Psychopharmacology and Pediatric Obesity

Raise awareness of the complex interplay between mental illness and obesity/metabolic disturbances in children

Dina Panagiotopoulos, MD, FRCPC
Clinical Professor of Pediatrics, UBC
Endocrinologist, BC Children's Hospital
Medical Director, Provincial Mental Health Metabolic Program
Clinician Scientist, BC Children's Hospital Research Institute

6th Conference on Recent Advances in the Prevention and Management of Childhood & Adolescent Obesity: Understanding the Interplay between Physical and Mental Health October 25, 2016

BC Mental Health & Addiction Services

Disclosure of Commercial Support

- **NONE**
- **No conflict of interest to declare.**

BC Mental Health & Addiction Services

Objectives

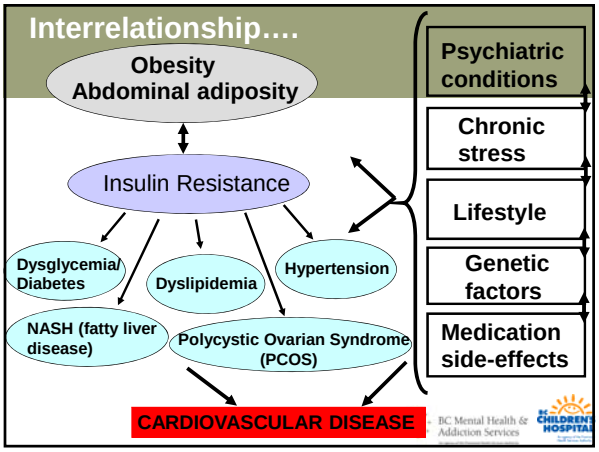
- Describe the complex inter-relationship between certain features of mental health conditions (MHCs), chronic stress, genetic factors, lifestyle issues & medications AND obesity/metabolic dysfunction in youth
- Identify risk for obesity and metabolic dysfunction in children treated with the most commonly prescribed classes of psychotropic medications with a focus on second-generation antipsychotics
- Discuss potential management strategies for psychotropic-related obesity

BC Mental Health & Addiction Services

Background

- 15% of children and youth in Canada will suffer from mental illness at one point in time
- Many will undergo a combination of non-pharmacologic and pharmacologic interventions
- Pharmacological interventions:
  - Second-generation antipsychotics (SGAs)
  - Antidepressants (e.g., SSRIs, SNRIs)
  - Mood stabilizers (e.g., lithium, valproic acid)

Interrelationship….



Increased Cardiovascular Disease and Reduced Life Expectancy

- Adults with severe mental illness (e.g., schizophrenia, major depressive disorder, or bipolar disorder) have a reduced life expectancy compared to the general population.
- Mortality due to myocardial infarction
  - 19% greater among persons with any mental illness
  - 34% greater in individuals with schizophrenia compared to a control population
- 15-25 yrs of reduced life expectancy secondary to
  - combined effect of the burdens of psychiatric illness and the side effects related to the medications used to treat mental illness

Druss BG, et al. Arch Gen Psychiatry 2001;58(6):565-72.
Hennekens CH, et al. Am Heart J 2005;150(6):1115-21.

Psychiatric conditions and Obesity/Metabolic Disturbances: A Complex Inter-relationship!

Chicken or the Egg?

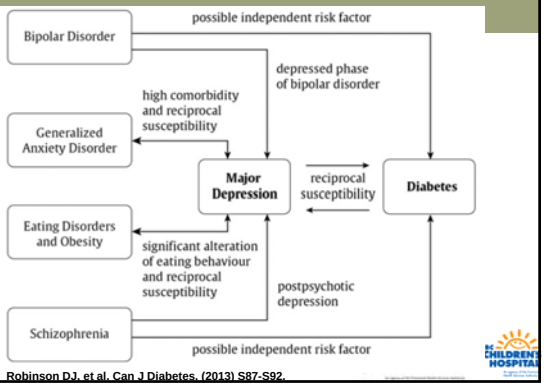
Obesity influencing psychological distress/mental illness

- In adults, obesity is associated with a 25% increased odds of developing mood and anxiety disorders (Simon GE, et al. Arch Gen Psychiatry. 2006.)
- In Canadian children, the odds of developing low self-esteem four years later were greater (OR=1.36) for those who were obese than those normal weight (Wang F, et al. 2009.) ; similar studies in Hispanic and non-Hispanic white females (French SA, et al. 1995; Strauss RS. 2000)
- Obese female adolescents become adults who earn lower wages, & have an increased risk of living in poverty; Obese male adolescents are less likely to marry as adults (Gortmaker SL, et al. 1993.; Sargent JD, 1994)
- Pre-existing obesity in childhood shown to be an independent predictor of adolescent-onset bipolar disorder (OR= 1.58) (Jerrell et al., J Clin Psychiatry 2010.)
- Chronic obesity associated with oppositional defiant disorder in both sexes and depressive disorders in boys (Mustillo S, et al. Pediatrics, 2003.)

Mental illness influencing obesity

- In adults, 2x increased odds of obesity for both people living with schizophrenia and bipolar disorder (DeHert et al. 2009)
- In children, having depressed mood at baseline without obesity at baseline independently predicted (OR = 2.05) obesity at 1 year follow-up (Goodman E, et al. 2002.)
- Childhood depression is associated with an increased BMI into adulthood (Pine DS et al, et al. Pediatrics, 2001.)
- Association between ADHD symptoms and OW/OB in adolescent girls (van Egmond-Fröhlich AW, et al. Int J Obesity (London) 2012)
- Adolescents with bipolar disorder had an increased odds of obesity (OR=1.92) and type 2 diabetes (OR=1.59) compared to control youth

Influence of mental illness on diabetes risk

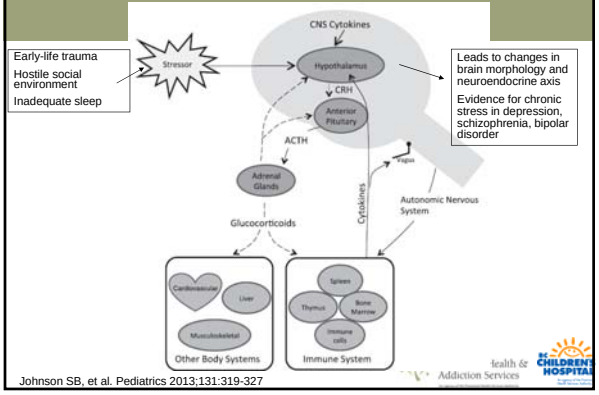


Robinson DJ, et al. Can J Diabetes. (2013) S87-S92.

Shared Neurobiological Mechanism Between Mental Illness and Obesity?

Chronic Stress?

Chronic Stress: HPA axis



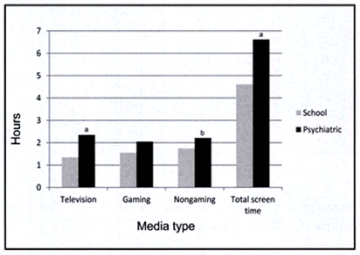
Johnson SB, et al. Pediatrics 2013;131:319-327

Other Contributing Lifestyle Factors?

- Physical inactivity/Sedentary behaviour including excess screen time
- Sleep disturbances
- Sugar-sweetened beverage consumption
- Smoking

Lifestyle: Excess screen time

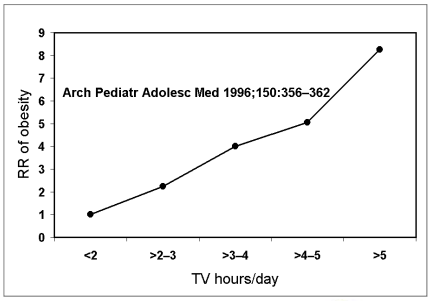
Figure 1 Amounts of time spent on different electronic media in youth seen in psychiatric clinic and school populations



[a]$P < 0.05$, [b]$P < 0.1$, after controlling for SES and sex

Baer S et al. Can J Psychiatry 2012; 57(12):728-35

Lifestyle: Excess screen time



Arch Pediatr Adolesc Med 2003;157:725–727

Lifestyle: Sleep disturbances

- Sleep disturbances highly prevalent in many mental health conditions:
  - Autism spectrum disorders (Cortesi et al. 2010; Miano et al. 2010)
  - Mood disorders, bipolar disorder (Mindell JA et al. 2003; Richardson MA et al. 2007; Lofthouse N, et al. 2010)
  - ADHD (Bends et al. 2010; Sung et al. 2008; Weiss et al. 2006)
  - Anxiety disorders (e.g. Generalized Anxiety Disorder, Separation Anxiety) (Richardson et al. 2007)
  - FASD (Jan JE et al. 2010)
- In healthy adolescents, higher sleep disturbance scores associated with: (Narang I et al. CMAJ, 2012).
  - Cardiovascular risk (OR 1.43 [95% CI 1.16 – 1.77])
  - Hypertension (OR 1.44 [95% CI 1.02 – 2.05])
  - Elevated non-HDL cholesterol (OR 1.28 [95% CI 1.00 – 1.64])

BC Mental Health & Addiction Services

Psychopharmacology

Medication side-effects: an under-recognized problem?

-Second-generation antipsychotics (SGAs)
-Antidepressants (SSRIs)
-Mood stabilizers (lithium, valproate)

BC Mental Health & Addiction Services

Second Generation (Atypical) Antipsychotics (SGAs)

- Risperidone (Risperdal®)
- Quetiapine (Seroquel®)
- Olanzapine (Zyprexa®)
- Aripiprazole (Abilify®)
- Ziprasidone (Zeldox®)
- Clozapine (Clozaril®)
- Paliperidone (Invega®)

Atypicality:

- 5-HT 2a blockade & D2 blockade
- Significantly decreased risk of extra-pyramidal symptoms

BC Mental Health & Addiction Services

Rapid Increase in Antipsychotic Prescriptions to Children and Adolescents

United States

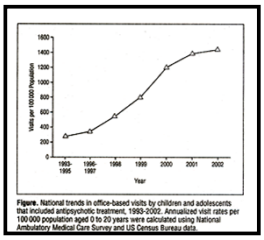
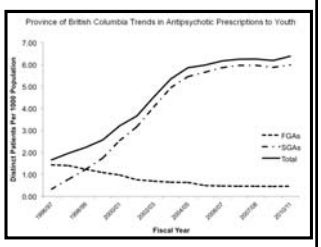


Figure. National trends in office-based visits by children and adolescents that included antipsychotic treatment, 1993-2002. Annualized visit rates per 100 000 population aged 0 to 20 years were calculated using National Ambulatory Medical Care Survey and US Census Bureau data.

Olfson et al. (2006). Archives of General Psychiatry, 63: 679-685

British Columbia, Canada



Ronsley R et al. (2013). Canadian Journal of Psychiatry

RCT-supported evidence for SGA use in kids is LIMITED

- All SGA use in children in Canada is off-label*

Indication	Target Symptoms
Autism† and Pervasive Developmental Disorders	Irritability, Aggression
Bipolar I Disorder †	Manic or mixed episodes
Conduct Disorder	Aggression
Developmental Disabilities	Aggression, Self-injurious behaviour
Disruptive Behaviour Disorder	Conduct problems, Irritability, Hyperactivity, Aggression
Tourette Syndrome	Tics
Schizophrenia †	Positive and negative symptoms

*except for Aripiprazole for youth aged 15-17 with schizophrenia and 13-17 yo with manic/mixed episodes of BP I

† = FDA approvals

Panagiotopoulos et al. (2010), J Can Acad Child Adolesc Psychiatry. 19(2):124-37.

www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm094303.htm

For what symptoms and diagnoses are SGAs prescribed in kids in Canada?

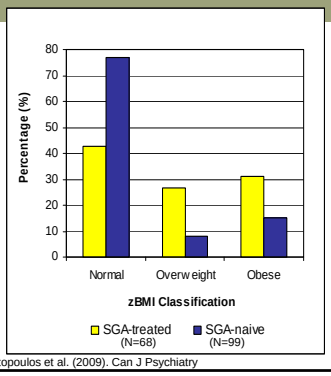
Percentage of prescribers by indication

Indication	%
Schizophrenia	**78.8**
Bipolar mood disorder	**81.8**
Depression	**30.0**
Tourette syndrome	**73.5**
Eating disorders	**25.0**
Obsessive-compulsive disorder	**52.3**
Posttraumatic stress disorder	**33.5**
Other anxiety disorders	**30.0**
Pervasive developmental disorder	**80.4**
Mental retardation	**48.2**
Attention-deficit hyperactivity disorder	**51.2**
Oppositional defiant disorder	**51.2**
Conduct disorder	**50.4**
Impulsivity	**65.3**
Poor frustration tolerance	**74.3**
Affective dysregulation	**84.7**
Insomnia	**35.9**

Survey of Canadian pediatricians and psychiatrists

Doey T et al. Canadian J of Psych (2007) 52: 363-368

Increased Risk of Overweight/Obesity



SGA-treated: 57.5%

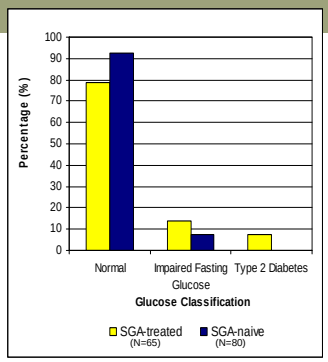
vs.

SGA-naïve: 23%

P<0.01 by Two-Way Chi Square

Panagiotopoulos et al. (2009). Can J Psychiatry

Increased Risk of Glucose Intolerance



SGA-treated: 21.5%

vs.

SGA-naïve: 7.5%

P=0.014 by Two-Way Chi Square Analysis

Panagiotopoulos et al. (2009). Can J Psychiatry

JAMA

Online article and related content current as of October 28, 2009.

Cardiometabolic Risk of Second-Generation Antipsychotic Medications During First-Time Use in Children and Adolescents

Christoph U. Correll; Peter Manu; Vladimir Olshanskiy; et al.

JAMA. 2009;302(16):1765-1773 (doi:10.1001/jama.2009.1549)

Nonrandomized Second-Generation Antipsychotic Treatment Indications, Effectiveness and Tolerability in Youth (SATIETY) cohort study

- Patients aged 4-19 years with 1 week or less of lifetime antipsychotic treatment
- 272 patients were included in analysis with a mean antipsychotic exposure time of 10.8 weeks

Mean Weight Gain (Kg)

SGA	Weeks 0-4	Weeks 0-8	Weeks 0-12
Olanzapine (n=45)	4.52*	6.68*	8.54*
Quetiapine (n=36)	2.87*	4.85*	6.06*
Risperidone (n=135)	2.72*	4.63*	5.34*
Aripiprazole (n=41)	1.61*	3.34*	4.44*
Untreated (n=15)	1.00	0.78	0.19

Correll, C. U. et al. JAMA 2009;302:1765-1773

BC Mental Health & Addiction Services

Mean Increase in Waist Circumference (cm)

SGA	Weeks 0-4	Weeks 0-8	Weeks 0-12
Olanzapine (n=45)	4.09*	6.79*	8.55*
Risperidone (n=135)	2.85*	4.60*	5.10*
Quetiapine (n=36)	2.74*	4.50*	5.27*
Aripiprazole (n=41)	2.20*	4.28*	5.40*
Untreated	0.84	0.94	0.70

Correll, C. U. et al. JAMA 2009;302:1765-1773.

BC Mental Health & Addiction Services

Transition to Overweight or Obesity

Weight gain	Total (N=272)	Olanzapine (n=45)	Risperidone (n=135)	Quetiapine (n=36)	Aripiprazole (n=41)	Comparison group (n=15)
≥7%	169 (62.1%)	38 (84.4%)	87 (64.4%)	20 (55.6%)	24 (58.4%)	0
≥14%	75 (27.6%)	23 (51.1%)	34 (25.2%)	11 (30.6%)	7 (17.1%)	0
≥21%	24 (8.8%)	11 (24.4%)	9 (6.7%)	2 (5.6%)	2 (4.9%)	0
Transition to OW or OB	47 (17.3%)	10 (22.2%)	19 (14.1%)	13 (36.1%)	4 (9.8%)	1 (6.6%)

BC Mental Health & Addiction Services

Prospective 12-month cohort study (n=37)

[Ronsley R. et al. Can J Psychiatry 2015]

Table 2 Change to anthropometric parameters at 6 and 12 months

	6 months		12 months	
Variable	Mean (95% CI)	*P*	Mean (95% CI)	*P*
Weight, kg				
All	7.9 (6.5 to 9.3)	<0.001	10.3 (8.1 to 12.4)	<0.001
Risperidone	8.6 (6.6 to 10.5)	<0.001	10.8 (7.9 to 13.7)	<0.001
Quetiapine	7.2 (5.1 to 9.2)	<0.001	9.7 (6.5 to 12.8)	<0.001
BMI kg/m^2				
All	2.81 (2.26 to 3.37)	<0.001	3.34 (2.52 to 4.16)	<0.001
Risperidone	2.90 (2.14 to 3.67)	<0.001	3.51 (2.40 to 4.62)	<0.001
Quetiapine	2.71 (1.90 to 3.52)	<0.001	3.14 (1.94 to 4.35)	<0.001
BMI *z* score				
All	0.68 (0.51 to 0.86)	<0.001	0.69 (0.45 to 0.93)	<0.001
Risperidone	0.75 (0.51 to 0.99)	<0.001	0.78 (0.45 to 1.11)	<0.001
Quetiapine	0.60 (0.35 to 0.85)	<0.001	0.59 (0.23 to 0.95)	<0.001
BMI percentile				
All	19.82 (14.39 to 25.26)	<0.001	19.70 (12.51 to 26.88)	<0.001
Risperidone	21.73 (14.24 to 29.22)	<0.001	22.85 (13.09 to 32.62)	<0.001
Quetiapine	17.69 (9.79 to 25.58)	<0.001	16.16 (5.55 to 26.76)	<0.001
WC, cm				
All	8.8 (6.8 to 10.9)	<0.001	10.3 (8.0 to 12.7)	<0.001
Risperidone	10.8 (7.9 to 13.6)	<0.001	11.5 (8.1 to 14.8)	<0.001
Quetiapine	6.9 (4.0 to 9.8)	<0.001	9.1 (5.9 to 12.4)	<0.001

Prospective 12-month cohort study (n=37)

[Ronsley R. et al. Can J Psychiatry 2015]

Table 4 New-onset metabolic complications identified at 6 and 12 months

	Incidence, *n*/*N*[a] (%)	
Variable	6 months	12 months
Overweight or obese		
All	10/29 (34.5)	13/29 (44.8)
Risperidone	5/15 (33.3)	6/15 (40.0)
Quetiapine	5/14 (35.7)	7/14 (50.0)
WC ≥ 90th percentile		
All	6/27 (22.2)	6/27 (22.2)
Risperidone	3/14 (21.4)	3/14 (21.4)
Quetiapine	3/13 (23.1)	3/13 (23.1)

BC Mental Health & Addiction Services

Original Investigation

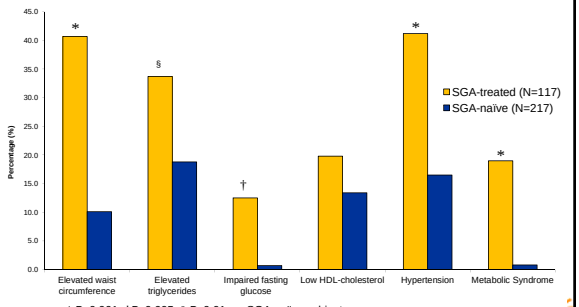
Antipsychotics and the Risk of Type 2 Diabetes Mellitus in Children and Youth

JAMA Psychiatry Published online August 21, 2013

William V. Bobo, MD, MPH; William O. Cooper, MD, MPH; C. Michael Stein, MB, ChB; Mark Olfson, MD, MPH; David Graham, MD, MPH; James Daugherty, MS; D. Catherine Fuchs, MD; [illegible]

3-fold increase risk of type 2 diabetes in SGA users!

Increased Prevalence of the Metabolic Syndrome and its Components



* *P*<0.001 †*P*=0.005 § *P*=0.01 *vs.* SGA-naïve subjects

Panagiotopoulos et al. (2012). Can J Psychiatry

Role of Genetic Polymorphisms

Citation: Transl Psychiatry (2012) 2, e71; doi:10.1038/tp.2011.68

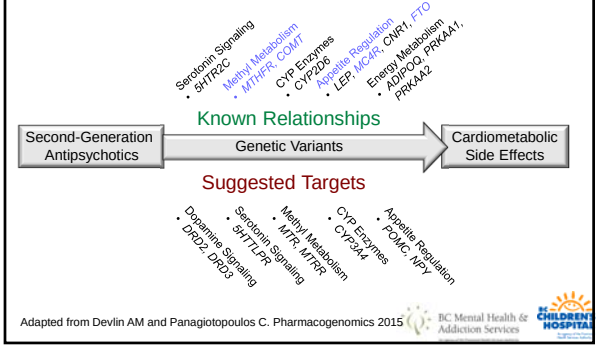
www.nature.com/tp

Cardiometabolic risk and the *MTHFR* C677T variant in children treated with second-generation antipsychotics

AM Devlin, YF Ngai, R Ronsley and C Panagiotopoulos

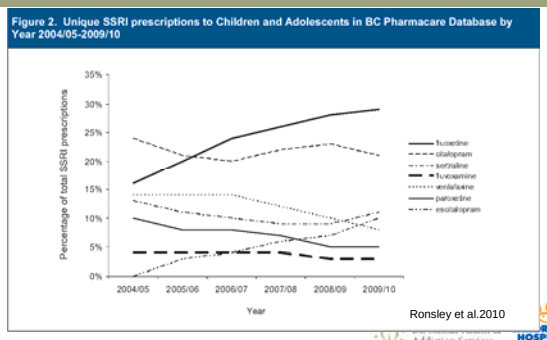
- MTHFR T allele is associated with risk for cardiovascular disease, and features of MetS in adults without psychiatric illness
- In a separate cohort, we demonstrated that the T allele was associated with a **6-fold** increased odds ratio of metabolic syndrome in SGA-treated children

Gene Variants that may Predict Obesity/Metabolic Risk in SGA-Treated Children



Adapted from Devlin AM and Panagiotopoulos C. Pharmacogenomics 2015

Prescription rates of SSRIs in pediatric patients



Ronsley et al.2010

Adults: SSRIs and Obesity/ Metabolic effects

- Treatment associated with
  - Obesity (OR 1.38, 95% CI 1.03-1.87) [Reader et al. 2006]
  - Abdominal obesity (OR 1.40, 95% CI 1.08-1.81) [Reader et al. 2006]
  - Hypercholesterolemia; (OR 1.36, 95% CI 1.07-1.73) [Reader et al. 2006]
  - Hypertriglyceridemia [Kesim et al., 2011]
  - Increased serum insulin [Kesim et al., 2011]
  - Type 2 diabetes (HR 1.10, 95% CI 1.00-1.22) [Pan et al., 2012]
- Interpretation complicated by the fact that depression is independently associated with metabolic complications (Takeuchi,T. 2009; Pyykkonen,A.J. 2012)

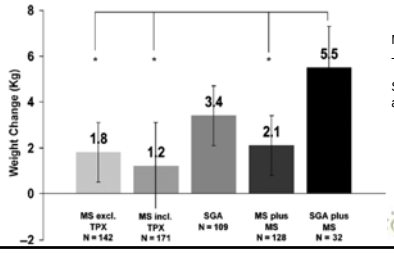
SSRIs and Obesity/metabolic complications in Children

- Current published data are limited in adolescents
- Short-term prospective study observed a significant decrease of weight after 19-week fluoxetine therapy (1.2 kg ± 2.7 vs. 2.3 kg ± 2.6; p = 0.008) (Nilsson et al. 2004)
- Prospective 24-week RCT in treatment-resistant depression found increase in BMI and weight gain was greater in those treated with SSRIs, particularly paroxetine and citalopram, compared with those treated with either venlafaxine or fluoxetine. (Mansoor et al. 2013)

Mood stabilizers and weight gain in children with bipolar disorder

- Systematic review of 19 short-term studies including 24 medication trials in 684 patients
- Weight gain observed in 18 (75%) of trials; weight loss only seen in 2 studies of TPX

Correll C. J Am Acad Child Adolesc Psychiatry. 2007.



MS: mood stabilizer

TPX: topiramate

SGA: second-generation antipsychotic

BC Mental Health & Addiction Services

BC Children's Hospital

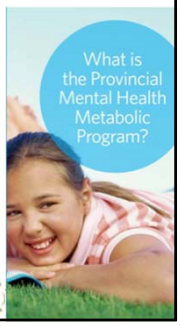
Treatment/Prevention of Obesity in Children with Mental Illness treated with Psychotropics

BC Mental Health & Addiction Services

BC Children's Hospital

Provincial Mental Health Metabolic Program in BC

- Provides specialized care to children and youth with mental health disorders who are at risk for, or are experiencing obesity and metabolic side effects associated with the use of psychotropics.
- Multidisciplinary team includes a pediatric endocrinologist, child and youth psychiatrist, nurse practitioner, dietitian, physiotherapist
  - Lifestyle counselling/freq contact/support



Healthy Living Toolkit for Professionals

- The Healthy Living Toolkit for Professionals addresses how to help families make changes to eating, physical activity, sleep and stress management in the context of MH condition.
- Modules include:
  - Getting Started (a suggested approach to using the toolkit)
  - Healthy eating
  - Physical activity
  - Sleep
  - Stress management

http://keltymentalhealth.ca/toolkits

Healthy Living Toolkit for Professionals

- Sections include:
  - Key Messages
  - Discussing Healthy Living with Children and Youth
  - Addressing Challenges to Healthy Living
  - Medications and their Effects on Healthy Living
  - Resources and Handouts

SMART Goal Setting

- SMART goal setting has been found to help children maintain focus and provides structure in changing behaviour

Setting S.M.A.R.T. Goals:

S: Specific (What do you want to do?)

M: Measurable (How much and how often?)

A: Action Plan (How will you do it?)

R: Realistic (Can you do it? 1-10 Scale)

T: Timely (When will you do it/review it?)

BC Mental Health & Addiction Services

BC CHILDREN'S HOSPITAL

Healthy Living Toolkit Instructional Videos

5 videos produced to demonstrate SMART Goal-Setting using the Healthy Living Toolkits

Family Toolkit:
- **Physical Activity**
- **Healthy Eating**

http://keltymentalhealth.ca/toolkit-families

Professionals Toolkit:
- **Physical Activity**
- **Nutrition**
- **Sleep**

http://keltymentalhealth.ca/toolkit-professionals

Healthy Living Toolkit for Families

- Developed in partnership with The F.O.R.C.E. Society for Kids' Mental Health

  The F.O.R.C.E. (Families Organized for Recognition and Care Equality) is a non-profit, BC-based organization that aims to support and empower families and work collaboratively with professionals and systems in understanding and meeting the mental health needs of families.
- Information is consistent with the Healthy Living Toolkit for Professionals

http://keltymentalhealth.ca/toolkits

Translation: FA FR KO PA SC TC

Patient & Family Guide to Second-Generation Antipsychotics

http://www.bcchildrens.ca/our-services/mental-health-services/metabolic-program

Metabolic Assessment, Screening & Monitoring Tool


METABOLIC ASSESSMENT, SCREENING AND MONITORING TOOL

P1


P2

Program Evaluation

Table 2. Change in Anthropometric, Laboratory, Physical Activity, and Nutrition Parameters for those Elevated or Abnormal at First Clinic Visit

Variables	n	Median (95% CI) Baseline (First Visit)	Median (95% CI) Follow-up (Last Visit)	p
Overweight or Obese				
BMI z-score	180	2.54 (2.27, 2.70)	2.51 (2.34, 2.75)	**0.005**
WC z-score		1.70 (1.61, 1.78)	1.66 (1.53, 1.76)	**0.001**
High WC (WC ≥ 90th Percentile)				
BMI z-score	147	2.74 (2.61, 2.96)	2.78 (2.56, 2.91)	**0.016**
WC z-score		1.86 (1.74, 1.92)	1.78 (1.68, 1.84)	**0.010**
IFG (FG ≥ 5.7 mmol/L)				
Fasting Glucose, mmol/L	46	5.9 (5.8, 6.4)	5.2 (5.0, 5.4)	**< 0.001**
Fasting insulin				
Insulin, µU/L	232	104.0 (93.1, 118.0)	120.0 (104.2, 142.5)	0.382
Prolactin (PRL > 20 mmol/L)				
Prolactin, mmol/L	134	36.8 (29.1, 45.9)	13.2 (10.3, 19.1)	**< 0.001**
High LDL (LDL ≥ 2.85 mmol/L)				
LDL, mmol/L	102	3.3 (3.2, 3.5)	3.1 (2.9, 3.3)	**0.003**
Low HDL (HDL ≤ 1.03 mmol/L)				
HDL, mmol/L	78	0.9 (0.9, 1.0)	1.0 (0.9, 1.0)	**0.014**
High Triglycerides (≥ 1.7 mmol/L)				
Triglycerides, mmol/L	80	2.2 (2.2, 2.4)	1.6 (1.4, 1.8)	**< 0.001**
High Cholesterol (≥ 4.4 mmol/L)				
Total Cholesterol, mmol/L	130	5.2 (5.0, 5.3)	4.8 (4.6, 5.0)	**< 0.001**

Program Evaluation

Variables	Median (95% CI) Baseline (First Visit)	Median (95% CI) Follow-up (Last Visit)	p
Physical Activity Parameters			
Estimated VO_2 Peak	31.0 (29.8, 33.0)	33.4 (31.2, 35.9)	**0.004**
Screen Time per week, minutes	1,260 (853, 1,260)	1,260 (1,260, 1,564)	0.312
Activity per week, minutes	182 (150, 210)	240 (195, 272)	**0.002**
Nutrition Parameters			
# of SSB Consumed per week, time	3 (2, 7)	1 (1, 2)	**0.012**
# of Fast Food Eaten per week, time	0.5 (0.5, 1.0)	0.5 (0.5, 1)	0.276
# of Breakfast Eaten per week, time	7 (7, 7)	7 (7, 7)	0.880
Client Service Plan Sent, No. (%)	105 (43.2)	179 (74.6)	**< 0.001**
Healthy Living Goal Set, No. (%)	205 (84.4)	193 (80.8)	0.296

BC Mental Health & Addiction Services

Metformin

Studies limited by short duration of follow-up, small subject numbers, and variability in SGA-treatment

Klein et al. (2006): double blind randomized study:

- improvement in weight, BMI z-score, insulin sensitivity in patients (on olanzapine, risperidone or quetiapine) treated with metformin over 16 weeks

Arman et al. (2008): double blind, randomized study:

- mean weight and BMI improved in risperidone treated patients over first 4 weeks compared with placebo but no difference by 12 weeks

Morrison et al. (2002): open label, prospective cohort study

- 15/19 patients lost weight on metformin over 12 weeks

Shin et al. (2009): open label, prospective cohort study

- no weight loss while treated with metformin but no further weight gain

Other medications

Systematic review (Maayan, Vakhrusheva & Correll 2010) of 32 studies and 15 different medications used in the management of weight gain

- Total number of patients was small, and only 5 medications demonstrated small weight loss when compared to placebo:
  - Metformin (n=334)
  - D-fenfluramine (n=16)
  - Sibutramine (n=55)
  - Topiramate (n=133)
  - Reboxetine (n=79)
- Insufficient evidence to support routine clinical usage of these agents

Summary

- There is a complex inter-relationship between psychiatric illness and obesity/metabolic co-morbidities modulated by
  - Individual mental health condition
  - Chronic stress
  - Lifestyle risk factors (poor nutrition, physical inactivity, poor sleep, smoking)
  - Genetics
  - Psychotropic medication side-effects
- Clinicians need to be aware of these health risks so that they can monitor and pro-actively counsel and treat their patients for these co-morbidities to prevent increased morbidity and mortality from diabetes and cardiovascular disease

Thank you!

Questions or Comments?

Dr. Dina Panagiotopoulos:
dpanagiotopoulos@cw.bc.ca

BC Mental Health & Addiction Services

BC Children's Hospital