The 5As of Pediatric Obesity Management

CHEO’s Centre for Healthy Active Living
There is no wrong way to have a body

All bodies are unique and essential. All bodies are whole. All bodies have strengths and needs that must be met. We are powerful not despite the complexities of our bodies but because of them. We move together, with no body left behind.

Aurora Levins Morales and Patty Berne
Disability and health activists

Moving together with our differences, that’s when we can really make important change
Living with Obesity

• Your body is ALWAYS worthy of care

• Your body is ALWAYS worthy of intervention when it is in trouble

• Your body is NOT taking up too much space

• Nikki Masse (Living with Obesity)
Objectives

• Introduce the 5As of Pediatric Obesity Management

• Review the 4Ms Framework for the assessment of obesity related complications, root causes of obesity, drivers of weight gain and barriers to weight management

• Apply the Edmonton Obesity Staging System for Pediatrics to better determine health risk and health care needs in pediatric obesity assessment and management
Disclosures

• Faculty: Stasia Hadjiyannakis

• Relationships with commercial interests:
  • NovoNordisk, Honorarium for invited lecture
  • Rhythm Pharmaceuticals: Advisory Board

• This program has received financial support from the Ministry of Health
5As Framework for Obesity Management

Arya M. Sharma, MD/PhD, FRCPC
Scientific Director & CEO
Canadian Obesity Network

5As of Pediatric Obesity Management

Canadian Obesity Network

Canadian Obesity Network
Centre for Healthy Active Living
Key Principles
Key Principles

Obesity Management is About Improving Health and Well-being, and not Simply Reducing Numbers on the Scale
Key Principles

Weight bias can be a barrier to weight management
Key Principles

Interventions should include addressing ‘root causes’ of obesity and removing roadblocks for families to make healthy changes.
Key Principles

A Child’s ‘Best’ BMI May Never Be His or Her ‘Ideal’ BMI
Key Principles

Success is different for every child and family
WHO Definition:

Overweight and obesity are defined as abnormal or excessive fat accumulation that presents a risk to health. A crude population measure of obesity is the body mass index (BMI)
Obesity is Defined as BMI > 95th%
# Obesity Class

<table>
<thead>
<tr>
<th>Classification</th>
<th>CDC</th>
<th>WHO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>95th to 120% of 95th%</td>
<td>Z- Score +2 to 3</td>
</tr>
<tr>
<td>Class II*</td>
<td>120 to 140% of 95th%</td>
<td>Z- Score +3 to 4</td>
</tr>
<tr>
<td>Class III*</td>
<td>Greater than 140% of 95th%</td>
<td>Z-Score greater than 4</td>
</tr>
</tbody>
</table>

*severe obesity
Expanded BMI Curve
Limitations of BMI Classification Systems

Jeff
12 y/o, BMI 32 kg/m²
Excels in school, has many friends. Active with hockey and soccer. Has supportive parents. Has no biochemical or clinical evidence of weight related health complications.

Aaron
12 y/o, BMI 32 kg/m²
Has ADHD and a non-verbal learning disability. Is being bullied at school and has few friends. He has type 2 diabetes. Lives in unsafe neighbourhood with limited opportunities for play.
Edmonton Obesity Staging System

- Risk-stratification system that classifies adults with obesity into 5 graded categories based on morbidity and health-risk profiles

- EOSS independently predicted increased mortality even after adjustment for common methods of classifying obesity
Survival Curves diverge when stratified by EOSS score but not BMI Class.
<table>
<thead>
<tr>
<th>Stage</th>
<th>Metabolic</th>
<th>Mechanical</th>
<th>Mental</th>
<th>Milieu</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No metabolic abnormalities</td>
<td>No functional limitations</td>
<td>No psychopathology</td>
<td>No parental, familial or social environment concerns</td>
</tr>
<tr>
<td>1</td>
<td>Sub-clinical risk factors (Acanthosis Nigricans, pre-hypertension, IFG/IGT, mild lipid abnormalities, mild elevation in transaminases, mild to moderate fatty infiltration of liver)</td>
<td>Mild OSA not requiring PAP therapy, mild MSK pain and/or dyspnea not interfering with ADL</td>
<td>Mild psychopathology, ADHD, LD, mild body image pre-occupation, occasional emotional/binge eating, bullying, mild developmental delay</td>
<td>Minor problems in relationships, minor limitations in caregivers ability to support child’s needs</td>
</tr>
<tr>
<td>2</td>
<td>Type 2 Diabetes, Hypertension, moderate lipid abnormalities, moderate elevation of transaminases and/or severe fatty infiltration of liver, PCOS, asymptomatic gall stones</td>
<td>OSA requiring PAP therapy, GERD, MSK pain limiting activity, moderate limitations in ADLs</td>
<td>Major depression, anxiety, school absenteeism, frequent binging, significant bullying (school or home), significant body image disturbance, moderate developmental delay</td>
<td>Moderate problems in relationships, significant limitations in caregivers ability to support child’s needs</td>
</tr>
<tr>
<td>3</td>
<td>Uncontrolled T2DM (+/- complications), hypertension, FSGS, markedly elevated liver enzymes and/or liver dysfunction, symptomatic gall stones, marked lipid abnormalities</td>
<td>OSA requiring PAP therapy and suppl. oxygen, limited mobility, shortness of breath sitting/sleeping</td>
<td>Uncontrolled psychopathology, school refusal, daily binge eating, severe body image disturbance</td>
<td>Severe problems in relationships, caregivers unable to support child’s needs - may include exposure to family violence, dangerous environment (home, neighbourhood, school</td>
</tr>
</tbody>
</table>
EOSS-P

Impact of Genetics

- 50 – 90% of our risk for obesity comes from our genes
  - Some people are at greater risk for developing obesity and some are at less risk

- Epigenetic Changes:
  - Pregnancy and birth factors
  - Gut microbiome/exposure to antibiotics
  - Trauma (intergenerational)
  - Environmental exposures
Sensitivity to weight promoting environments and behaviours modified through genetic and pre-natal programming

Beyerlein et al, PLoS one (2011)
Neuroendocrine Control of Energy Balance

Science, Feb 7, 2003
Additional weight loss can only be achieved by a more severe diet and further increases in physical activity.
## Expected changes in weight

<table>
<thead>
<tr>
<th>Change in weight</th>
<th>Lifestyle</th>
<th>Medication</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 5%</td>
<td>2 to 15%</td>
<td>20 to 40%</td>
<td></td>
</tr>
</tbody>
</table>

ASK for Permission to Discuss Weight

ASSIST in addressing drivers & barriers, offer education & resources, refer to provider, and arrange follow-up

ASSESS obesity related risk and potential ‘root causes’ of weight gain

AGREE on a realistic SMART plan to achieve health behaviour outcomes

ADVISE on obesity risks, discuss benefits & options
Weight is a sensitive issue. Many children and parents may be embarrassed or fear blame and stigma, so ‘asking’ is an important first step.
When ASKing...

• Do you have any concerns about your/your child’s health?

• Do you have any concerns about your/your child’s weight?
  • What are your concerns about your/your child’s weight?
  • How does your/your child’s weight impact you/them?
ASSESS obesity related risk and potential ‘root causes’ of weight gain
Create a Weight-Friendly Practice

• **Facilities:** wide doors, large restrooms, floor-mounted toilets

• **Scales:** over 350lb/160kg, wheel-on accessible, located in private area and used with sensitive weighing procedures

• **Waiting room:** sturdy, armless chairs, appropriate reading material – no glossy fashion magazines

• **Exam room:** appropriate-sized gowns, wide and sturdy exam tables, extra-large blood pressure cuffs, longer needles and turniquets, long-handled shoe horns
Obesity Class
BMI for age percentiles

Obesity Stages (EOSS-P*)

0 No Apparent Risk Factors
1 Subclinical Risk Factors
2 Chronic Disease
3 Uncontrolled Chronic Disease

* Edmonton Obesity Staging System - Pediatrics
Etiology of Pediatric Obesity

**Endocrine**
- Low growth velocity
- Hypothyroidism
- Growth Hormone Deficiency
- Cushing’s Syndrome

**Monogenic**
- Obesity onset before 6 months of age
  - Increased appetite
- MC4R defect/Leptin deficiency

**Genetic Syndrome**
- Dysmorphic features
- Neurocognitive delay
- Prader Willi Syndrome
- Bardet Biedl Syndrome
- Alstrom

**CNS/hypothalamic damage**
- Hypothalamic obesity
- Increased appetite
- Decreased energy expenditure
- Hypopituitarism

**Acquired/Polygenic***
- Normal or increased growth velocity
- Highly heritable
- Intrauterine exposures

*most common form of pediatric obesity

ASSESS
The 4 M’s of Pediatric Obesity

Mental
- Anxiety
- Depression
- Body image
- ADHD
- Learning disorder
- Sleep disorder
- Eating disorder
- Trauma

Mechanical
- Sleep apnea
- MSK pain
- Reflux disease
- Stress incontinence
- Encopresis
- Intertrigo

Metabolic
- IGT/T2DM
- Dyslipidemia
- Hypertension
- Fatty liver
- Gallstones
- PCOS
- Medication
- Genetics

Milieu
- Parent health/disability
- Family stressors
- Family income
- Bullying/Stigma
- School attendance
- School support
- Neighbourhood safety
- Medical insurance
- Accessible facilities
- Food Environment
- Opportunities for physical activity
| Stage 0 | Metabolic: No metabolic abnormalities  
Mechanical: No functional limitations  
Mental: No psychopathology  
Milieu: No parental, familial or social environment concerns |
| Stage 1 | Metabolic: Sub-clinical risk factors (Acanthosis Nigricans, pre-hypertension, IFG/IGT, mild lipid abnormalities, mild elevation in transaminases, mild to moderate fatty infiltration of liver)  
Mechanical: Mild OSA not requiring PAP therapy, mild MSK pain and/or dyspnea not interfering with ADL  
Mental: Mild psychopathology, ADHD, LD, mild body image pre-occupation, occasional emotional/binge eating, bullying, mild developmental delay  
Milieu: Minor problems in relationships, minor limitations in caregivers ability to support child’s needs |
| Stage 2 | Metabolic: Type 2 Diabetes, Hypertension, moderate lipid abnormalities, moderate elevation of transaminases and/or severe fatty infiltration of liver, PCOS, asymptomatic gall stones  
Mechanical: OSA requiring PAP therapy, GERD, MSK pain limiting activity, moderate limitations in ADLs  
Mental: Major depression, anxiety, school absenteeism, frequent binging, significant bullying (school or home), significant body image disturbance, moderate developmental delay  
Milieu: Moderate problems in relationships, significant limitations in caregivers ability to support child’s needs |
| Stage 3 | Metabolic: Uncontrolled T2DM (+/- complications), hypertension, FSGS, markedly elevated liver enzymes and/or liver dysfunction, symptomatic gall stones, marked lipid abnormalities  
Mechanical: OSA requiring PAP therapy and suppl. oxygen, limited mobility, shortness of breath sitting/sleeping  
Mental: Uncontrolled psychopathology, school refusal, daily binge eating, severe body image disturbance  
Milieu: Severe problems in relationships, caregivers unable to support child’s needs - may include exposure to family violence, dangerous environment (home, neighbourhood, school |

**EOSS-P: Edmonton Obesity Staging System – Pediatrics Staging Tool**
Jeff - 12 yo BMI 32 kg/m² - Class II Obesity

Mental
- No mood or anxiety concerns
- No learning difficulties or developmental concerns
- Positive body image
- No emotional or binge eating
  *Stage 0*

Mechanical
- No MSK concerns
- No symptoms of OSA
- No mobility difficulties
  *Stage 0*

Metabolic
- Normal blood pressure
- No Acanthosis Nigricans
- Normal blood sugars, A1C, lipid profile, liver enzymes
  *Stage 0*

Milieu
- Well supported at home and at school
- Good opportunities for activity
- Healthy home food environment
- No active familial stressors
  *Stage 0*

EOSS-P Stage 0
Aaron - 12 yo BMI 32 kg/m²- Class II Obesity

Mental
- ADHD
- Non-verbal learning disorder
  - *Stage 1*

Mechanical
- No MSK concerns
- No symptoms of OSA
- No mobility difficulties
  - *Stage 0*

Metabolic
- Type 2 Diabetes without complications
  - *Stage 2*

Milieu
- Significant bullying-leading to school refusal
- Socially isolated
- Unsafe neighbourhood
  - *Stage 3*

EOSS-P Stage 3
Oscar 15 yo, male, BMI 44 kg/m²

**Mental**
- ADHD (untreated)
- Nonverbal Learning Disability (stage 2)

**Mechanical**
- Sleep apnea non-adherent with BiPAP (stage 2)

**Metabolic**
- Type 2 Diabetes (A1C 12.2) (stage 2)
- Dyslipidemia (stage 3)

**Milieu**
- Combined family income (< $25000)
- Maternal type 2 diabetes complications
- Maternal eating disorder
- Bullied at school
- School refusal
- Frequent suspensions (stage 3)

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EOSS-P Stage 3
Obesity Complications, Barriers & Drivers - *OSCAR*

<table>
<thead>
<tr>
<th><strong>Metabolic</strong></th>
<th>Type 2 Diabetes with high A1C – 12.2 Dyslipidemia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanical</strong></td>
<td>OSA- non-adherent with BiPAP</td>
</tr>
<tr>
<td><strong>Mental Health</strong></td>
<td>ADHD (not on treatment), non-verbal LD</td>
</tr>
<tr>
<td><strong>Milieu</strong></td>
<td>School refusal- frequent suspensions, detentions, maternal diabetes with complications, maternal eating disorder, household income less than $25,000/year</td>
</tr>
<tr>
<td><strong>Drivers</strong></td>
<td>Skipped breakfast and lunch- with high hunger later in the day, Lack of formal meals and snacks, High Sweetened Beverage Consumption, Untreated ADHD, Insufficient Sleep</td>
</tr>
<tr>
<td><strong>Barriers</strong></td>
<td>Financial Limitations, Inadequately treated OSA, Untreated ADHD, Maternal Health and Mental Health Issues</td>
</tr>
</tbody>
</table>
### 4 Pillars of Lifestyle Interventions

| Mental Health | • Stress management  
|               | • Body image  
|               | • Self-confidence  
|               | • Manage mood & mental health |
| Nutrition     | • When, where & who we eat with  
|               | • Hunger management – keeping our bodies fueled  
|               | • Healthy relationship with food |
| Sleep         | • Regular sleep & wake time  
|               | • Good quantity & quality of sleep |
| Activity      | • Opportunities for organized & free play  
|               | • Manage screen time |

- Choose long-term strategies & sustainable behaviours
- Avoiding “quick-fixes”
Advise on Family-Based Management Options

Sleep
- Management interventions can significantly improve eating and activity behaviours as well as mood and school performance.

Eating Behaviours
- Should focus on eating & drinking hygiene. Extreme and “fad” diets are not sustainable in the long-term.

Physical Activity
- Interventions should aim at reducing sedentariness and increasing daily physical activity levels to promote fitness, overall health, and general well-being, rather than focusing on “burning calories”.
## Advise on Family-Based Management Options

<table>
<thead>
<tr>
<th><strong>Sedentary Behaviour</strong></th>
<th>• should be limited through minimizing recreational screen time to less than 2 hours per day, choosing active transportation over motorized, and increasing active play and active family time.</th>
</tr>
</thead>
</table>
| **Mental Health**       | • treatment referrals to help manage underlying /co-morbid psychological issues  
• interventions can improve body-esteem, self-esteem, reduce emotional eating, and promote coping strategies. |
| **Bariatric Surgery**   | • may be considered for adolescents who’ve reached their final adult height, with BMI>40, and with obesity related health complications. Candidates & their families are required to have completed a multidisciplinary 6-month presurgical intervention. |
Pharmacotherapy

Setmelanotide/Imcivree (FDA)

- Age 6 and older with:
  - POMC deficiency
  - PCSK1 deficiency (impaired POMC processing)
    - Obesity; malabsorptive diarrhea; hypogonadotrophic hypogonadism; altered thyroid and adrenal function
  - Leptin Receptor Deficiency
  - Bardet Biedl Syndrome
  - Outcomes: 80% lost more than 10% of their body weight
Pharmacotherapy (GLP-1 Agonists)

Liraglutide (3 mg sc daily) (FDA and Health Canada):
• Age 12-17, body weight of >60 kg; BMI > 30 kg/m2 or > 27 kg/m2 with at least one weight related comorbidity
• Reduction in BMI of at least 5% in 45%

Semaglutide 2.4 mg sc weekly – (FDA Approval)
• Age 12-17, body weight of >60 kg; BMI > 30 kg/m2 or > 27 kg/m2 with at least one weight related comorbidity
• Mean change in BMI 16.1%
• A BMI reduction of at least 5% in 77%
Pharmacotherapy in Canada

• Liraglutide/Saxenda/Victoza (GLP-1 agonist)- Approved for 12 + years of age for weight management and 18+ years of age for T2DM
• Semaglutide/Ozempic/Wegovy- (GLP-1 agonist)- Approved for 18 + years of age for weight management and Type 2 Diabetes
• Naltrexone-bupropion/Contrave- Approved for 18 + years of age for weight management
• Orlistat/Xenical- Approved for 12 + years of age for weight management
Bariatric Surgery
Bariatric Surgery

• BMI greater than 35 kg/m² - clinically significant complications (OSA; T2DM; IIH, NAFLD, Blount Disease, SCFE, GERD, HTN)
• BMI greater than 40 kg/m²
• Outcomes (3 years):
  • 29% reduction in weight (mean 8 year follow up)
  • 95% resolution of T2DM
  • 74% resolution of HTN
  • 66% resolution of dyslipidemia
• Complications
  • Mortality – 0.3%
  • Minor surgical complications – 15%
  • Major surgical complications - 8%
  • Micronutrient deficiencies- (Fe – 66%; B12 8%; folate 6%)
AGREE on realistic weight-loss expectations and on a SMART plan to achieve behavioural goals

ASSIST in addressing drivers & barriers, offer education & resources, refer to provider, and arrange follow-up
• Agree on Behaviour Change Outcomes

• Agree on Sustainable Behavioural Goals and Health Outcomes

• Agree on Management Plan
ASSIST

• Assist Families in Identifying and Addressing Drivers and Barriers

• Provide Education and Resources

• Refer to Appropriate Provider

• Arrange Follow-Up
Conclusions

• Obesity is a heterogeneous, chronic, often treatment resistant disease

• A comprehensive assessment of Obesity related complications, drivers and barriers is essential in order to guide an effective management plan
5As Team

- Stasia Hadjiyannakis MD, FRCPC
- Annick Buchholz, PhD, CPsych
- Laurie Clark, PhD, CPsych
- Jane Rutherford, MSc
- Geoff Ball, PhD, RD
- Tracey Bridger, MD, FRCPC
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- Arya Sharma, MD, PhD, FRCPC
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- Kristi Adamo, PhD
- Jane Rutherford, MSc
- Laurie Clark, PhD
- Katie Baldwin, MD
- Charmaine Mohipp, MA
- Mary Ann Matzinger, MD
- Franco Momoli, PhD
Questions?
Liraglutide in youth with obesity

<table>
<thead>
<tr>
<th></th>
<th>Liraglutide (3.0 mg) + Lifestyle Therapy</th>
<th>Placebo + Lifestyle Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>125</td>
<td>126</td>
</tr>
<tr>
<td>Change in BMI standard-deviation score at 56 wk</td>
<td>−0.23±0.05</td>
<td>−0.00±0.05</td>
</tr>
<tr>
<td>Estimated treatment difference, −0.22; 95% CI, −0.37 to −0.08; P=0.002 in favor of liraglutide</td>
<td>64.8% P&lt;0.001</td>
<td>36.5%</td>
</tr>
</tbody>
</table>

A.S. Kelly et al. 10.1056/NEJMoa1916038

The NEW ENGLAND JOURNAL of MEDICINE

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GLP-1 Activity
Health Canada Approval - Feb, 2021

Saxenda

- Age 12-17, body weight of >60 kg; BMI > 30 kg/m² or > 27 kg/m² with at least one weight related comorbidity
- Reduction in BMI of at least 5% in 45%
- Side effects:
  - Nausea
  - Diarrhea
  - Constipation
- Contraindications
  - Family history of medullary thyroid carcinoma or MEN2
  - Past history of pancreatitis
Socio-Demographic factors

Childhood Obesity Rates and Trends

Obesity rates by race, ethnicity and household income among youth ages 10-17 nationwide:

- American Indian/Alaska Native: 28.7%
- Black: 23.8%
- Hispanic: 21.4%
- White: 12.1%
- Asian: 8.1%
- Lowest income: 23.1%
- Highest income: 8.6%
GENE-Environment interaction

**Socio-biological pathways**

**Structural**: Aspects of social organisation that disadvantage a proportion of the population and negatively affect their health OR confer advantage and benefit health (e.g., distribution of wealth, quality of housing stock, distribution of medical care)

**Behavioural**: Habits/behaviours related to health and are subject—albeit via constrained choice—to individual decision-making (structure/agency).

**Inter-personal**: Aspects of social interaction, social participation, social integration and social support.

**Material**: Living (bacteria, viruses) and inert (asbestos, folic acid) materials which that impact body’s structure and immune system. Can be beneficial or pathological.

**Psycho-social**: Social events and circumstances that trigger physiological effects via neurological and hormonal pathways from perception and emotions to the central nervous system.

**Epigenetic**: Ability of the social environment to trigger or suppress gene expression and activation.

(Blane et al., 2013)
Body weight is regulated by THE BRAIN

Appetite Control: The Brain

We all inherit a unique appetite system which evolved to protect us when food was scarce.
We cannot think ourselves LESS HUNGRY or MORE FULL.

REWARD OF FOOD
- Mesolimbic Reward Pathway
- Mediates Reward, Desire & Drive for activities needed to survive
- Responds to triggers: environment emotions, smell/sight, memory etc
- “Craving/Wanting”

DECISION MAKING (EXECUTIVE FUNCTION)
- Prefrontal Cortex
- Attention, Planning, Impulse Control, Problem Solving
- Juggling multiple tasks
- Integrates Thoughts & Feelings into Behaviours
- Decides when/what to eat

BODY HUNGER (HOMEOSTATIC EATING)
- Hypothalamus - regulates Energy Balance
- Controls Hunger & Fullness
- Responds to peripheral signals (hormones)
- Instinctive/Unconscious
- Defends against Weight Loss & Encourages Weight Regain (Set Point)

DOPAMINE RECEPTORS control the motivation to eat
OPIOID and CANNABINOIDS RECEPTORS control the pleasure associated with food

LEPTIN from fat cells decreases hunger
GHRELIN from stomach increases hunger
GLP-1 and CCK from the gut increase satiety

www.mybestweight.ie
Liraglutide in youth with T2DM
<table>
<thead>
<tr>
<th>Disorder</th>
<th>Description</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanocortin receptor 4</td>
<td>Most common monogenic form of obesity (5%) of those with severe obesity</td>
<td>Increased linear growth; hyperphagia</td>
</tr>
<tr>
<td>Leptin receptor</td>
<td>2-3% of infant severe obesity in consanguineous families</td>
<td>Hyperphagia; early onset obesity; immune dysfunction; central hypothyroidism; hypogonadotropic hypogonadism</td>
</tr>
<tr>
<td>Leptin deficiency</td>
<td>1% of infant severe obesity in consanguineous families</td>
<td>Responds to leptin</td>
</tr>
<tr>
<td>POMC mutations</td>
<td>Loss of melanocortin signaling, ACTH and MSH deficiency</td>
<td>Adrenal crisis; pale/red hair</td>
</tr>
<tr>
<td>PCSK1 mutation</td>
<td>Unable to activity POMC, TRH, proinsulin, proglucagon, proGnRH</td>
<td>Small bowel enteropathy, FTT in infancy; severe obesity and multiple endocrinopathies</td>
</tr>
<tr>
<td>SIM1 mutations</td>
<td>Transcription factor in PVN</td>
<td>Hyperphagia; subset with ASD</td>
</tr>
<tr>
<td>Brain Derived Neurotrophic factor (BDNF)</td>
<td>Unclear mechanism</td>
<td>Severe obesity; neurocognitive delay</td>
</tr>
<tr>
<td>16p11.2 deletion</td>
<td>Involved in leptin and insulin signaling</td>
<td>Developmental delay; ASD; severe obesity; severe insulin resistance</td>
</tr>
<tr>
<td>6q16 deletion</td>
<td>Impact SIM1</td>
<td>PWS like; hypopit; severe obesity</td>
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