



Equitable diagnosis for autism in adolescence
and adulthood: Learning from sex, gender, and
social developmental perspectives

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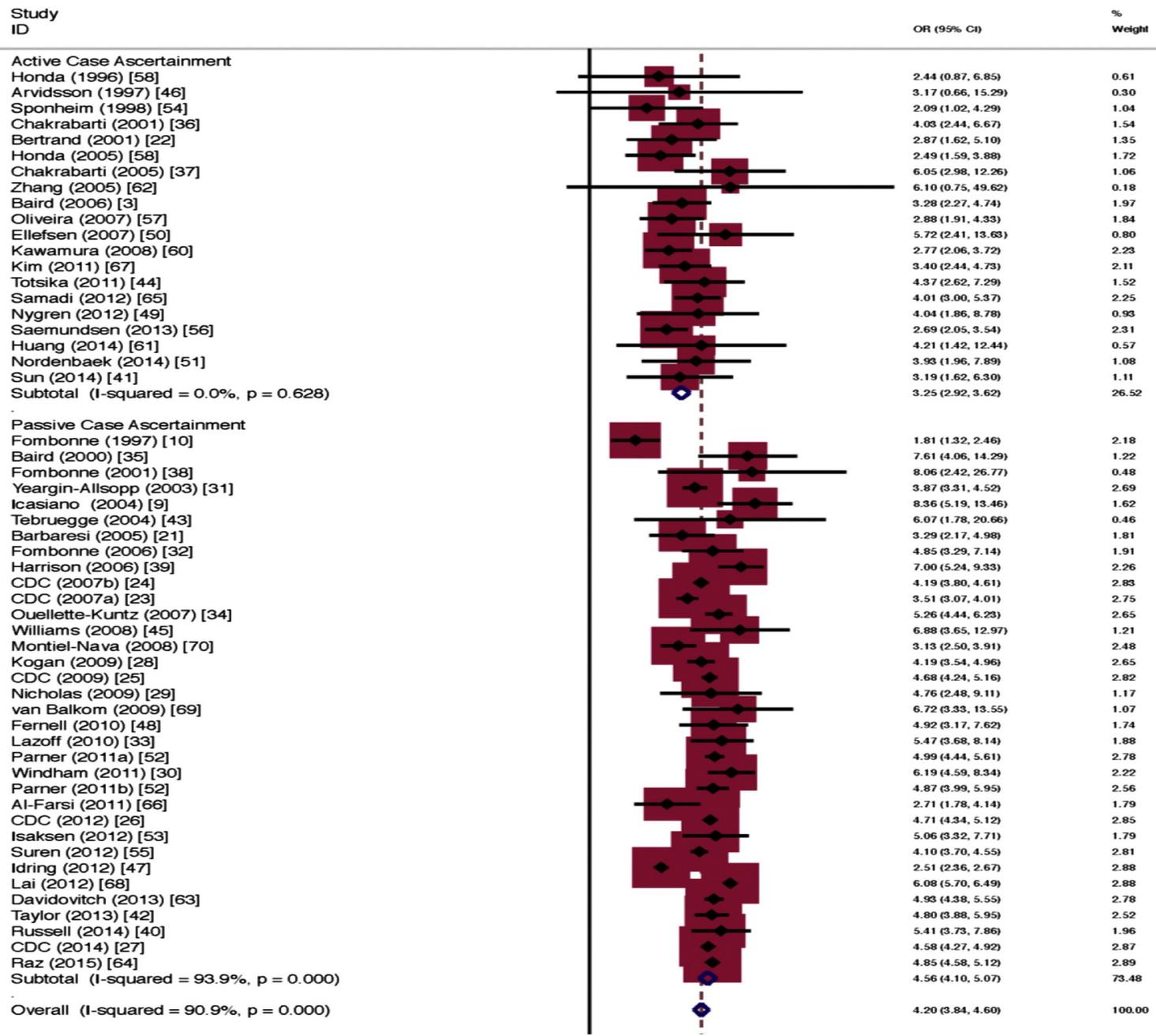
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Disclosure

Presenter: Meng-Chuan Lai (Staff Psychiatrist & Clinician Scientist, Centre for Addiction and Mental Health [CAMH]; Associate Professor, University of Toronto)

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- Consulting Fees: none
- Patents: none



Although overall ratio
4.20 (3.84 – 4.60) ...

‘Active’ Case Ascertainment
3.25 (2.92 – 3.62)

‘Passive’ Case Ascertainment
4.56 (4.10 – 5.07)

Why should we care about sex & gender in autism?

Clinical care
(diagnosis,
behavioural
presentation,
health status,
supports)

How do sex & gender modulate recognition, presentation, adaptation & developmental changes?

Biological
heterogeneity

(How) Are the biological substrates of autism differ by sex & gender?

Aetiologies

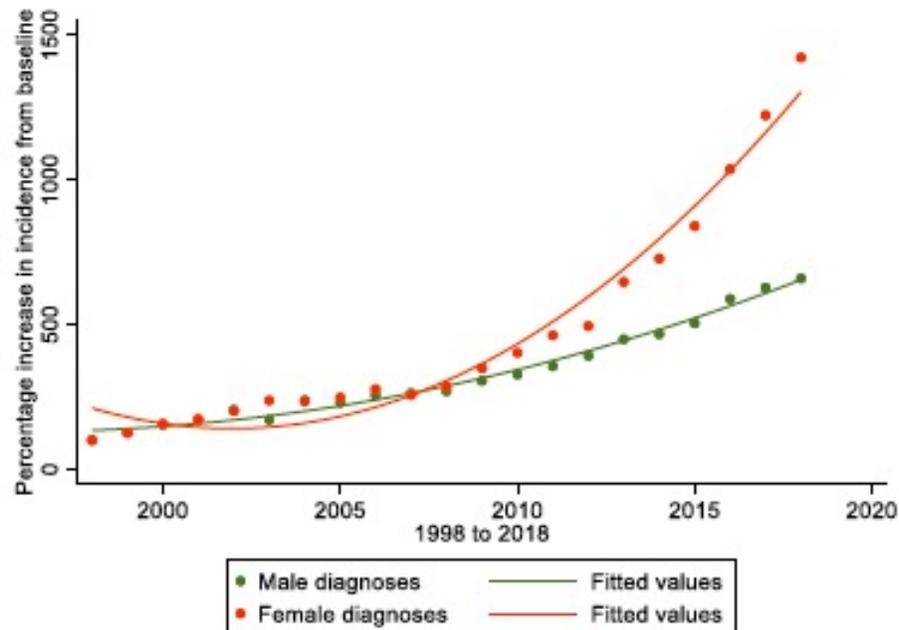
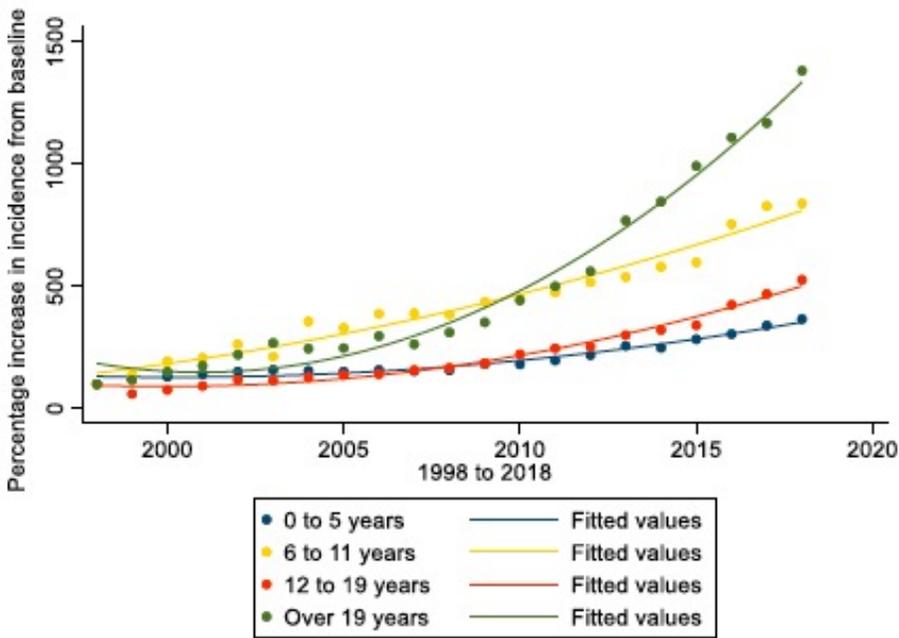
What underlies 'female protection'?

Are there converging mechanisms underlying sex differentiation, gender socialization, & the emergence of autism?

Caveats in current knowledge/literature:

- *Many under-represented populations*
- *A lack of appreciation of multi-faceted sex and gender factors*

Status Quo: Autism tends to be recognized & diagnosed later in females than in males (assigned sex at birth)



2002 US CDC autism surveillance data:

“The median age of identification for female subjects (6.1 years) was significantly older than that for male subjects (5.6 years)... Females in our sample were identified at a later age despite a tendency to be more cognitively impaired.”

Shattuck et al., 2009, *JAACAP*

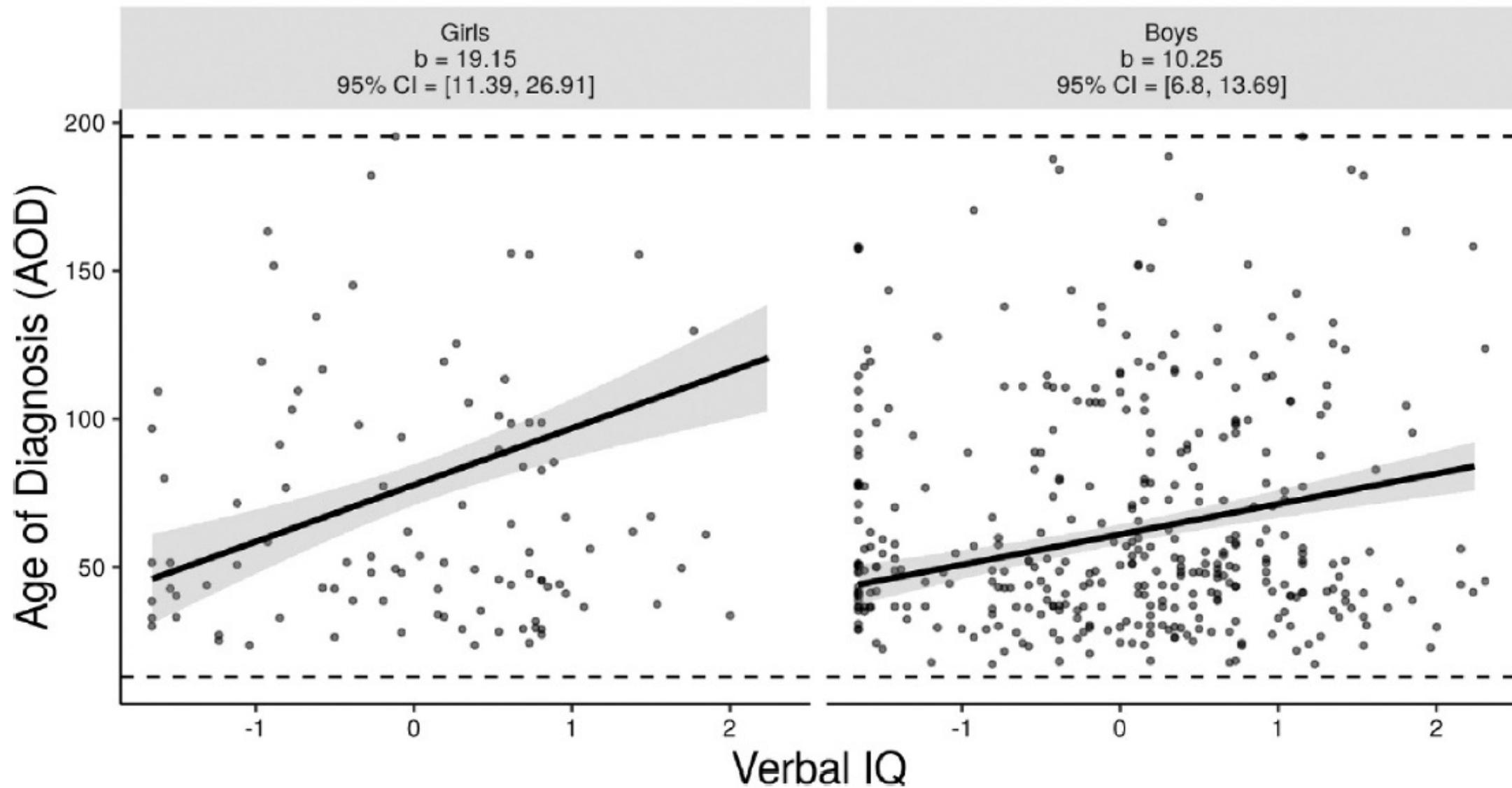
1998-2018 UK Clinical Practice Research Datalink (CPRD) primary care database:

“The mean age at which males received a diagnosis across the whole dataset was 12.3 years old (SD = 11.5) and for females 14.9 years old (SD = 12.4).”

Russell et al., 2021, *JCPP*

Reason 1: Expectancy bias, gender stereotypes, & diagnostic overshadowing may impede timely & accurate recognition of autism in non-male individuals (assigned sex at birth)

Level of Moderator (Sex)



Netherlands Autism Register: N=1019 (494 M, 525 F), >16 y/o

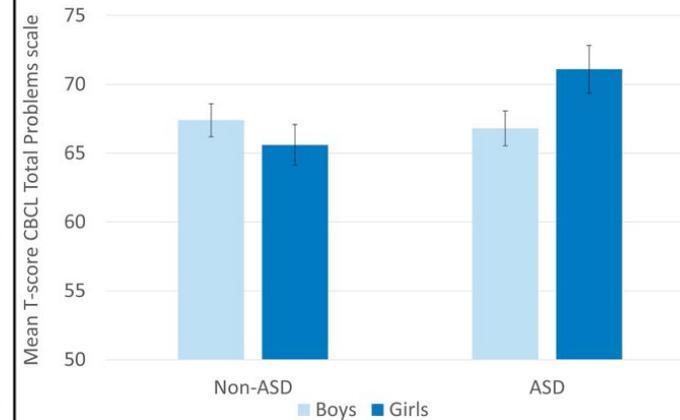
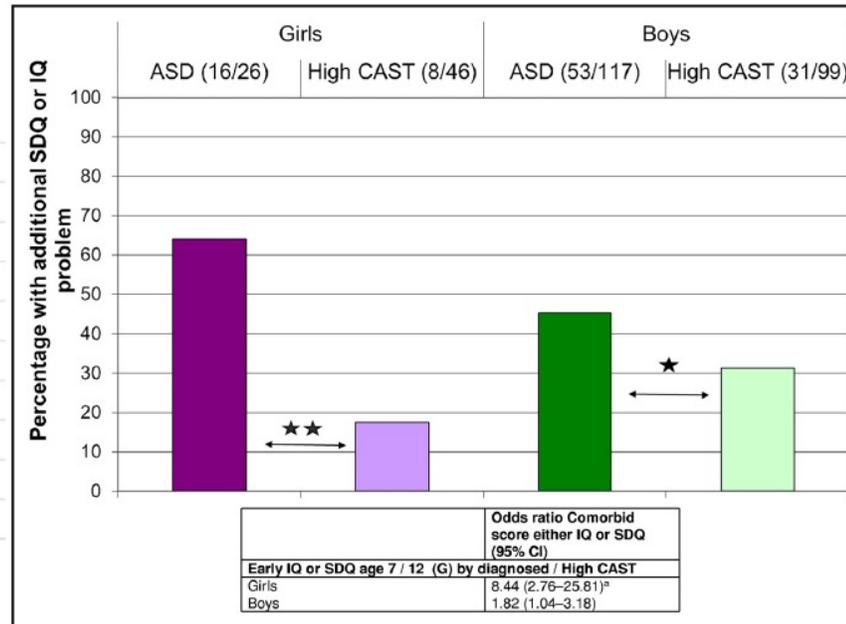
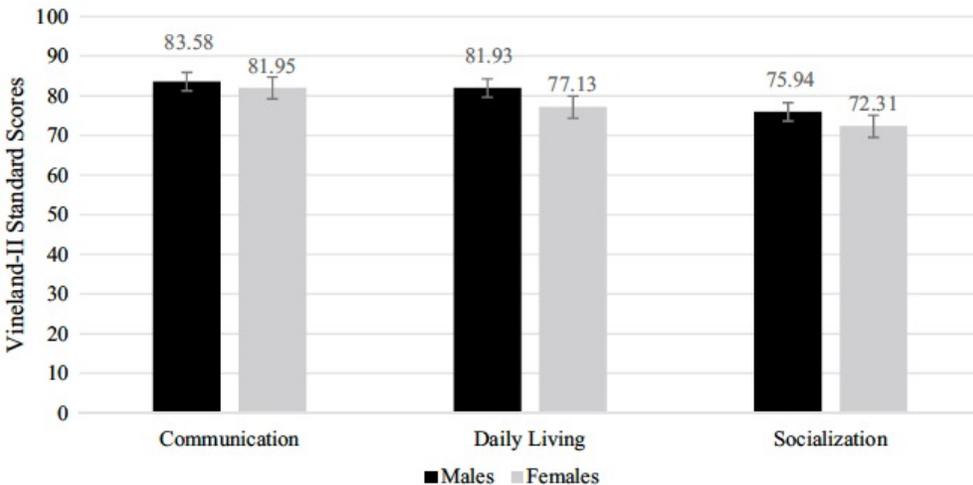
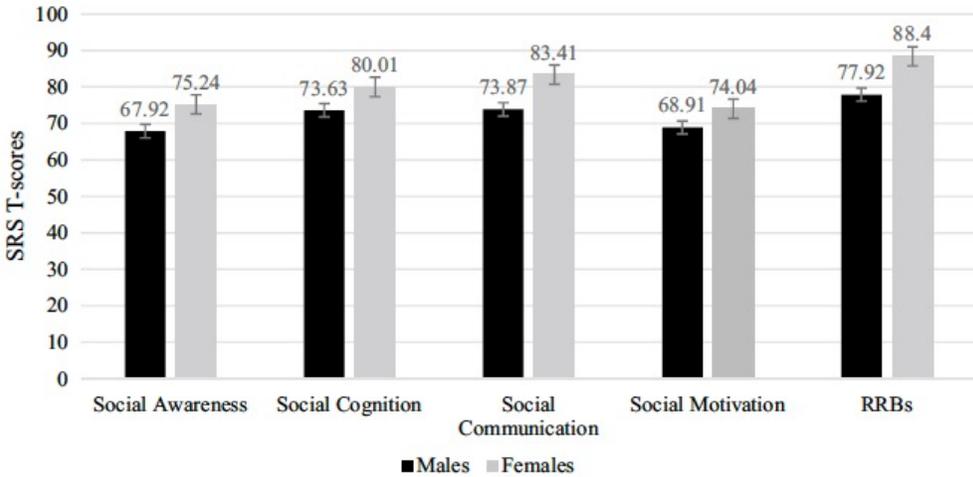
Observed rates of prior diagnoses that were no longer present post-autism diagnosis for specific psychiatric conditions, and logistic regression parameters.

	Prior diagnoses no longer present post-autism diagnosis												
	Male		Female		Total		Logistic Regression						
	N	%	N	%	N	%	b	SE	Wald χ^2	p	OR	Wald 95% CI	
At least one prior diagnosis no longer present post-autism diagnosis	135	27.3	247	47	382	37.5	0.89	.17	42.23	<.001***	2.45	1.87	3.12
Personality Disorders	35	7.1	115	21.9	150	14.7	1.46	.21	46.75	<.001***	4.30	2.83	6.53
Mood Disorders	26	5.3	70	13.3	96	9.4	1.12	.25	20.53	<.001***	3.06	1.89	4.96
Anxiety Disorders	23	4.7	66	12.6	89	8.7	1.02	.26	16.04	<.001***	2.78	1.69	4.60
Burnout/Chronic Fatigue	11	2.2	41	7.8	52	5.1	1.61	.36	19.98	<.001***	5.00	2.47	10.13
Eating Disorders	3	0.6	26	5.0	29	2.8	2.18	.62	12.33	<.001***	8.85	2.62	29.91
Attention-Deficit/ Hyperactivity Disorder	15	3.0	24	4.6	39	3.8	.37	.34	1.13	.287	1.44	.74	2.82
Trauma-related Disorders	5	1.0	15	2.9	20	2.0	1.27	.54	5.54	.019	3.54	1.24	10.15
Oppositional Defiant Disorder/ Conduct Disorder	13	2.6	7	1.3	20	2.0	-.65	.49	1.81	.179	.52	.20	1.35
Substance Use Disorder	9	1.8	7	1.6	16	1.6	-.04	.53	.00	.947	.97	.34	2.72

“...the delay in receiving an autism diagnosis was 1.5 years in boys and 2.6 years in girls with pre-existing ADHD, compared with boys and girls without prior ADHD”

Autistic boys and girls (mean=10 years) *matched on ADOS scores*

“...females who ultimately met criteria on gold-standard diagnostic measures were more severely affected in real-world settings than their male counterparts.”

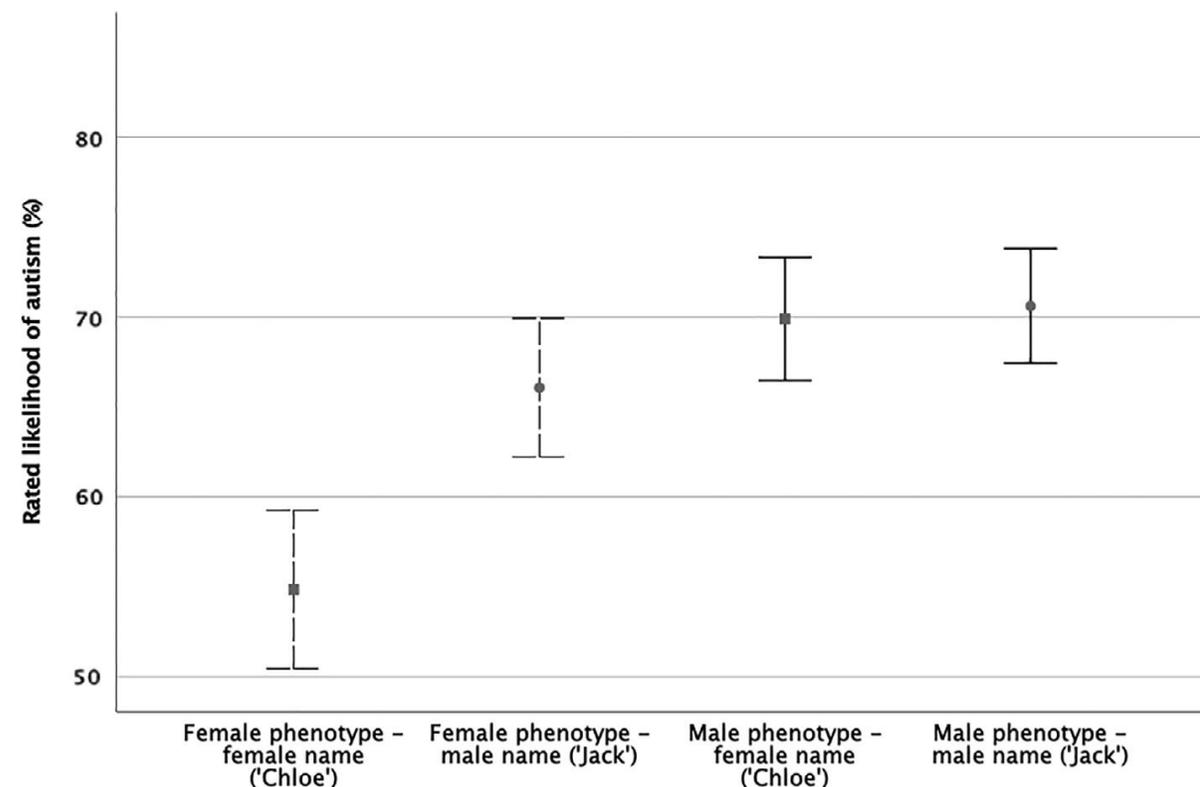


Recognition of Girls on the Autism Spectrum by Primary School Educators: An Experimental Study

Alana Whitlock, Kate Fulton, Meng-Chuan Lai , Elizabeth Pellicano , and William Mandy 

Vignette type	Word length	Core characteristic 1	Core characteristic 2	Core characteristic 3	Core characteristic 4
Female autism phenotype	180	Difficulty socializing, (higher friendship interest)▲ "best friends with another girl in the class, Mia, although Chloe does not seem to be friends with any of the other children"	Restricted interest (social/animal focused)▲ "Chloe loves meerkats, and has pictures of them over her books, and will often reference them in her creative writing"	Camouflage/ Mimicking▲ "Chloe will also copy a lot of Mia's behaviors"	Autism-related emotional/ behavioral problem▲ "she is a fussy eater and will leave a fair amount of her food every lunchtime"
Male autism phenotype	195	Difficulty socializing "He tries to join in with the other children but tends to be ignored"	Restricted interest "if there is any free time in the classroom, Jack will spend it playing with his Harry Potter cards."	Difficulty with change "He likes the routine of the classroom, but you have noticed that he can struggle moving from playtime back to the classroom"	Autism-related emotional/ behavioral problem "He has been involved in a couple of arguments and fights with his peers"

"...a significant **main effect of both gender and presentation** on estimations of the child in the vignette being autistic: a bias against girls and the 'female autism phenotype'. There was also an **interaction**: female gender had an effect on ratings of the 'female phenotype', but not on the 'male phenotype' vignette."



Reason 2: Sex- and gender-related factors can modulate autistic behavioural presentations and their developmental trajectories

Fewer RRB on conventional measures in girls, and age-related differences

From a 27-site integrative analysis (N=8,985)

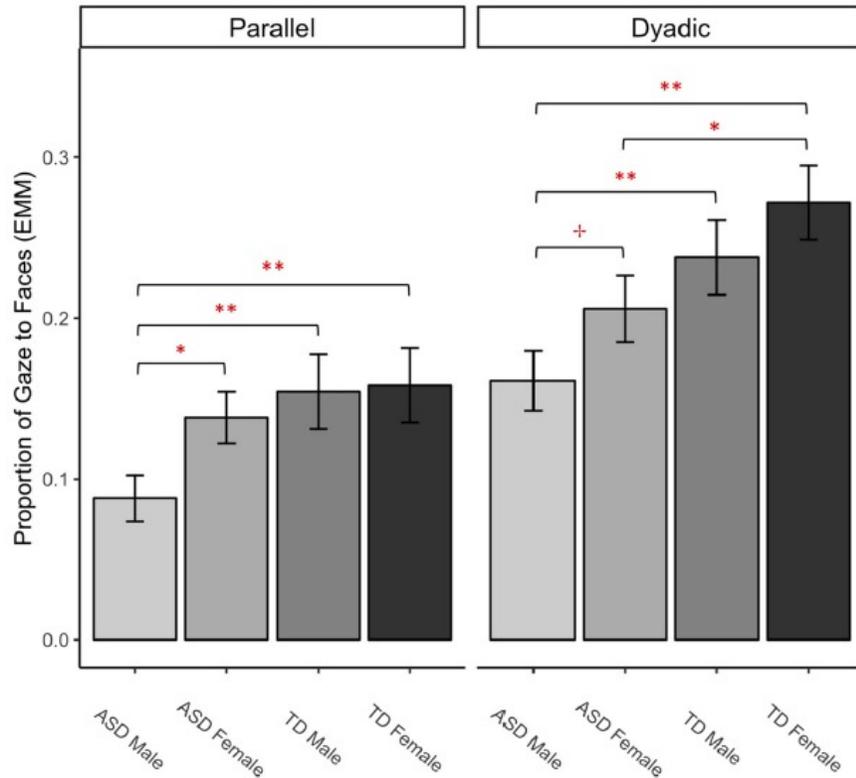
- ***“Boys received more severe RRB scores than girls on both the ADOS and ADI-R (age 4+ algorithm)”***
- ***“Girls received more severe scores than boys on both SRS indices [of social-communication and RRB], which emerged in adolescence”***
- ***“Among children who ultimately receive a clinical ASD diagnosis, severity estimates do not systematically differ to such an extent that sex-specific scoring procedures would be necessary”***
- ***“we could not address sex differences in phenotypic aspects **outside of these scores** [i.e. ADI-R, ADOS, SRS]”***

Within RRBI

- Diagnosed autistic boys have more repetitive motor behaviours, more circumscribed interests, and less compulsions and self-injurious behaviours than diagnosed autistic girls, with no differences in insistence on sameness
- Conventional screeners (e.g., M-CHAT, SCQ) may under-identify RRBI in toddler and preschool-aged girls

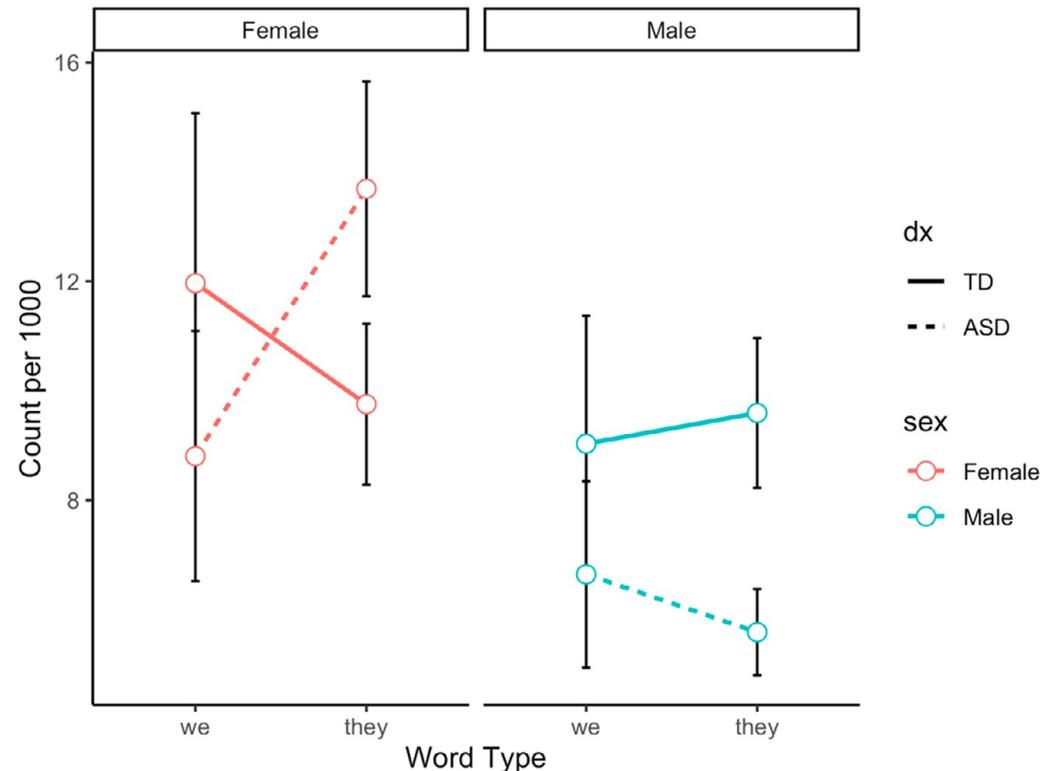
Presentations not well captured by conventional measures

Example 1: Social attention & linguistic characteristics

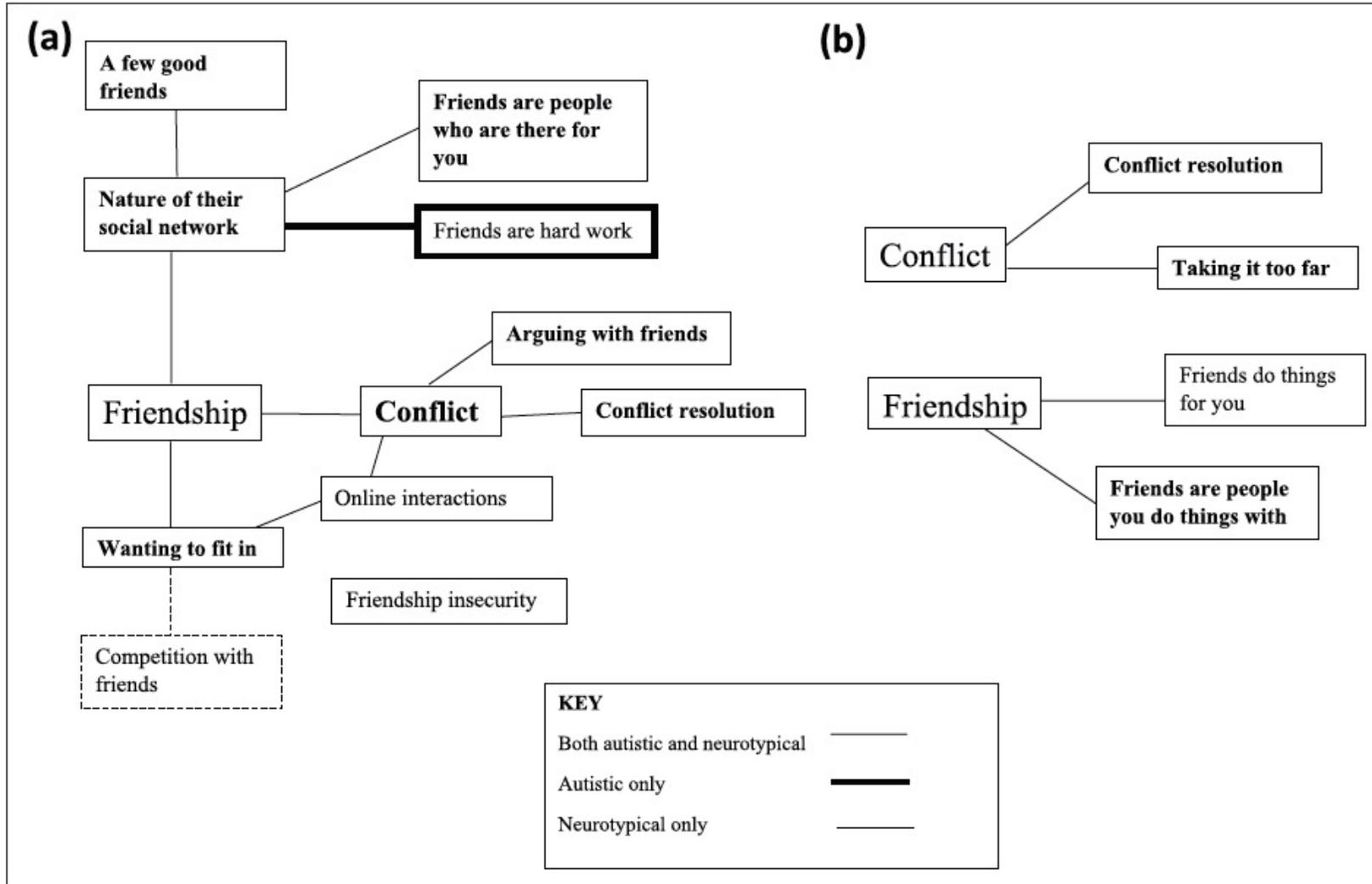


Natural language markers of social phenotype in girls with autism

Amber Song,¹ Meredith Cola,² Samantha Plate,³ Victoria Petrulla,² Lisa Yankowitz,^{2,4} Juhi Pandey,^{2,5} Robert T. Schultz,^{2,6} and Julia Parish-Morris^{2,5}



Example 2: Friendship and social motivation



46 adolescents with special education needs, attending special schools in England

102 adolescents in the general community attending mainstream education

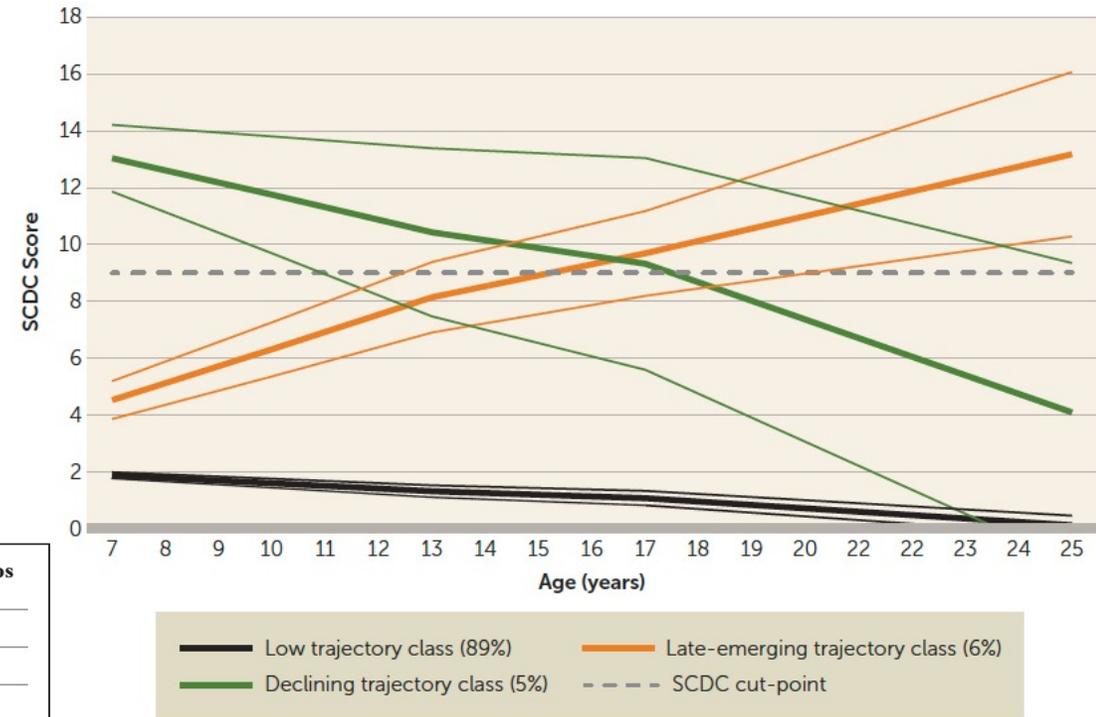
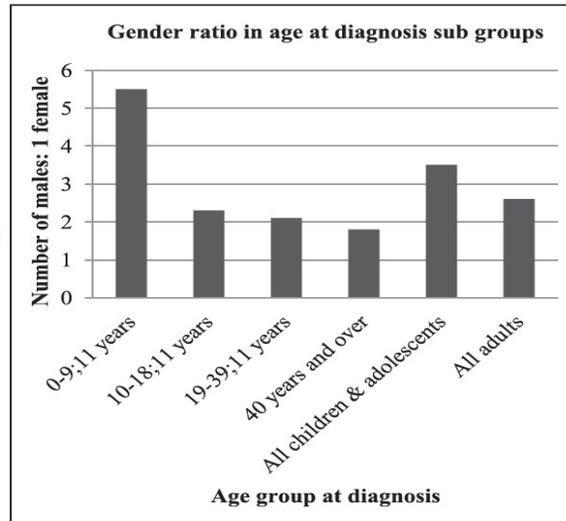
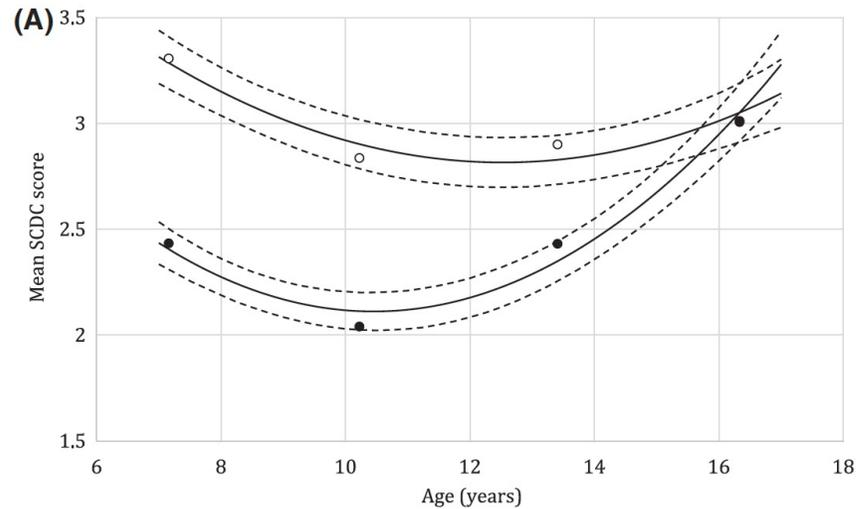
“...in many ways, the friendships and social experiences of autistic girls are similar to those of neurotypical girls.”

“Autistic girls, however, have significantly more social challenges than their neurotypical peers, experiencing more conflict and finding that conflict harder to manage successfully.”

Figure 1. Diagram showing the themes emerging from interviews with adolescent (a) girls and (b) boys. Bold lines denote themes unique to autistic participants and dashed lines denote themes unique to neurotypical participants. Bold text denotes the most common themes.

Example 3: (Social) developmental context and changes

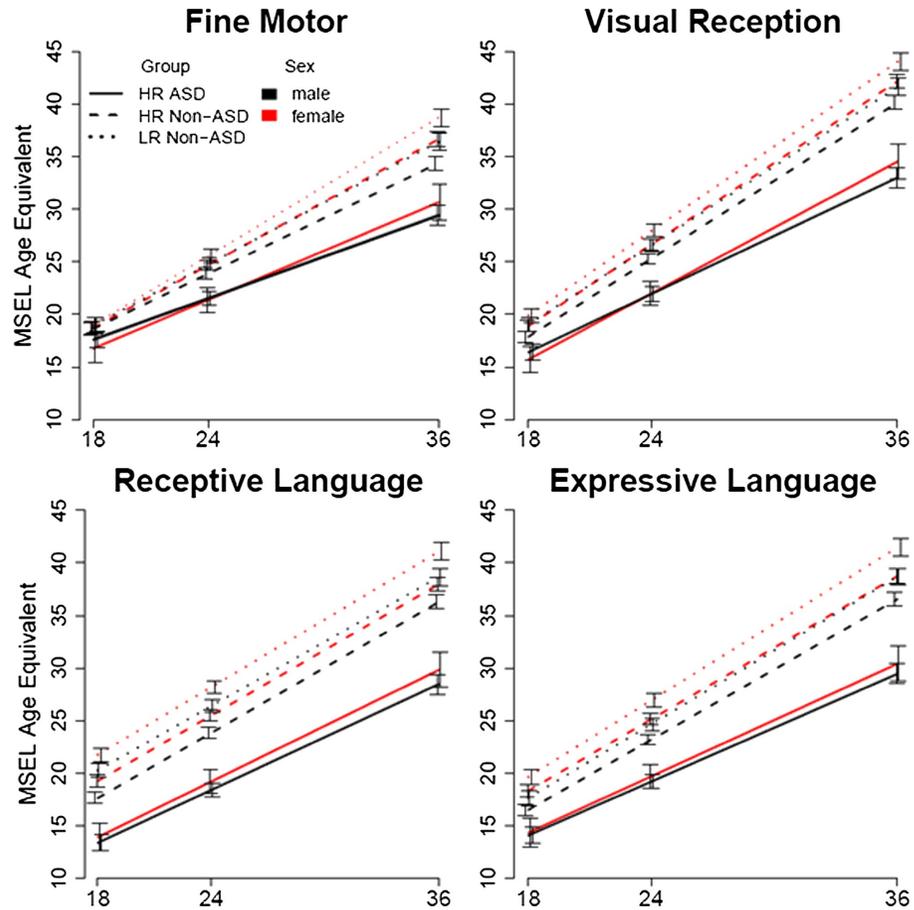
ALSPAC (UK birth cohort): 9744 children in the general population; 4784 males and 4960 females



ALSPAC: 8094 children in the general population; 4067 males and 4027 females

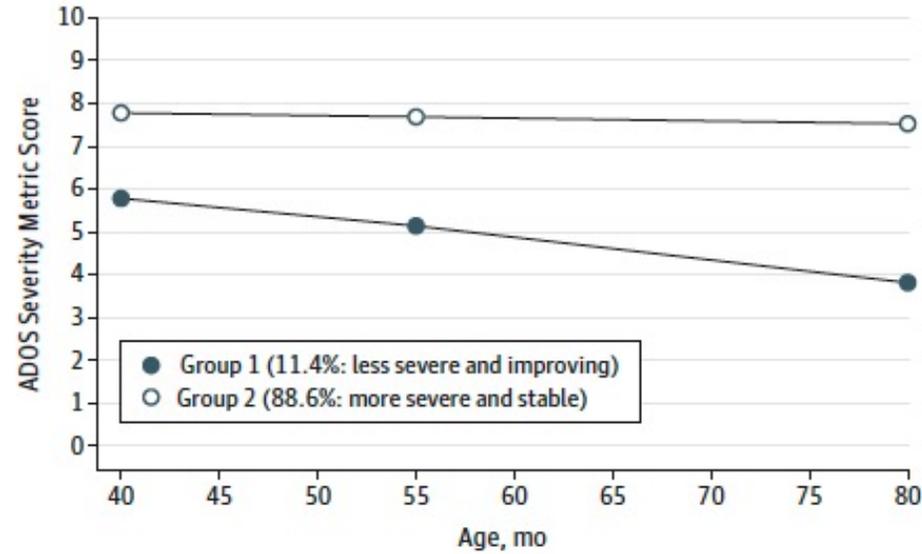
Baby Siblings Research Consortium:

total 1824 infants; 193 autistic boys, 59 autistic girls

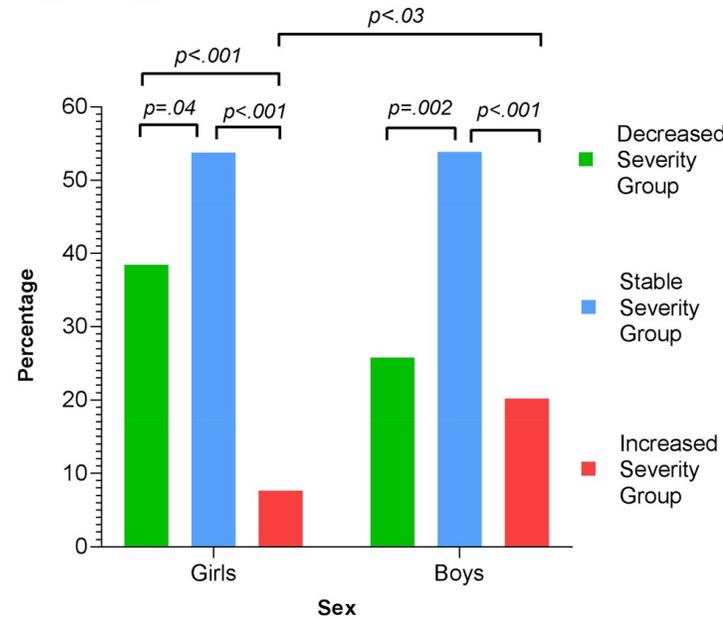
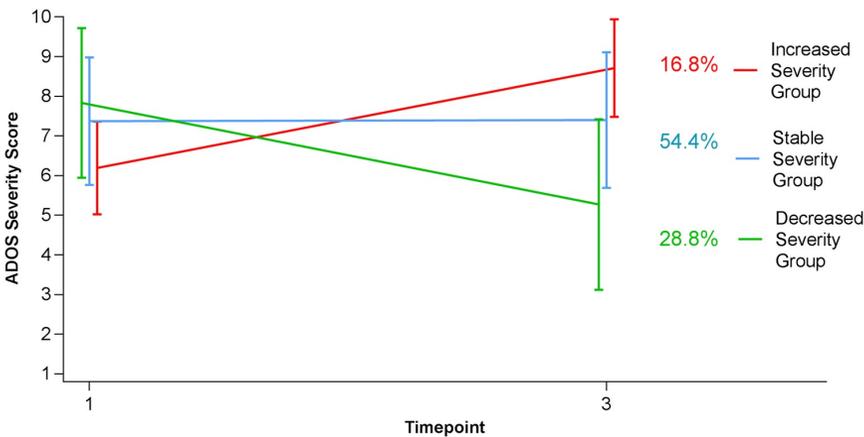


Pathways in ASD: 355 autistic boys, 66 autistic girls

Figure 1. Developmental Trajectories of Autistic Symptom Severity



Autism Phenome Project: 89 autistic boys, 36 autistic girls



Example 4: Social coping ('masking', 'camouflaging', 'passing as non-autistic')

Compensation = finding ways around things that are naturally difficult

Example:

Forcing yourself to make eye contact with someone

Masking = hiding parts of your autism

Example:

Not talking about something you are really interested in

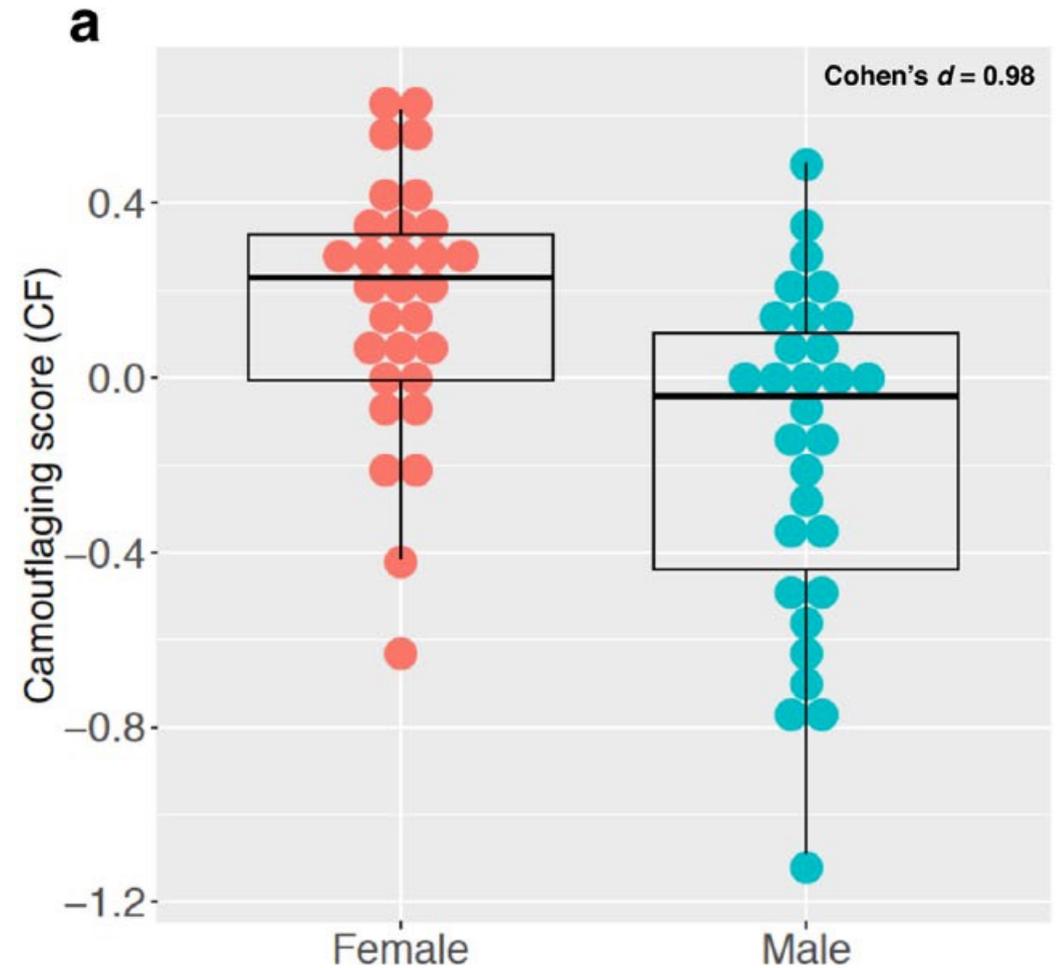
Assimilation = trying to fit in with everyone else so people don't notice you are different

Example:

Talking to a stranger in a shop even if you don't want to

Development and Validation of the Camouflaging Autistic Traits Questionnaire (CAT-Q)

Laura Hull^{1,6} · William Mandy¹ · Meng-Chuan Lai^{2,3,4} · Simon Baron-Cohen³ · Carrie Allison³ · Paula Smith³ · K. V. Petrides⁵



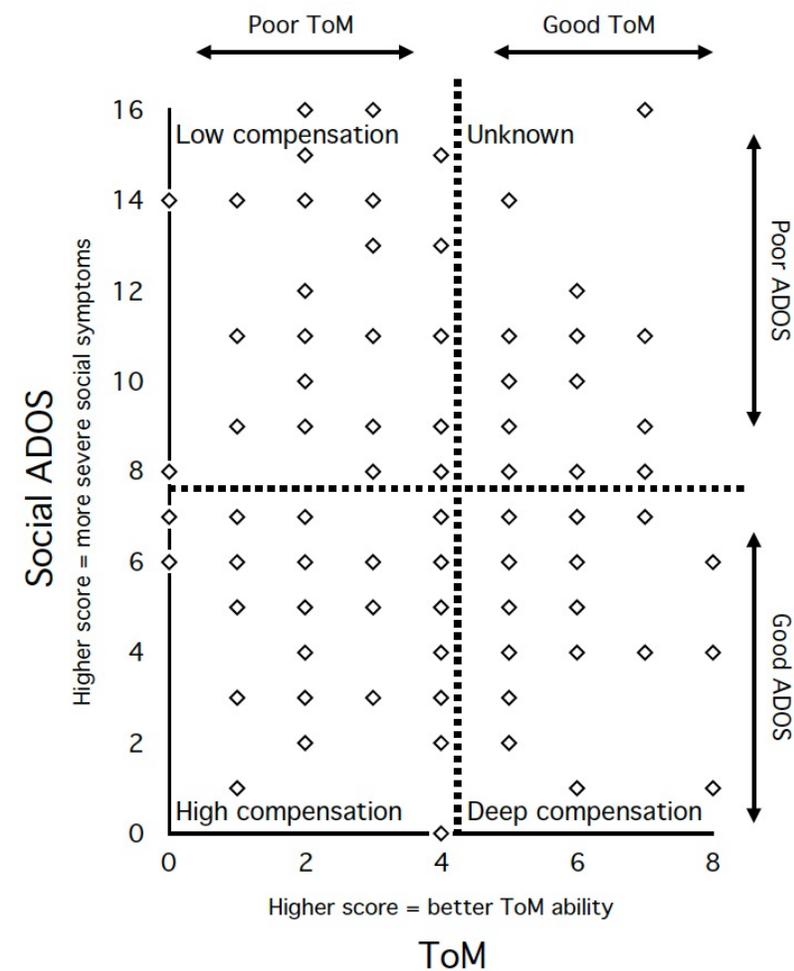


Playground behaviour

	<u>TD boys</u>	<u>TD girls</u>	<u>ASD boys</u>	<u>ASD girls</u>
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Games	41.50 (35.91)	13.75 (27.84)	10.87 (18.63)	6.68 (12.63)
Joint Engage	31.67 (31.44)	52.08 (35.01)	23.55 (27.80)	39.00 (31.46)
Solitary	3.81 (6.91)	7.92 (14.46)	43.57 (33.90)	26.69 (28.51)

Reciprocity in Interactive Drawing Test



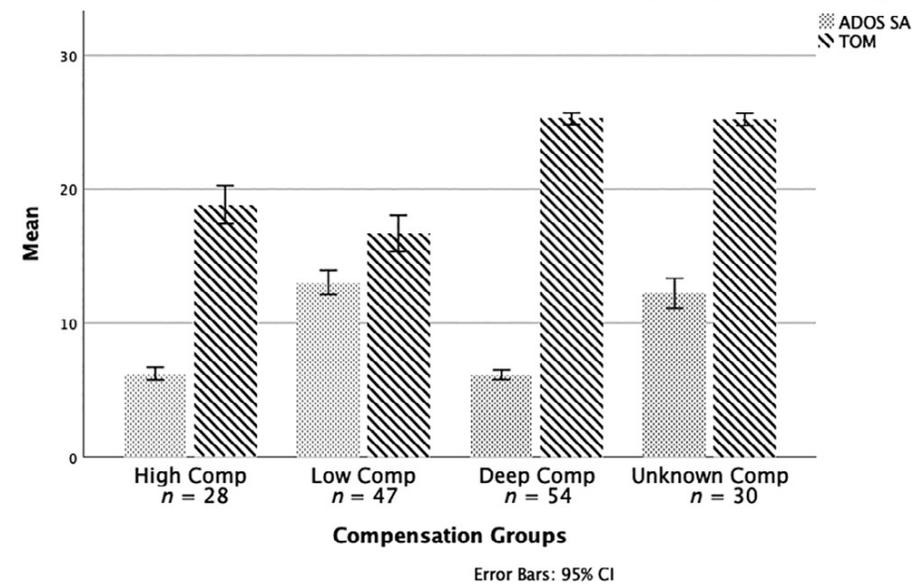


High vs. low compensator: **Higher IQ, EF, but more anxiety**

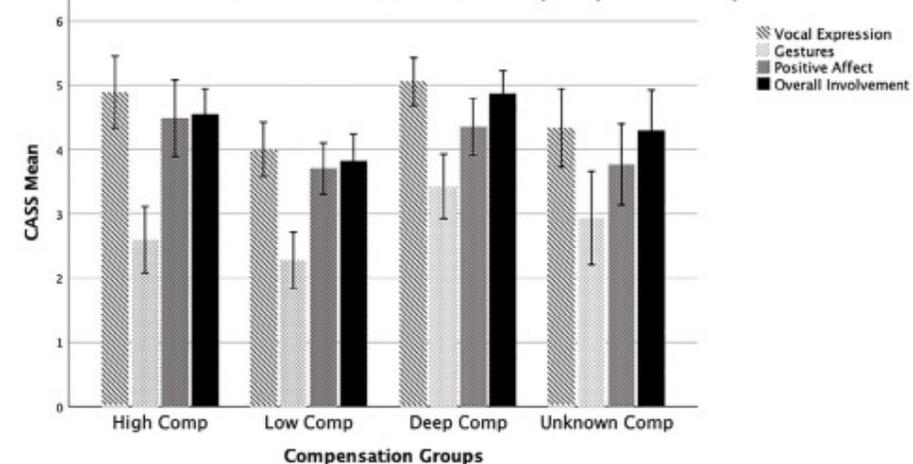
High vs. low compensator: **stronger social engagement and communication behaviors**

Higher self-reported camouflaging: **Better EF, more anxiety**

Clustered Bar Mean of ADOS SA and TOM by Compensation Group



Clustered Bar Mean of CASS Variables by Compensation Group



“You Must Become a Chameleon to Survive”: Adolescent Experiences of Camouflaging

Courtney J. Bernardin¹ · Erica Mason² · Timothy Lewis³ · Stephen Kanne⁴

Bernardin et al., 2021, *JADD*

Table 1 Summary of patterns in camouflaging motivations and consequences

Patterns by diagnosis	<i>Neurotypical participants</i> Motivation: To fit in and make friends Positive consequence: To be perceived positively, to gain future opportunities	<i>Autistic participants</i> Motivation: To avoid negative experiences Positive consequence: To make and keep friends
Patterns by sex	<i>Male participants</i> Camouflaging is easy Feel positive or neutral after	<i>Female participants</i> Camouflaging is difficult Feel negative or drained after
Patterns by sex within autistic participants	<i>Autistic males</i> Least likely to feel inauthentic after camouflaging Most likely to say nothing bad comes from camouflaging Most likely to be unsure of motivation for camouflaging	<i>Autistic females</i> Camouflage to avoid negative perceptions and avoid teasing/bullying Some described camouflaging in order to hide autism from others

Camouflaging in autism: A systematic review

Julia Cook^{a,*}, Laura Hull^a, Laura Crane^b, William Mandy^a

A Systematic Review of Passing as Non-autistic in Autism Spectrum Disorder

Erin J. Libsack¹ · Elliot Gavin Keenan² · Caroline E. Freden¹ · Julianne Mirmina¹ · Nathaniel Iskhakov¹ · Darsiya Krishnathasan¹ · Matthew D. Lerner¹

A systematic review on autistic people’s experiences of stigma and coping strategies

Emeline Han¹ | Katrina Scior² | Katerina Avramides³ | Laura Crane¹

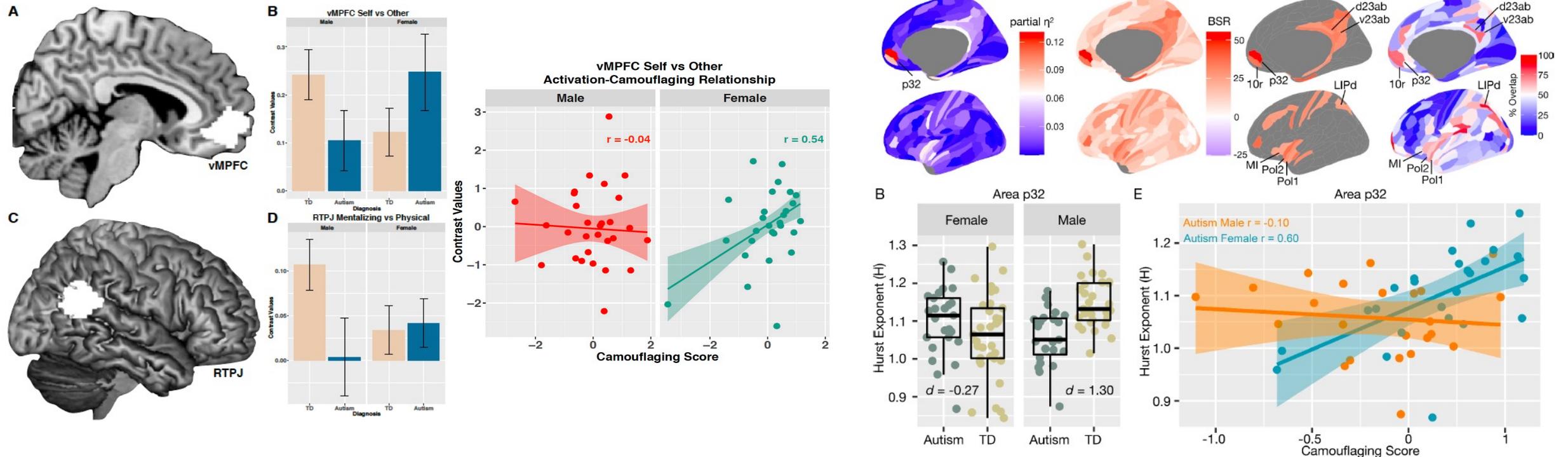
What 'camouflaging' is & is not

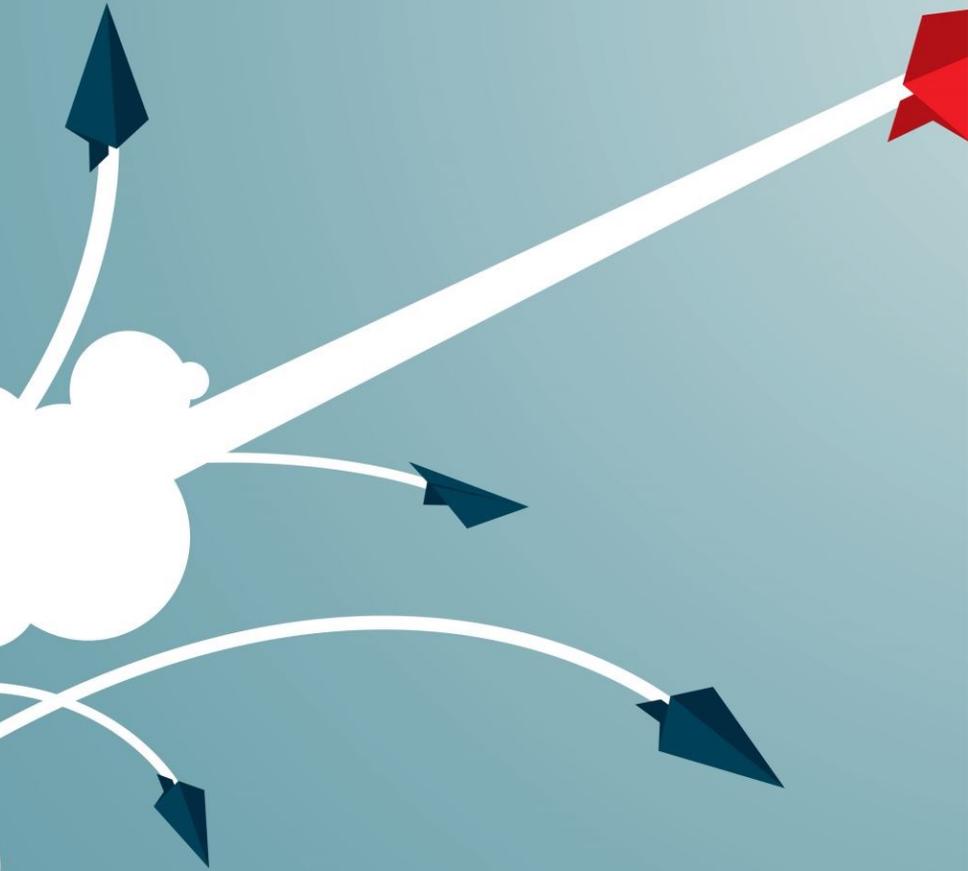
Coping responses to neurotypical social contexts
 Various measurements (*reflective, discrepancy, vs. real-world behaviour*) but construct validity remains to be established
 NOT sex/gender-specific
 NOT an autism subtype

What 'camouflaging' overlaps/intersects with

Impression management	Compensation	False self Persona etc.
Passing	Masking	
Cultural assimilation	Imitation	
Social coping / adaptation etc.	Trained social skills etc.	

Lai et al., 2021, *JCPP*





Exchange, Q & A, and a short break

*Autism diagnostic assessment in youth
and adults: A brief overview*

Prevalence in adulthood (England)

Table 1. Weighted Cumulative Estimates of Respondents per 1000 Population for ADOS-4 Cut-offs

ADOS-4 Cut-off	Unweighted Base (n = 2828)	Weighted Base (n = 7333)	Weighted Estimate Rate per 1000 Population (95% CI)
≥7	32	108	14.7 (7.0-22.5)
≥8	26	88	12.0 (4.9-19.1)
≥9	20	75	10.2 (3.4-17.0)
≥10 ^a	19	72	9.8 (3.0-16.5)
≥11	16	65	8.9 (2.2-15.5)
≥12	12	47	6.4 (0.6-12.3)
≥13	10	44	6.0 (0.2-11.8)

Male gender was a strong predictor of autism only in those with no or mild intellectual disability (adjusted OR = 8.5, 95% CI 2.0–34.9; interaction with gender, P = 0.03)

"Few adults with autism have intellectual disability; however, autism is more prevalent in this population."

"Autism measures may miss more women with autism."

Identification and initial assessment of possible autism

1.2.2 Consider assessment for possible autism when a person has:

- one or more of the following:
 - persistent difficulties in social interaction
 - persistent difficulties in social communication
 - stereotypic (rigid and repetitive) behaviours, resistance to change or restricted interests, **and**
- one or more of the following:
 - problems in obtaining or sustaining employment or education
 - difficulties in initiating or sustaining social relationships
 - previous or current contact with mental health or learning disability services
 - a history of a neurodevelopmental condition (including learning disabilities and attention deficit hyperactivity disorder) or mental disorder.

Approaches

Multi-informant, multi-disciplinary comprehensive clinical assessment is still the gold standard

Properly take into account subjective experiences (beyond the scores on screening measures [which often reflect dimensional traits])

Psychometric properties of questionnaires and diagnostic measures for autism spectrum disorders in adults: A systematic review

Sarah Wigham¹, Jacqui Rodgers¹, Tom Berney²,
Ann Le Couteur^{2,3}, Barry Ingham^{1,3} and Jeremy R Parr^{1,3}

- *“Sensitivity and specificity of structured questionnaires were best for individuals with previously confirmed autism spectrum disorder diagnoses and reduced in participants referred for diagnostic assessments, with discrimination of autism spectrum disorder from mental health conditions especially limited.”*
- *“For adults with intellectual disability, diagnostic accuracy increased when a combination of structured questionnaires were used.”*
- *“Evidence suggests some utility of diagnostic measures in identifying autism spectrum disorder among clinic referrals, although specificity for diagnosis was relatively low.”*
- *“In mental health settings, the use of a single structured questionnaire is unlikely to accurately identify adults without autism spectrum disorder or differentiate autism spectrum disorder from mental health conditions.”*

Semi-structured interview for developmental history

- Autism Diagnostic Interview-Revised (ADI-R)
- The Developmental, Dimensional and Diagnostic Interview (3Di) (Skuse et al., 2004, *JAACAP*)
- The Diagnostic Interview for Social and Communication Disorders (DISCO) (Leekam et al., 2002, *JCPP*)
- The Asperger Syndrome Diagnostic Interview (ASDI) (Gillberg et al., 2001, *Autism*)
- The Developmental, Dimensional and Diagnostic Interview, Adult version (3Di-Adult) (Mandy et al., 2017, *JADD*)

Semi-structured observational interview with the youth/adult

- Autism Diagnostic Observation Schedule-2 (ADOS-2), Module 4
 - But note: a negative result does not rule out autism in adults

The Adult Asperger Assessment (AAA) (Baron-Cohen et al., 2005, *JADD*)

- Utilizing information from screening questionnaires to facilitate clinical interview
- Detailed exploration of communication aspects

Challenges of making a first autism diagnosis in adulthood

Practical reasons

- Informant for developmental history not available
- Validity and reliability of recall

Developmental reasons

- Varied adulthood social-communicative developmental trajectories vs. 'functional impairment'
- Learnt behaviours (e.g., 'camouflaging')

Clinical reasons

- High co-occurrence with other conditions
- Bi-directional diagnostic overshadowing

What is a diagnosis for? Why one needs a diagnosis, and when? Who has the power to diagnose?

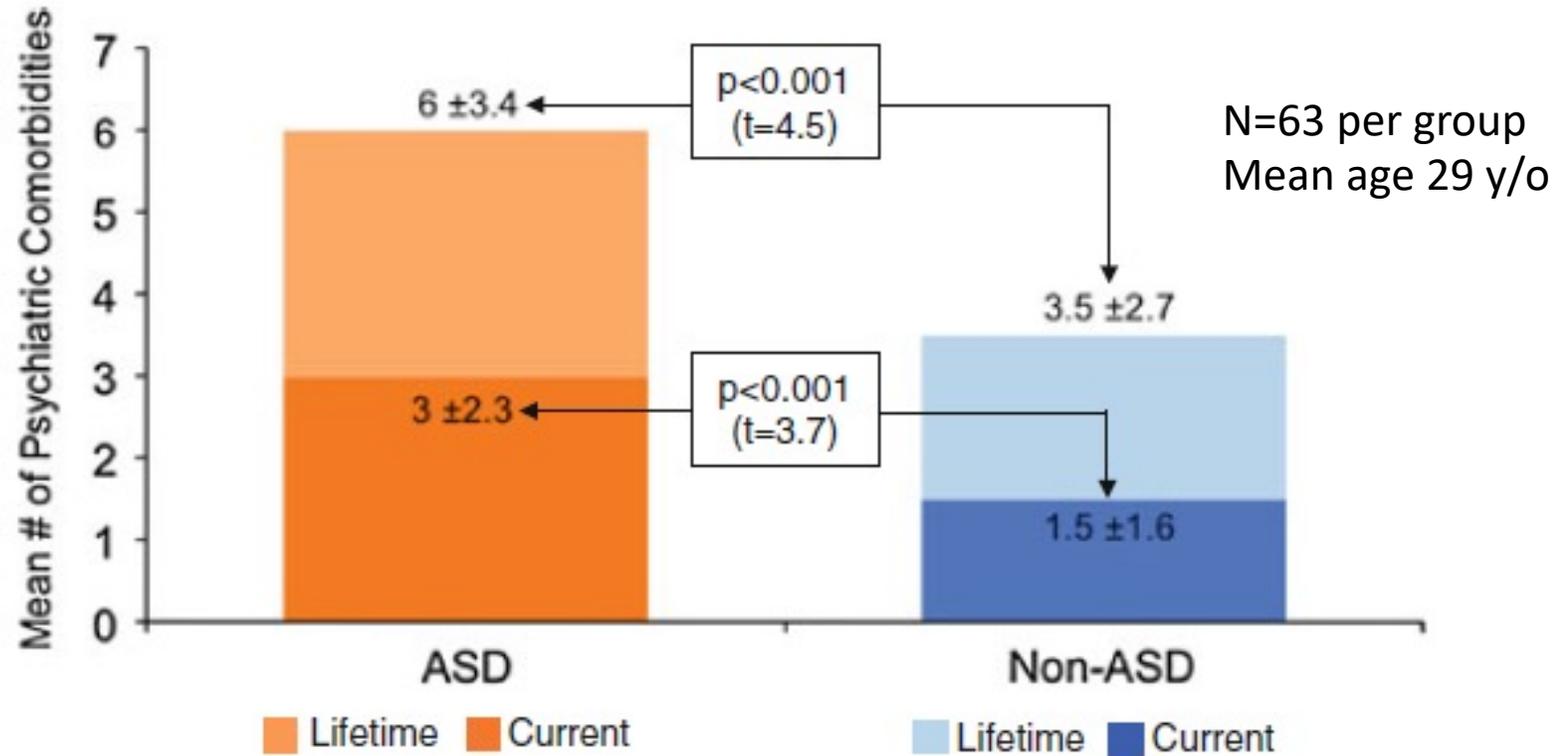


Fig. 2 Mean number of psychiatric comorbidities in psychiatrically referred adult populations with and without ASD

Compared to other psychiatric outpatients, autistic adults have significantly higher numbers of comorbidities, particularly MDD and multiple anxiety disorders.

Table 4: Lifetime rate of axis-II disorders in adults with autism spectrum disorders (N = 117)

	Criteria met DSM-IV															
	Autistic disorder (N=5)		Asperger's disorder (N=62)		PDD NOS (N=50)		Total (N=117)		AS – PDD NOS ^a		Male (N=77)		Female (N=40)		Male – Female ^a	
	N	%	N	%	N	%	N	%	χ^2 (df = 1)	p	N	%	N	%	χ^2 (df = 1)	p
Personality disorders																
≥ 1 PD	1	20	42	68	30	60	73	62	0.72	0.43	46	60	27	68	0.68	0.43
≥ 2 PD	0	0	25	40	16	32	41	35	0.83	0.43	28	36	13	33	0.18	0.84
≥ 3 PD	0	0	11	18	9	18	20	17	0.00	1.00	13	17	7	18	0.01	1.00
Paranoid	0	0	12	19	10	20	22	19	0.01	1.00	15	20	7	18	0.07	1.00
Schizotypal	0	0	10	16	5	10	15	13	0.90	0.41	12	16	3	8	1.54	0.26
Schizoid	0	0	13	21	12	24	25	21	0.15	0.82	11	14	14	35	6.72	0.02
Histrionic	-	-	-	-	-	-	0	0	-	-	-	-	-	-	-	-
Narcissistic	0	0	1	2	2	4	3	3	0.61	0.59	2	3	1	3	0.00	1.00
Borderline	0	0	4	7	6	12	10	9	1.05	0.34	4	5	6	15	3.24	0.09
Antisocial	0	0	0	0	4	8	4	3	5.14	0.04	3	4	1	3	0.16	1.00
Avoidant	0	0	18	29	11	22	29	25	0.62	0.52	21	28	8	20	0.81	0.50
Dependent	0	0	2	3	4	8	6	5	1.24	0.41	3	4	3	8	0.70	0.41
Obsessive	1	20	25	40	11	22	37	32	4.26	0.04	23	30	14	35	0.32	0.68
PD NOS	-	-	-	-	-	-	0	0	-	-	-	-	-	-	-	-

^aFisher's exact χ^2 test

Netherlands Autism Register
 N=1019 (494 M, 525 F), >16 y/o

Observed rates of prior diagnoses that were no longer present post-autism diagnosis for specific psychiatric conditions, and logistic regression parameters.

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Burnout/Chronic Fatigue	11	2.2	41	7.8	52	5.1	1.61	.36	19.98	<.001***	5.00	2.47	10.13
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Attention-Deficit/ Hyperactivity Disorder	15	3.0	24	4.6	39	3.8	.37	.34	1.13	.287	1.44	.74	2.82
Trauma-related Disorders	5	1.0	15	2.9	20	2.0	1.27	.54	5.54	.019	3.54	1.24	10.15
Oppositional Defiant Disorder/ Conduct Disorder	13	2.6	7	1.3	20	2.0	-.65	.49	1.81	.179	.52	.20	1.35
Substance Use Disorder	9	1.8	7	1.6	16	1.6	-.04	.53	.00	.947	.97	.34	2.72

	Relation to autism spectrum conditions
Anxiety disorders	Mostly comorbid
Social anxiety disorder	Differential and comorbid
Depressive disorders	Comorbid
Obsessive-compulsive disorder	Overlapping, differential, and comorbid
Psychotic disorders	Differential and comorbid
Bipolar disorders	Comorbid
Schizoid personality disorder	Overlapping, differential, and comorbid
Schizotypal personality disorder	Overlapping, differential, and comorbid
Paranoid personality disorder	Differential and comorbid
Borderline personality disorder	Differential and comorbid
Antisocial personality disorder	Differential and comorbid
Narcissistic personality disorder	Differential and comorbid
Histrionic personality disorder	Differential (unlikely to co-occur)
Obsessive-compulsive personality disorder	Overlapping, differential, and comorbid
Avoidant personality disorder	Differential and comorbid
Dependent personality disorder	Differential and comorbid
Attention deficit hyperactivity disorder	Differential and comorbid
Language disorders	Differential and comorbid
Disorders of motor development	Comorbid
Tic disorders	Comorbid
History of social deprivation, maltreatment, or extended treatment in an institution or hospital	Differential
Eating disorders	Comorbid
Gender dysphoria	Comorbid
Substance misuse	Comorbid

Table 2: Comorbid, overlapping, and differential diagnoses to autism spectrum conditions in adults



'Not at the diagnosis point': Dealing with contradiction in autism assessment teams

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^c University of Cambridge, Department of Psychiatry, Douglas House, 18b Trumpington Road, Cambridge, CB2 2AH, UK

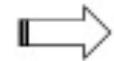
"We identified a three-part interactional pattern which allows clinicians to forward evidence for and against a diagnosis, facilitates their collaborative decision-making process and enables them to build a plausible narrative which accounts for the diagnostic decision. Pragmatism was found to operate as a strategy to help assign diagnosis within a condition which, diagnostically, is permeated by uncertainty and contradiction."

1. Constraining preface (*sets constraints for discussion*)

2. Contradictory account (*complicating factor*)

3. Re-alignment (*offers an explanation for and then realigns conflicting account to the diagnostic narrative*)

+ Helpfulness (*outlines the pragmatic outcome – temporally flexible*)



Pragmatic, coherent diagnostic narrative

Table 2. Final 11 statements describing characteristics of optimal autism assessment services for adults.

Referral process/pre-assessment

- Services across primary, secondary and specialist care should have access to a clear pathway of how people can access a local autism diagnostic assessment service
- Autism diagnostic services should give an update to people on their waiting list, for example, when it is around 12, 6 and around 3 months until their assessment if resources are available
- Information on autistic characteristics and co-existing conditions should be sought from informants and clinicians, before the assessment takes place to allow individualised planning of the assessment process and to give clinical context
- Autism diagnostic services should provide information to people before their assessment such as directions, a clear description of what will happen during the assessment, the environment and people they will meet (this may include photographs)

Diagnostic assessment

- There should be a separately resourced specialist multidisciplinary service within the 'secure estate' (e.g. prison, medium and low secure units) for diagnosis of autism and co-occurring mental and physical health problems
- As part of diagnostic assessment, with consent, services should always try to gather developmental and/or current information about social communication ability, rigidity/repetitive behaviours and co-occurring conditions. This could be from a family member or another person who knew/knows the person well (e.g. friend, tutor or employer)
- All autism diagnostic services should include someone trained in the use of a standardised observational tool, so it can be used if needed
- Training on use of standardised diagnostic tools should be available for autism diagnostic service members
- The core autism diagnostic multidisciplinary service should include a clinician with expertise identifying mental health conditions

Training/consultancy

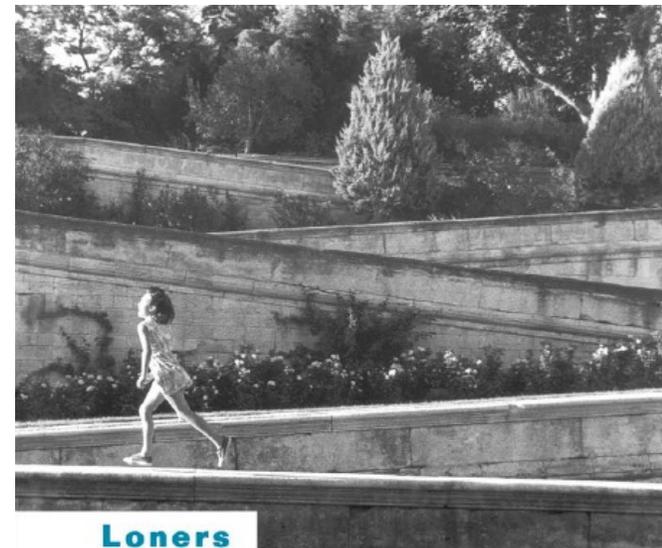
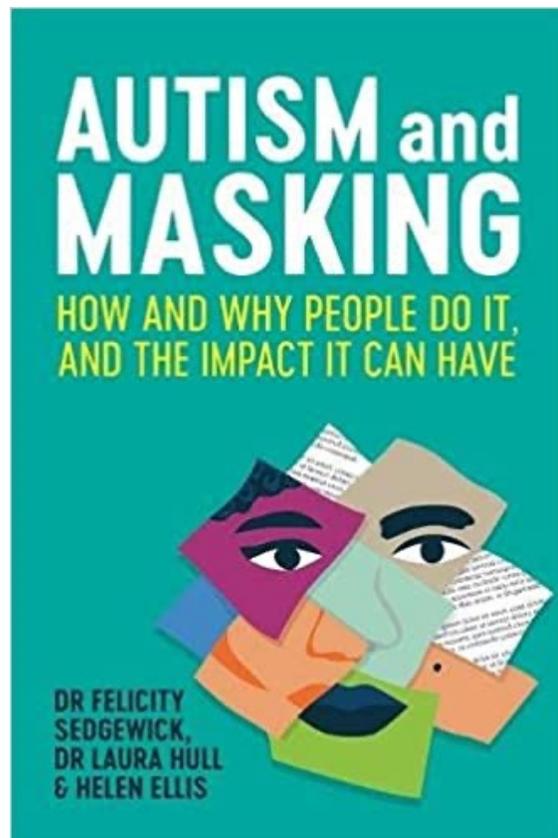
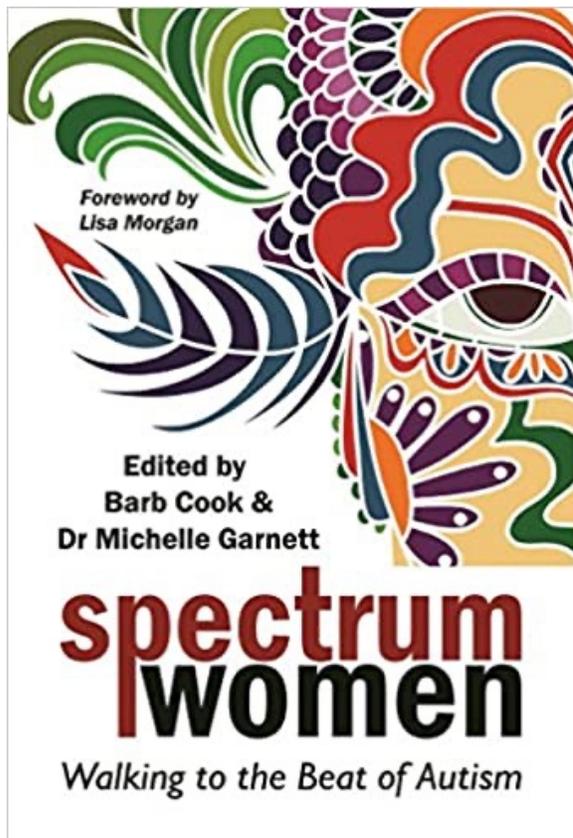
- Delivering training to others should be part of an autism diagnostic service's commissioned service specification (as opposed to being ad hoc)
 - A national network of multidisciplinary health professionals who work in autism diagnostic services should be created. There should be opportunities for meetings focusing on topics such as exchange of ideas, peer support and information sharing
-

*How do we achieve
equitable recognition
of autism across sexes
and genders?*



The first account of the syndrome Asperger described? Part 2: the girls

Charlotte Simmonds¹  · G. E. Sukhareva²



Loners

The Life Path of Unusual Children

Sula Wolff

Foreword by Leon Eisenberg, MD
Harvard Medical School



Rethinking (& re-calibrating) autism; Improving recognition

~~Female autism phenotype?~~

Nuanced autism presentations
modulated by sex- or gender-
related factors

A1: Social-emotional reciprocity

- Attention and interest to social stimuli can be present to some extent, and modulated by gendered contexts and upbringing
- Conversation may be superficially back and forth (sometimes with scripted politeness, well-rehearsed in asking questions, or seemingly 4-way but mostly offering own experiences/views), but reciprocity difficulty arises with topic shifting, unfamiliar contexts, or increasing complexity (e.g., more than 2 people conversing)
- Conversation reciprocity improves and becomes more natural when talking about interests
- Can have intact affective empathy and show sympathy (including towards animals)

A2: Non-verbal communication

- Non-verbal expressions (e.g., eye contact, facial expression orientation, conventional, descriptive, and emphatic gestures) can be superficially present, though can be exaggerated, inflexible, or with insufficient integration across modalities and with verbalization
- Understanding neurotypical non-verbal communications may be the main challenge
- Subjectively reporting learnt and forced alternative ways of making eye contact (e.g., looking at other's forehead or nose) and facial expression orientation throughout childhood/teenage—this effort can disrupt verbal exchange, objectively shown as reduced integration of verbal and non-verbal communication

A3: Developing, maintaining, & understanding relationships

- Interests to social relationships and peer interaction can be present, with developmentally appropriate desire for friendships, yet finding them difficult to navigate and manage
- Social awareness can be present to certain levels
- Tend to be naïve in relationships
- May prefer to be alone in neurotypical social situations, but can have close friends especially when there are shared characteristics or interests
- Can figure out neurotypical others' thoughts and feelings with deliberate efforts, but intuitive understanding is still challenging
- Can invest large amounts of energy preparing for social interactions, and feeling exhausted and drained afterwards

B1: Stereotypy & repetitiveness

- Repetitiveness may not be apparent motor mannerisms
- Stereotypy can manifest as idiosyncratic language expression, including unusually formal, pedantic, detailed, or precise language

B2: Insistence on sameness

- Can be perceived as perfectionism or preoccupation with details
- Can manifest as strictly following rules, “black and white” thinking, or insisting on believed truth (when co-existing with A3 features)

B3: Circumscribed interests

- Content of circumscribed interest can be typical to neurotypical and gendered contexts
- Despite ego-syntonic, engagement with circumscribed interest can be exhaustive
- Circumscribed interests can be used as social currency

B4: Idiosyncratic sensory responses

- Both hyper- and hypo-responsivity can be present within the same or across different sensory modalities
- Can also present as enhanced perception
- Can also present as difficulties in interoception
- Can manifest as eating problems
- Can be associated with choices of clothing and appearance not fitting stereotypical gender expectations

C: Evident characteristics in early developmental period but may not fully manifest until demands exceed capacity, or masked by learnt strategies

- **Impression management** of the individual and socio-cultural (including gendered) expectations may lead to learned modification of own behaviours across development, resulting in attenuated autistic behavioural presentations (a process termed “autistic camouflaging”, “masking”, or “passing as non-autistic”, etc.) that render some, but not all, cardinal features of autism less apparent.
- However, **impression management is not autism-specific nor diagnostic for autism.** Positive subjective reports of developmental experiences of intention and efforts to “camouflage/mask/pass” and the cognitively taxing nature due to autistic cognition and executive function challenges, alongside collateral information of evident autistic features in early years (i.e., childhood), are key to autism diagnostics in this scenario.

C: Evident characteristics in early developmental period but may not fully manifest until demands exceed capacity, or masked by learnt strategies

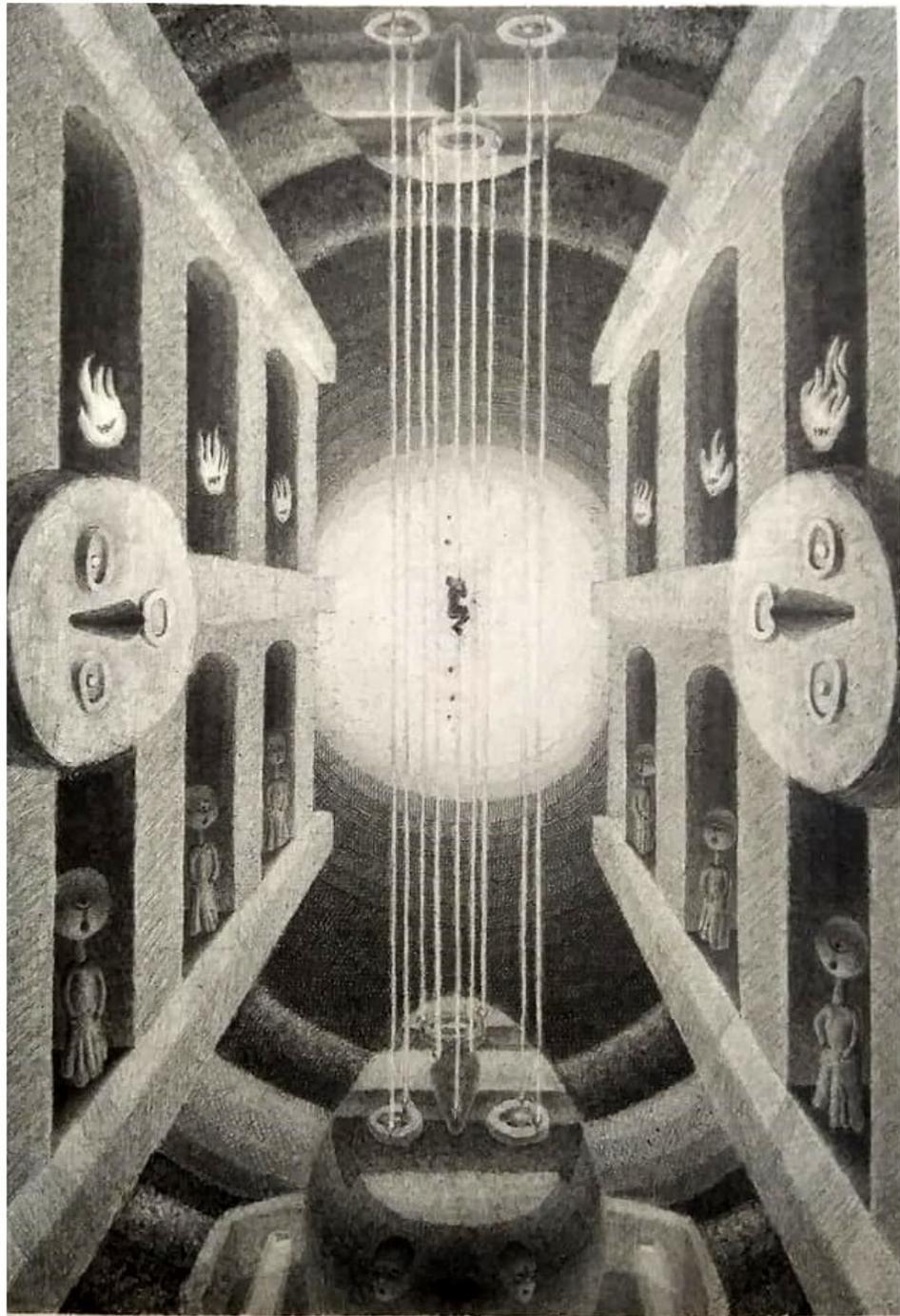
- **Autistic “camouflaging/masking/passing” should be recognizable**
- 1. There should be autistic features early in life to be masked or compensated for, when camouflaging efforts started
- 2. There should be repeated camouflaging practices/rehearsals that the individual exercised over time, so it was less successful initially but over time they were better at it
- 3. Even when an autistic person masters camouflaging, there should still be observable signs of this effort, including (i) the exhaustion and withdrawal afterwards (e.g., signs of “autistic burnout”), (ii) inflexibility across contexts (e.g., much more difficult in the “cocktail party” scenario), and (iii) subtle de-synchronization during interpersonal interactions, “out of sync” episodes, and efforts to keep up with synchronization
- Hence, social-behavioural differences may manifest and become more observable over time during long interactions, and especially in novel or unpredictable settings.

D: Clinically significant impairment in current functioning

- Despite superficially intact functioning, can easily feel exhausted due to impression management efforts
- Subjective distress should also be considered for making a clinical diagnosis
- Context dependence of functioning is not uncommon: e.g., keeping oneself together in public (e.g., at school, workplace) but experiencing/expressing substantial emotion regulation challenges (e.g., burnout, meltdown) in private settings (e.g., at home)
- Frequently requiring time alone to recover and restore energy
- Overall, **the clinical diagnosis is based on the Gestalt of behavioural-cognitive patterns and their developmental profiles, and that functional and wellbeing impacts are directly associated with this Gestalt (in neurotypical contexts)**

Associated features that commonly co-exist

- Can be much clouded by emotional dysregulation (e.g., “ambivalence of emotions” as per Sukhareva)
- Can have co-existing difficulties in understanding own emotions (i.e., alexithymia) and other’s emotions, accompanied by long processing time or difficulty differentiating emotions
- Childhood imaginative/pretend play (e.g., doll play) can be present, but is often predominated by setting up toys and scenes, scripted (even interactive), with limited reciprocity (even with the presence of agency using dolls/figures)
- Good structural language ability, especially in expression (including hyperlexia)
- Executive function difficulties and motor challenges may be common
- Body focused repetitive behaviours may be common
- Do not reach the level of adaptation or achievement expected given the intelligence level
- Increased variance and fluidity in gender expression and identity, as well as sexual orientation and sexual identity



Appreciating Subjective Experiences

這是我面對社交時，心底浮現的畫面。我要在心裡模仿別人的表情，還要花很多時間，才能勉強讀出表情背後一兩成的含意。所以畫中臉上的五官彼此用線連著，而我在中間艱辛的攀爬著。

This picture is what comes to my mind when I am faced with social interactions. To understand what other people mean behind their facial expressions, I need to imitate their expressions in my head, and it takes a lot of time to barely make out part of the meaning. That's why the features of the faces are connected to each other in this picture, and I am the one in the middle, struggling up the threads.

And let's not forget: Health care needs in autistic people (particularly in girls/women and gender-diverse people)

	Number of datapoints in meta-analysis*	Autism population sample size (n)	Autism population		General population prevalence (95% CI or SE)	Subgroup moderator analysis				
			Pooled prevalence (95% CI; 95% PI)	I ² (95% CI; p value†)		Prevalence in population or registry-based studies (95% CI; 95% PI)	Prevalence in clinical sample-based studies (95% CI; 95% PI)	R ² (QE p value)	I ² (95% CI)	QM p value
Attention-deficit hyperactivity disorder	89	210 249	28% (25-32; 4-63)	99.65% (99.55-99.85; <0.0001)	7.2% (6.7-7.8; point prevalence, aged ≤18 years) ⁴⁶	22% (17-26; 1-55)	34% (29-39; 7-69)	2.05% (<0.0001)	99.64% (99.60-99.84)	0.0004
Anxiety disorders	68	169 829	20% (17-23; 2-48)	99.53% (99.42-99.87; <0.0001)	7.3% (4.8-10.9; current prevalence, across ages) ⁴⁷	15% (11-19; 0.5-42)	26% (22-31; 1-56)	0% (<0.0001)	99.54% (99.20-99.85)	0.0002
Depressive disorders	65	162 671	11% (9-13; 0-33)	99.41% (99.39-99.81; <0.0001)	4.7% (4.4-5.0; point prevalence of MDD, across ages) ⁴⁸	8% (5-11; 0.01-28)	14% (11-18; 1-38)	0.23% (<0.0001)	99.40% (99.37-99.80)	0.0003
Bipolar and related disorders	38	153 192	5% (3-6; 0-19)	99.50% (99.40-99.82; <0.0001)	0.71% (0.56-0.86) for bipolar I; and 0.50% (0.35-0.64) for bipolar II (1-year prevalence, across ages) ⁴⁹	3% (2-5; 0-16)	7% (4-10; 0-24)	0.35% (<0.0001)	99.50% (99.48-99.81)	0.018
Schizophrenia spectrum and psychotic disorders	42	166 627	4% (3-5; 0-14)	99.18% (99.00-99.87; <0.0001)	0.46% (0.41-0.50; 1-year prevalence, across ages) ⁵⁰	2% (1-4; 0-11)	7% (4-9; 0-19)	0% (<0.0001)	99.18% (99.01-99.84)	0.0004
Obsessive-compulsive and related disorders	47	53 243	9% (7-10; 1-21)	96.85% (96.75-99.87; <0.0001)	0.7% (0.4-1.1; 1-year prevalence, aged ≥18 years) ⁵¹	4% (2-6; 0-13)	12% (10-15; 3-26)	12.51% (<0.0001)	96.20% (96.17-99.37)	<0.0001
Disruptive, impulse-control, and conduct disorders	50	140 946	12% (10-15; 0-36)	99.52% (99.47-99.90; <0.0001)	8.9% (SE 0.5; 1-year prevalence, aged ≥18 years) ⁵²	7% (4-10; 0-28)	22% (17-27; 3-50)	0% (<0.0001)	99.53% (99.42-99.88)	<0.0001
Sleep-wake disorders	26	190 963	13% (9-17; 0-43)	99.87% (99.78-99.93; <0.0001)	3.7% (NA; 1-year prevalence, aged ≤18 years) ⁵³	11% (7-17; 0-39)	16% (8-25; 0-47)	8.52% (<0.0001)	99.85% (99.77-99.91)	0.356

Age effect: ADHD, depression, bipolar, SSD
Sex/gender effect: depression

ID effect: SSD
Human Development Index effect: OCD

Lai et al., 2019,
Lancet Psychiatry



Physical health of autistic girls and women: a scoping review

Caroline Kassee^{1,2†}, Stephanie Babinski^{2,3†}, Ami Tint^{1,4}, Yona Lunsky^{4,5}, Hilary K. Brown^{2,6},
Stephanie H. Ameis^{1,4,5,7}, Peter Szatmari^{1,5,7}, Meng-Chuan Lai^{1,4,5,7,8,9,10†} and Gillian Einstein^{2,8,11,12†}

AUTISTIC GIRLS & WOMEN

vs. AUTISTIC
BOYS & MEN

HIGHER OVERALL PHYSICAL
HEALTH CHALLENGES

HIGHER PREVALENCE OF EPILEPSY

7.0% of autistic girls/women
3.9% of autistic boys/men
(0.73% of general population boys/men)

vs. NON-AUTISTIC
GIRLS & WOMEN

HIGHER OVERALL PHYSICAL
HEALTH CHALLENGES

HIGHER PREVALENCE OF EPILEPSY

7.0% of autistic girls/women
0.69% of general population girls/women

HIGHER PREVALENCE OF ENDOCRINE AND
REPRODUCTIVE HEALTH ISSUES, e.g. PCOS

7.8% of autistic girls/women
3.5% of general population girls/women

Kassee & Babinski et al., 2020, *Mol Autism*

Key Practical Implications

- **Clinicians need to regularly monitor and address physical health care needs for autistic people, especially female individuals.**
- **Particular attention should be paid to the risks of epilepsy, endocrine and reproductive health issues, and other neurological, gastrointestinal, metabolic, nutritional, and immune conditions.**
- **Developing a women's health lens when providing clinical care to autistic girls/women is essential.**

Autism, neurodevelopmental conditions, and gender diversity

675 adolescents (age >15) and adults registered in the Netherlands Autism Register (NAR)

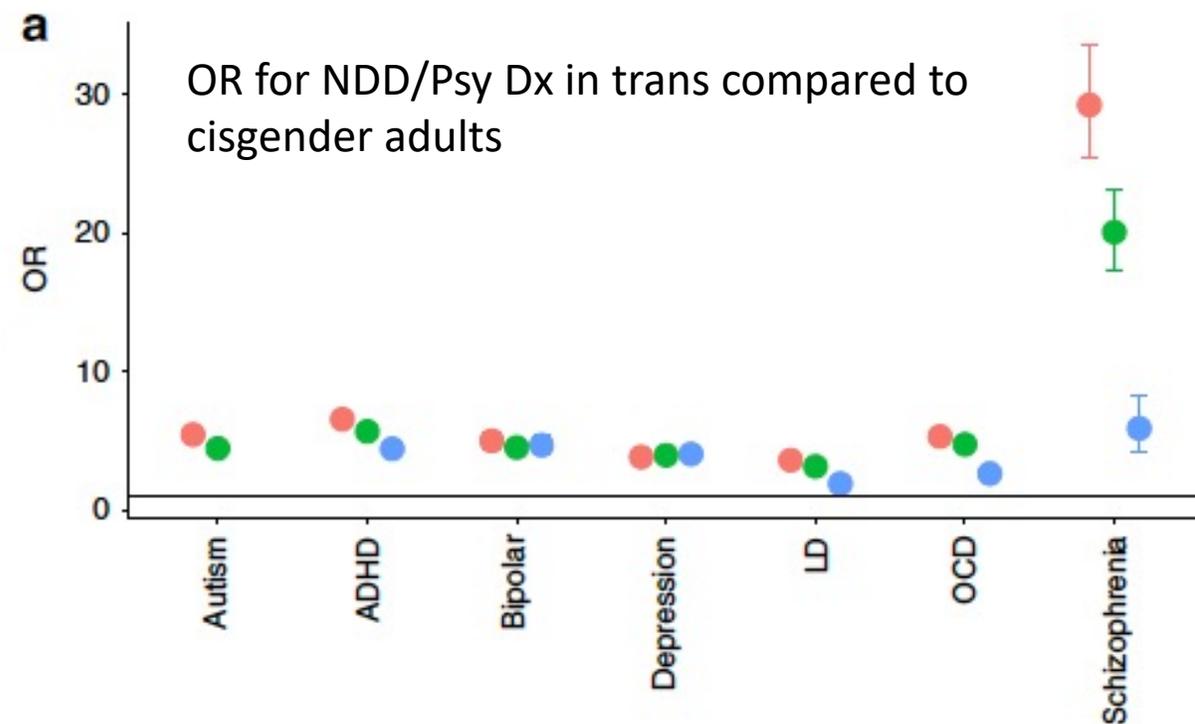
Table 2 Assigned gender at birth and gender identity

Assigned gender at birth	Male n (%)		Female n (%)	
	ASD (n=316)	TD (n=3927)	ASD (n=343)	TD (n=4137)
Feels male	299 (91.7)		3 (0.9)	
Partly male, partly female	10 (3.1)		31 (8.9)	
Not male, nor female	2 (0.6)		26 (7.4)	
don't know (yet)	4 (1.2)		9 (2.6)	
Different (e.g. human, no sex)	8 (2.5)		8 (2.3)	
Feels female	3 (0.9)		272 (77.9)	

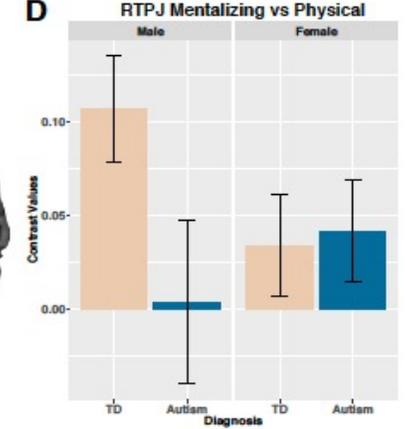
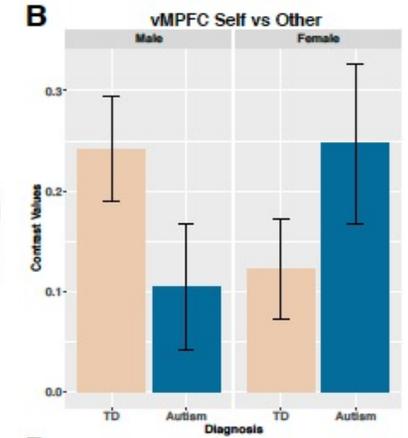
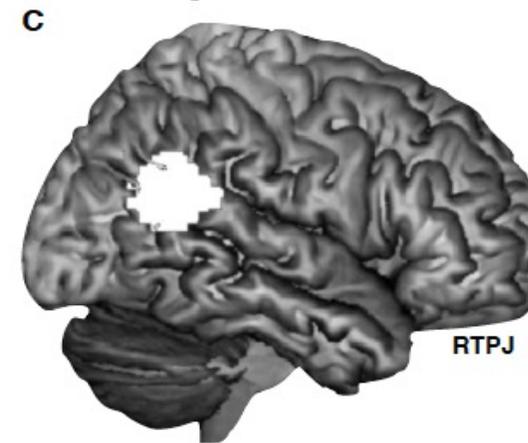
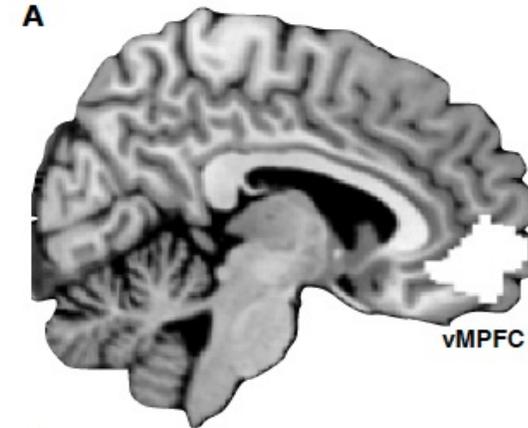
n (%)	Men		Women	
	ASD (n=316)	TD (n=3927)	ASD (n=343)	TD (n=4137)
Feels attracted to				
Men only	16 (5.1)	150 (3.8)	194 (56.6) ^{***a}	3601 (87)
Both men and women	27 (8.5)	184 (4.7)	77 (22.4)	418 (10.1)
Women only	258 (81.6) ^{***a}	3549 (90.4)	21 (6.1)	53 (1.3)
None of these	15 (4.7)	44 (1.1)	51 (14.9)	65 (1.6)
In a relationship	158 (50) ^{**}	2916 (74.3)	162 (47.2) ^{**}	2923 (70.7)
With a man	8 (5.1)	113 (3.9)	151 (93.2)	2861 (97.9)
With a woman	150 (94.9)	2803 (96.1)	11 (6.8) [*]	62 (2.1)
Living together with partner	136 (86.1)	2450 (84)	130 (80.2)	2324 (79.5)

Elevated rates of autism, other neurodevelopmental and psychiatric diagnoses, and autistic traits in transgender and gender-diverse individuals

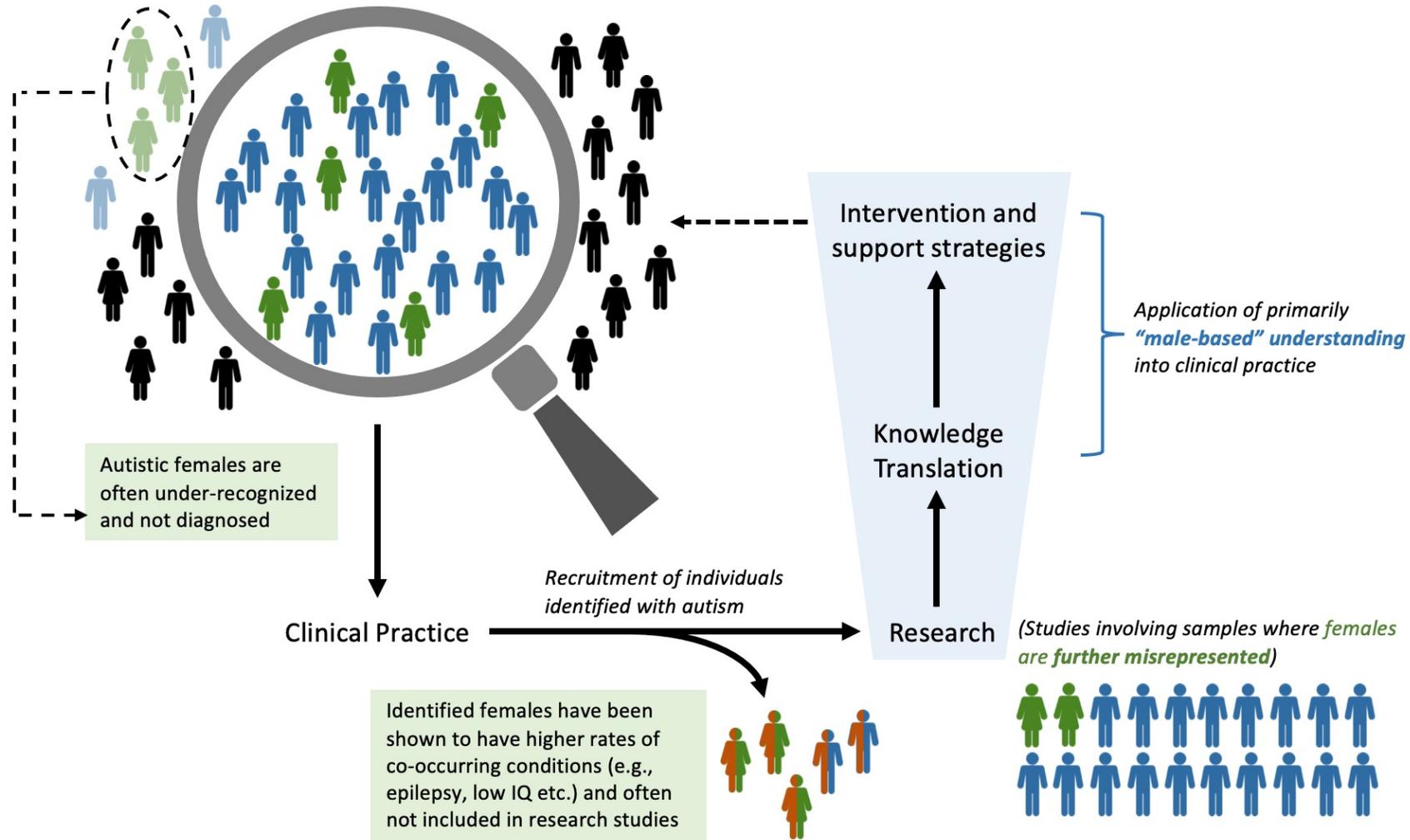
Varun Warriar¹, David M. Greenberg^{1,2}, Elizabeth Weir¹, Clara Buckingham¹, Paula Smith¹, Meng-Chuan Lai^{1,3,4}, Carrie Allison¹ & Simon Baron-Cohen¹



Human beings grow and develop; Environment and contexts matter



Addressing existing knowledge and practical biases; Considering intersectionality



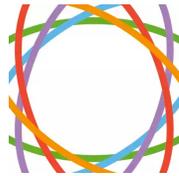
Sincere thanks to everyone who cares about autistic people and contributes to science 🙏



CIHR IRSC



Canadian Institutes of Health Research
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ONTARIO BRAIN INSTITUTE
INSTITUT ONTARIEN DU CERVEAU



POND NETWORK

Province of Ontario Neurodevelopmental Disorders



ORGANIZATION FOR AUTISM RESEARCH

camh

Centre for Addiction and Mental Health



INSAR

International Society for Autism Research



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