

---

---

**Autisme Spectrum Disorder**

**&**

**AHDH**

**Mutually Exclusive?!? a Clinical Issue**

**Rutger Jan van der Gaag MD PhD**

**UMC St. Radboud / Karakter UCN**

**University Department Child & Adolescent Psychiatry**

**Nijmegen, the Netherlands**

# Disclosure

---

Rutger Jan van der Gaag

- has received grants from Eli Lilly for drug research trials
- he is on the speakers list for both Eli Lilly and Jansen Cilag

# Outline

---

- Introduction
- ASD & ADHD mutually exclusive?
- Is hyperactivity in ASD always ADHD?  
clinical pitfalls
- Management of co-morbidity
- Tentative conclusions

# Preemption rules in DSM

&

---

---

## clinical reality

- DSM IV has a “pre-emption” rule that says that ASD/PDD prevails over ADHD
- This implies that they cannot be classified conjointly... but could occur simultaneously

# Preemption rules in DSM & clinical reality

---

- This rule has hindered the heuristic effect of classification that is to stimulate research in unknown area's
- It has been longtime abided to strictly:
  - PubMed gives 90 hits on Autism & ADHD
  - 87 from after 2000!

# Research Issues

---

- More emphasis clinical managing issues such as
  - social problems in ADHD
    - Carpenter Rich E, Social functioning difficulties in ADHD: association with PDD risk. Clin Child Psychol Psychiatry. 2009
    - Nijmeijer JS, et al. PDD symptoms in ADHD, an independent familial trait? J Abnorm Child Psychol. 2009

# Research Issues

---

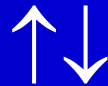
- More emphasis clinical managing issues such as
  - Hyperactivity in ASD
    - Martin et al. 1999

# ADHD & ASD

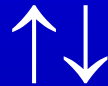
## differences - similarities

---

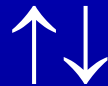
(Epi)Genetics



Brain structure & Physiology



Neuropsychology



Clinical Picture



# ADHD & ASD

## differences - similarities

---

---

### (Epi)Genetics

- 1 Ben-Shachar S et al., Microdeletion 15q13.3: a locus with incomplete penetrance for autism, mental retardation, and psychiatric disorders. *J Med Genet.* 2009 Jun;46(6):382-8. Epub 2009
- 2: Gadow KD et al. Association of ADHD, tics, and anxiety with dopamine transporter (DAT1) genotype in autism spectrum disorder. *J Child Psychol Psychiatry.* 2008
- 3: Niklasson L, ADHD, mental retardation and behavior problems in 100 individuals with 22q11 deletion syndrome. *Res Dev Disabil.* 2009
- 4: de Krom M et al. A common variant in DRD3 receptor is associated with autism spectrum disorder. *Biol Psychiatry.* 2009 Apr 1;65(7):625-30.
- 5: Nijmeijer JS, et al. PDD symptoms in ADHD, an independent familial trait? *J Abnorm Child Psychol.* 2009
- 6: Reiersen AM et al. Evidence for shared genetic influences on self-reported ADHD and autistic symptoms in young adult Australian twins. *Twin Res Hum Genet.* 2008 Dec;11(6):579-85. PubMed PMID: 19016613.

# ADHD & ASD

## differences - similarities

---

### Neuropsychology

- **Executive Functioning**

- Bramham J et al. Executive functioning differences between adults with attention deficit hyperactivity disorder and autistic spectrum disorder in initiation, planning and strategy formation. *Autism*. 2009 –
- White S, O'Reilly H, Frith U. Big heads, small details and autism. *Neuropsychologia*. 2009

- **Attention**

directed – sustained - distractability

# ADHD & ASD

## differences - similarities

---

### Brain structure & physiology

- different growth rates:
  - bigger brains ASD
  - smaller hemispheres in ADHD
- cerebellum?

Tiemeier H et al. Cerebellum development during childhood and adolescence: a longitudinal morphometric MRI study. *Neuroimage*. 2009

# ADHD & ASD

## differences - similarities

---

### Clinical Picture

- When is it appropriate to diagnose ADHD in presence of ASD
  - HYPERACTIVITY ???
  - INATTENTION ???
  - IMPULSIVITY ???

In other words meeting the criteria for ADHD does not imply that comorbid ADHD in se is in play!

# ADHD & ASD

## differences - similarities

---

### Clinical Picture

- HYPERACTIVITY in ASD 60% (Martin et al 1999)
- In our sample (G van de Loo ea) HYPERACTIVITY in 60-70% as a reported symptom but in only 23 cases in 145 consequent ASD children/adolescents with hyperactivity in fact genuine comorbid ADHD
- ADHD symptoms in ASD 40-60% (Hazell et al RUPP 2005) NB with far lower response rate to stimulants (49%) and lower effect size (0,2-0,4)

# Clinical Assessment

---

- “Functional Clinical” appraisal of symptoms of ADHD in individuals with ASD
- Neuropsychological assessment of IQ profile – Attentional functioning – Executive Functioning – Central Coherence

# Managing Hyperactivity in ASD

---

---

- “back to basics”
  - Considering Hyperactivity and/or an increase of stereotypies as a reflection of information overload and too much pressure on every day demands in ASD

# Managing ADHD in ASD

---

- None pharmacological interventions
  - at home – in school – daytime activity centers
  - Structuring
    - Time
    - Space
    - Persons
    - Activities



# Managing ADHD in ASD

---

## Pharmacological interventions

- these are all “off label”
- thus pose strict conditions for informed consent
- PM a case for clinical double-blind placebo controlled trials in individuals with target symptom monitoring

# Managing ADHD in ASD

---

## Pharmacological interventions

- **STIMULANTS**
  - Several well conducted studies
  - Handen et al. (2000) – RUPP (2005)
    - Smaller response rates (40-49%)
    - Smaller effect sizes (0,2-0,4)
    - Higher discontinuation (20%) due to mild adverse effects

# Managing ADHD in ASD

---

## Pharmacological interventions

- **ATOMOXETINE**

- promising Pilot studies (Troost 2006 – Posey 2006)
- recent completed multisite study over 100 patients ASD/ADHDpositive with positive effects reported on the RADAR study by Mirjam Hafterkamp et al. ESCAP 2009

# Managing ADHD in ASD

---

## Pharmacological interventions

- Alpha agonist
  - classic study on effect of clonidine (Jaselskis et al 1992) high effect on reported reduction of “irritability” (by 33%) by parents and teachers

# Managing ADHD in ASD

---

## Pharmacological interventions

- Second generation neuroleptics
  - Risperidone (McCracken 2002 – RUPP 2005 RTC):
    - Significant effects on behavior
    - Weight gain
    - Anxiety as a prominent side effect in this group
  - Olanzapine (Hollander et al 2006 RTC)
    - Clinical improvement “more reachable”
    - Weight gain ++

# Managing ADHD in ASD

---

## Pharmacological interventions

- Second generation neuroleptics
  - Quetiapine (Malone et al. 2001 RTC)
    - Clinical improvement on restlessness
  - Aripiprazole (Strigler 2006 Open label)
    - Strong effect on anxiety - confusability

# Managing ADHD in ASD

---

## Pharmacological interventions

- Clinicians tend to combine stimulants and neuroleptics
- Though rationally illogical
  - pharmaceutically safe and
  - clinically effective

# CONCLUSIONS

---

- ADHD and ASD are genetically linked and have an important clinical overlap that should be carefully considered



# CONCLUSIONS

---

- In clinical practice the ASD management should prime above interventions for ADHD

# CONCLUSIONS

---

- Untangling the psychophysiological mechanisms and the pharmacogenetics will lead to more rational approaches

[R.vanderGaag@karakter.com](mailto:R.vanderGaag@karakter.com)

---

Thanks for your kind attention