Supporting Educators with Research Based Insights

Evdokia Anagnostou, MD
Professor, Department of Pediatrics, University of Toronto
VP research and Director Bloorview Research Institute
Senior Clinician Scientist, Bloorview Research Institute
Dr Stuart D. Sims Chair in Autism

Holland Bloorview
Kids Rehabilitation Hospital

A world of possibility

Transformative Care, Inclusive World:
Holland Bloorview 2030

Why research matters and where to go next

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A world of possibility

Transformative Care, Inclusive World:
Holland Bloorview 2030

Disclosures - Positionality

- Funding:
  - Ontario Brain Institute, Canadian Institutes of health (CIHR), NIH, DoD, HRSA, NCE-NeuroDevNet, Autism Speaks, Brain Canada, Azrieli Foundation, Ontario Ministry of Health, Genome Canada
  - Pharma grant support: ROCHE, Anavex, Maplight, Neuren
  - In kind support: AMO pharma; Simons foundation –CRA
  - Consultation: ROCHe, Quadrant, Ono, Impel, Cell EI, Acadia
- Patents:
  - Anxiety meter Patents #: 14/755/084, United States, Patents #: 2,895,954, Canada

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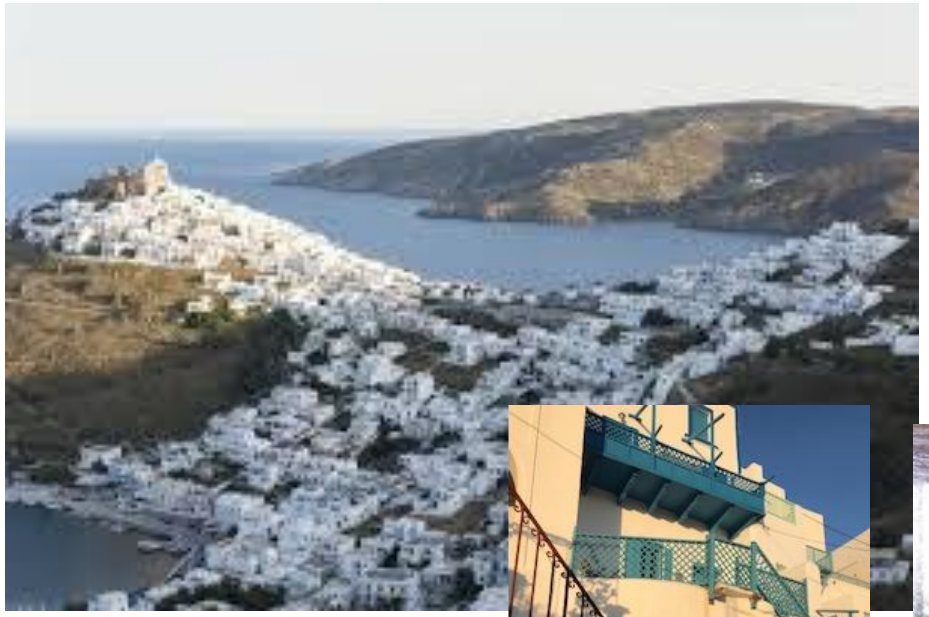
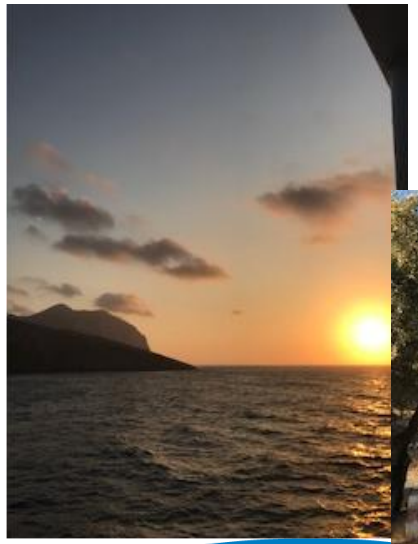




No boundaries

Bloorview
RESEARCH INSTITUTE

McGill | Faculty of Medicine and Health Sciences

UNIVERSITY OF TORONTO

No boundaries

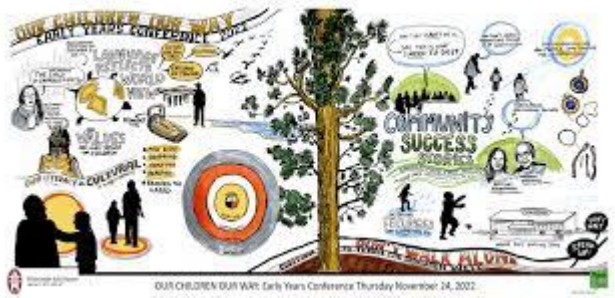
Bloorview
RESEARCH INSTITUTE

Why research

- What is the question, what is the goal:
  - *A good life for every child, youth, adult, community*

- Aristotle
  Eudaimonia (Flourishing)
  meaning, purpose
  action

- Ojibwe
  Mino-bimaadiziwin
- Cree
  Miyo-pimâtisiwin



Balance: It requires tending to all four areas: physical, mental, emotional, and spiritual.

A good life

Influenced by

- Individual characteristics
- Community
- Cultural concepts of “happiness”

Precision Health

Precision health

A proactive and personalized approach to care where interventions, services, and accommodations are informed by each individual's biology and environment, including their genetics, neurobiology, clinical presentation, and sociodemographic context.

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Needs based Care

Needs-based care:

a structured and standardized model, focuses on identifying and addressing individual needs of

- patients, clients
- Health workforce planning (Murphy et al 2017)

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Why diagnoses?

Why do we use diagnostic labels?

- Define the nature of difference
- Explanatory power
- Identify needs, current and future to guide
  - Future expectations / planning / anticipatory guidance
  - Treatment / Intervention
- Care System organization
- Identity implications

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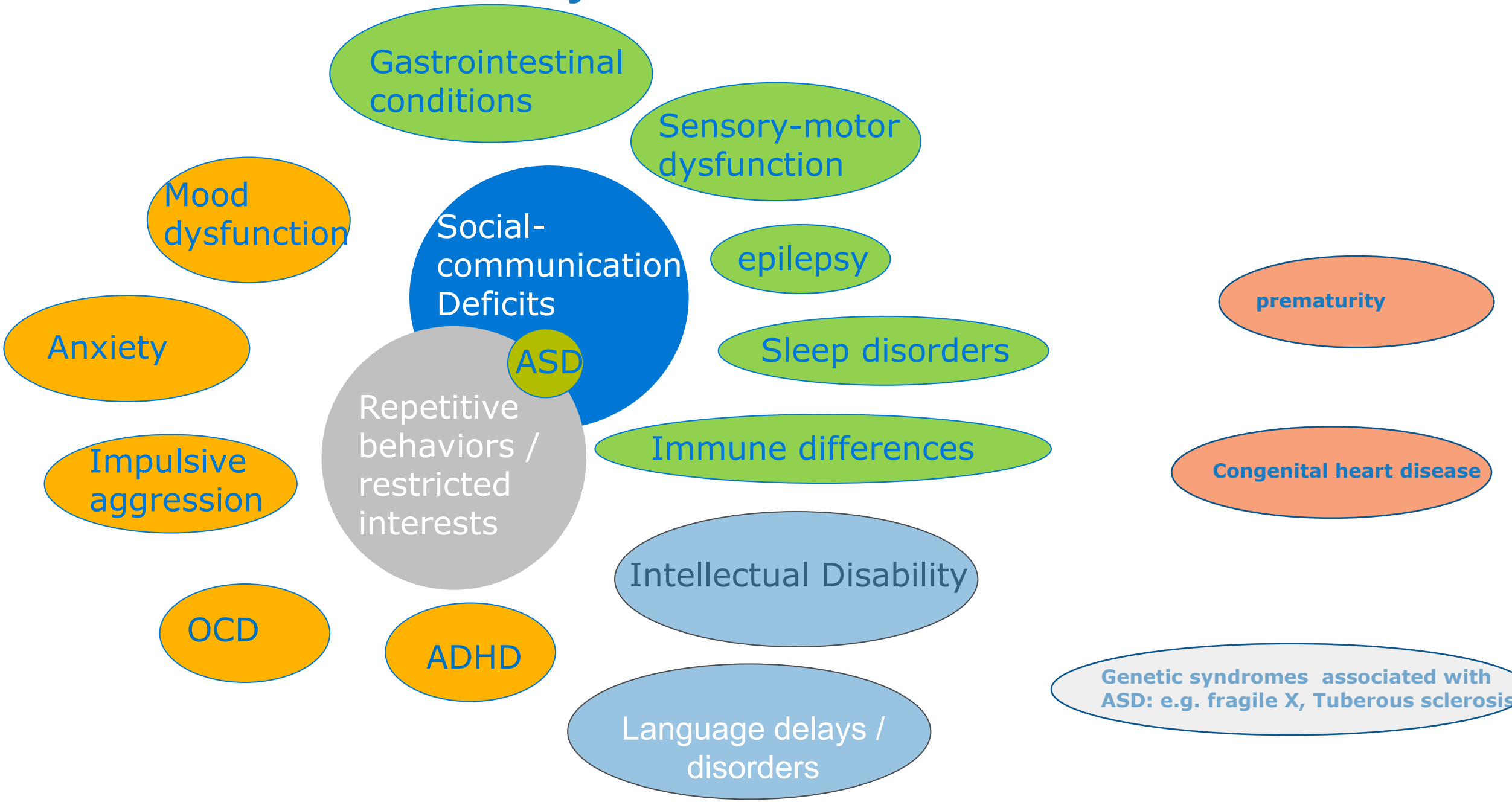
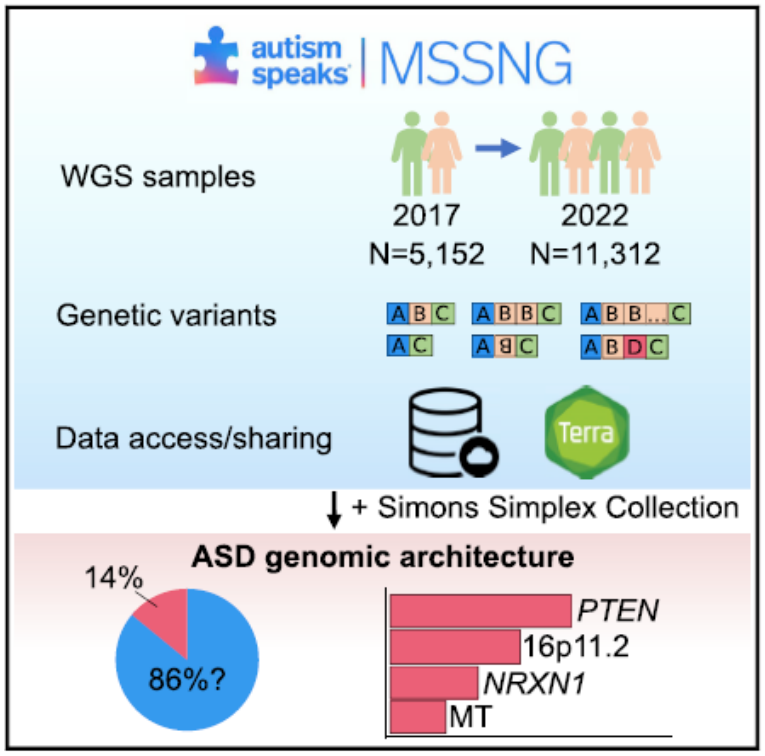
Why precision health in neurodevelopmental conditions

When it comes to neurodivergence, our diagnosis labels don’t always align with distinct differences in behaviour, neurobiology, or patient priorities.

Diversity in Clinical Presentations



Diversity in genomic architecture



Genomic architecture of autism from comprehensive whole-genome sequence annotation

Cell *185*, 4409–4427, November 10, 2022

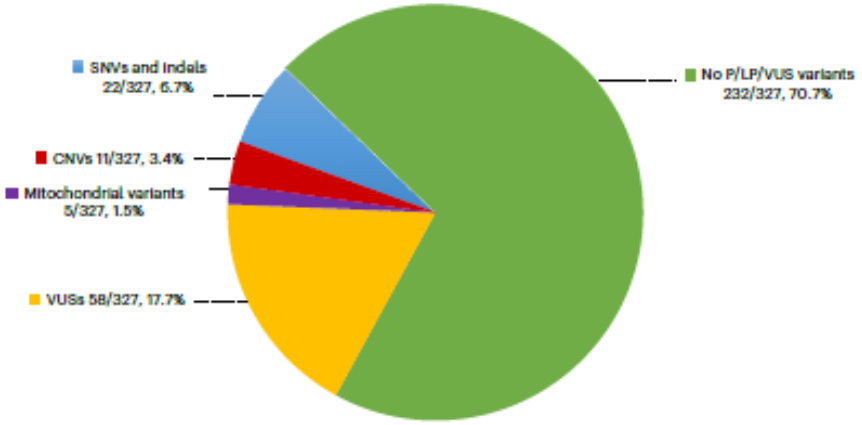
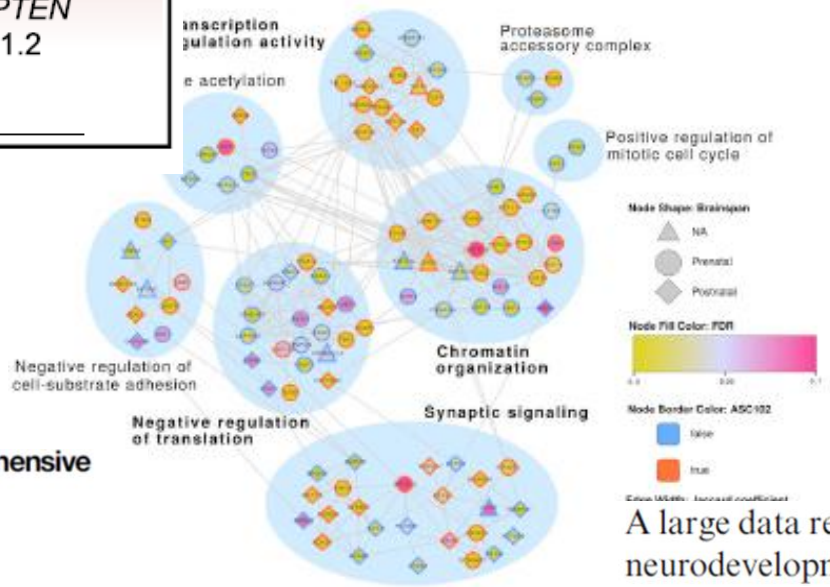


Fig. 1 | The number (%) of cases with subtypes of variants of potential clinical relevance in CP. Numbers and percentages of cases with each class of variants (P/LP/VUS) identified in the CP cohort.

Comprehensive whole-genome sequence analyses provide insights into the genomic architecture of cerebral palsy: Fehlings et al, Nature Genetics, 2024

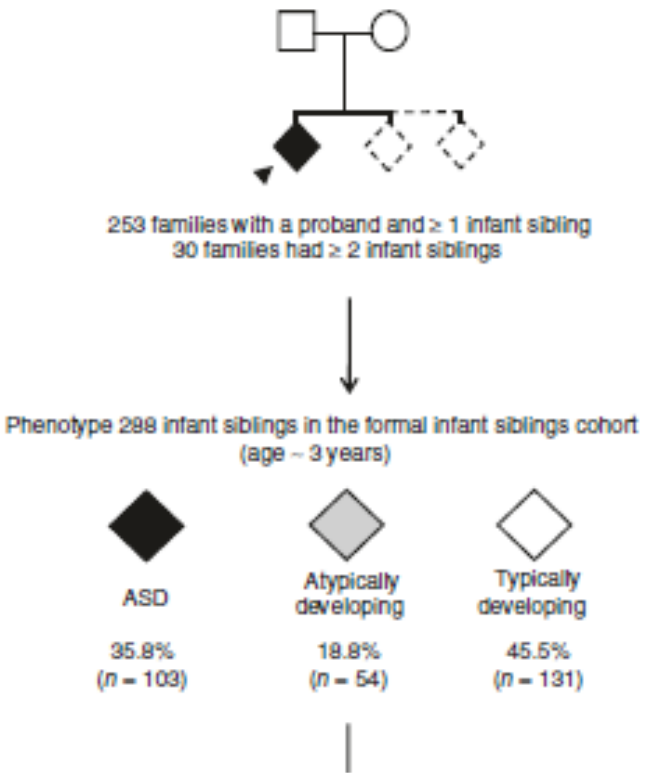


No genomic variants have been found to date to be NDD specific

A large data resource of genomic copy number variation across neurodevelopmental disorders

NPJ Genom Med. 2019; 4: 26.

Diversity in genomic architecture



PPV for ASD: 46%

PPV for NDD: 85%

OPEN

Predictive impact of rare genomic copy number variations in siblings of individuals with autism spectrum disorders

L. D'Abate[1,2], S. Walker[1], R.K.C. Yuen[1,2], K. Tammimies[1,3,4], J.A. Buchanan[1], R.W. Davies[1], B. Thiruvahindrapuram[1], J. Wei[1], J. Brian[5], S.E. Bryson[6], K. Dobkins[7], J. Howe[1], R. Landa[8], J. Leef[5], D. Messinger[9], S. Ozonoff[10], I.M. Smith[6], W.L. Stone[11], Z.E. Warren[12], G. Young[10], L. Zwaigenbaum[13] & S.W. Scherer[1,2,14*]

POND NETWORK

Province of Ontario Neurodevelopmental Disorders

Jason Lerch, PhD
University of Oxford

Holland Bloorview Kids Rehabilitation Hospital

University of Oxford

LAWSON HEALTH RESEARCH INSTITUTE

Western

ONTARIO BRAIN INSTITUTE

Master Observation Trial

>10 years

University of Toronto

McMaster University

Queen's University

SickKids

King's College London

Université de Montréal

IC/ES

Genomics

Behaviour

Cognition

Epigenetics

Imaging

Immune

Endocrine

Clinical Trials

IPS Cells

Mouse Models

AI

Biostatistics

Knowledge Translation

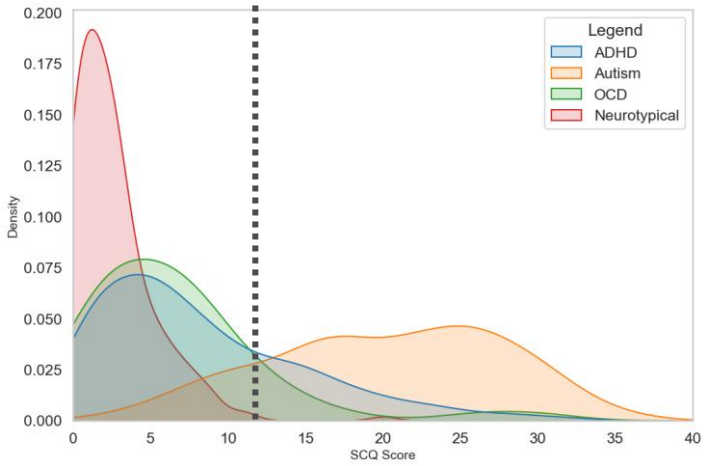
>30 Investigators

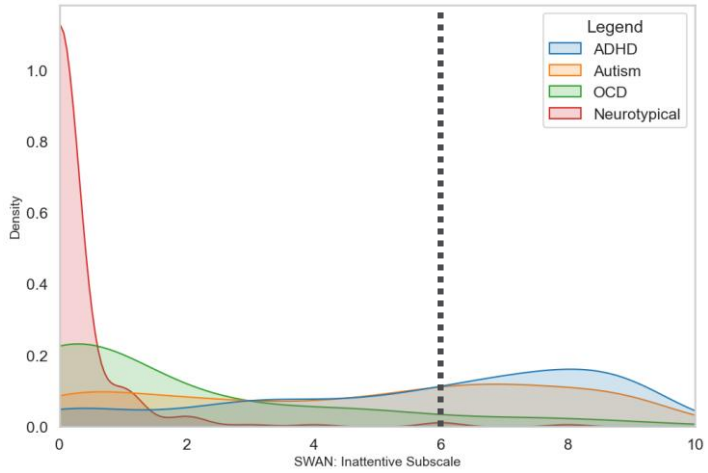
Patient advisory Committee

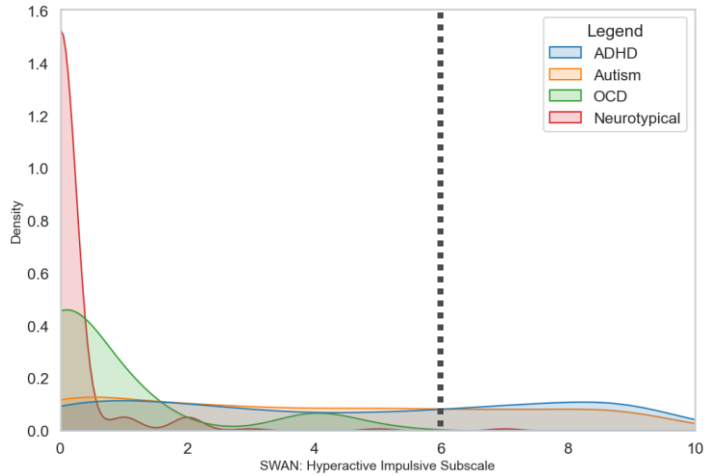
Youth advisory Committee

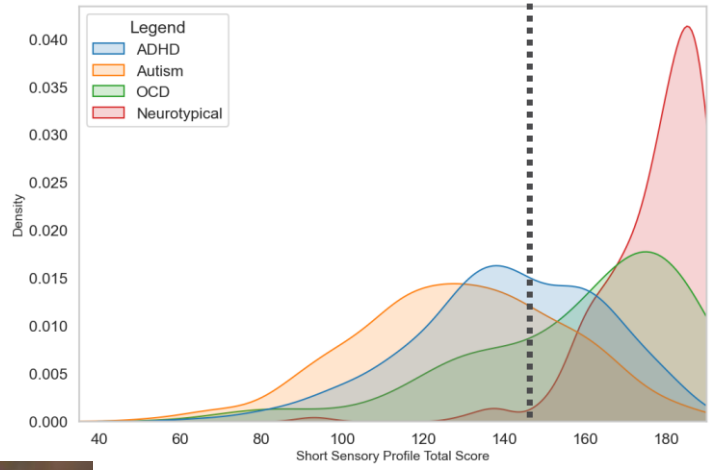
https://pond-network.ca/

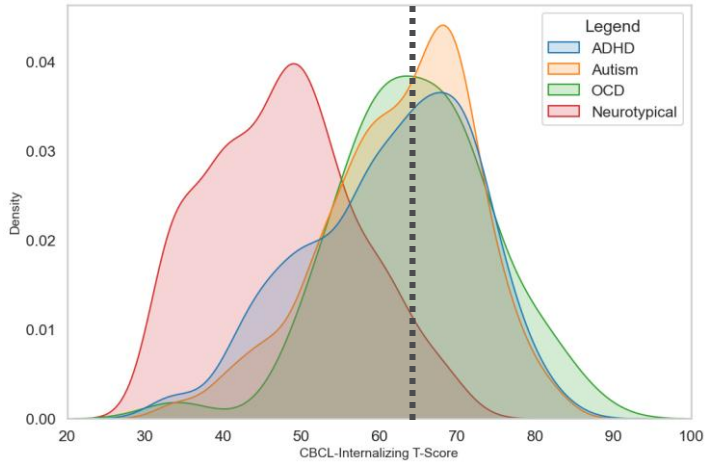
~4000 participants

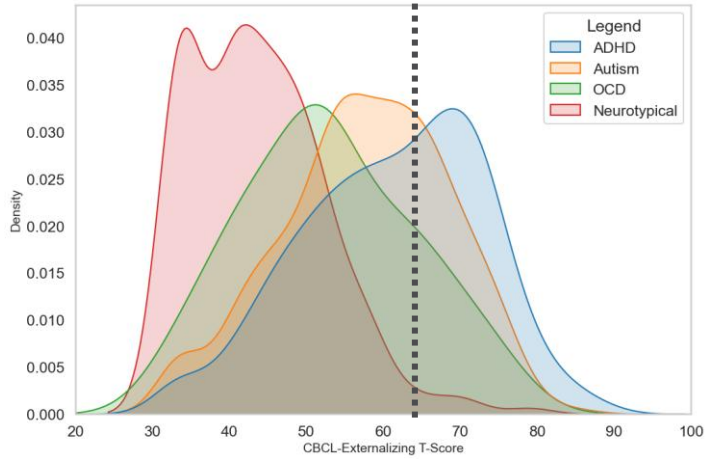












Azadeh Kushki, PhD

N_autism = 1535; N_ADHD=1287; N_OCD=296; N_neurotypical = 395

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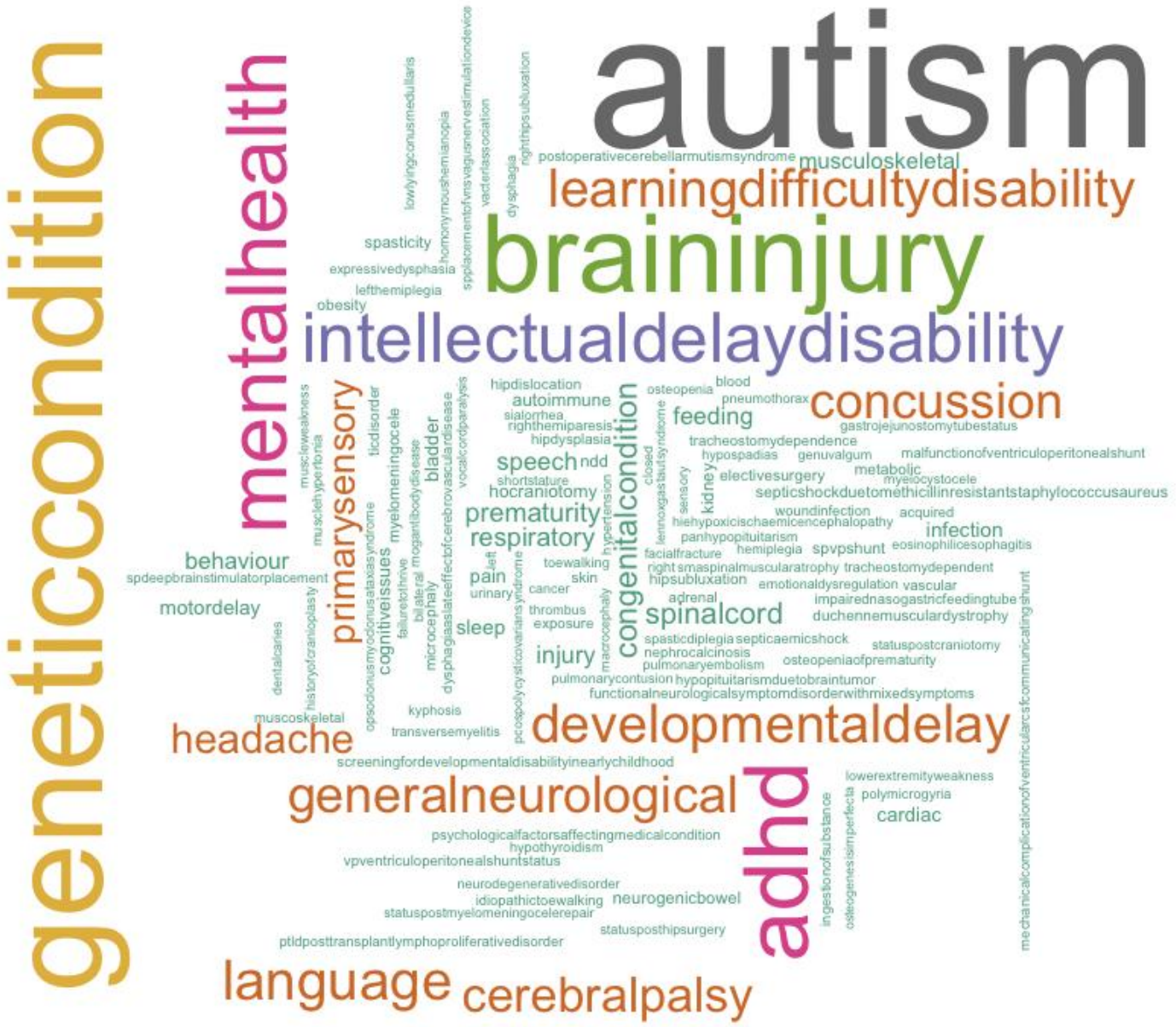
Most frequently entered:

Autism (32%)
Genetic condition (19%)
ADHD (14%)
Brain injury (12%)
Intellectual disability/delay (10%)
Mental health (10%)

2.4 Average number of diagnoses

24 Maximum number of diagnoses

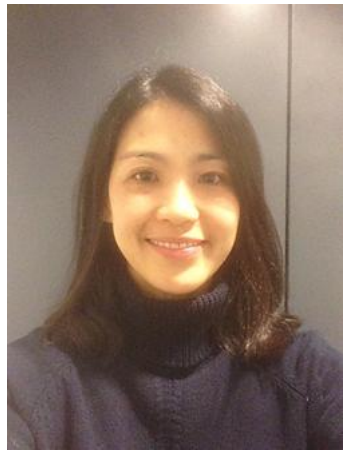


Jason Lerch, PHD
University of Oxford

Margot Taylor, PHD
University of Toronto

Azadeh Kushki, PHD
University of Toronto

Marlee VandeWouw
PHD candidate
University of Toronto



Eunjung Choi, PHD
Western University

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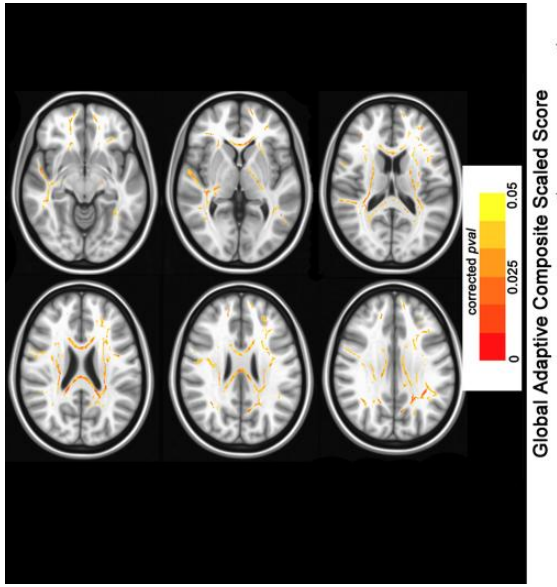
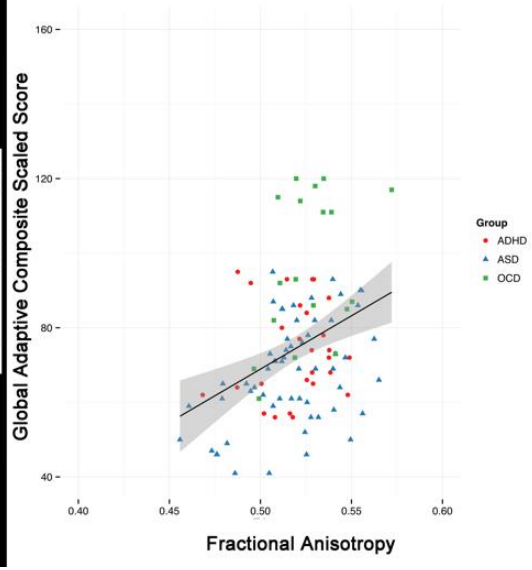
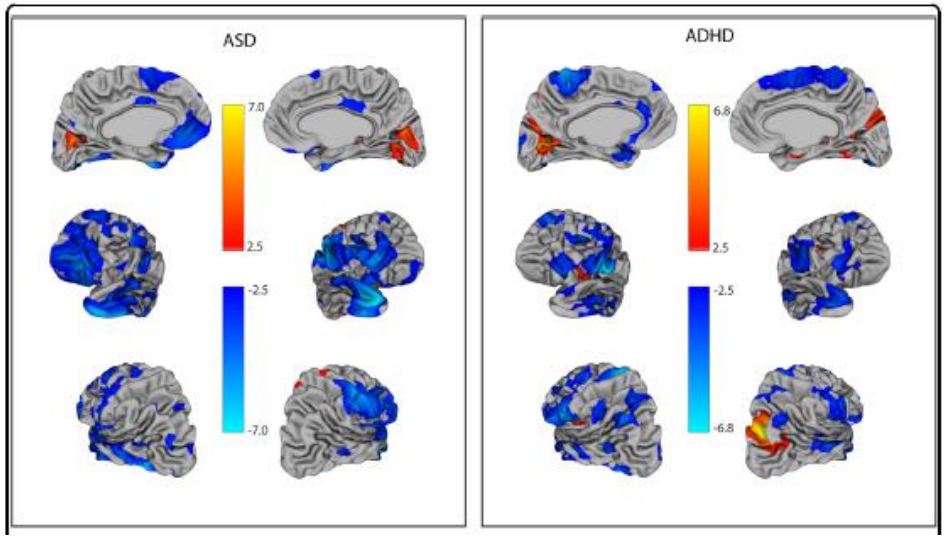
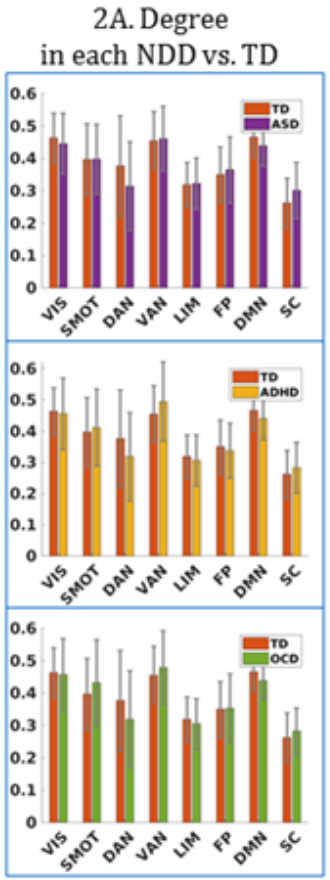
Neuroimaging core

Brain imaging:
opportunity to explore unique signatures?









A Diffusion Tensor Imaging Study in Children With ADHD, Autism Spectrum Disorder, OCD, and Matched Controls: Distinct and Non-Distinct White Matter Disruption and Dimensional Brain-Behavior Relationships

Stephanie H. Ameis, M.D., M.Sc., Jason P. Lerch, Ph.D., Margot J. Taylor, Ph.D., Wayne Lee, M.Sc., Joseph D. Viviano, M.Sc., Jon Pipitone, M.Sc., Arash Nazeri, M.D., Paul E. Croarkin, D.O., M.Sc., Aristotle N. Voineskos, M.D., Ph.D., Meng-Chuan Lai, M.D., Ph.D., Jennifer Crosbie, Ph.D., Jessica Brian, Ph.D., Noam Soreni, M.D., Russell Schachar, M.D., Peter Szatmari, M.D., Paul D. Arnold, M.D., Ph.D., Evdokia Anagnostou, M.D.

AJP in Advance (doi: 10.1176/appi.ajp.2016.15111435)

Translational Psychiatry

ARTICLE Open Access

Structural neuroimaging correlates of social deficits are similar in autism spectrum disorder and attention-deficit/hyperactivity disorder: analysis from the POND Network

NeuroImage: Clinical

Beyond diagnosis: Cross-diagnostic features in canonical resting-state networks in children with neurodevelopmental disorders

Eun Jung Choi, Marlee M. Vandewouw, Margot J. Taylor, Paul D. Arnold, Jessica Brian, Jennifer Crosbie, Elizabeth Kelley, Meng-Chuan Lai, Xudong Liu, Russell J. Schachar, Jason P. Lerch, Evdokia Anagnostou

Mouse models of autism

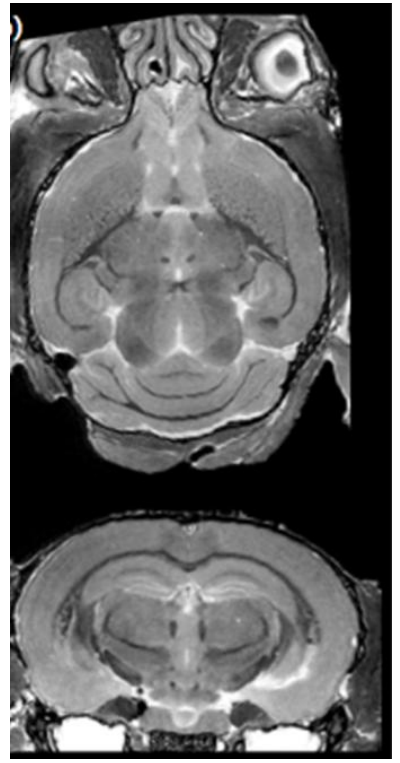
Of mice and men

Start with human genetics

Knock out or modify identified genes

Phenotype for brain and behaviour

>100 Genotypes



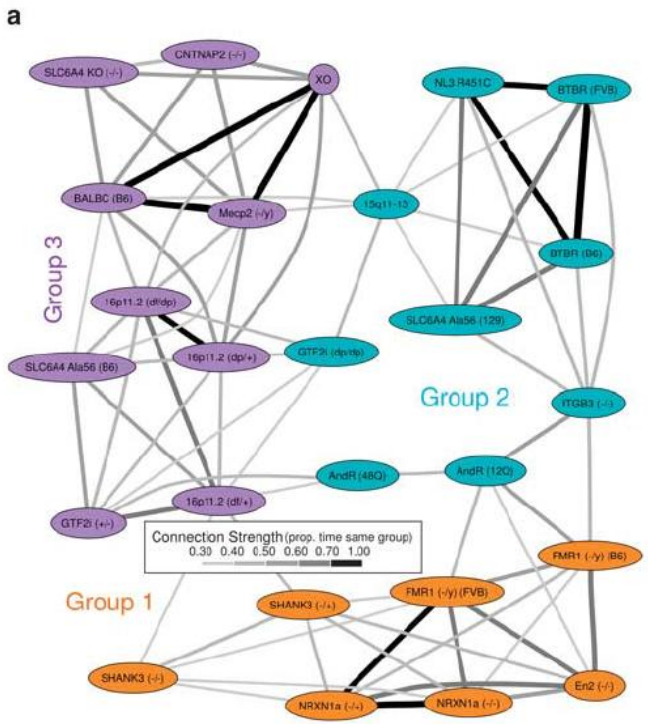
Molecular Psychiatry (2015) 20, 118–125

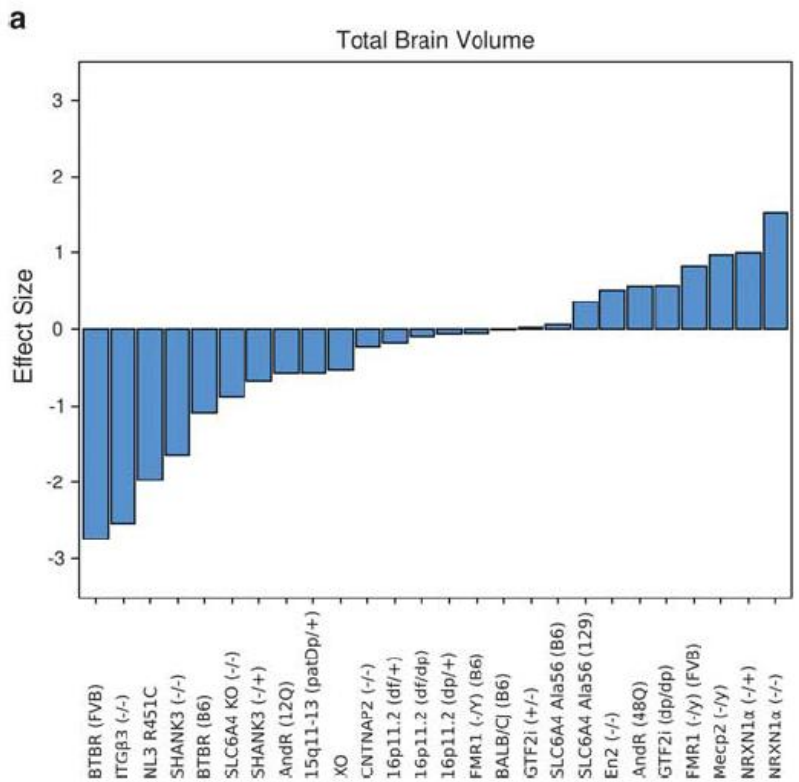
www.nature.com/mp

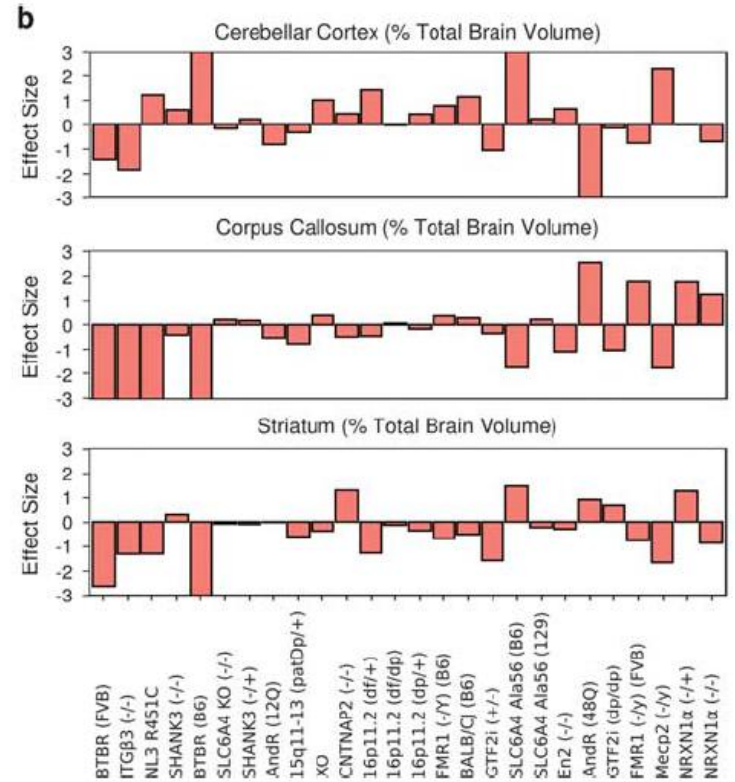
ORIGINAL ARTICLE

Clustering autism: using neuroanatomical differences in 26 mouse models to gain insight into the heterogeneity

J Ellegood[1], E Anagnostou[2], BA Babineau[3], JN Crawley[3,4], L Lin[5], M Genestine[5], E DiCicco-Bloom[5], JKY Lai[6], JA Foster[6], O Peñagarikano[7], DH Geschwind[7], LK Pacey[8], DR Hampson[8], CL Laliberté[1], AA Mills[9], E Tam[10], LR Osborne[10], M Kouser[11], F Espinosa-Becerra[11], Z Xuan[11], CM Powell[11], A Raznahan[12], DM Robins[13], N Nakai[14], J Nakatani[14], T Takumi[14], MC van Eede[1], TM Kerr[15], C Muller[15], RD Blakely[15], J Veenstra-VanderWeele[15], RM Henkelman[1,16] and JP Lerch[1,16]







Several clustering studies have shown misalignment between brain similarity and diagnostic labels.

ARTICLE Open Access

Examining overlap and homogeneity in ASD, ADHD, and OCD: a data-driven, diagnosis-agnostic approach

Azadeh Kushki[1,2], Evdokia Anagnostou[1,3], Christopher Hammill[4], Pierre Duez[5], Jessica Brian[1,3], Alana Iaboni[1], Russell Schachar[6,7], Jennifer Crosbie[6,7], Paul Arnold[8] and Jason P. Lerch[4,9,10]

ORIGINAL ARTICLE

Cross-Diagnosis Structural Correlates of Autistic-Like Social Communication Differences

Azadeh Kushki[1,2], Robyn E. Cardy[1,2], Sina Panahandeh[1,2], Mahan Malihi[1,2], Christopher Hammill[3], Jessica Brian[1,4], Alana Iaboni[1], Margot J. Taylor[5,6], Russell Schachar[7,8], Jennifer Crosbie[7,8], Paul Arnold[9], Elizabeth Kelley[10], Muhammad Ayub[11], Robert Nicolson[12], Stelios Georgiades[13], Jason P. Lerch[3,14,15] and Evdokia Anagnostou[1,4]

Investigating heterogeneity across autism, ADHD, and typical development using measures of cortical thickness, surface area, cortical/subcortical volume, and structural covariance

Younes Sadat-Nejad[1,2], Marlee M. Vandewouw[1,2], R. Cardy[1], J. Lerch[3,4,5], M. J. Taylor[6,7], A. Iaboni[1], C. Hammill[3], B. Syed[3], J. A. Brian[1,8], E. Kelley[9,10,11], M. Ayub[11], J. Crosbie[12,13], R. Schachar[12,13], S. Georgiades[14], R. Nicolson[15], E. Anagnostou[1,8] and A. Kushki[1,2*]

JAMA Network | Open

Original Investigation | Imaging

Identifying Replicable Subgroups in Neurodevelopmental Conditions Using Resting-State Functional Magnetic Resonance Imaging Data

Marlee M. Vandewouw, MASc; Jessica Brian, PhD; Jennifer Crosbie, PhD; Russell J. Schachar, MD; Alana Iaboni, PhD; Stelios Georgiades, PhD; Robert Nicolson, MD; Elizabeth Kelley, PhD; Muhammad Ayub, MD; Jessica Jones, MD; Margot J. Taylor, PhD; Jason P. Lerch, PhD; Evdokia Anagnostou, MD; Azadeh Kushki, PhD

Ho
Kids

JAMA Network | Open

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Figure 2. Clustering Results

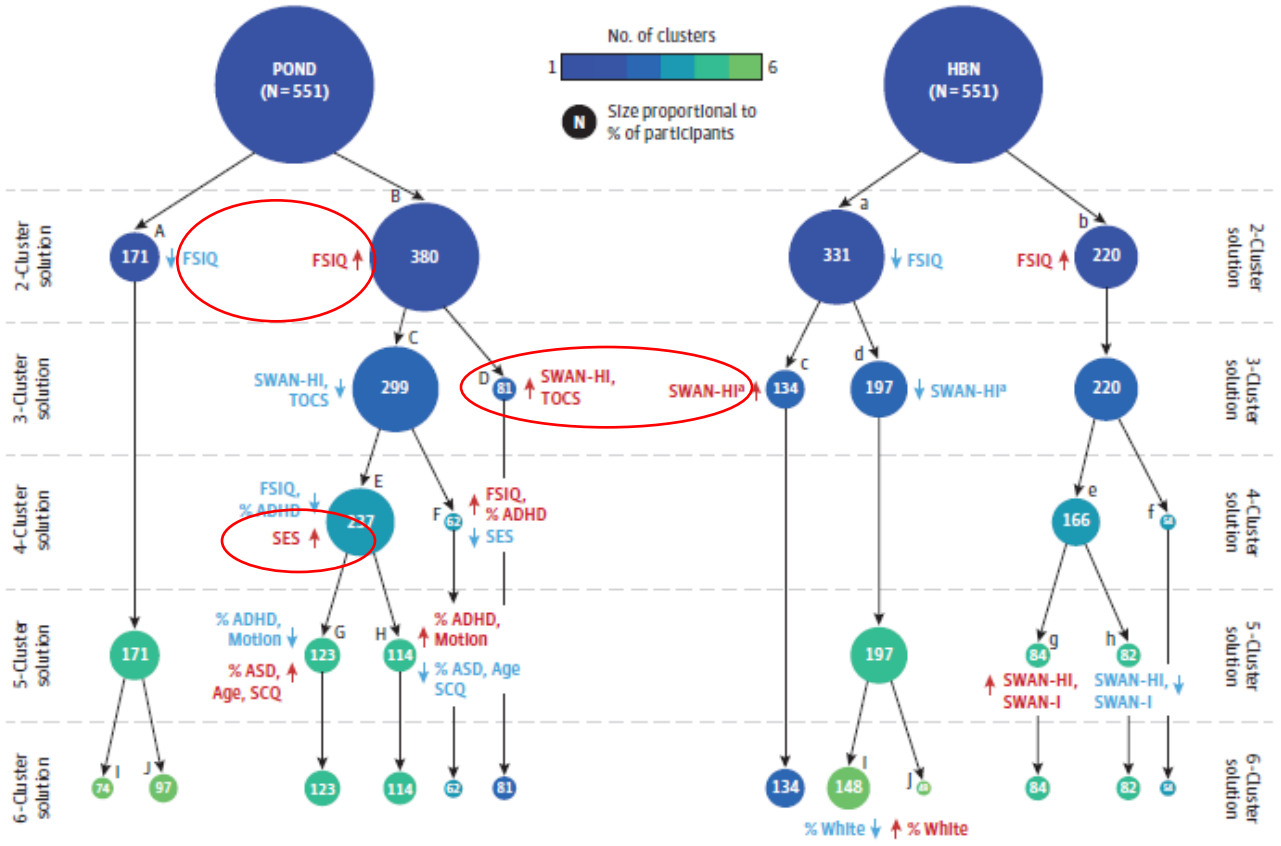
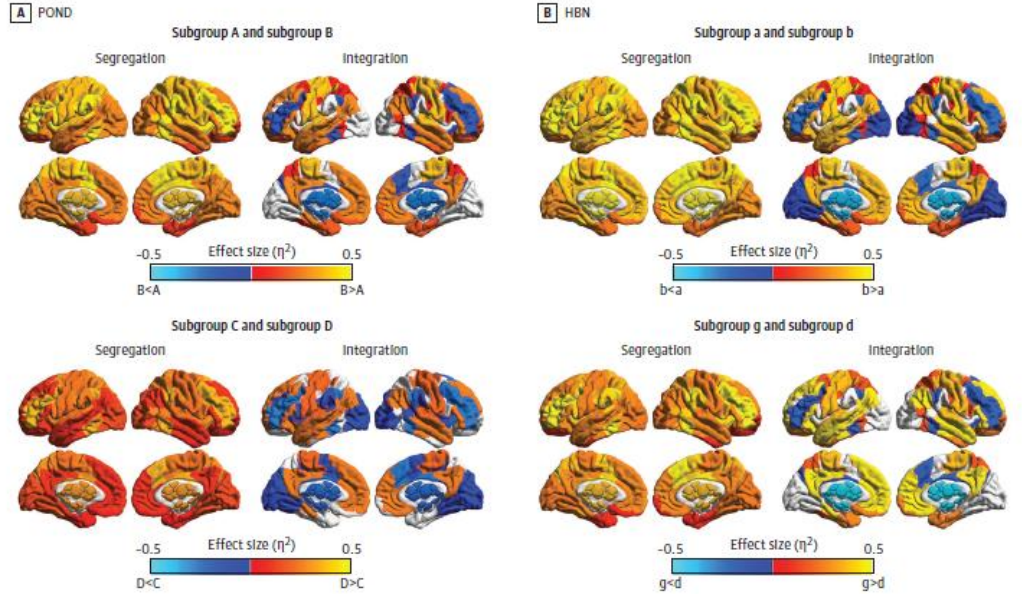


Figure 3. Between-Subgroup Differences in Brain Measures



POND
HBN

How do labels align with priorities

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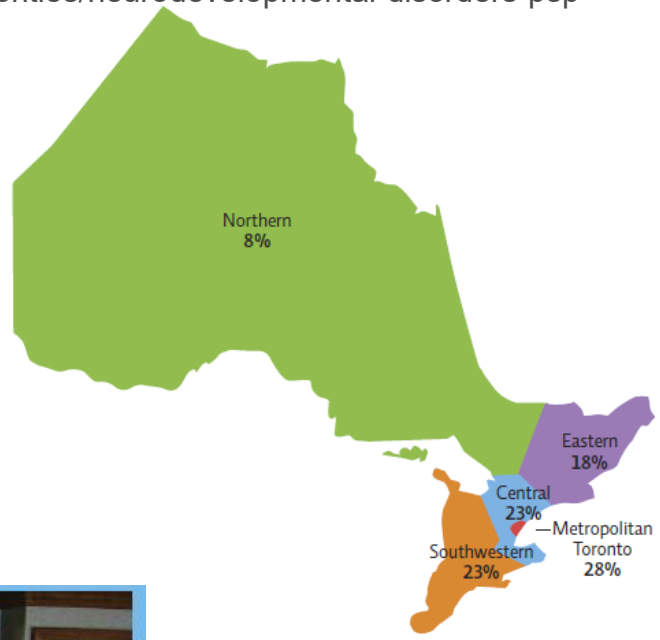
Kids Rehabilitation Hospital

Heterogeneity in lived experience

- James Lind Alliance Canadian Priorities

https://braininstitute.ca/resources/setting-research-priorities/neurodevelopmental-disorders-psp



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The Top 10

The Top 10 research priorities from the neurodevelopmental disorder community are:

1. What are the most effective treatment options/plans (e.g., timing, frequency, duration, type, intensity or dosage) for individuals with neurodevelopmental disorders for both short and long-term benefits?
2. How can system navigation be organized in a manner that enables coordinated services and supports across the lifespan for individuals with neurodevelopmental disorders and their families??
3. Which biological treatments (including medications, gene therapy, stem cell therapy, etc.) are effective for neurodevelopmental disorders and associated symptoms?
4. Which child and family-centered interventions or approaches promote optimal individual and family functioning?
5. Which interventions best help individuals with neurodevelopmental disorders develop emotional and behavioural regulation (including increasing impulse control and reducing compulsive behaviour)?
6. Which resources are needed to more effectively address the health, social and emotional needs of families or caregivers of individuals with neurodevelopmental disorders?
7. How can treatment decisions for individuals with neurodevelopmental disorders be more precise (i.e., based on the diagnosis, age, functional need of the individual)?
8. Which are the most effective pharmacological and non-pharmacological treatments for aggressive and self-injurious behaviour in individuals with neurodevelopmental disorders?
9. Which are the most effective pharmacological and non-pharmacological intervention(s) to reduce anxiety in individuals with neurodevelopmental disorders?
10. Which interventions are most effective to help individuals with neurodevelopmental disorders improve their social skills and develop and maintain social relationships?

What predicts quality of life?

scientific reports

Check for updates

OPEN

Predictors of health-related quality of life for children with neurodevelopmental conditions

Maryam Mahjoob[1], Robyn Cardy[2], Melanie Penner[2], Evdokia Anagnostou[2], Brendan F. Andrade[3], Jennifer Crosbie[4], Elizabeth Kelley[5], Muhammad Ayub[6], Muhammad Ayub[5], Jessica Brian[2], Alana Iaboni[2], Russell Schachar[4], Stelios Georgiades[7], Rob Nicolson[8], Jessica Jones[6] & Azadeh Kushki[2]✉

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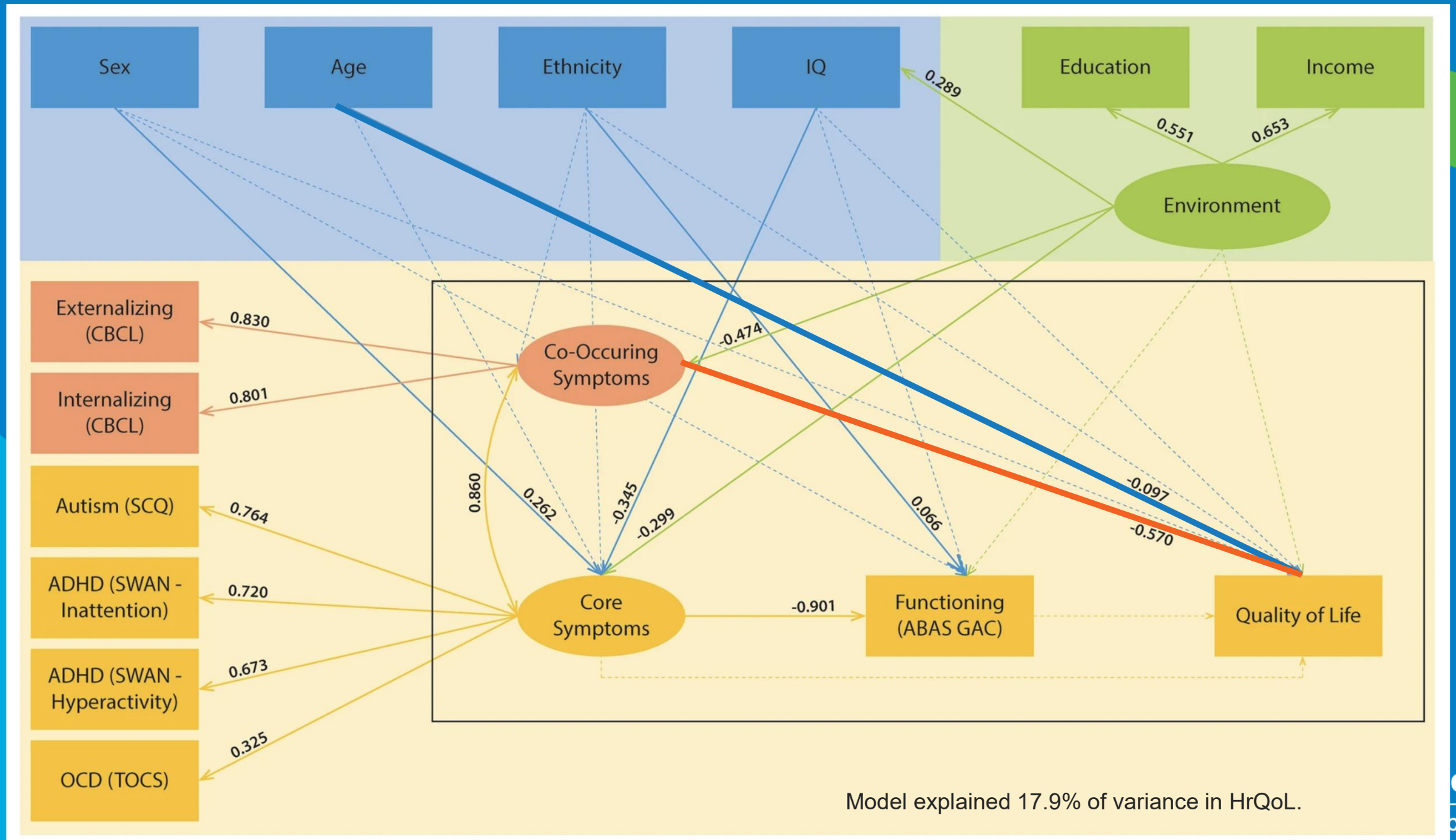
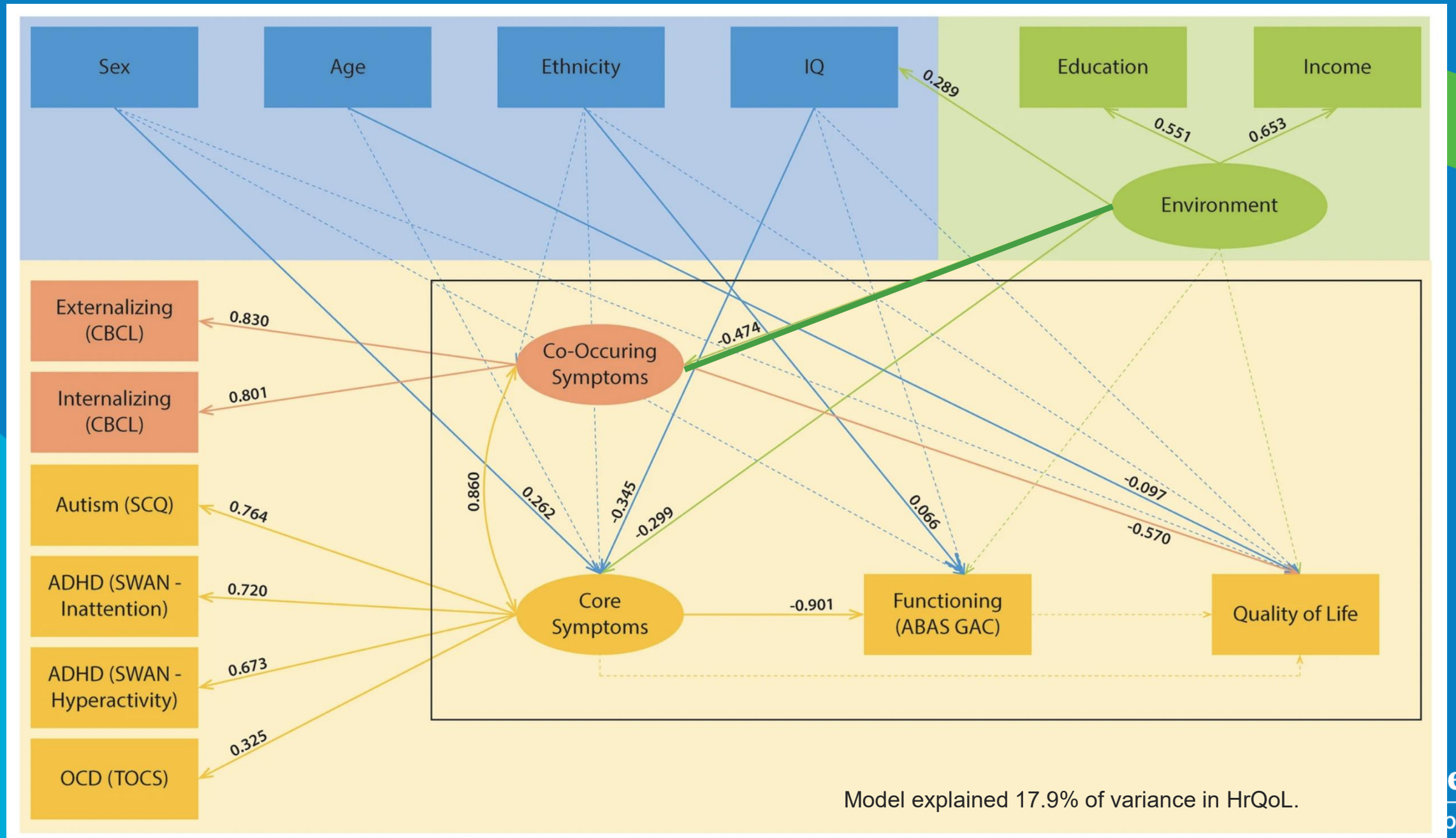
NSERC CRSNG

CIHR IRSC



Model explained 17.9% of variance in HrQoL.



Model explained 17.9% of variance in HrQoL.

Why do we use diagnostic labels?

- Define the nature of difference - poor
- Explanatory power – potential but limited
- Identify needs, current and future to guide – some but inadequate
  - Future expectations / planning / anticipatory guidance
  - Treatment / Intervention
- Health System organization
- Identity implications

Can we do better?

Holland Bloorview
Kids Rehabilitation Hospital

What predicts mental health outcomes?

Translational Psychiatry

www.nature.com/tp

ARTICLE OPEN

Check for updates

Using deep learning to predict internalizing problems from brain structure in youth

Marlee M. Vandewouw[1,2✉], Bilal Syed[3], Noah Barnett[4], Alfredo Arias[5], Elizabeth Kelley[6,7], Jessica Jones[6,7], Muhammad Ayub[6,8], Alana Iaboni[1], Paul D. Arnold[9,10], Jennifer Crosbie[11,12], Russell J. Schachar[12,13], Margot J. Taylor[11,14,15,16], Jason P. Lerch[11,17,18], Evdokia Anagnostou[1,11] and Azadeh Kushki[1,2]

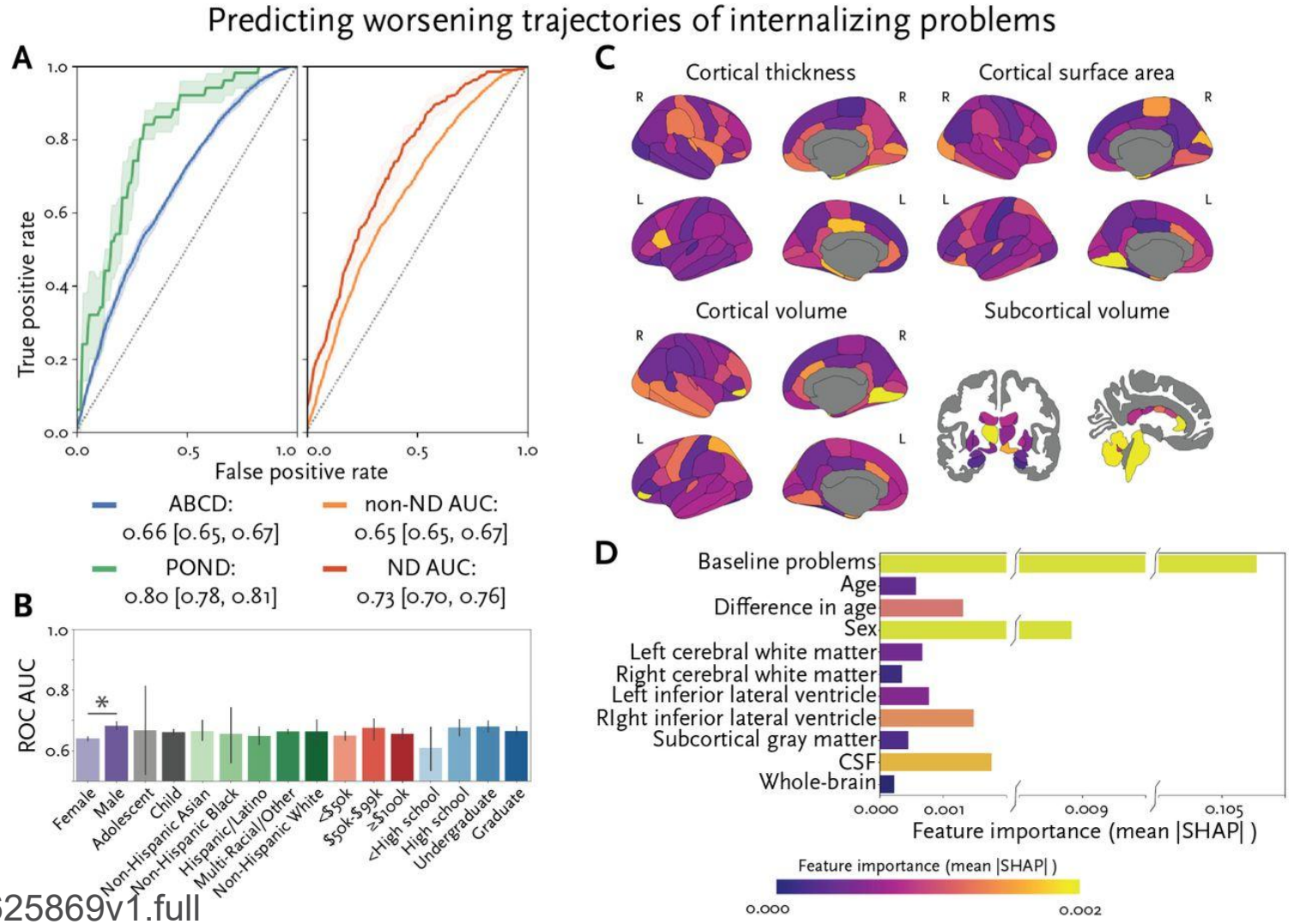
POND NETWORK
Province of Ontario Neurodevelopmental Disorders

NSERC CRSNG

CIHR IRSC

Predicting long term trajectories

- Datasets
  - ABCD (release 5.1)
  - HBN (Release 10)
  - HCP-D (Release 2)
  - POND
- Total sample: 14,523



https://www.biorxiv.org/content/10.1101/2024.11.28.625869v1.full

Getting closer to care:
AI + real world data

Transformative Care,
Inclusive World:
Holland Bloorview 2030

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Can we predict responses to pharmacological interventions?

medRxiv

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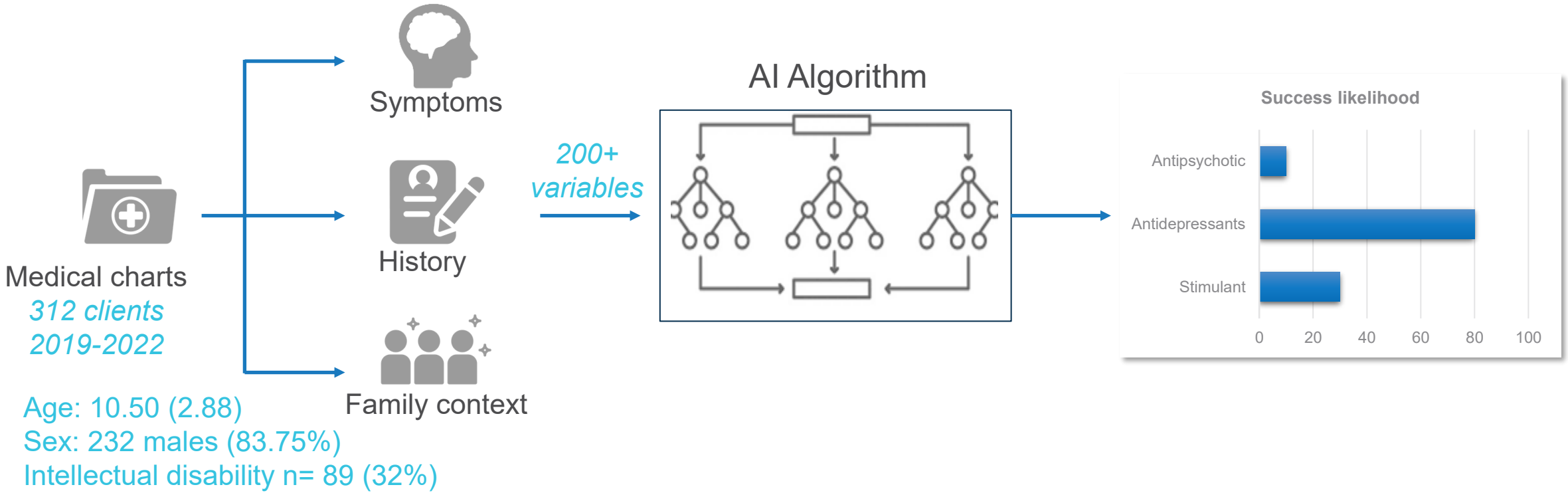
A precision health approach to medication management in neurodevelopmental conditions: a model development and validation study using four international cohorts

Marlee M. Vandewouw, Kamran Niroomand, Harshit Bokadia, Sophia Lenz, Jesiqua Rapley, Alfredo Arias, Jennifer Crosbie, Elisabetta Trinari, Elizabeth Kelley, Robert Nicolson, Russell J. Schachar, Paul D. Arnold, Alana Iaboni, Jason P. Lerch, Melanie Penner, Danielle Baribeau, Evdokia Anagnostou, Azadeh Kushki

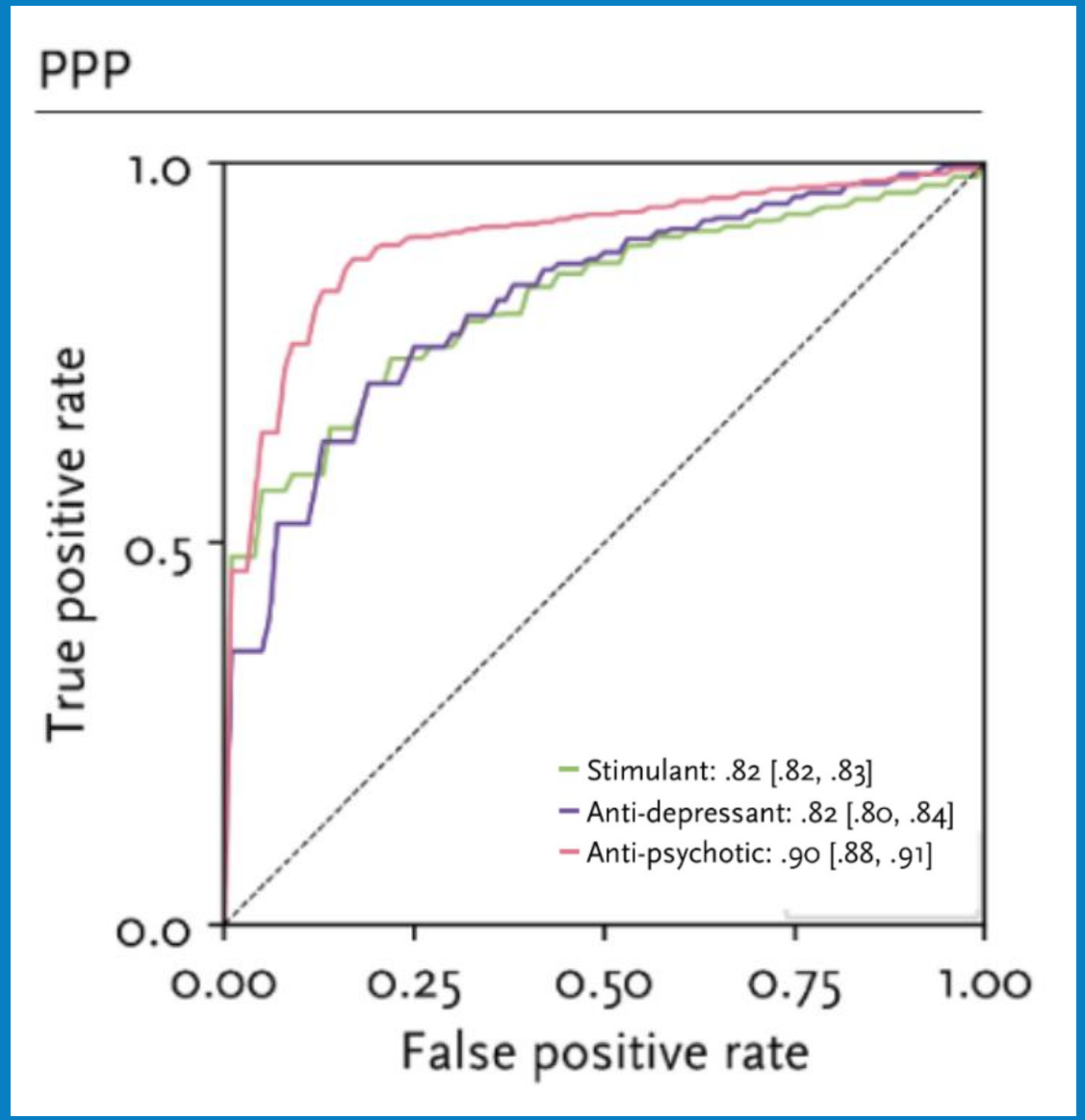
NSERC CRSNG

CIHR IRSC

Electronic Medical Records



Age: 10.50 (2.88)
Sex: 232 males (83.75%)
Intellectual disability n= 89 (32%)



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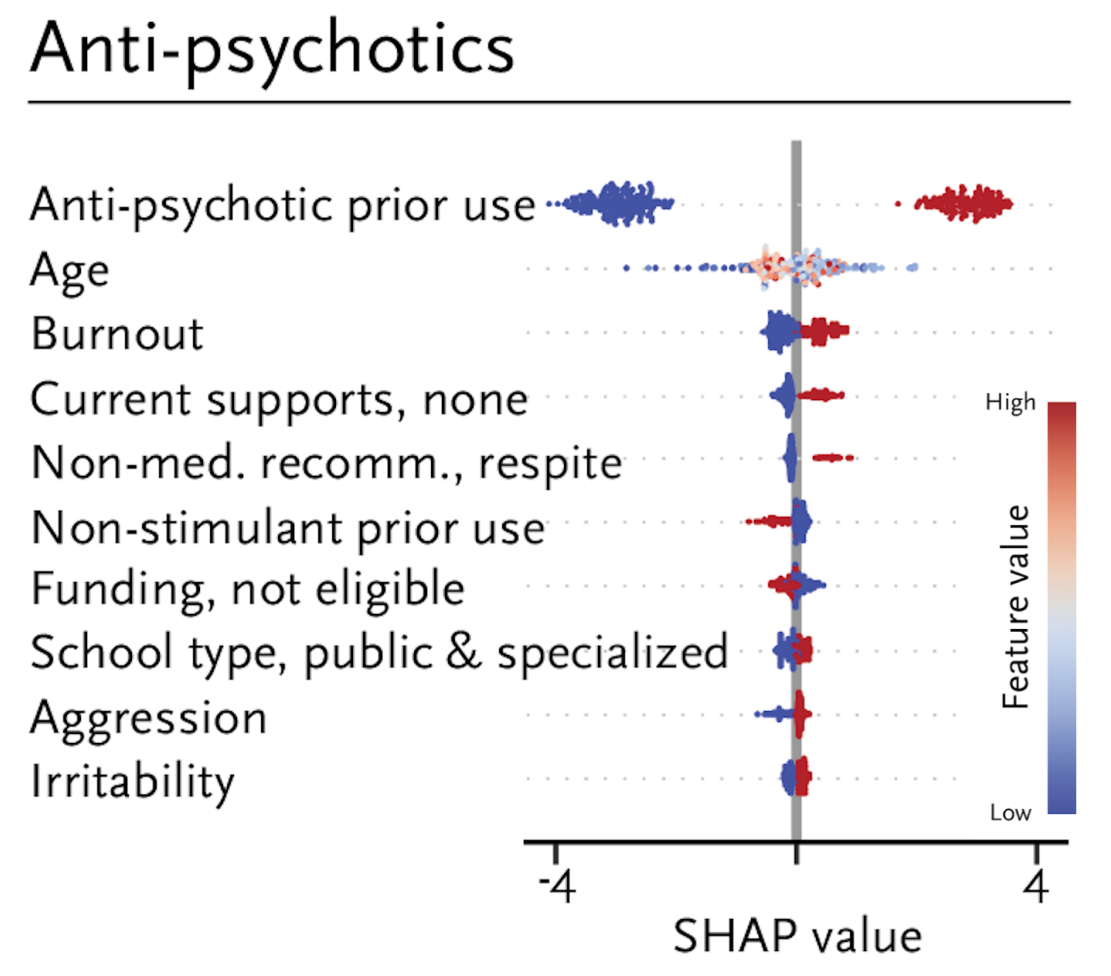
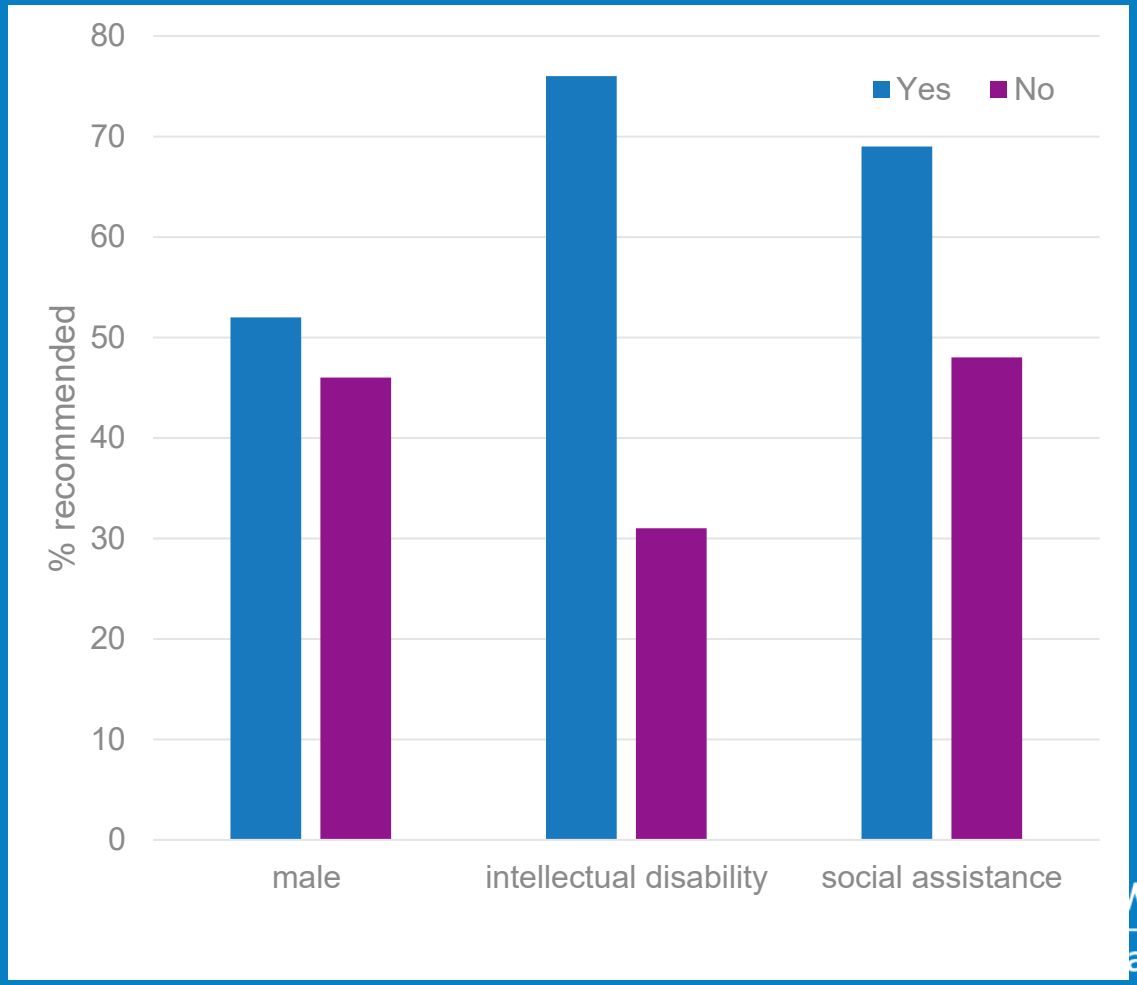
Who is Disadvantaged?





Medium

Search

The Ethics of Fairness in AI and What I Learned Through Self-Reflection

Eric Wan Follow 5 min read · Apr 7, 2025

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“Fairness isn’t real until someone chooses it.

… Some people assume machines are neutral. That technology is cold and clean and free from bias.

But the more you look at AI, the more you realize, it’s only as fair as the people who train it.

… Bias in, bias out.”

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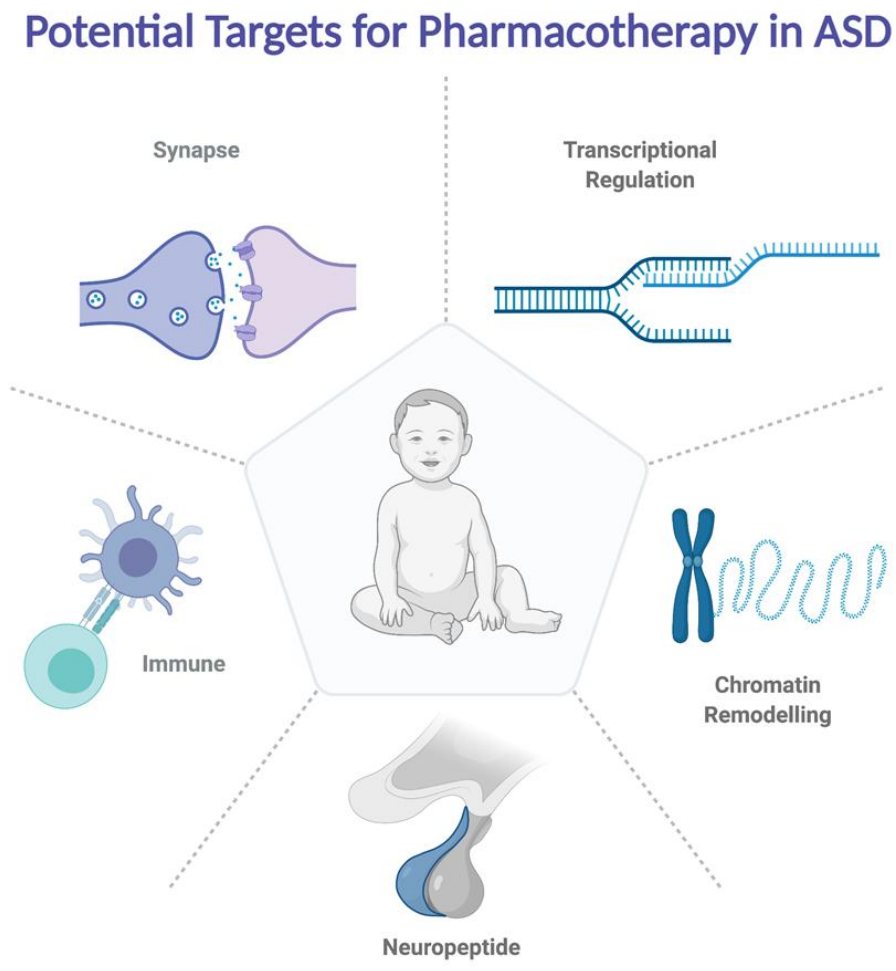
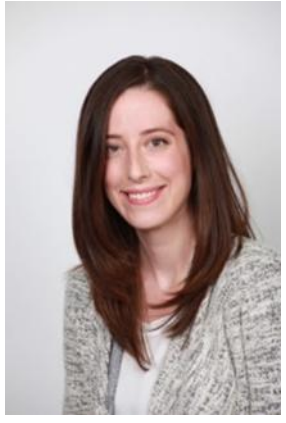
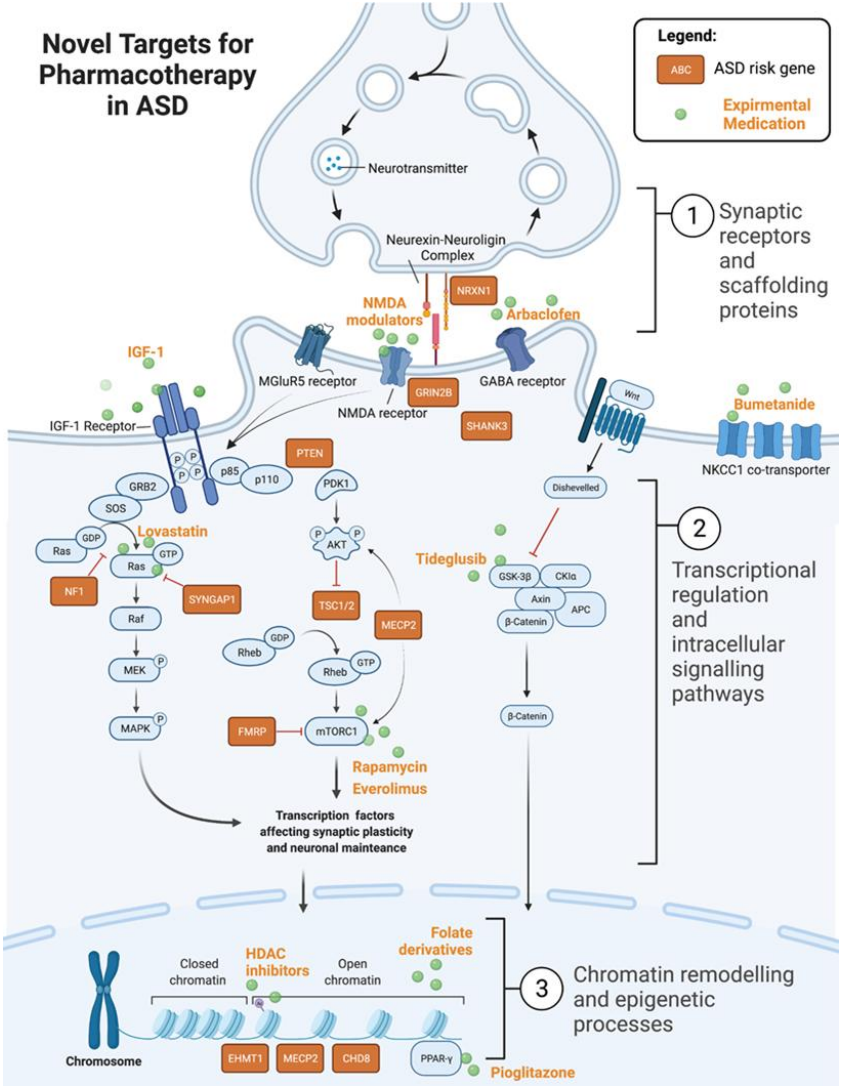
Precision therapies

Baribeau et al Pharmacol Reviews, 2022







E:I dynamics

▸ Mol Psychiatry. Author manuscript; available in PMC: 2019 Sep 12.

Published in final edited form as: Mol Psychiatry. 2019 May 14;24(9):1248–1257. doi: 10.1038/s41380-019-0426-0

Excitation-inhibition balance as a framework for investigating mechanisms in neuropsychiatric disorders

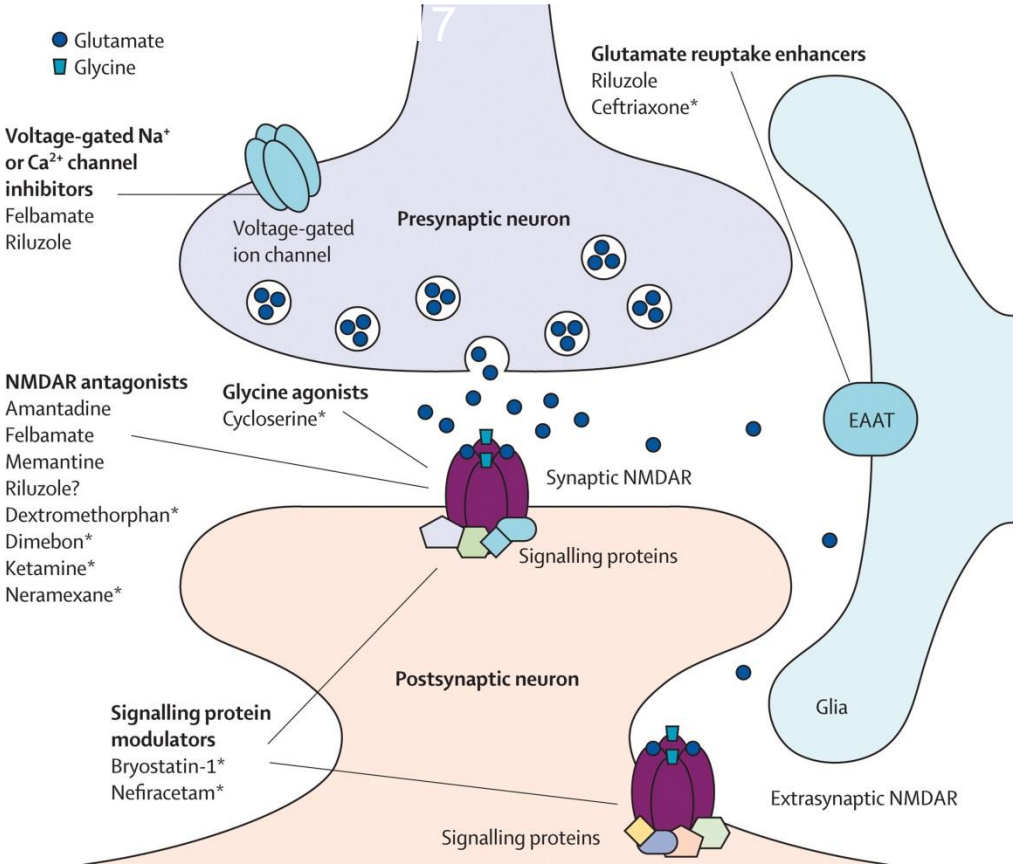
Vikaas S Sohal [1], John L R Rubenstein [1]

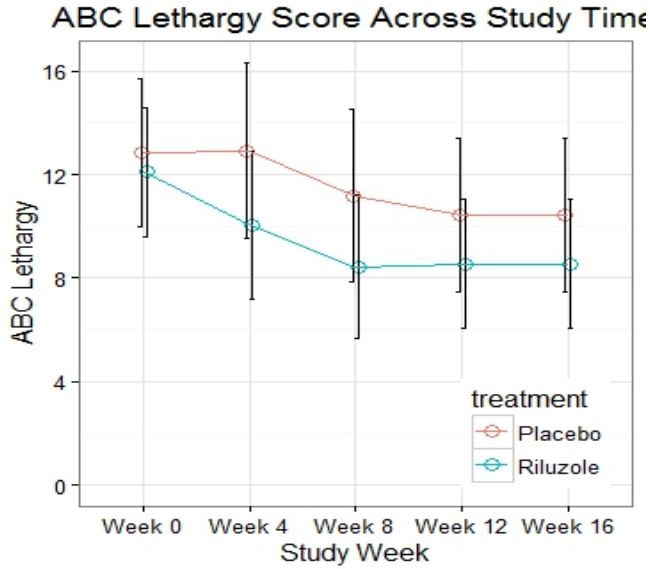
▸ Author information ▸ Article notes ▸ Copyright and License information

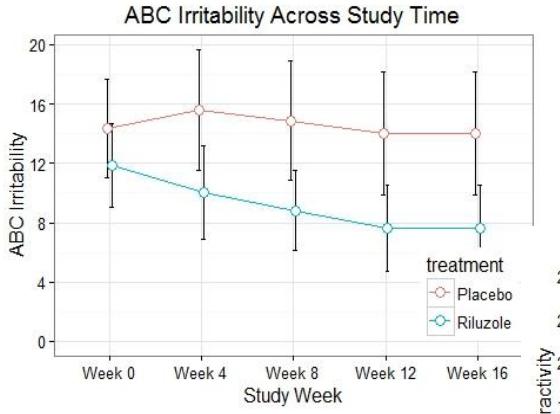
balancing of excitatory and inhibitory synaptic inputs to modulate neural circuit excitability, amplitude and timing of neural activity, information gating.

Riluzole vs placebo in AS

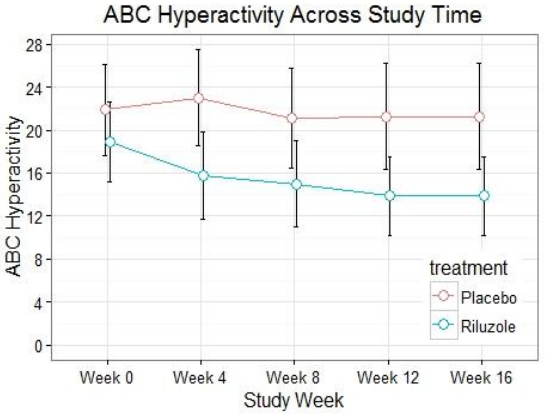
(co-Pis: Rob Nicolson, Terry Bennet)







P=0.02; d=0.4
Coeff estimate for riluzo



p= 0.02; d= 0.45,

Rob Nicolson
Lawson /Western

Janys Lim

Lucia Capano
Queens U

Julia Frei
McMaster U

Celso Arango

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Marg Spoelstra
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Noah Barnett

Clinicaltrials.gov:
***NCT03887676,* NCT03682978**

Karen Walton – Bowen,
CRA/Simons

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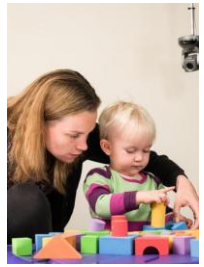
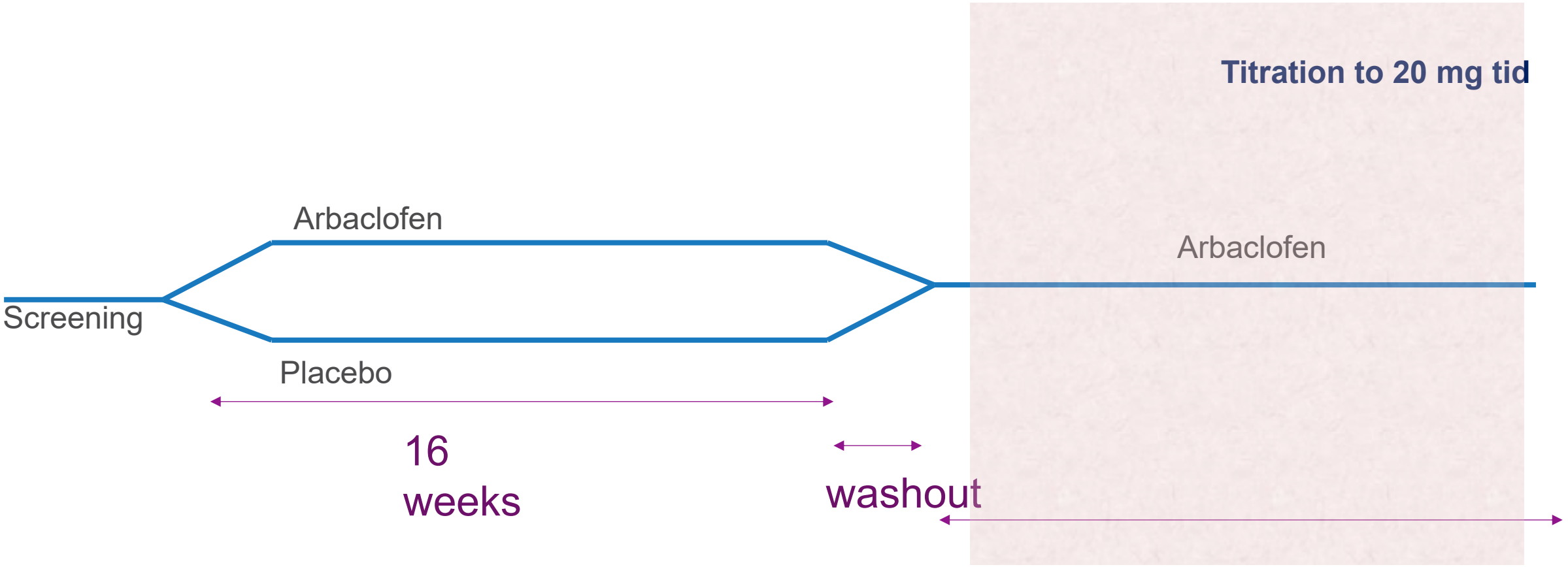
Aims-2 Trials
A- Reps



Emily
Jones
Birkbeck

The ARBA/EU studies - Methods



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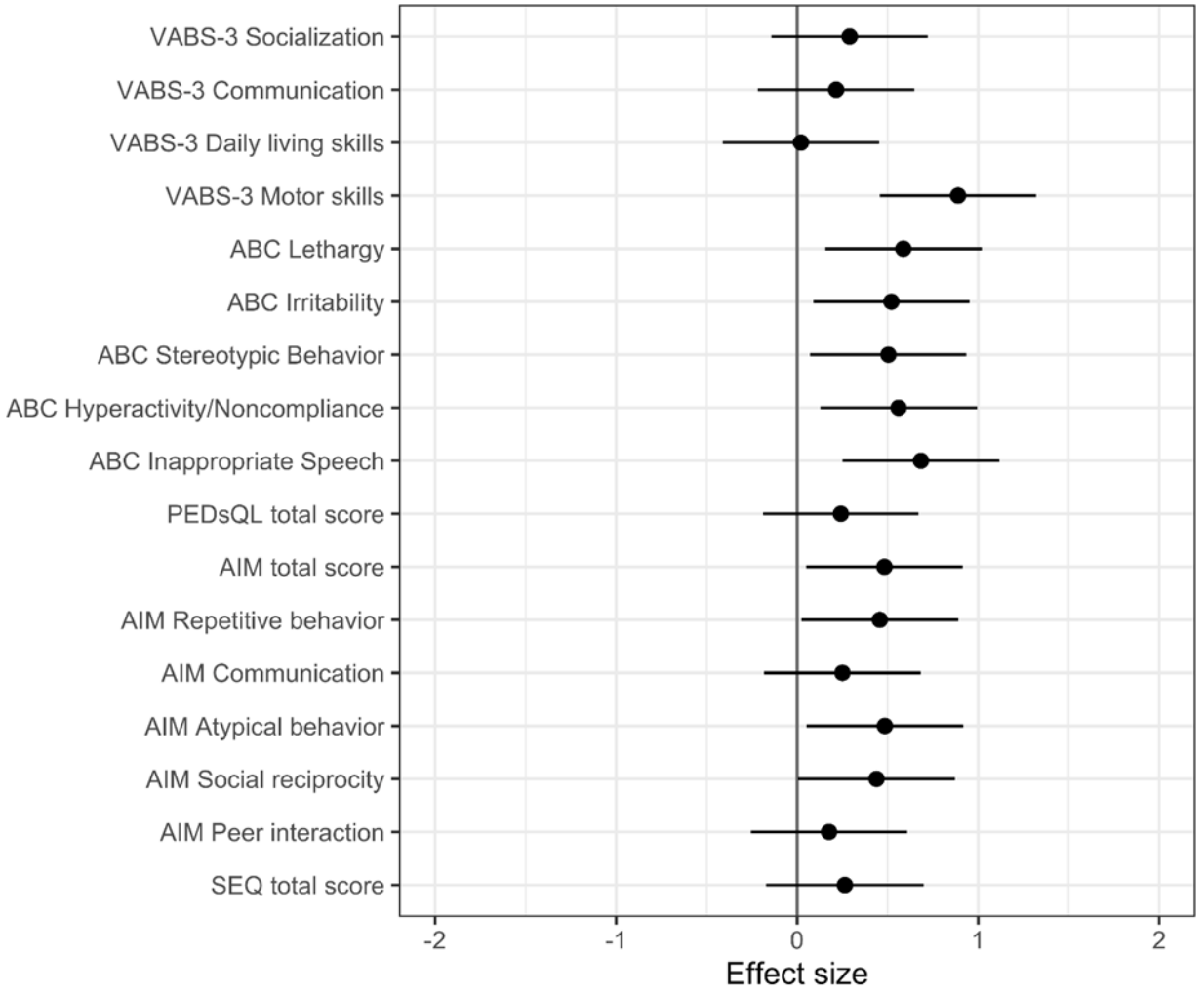
Who participated

	EUROPE		CANADA		ALL	
	Placebo	**Arbaclofen**	**Placebo**	**Arbaclofen**	**Placebo**	**Arbaclofen**
n	63	59	45	45	108	104
Age (years)	12.1 (3.2)	11.4 (3.2)	12.4(3.5)	12.4(3.3)	12.2(3.3)	11.8(3.2)
Male:Female	52:11	50:9	35:10	37:8	87:21	87:17
VIQ	98.1 (21.0)	96.3 (20.5)	91.0(22.4)	89.2(18.5)	95.1(21.6)	93.3(19.7)
NVIQ	100.1(15.9)	96.0 (18.0)	96.6(19.2)	97.0(20.9)	98.6(17.3)	96.4(19.3)
FSIQ	99.1 (16.5)	96.4 (17.3)	93.6(20.6)	92.5(19.1)	97.9(18.3)	94.8(18.1)

Data from Canadian Children/youth



Arbaclofen-Placebo group difference

week 16 after controlling for baseline score and age

MCID (Silkey et al 2022): –4.5 (–7.61, 1.37)

	Canada	Europe	All
AIM – Total	**-15.50(6.98), p=.03** [-29.40, -1.60]	**-13.95(6.01), p=.02**	**-14.91(4.54), p=.001** [-23.82, -6.00]
AIM – repetitive behaviour	**-3.41(1.62), p=.04** [-6.64, -0.18]	-2.01(1.69), p=.23	**-2.98(1.16), p=.01** [-5.26, -0.70]
AIM - communication	-1.53(1.33), p=.25 [-4.17, 1.12]	-1.78(1.01), p=.08	**-1.69(0.80), p=.04** [-3.26, -0.11]
AIM – atypical behaviour	**-3.27(1.47), p=.03** [-6.19, -0.35]	**-5.00(1.53), p=.001**	**-4.17(1.06), p<.001** [-6.25, -2.10]
AIM – social reciprocity	**-2.29(1.14), p=.05** [-4.55, -0.032]	-1.30(1.08), p=.23	**-1.79(0.78), p=.02** [-3.32, -0.25]
AIM – peer interaction	-0.79(0.98), p=.42 [-2.74, 1.15]	**-2.76(1.08), p=.01**	**-1.70(0.72), p=.02** [-3.12, -0.28]

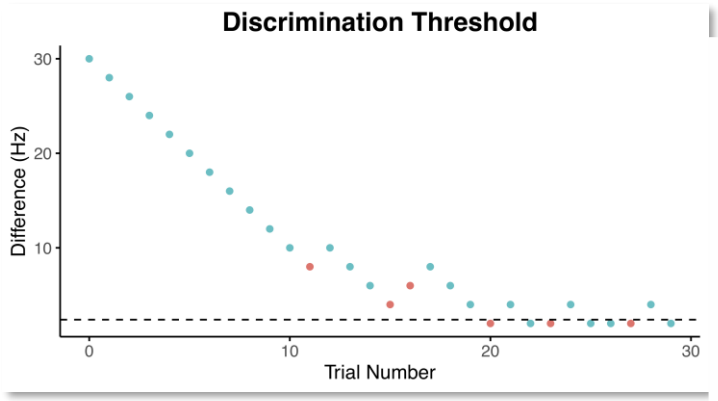
Arbaclofen-Placebo group difference

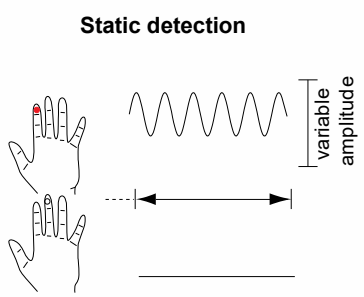
week 16 after controlling for baseline score and age

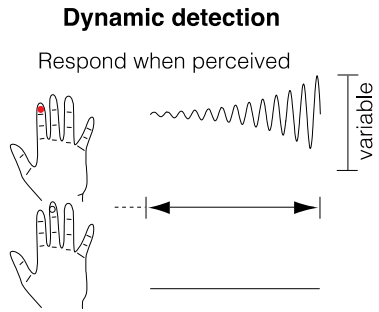
	Canada	Europe	All
ABC – Irritability	**-2.54(1.061), p=.02** [-4.65, -0.43]	-1.58(1.25), p=.21	**-2.20(0.81), p=.007** [-3.78, -0.61]
ABC – Social withdrawal	**-2.95(1.09), p=.008** [-5.81, -0.25]	**-3.17(1.25), p=.01**	**-3.09(0.82), p=.0002** [-4.70, -1.48]
ABC – Stereotypic behaviour	**-1.37(0.59), p=.02** [-2.54, -0.19]	-0.69(0.60), p=.25	**-1.03(0.42), p=.01** [-1.85, -0.21]
ABC – Hyperactivity	**-3.35(1.30), p=.01** [-5.94, -0.77]	**-3.01(1.35), p=.03**	**-3.29(0.93), p=.0004** [-5.11, -1.46]
ABC – Inappropriate speech	**-1.17(0.37), p=.002** [-1.91, -0.43]	-8.10(4.96), p=.11	**-1.27(0.37), p=.0006** [-2.00, -0.55]

What predicted which kids/youth did well

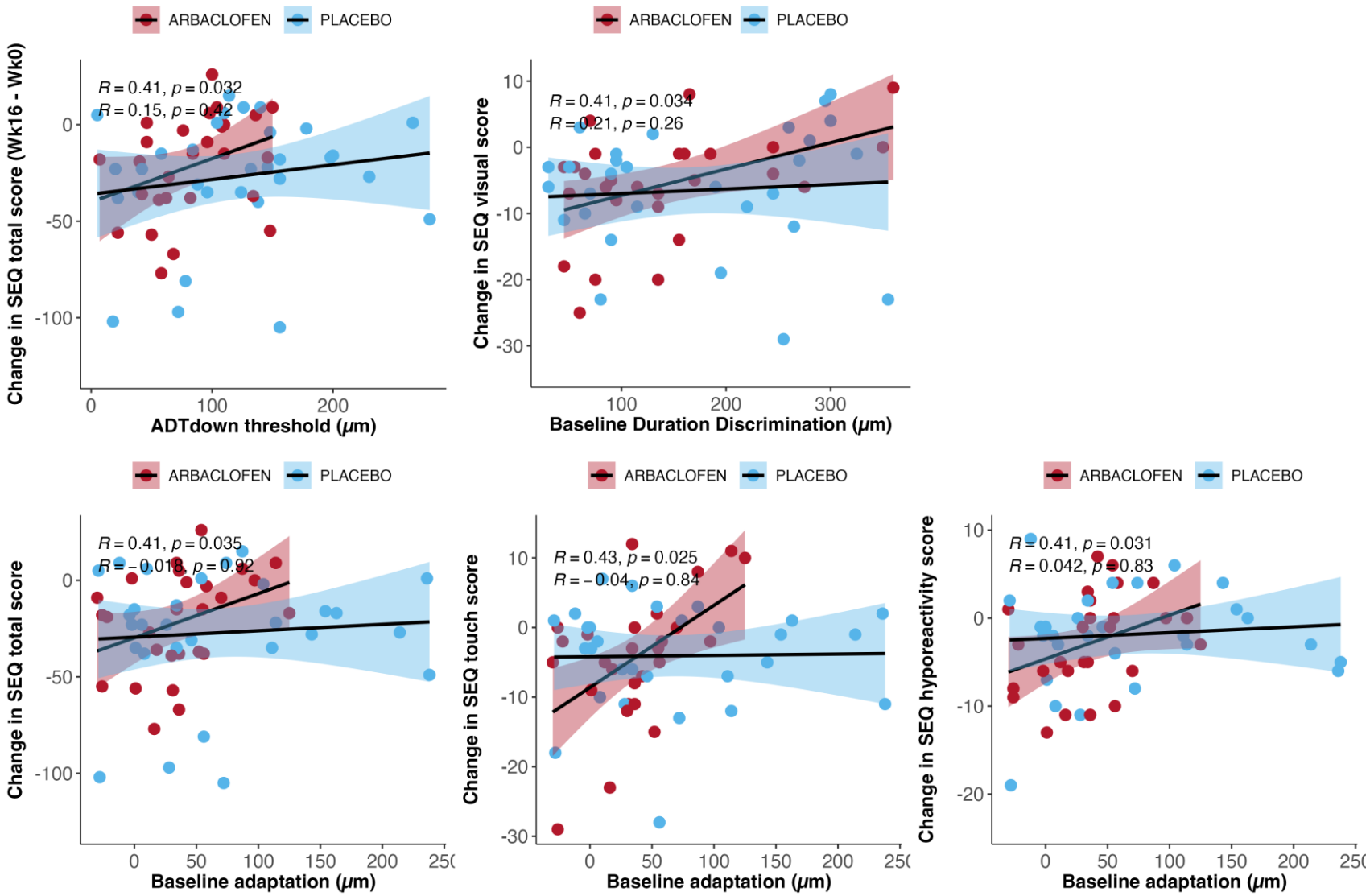
- EEG, Braingage
- Example: Braingage: sensory processing and GABA B
  - Associates with GABRB3 (Tavassoli et al. Mol. Aut. 2012)
  - Related to ($GABA_B$?) somatosensory gating (Blankenburg et al. Sci. 2003, Favorov and Kursun, J Neurophys. 2012, Iliapolos et al. Cereb Cortex 2021) and feed-forward inhibition



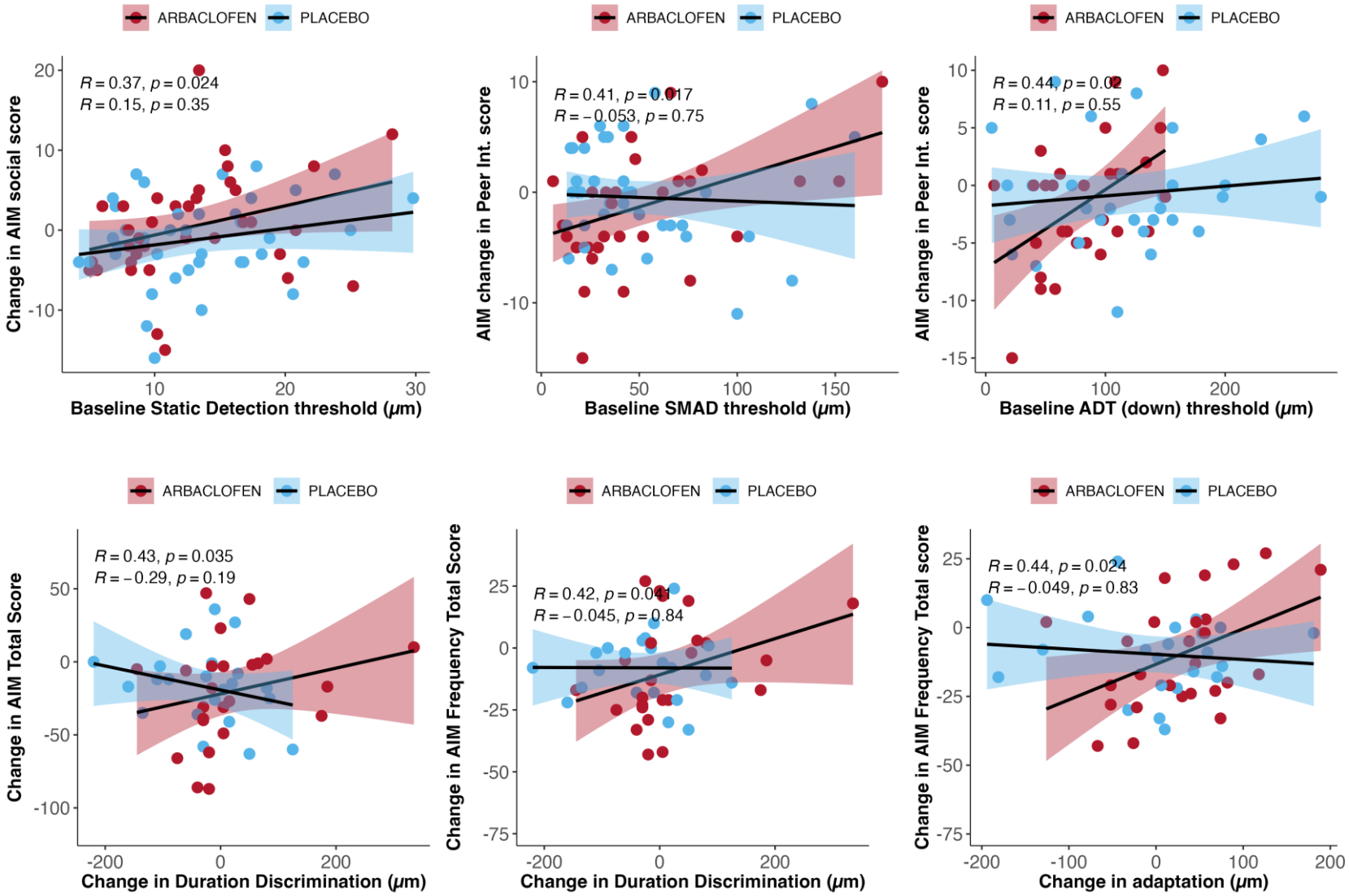




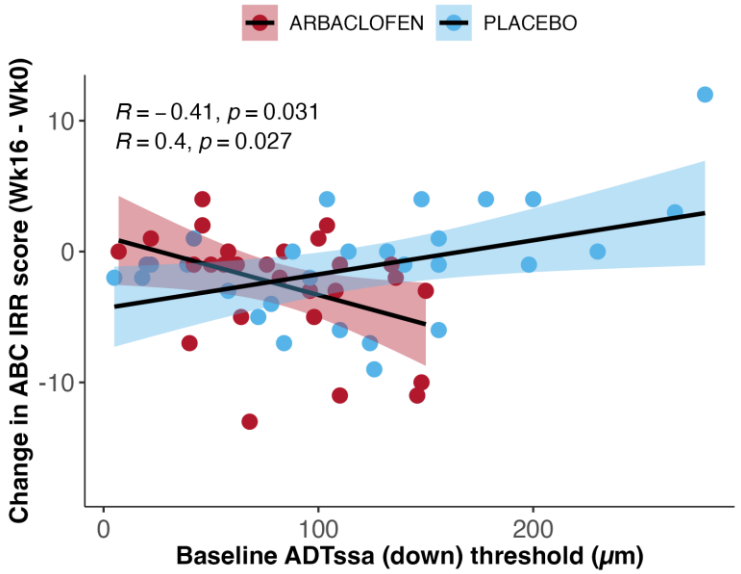
Sensory experiences

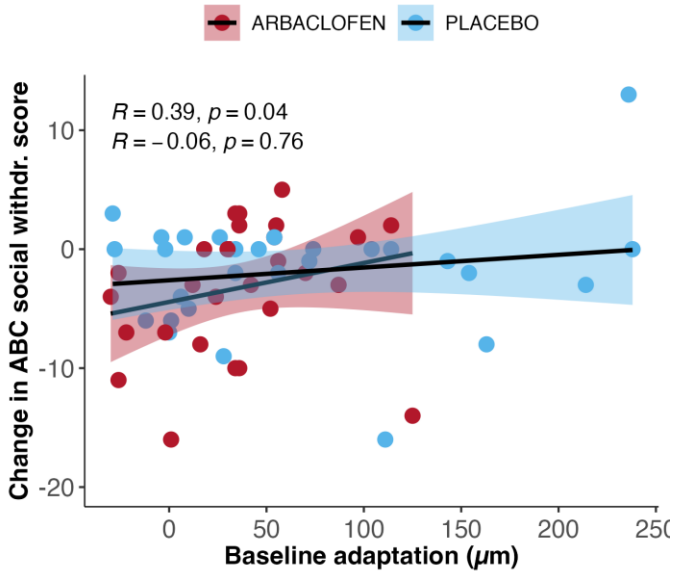


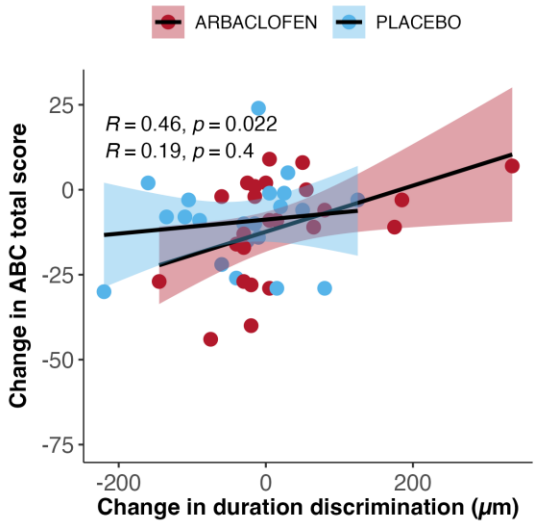
AIM

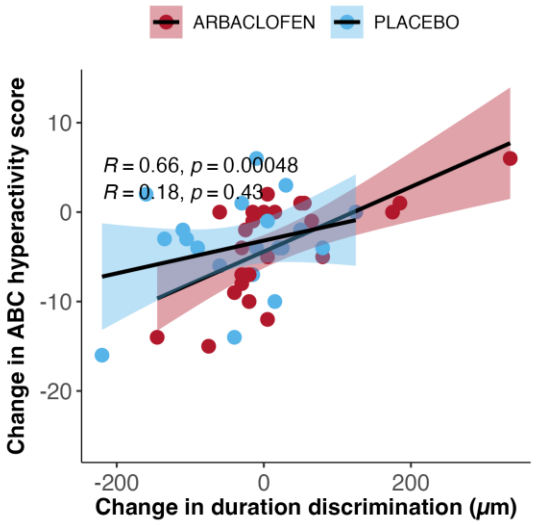

ARBACLOFEN
PLACEBO
R = 0.37, p = 0.024
R = 0.15, p = 0.35
Change in AIM social score
Baseline Static Detection threshold (μm)
R = 0.41, p = 0.017
R = −0.053, p = 0.75
AIM change in Peer Int. score
Baseline SMAD threshold (μm)
R = 0.44, p = 0.02
R = 0.11, p = 0.55
AIM change in Peer Int. score
Baseline ADT (down) threshold (μm)
R = 0.43, p = 0.035
R = −0.29, p = 0.19
Change in AIM Total Score
Change in Duration Discrimination (μm)
R = 0.42, p = 0.041
R = −0.045, p = 0.84
Change in AIM Frequency Total Score
Change in Duration Discrimination (μm)
R = 0.44, p = 0.024
R = −0.049, p = 0.83
Change in AIM Frequency Total score
Change in adaptation (μm)

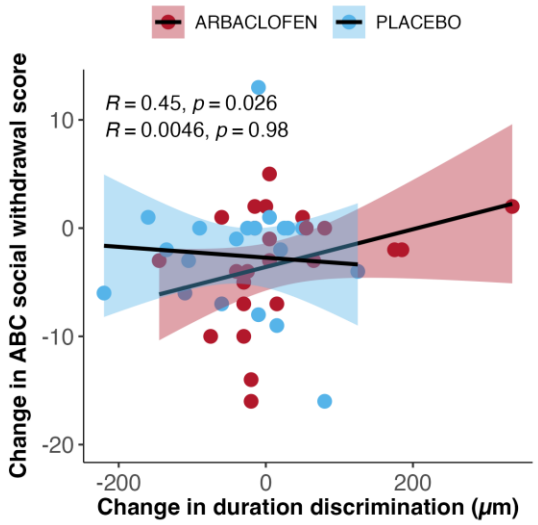
ABC

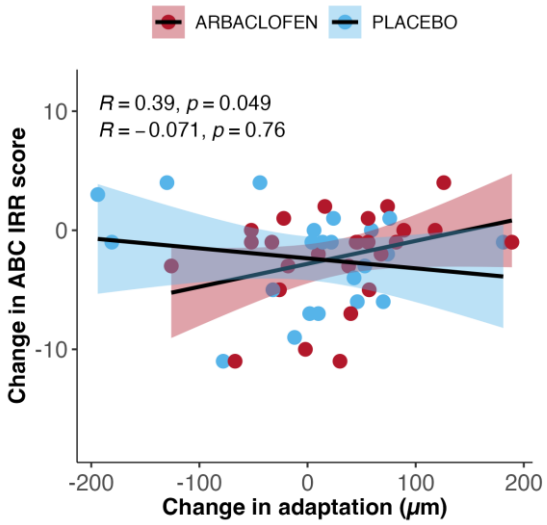

ARBACLOFEN
PLACEBO
R = −0.41, p = 0.031
R = 0.4, p = 0.027
Change in ABC IRR score (Wk16 - Wk0)
Baseline ADTssa (down) threshold (μm)


ARBACLOFEN
PLACEBO
R = 0.39, p = 0.04
R = −0.06, p = 0.76
Change in ABC social withdr. score
Baseline adaptation (μm)


ARBACLOFEN
PLACEBO
R = 0.46, p = 0.022
R = 0.19, p = 0.4
Change in ABC total score
Change in duration discrimination (μm)


ARBACLOFEN
PLACEBO
R = 0.66, p = 0.00048
R = 0.18, p = 0.43
Change in ABC hyperactivity score
Change in duration discrimination (μm)

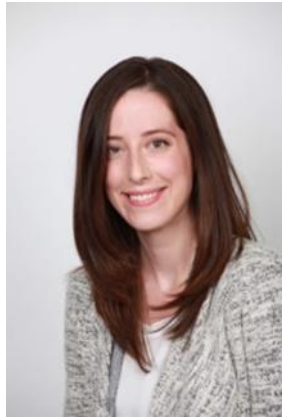

ARBACLOFEN
PLACEBO
R = 0.45, p = 0.026
R = 0.0046, p = 0.98
Change in ABC social withdrawal score
Change in duration discrimination (μm)

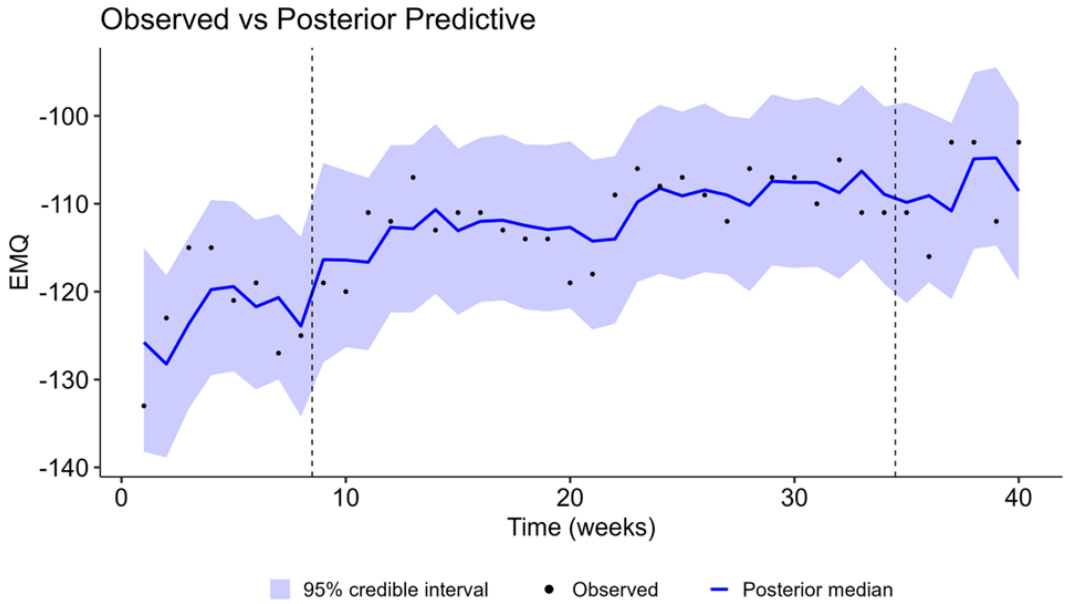

ARBACLOFEN
PLACEBO
R = 0.39, p = 0.049
R = −0.071, p = 0.76
Change in ABC IRR score
Change in adaptation (μm)

Single case, N-of-1 and ‘small-n’ trial designs

RareKids CAN

- KCNC1-related disorder (RD)





Families step up to find gene therapies for diseases too rare for research firms

CARLY WEEKS
The Globe and Mail
Published March 29, 2024
Updated 6 hours ago

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Build a Canadian National Clinical Trials Network

- Leverage experience in building clinical trials network in POND, funded by OBI, to invite all common (e.g., ASD, ADHD, ID, OCD, CP, other neuromotor) and rare NDDs (e.g., Fragile X, Rett Syndrome, Tuberous sclerosis), and exposures that adversely impact neurodevelopment (e.g. prematurity, toxic exposures) across the life span

Vision:

- National network of 14 clinical trial-ready sites
- Regulatory training and readiness at all sites
- Develop & share protocols
- Leverage Canadian efforts for Common ethics approval process
- Continuous quality control
- Leverage efforts for ethical sharing of data

- Need: Anxiety: common, impairing , transdiagnostic, prioritized by patient groups

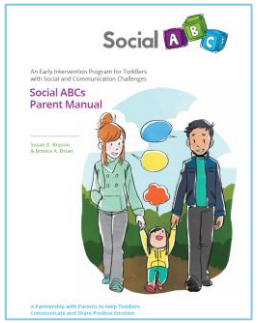
How we will personalize:

Pharmacogenetics; ANS/arousal regulation

The Social ABCs

Les ABC sociaux[MD] Social ABC[TM]

What is the Social ABCs?



- Developed in Canada – J Brian (Toronto) & S Bryson (Halifax)
- **Caregiver-mediated** NDBI (ABCs of learning in a developmental context)
- Focused (relatively brief: 6 or 12 weeks) + Manualized
- For toddlers with ASD or **related social-communication challenges** (12 – 42 mos)
- **Supported by a solid evidence base** from research and community evaluation

Where is it available?

- CANADA
  - Ontario: Government-funded post-diagnosis (10+ community sites)
  - Other Canadian provinces:
    - Nova Scotia & Alberta (research)
    - PEI (clinical; province-wide; pre-dx); Manitoba (in training!), BC in 2026
- GLOBALLY: India (Goa), Israel, France

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NDBI: Naturalistic Developmental Behavioural Intervention

Social ABCs pipeline - *from development to deployment*

- Research (Funded by CIHR, KBHN, Brain Canada, Azrieli Foundation)
- Implementation
- International partnerships
- Leveraged government funding (ON: MCYS/ MCCSS; PEI: Health)

Proof of concept:
Development of 12-week individual model: acceptability, feasibility +pilot evaluation
[2007-2011]

Efficacy:
Original 12-wk individual model:
Cross-site RCT
[2013-2015]
ON, NS

ECE training:
Feasibility +pilot evaluation
[2014-2016]

Attention training booster:
12-wk individual model +attention co-intervention **RCT**
[2016-2020]
ON, AB, NS

Effectiveness
Community Implementation + evaluation
Research-community partnership [2016-2019]
MCYS Demo Project

Group model:
Adapted 6-wk model + pilot evaluation:
In-person vs. virtual
[2018-2020]
ON, NS, AB

International partnerships
India, Israel, France
[ongoing]

Efficacy:
Group Social ABCs virtual delivery **RCT**
[2022-2025]

Spread - Infant and child development sector in new 2 provinces (KBHN)
MB and BC
2025 - 2006

Spread
Community implementation via public providers
2020 – ongoing
ON*, PEI, AB
**MCCSS – OAP CMEY*

We are HERE!

Future-state:
Wide-scale community implementation → widespread access!

10 autism service agencies in Ontario!
OAP - CMEY

Ontario
Ministry of Children, Community and Social Services

Social ABCs™ Les ABCs sociaux™

Social ABCs – Overview of main outcomes

Caregiver

- Learn new strategies (fidelity)
- Experience self-efficacy
- *Parenting stress decreases*

Toddler

- Gains in social communication
- Positive affect / enjoyment
- Social orienting

Babies too!

Dyad

- Sharing positive emotions together
- Orienting to each other
- Empowerment

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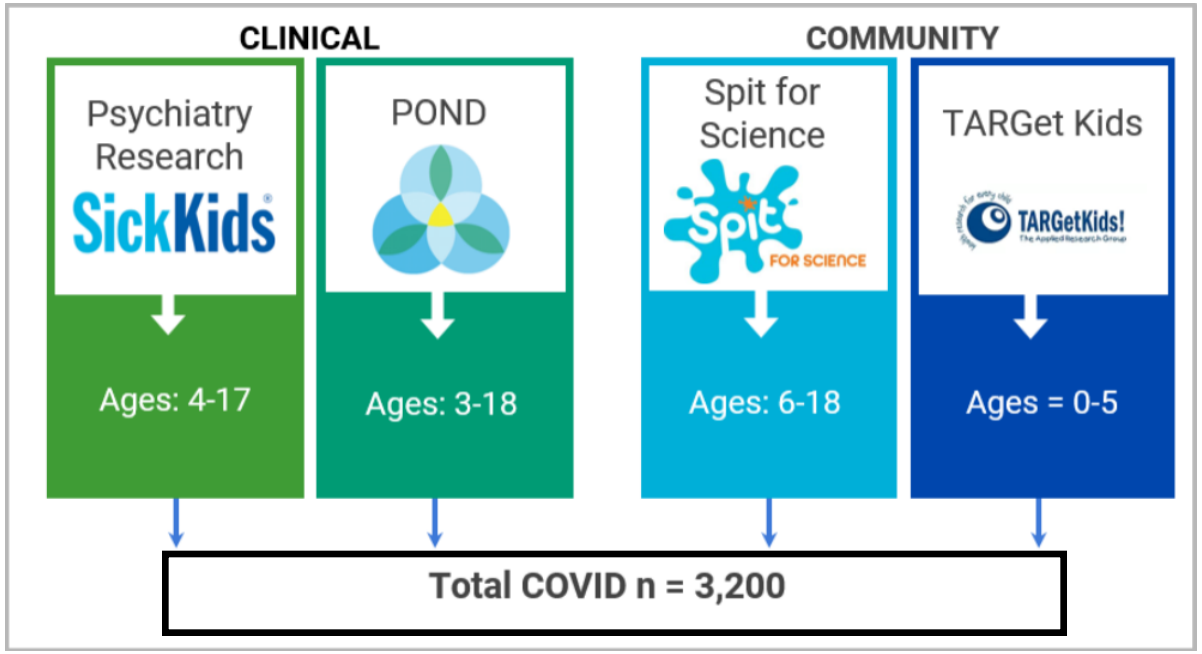
Neuro-affirmative care

- Principle 1: acceptance of autistic ways of being, honour individual strengths, interests and learning styles
- Principle 2: Rights based care: all have the right to safety, security, warmth, and trusting relationships; consistency, predictability, clear expectations and boundaries; access to preferred activities and items; and effective opportunities to learn new things
- To teach or not to teach:
  - Misconception: neuro-affirmative care not consistent with effective teaching

Real-Time Monitoring of Mental Health Impact of COVID-19 on Canadian Children, Youth and Families



CRISIS AFAR: An International Collaborative Study of the Impact of the COVID-19 on youth with NDDs (Lead: A. DiMartino)

Daphne Korczak, MD (PI)

Psychiatry UNIVERSITY OF TORONTO | SickKids Centre for Brain & Mental Health | CIHR IRSC | Ontario Ministry of Health | The Edwin S. H. Leong Centre for Healthy Children UNIVERSITY OF TORONTO

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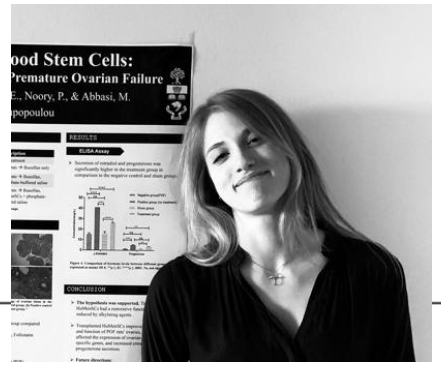
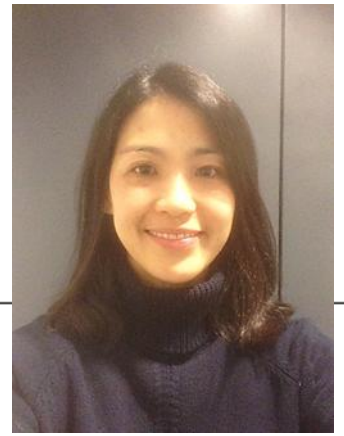
Original Article





OXFORD

Original Article

Mental health profiles of autistic children and youth during the COVID-19 pandemic

Marina Charalampopoulou BSc[1,*], Eun Jung Choi PhD[1,*], Daphne J. Korczak MD[2,3], Katherine T. Cost PhD[2], Jennifer Crosbie PhD[2,3], Catherine S. Birken MD MSc FRCPC[4,5], Alice Charach MD[2,3,5,6], Suneeta Monga MD[2,3], Elizabeth Kelley PhD[7,8], Rob Nicolson MD[9], Stelios Georgiades PhD[10], Muhammad Ayub MD[8], Russell J. Schachar MD[2,3], Alana Iaboni PhD[1], Evdokia Anagnostou MD[1,4]

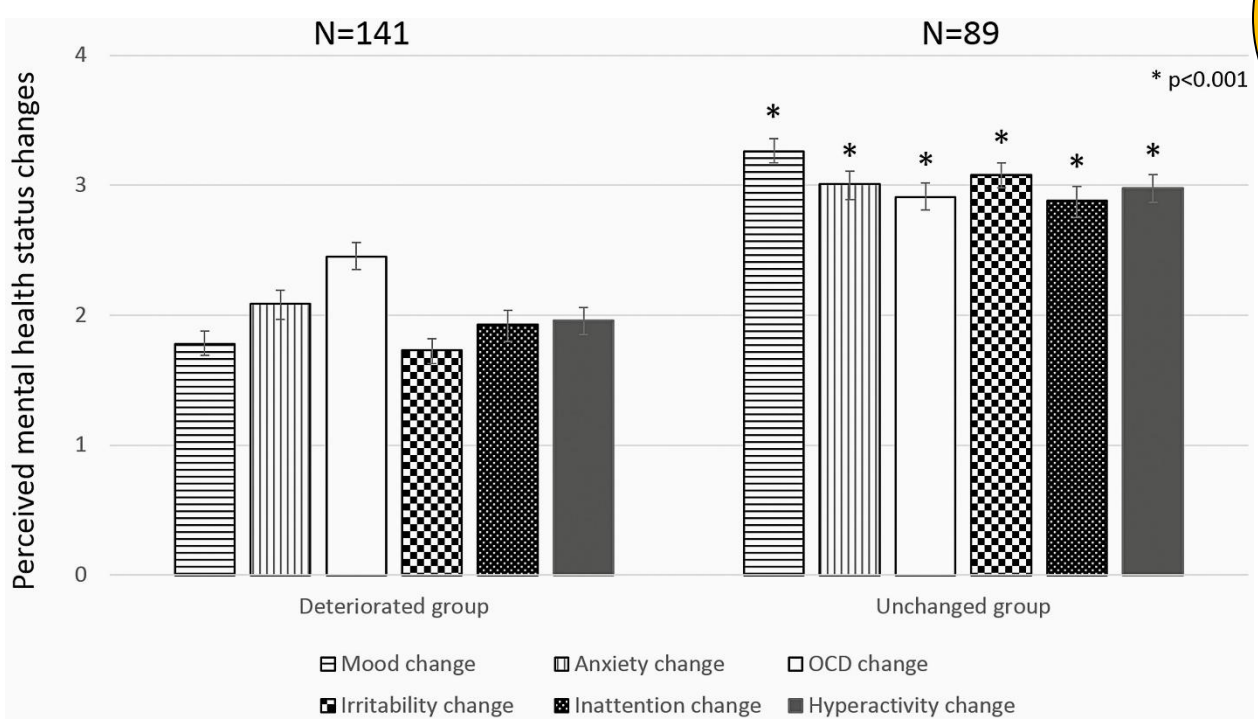
Figure 2. MH changes were examined in six measures (Mood, Anxiety, OCD symptom, Irritability, Inattention, …

COVID stress / material deprivation

Pre-existing internalizing symptoms

Parental mental health

Loss of School / medical services

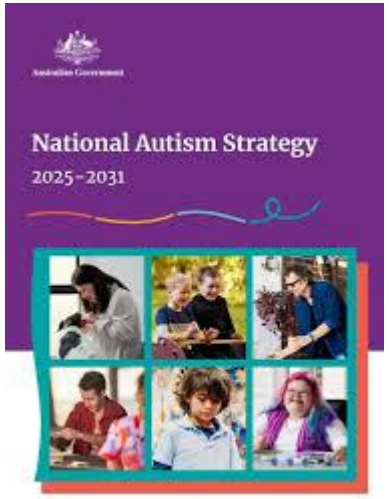


Good parental mental health / Financial security

Priority Area 3 : Data Collection, Public Health Surveillance, and Research.

Strengthening Data: Collecting comprehensive data across all age groups and regions, including diverse demographics and co-occurring conditions.

- **Research & Surveillance:** Establishing a national research network, advancing inclusive research guidelines, and promoting autistic participation in research.
- **Informing Policy:** Using research and surveillance data to improve outcomes and guide evidence-based policy decisions.
- **Clinical Guidelines:** Updating national guidelines for screening, diagnosis, and services.



National Autism Network
Réseau national de l'autisme

Thank you to families, children, youth and adults who participate in research

ONTARIO BRAIN INSTITUTE
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Brain Canada Foundation

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