cohort to the 6584 children born to women with epilepsy, the absolute risk of autism spectrum disorder among 432 children exposed to valproate was 4.15% (95% CI, 2.20%-7.81%) (adjusted HR, 1.7 [95% CI, 0.9-3.2]), and the absolute risk of childhood autism was 2.95% (95% CI, 1.42%-6.11%) (adjusted HR, 2.9 [95% CI, 1.4-6.0]) vs 2.44% (95% CI, 1.88%-3.16%) for autism spectrum disorder and 1.02% (95% CI, 0.70%-1.49%) for childhood autism among 6152 children not exposed to valproate.

CONCLUSIONS AND RELEVANCE:

Maternal use of valproate during pregnancy was associated with a significantly increased risk of autism spectrum disorder and childhood autism in the offspring, even after adjusting for maternal epilepsy. For women of childbearing potential who use antiepileptic medications, these findings must be balanced against the treatment benefits for women who require valproate for epilepsy control.

How animal models can reveal the biological basis of autism: current and future directions

Jørgen Scheel-Krüger,
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Social interactions are performed by all species of the animal kingdom and are an essential part of survival. Social dysfunction represents a key feature in several psychiatric disorders, including autism, schizophrenia, depression and drug dependence. Unfortunately this key feature remains largely untreated by current medication. It is thus imperative for the development of effective drug treatments of social dysfunctions that we study social behaviour across species, to translate later to the human condition.

Regarding autism there is currently an intense activity in big pharma and at several universities working with various preclinical rodent models of social deficits, which hopefully may translate to some forms of autism. This interest is based on the fact that no drug treatment of today is able to ameliorate the core syndrome of autism: the social behavioural deficits. Current drug treatments are only aimed at reducing co-morbid symptoms of autism, which include repetitive behavior, hyperactivity and inattention (ADHD), irritability and aggression, symptoms that are often seen in early childhood.

Autism represents a gene dependent neurodevelopmental disorder, which in addition to complex interactions of several genetic mutations also seems highly dependent on internal and external factors which produce epigenetic modulations of critical risk genes. Some findings from the current status of these models will be presented.

Recent data from our CFIN autism team suggest that prenatal exposure of valproate (VPA) could provide an animal model for autism with reduced social interaction. In the clinic, it is well known that prenatal exposure to the antiepileptic drug VPA to epileptic women is a high risk factor for cognitive dysfunction in the offspring, which may include autism spectrum disorders. In our model, pregnant rats received a sub-chronic daily administration of VPA at 20 or 100mg/kg from day 12 until the end of pregnancy. This model is thus designed to mimic the human clinical condition with VPA administered chronically to pregnant women with epilepsy. Our model differs from the original VPA model in which only one single high neurotoxic dose of VPA (600mg/kg) is injected at day 12.5 of pregnancy.

The present acute high dose model shows reduced numbers of neurons and various behavioural changes. In contrast, we observe in our new low dose subchronic model increases in neuronal cortical cell numbers in the offspring, a finding we suggest may be related to the stimulatory trophic effect of GABA on the migration of early embryonic cells in the fetal brain tissue in addition to a histone modulation of the DNA chromatine. Our finding of increased cell number is consistent with the results of Courchesne et al (Courchesne E, et al. Neuron number and size in prefrontal cortex of children with autism. JAMA. 2011;306(18):2001-10) reporting an abnormal excess of neurons in the

prefrontal cortex of autistic males. In our model, we also observe decreased juvenile play behavior in young, male VPA rats, consistent with the social deficit observed in human autism. These VPA-rats had a marked decrease in the level of striatal serotonin, a finding consistent with the involvement of serotonin in social play behavior. The adult VPA rats showed enhanced performance in the object recognition test. Ongoing studies are aimed to elucidate the role of the social neurotransmitters involved, serotonin, GABA, dopamine, oxytocin and vasopression.