Donders Institute
for Brain, Cognition and Behaviour

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ADHD and ASD: two manifestations of the same disorder?

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Radboud University Nijmegen

Potential Conflict of Interest - Jan Buitelaar

	Speaker	Advisory Board	Research Support	Involved in clinical trials
Lilly	X	X	X	X
Janssen Cilag	X	X		X
Medice	X			
Shire		X	X	X
Pfizer		X		
Novartis		X		
Otsuka/BMS		X		
Servier		X		
Roche		X		
Vifar			X	

TS-EUROTRAIN

NWO

ZonMw

Hersenstichting Nederland

NATIONAL INSTITUTES OF HEALTH

Brainview

TRAINING NETWORK ADHD & AUTISM MiND

Social-communication deficits

Fixated interests and repetitive behaviours

ADHD - Core Symptom Areas

ADHD and ASD: two manifestations of the same disorder?

These neurodevelopmental disorders are thought to result from the disruption of normal brain development and related neurobiological mechanisms during the prenatal and early postnatal period

Outline of the talk

- **Clinical issues**
- Genetics
- Cognitive measures
- Brain function and structure
- Implications – new concepts

Autism Spectrum Disorder versus ADHD

ASD and ADHD are developmental disorders with early onset and strong persistence over time

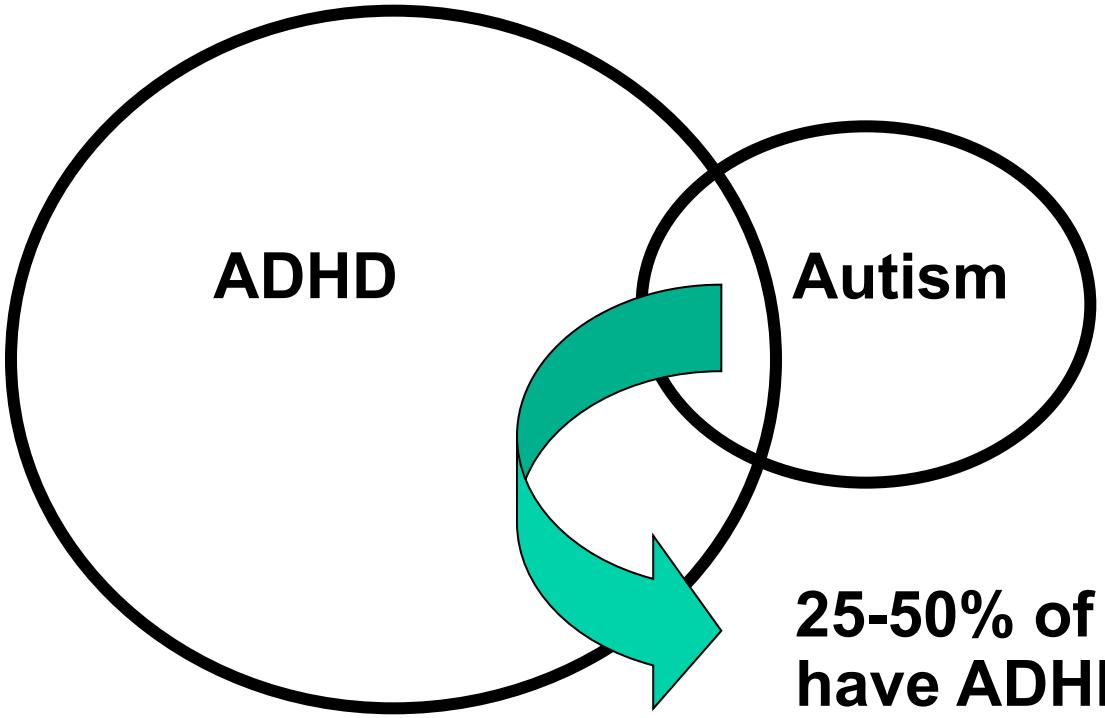
ASD

- **Onset before age 3**
- **>90% persistence into adulthood**

ADHD

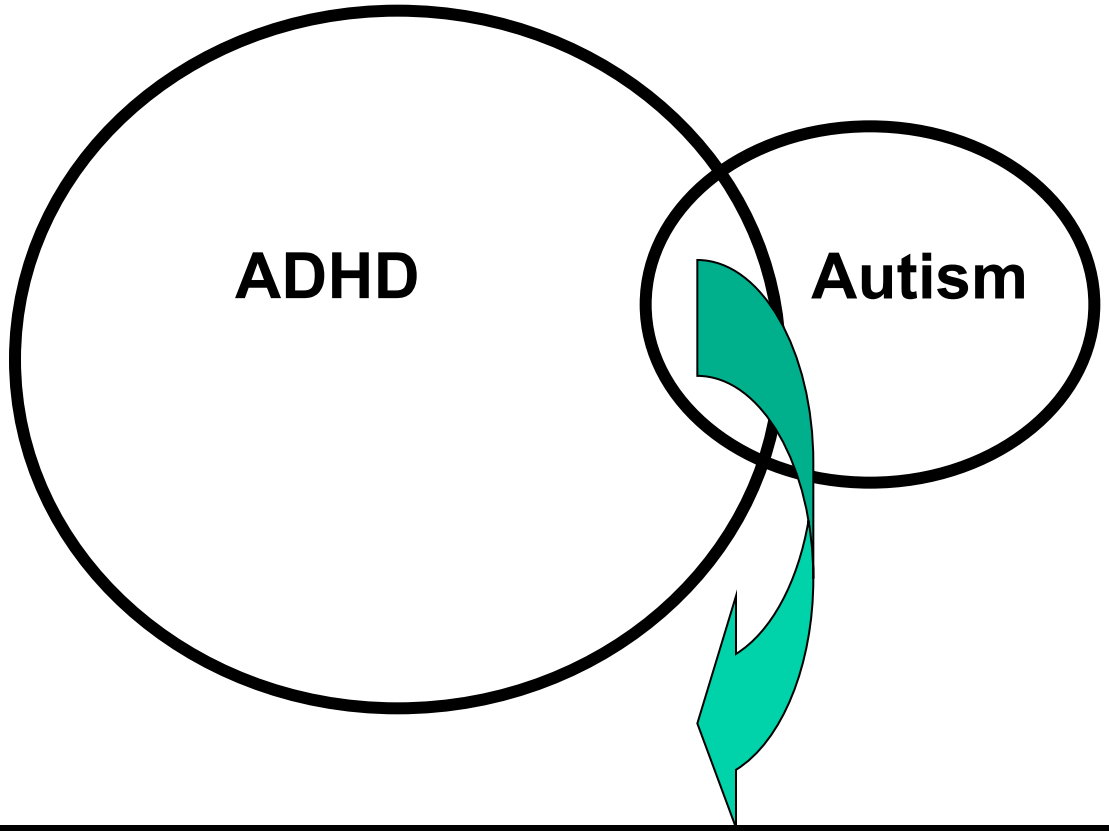
- **Onset before age 12**
- **About 50% have onset at 2-3 year**
- **70% persistence into adolescence**
- **30-50% persistence into adulthood**

Clinical overlap between ASD and ADHD



25-50% of subjects with ASD have ADHD symptoms that merit clinical treatment (for review see Rommelse et al. Eur Child Adolesc Psychiatry 2010,19:281-95.)

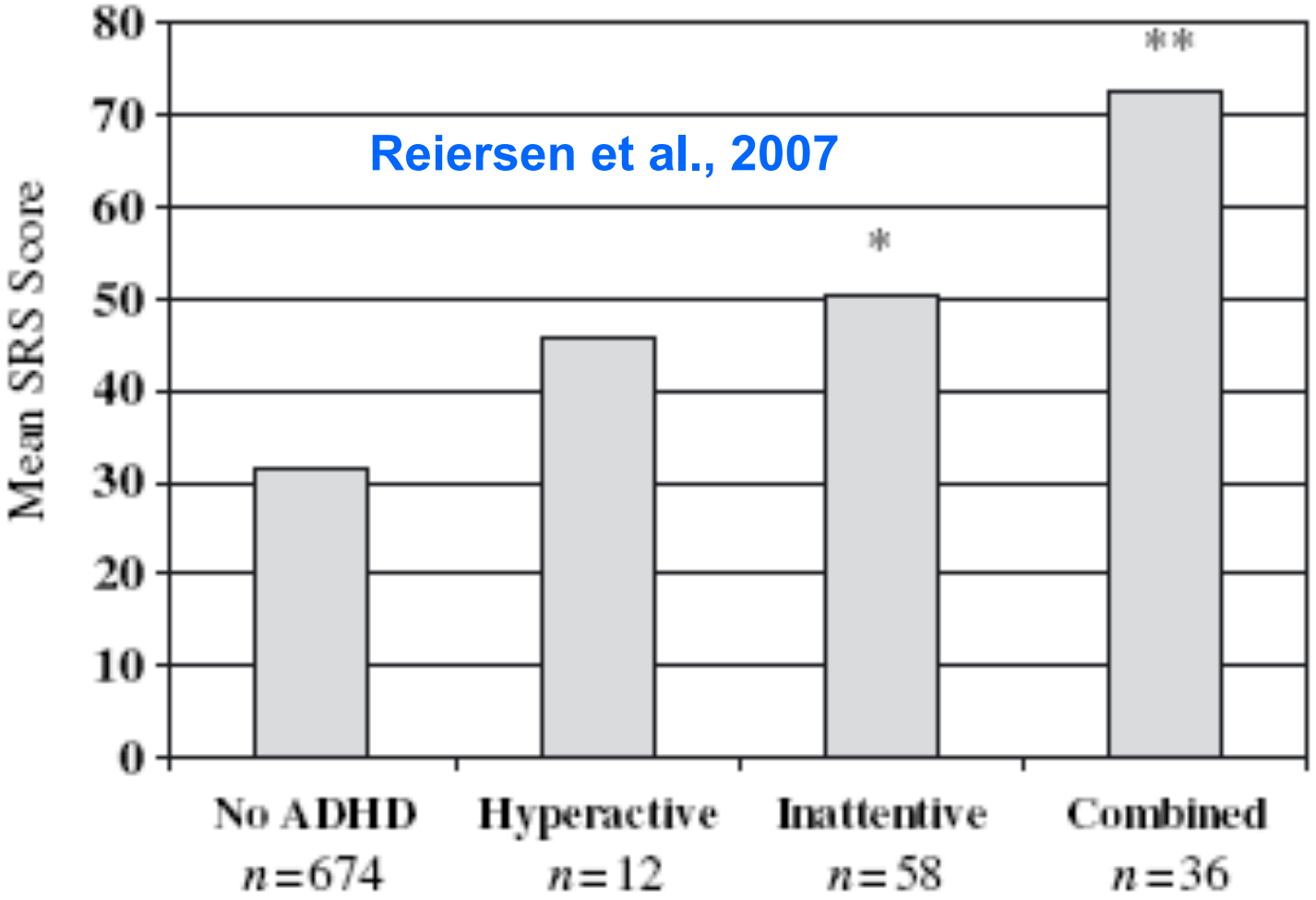
Clinical overlap between ADHD and ASD



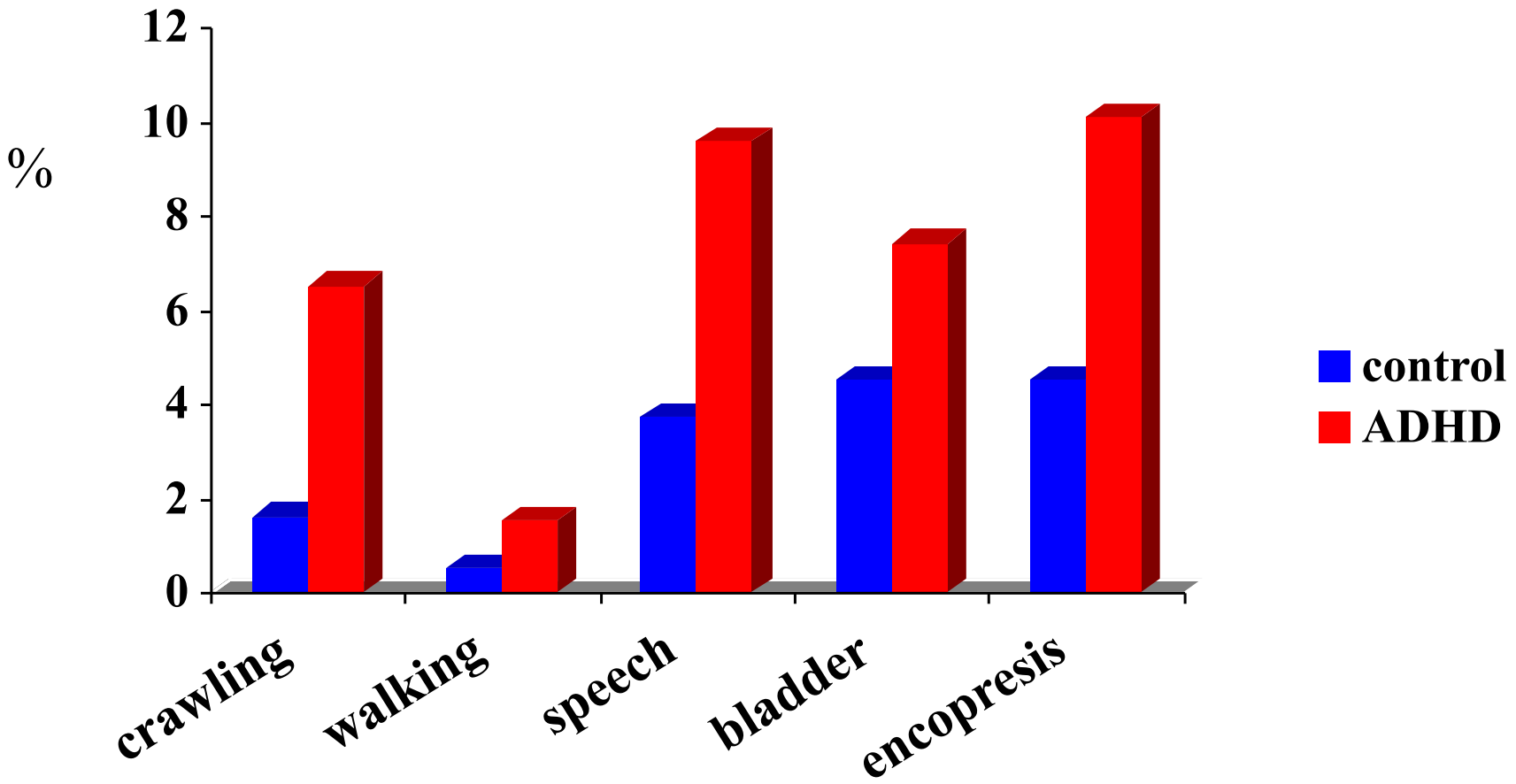
Inattention as the linking pin ?

25-50% of children with ADHD are severe socially disabled and/or have at least mild ASD symptoms (Green et al., 1996; Luteijn et al., 2000; Goldstein and Schwebach, 2004; Mulligan et al., 2009; Nijmeijer et al., 2008; Santosh and Mijovic, 2004). This also applies to population samples (Reiersen et al., 2007) (for review see Rommelse et al., 2010).

Clinical overlap between ADHD and ASD - population-based sample

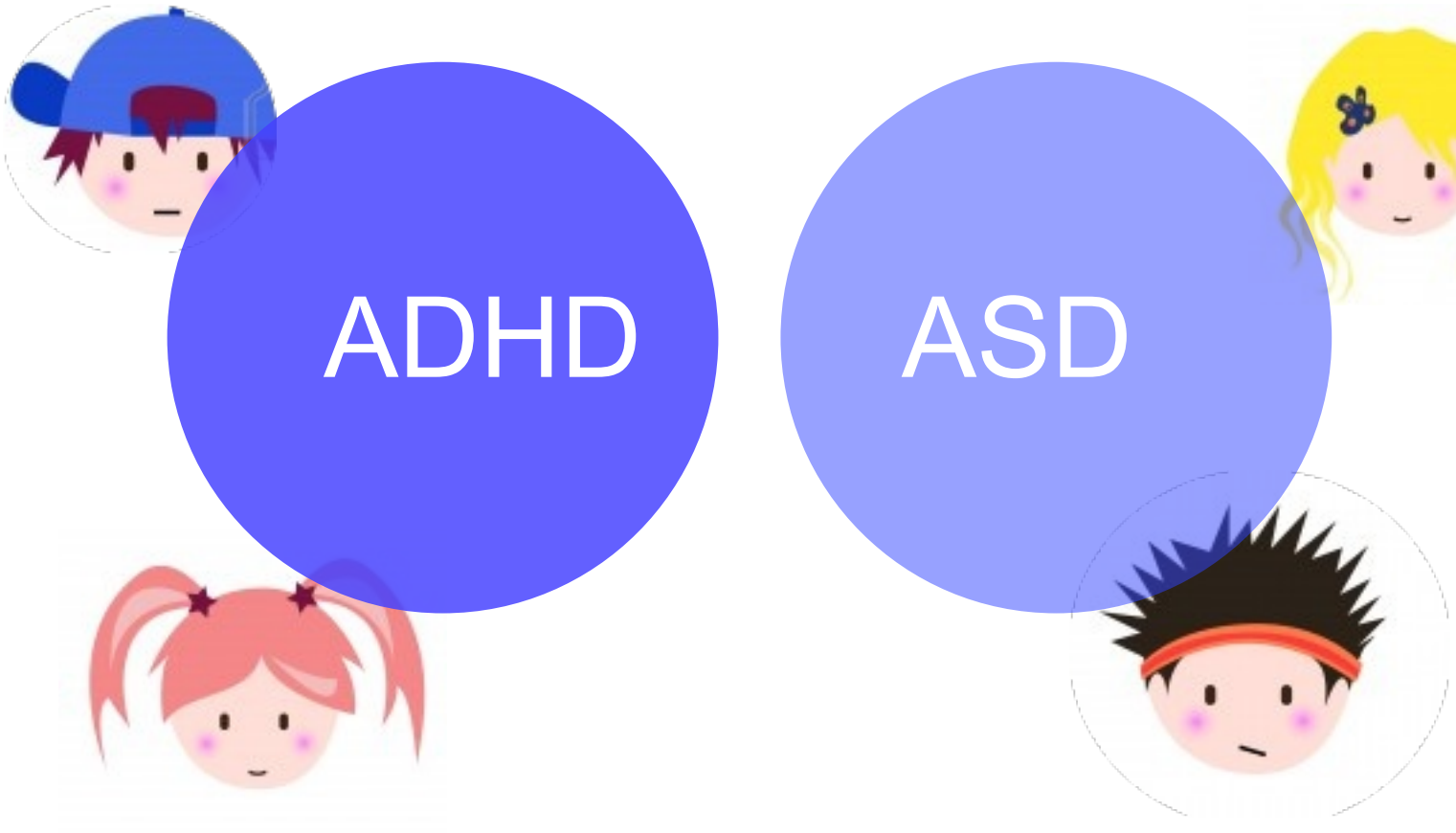


ADHD and developmental problems

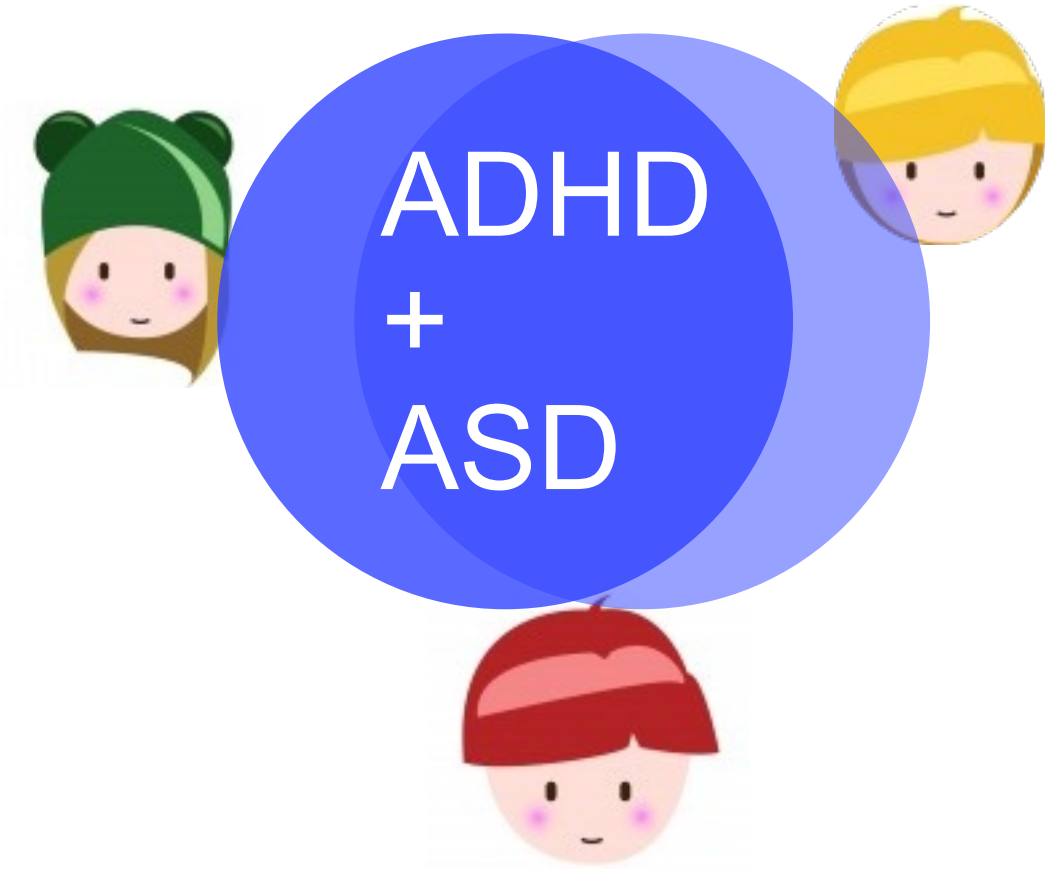


Hartsough & Lambert, 1985

ADHD and ASD



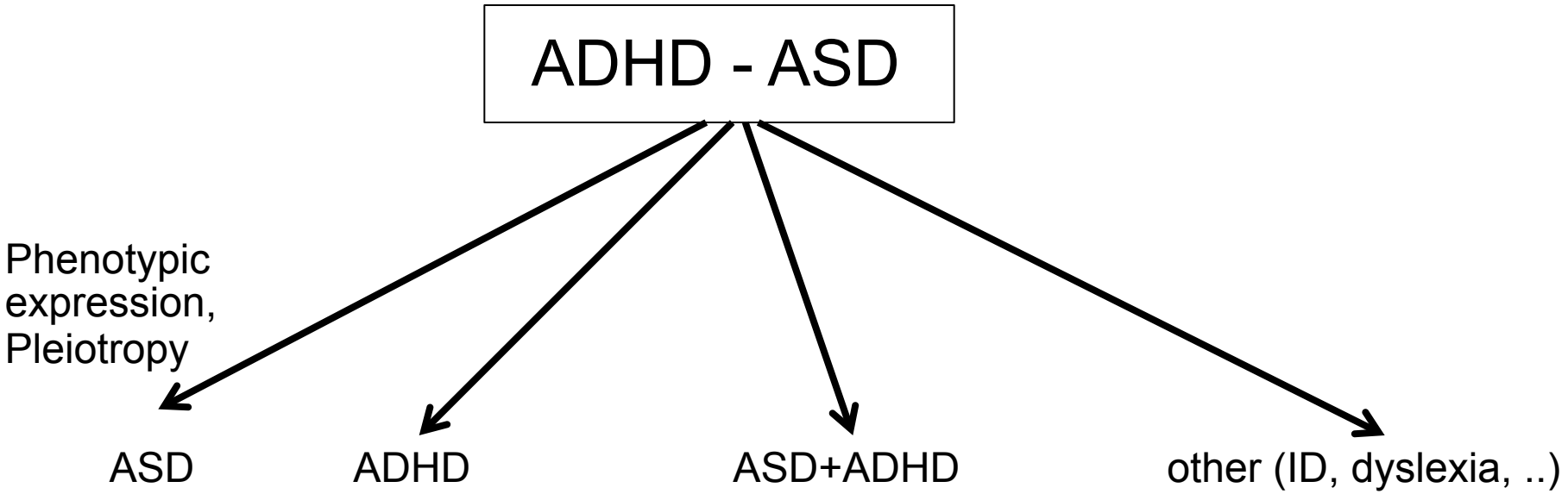
ADHD and ASD



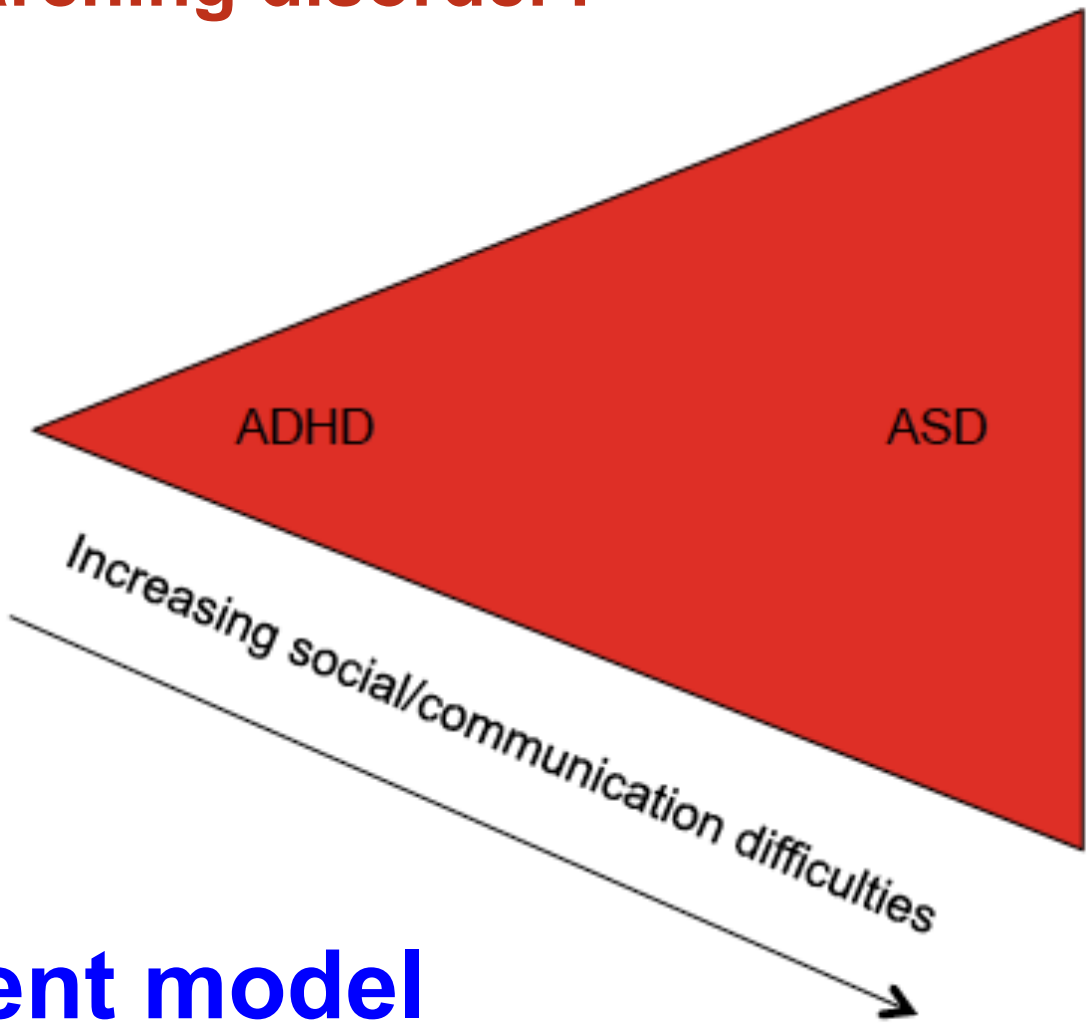
Theoretical models for overlap – co-occurrence

- One overarching disorder
- Common cause – shared risk factors
  - Genetic factors
  - Environment (e.g. obstetric adversity)
- Common neurobiological substrate
- Disorder A causes disorder B
- Disorder A is risk factor to disorder B
- Overlap in defining symptoms

One overarching disorder

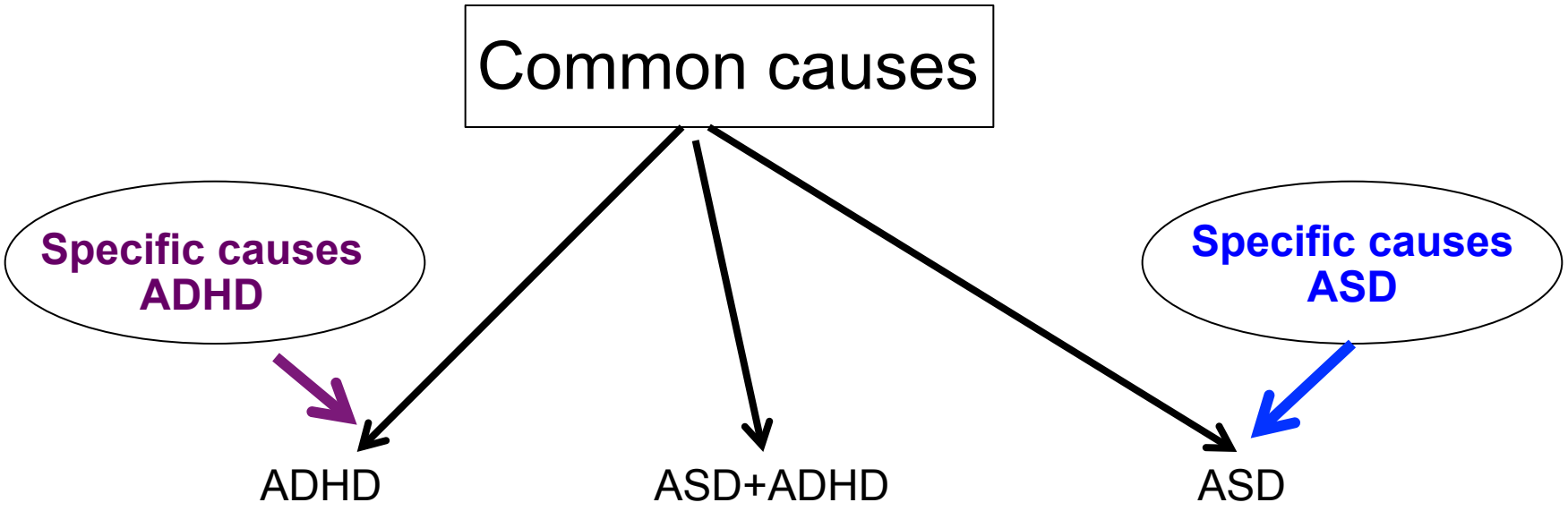


Are ASD and ADHD different manifestations of one overarching disorder?

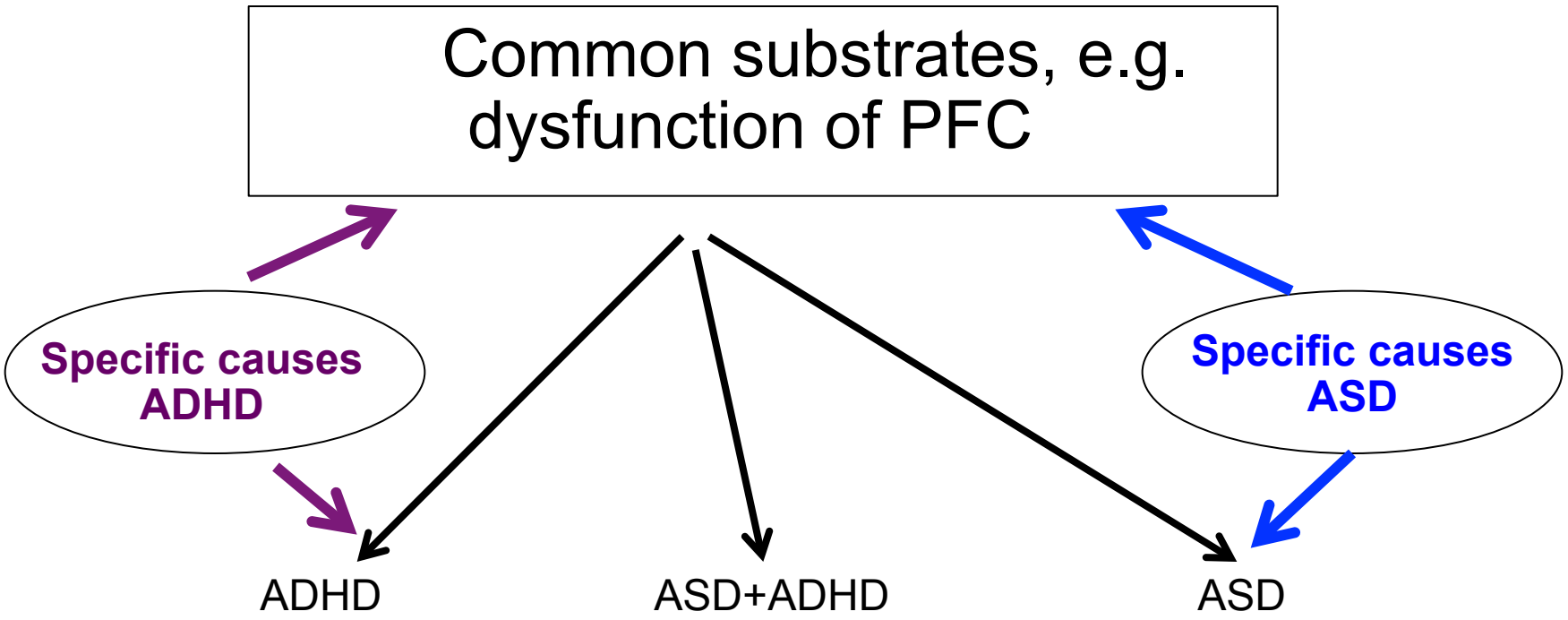


Gradient model

Different disorders with common causes



Different disorders with common neural substrates



Outline of the talk

- Clinical issues
- **Genetics**
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Clinical observations

Clinicians will rather often observe the following:

- Proband diagnosed with ASD
- Sibling later referred and diagnosed with ADHD (and ASD broad phenotype)
- Another sibling referred because of ADHD or dyslexia or social problems

Twin studies

- Genetic similarity
  - Monozygotic (MZ) twins (nearly) 100%
  - Dizygotic (DZ) twins ~ 50%

Estimated heritabilities

Disorder	heritability (%)	
Autism	90	(but lower in recent studies)
ADHD	80	
Schizophrenia	80	
Bipolair disorder	80	
Anorexia nervosa	70	

Shared genetic influences on ADHD and ASD symptoms

- TEDS (community sample of 6,771 twins 8 year old)
- Ratings on the Childhood Asperger Syndrome Test
- Ratings on the Conners' DSM-IV subscales.
- ASD and ADHD traits were significantly correlated in the general population (.54 for parent data, .51 for teacher data).
- **All genetic correlations were >.50**
- **Higher genetic correlations at more extreme levels of ADHD and ASD**

Ronald et al., 2008, J Child Psychol Psychiatry 49:535-42

Shared genetic influences on ADHD and ASD symptoms

- Adult sample of 674 young Autralian Twins
- Self-report data from 11 SRS items and 12 DSM-IV ADHD symptoms
- Phenotypic correlation between ASD and ADHD symptoms was moderate.
- ADHD and ASD traits were both moderately heritable.
- **The genetic correlation between SRS and ADHD was 0.72**

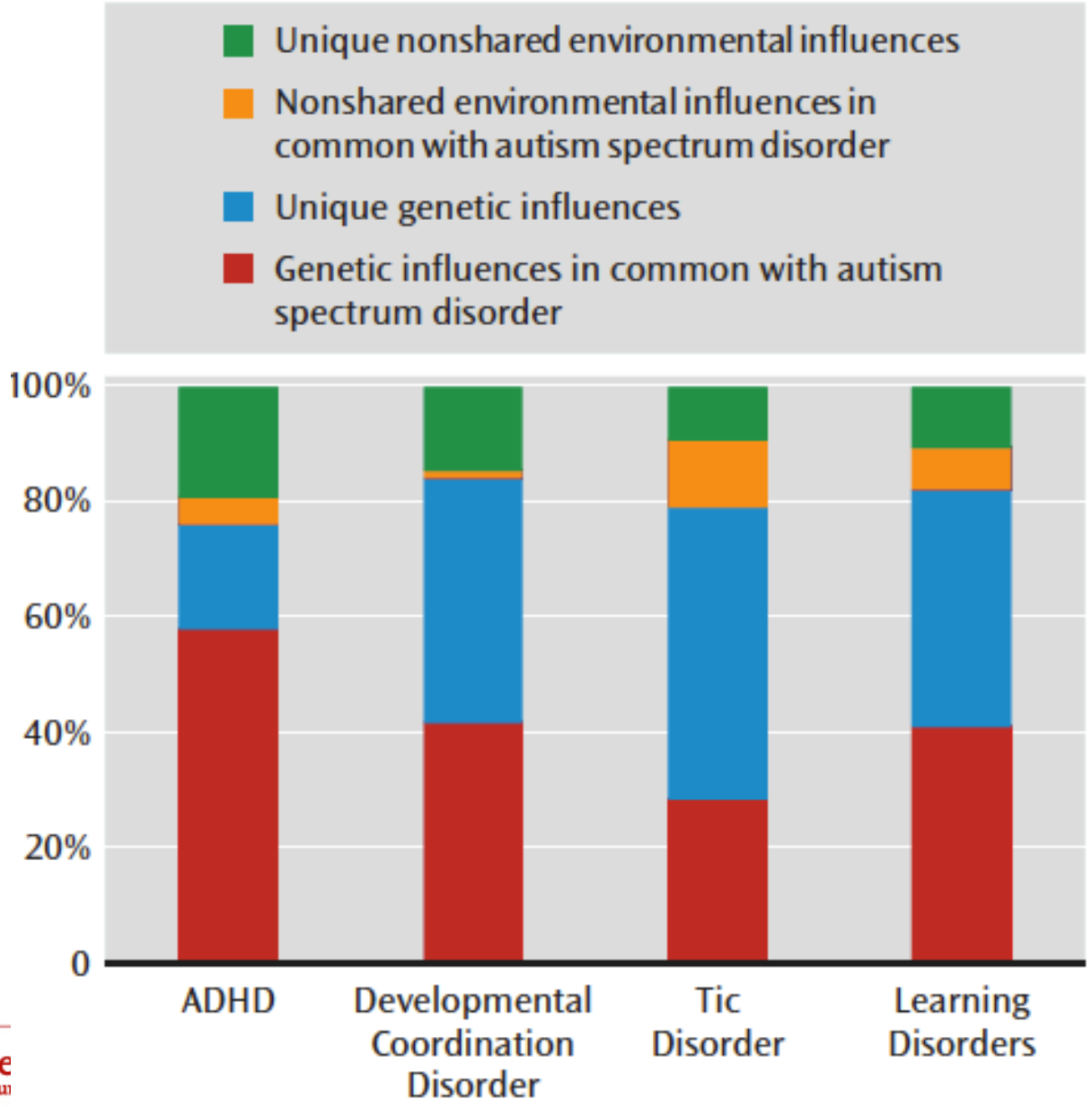
Reiersen et al., 2008, Twin Res Hum Genet 11:579-85

Shared genetic influences on ADHD and ASD symptoms

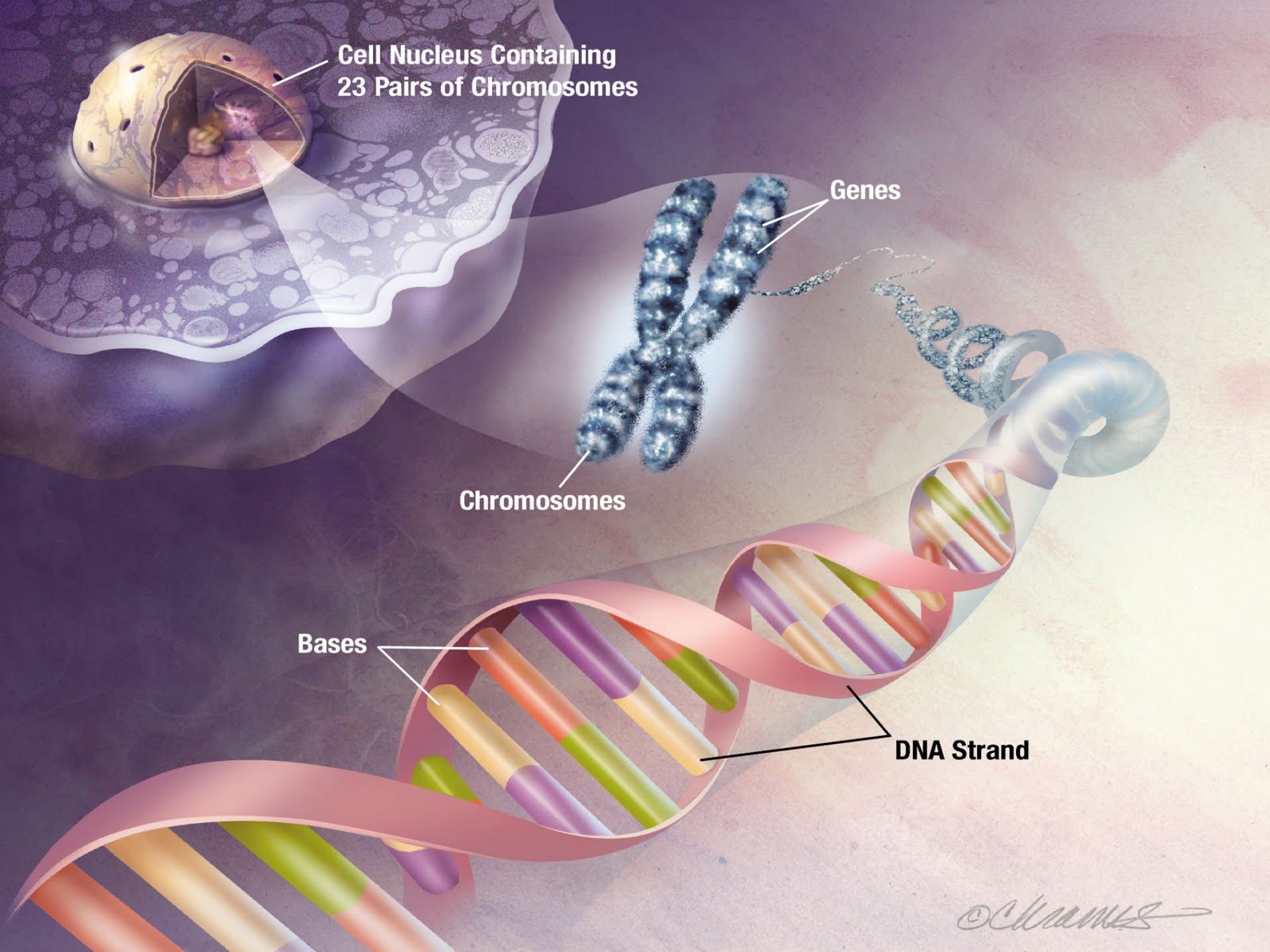
- 9- and 12-year-old Swedish twin pairs born between 1992 and 2000 (N=10,895) Lichtenstein et al., 2010, Am J Psychiatry

Disorder	Genetic Effects	95% CI
Autism spectrum disorders	0.80	0.29–0.91
ADHD	0.79	0.61–0.88
Developmental coordination disorder	0.70	0.35–0.83
Tic disorder	0.56	0.37–0.68

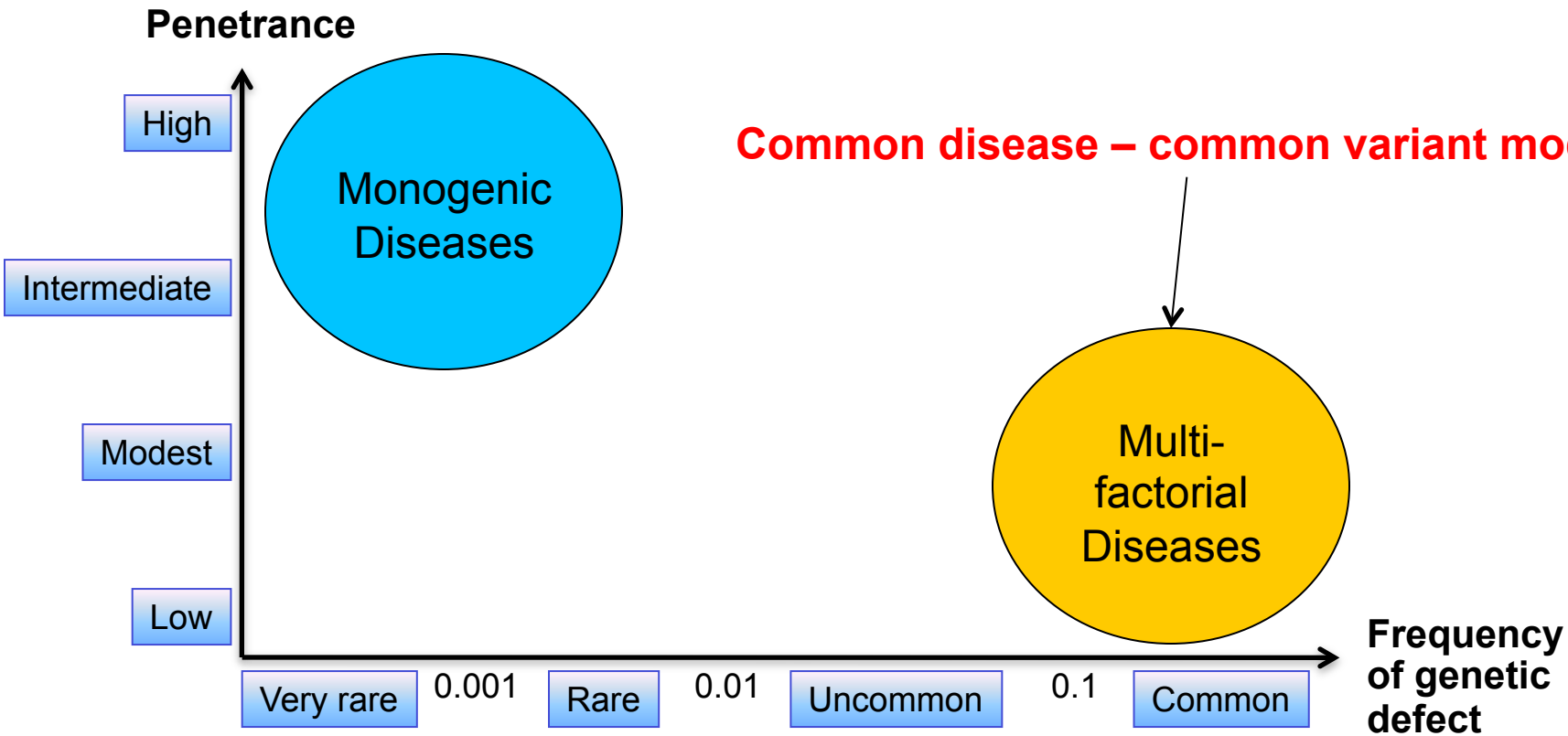
Shared genetic influences on ADHD and ASD symptoms



Lichtenstein et al., 2010, Am J Psychiatry

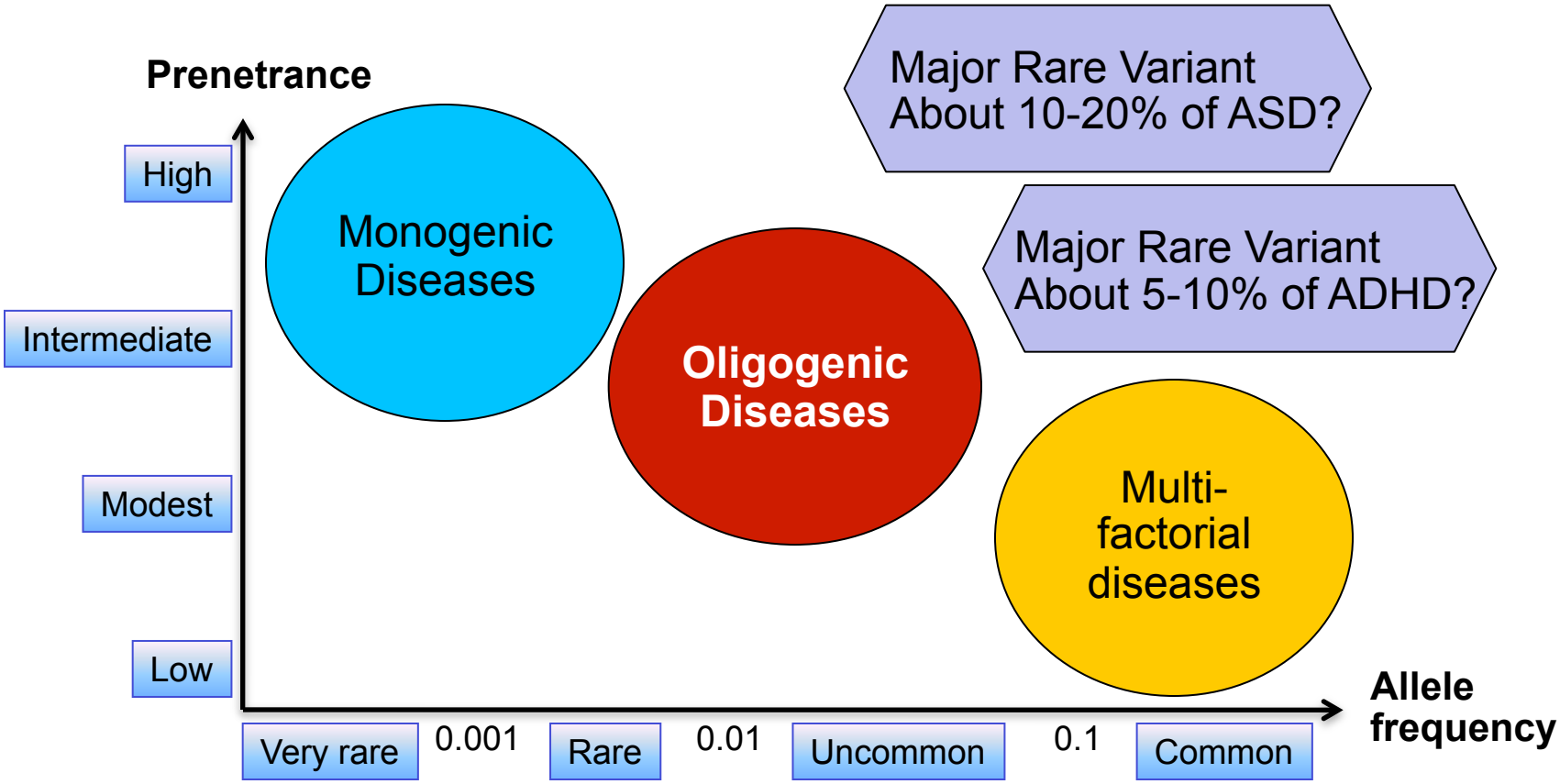

Cell Nucleus Containing
23 Pairs of Chromosomes
Genes
Chromosomes
Bases
DNA Strand

Causes of genetic disease



(adapted from McCarthy et al., 2008)

Causes of genetic disease



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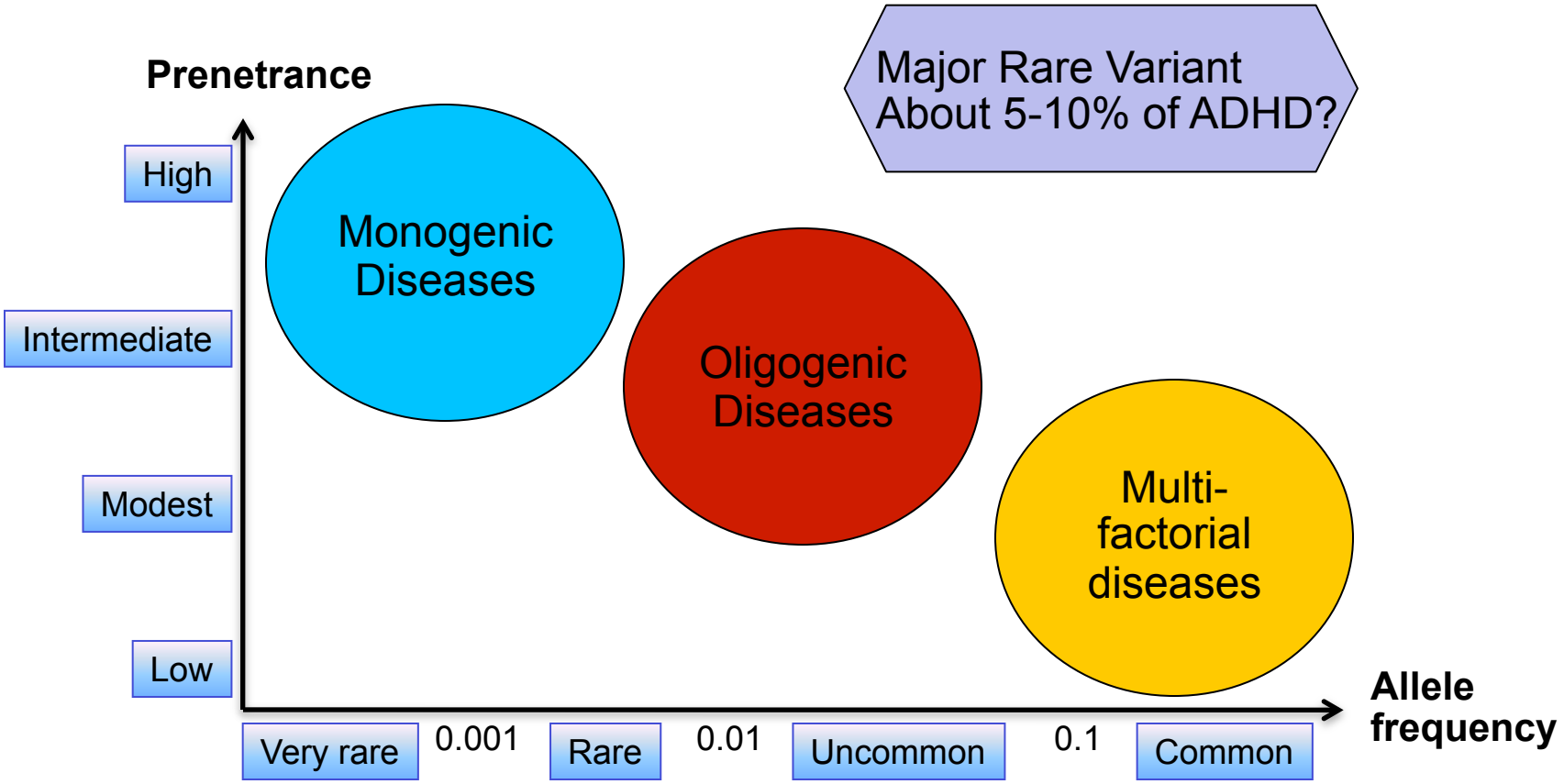
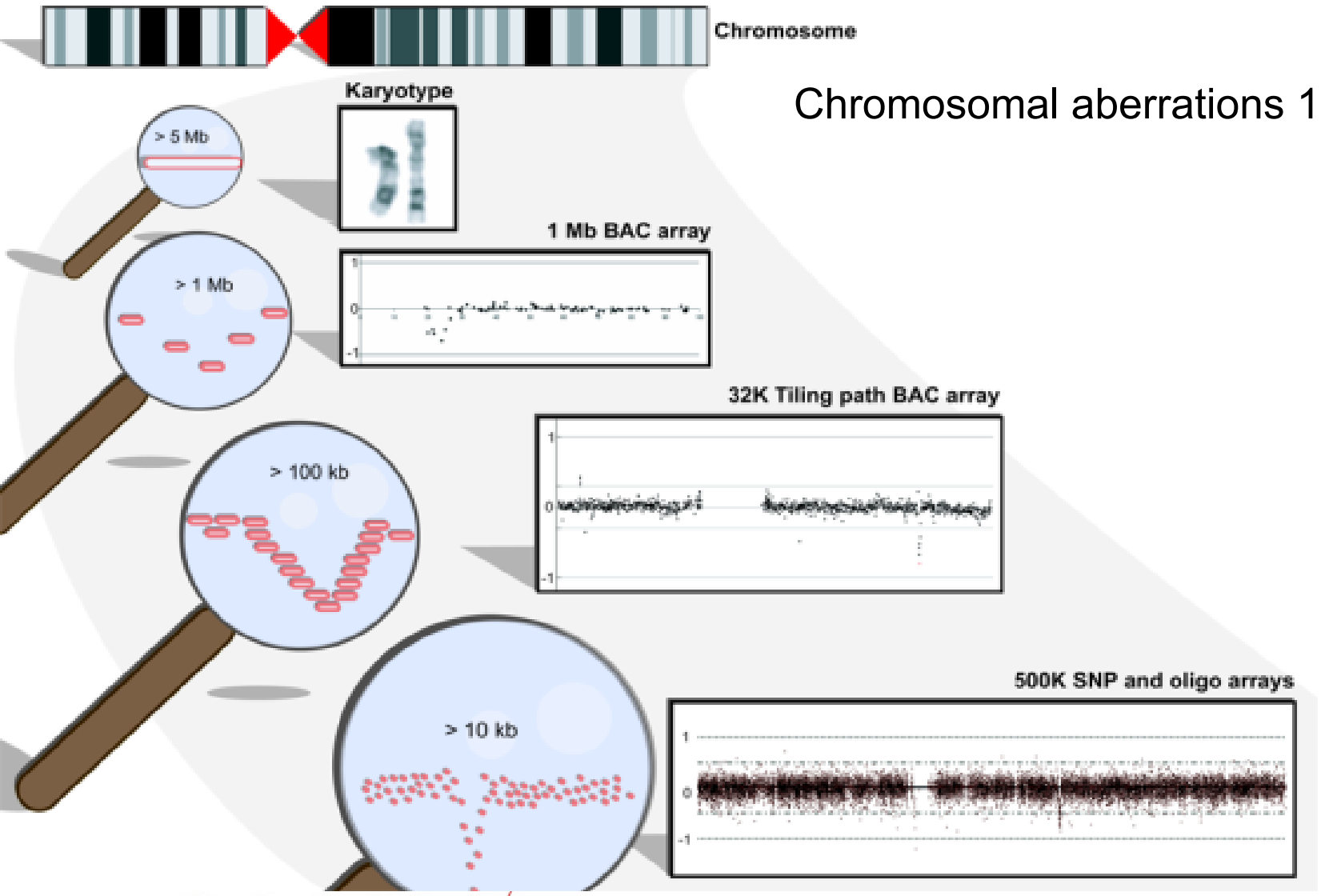
Causes of genetic disease

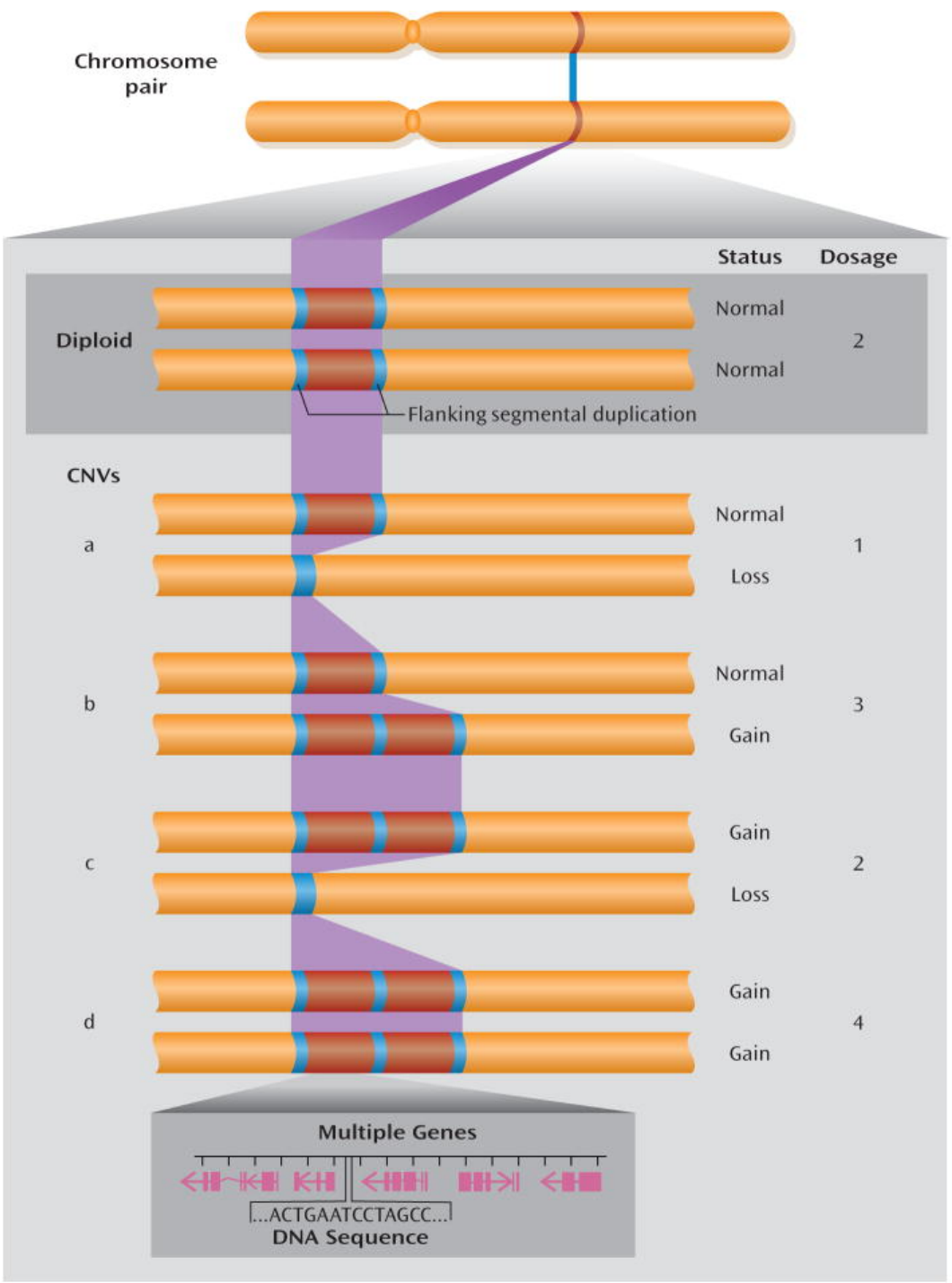


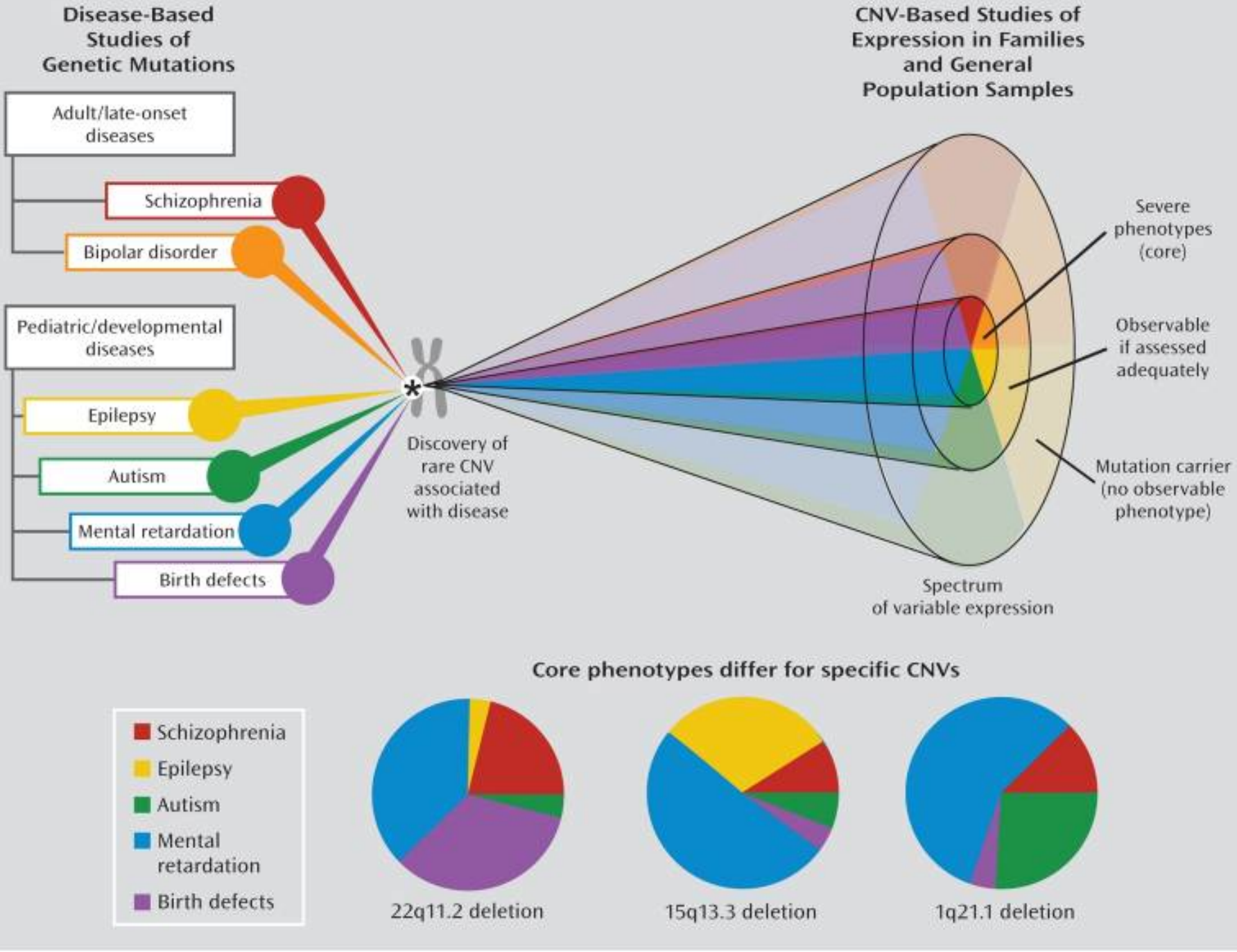
(adapted from McCarthy et al., 2008)

Copy Number Variation

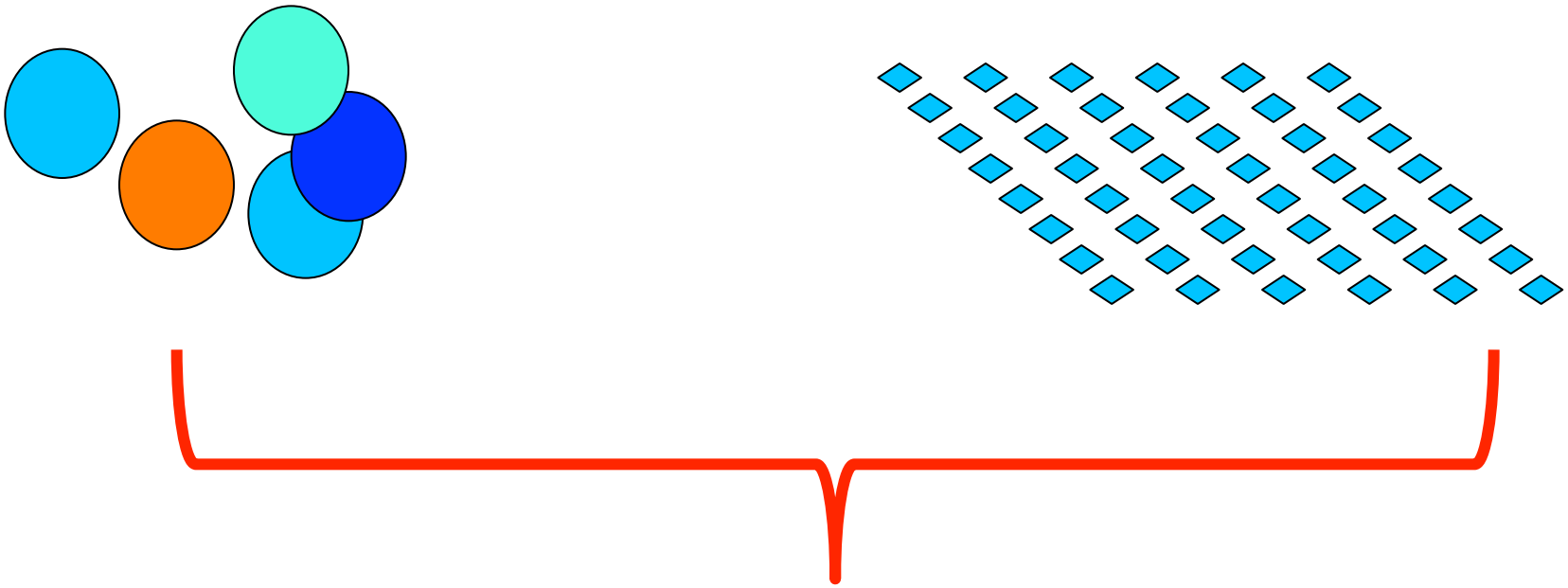


Chromosomal aberrations 1kb – 3Mb

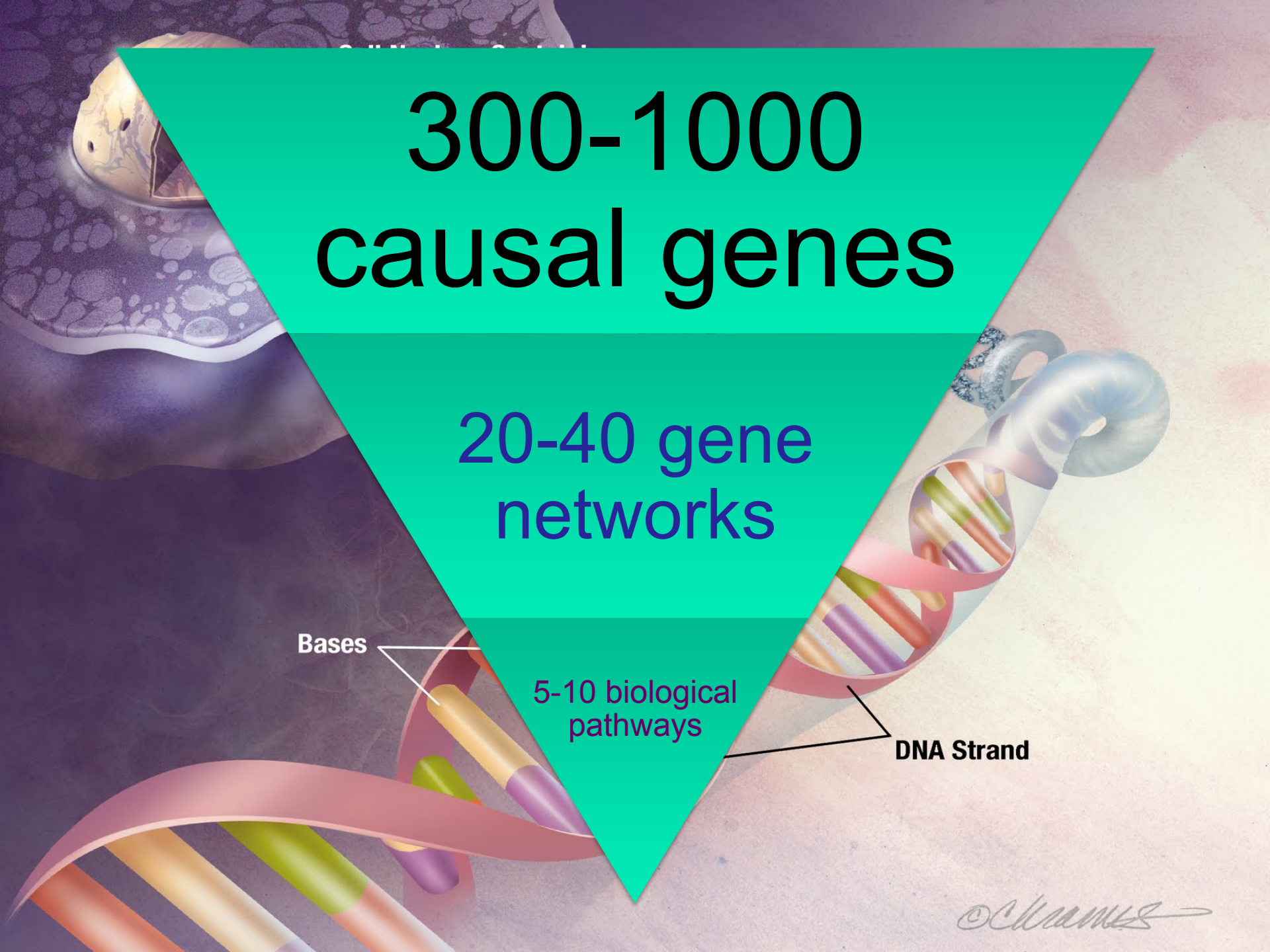

Chromosome pair
Status
Dosage
Diploid
Normal
Normal
2
Flanking segmental duplication
CNVs
a
Normal
Loss
1
b
Normal
Gain
3
c
Gain
Loss
2
d
Gain
Gain
4
Multiple Genes
...ACTGAATCCTAGCC...
DNA Sequence


Disease-Based Studies of Genetic Mutations
Adult/late-onset diseases
Schizophrenia
Bipolar disorder
Pediatric/developmental diseases
Epilepsy
Autism
Mental retardation
Birth defects
Discovery of rare CNV associated with disease
CNV-Based Studies of Expression in Families and General Population Samples
Severe phenotypes (core)
Observable if assessed adequately
Mutation carrier (no observable phenotype)
Spectrum of variable expression
Core phenotypes differ for specific CNVs
Schizophrenia
Epilepsy
Autism
Mental retardation
Birth defects
22q11.2 deletion
15q13.3 deletion
1q21.1 deletion

Rare and common variants - integration



Rare and common variants converge into the same gene-protein networks


300-1000
causal genes
20-40 gene
networks
5-10 biological
pathways
Bases
DNA Strand

SNPs – Single Nucleotide Polymorphisms

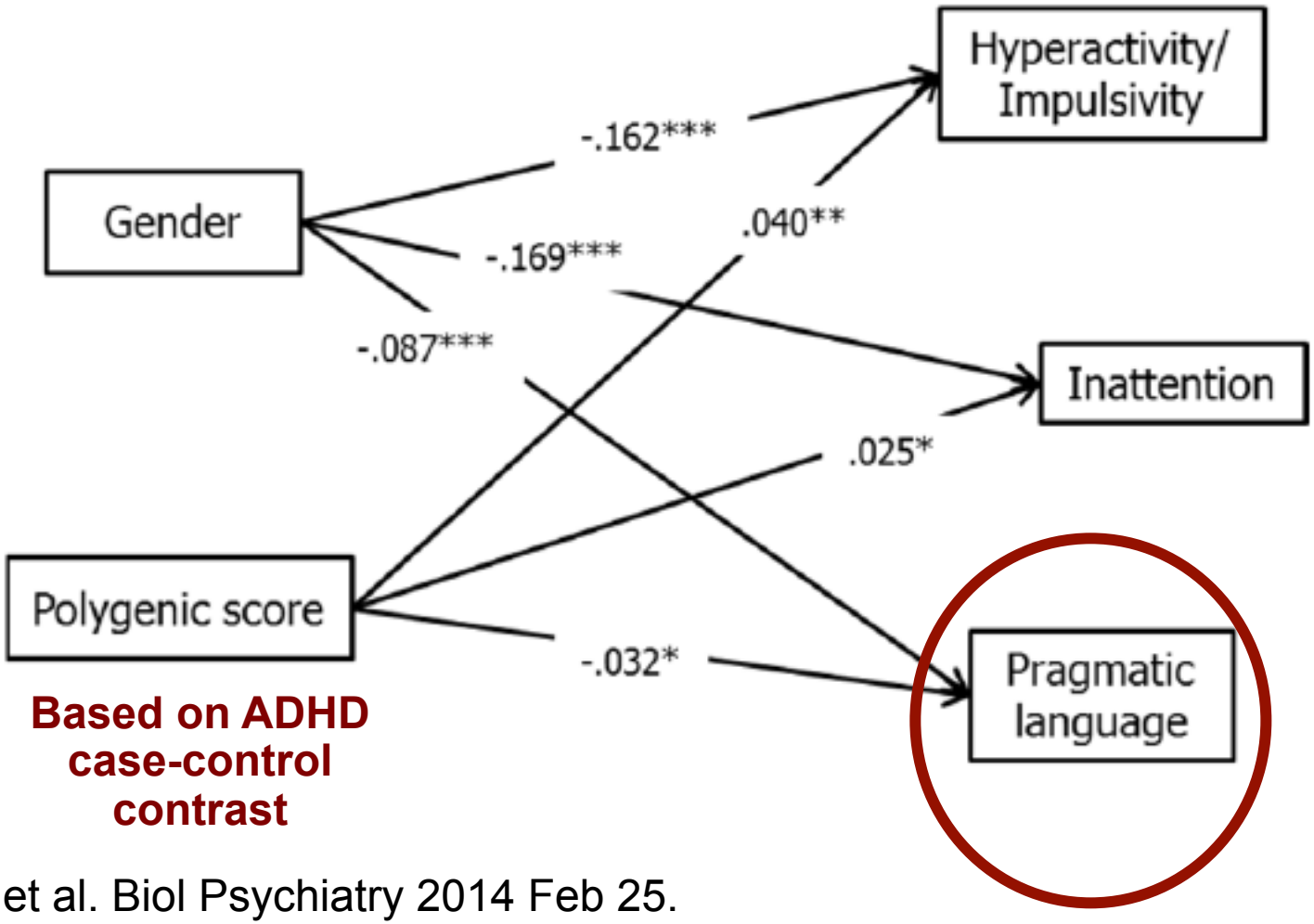
13.000.000 SNPs in human genome
- used as landmark for chromosomal location
- may change function/regulation of a gene product

Genetic Risk for ADHD Contributes to Neurodevelopmental Traits in the General Population

- Polygenic risk scores were calculated in the ALSPAC population sample (N = 8229) based on a discovery case-control genome-wide association study of childhood ADHD.
- Regression analyses were used to assess whether polygenic scores predicted ADHD traits and ASD-related measures (pragmatic language abilities and social cognition) in the ALSPAC sample.
- Polygenic risk for ADHD showed a positive association with ADHD traits (hyperactive-impulsive, p = .0039; inattentive, p = .037)
- Polygenic risk for ADHD was also negatively associated with pragmatic language abilities (p = .037) but not with social cognition (p = .43).

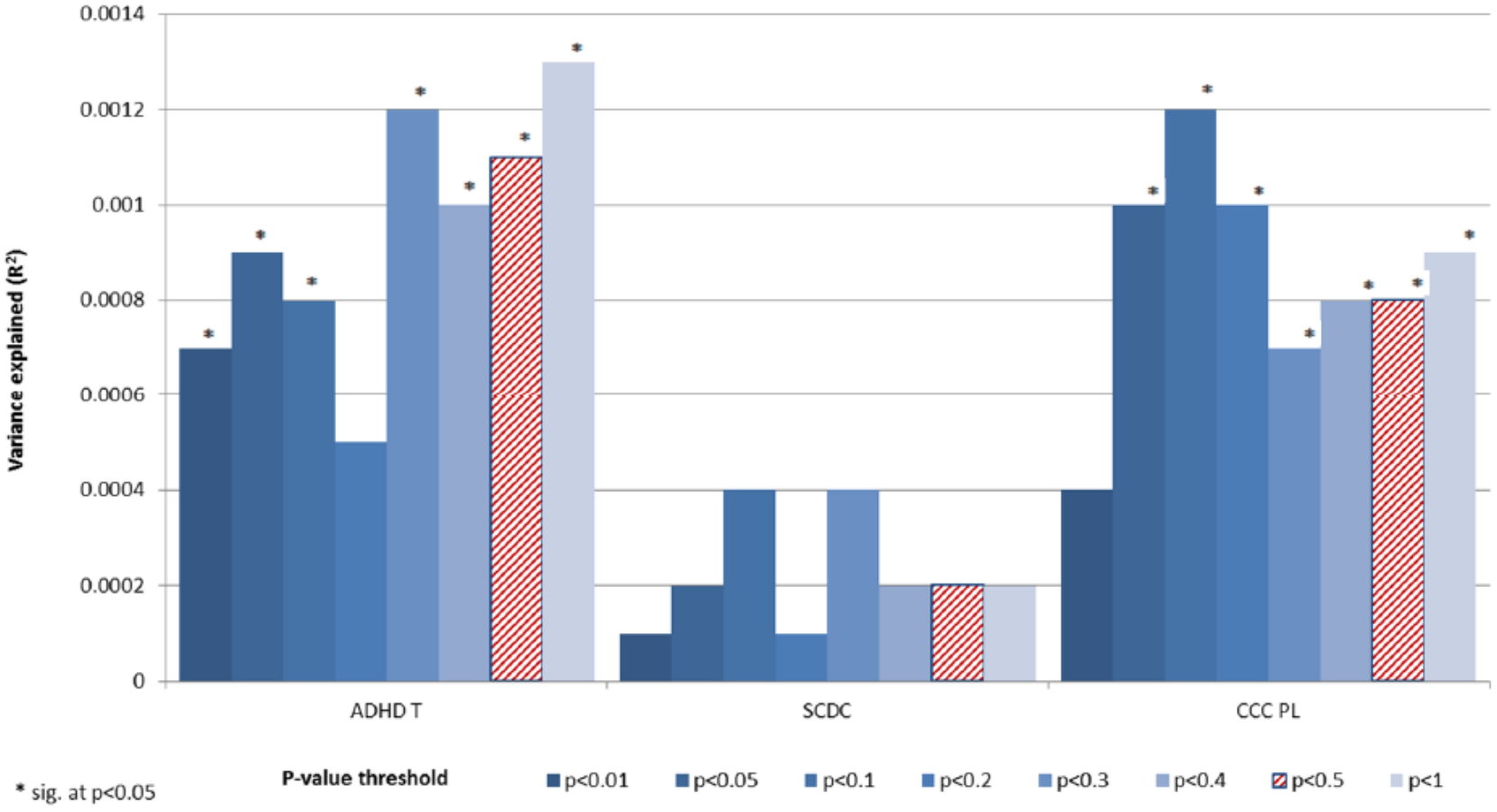
Martin et al. Biol Psychiatry 2014 Feb 25

Polygenic score predicting multiple correlated outcomes



Martin et al. Biol Psychiatry 2014 Feb 25.

Polygenic score predicting multiple correlated outcomes



Martin et al. Biol Psychiatry 2014 Feb 25.

Biological overlap of ADHD and ASD: evidence from copy number variants

Table 1

Number of Pathways Achieving Given Levels of Enrichment Significance ($p < .05$, $p < .01$, $p < .001$) in the Autism Spectrum Disorder (ASD) Dataset That Were Also Significantly Enriched at the Same Significance Level in the Attention-Deficit/Hyperactivity Disorder (ADHD) Sample

CNV Type (ASD)	$p < .05$		$p < .01$		$p < .001$	
	No. of Pathways	*p*	No. of Pathways	*p*	No. of Pathways	*p*
De novo	58	.006	9	.016	1	.021
Inherited	72	.001	16	.004	1	.019
All	100	<.001	20	.001	1	.017

Note: *p* Values are given for the test of whether the number of enriched pathways is greater than would be expected by chance. CNV = copy number variant; de novo = confirmed not to have been transmitted from either parent.

Martin et al. J Am Acad Child Adolesc Psychiatry 2014 Jul;53(7):761-70

Biological overlap of ADHD and ASD: evidence from copy number variants

- After correction for multiple testing, genes involved in 3 biological processes (**nicotinic acetylcholine receptor signalling pathway, cell division, and response to drug**) showed significant enrichment for case CNV hits in the combined ADHD and ASD sample.

- The results of this study indicate the presence of significant overlap of shared biological processes disrupted by large rare CNVs in children with these 2 neurodevelopmental conditions.

Martin et al. J Am Acad Child Adolesc Psychiatry 2014 Jul;53(7):761-70

Conclusions sofar

- Evidence for genetic overlap between autism and ADHD
- Multifactorial and oligogenetic forms
- Both disorders of synaptic structure/ efficiency, cell adhesion, neurite outgrowth, signalling pathways

Outline of the talk

- Clinical issues
- Genetics
- **Cognitive measures**
- Brain function and structure
- Implications – new concepts

Cognitive deficits

- Both ASD as ADHD are heterogenous at the cognitive level
- Data suggest multiple impairment models rather than one universal or primary cognitive deficit

Anoek Oerlemans

Jolanda van der Meer

Catharina Hartman

Nanda Rommelse

Are ASD and ADHD different manifestations of one overarching disorder?

- Latent class analysis (LCA) was performed on Social Communication Questionnaire (SCQ) and Conners' Parent Rating Scale (CPRS-R:L) data of **644 children**.
- Classes were compared for comorbid symptoms and their cognitive profiles of motor speed and variability, executive functioning, attention, emotion recognition and central coherence.

Van der Meer, Oerlemans, van Steijn, Lappenschaar. de Sonneville, Buitelaar, Rommelse J Am Acad Child Adolesc Psychiatry. 2012 Nov;51(11):1160-1172.

Are ASD and ADHD different manifestations of one overarching disorder?

Table 1. Demographic characteristics of the children in the distinct classes.

	Normal N=418		ADHD N=109		ADHD(+ASD) N=59		ASD(+ADHD) N=58		Contrasts based on *p*-values of .05
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	
Age	9.5	2.4	9.9	2.8	11.2	3.3	11.5	2.7	Normal = ADHD < ADHD(+ASD) = ASD(+ADHD)
% male	45.7		66.1		81.4		86.2		Normal = ADHD < ADHD(+ASD) = ASD(+ADHD)
IQ	111.7	18.7	107.1	19.1	101	21.2	105.5	19.7	Normal > ADHD(+ASD)
SCQ	4.1	4.4	6.9	4.7	16.3	7.2	23	6	Normal < ADHD < ADHD(+ASD) < ASD(+ADHD)
Inatt	47.3	6	64.7	8.3	73.3	8.8	62.6	8.2	Normal < ADHD = ASD(+ADHD) < ADHD(+ASD)
Hyp/Imp	48.2	6.7	64.8	9.8	79.8	8.2	66.7	11.2	Normal < ADHD = ASD(+ADHD) < ADHD(+ASD)

Van der Meer, Oerlemans, van Steijn, Lappenschaar. de Sonneville, Buitelaar, Rommelse J Am Acad Child Adolesc Psychiatry. 2012 Nov;51(11):1160-1172.

Hypotheses

H1: overarching disorder hypothesis: If true, symptomatic expression can be regarded as 'noise' and classes will more similar than different in associated traits

➔ **LC1 = LC2 = LC3 = …**

H2: ADHD is a less severe subtype within the ASD spectrum. LCA will then identify at least one ADHD class without ASD symptoms, but no ASD class without ADHD symptoms, and all classes will show rather similar associated traits

➔ **LC1 (ADHD) < LC2 (ASD) < LC3 (ADHD+ASD).**

Van der Meer, Oerlemans, van Steijn, Lappenschaar. de Sonneville, Buitelaar, Rommelse J Am Acad Child Adolesc Psychiatry. 2012 Nov;51(11):1160-1172.

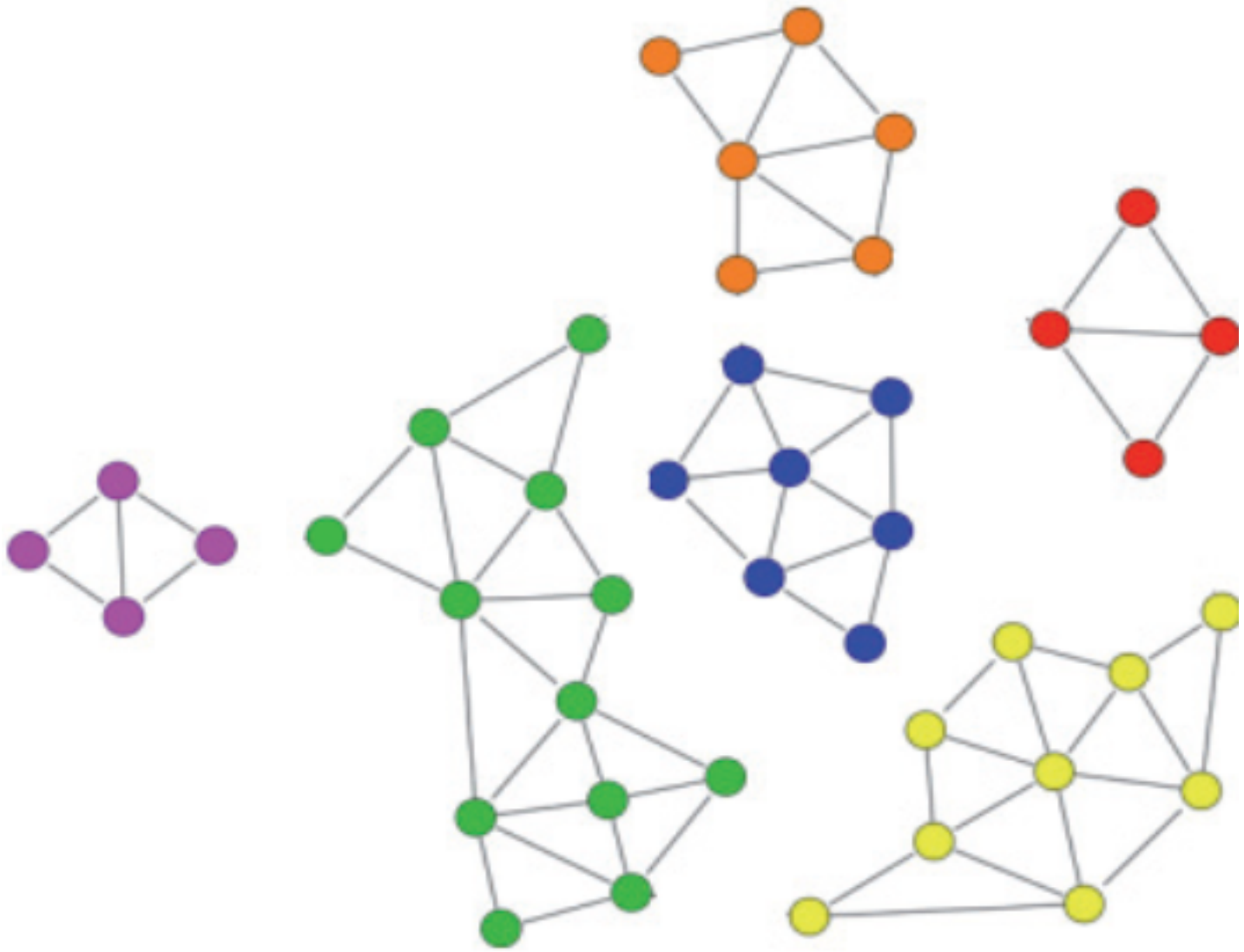
Hypotheses

Ho: Alternatively, ASD and ADHD do not constitute different expressions of one overarching disorder. In this case, the LCA will identify at least some classes with pure ADHD or ASD symptoms. Further, the classes will be more different than similar in terms of associated traits

➔ **LC1 ≠ LC2 ≠ LC3 …**

Van der Meer, Oerlemans, van Steijn, Lappenschaar. de Sonneville, Buitelaar, Rommelse J Am Acad Child Adolesc Psychiatry. 2012 Nov;51(11):1160-1172.

Latent Class Analysis



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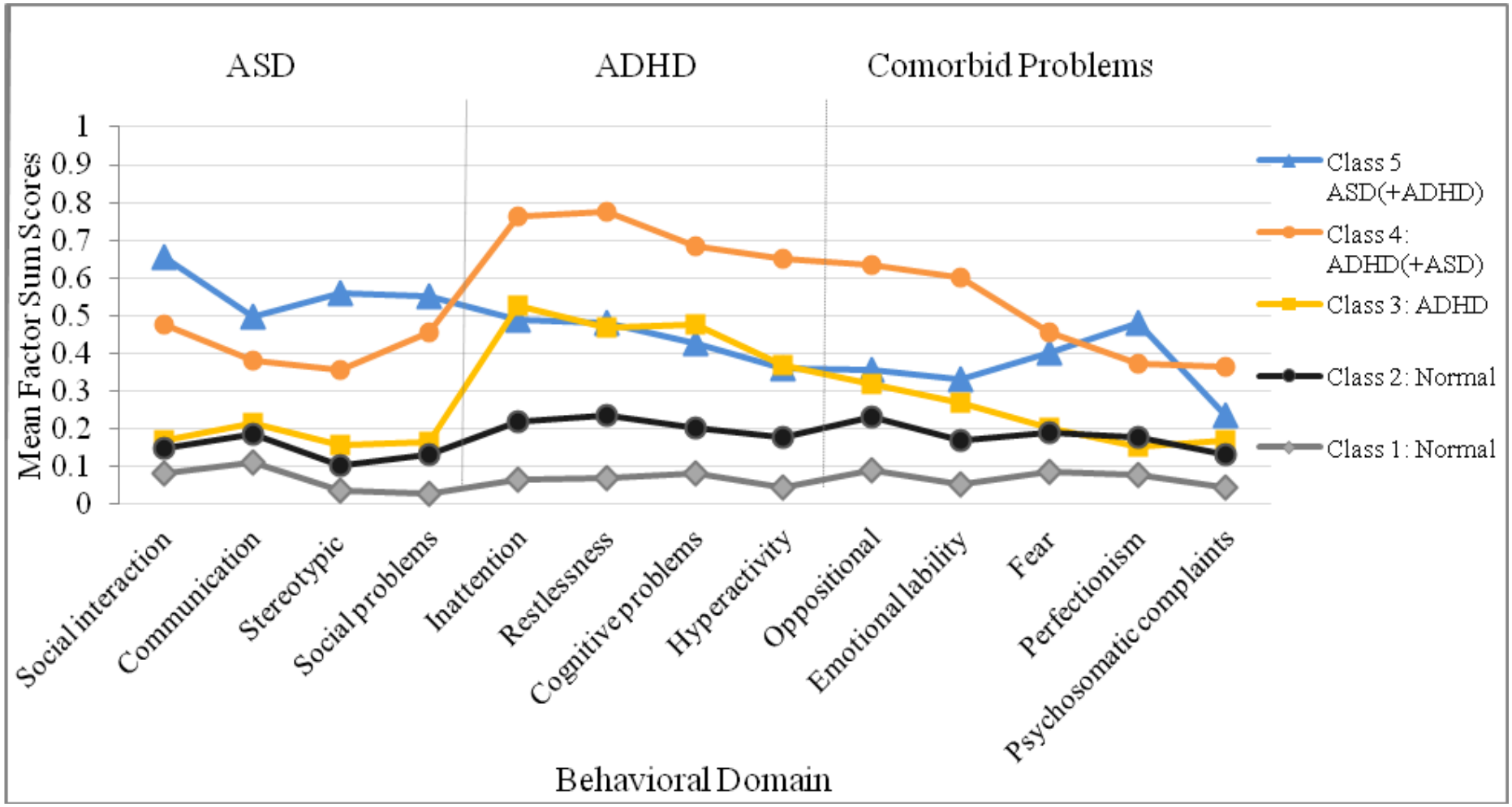

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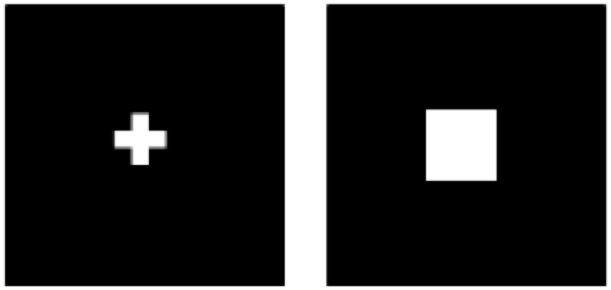
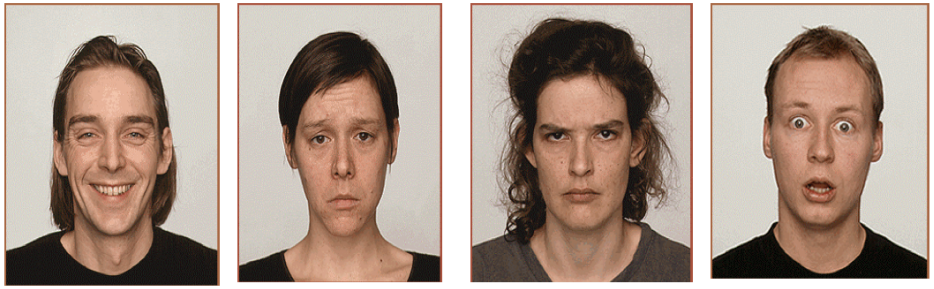
Cognitive tests

a. Baseline speed and variability



Fixation Signal

b. Facial emotion recognition



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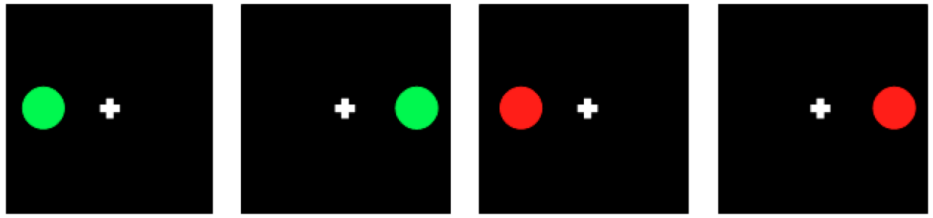
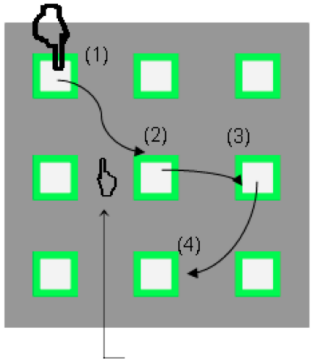
Cognitive tests

c. Inhibition and cognitive flexibility: compatible and incompatible trials.



Left compatible Right compatible Left incompatible Right incompatible

d. Visuo-spatial attention and working memory.



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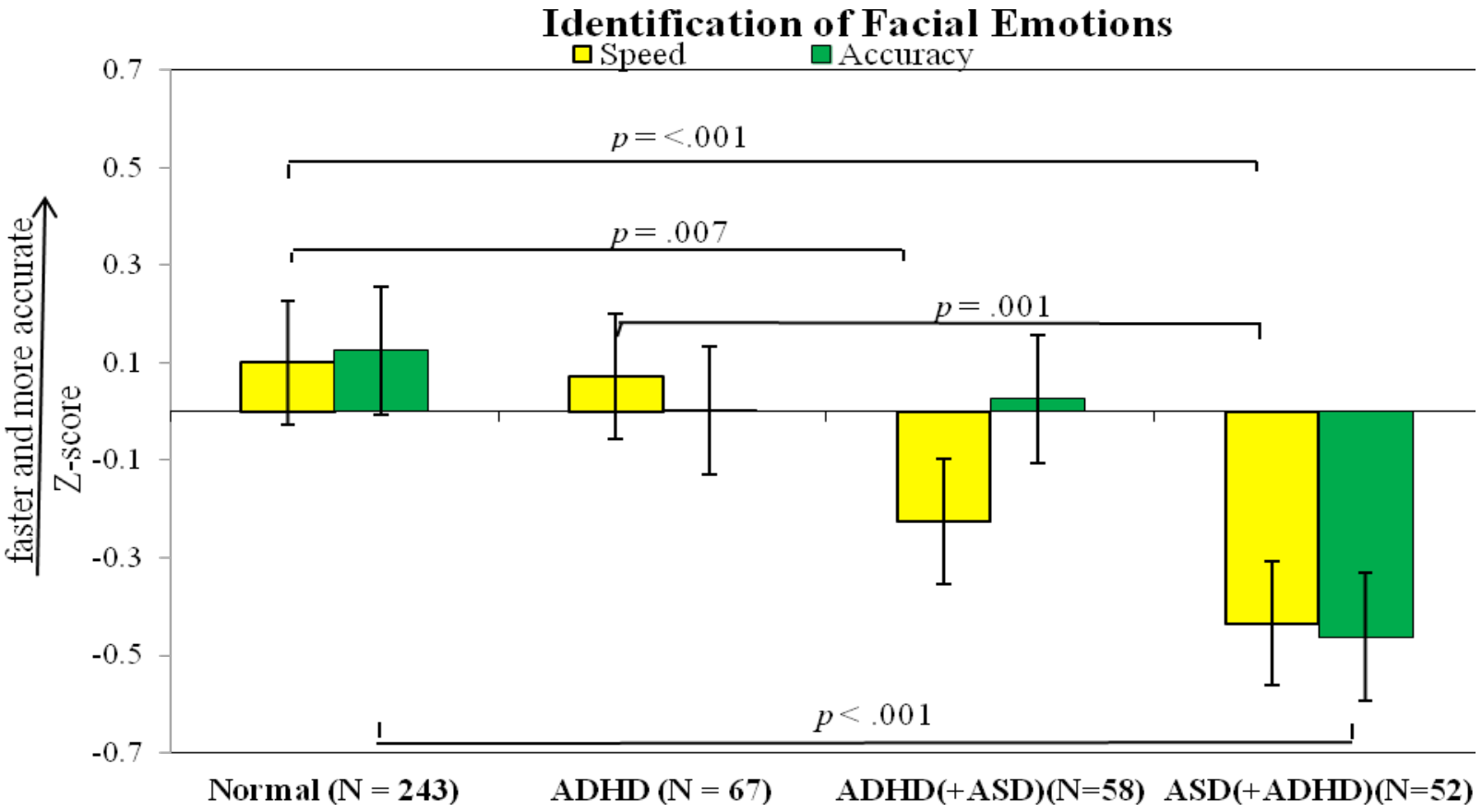

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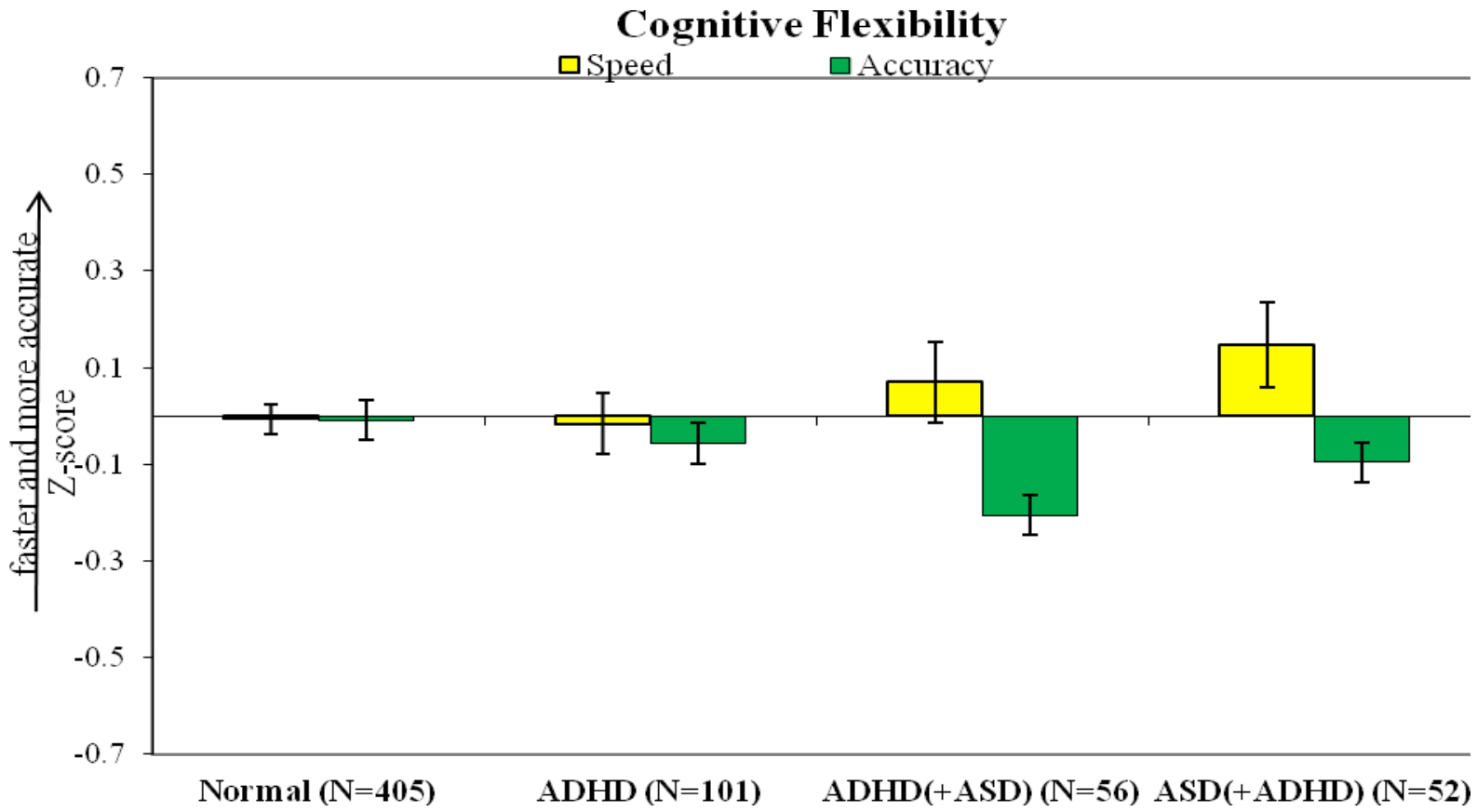
Are ASD and ADHD different manifestations of one overarching disorder?



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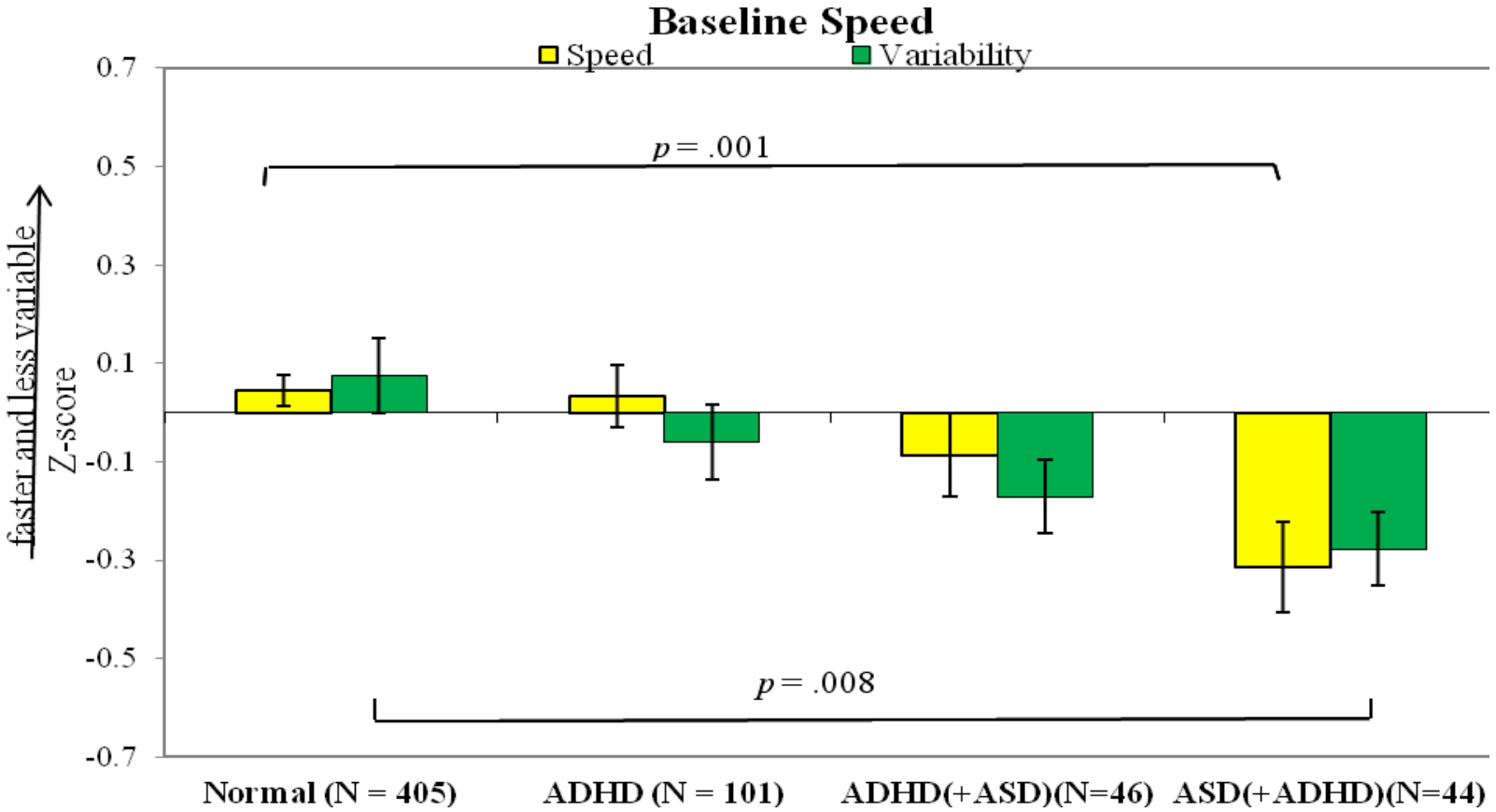

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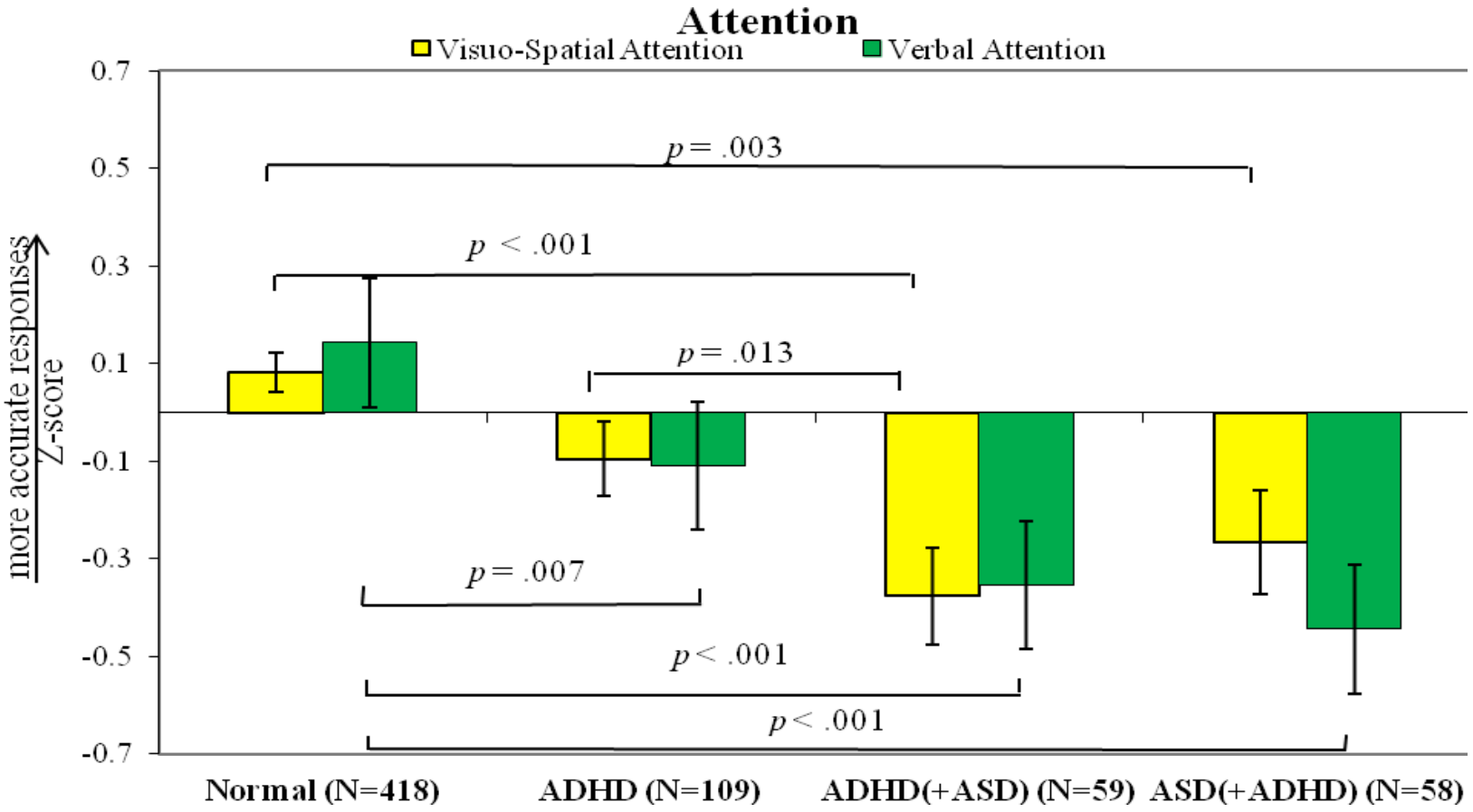

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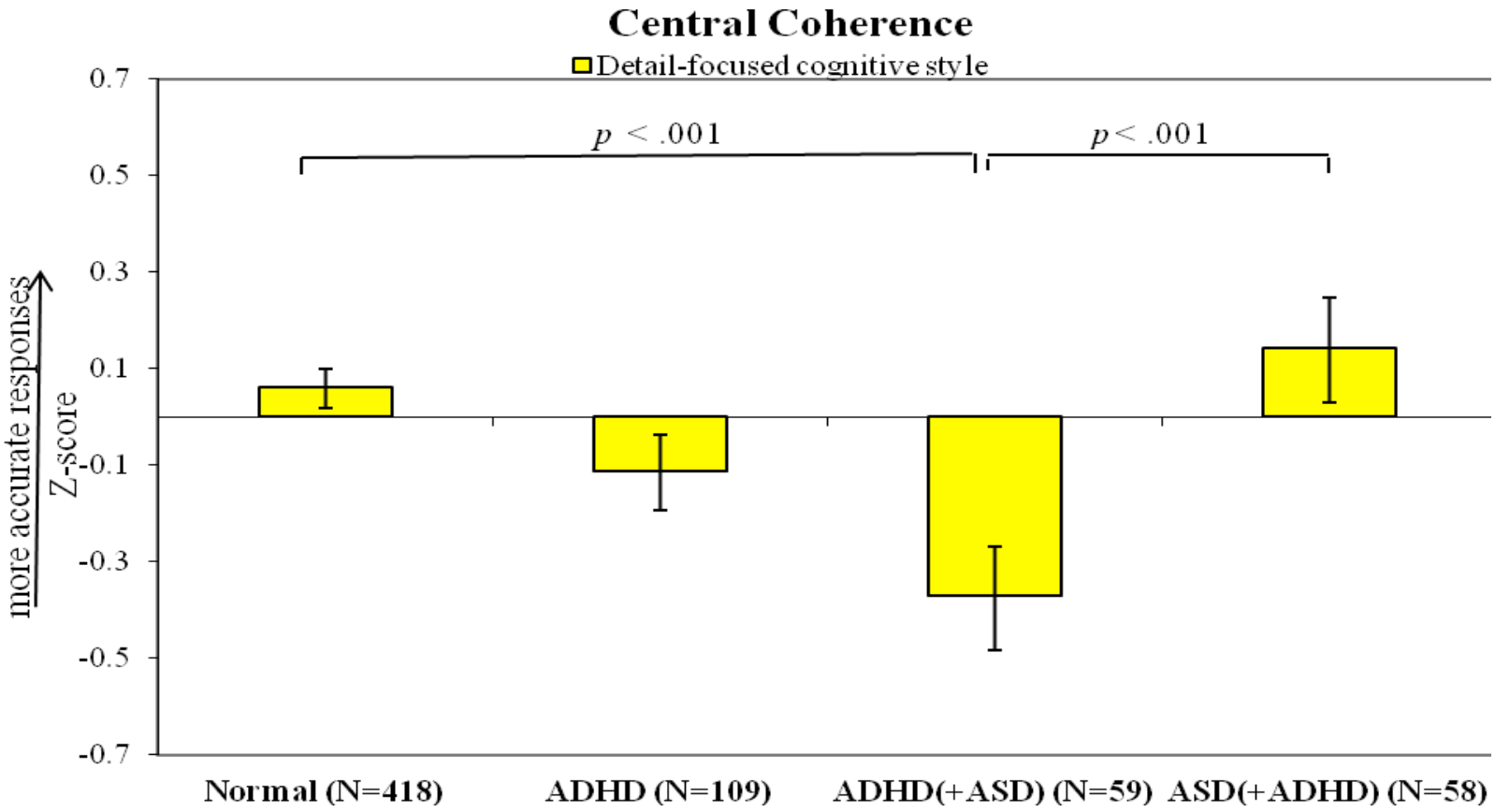

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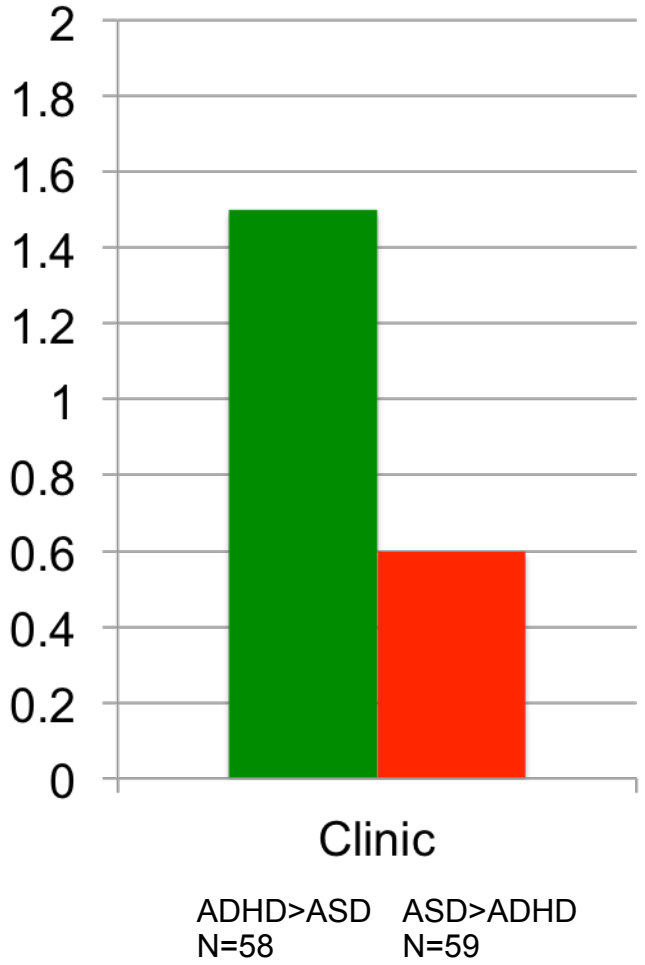
Are ASD and ADHD different manifestations of one overarching disorder?

2 classes with high scores on ASD and ADHD symptoms, however with strongly different performance on visuo-spatial skills



Van der Meer, Oerlemans, van Steijn, Lappenschaar. de Sonneville, Buitelaar, Rommelse J Am Acad Child Adolesc Psychiatry. 2012 Nov;51(11):1160-1172.

Gradient overarching disorder hypothesis

- In support
  - an ADHD class without ASD symptoms
  - absence of an ASD class without ADHD symptoms
  - cognitive functioning of the simple ADHD-class is less impaired than that of both comorbid classes.
- In conflict
  - severity of ADHD, comorbid oppositional and anxiety symptoms and cognitive problems were not the highest in the ASD(+ADHD) class
  - some specificity of cognitive deficits across classes.

Homogeneous combinations of ASD-ADHD traits and their cognitive and behavioral correlates in a population-based sample

- Sofar, approaches to identify more homogeneous subgroups have studied variability only in the affected population.
- Here we aim to identify subgroups of children with distinct ASD -ADHD trait profiles **in the general population,** using measures sensitive across the ASD and ADHD trait continua, including the unaffected ends, and show how these subgroups differ in terms of cognitive functioning.

Van der Meer, Lappenschaar, Hartman, Greven, Buitelaar, Rommelse. J Attention Disorders 2014

Homogeneous combinations of ASD-ADHD traits and their cognitive and behavioral correlates in a population-based sample

- We examined continuously distributed ASD and ADHD traits in relation to other internalizing and externalizing problems and cognitive functions in **378 children (6-13 years) from a population sample**.
- Latent class analyses (LCA) were conducted on the Autism Quotient (AQ) and the Strengths and Weaknesses of ADHD symptoms and Normal behavior (SWAN) rating scale.

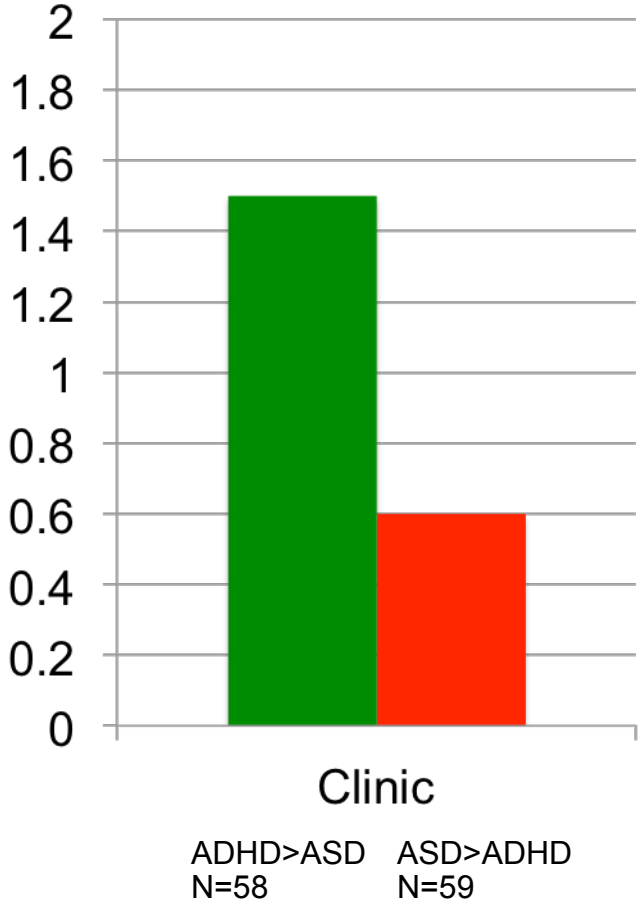
Van der Meer, Lappenschaar, Hartman, Greven, Buitelaar, Rommelse. J Attention Disorders 2014

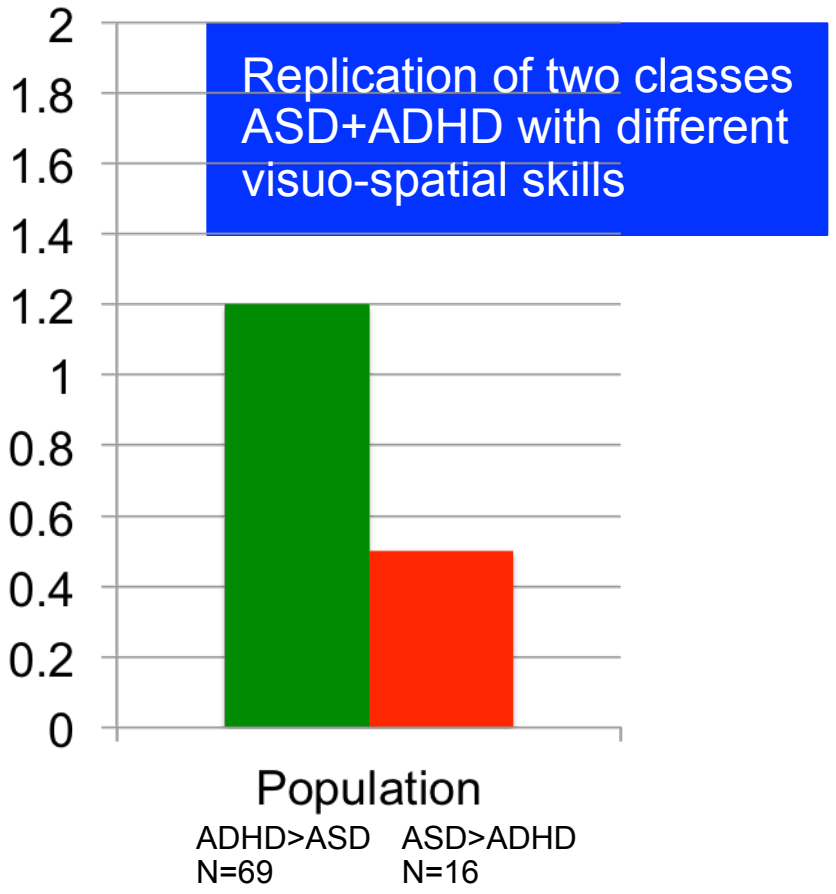
Homogeneous combinations of ASD-ADHD traits and their cognitive and behavioral correlates in a population-based sample

- In addition to three concordant classes with low (10.1%), medium (54.2%) or high (13.2%) scores on both traits, LCA revealed **two discordant classes with more ADHD than ASD characteristics (ADHD>ASD, 18.3%) and vice versa (ASD>ADHD, 4.2%).**
- Classes were **dissociated in visual-spatial functioning**, with ASD>ADHD exhibiting superior, and ADHD>ASD and the class with high scores on both traits, inferior performances.

Van der Meer, Lappenschaar, Hartman, Greven, Buitelaar, Rommelse. J Attention Disorders 2014

Are ASD and ADHD different manifestations of one overarching disorder?





Van der Meer, Oerlemans, van Steijn, Lappenschaar. de Sonneville, Buitelaar, Rommelse J Am Acad Child Adolesc Psychiatry. 2012 Nov;51(11):1160-1172; Van der Meer, Lappenschaar, Hartman, Greven, Buitelaar, Rommelse. J Attention Disorders 2014

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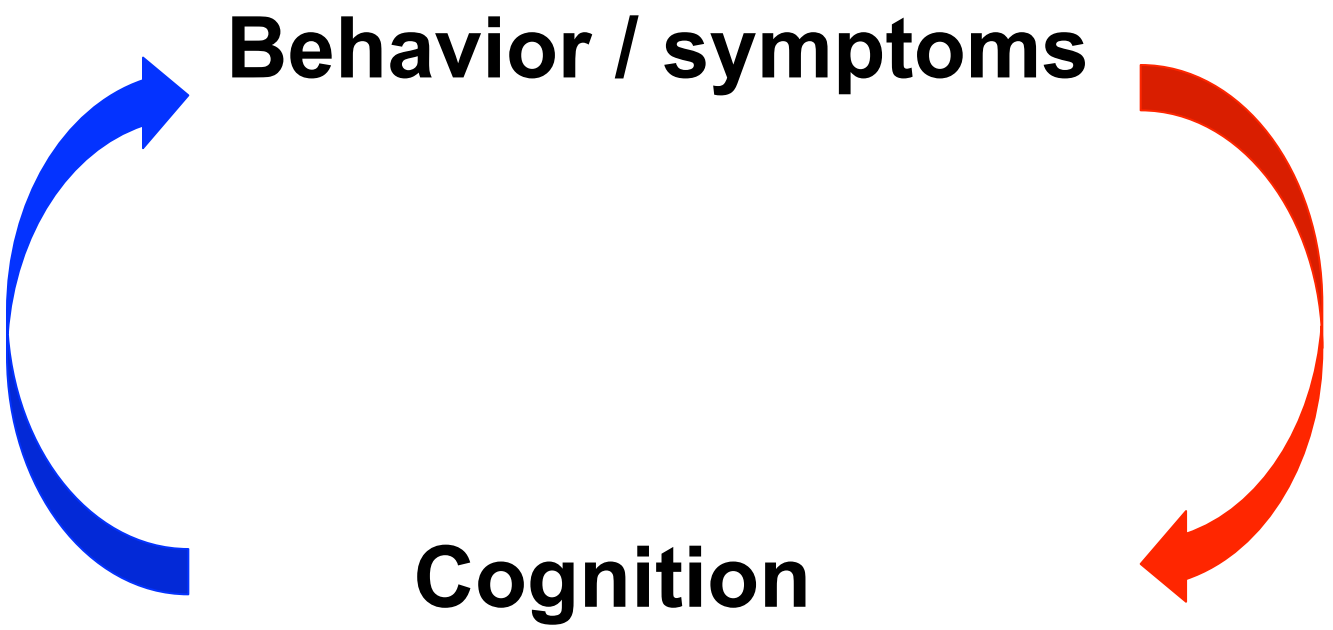
Homogeneous combinations of ASD-ADHD traits and their cognitive and behavioral correlates in a population-based sample

Conclusions

- A minority of children displays atypical discordant trait profiles characterized by differential visual-spatial functioning.
- This dissociation was previously also reported in clinical classes with ASD and ADHD, suggesting that heterogeneity in ASD and ADHD is rooted in heterogeneity present in the lower unaffected end of the distribution

Van der Meer, Lappenschaar, Hartman, Greven, Buitelaar, Rommelse. J Attention Disorders 2014

Cognitive subtyping



Using cognitive subtyping to examine the relationship between ASD and ADHD

Description of the Cognitive Measures

Task	Measurement potential	Dependent variable(s)
Baseline Speed[a,b]	Speed and variability of motor output as response to external cue	Mean reaction time (ms) and variability (SD of reaction time in ms)
Digit Span (WISC-III)[a,c]	Verbal Attention	Number of correct reproduced digits in identical (forward) order
	Verbal Working Memory	Number of correct reproduced digits in reversed (backward) order
Visuo-Spatial Sequencing[a,b]	Visuo-Spatial Attention	Number of correct reproduced sequences in identical (forward) order
	Visuo-Spatial Working Memory	Number of correct reproduced sequences in reversed (backward) order
Block Patterns (WISC-III)[a,c]	Visual pattern recognition	Number of correct and timely completed geometric designs
Facial Emotion Recognition[a,b]	Capacity to identify the facial emotional expression of happiness, sadness, anger and anxiety.	Mean reaction time (ms) and accuracy on four emotions

Rommelse, Van der Meer, Hartman, Buitelaar (under review)

Using cognitive subtyping to examine the relationship between ASD and ADHD

- Latent class analyses (LCA) were performed on motor speed and variability, verbal and visual-spatial attention, verbal and visual-spatial working memory, visual pattern recognition and emotion recognition in 360 participants from a **population based sample** and 254 participants from **a clinic based sample** (5 -17 years).
- Classes were compared on several behavioral symptom scales.

Rommelse, Van der Meer, Hartman, Buitelaar (under review)

Using cognitive subtyping to examine the relationship between ASD and ADHD

- LCAs in the population and clinic samples revealed a similar four class solution typified by qualitatively different speed-accuracy trade-offs:
  - *high accuracy-medium speed* (21.9% of the population sample and 16.5% of the clinic sample),
  - *medium accuracy-high speed* (24.2% and 24.4%),
  - *low accuracy-medium speed* (35.3% and 39.0%) and
  - *low accuracy-low speed* (18.6% and 20.0%).

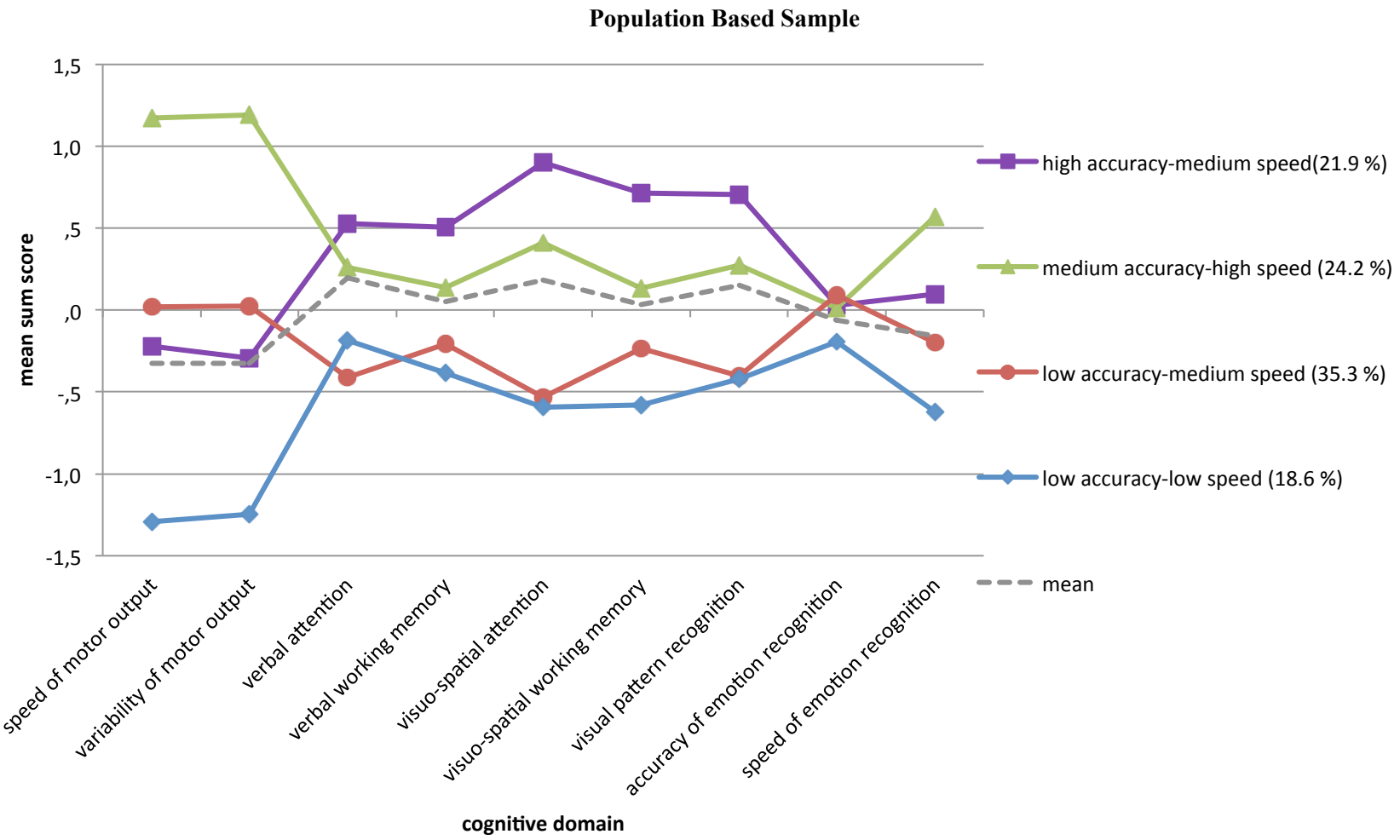
Rommelse, Van der Meer, Hartman, Buitelaar (under review)

Using cognitive subtyping to examine the relationship between ASD and ADHD

- These classes were respectively associated with lowest en highest levels of ASD and ADHD symptoms in the clinical sample, with an overall strong predictive effect.
- Associations with clinical symptoms were much weaker in the population sample.
- Classes were not characterized by domain specific cognitive strengths or weaknesses.

Rommelse, Van der Meer, Hartman, Buitelaar (under review)

Using cognitive subtyping to examine the relationship between ASD and ADHD



Rommelse, Van der Meer, Hartman, Buitelaar (under review)

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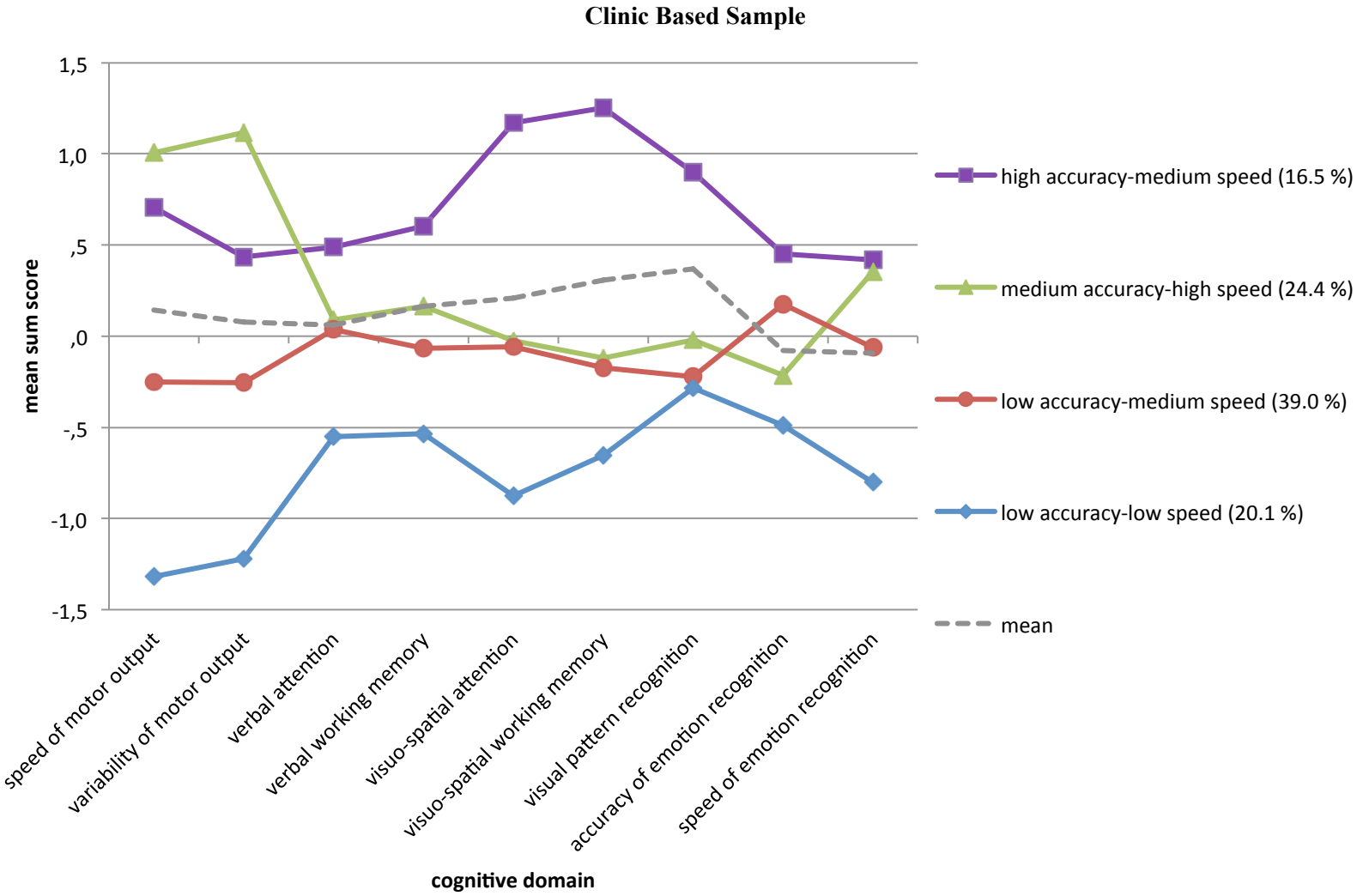

Rommelse, Van der Meer, Hartman, Buitelaar (under review)

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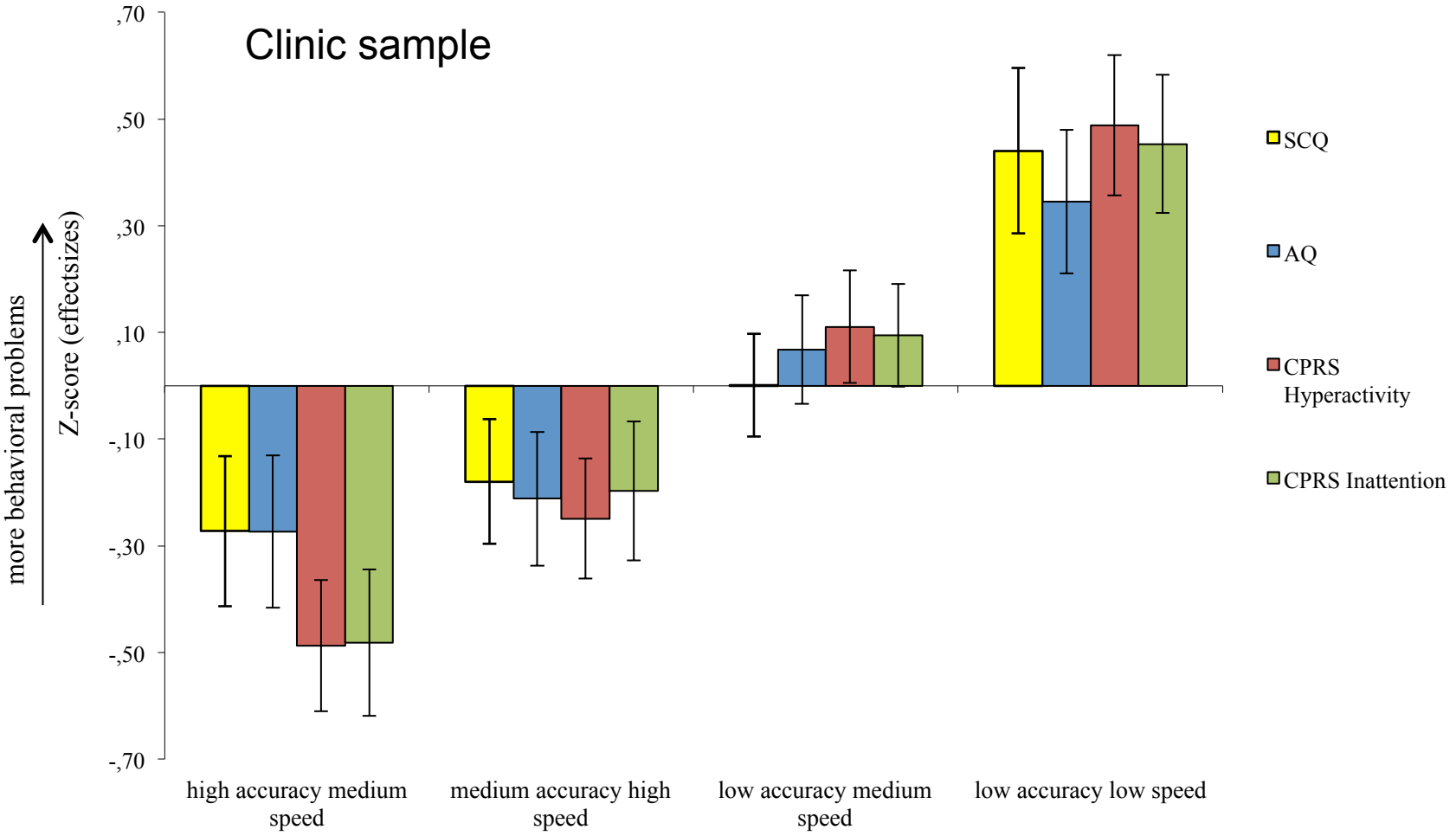

Rommelse, Van der Meer, Hartman, Buitelaar (under review)

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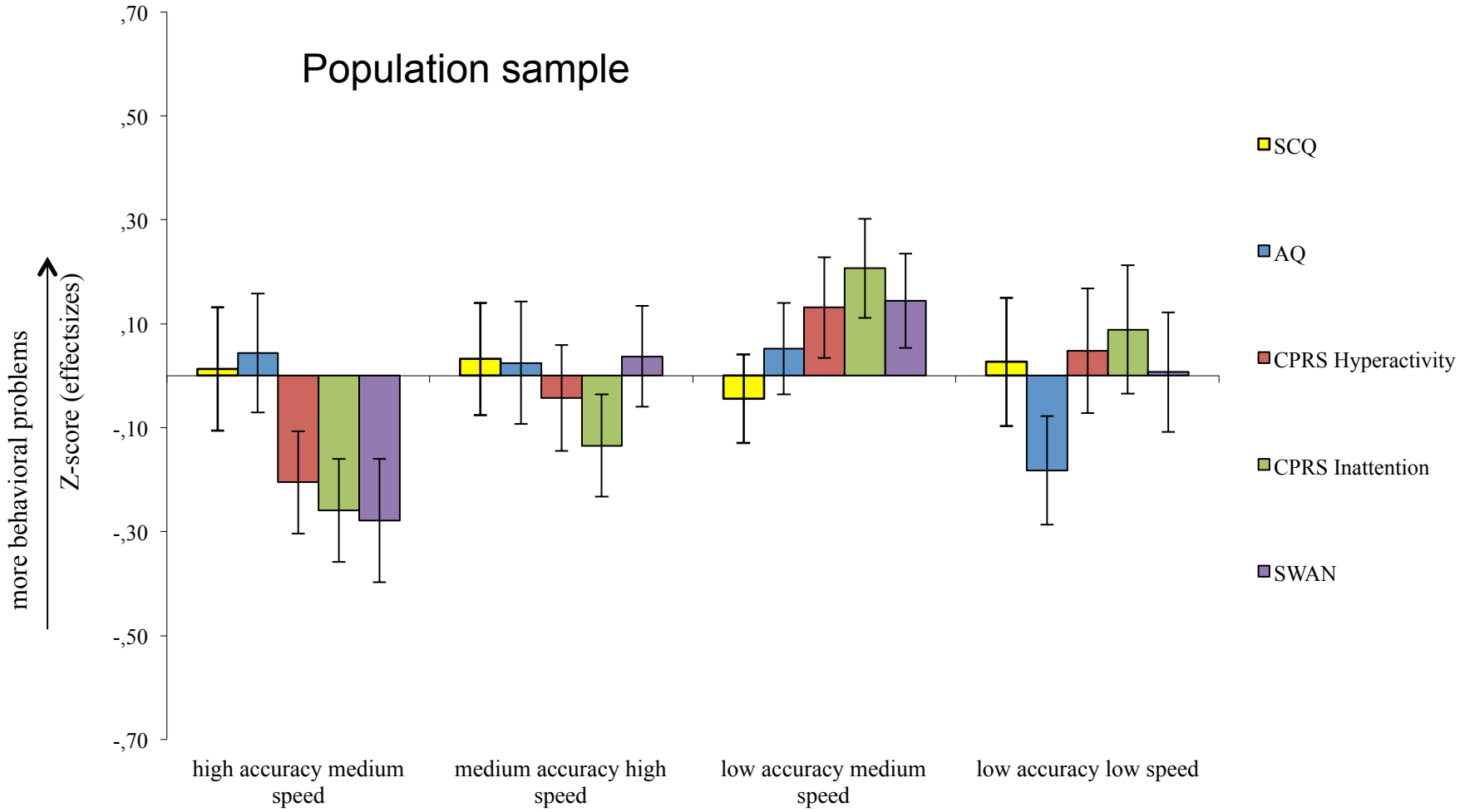

Rommelse, Van der Meer, Hartman, Buitelaar (under review)

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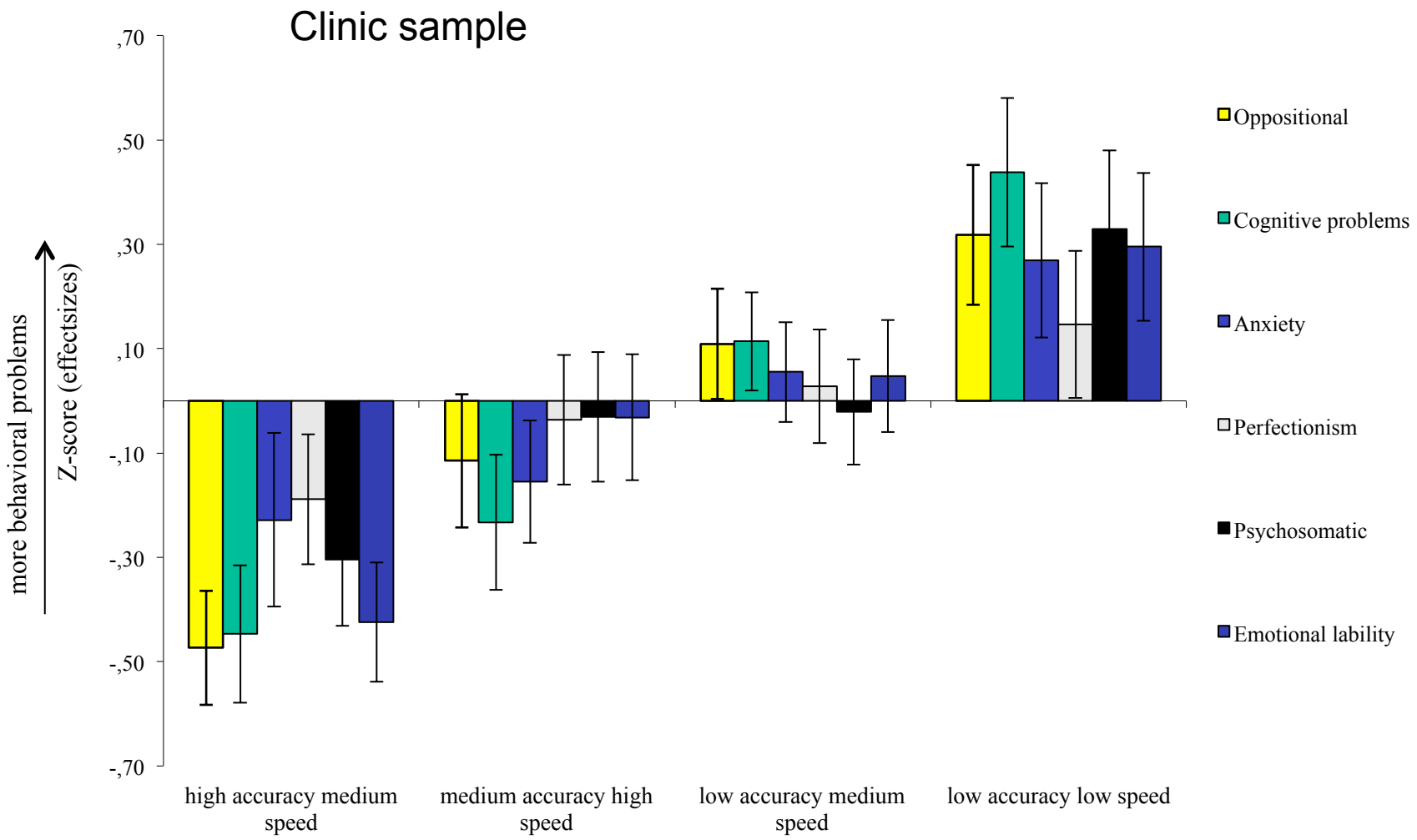

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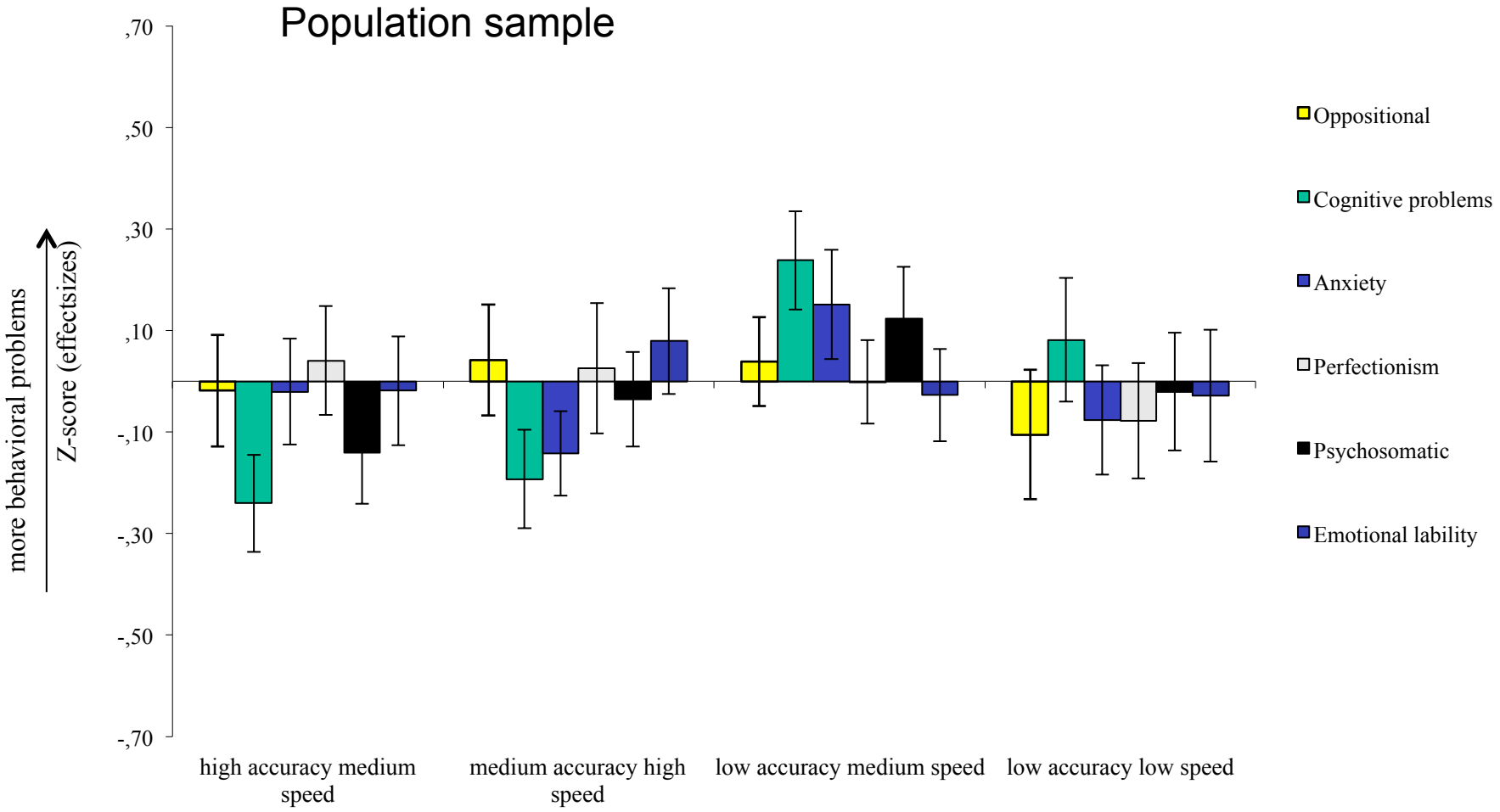
Using cognitive subtyping to examine the relationship between ASD and ADHD



Rommelse, Van der Meer, Hartman, Buitelaar (under review)

Using cognitive subtyping to examine the relationship between ASD and ADHD

Conclusions

- Cognitive subtyping appears a powerful strategy to uncover the mechanisms underlying ASD and ADHD.
- Do the cross-domain generic cognitive factors have a specific neural architecture: MRI studies needed.
- The weak associations between cognition and behavior in the population sample suggest that cognitive functioning may only predict behavior when other risk or protective factors are present.

Rommelse, Van der Meer, Hartman, Buitelaar (under review)

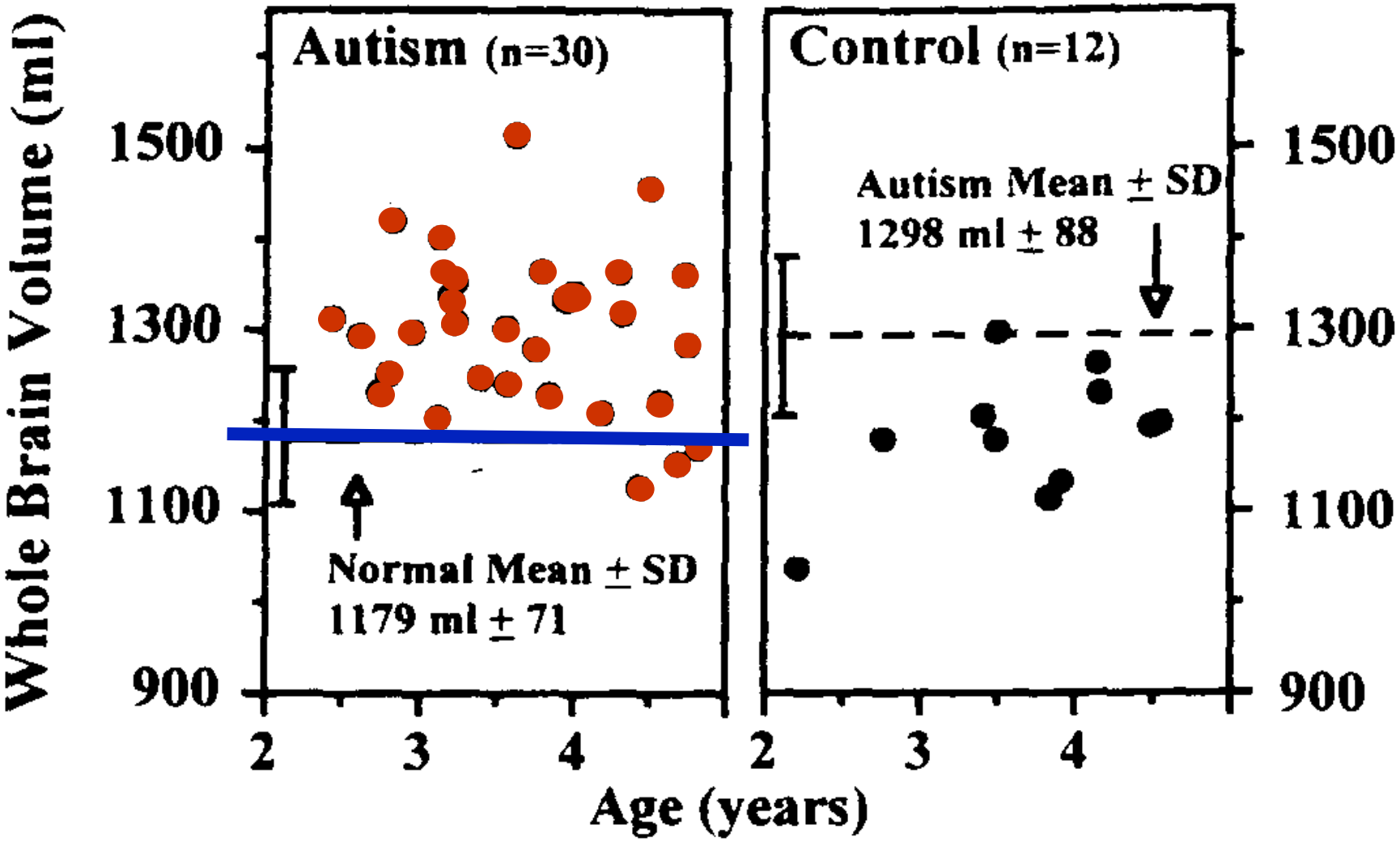
Conclusions

- There is clinical and genetic overlap between autism and ADHD
- Behaviour ➔ cognition and comorbidity: some evidence for autism and ADHD as part of an overarching disorder
- Cognition ➔ behavior: speed-accurary trade-off; general principle of neural architecture

Outline of the talk

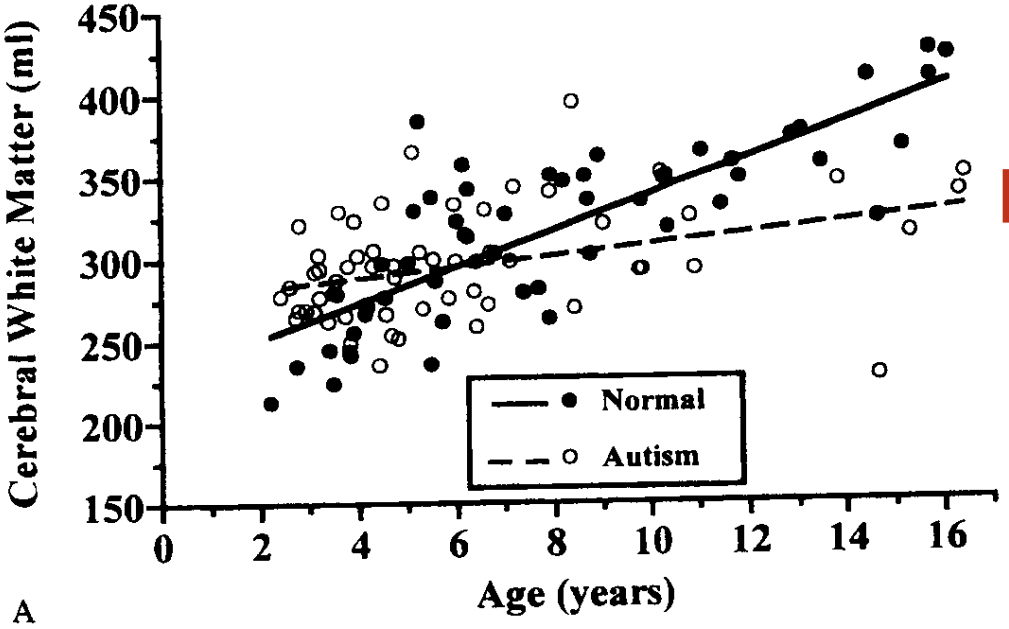
- Clinical issues
- Genetics
- Cognitive measures
- **Brain function and structure**
- Implications – new concepts

Whole brain volume in 2-4 year olds (autism vs controls)



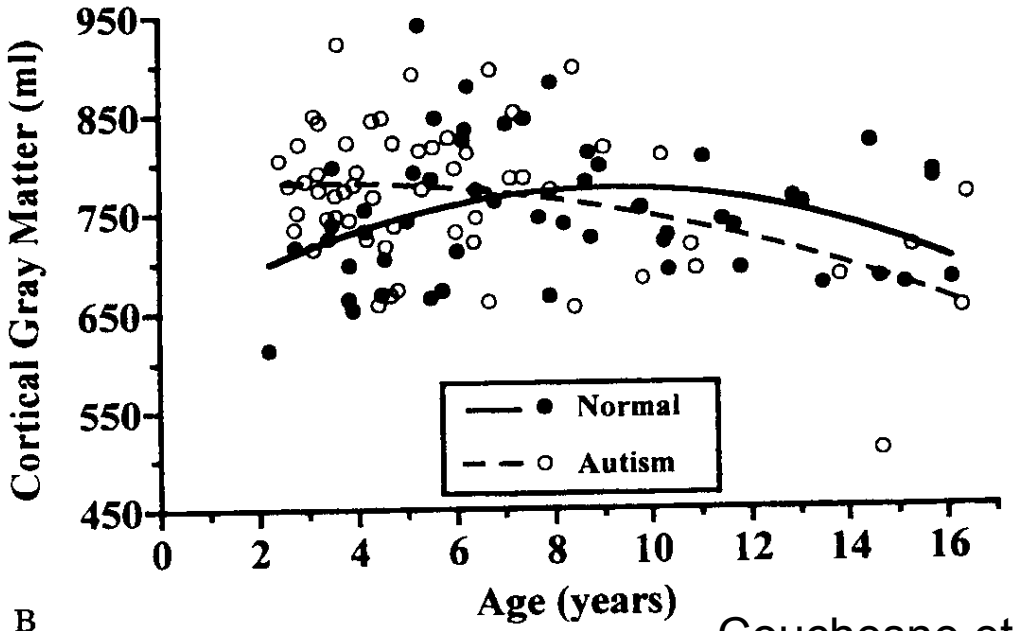
Courchesne et al., Neurology, 2001, 57, 245-254

Brain Volumes in ASD



A

Volume of cerebral white matter

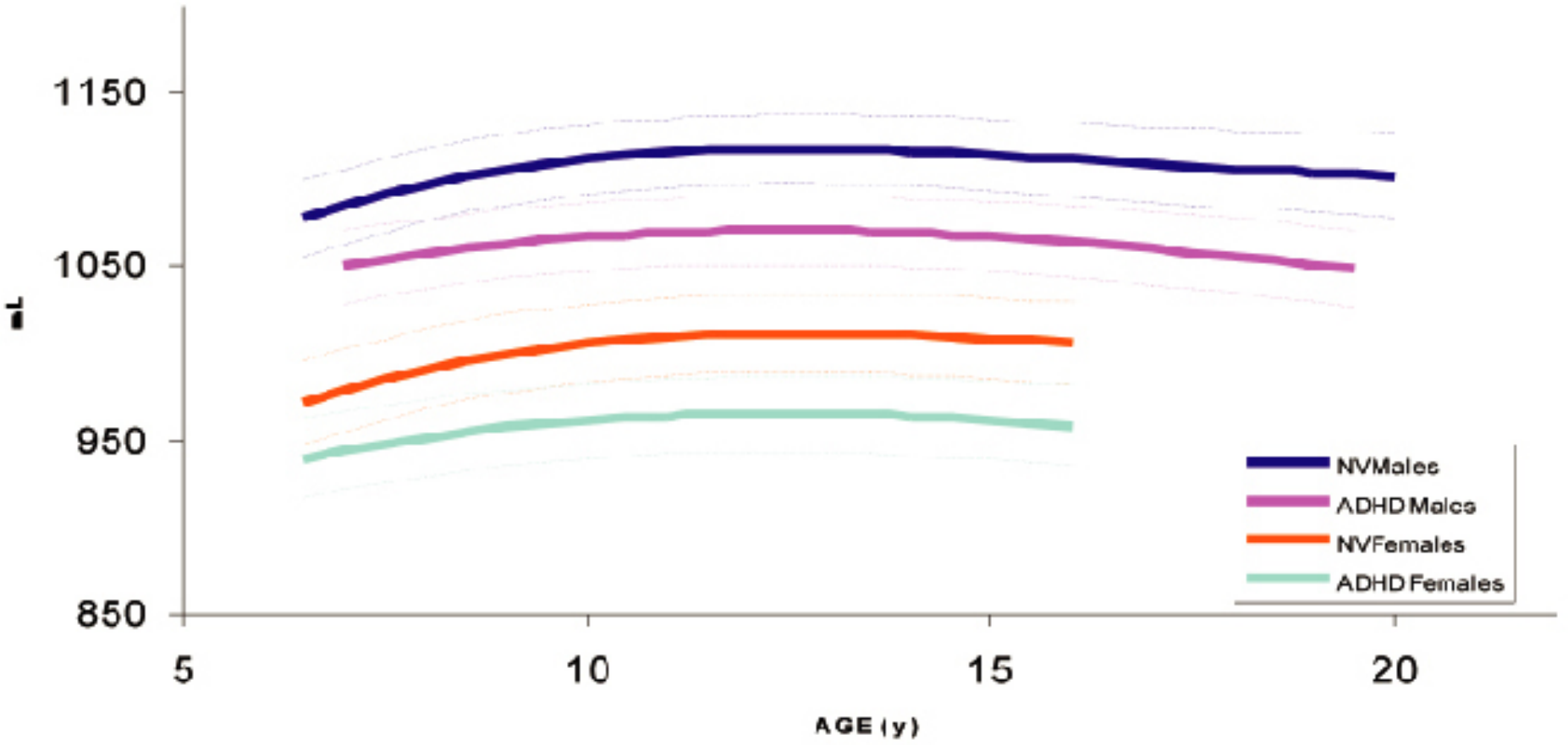


B

Volume of cerebral gray matter

Couchesne et al., 2001

Brain volumes in ADHD

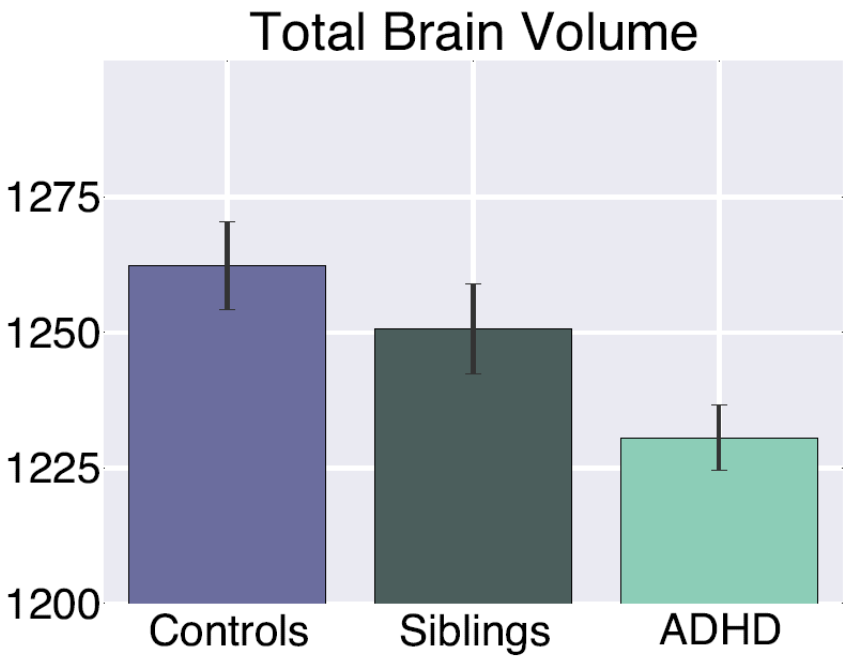


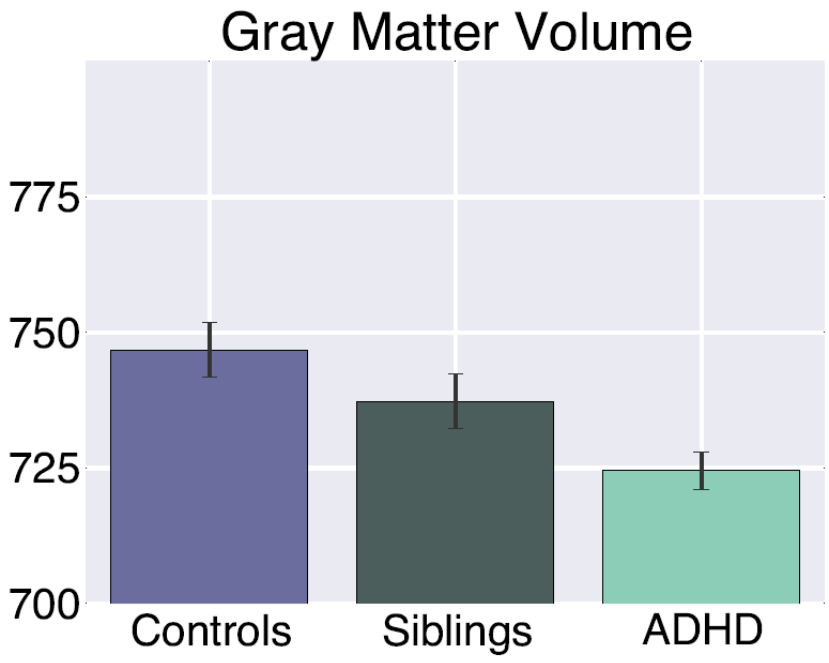
Castellanos et al., 2002

Total brain volume (= total gray + white matter)

Greven et al. JAMA Psychiatry 2015

- Main effects of ADHD diagnosis on **total brain** and **total gray matter** volumes
  - Total brain 32ml (**2.5%**), total gray matter 22ml (**3%**) smaller in subjects with ADHD
- No diagnosis x age effects





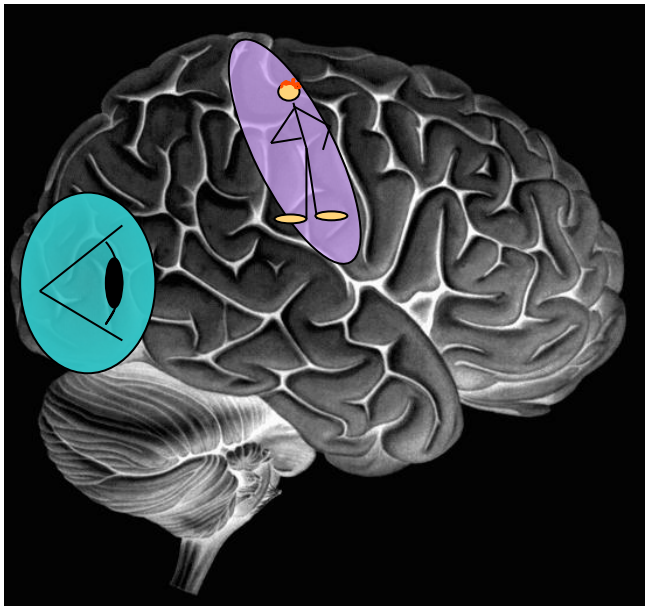
Principles of Organisation

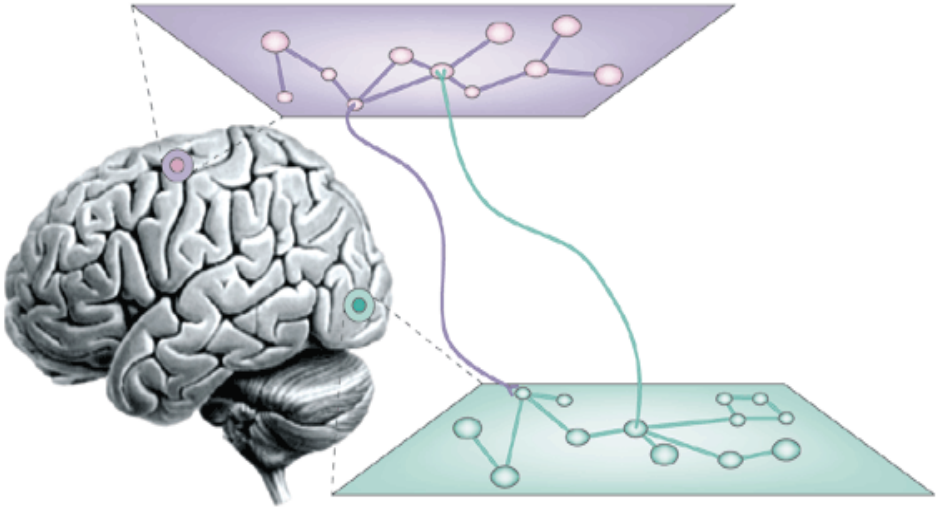
Functional specialization

Localisation

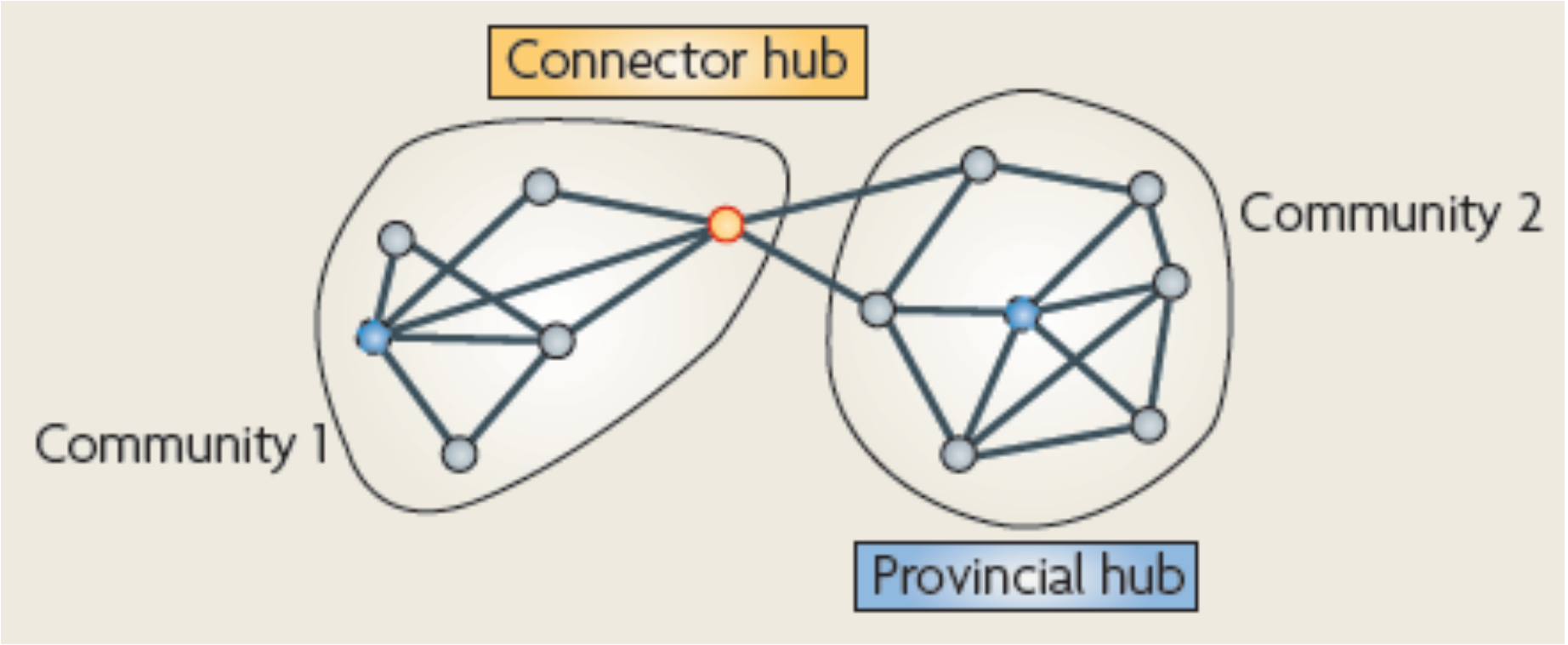
Functional integration

Connectivity



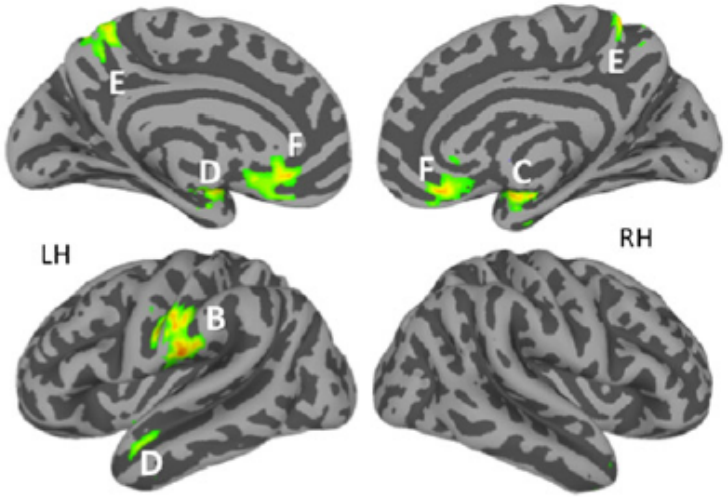


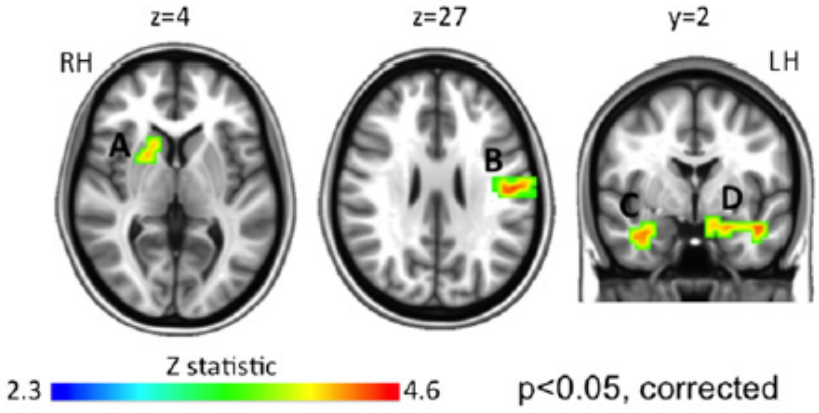
Neuronal network analysis



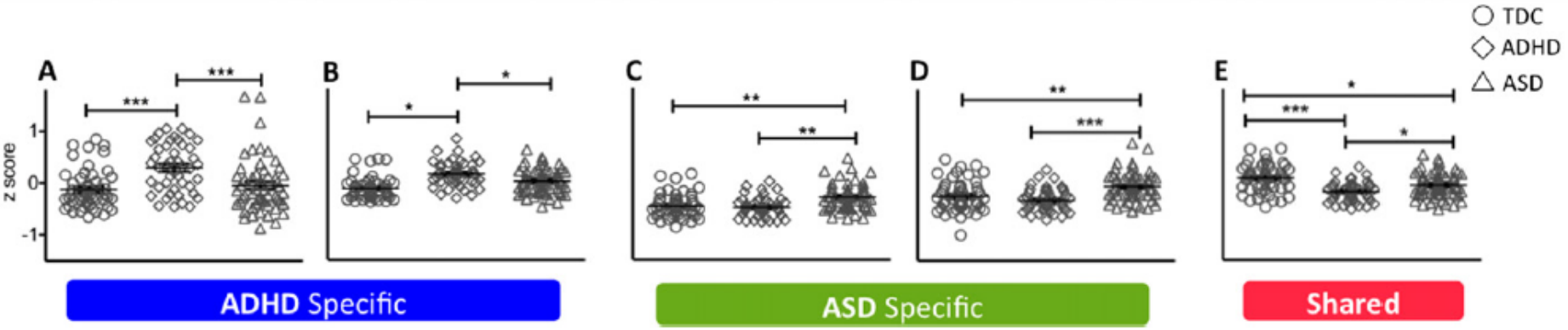
Distinct and shared intrinsic functional network centrality in ASD and ADHD

One-way ANCOVA





Post-Hoc

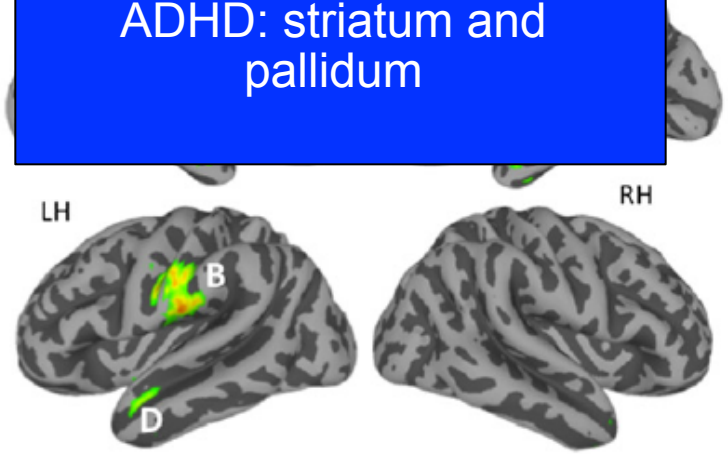


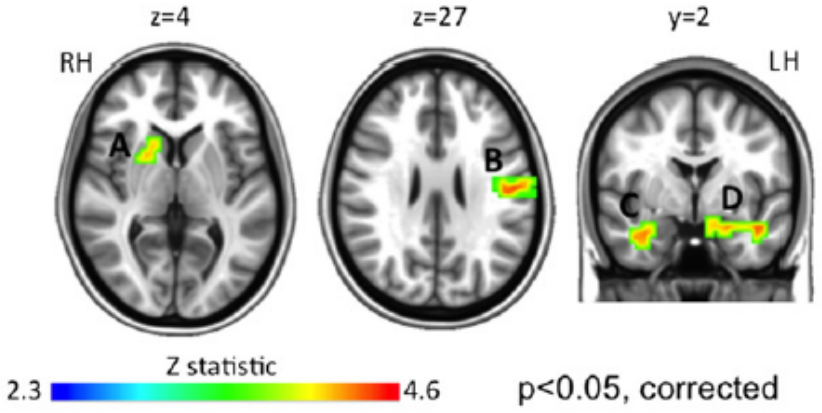
Di Martino et al. Biol Psychiatry 2013

Distinct and shared intrinsic functional network centrality in ASD and ADHD

One-way ANCOVA

ADHD: striatum and pallidum





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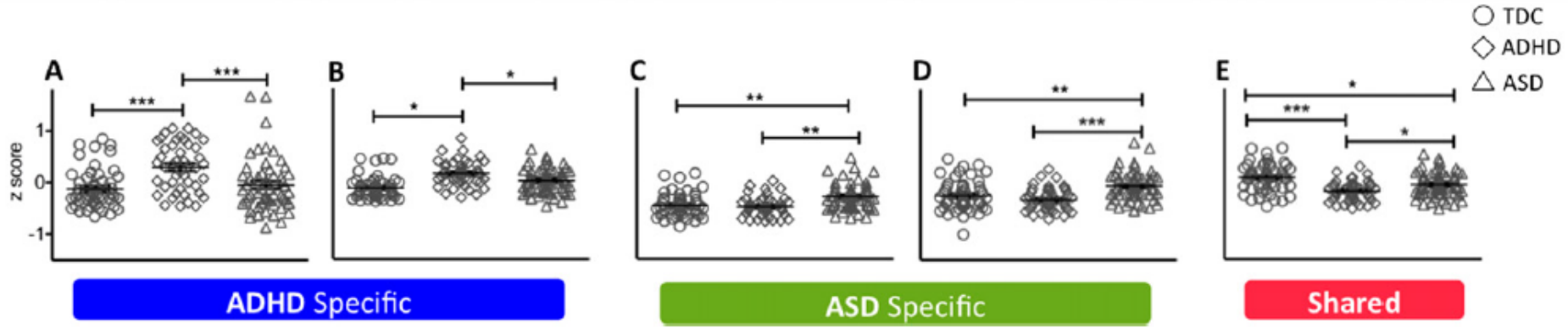
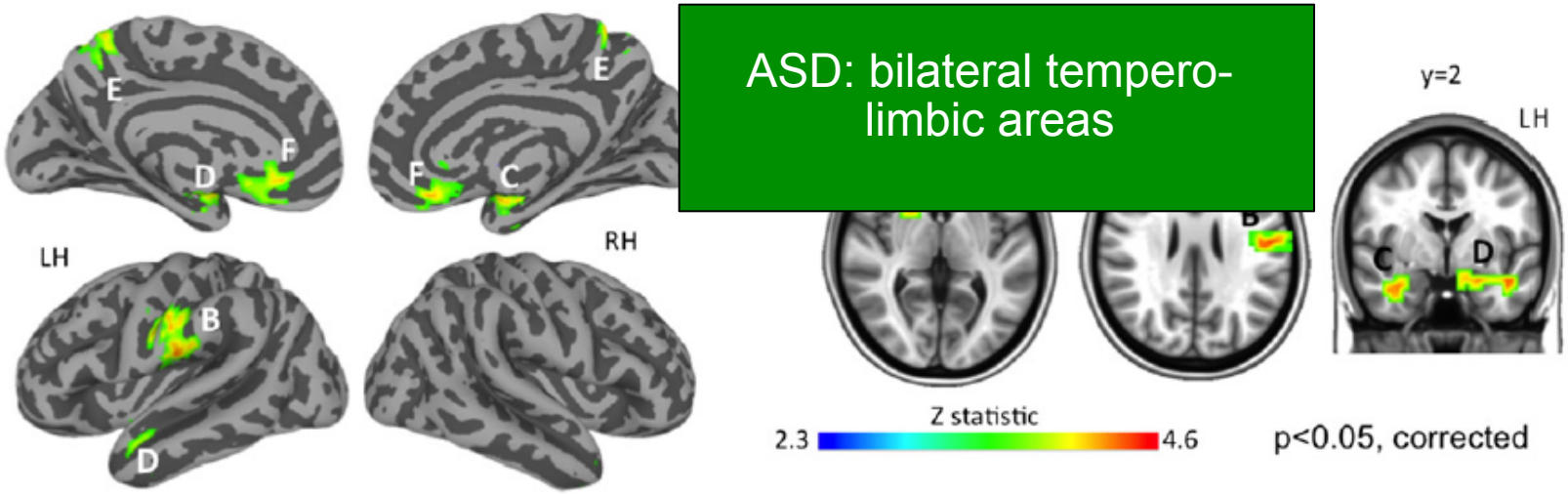


Di Martino et al. Biol Psychiatry 2013

Distinct and shared intrinsic functional network centrality in ASD and ADHD

One-way ANCOVA



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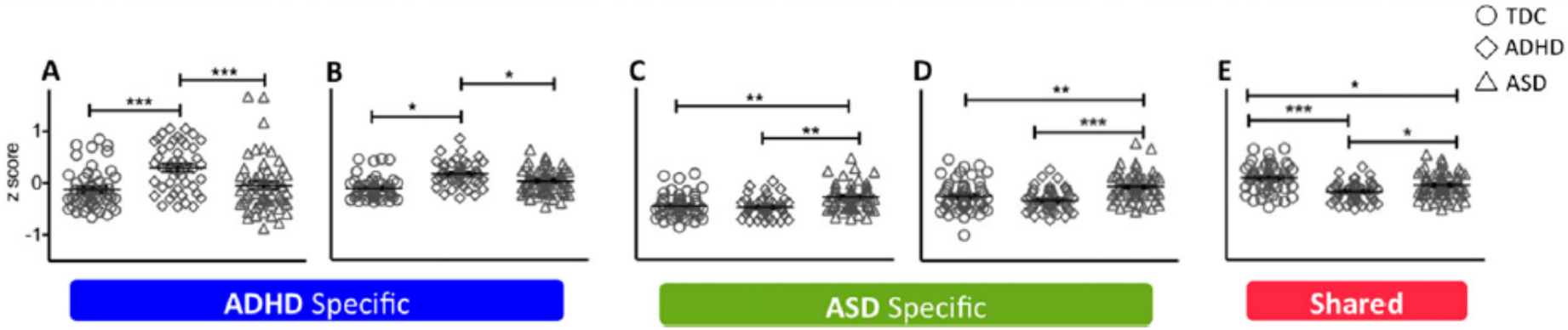

Di Martino et al. Biol Psychiatry 2013

Distinct and shared intrinsic functional network centrality in ASD and ADHD

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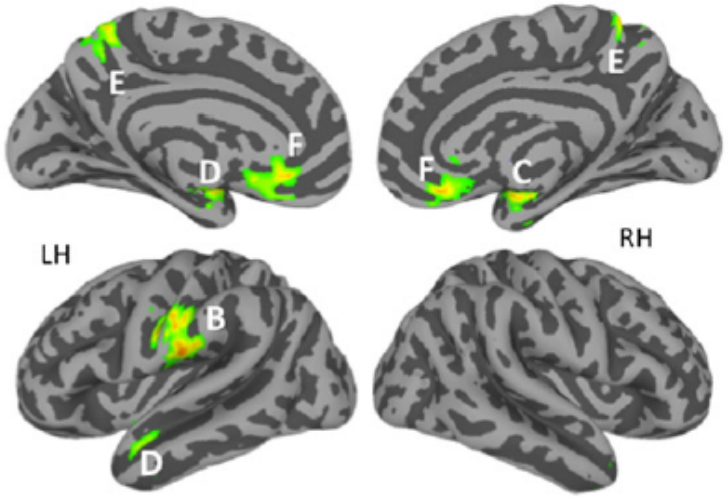
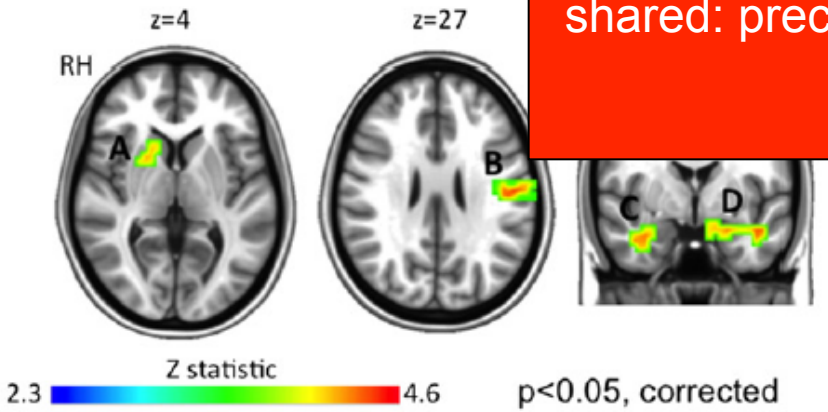
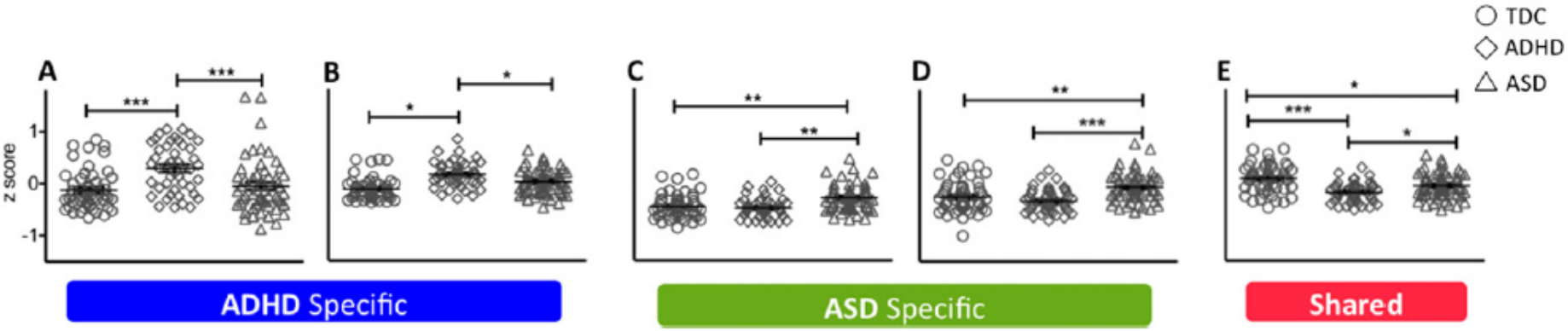




shared: precuneus

Post-Hoc



Di Martino et al. Biol Psychiatry 2013

Conclusion

- ASD and ADHD are disorders of brain development and brain connectivity
- Sofar, stronger evidence for distinct than for shared neural correlates
- However, studies with small samples and DSM-based

Outline of the talk

- Clinical issues
- Genetics
- Cognitive measures
- Brain function and structure
- **Implications – new concepts**

Implications

- Integrate / combine research on ASD and ADHD
- Apply theories on ASD to ADHD and vice versa
- Apply research approach used in ASD to ADHD and vice versa

Implications

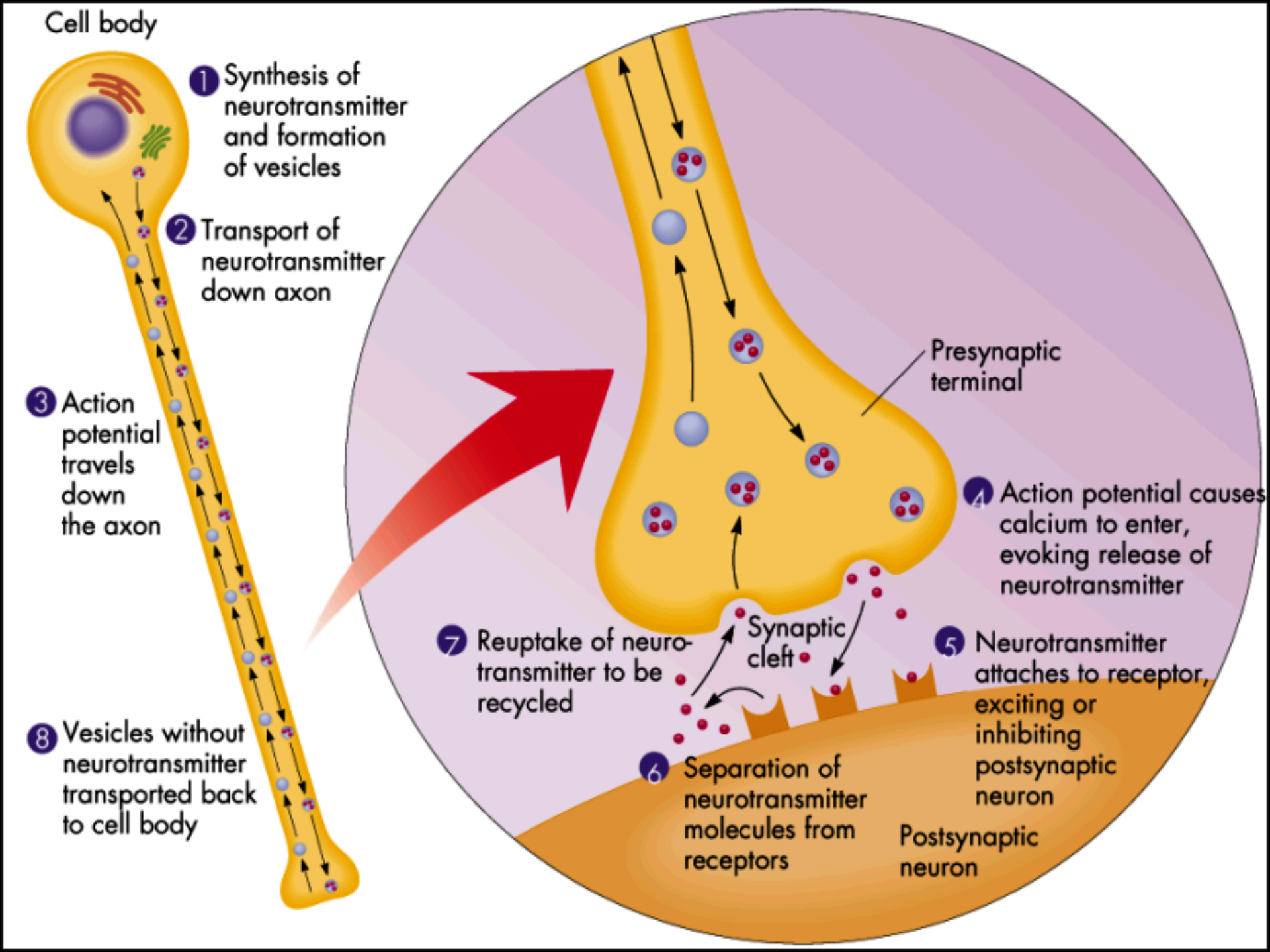
- I

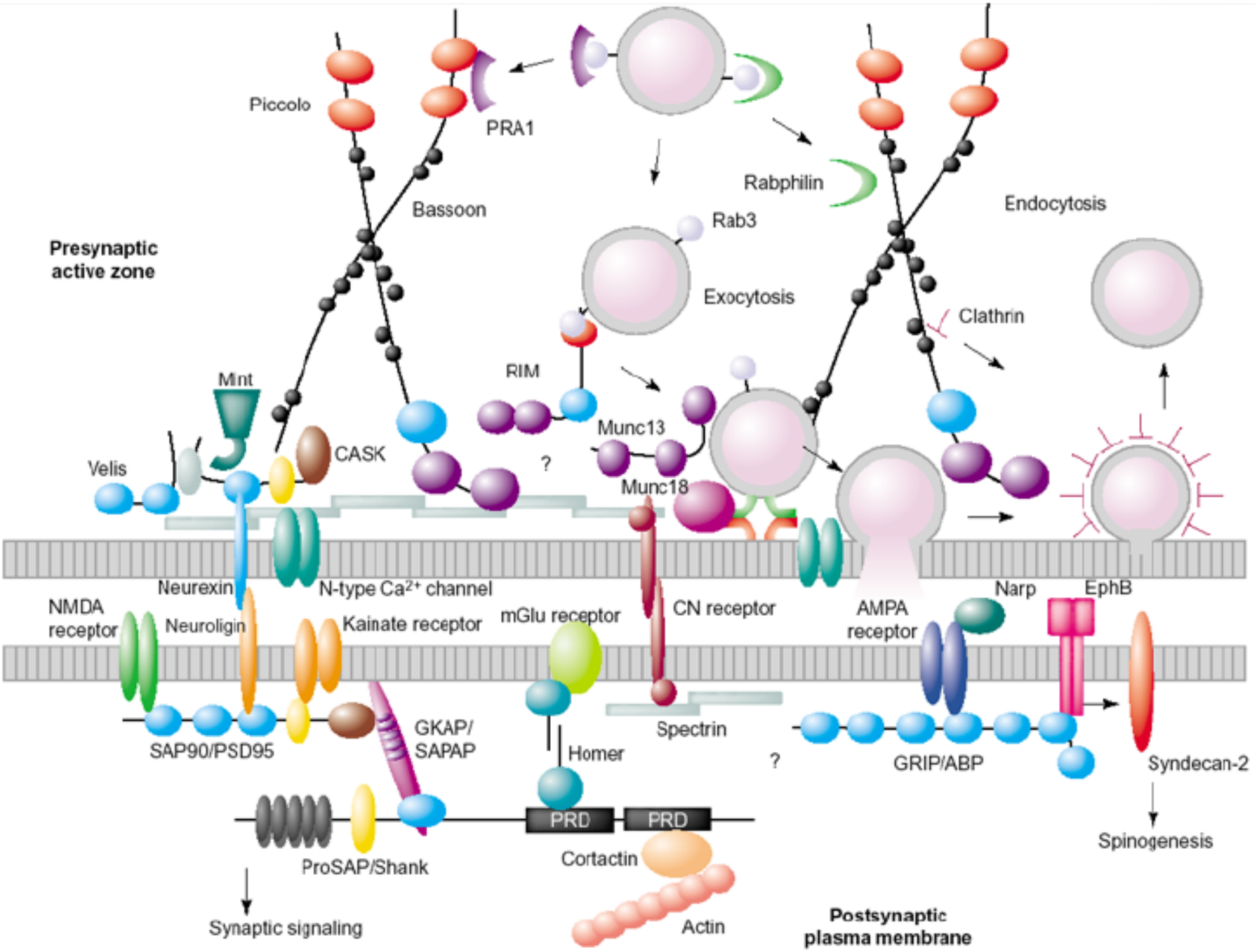
Theories

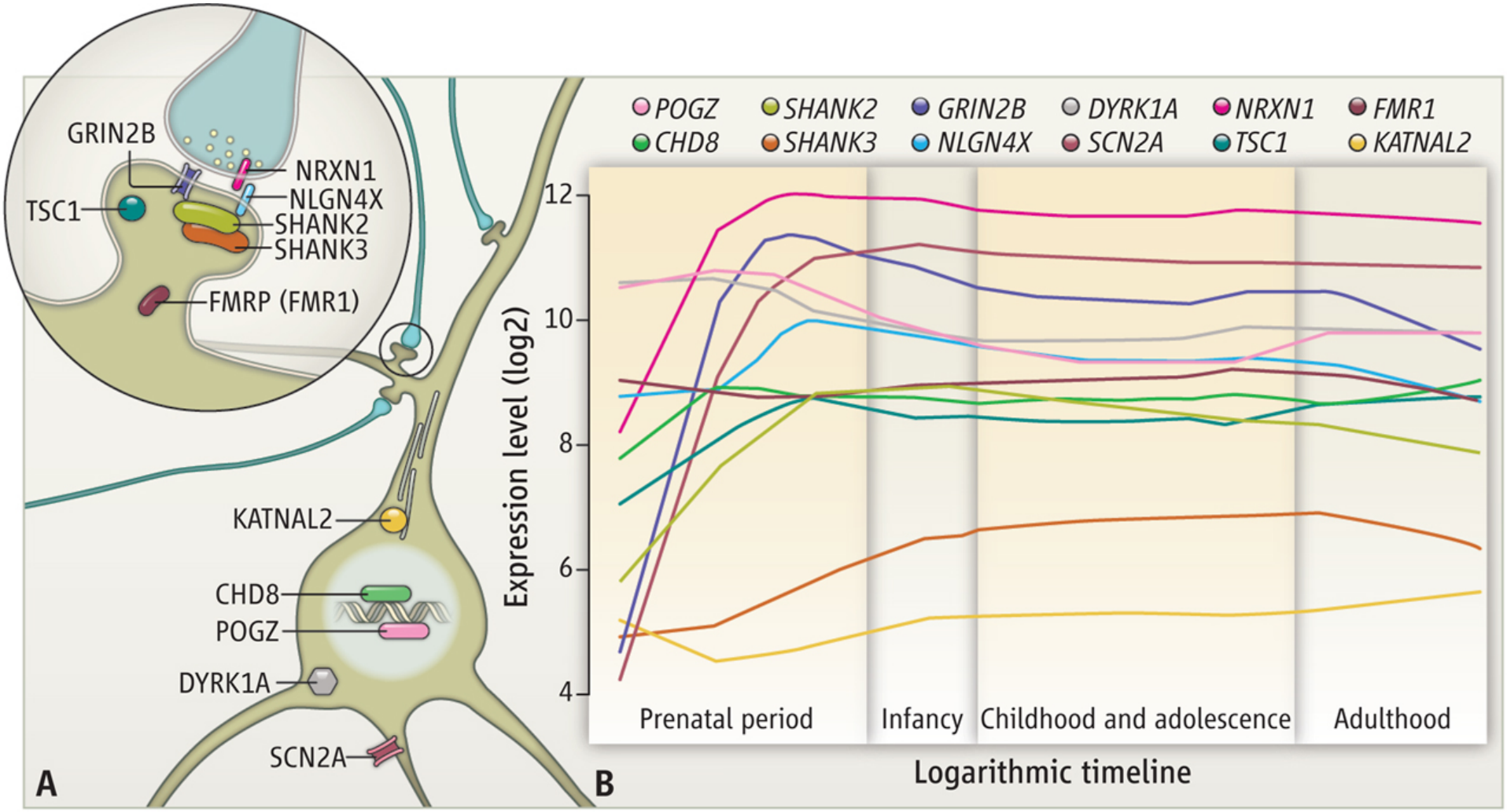
1.predictive coding – brain as a prediction machine
2.failure of modularisation
3.connectivity account
4.different factors involved in etiology/genesis versus remission/recovery
5.symptoms = secundary brain response to primary synaptic dysfunction
6.secundary brain disease due to primary systemic disease (inflammation, microbiome, mitochondrial disease)
7.etiology/onset due to failing / weak EF

ADHD and ASD: two manifestations of the same disorder?

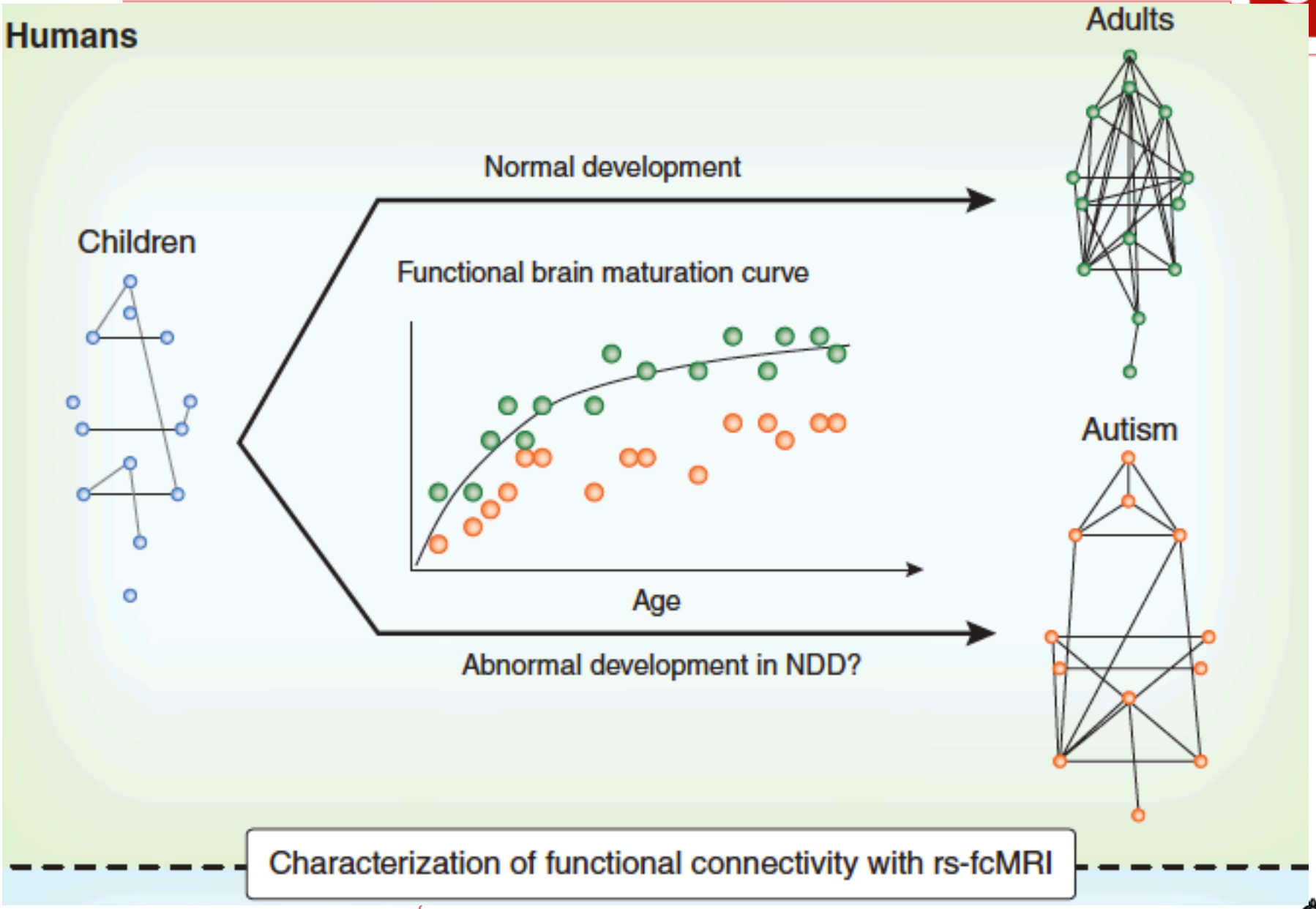
These neurodevelopmental disorders are thought to result from the disruption of normal brain development and related neurobiological mechanisms during the prenatal and early postnatal period


Cell body
1 Synthesis of neurotransmitter and formation of vesicles
2 Transport of neurotransmitter down axon
3 Action potential travels down the axon
8 Vesicles without neurotransmitter transported back to cell body
Presynaptic terminal
4 Action potential causes calcium to enter, evoking release of neurotransmitter
Synaptic cleft
5 Neurotransmitter attaches to receptor, exciting or inhibiting postsynaptic neuron
7 Reuptake of neuro-transmitter to be recycled
6 Separation of neurotransmitter molecules from receptors
Postsynaptic neuron

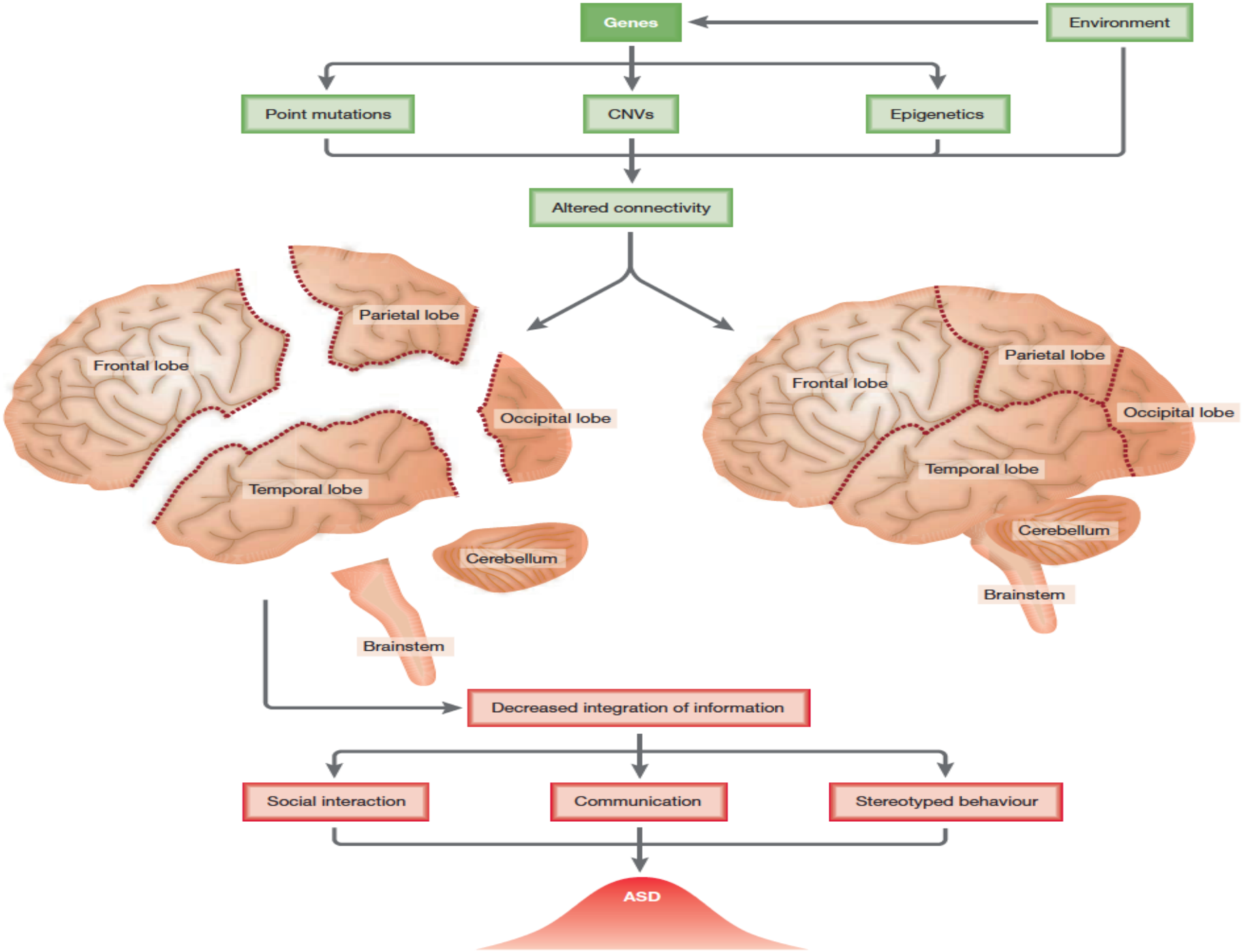

Piccolo
PRA1
Bassoon
Rabphilin
Rab3
Endocytosis
Presynaptic
active zone
Exocytosis
Clathrin
RIM
Mint
Munc13
CASK
Velis
?
Munc18
Neurexin
N-type Ca2+ channel
NMDA
receptor
Neuroligin
Kainate receptor
mGlu receptor
CN receptor
AMPA
receptor
Narp
EphB
GKAP/
SAPAP
Spectrin
SAP90/PSD95
Homer
?
GRIP/ABP
Syndecan-2
PRD
PRD
Spinogenesis
ProSAP/Shank
Cortactin
Synaptic signaling
Actin
Postsynaptic
plasma membrane

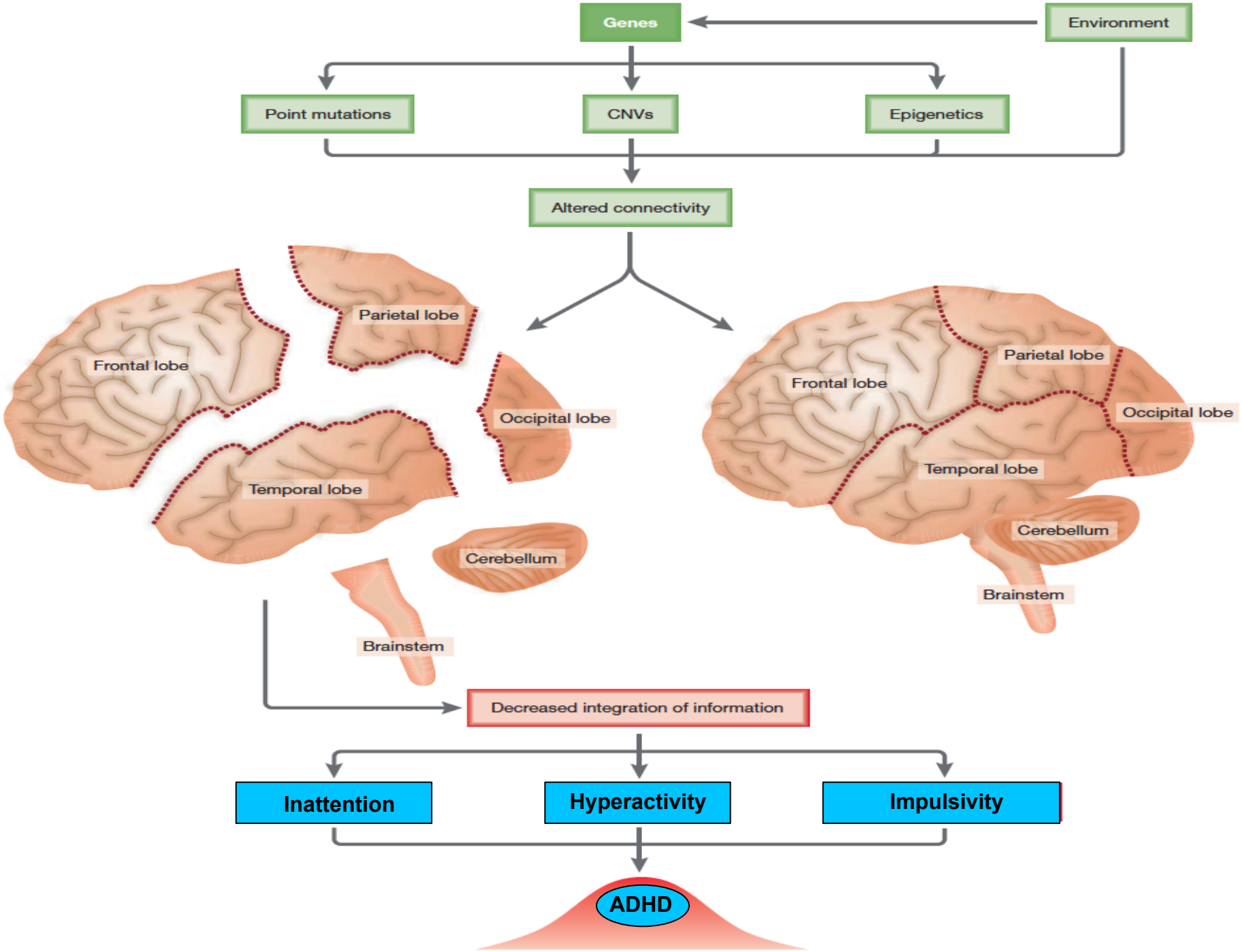

GRIN2B
NRXN1
TSC1
NLGN4X
SHANK2
SHANK3
FMRP (FMR1)
KATNAL2
CHD8
POGZ
DYRK1A
SCN2A
A
POGZ
SHANK2
GRIN2B
DYRK1A
NRXN1
FMR1
CHD8
SHANK3
NLGN4X
SCN2A
TSC1
KATNAL2
Expression level (log2)
12
10
8
6
4
Prenatal period
Infancy
Childhood and adolescence
Adulthood
Logarithmic timeline
B

Autism and ADHD: developmental disorders



Characterization of functional connectivity with rs-fcMRI


Genes
Environment
Point mutations
CNVs
Epigenetics
Altered connectivity
Parietal lobe
Frontal lobe
Occipital lobe
Temporal lobe
Cerebellum
Brainstem
Parietal lobe
Frontal lobe
Occipital lobe
Temporal lobe
Cerebellum
Brainstem
Decreased integration of information
Social interaction
Communication
Stereotyped behaviour
ASD

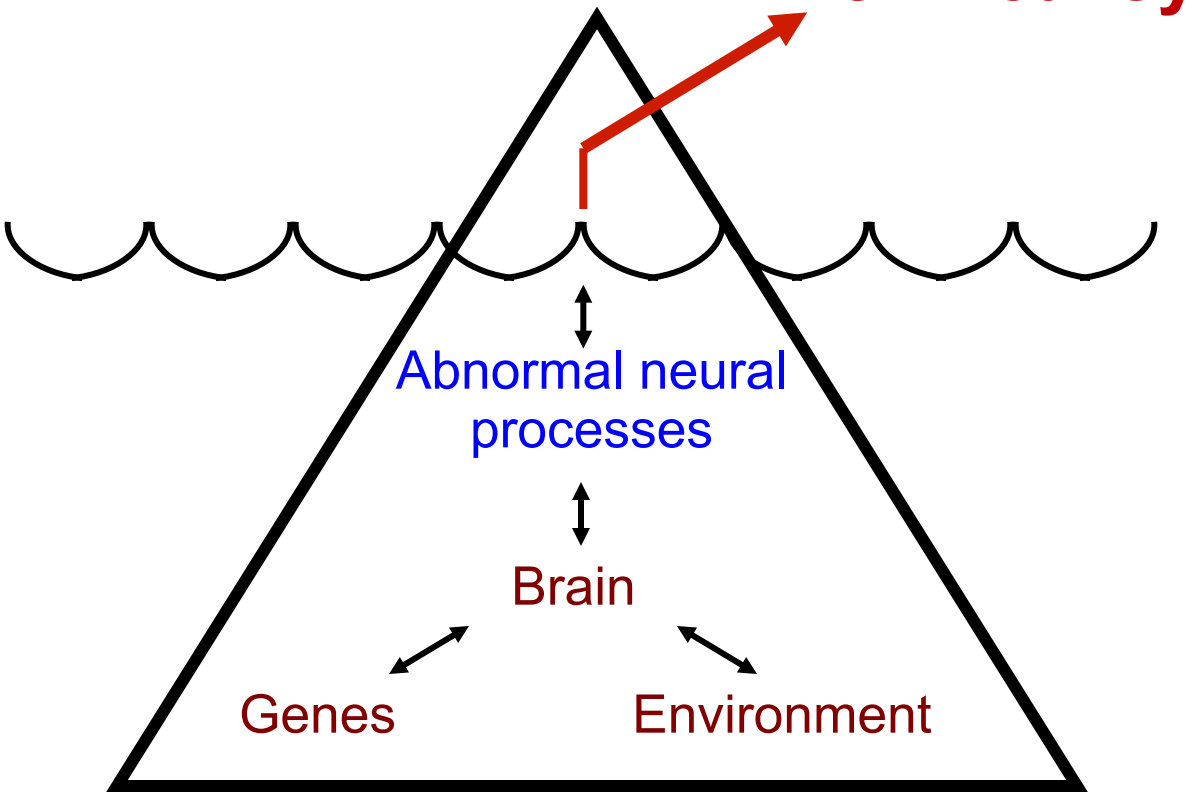

Genes
Environment
Point mutations
CNVs
Epigenetics
Altered connectivity
Parietal lobe
Frontal lobe
Occipital lobe
Temporal lobe
Cerebellum
Brainstem
Parietal lobe
Frontal lobe
Occipital lobe
Temporal lobe
Cerebellum
Brainstem
Decreased integration of information
Inattention
Hyperactivity
Impulsivity
ADHD

Neurodevelopmental disorder

This is different from a cerebral lesion in a mature brain

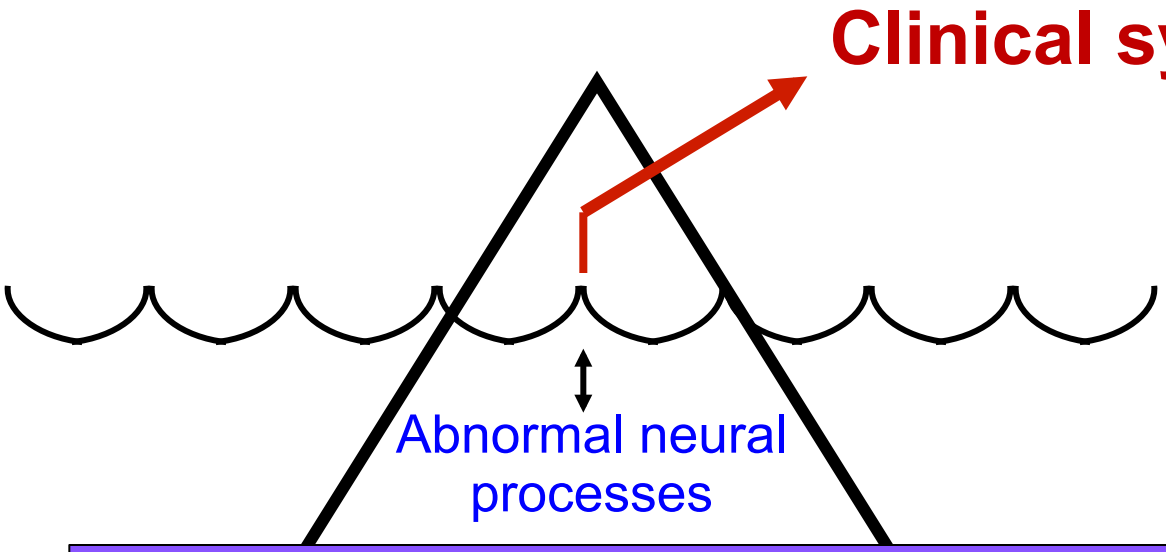
Wide spread ramifications of neural dysfunction towards a variety of clinical symptoms

Clinical symptoms



Compensatory processes may mask primary deficits

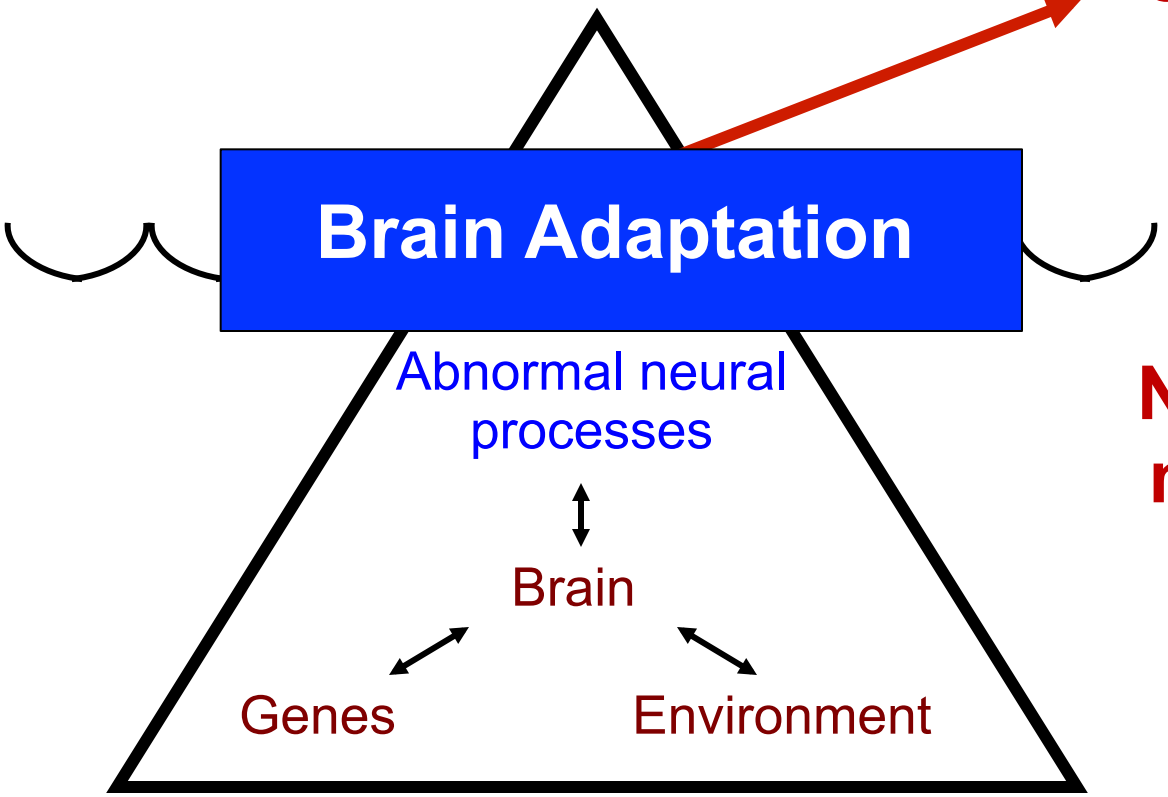
What is the problem ?



Noisy, less efficient information processing

Noise can be productive: leads to finetuning and optimisation

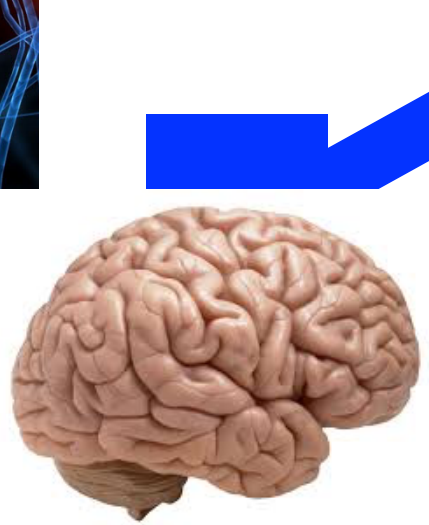
Too much noise is harmful



Clinical symptoms due to brain adaptation

Not due to primary molecular / neural problems

Brain Adaptation and Alternative Developmental Trajectories



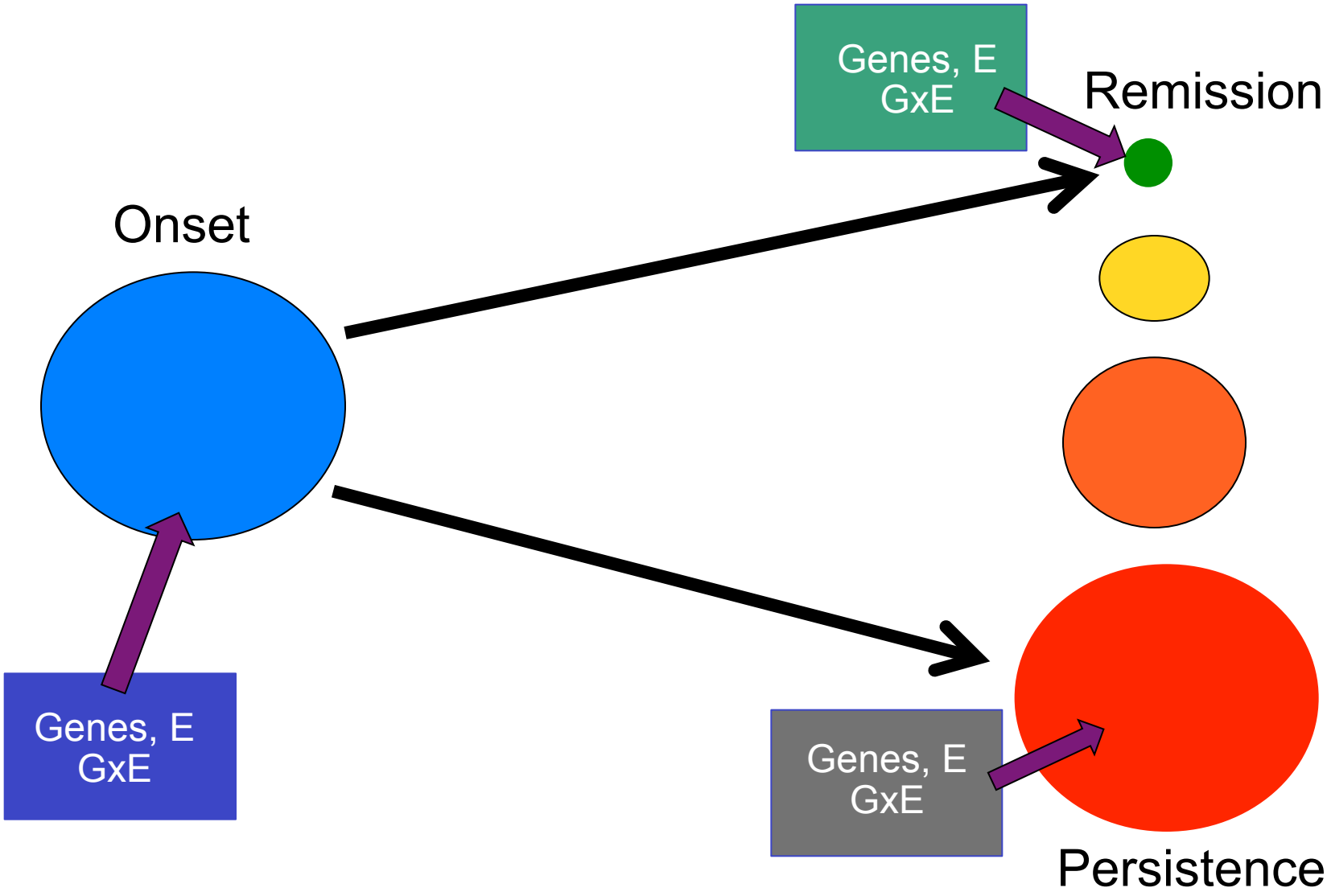
1. Redundancy
2. Reorganization
3. Niche Construction
4. Adjustment of Developmental rate

Johnson et al. Development and Psychopathology, 2015

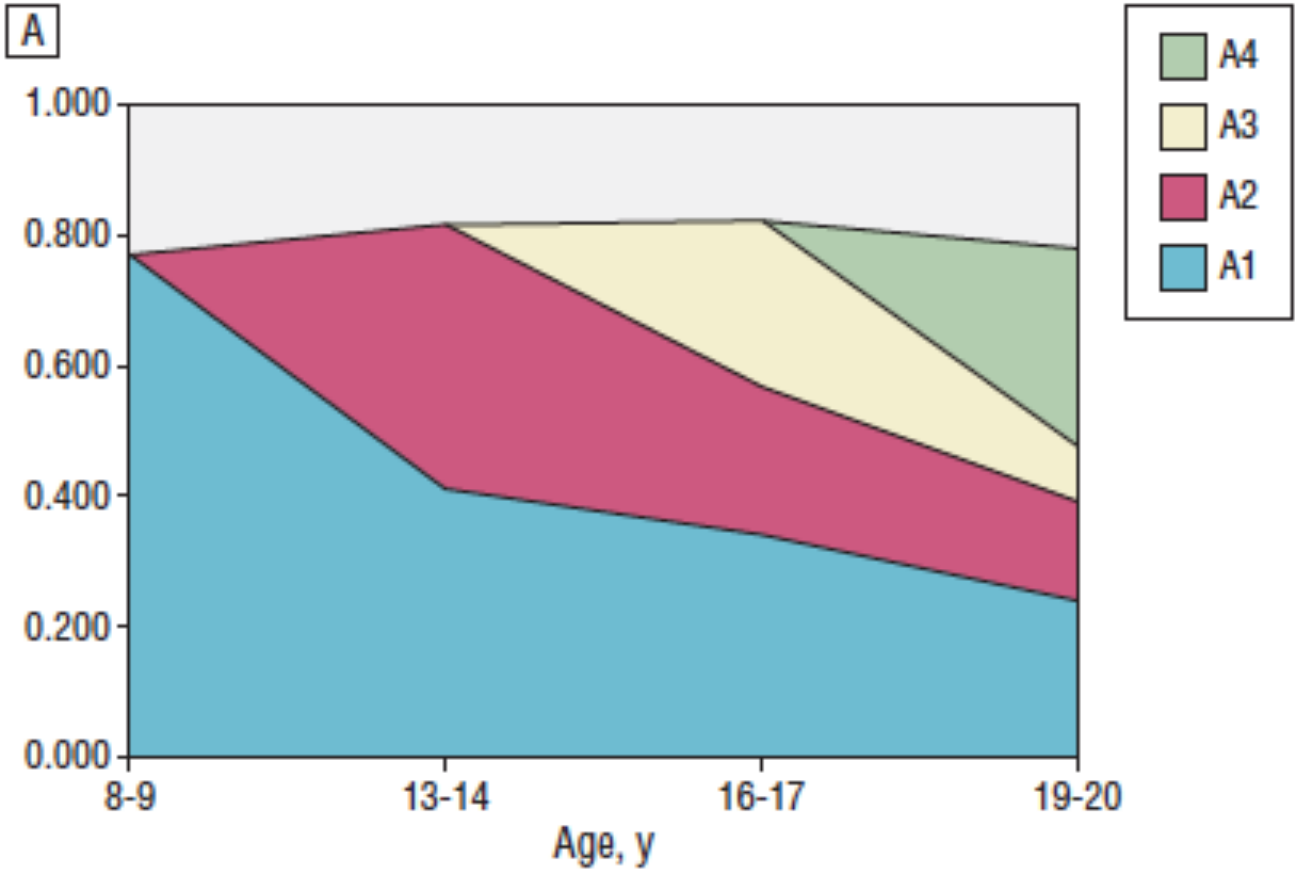
Implications – critical need of

- Studies of brain adaptation (genes and environmental factors)
- New interventions that not necessarily try to remediate the primary problems
- Studies in high-risk individuals (prior to developing symptoms, less confounded by later brain adaptation)

Onset versus Persistence vs Remission

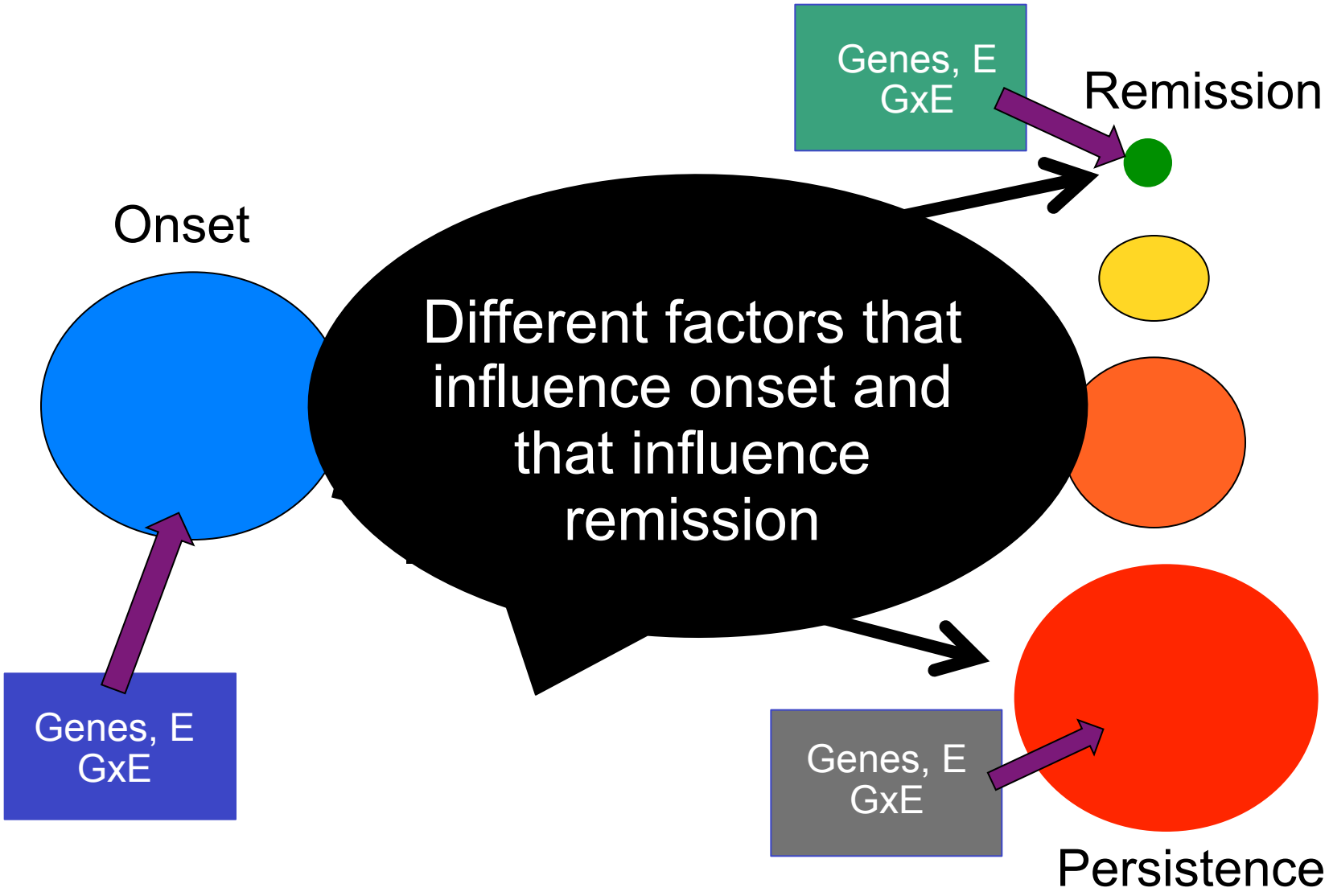


Dynamics of Genetic and Environmental Risk Factors

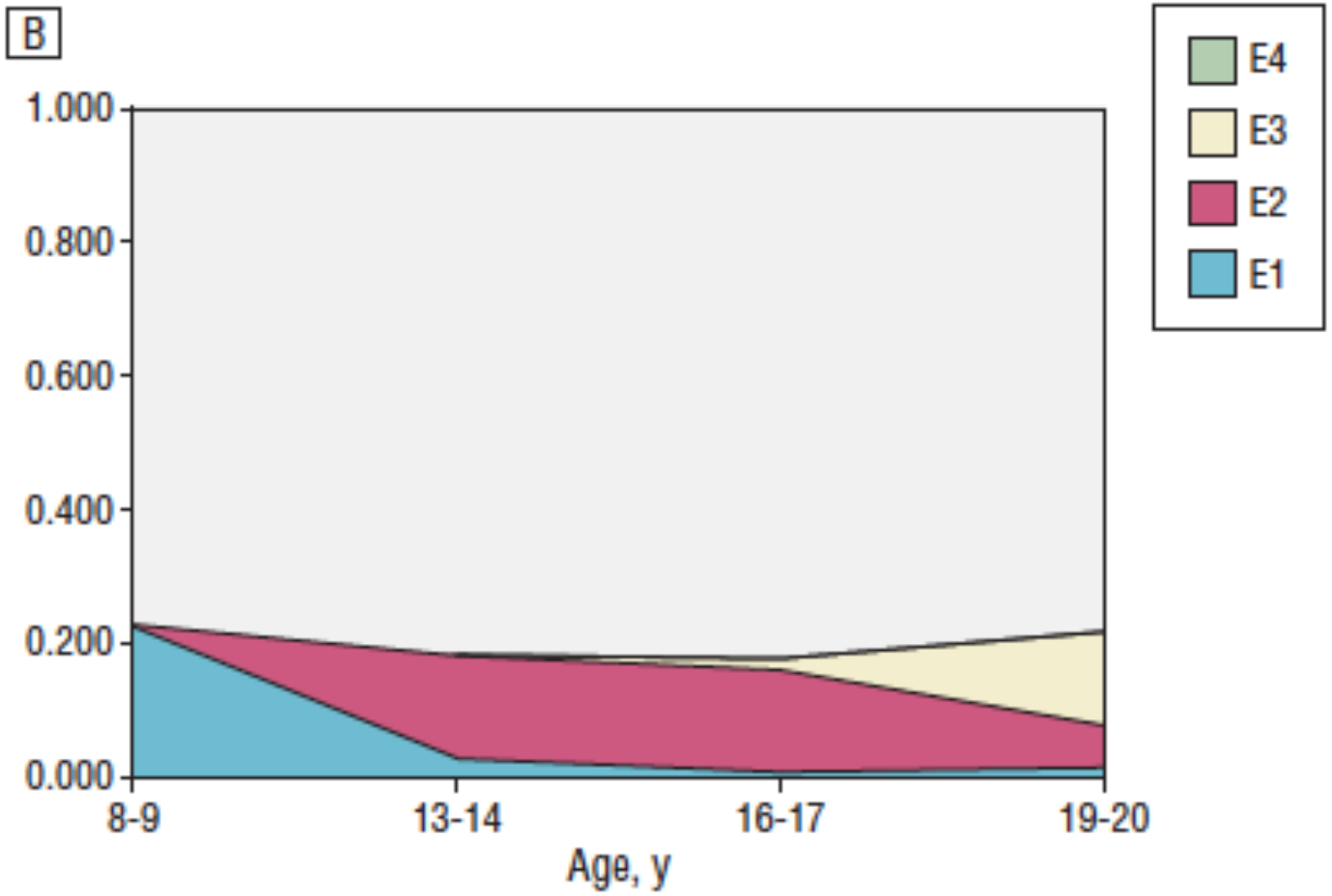


Chang et al. JAMA Psychiatry 2013

Onset versus Persistence vs Remission

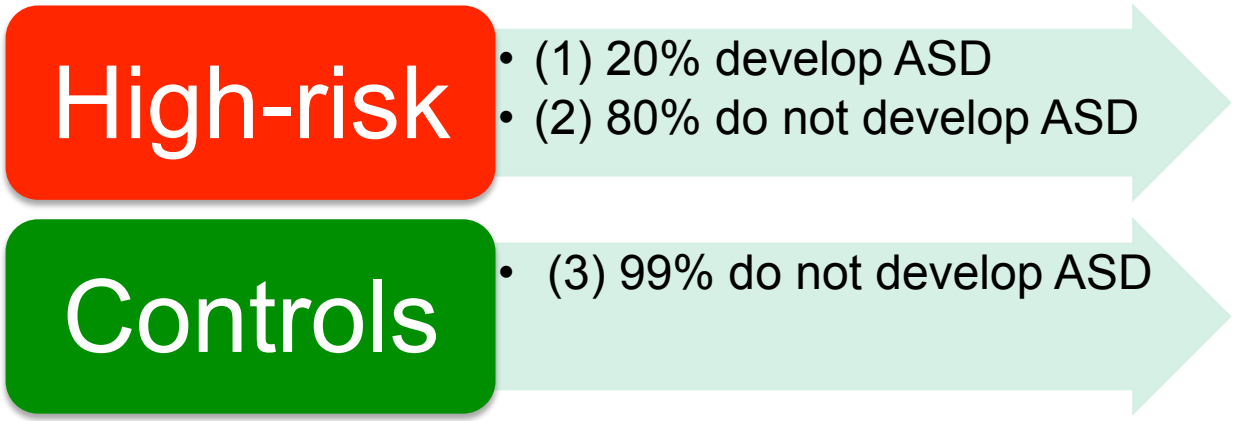


Dynamics of Genetic and Environmental Risk Factors



The high-risk infant study design

- Participants are younger siblings of children with autism
- 20% of this group will develop autism (cf. 1% of the general population)



- Data of a European multi-site longitudinal study will be used
- Infants tested at 4, 10, 14, 24, and 36 months of age

EU-AIMS
Autism Research in Europe

The high-risk infant study design

- Participants are younger siblings of children with autism
- 20% of this gr… …e general population

H…

Cont…

Extend to high-risk for ADHD

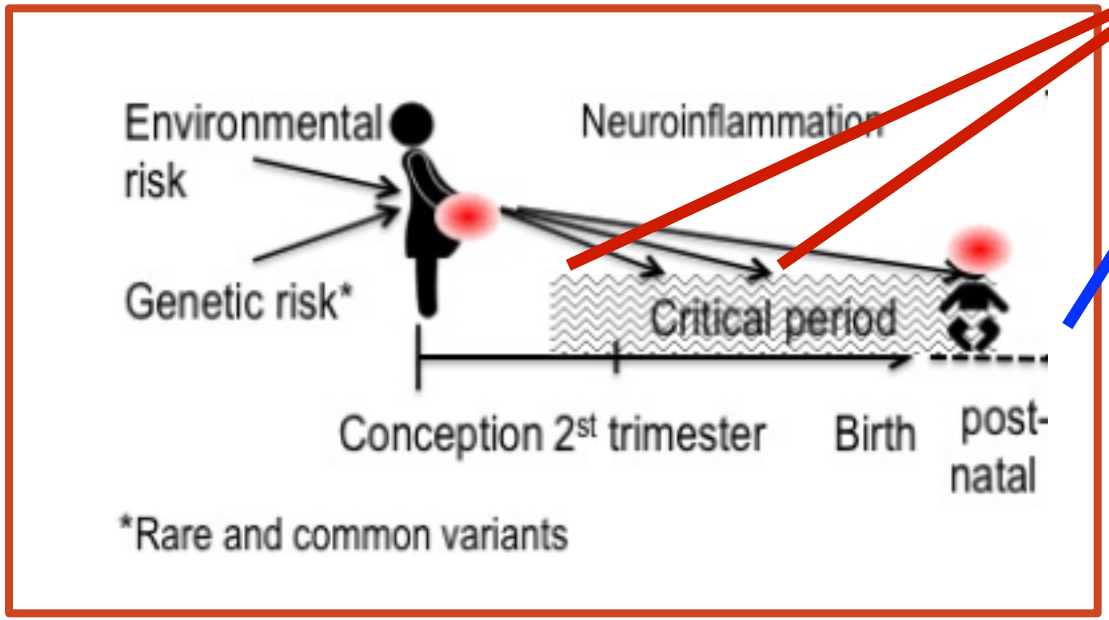
- Data of a European …lti-site longitudinal study will be used
- Infants tested at 4, 10, 14, 24, and 36 months of age

EU-AIMS
Autism Research in Europe

Developmental Hypotheses

A. Risk factors

1. Pre/perinatal environmental risk factors
2. Genes (common, rare variants)
3. Neuroinflammation
4. Critical period, timing



Autism – early

ADHD - later

Getting answers from babies

More on the overlap between ASD and ADHD in the next symposium S6-03 17.00 – 18.30 in the Paris room

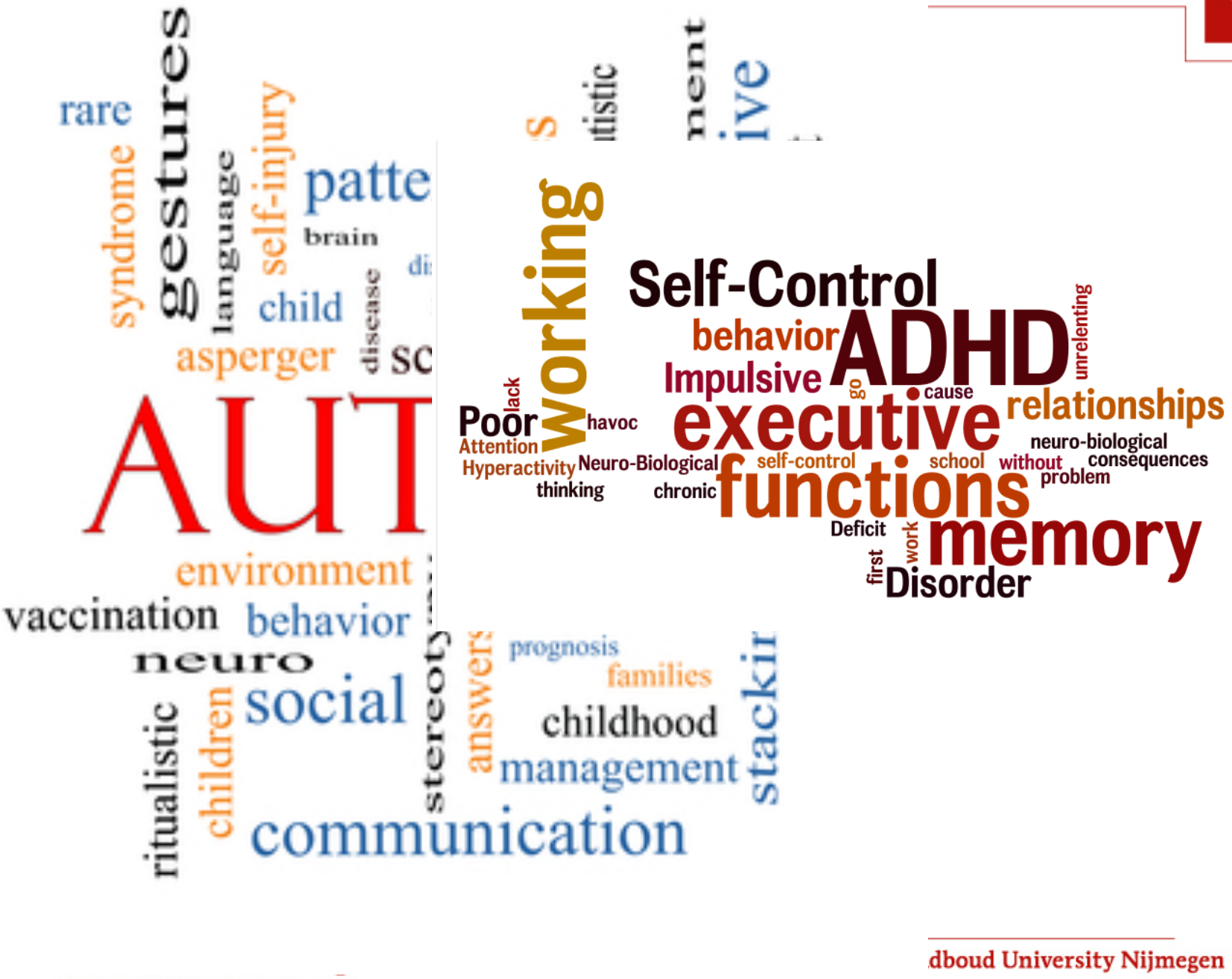
Review

Getting answers from babies about autism

Trends in Cognitive Science, 2009

Mayada Elsabbagh and Mark H. Johnson

Centre for Brain and Cognitive Development, Birkbeck, University of London, Henry Wellcome Building, London, WC1E 7HX, UK


rare
gestures
syndrome
language
self-injury
patte
brain
child
asperger
disease
AUT
environment
vaccination
behavior
neuro
social
ritualistic
children
stereoty
answers
prognosis
families
childhood
management
communication
stackir
working
Self-Control
behavior
ADHD
Impulsive
unrelenting
go
cause
relationships
Poor
lack
havoc
executive
Attention
Hyperactivity
Neuro-Biological
thinking
chronic
self-control
school
without
neuro-biological
consequences
problem
functions
Deficit
work
first
memory
Disorder

Questions?