Nutritional and environmental influences on neurodevelopment

International Society for Orthomolecular Medicine

INTRODUCTION

Neurodevelopmental disorders: Definitions and scope of the problem

Introduction

- Children with neurodevelopmental disorders/disabilities (NDD/D) or "neurodisability" are the largest identifiable subpopulation of children with disabilities and account for 7% to 14 % of all children in developed countries.
- Diagnoses under NDD/D include autism spectrum disorders (ASD), intellectual or learning disabilities, attention-deficit/ hyperactivity disorder (ADHD), cerebral palsy, and Down and fetal alcohol syndromes.

Child functional characteristics explain child and family outcomes better than diagnosis: Population-based study of children with autism or other neurodevelopmental disorders/disabilities
Health Reports. Statistics Canada. 2016.

Developmental delay

- Children with sustained developmental delay are at higher risk of learning difficulties, behavioural problems and functional impairments later in life.
- Many factors are associated with increased risk of developmental delay, including poor maternal health during pregnancy, birth complications, infections, genetic characteristics, exposure to toxins, trauma, maltreatment and possibly low socioeconomic status.

Developmental delay sequelae

Early Neurodevelopment and Self-Reported Adolescent Symptoms of Depression and Anxiety in a National Canadian Cohort Study
PLoS ONE. 2013 8(2): e56804.

- 3508 Canadian children who participated in a nationally representative prospective cohort study.
- Cohort members who displayed delayed developmental milestones in early childhood were more likely to experience higher levels of depressive and anxious symptoms as adolescents.

Autism Spectrum Disorder Among Children And Youth In Canada 2018
A Report of the National Autism Spectrum Disorder Surveillance System, Public Health Agency of Canada 2018

Statistics are from 2015 (reported 2018)

What is autism spectrum disorder (ASD)?

- ASD is a neurodevelopmental disorder that includes impairments in language, communication skills, and social interactions combined with restricted and repetitive behaviours, interests or activities.
- Signs of ASD are typically detected in early childhood.
- Diagnosis of ASD is 4 to 5 times more common in boys than girls.

A spectrum disorder

- Each person with ASD is unique and will have different symptoms, deficits and abilities.
- Because of the range of characteristics, this condition is named a "spectrum" disorder.
- Ones' abilities and deficits can fall anywhere along a spectrum, and thereby, support needs may range from none to very substantial.
- It is a complex life-long condition that impacts not only the person with ASD, but their families, caregivers and communities.

ASD prevalence

- Approximately 1 in 66 children and youth are diagnosed with ASD in Canada
- A critical review of 42 studies found that the mean age at diagnosis for these studies ranged from 3–10 years old.
- In a more recent study the median age at diagnosis was 5.3 years old, with a range of age of diagnosis from 2–17 years old.

1 in 42 males were diagnosed with ASD

1 in 165 females were diagnosed with ASD

Autism by the numbers: Economic costs to families, society

Costs of Autism Spectrum Disorders in the United Kingdom and the United States
JAMA Pediatrics. 2014 168(8): 721-728.

- The economic effect of ASDs on individuals with the disorder, their families, and society as a whole is poorly understood and has not been updated in light of recent findings.
- Main outcomes and measures: Mean annual medical, nonmedical, and indirect economic costs and lifetime costs were measured for individuals with ASDs, separately for those with and without intellectual disability in the U.S. and the U.K.
- The cost of supporting an individual with an ASD and intellectual disability during his or her lifespan was $2.4 million in the United States.
- The cost of supporting an individual with an ASD without intellectual disability was $1.4 million.
- The largest cost components for children were special education services and parental productivity loss (lost work hours).
- During adulthood, residential care or supportive living accommodation and individual productivity loss contributed the highest costs.
- Medical costs were much higher for adults than for children.
- The substantial direct and indirect economic effect of ASDs emphasizes the need to continue to search for effective interventions that make best use of scarce societal resources.
- The enormous effect on families also warrants policy attention.

Autism by the numbers: Forecasting economic burden

Brief Report: Forecasting the Economic Burden of Autism in 2015 and 2025 in the United States
Journal of Autism and Developmental Disorders. 2015 45(12): 4135-4139.

- The cost of supporting an individual with an ASD and intellectual disability during his or her lifespan was $2.4 million.
- Cost without intellectual disability was $1.4 million.
- Few US estimates of the economic burden of autism spectrum disorders (ASD) are available and none provide estimates for 2015 and 2025.
- Forecast: annual direct medical, direct non-medical, and productivity costs combined will be $268 billion (range $162–$367 billion; 0.884–2.009 % of GDP) for 2015.
- Forecast: $461 billion (range $276–$1011 billion; 0.982–3.600% of GDP) for 2025.
- ASD costs exceed those of stroke and hypertension.
- If the prevalence of ASD continues to grow as it has in recent years, ASD costs will likely far exceed those of diabetes and ADHD by 2025.

CANADIAN POLITICS

Over 16,000 children on Ontario wait lists for autism services: More kids are waiting than getting support

- some families are waiting years for services – so long that the efficacy of treatment declines.

National Post
https://nationalpost.com/news/politics/over-16000-children-on-ontario-wait-lists-for-autism-services-some-families-are-waiting-years-for-help

Autism: Not early enough

Cost-effectiveness of Wait Time Reduction for Intensive Behavioral Intervention Services in Ontario, Canada
JAMA Pediatrics. 2017 171(1): 23-30.

IMPORTANCE Earlier access to intensive behavioural intervention (IBI) is associated with improved outcomes for children with severe autism spectrum disorder (ASD); however there are long waiting times for this program. No analyses have been performed modeling the cost-effectiveness of wait time reduction for IBI.

Autism: Reducing wait times

- Mean starting ages for IBI (Intensive Behavioural Intervention) were 5.24 years for CWT (Current Wait Time), 3.89 years for RWT (Reduced Wait Time), and 2.71 years for EWT (Eliminated Wait Time)
- Cost of IBI valued at $56 000 per child per year, mean duration of 2 years
- Government: EWT was the dominant strategy, generating the most DFLYs for $53K less per individual to 65 years of age than CWT
- Society: EWT produced lifetime savings of $267K per individual compared with CWT
- Current disparity between IBI service needs and the amount of IBI being delivered in the province of Ontario, with long term effects
- Waiting lists increasing much faster than the number of children receiving IBI
- Eliminating wait times for IBI – potential to result in better treatment and adult outcomes for many children
- Substantial cost savings from the perspectives of the provincial government and society

Mental health disorders standard of care

Mental health disorders: Standard of care

- "*To include what's outside the box does not exclude what's inside*." Bo Jonnson
- History; Exam; Lab work; Diagnosis
- Psychiatry referral (Developmental Paediatrician)
- Psychoactive medication
- Psychotherapy; CBT (Autism: Applied Behaviour Analysis/ABA, Intensive Behavioural Intervention/IBI, Speech Therapy, Occupational Therapy)
- Professional and personal support network
- Institutional care

Adverse effects of psychotropic medications in children

- Despite limited information related to efficacy in children, psychotropic medications are commonly prescribed as a first-line treatment for a range of psychiatric diagnoses in children in a variety of clinical settings.
- Usage has increased over the past three decades.
- Although psychotropic medications are often effective at treating psychiatric symptoms, the risk of adverse effects (AE) in children is unclear.

Adverse Effects of Psychotropic Medications in Children: Predictive Factors
Journal of Canadian Academy of Child and Adolescent Psychiatry. 2014 23(3): 218–225.

Second-generation antipsychotics in children

- Treatment with quetiapine has considerably reduced irritability and improved his quality of life. Patient's mother has stated that her child's clothes are no longer fitting because his waist size has increased substantially, and that he has gained 5 kg since treatment initiation 8 weeks ago.
- Despite known metabolic side effects such as weight gain, excess visceral adiposity, dyslipidemia, and glucose intolerance or diabetes, many patients must continue with treatment.
- In Canada, aripiprazole is approved for those aged 15 to 17 with schizophrenia and those aged 13 to 17 with manic or mixed episodes of bipolar I disorder.
- Olanzapine is available for both schizophrenia and bipolar disorder in those aged 13 to 17.
- Second-generation antipsychotics (SGA) are also prescribed for irritability associated with autism spectrum disorder.
- Canada saw a 33% rise in SGA prescriptions from 2010 to 2013.
- Treatment with risperidone and quetiapine over 52 weeks in children (mean age was 14.1 years) showed an average weight gain of 9.7 kg.
- Children who are prescribed SGAs are at risk of developing metabolic side effects with a potential effect on their future cardiovascular health.
- Children should always be given the lowest therapeutic dose.

Second-generation antipsychotics in children
Canadian Family Physician. 2018 64(9): 660-662.

Use of natural health products (NHPs) in children

- Overall, 18.8% of family physicians said they regularly or frequently asked about NHP use; 24.7% counseled patients about potential harms. Only 1.9% of physicians believed NHPs were usually beneficial.
- 8.4% thought they were usually harmful.
- 59.7% said they never recommend NHPs for children, and a further 37.0% said they would only "sometimes" recommend NHPs

Use of Natural Health Products in Children
Canadian Family Physician. 2013 59(8): e357-e363.

The scope: Conclusions

- There is a GAP in care
- Emphasis needs to be primary prevention
- A role to play for lifestyle factors and modification
- Need to start very young - identify at risk children; provide for basic needs, including nutrition; modify potential maternal risk factors

How to fill the gap?
What might Osler say?
Sir William Osler: (1849-1919)

- Canadian physician - born in Bond Head, Ontario
- one of the "Big Four" founding professors at Johns Hopkins
- the father of modern medicine – brought medical students to the hospital wards to learn at the bedside - established medical residency
- also considered the father of psychosomatic medicine – understood the role of psychology in human illness

Oslerisms

- "Observe, record, tabulate, communicate. Use your five senses. Learn to see, learn to hear, learn to feel, learn to smell, and know that by practice alone you can become expert."
- "It is much more important to know what sort of a patient has a disease than what sort of a disease a patient has."
- "There are, in truth, no specialties in medicine, since to know fully many of the most important diseases a man must be familiar with their manifestations in many organs."
- "One of the first duties of the physician is to educate the masses not to take medicine."
- "The young physician starts life with 20 drugs for each disease, and the old physician ends life with one drug for 20 diseases."
- "Medicine is a science of uncertainty and an art of probability."

The name game

- "Normal"
- Speech Disorder
- Apraxia
- Seizure Disorder
- Learning Disability
- Dyslexia
- Oppositional Behaviour
- Antisocial Personality
- Hyperlexia
- Hyperactivity Disorder
- Attention Deficit Disorder
- Attention Deficit & Hyperactivity Disorder
- Asperger's Syndrome
- Autism Spectrum Disorder
- Pervasive Developmental Delay
- Global Developmental Delay

Genetics
Toxin Exposure
Diet Factors
Dysbiosis
Food Intolerances
Neuroinflammation

Model of chronic disease and clinical assessment

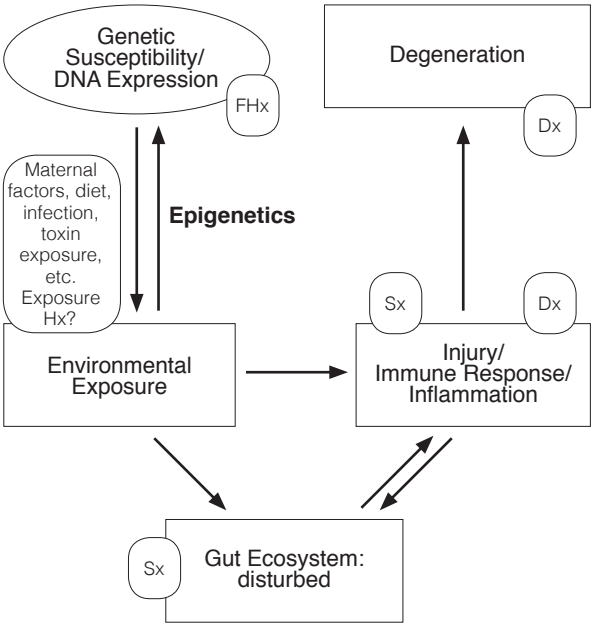


Image: **Molecular psychiatry Figure 1**

Image: **Molecular psychiatry Figure 2**

https://www.nature.com/articles/mp201233

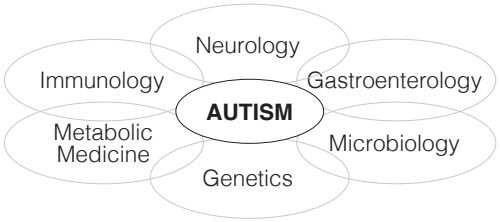
The neuroprogressive nature of major depressive disorder: pathways to disease evolution and resistance, and therapeutic implications
Molecular Psychiatry. 2013 18(5): 595-606.

Image: **The evolving understanding of bipolar depression neurobiology and the relation to diagnosis**

https://www.medscape.org/viewarticle/781133_transcript

The Evolving Understanding of Bipolar Depression Neurobiology and the Relation to Diagnosis
Medscape Education Psychiatry & Mental Health CME

ASD as multi-system disease with co-morbidities



A review of research trends in physiological abnormalities in autism spectrum disorders: immune dysregulation, inflammation, oxidative stress, mitochondrial dysfunction and environmental toxicant exposures
Molecular Psychiatry. 2012 17(4): 389–401.

References

A review of research trends in physiological abnormalities in autism spectrum disorders: immune dysregulation, inflammation, oxidative stress, mitochondrial dysfunction and environmental toxicant exposures
Molecular Psychiatry. 2012 17(4): 389–401.
https://doi.org/10.1038/mp.2011.165

Adverse Effects of Psychotropic Medications in Children: Predictive Factors
Journal of Canadian Academy of Child and Adolescent Psychiatry. 2014 23(3): 218–225.

Autism Spectrum Disorder Among Children And Youth In Canada 2018
A Report of the National Autism Spectrum Disorder Surveillance System, Public Health Agency of Canada 2018
https://www.canada.ca/en/public-health/services/publications/diseases-conditions/autism-spectrum-disorder-children-youth-canada-2018.html

Brief Report: Forecasting the Economic Burden of Autism in 2015 and 2025 in the United States
Journal of Autism and Developmental Disorders. 2015 45(12): 4135-4139.
https://doi.org/10.1007/s10803-015-2521-7

Child functional characteristics explain child and family outcomes better than diagnosis: Population-based study of children with autism or other neurodevelopmental disorders/disabilities
Health Reports. Statistics Canada. 2016
https://www150.statcan.gc.ca/n1/pub/82-003-x/2016006/article/14635-eng.htm

Cost-effectiveness of Wait Time Reduction for Intensive Behavioral Intervention Services in Ontario, Canada
JAMA Pediatrics. 2017 171(1): 23-30.
https://doi.org/10.1001/jamapediatrics.2016.2695

Costs of Autism Spectrum Disorders in the United Kingdom and the United States
JAMA Pediatrics. 2014 168(8): 721-728.
https://doi.org/10.1001/jamapediatrics.2014.210

Early Neurodevelopment and Self-Reported Adolescent Symptoms of Depression and Anxiety in a National Canadian Cohort Study
PLoS ONE. 2013 8(2): e56804.
https://doi.org/10.1371/journal.pone.0056804

National Post – https://nationalpost.com/news/politics/over-16000-children-on-ontario-wait-lists-for-autism-services-some-families-are-waiting-years-for-help

Second-generation antipsychotics in children
Canadian Family Physician. 2018 64(9): 660-662.
https://www.cfp.ca/content/64/9/660

The Evolving Understanding of Bipolar Depression Neurobiology and the Relation to Diagnosis
Medscape Education Psychiatry & Mental Health CME
https://www.medscape.org/viewarticle/781133_transcript

The neuroprogressive nature of major depressive disorder: pathways to disease evolution and resistance, and therapeutic implications
Molecular Psychiatry. 2013 18(5): 595-606.
https://doi.org/10.1038/mp.2012.33

Use of natural health products in children
Canadian Family Physician. 2013 59(8): e357-e363.
https://www.cfp.ca/content/59/8/e357

