ADHD and neurodivergence: a short history

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- Royalties from Wiley and payments from universities for talks go to Cardiff University
- ADHD Foundation Charity Board Member, Welsh Govt ND Ministerial Advisory Group co-chair, NHS England ADHD Taskforce Chair

1980s and early 1990s: NHS psychiatry, CAMHS

No learning about ADHD
Autism extremely rare
1 in 40,000

Limited UK research

Causal theories about role of parent/s:
e.g. in notes in one hospital
"schizophrenogenic mother",
"refrigerator parents"

How did I become interested in ADHD? Early 1990s

Early 1990s: family of 7 children with ADHD in my clinic

1992-1995: PhD : ADHD genetic influences

Stigma

ADHD in the beginning

Views about ADHD: “naughty children”, ”made up disorder”, “bad parenting” ”Ridiculous doing research on ADHD”

Co-diagnosis with autism/ASD not allowed

Our first large ADHD research study highlighted this was a problem

Behavioural problem like conduct disorder

Children grow out of it

What changed and what we learnt

Later 20th Century, 21st Century

- Increase in scientific research
- Focus on diagnoses in research
- Not just observations (clinicians describing people)
- Genetics, neuroscience challenges to prevailing beliefs about parents, “naughty children”

The Journal of Child Psychology and Psychiatry

INFANTILE AUTISM: A GENETIC STUDY OF 21 TWIN PAIRS

Susan Folstein, Michael Rutter

First published: September 1977 | https://doi.org/10.1111/j.1469-7610.1977.tb00443.x | Citations: 877

PDF TOOLS SHAR

Summary

A systematic study was made of a representative group of
MZ and 10 DZ) in which at least one twin showed the syndr
was a 36 per cent pair-wise concordance rate for autism in
cent concordance in DZ pairs. The concordance for cognitiv
cent in MZ pairs and 10 per cent in DZ pairs. It was conclud
hereditary influences concerning a cognitive deficit which i
to autism. In 12 out of 17 pairs discordant for autism, the p

nature genetics
ARTICLES
https://doi.org/10.1038/s41588-021-00899-8

Check for updates

Recent ultra-rare inherited variants implicate new autism candidate risk genes

Amy B. Wilfert[1], Tychele N. Turner[1,7], Shwetha C. Murali[1,2], PingHsun Hsieh[1], Arvis Sulovari[1], Tianyun Wang[1], Bradley P. Coe[1], Hui Guo[1,3], Kendra Hoekzema[1], Trygve E. Bakken[4], Lara H. Winterkorn[5], Uday S. Evani[5], Marta Byrska-Bishop[5], Rachel K. Earl[5], Raphael A. Bernier[6], The SPARK Consortium*, Michael C. Zody[5] and Evan E. Eichler[1,2]

Autism is a highly heritable complex disorder in which de novo mutation (DNM) variation contributes significantly to risk. Using whole-genome sequencing data from 3,474 families, we investigate another source of large-effect risk variation, ultra-rare variants. We report and replicate a transmission disequilibrium of private, likely gene-disruptive (LGD) variants in probands but find that 95% of this burden resides outside of known DNM-enriched genes. This variant class more strongly affects multiplex family probands and supports a multi-hit model for autism. Candidate genes with private LGD variants preferentially

nature neuroscience
ARTICLES
https://doi.org/10.1038/s41593-019-0527-8

Autism spectrum disorder and attention deficit hyperactivity disorder have a similar burden of rare protein-truncating variants

F. Kyle Satterstrom[1,2,3*], Raymond K. Walters[1,2,3], Tarjinder Singh[1,2,3], Emilie M. Wigdor[1,2,3], Francesco Lescai[4,5,6], Ditte Demontis[4,5,6], Jack A. Kosmicki[1,2,3], Jakob Grove[4,5,6,7], Christine Stevens[1], Jonas Bybjerg-Grauholm[4,8], Marie Bækvad-Hansen[4,8], Duncan S. Palmer[1,2,3], Julian B. Maller[1,2,3], iPSYCH-Broad Consortium[19], Merete Nordentoft[4,10], Ole Mors[4,11], Elise B. Robinson[1,2,3,12], David M. Hougaard[4,8], Thomas M. Werge[4,13,14], Preben Bo Mortensen[4,5,15,16], Benjamin M. Neale[1,2,3,17], Anders D. Børglum[4,5,6*] and Mark J. Daly[1,2,3,17,18*]

The exome sequences of approximately 8,000 children with autism spectrum disorder (ASD) and/or attention deficit hyperactivity disorder (ADHD) and 5,000 controls were analyzed, finding that individuals with ASD and individuals with ADHD had a similar burden of rare protein-truncating variants in evolutionarily constrained genes, both significantly higher than controls. This motivated a combined analysis across ASD and ADHD, identifying microtubule-associated protein 1A (*MAP1A*) as a new exome-wide significant gene conferring risk for childhood psychiatric disorders.

nature genetics
ARTICLES
https://doi.org/10.1038/s41588-018-0269-7

Discovery of the first genome-wide significant risk loci for attention deficit/hyperactivity disorder

Ditte Demontis[1,2,3,60], Raymond K. Walters[4,5,69], Joanna Martin[5,6,7], Manuel Mattheisen[1,2,3,8,9,10], Thomas D. Als[1,2,3], Esben Agerbo[1,11,12], Gísli Baldursson[13], Rich Belliveau[5], Jonas Bybjerg-Grauholm[3,14], Marie Bækvad-Hansen[3,14], Felecia Cerrato[5], Kimberly Chambert[5], Claire Churchhouse[4,5,15], Ashley Dumont[5], Nicholas Eriksson[16], Michael Gandal[17,18,19,20], Jacqueline I. Goldstein[4,5,15], Katrina L. Grasby[21], Jakob Grove[1,2,3,22], Olafur O. Gudmundsson[13,23,24], Christine S. Hansen[1,14,25], Mads Engel Hauberg[1,2,3], Mads V. Hollegaard[1,14], Daniel P. Howrigan[4,5], Hailiang Huang[4,5], Julian B. Maller[5,26], Alicia R. Martin[4,5,35], Nicholas G. Martin[21], Jennifer Moran[5], Jonatan Pallesen[1,2,3], Duncan S. Palmer[4,5], Carsten Bøcker Pedersen[1,11,12], Marianne Giørtz Pedersen[1,11,12],

Explicit diagnostic criteria

Six inattention symptoms

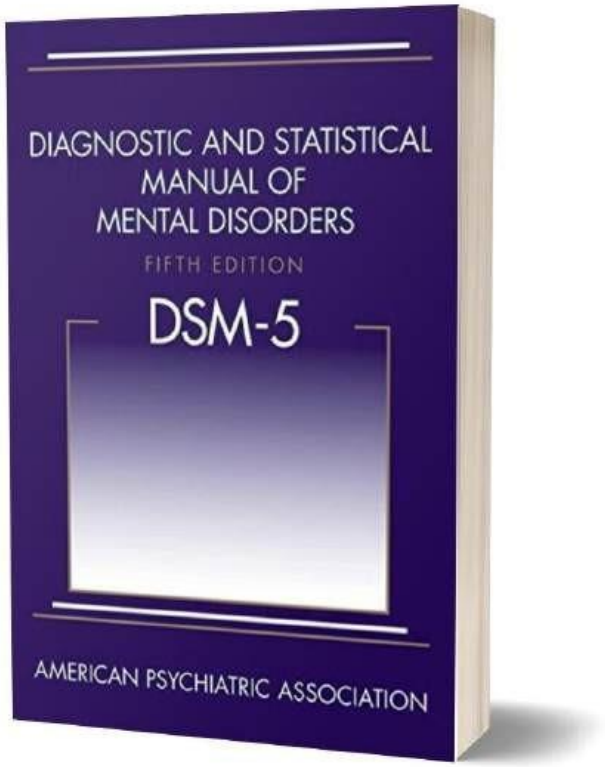
Six hyperactive-impulsive symptoms

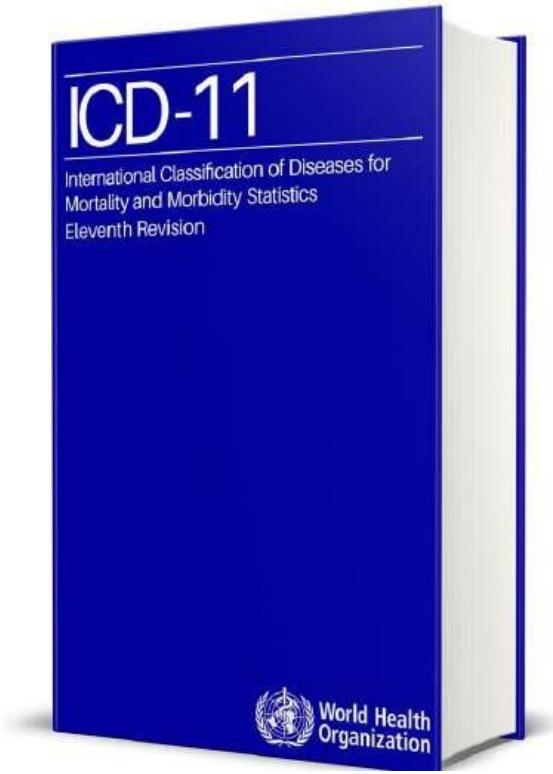
Onset in childhood

In school/another setting

Interferes with functioning

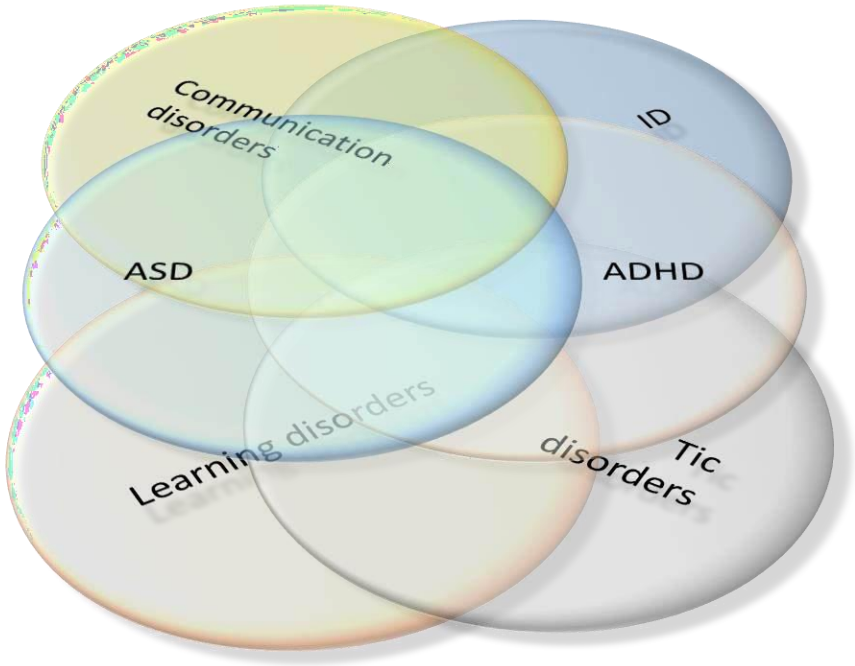
Our diagnostic categories: expert consensus, some research





What we learnt

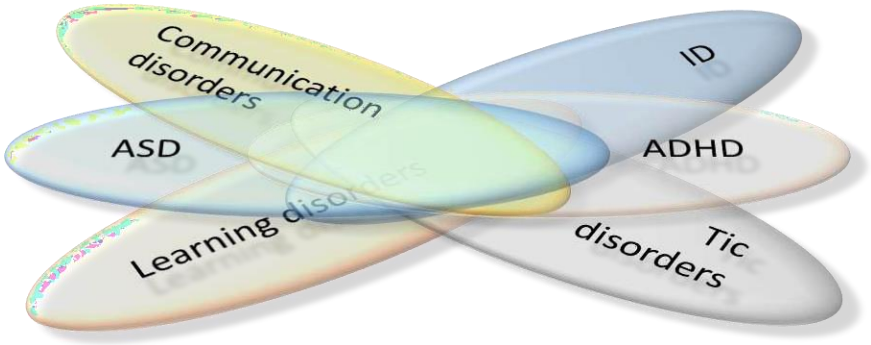
ND diagnosis and symptom overlaps are typical: co-occurrence is the norm



ID Intellectual disability
ASD Autism Spectrum Disorder

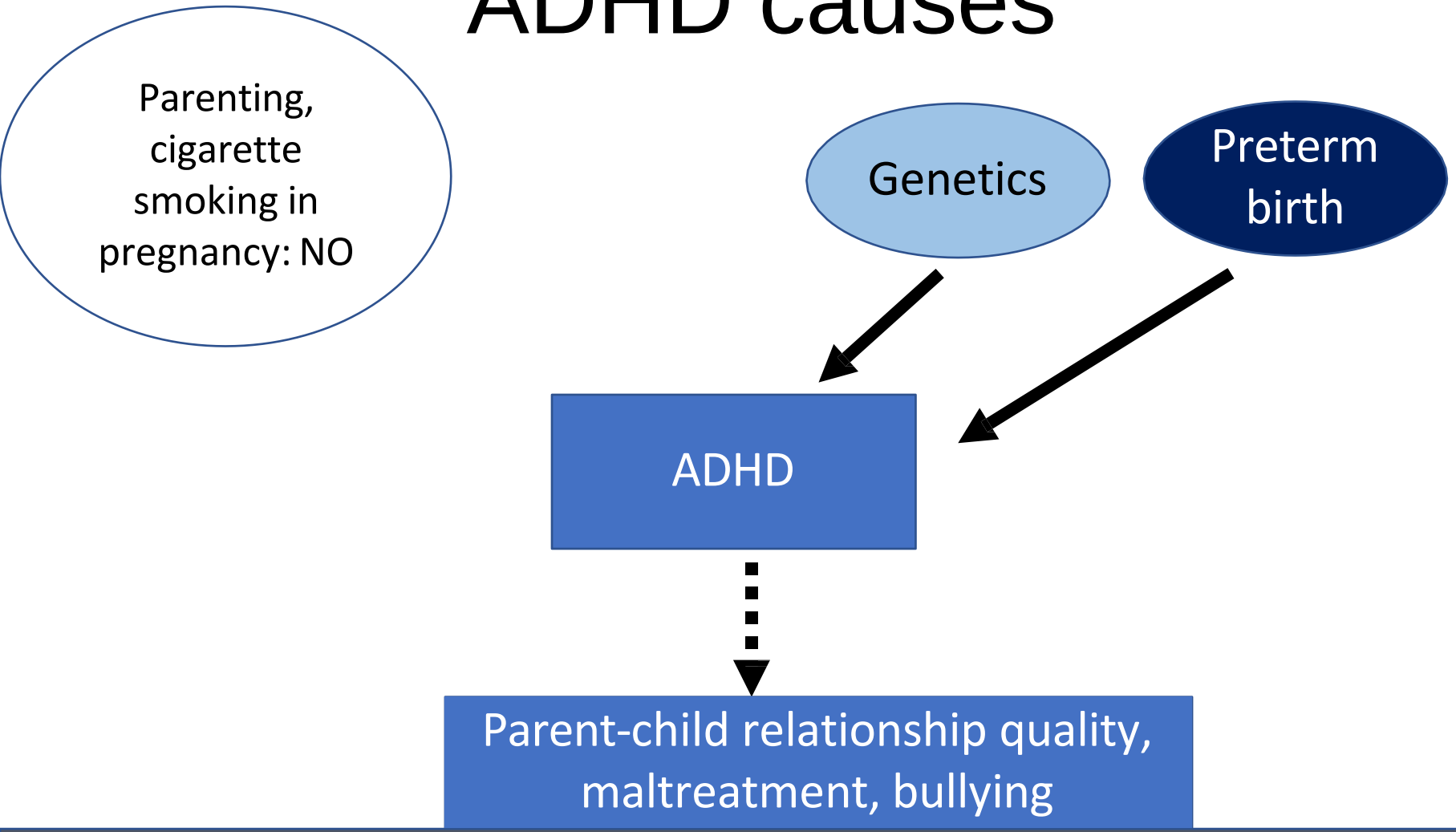
Thapar, Cooper & Rutter. Lancet Psychiatry 2017

ND overlaps in families



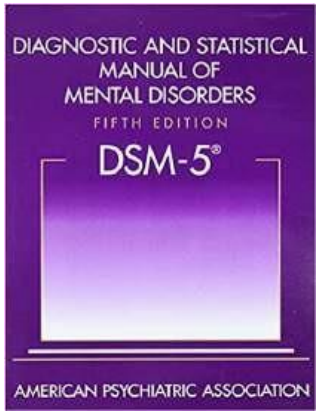
Thapar & Rutter, 2015

ADHD causes


Parenting, cigarette smoking in pregnancy: NO
Genetics
Preterm birth
ADHD
Parent-child relationship quality, maltreatment, bullying

Changes in diagnostic criteria 2013

- ADHD and ASD could be co-diagnosed
- Greater recognition ADHD and ASD occur across the cognitive ability spectrum
- Definitions of ASD change (1 in 100)



ADHD became grouped as a neurodevelopmental rather than behavioural disorder

- Specific learning disorders (involving reading, writing and arithmetic)
- Motor co-ordination and tic disorders
- Communication disorders
- Autism spectrum disorder (ASD)
- Attention deficit/hyperactivity disorder (ADHD)
- Intellectual disability (ID)
- Tic disorders

Rationale for ND grouping

- Early-onset
- Overlaps are typical
- Mainly non-episodic (i.e. remissions and relapses)
- Prominent cognitive, learning differences
- Maturational changes but for majority differences persist into adulthood

Thapar & Rutter, Rutters' Child and Adolescent Psychiatry, 6th edition 2015; Thapar, Cooper & Rutter, Lancet Psychiatry, 2017

Do children grow out of ADHD? ASD?

- Increased awareness of symptoms or challenges persisting into adulthood (15-80%)

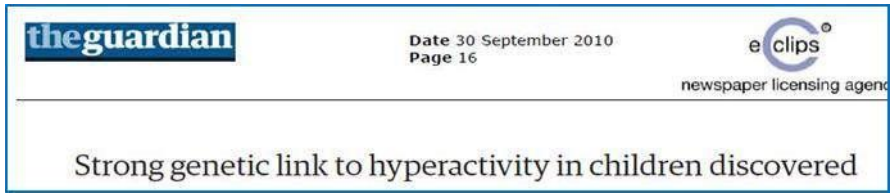
- Adult ADHD and ASD in psychiatry clinics e.g. depression or psychosis

Thapar et al. 2017; Lord et al. 2020; Catalá-López et al. 2022.

Learning disorders: adults

- Subtle language and motor differences
- Mid-life spelling /reading challenges

Stigma about ADHD: backlash against our research findings 2010


theguardian

Date 30 September 2010
Page 16

eclips newspaper licensing agenc

Strong genetic link to hyperactivity in children discovered

THE LANCET

D-09-07664R2

S0140-6736(10)61109-9 Funding: Wellcome, MRC

Rare chromosomal deletions and duplications in attention-deficit hyperactivity disorder: a genome-wide analysis

Nigel M Williams, Irina Zaharieva, Andrew Martin, Kate Langley, Kiran Mantripragada, Ragnheidur Fossdal, Hreinn Stefansson, Kari Stefansson, Pall Magnusson, Olafur O Gudmundsson, Omar Gustafsson, Peter Holmans, Michael J Owen, Michael O'Donovan, Anita Thapar

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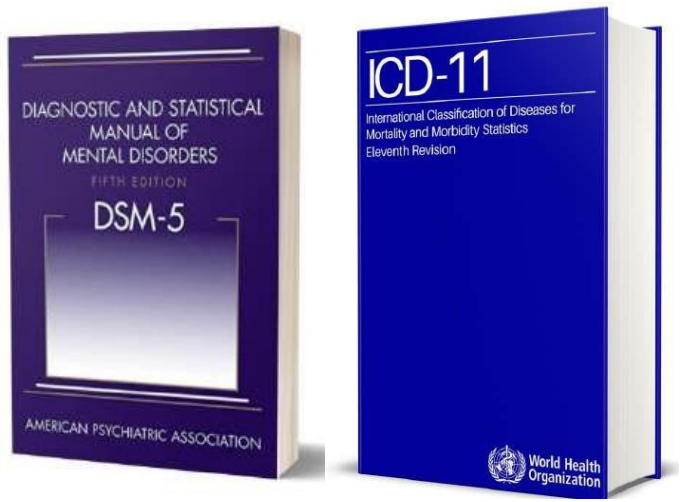
Challenges

Diagnostic categories are useful

Communicate

Yes/no decisions
e.g. treat with medication



People/families access support
Self understanding

Define similar groups of people when conducting research

Apply evidence from research on same category in clinic

Families/society: many want diagnosis

- People to understand why they/their loved one might be different even if “neurodivergence” is the term preferred by an individual
- Access to services and support
- Group membership

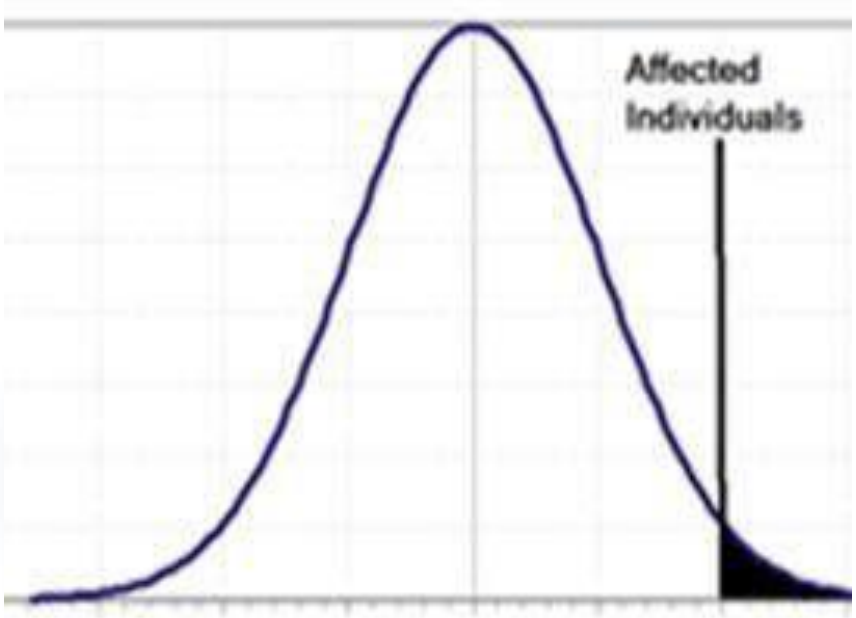
ADHD Foundation
The Neurodiversity Charity

National Autistic Society

But limitations to our diagnostic systems…..

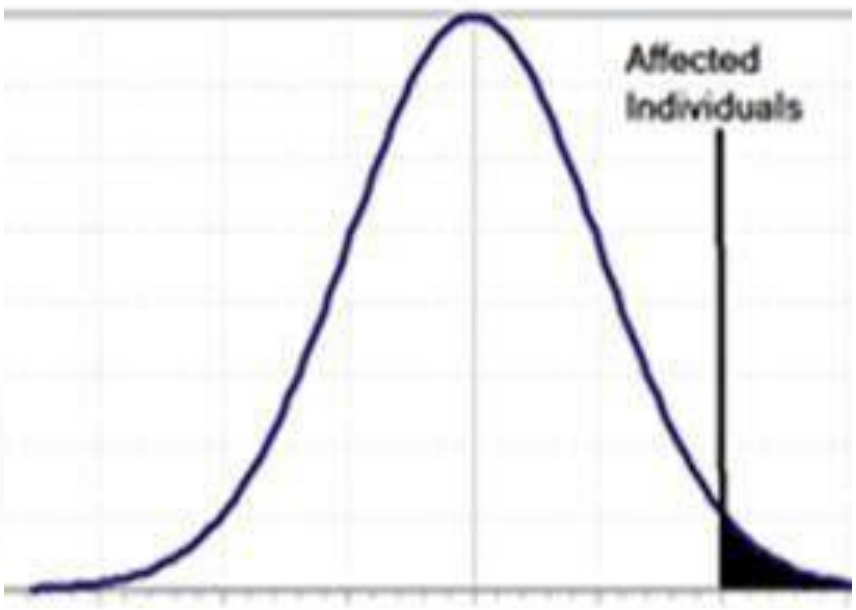
Challenge 1: ADHD does not behave as a clear-cut yes/no diagnostic category

Trait and disorder



- ADHD can be viewed as a trait or continuum as well as yes/no category
- Akin to blood pressure

ADHD



- No clear-cut point for adverse outcomes
- Subthreshold ADHD associated with risk
- All ND

e.g. Demontis et al. 2019;
Norbury 2014; Rutter 2013; Robinson et al. 2016;

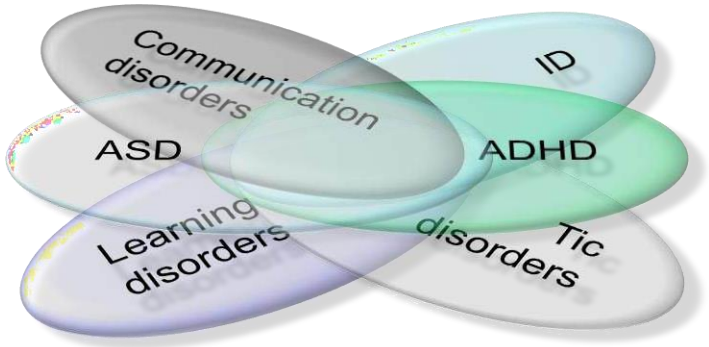
Challenge 2: same diagnosis, everyone is different

Same ADHD diagnosis: not the same

- Symptom differences e.g. greater inattention in females, different types of symptoms
- Differences in impairments

ADHD overlap with other NDDs

- Medical tradition of single diagnosis
- Challenged by overlaps



Challenge 3: Deficit focus

What about strengths?

- Personal attributes: e.g. kind, conscientious, cognitive abilities, personality, energy, innovation

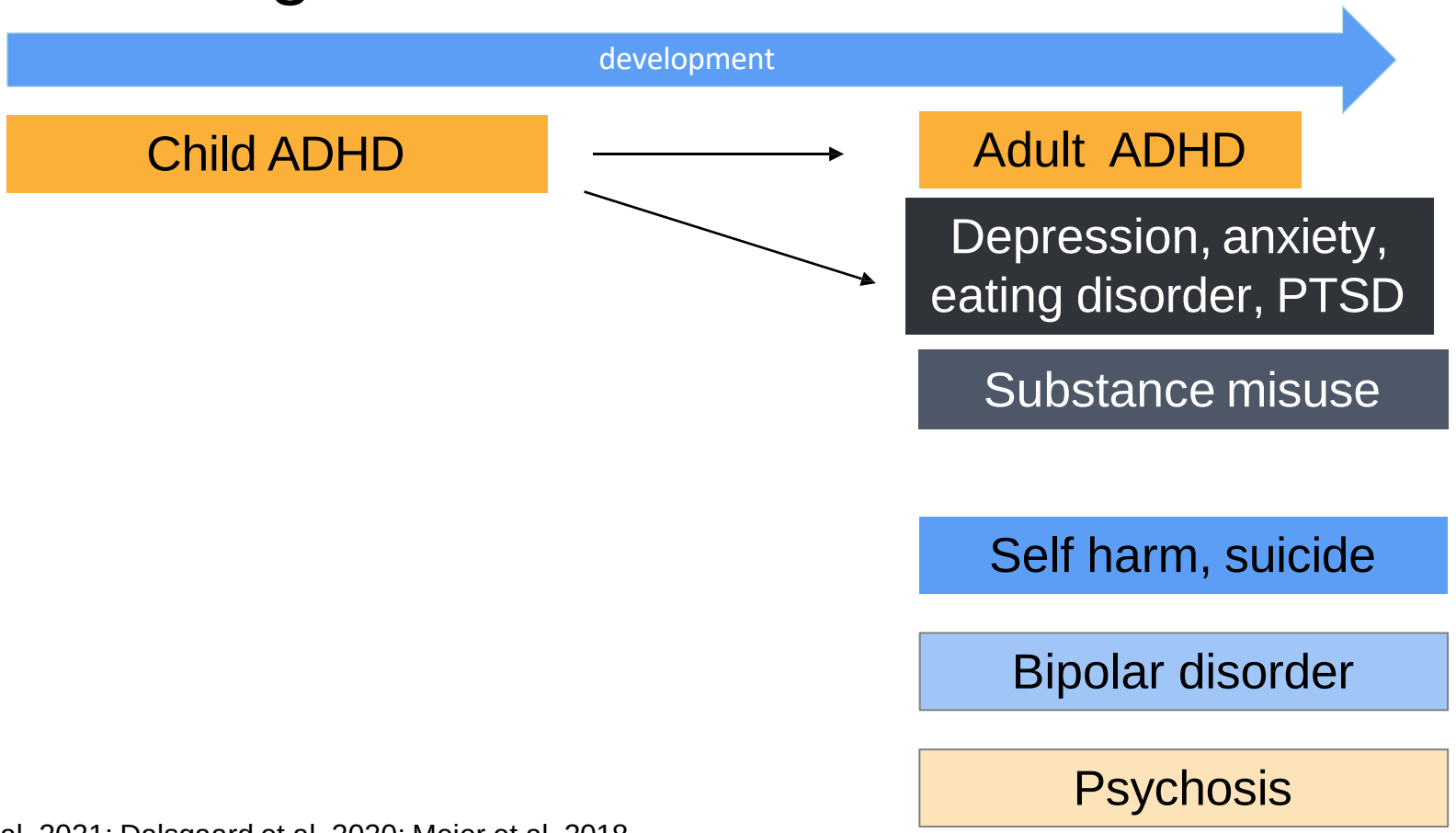
- Scaffolding in environment: family, parent, school, work, broader social context

Challenge 4: ND isolation from mental health

4-8 x increased rate of common and severe mental health problems

Earlier onset than neurotypical

Mental health: diagnostic transitions from ADHD



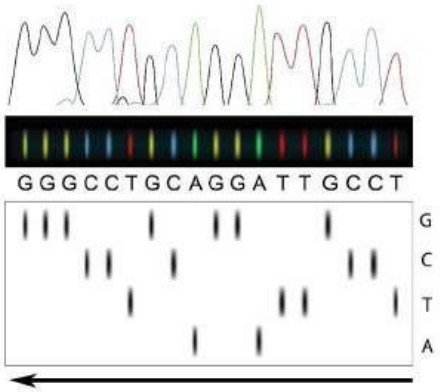
Salvi et al. 2021; Dalsgaard et al. 2020; Meier et al. 2018

Isolation from mental health: challenges

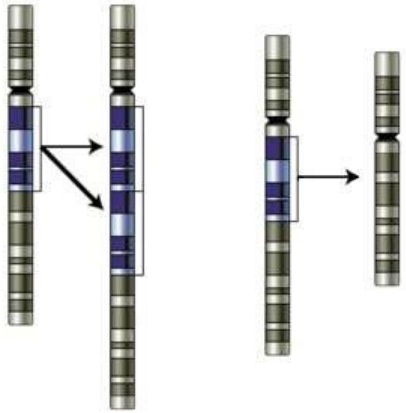
- ND in mental health services (more severe, “treatment resistant”, hospitalization, self-harm, early-onset depression)
- Recognising mental health problems in ND services
- Accessing mental health support and resources

Challenge 5: Over-reliance on diagnosis

Diagnoses are concepts not biologically defined entities



Biological signatures of diagnoses? No



Careful about reification of diagnostic criteria

- Our current ND diagnoses do not have clear-cut distinct biological signatures

- They are concepts that we use to help us clinically and for research

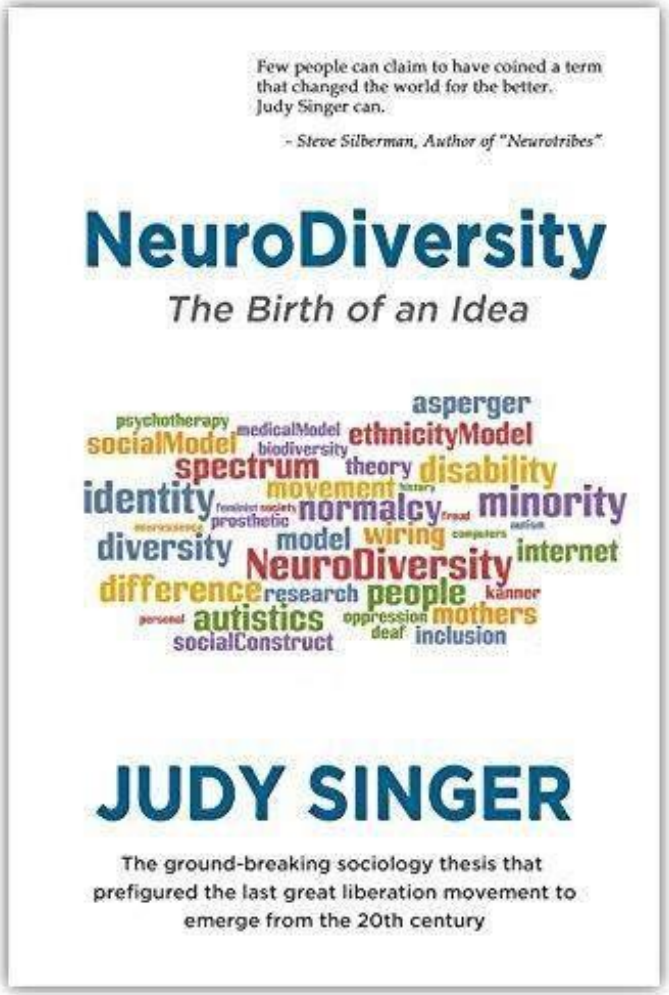
An alternative to diagnosis/medical approaches?

Social constructionist theory

- Opposes medical model which views disability as deficits or dysfunction in the individual and need to "cure" them

- Disability as socially constructed by society barriers, negative attitudes and exclusions

Neurodiversity



Neurodiversity: Judy Singer

- Does not totally agree with social constructionism
- Neurological diversity
- Focus on higher functioning ASD
- “A swing from nurture to nature”
- Social justice, civil rights

My own perspective: need both approaches

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Psychiatry

COMMENT | VOLUME 8, ISSUE 7, P559-561, JULY 01, 2021

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The neurodiversity concept: is it helpful for clinicians and scientists?

Edmund Sonuga-Barke • Anita Thapar

Published: May 10, 2021 • DOI: https://doi.org/10.1016/S2215-0366(21)00167-X • Check for updates

References

Article Info

Linked Articles

ADHD and autism spectrum disorder are conceptualised as discrete, categorical, neurodevelopmental disorders, which originate in early development [1] and are assumed to be the result of underlying brain dysfunction. [2] From one perspective, these definitions provide important clarity for clinical practice and ensure we are guided by research progress over the past 40 years. [3] By contrast, others have

Challenge 6: ADHD and ND can impact widely

What we know about ADHD and ND: research on outcomes

- Impacts on mental and physical health
- Educational achievement and inclusion, employment, poverty, homelessness
- Criminal justice system, looked after children

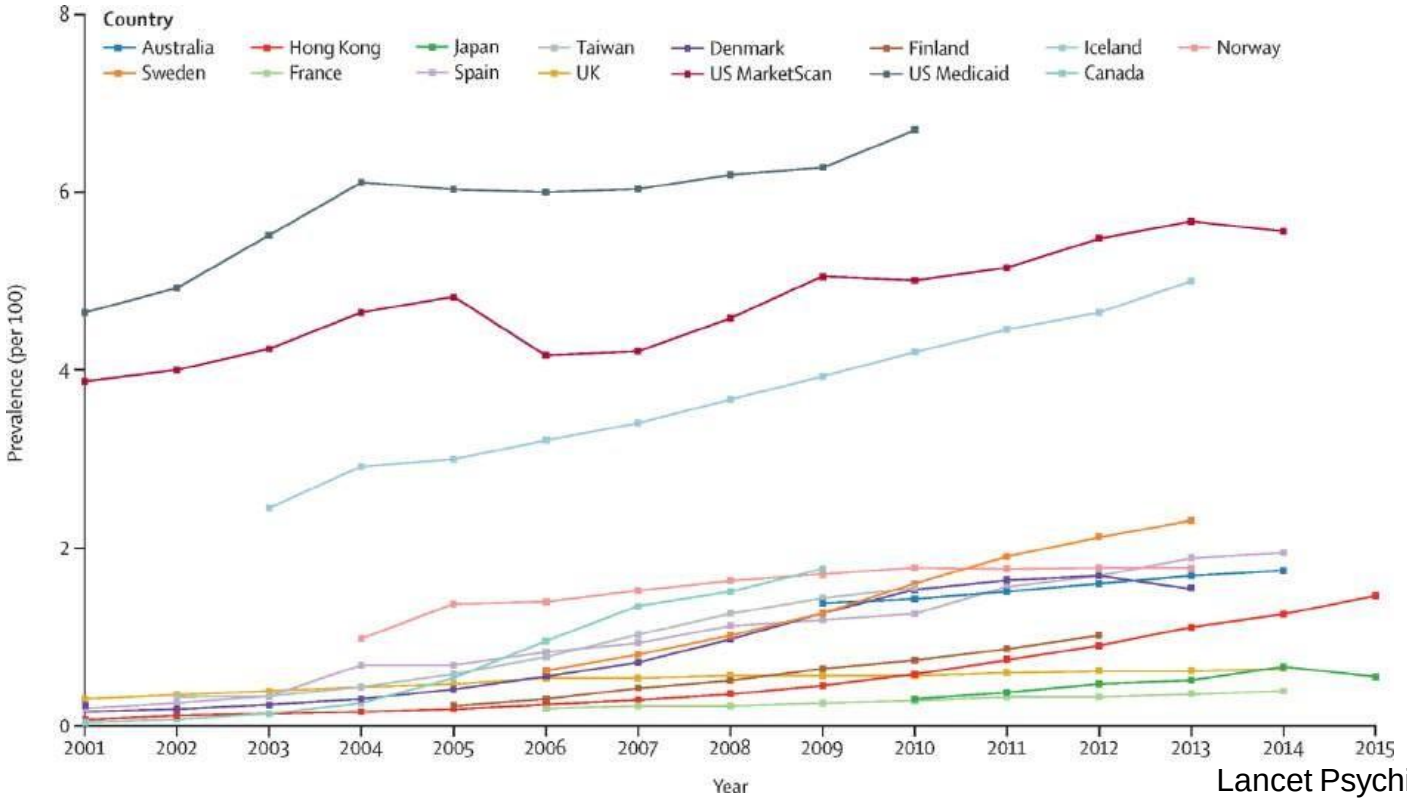
Different sectors need to work together and beyond diagnoses

- NHS, education, work, social care, criminal justice
- Diagnoses not designed around all needs e.g. for education, just medical /clinician decisions

Challenge 7: Services need redesign
Were set up as if ADHD/ND are rare

ADHD referral not needed and over-treated?

Still under-treated in the UK



Lancet Psychiatry, 2019

How do we deal with changes in recognition? Current NHS model is secondary care/specialist focused

Demand and capacity

Conclusions and future

Conclusions

- Much has changed and for the better
- ADHD recognized as neurodevelopmental, ND overlaps, understanding more about causes and outcomes, links with mental health, neurodivergence movement rather than deficit-focused models
- Wales is globally ahead in thinking

Cardiff University

- Understanding female ADHD
- Welsh and Swedish health data on ADHD and ND outcomes
- Understanding links with mental health e.g. depression
- Digital platform in Wales to monitor ND health and well-being, digital tools for mental health
- Impact of schools on ADHD mental health/wellbeing, what helps?
- European ADHD Research Network, World ADHD Federation, European ADHD Guidelines

Summary

- Current system relies on diagnoses not needs
- Diagnoses are yes/no but ND behaves as a spectrum
- Ignores co-occurrences across ND
- Ignores co-occurrence with mental health problems
- Diagnosis not developed to address needs in education, other sectors
- Not dispense completely with diagnosis but recognize its limitations

Diolch yn fawr/ thanks

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