Pathways to Eating in Children and Adolescents with Obesity

by

Hayyah Clairman

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Abstract

Objective: To determine whether treatment-seeking children and adolescents with obesity cluster into phenotypes based on known eating drivers and whether phenotypes can be distinguished based on clinical characteristics.

Methods: Latent Profile Analysis was used to cluster participants based on seven eating driver scores obtained from questionnaires. Analysis of variance was used to determine phenotype differences on clinical variables.

Results: Seven eating drivers clustered into three distinct phenotypes, namely: 1) loss of control eating, impulsivity, inattention (named LOCE-ADHD), 2) No elevated drivers (named No-ED), and 3) loss of control eating, emotional eating, external eating, restrained eating, hyperphagia (named Restrained-Triggered). LOCE-ADHD was younger, non-White, ate out or ordered in meals less frequently, and had lower BMI, decreased social functioning, and fewer diagnoses of depression than the other groups. Restrained-Triggered had the lowest body esteem.

Conclusions: Distinct eating phenotypes are found in youth with obesity that should be considered in treatment approaches.

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List of Abbreviations

AB	Alberta
aBIC	Sample size adjusted Bayesian Information Criterion
ADHD	Attention deficit hyperactivity disorder
AgRP	Agouti-related protein
AIC	Akaike Information Criterion
ANOVA	Analysis of variance
aOR	Adjusted odds ratio
BC	British Columbia
BESAA	Body Esteem Scale for Adolescents and Adults
BIC	Bayesian Information Criterion
BLRT	Bootstrap likelihood ratio test
BMI	Body mass index
CANPWR	CANadian Pediatric Weight-management Registry
CART	Cocaine- and amphetamine-regulated transcript
CCK	Cholecystokinin
CH	Children's Hospital
CHEO	Children's Hospital of Eastern Ontario
CI	Confidence interval
CIHR	Canadian Institutes of Health Research
CNS	Central nervous system
CRF	Case report form
DEBQ	Dutch Eating Behaviours Questionnaire
DEBQ-C	Dutch Eating Behaviours Questionnaire for Children
EAH	Eating in the Absence of Hunger
EDE	Eating Disorders Examination
EDE-Q	Eating Disorders Examination Questionnaire
GLP-1	Glucagon-like peptide-1
HQ	Hyperphagia Questionnaire
IPT	Interpersonal psychotherapy

LOCE	Loss of control eating
LPA	Latent profile analysis
NPY	Neuropeptide Y
ON	Ontario
POMC	Pro-opiomelanocortin
PVN	Paraventricular nucleus
PWS	Prader-Willi Syndrome
PYY	Peptide YY
QC	Quebec
SD	Standard deviation
SES	Socioeconomic status
SickKids	The Hospital for Sick Children
SNAP-IV	Swanson, Nolan, and Pelham-IV scale
SSRI	Selective serotonin reuptake inhibitor
STOMP	SickKids Team Obesity Management Program
SWAN	Strengths and Weaknesses of ADHD Symptoms and Normal Behaviour Scale
TFEQ	Three-Factor Eating Questionnaire
WHO	World Health Organization

Chapter 1 Introduction and Literature Review

1.1 Obesity Prevalence and Comorbidities

For over 15 years, the World Health Organization (WHO) has recognized obesity as a global health epidemic (Vandevijvere et al., 2015; WHO, 2000). In Canada, among children and adolescents aged 6-17 years, 13.1% were reported to be obese in 2013 (Rao et al., 2016) and in the United States, the prevalence in this age group was an alarming 20.5% (Ogden et al., 2016). While prevalence rates of overweight and obesity in children and adolescents aged 2 to 19 years seem to have plateaued in recent years, the prevalence of severe obesity in this age group has increased (Kumar and Kelly, 2017). The accumulation of excess body weight has become a significant economic and social burden because of associated medical and psychosocial consequences that can appear during childhood and persist into adulthood. These comorbidities include type 2 diabetes, sleep apnea, dyslipidemia and cardiac disease, hypertension, cancer, stroke, non-alcoholic fatty liver disease, musculoskeletal complications, eating disorders, anxiety, depression, and lower health-related quality of life (Kumar and Kelly, 2017; Yanovski, 2015).

Young adults with obesity require continual medical treatment for on-going and newly developed comorbidities, which may accrue over a lifetime (Lobstein et al., 2004). Despite the recent growth in weight-management programs for children and adolescents, current intervention models focus on very general (“one size fits all”) recommendations to modify nutritional intake and physical activity. In reality, however, variation exists in the underlying causes of obesity and, in particular, eating-related behaviours, and individualization of treatment should reflect this complexity. Health care providers require screening tools to assist them in

recognizing the various eating traits and behaviours that may underpin a child's excess weight gain (Wilfley, Vannucci, and White, 2010).

In individuals with obesity, common drivers of overeating that have been described include loss of control eating, emotional eating, response to external cues, restrained eating, hyperphagia, impulsivity, and inattention (Anderson et al., 2016; He, Cai, and Fan, 2017; Thamotharan et al., 2013; Braet et al., 2008; Fisher et al., 2007). Overall, however, research in pediatric obesity in this area remains extremely limited. Further understanding of the factors driving overeating in children and adolescents is needed to better understand the design and response of new approaches to treatment in this age group.

1.2 Appetite Regulation

Food intake in humans is regulated by an extremely complex interplay of physiological, environmental, and behavioural (both conscious and subconscious) factors (Farr, Li, and Mantzoros, 2016; Faulconbridge and Hayes, 2011; Hopkins et al., 2000). Eating is subject to feedback control from homeostatic, hedonic, and cognitive processes. The homeostatic system can be defined as the neural and hormonal pathways that regulate and maintain energy balance. In contrast, hedonic pathways are activated in response to the anticipated pleasure of eating, irrespective of energy status. Furthermore, cognitive processes of the brain's frontal lobe are involved in initiating or refraining from food consumption. In obesity, internal satiety cues may be dysregulated or otherwise overcome by internal or external factors, thus contributing to a positive energy status or overeating.

1.2.1 *Homeostatic Pathways*

Energy homeostasis is achieved through the balance of energy intake (food consumption) and energy expenditure (e.g. physical activity and normal physiological processes). This balanced energy state is attained through the integration by the central nervous system of input received from sensory properties of food, receptors in the gastrointestinal tract, the autonomic nervous system, metabolites in the circulatory system, and gut hormones (Coles, Birken, and Hamilton, 2016). Ghrelin, the only orexogenic hormone, is secreted from the stomach preprandially to increase hunger, promote energy intake and reduce energy expenditure (Faulconbridge and Hayes, 2011). Nutrient properties of food sensed in the oral cavity promote positive feedback communication to the brain (Faulconbridge and Hayes, 2011). Further downstream, satiation signals in the form of pancreatic and gut peptides (e.g. insulin, cholecystokinin, serotonin, peptide YY, glucagon-like peptide-1, glutamate, enterostatin) and gastric distension cause the activation of receptors on afferent fibres of the vagus nerve to communicate to the brain to inhibit feeding (Faulconbridge and Hayes, 2011). Circulating metabolites (e.g. glucose, free-fatty acids) and various regulatory hormones (e.g. insulin, gut peptides) released from gastrointestinal organs into the circulation cross the blood-brain barrier to communicate directly with receptors in the brain. Long-term regulators of energy set point and body weight are controlled primarily by an adipose tissue-containing hormone, leptin, and to a lesser extent insulin, that feedback to the hypothalamus (Farr, Li, and Mantzoros, 2016).

Within the hypothalamus, the arcuate nucleus assumes an integrational role, which involves neuronal signalling, based on peripherally-derived nutrient and hormonal input. Relevant neurons in the arcuate nucleus include those that increase the drive to eat and decrease energy expenditure, termed orexigenic, which express agouti-related protein (AgRP) and

neuropeptide Y (NPY) and conversely, those that inhibit food intake and increase energy expenditure, termed anorexigenic, which express pro-opiomelanocortin (POMC) and cocaine- and amphetamine-regulated transcript (CART) (Farr, Li, and Mantzoros, 2016). Leptin and insulin inhibit AgRP/NPY neurons while promoting the activation of POMC/CART neurons to induce satiety (Farr, Li, and Mantzoros, 2016). Subsequently, the released neurotransmitters signal further to other nuclei within the hypothalamus to modulate appetite (Farr, Li, and Mantzoros, 2016). Figure 1 provides an illustrative overview of homeostatic appetite pathways.

1.2.2 *Hedonic and Cognitive Pathways*

In addition to the homeostatic mechanisms controlling energy uptake and expenditure, other factors have an effect on food intake. Environmental factors may control access to food or desire to eat and include food availability, time, food features/cues (including sight and smell), social factors (including presence of family or friends), and emotions (Faulconbridge and Hayes, 2011). Behavioural factors may also influence conscious or subconscious control of eating and include dietary restraint, loss of control, sedentary behaviour, impulsivity, and inattention. The hypothalamus communicates with corticolimbic regions responsible for reward, memory, attention, emotion, and cognitive control (e.g. ventral tegmental area, nucleus accumbens, hippocampus, prefrontal cortex, amygdala) to stimulate food intake (Farr, Li, and Mantzoros, 2016; Faulconbridge and Hayes, 2011). Upon activation of structures within the reward circuit, a positive feedback mechanism is activated which releases humoral substances such as dopamine (Hopkins et al., 2000). Similar pathways involving reward circuitry have been implicated in drug and gambling addictions (Blum et al., 2015; Davis, 2009; Kelley et al.,

2002). Humoral substances act on both homeostatic and hedonic brain regions leading to positive feedback mechanisms which dominate metabolic mechanisms and lead to increased desire to eat (Faulconbridge and Hayes, 2011). Within the hypothalamus, NPY and other appetite-increasing hormones are released while insulin, leptin, and other satiety hormones are downregulated (Hopkins et al., 2000).

1.2.3 *Appetite Dysregulation*

In normal weight individuals, appetite hormones work in tightly regulated positive and negative feedback loops to maintain energy balance. However, there are numerous proposed mechanisms that result in a positive energy supply in individuals with obesity. While hedonic factors may initially drive the accumulation of excess body weight, homeostatic mechanisms may eventually become affected, including the development of leptin or insulin resistance, leading to reduced satiety, and further weight gain (Yu et al., 2015). Furthermore, studies have suggested that ghrelin levels are not decreased as quickly in response to food intake in obese compared to normal weight individuals leading to delayed feeding cessation. In Prader-Willi Syndrome (PWS), high ghrelin levels contribute to severe hyperphagia and compulsive food-seeking behaviours (Druce and Bloom, 2006). Within the hedonic system, the decreased availability of dopamine in obese individuals may lead to the pursuit of rewarding stimuli such as food to supplement this deficit (Farr, Li, and Mantzoros, 2016). Finally, in individuals with inattention or impulsivity, cognitive restraint may be reduced in response to hedonic pathway activation (Davis, 2009; Guerrieri, Nederkoorn, and Jansen, 2008).

In summary, both homeostatic and hedonic systems coordinate control of food intake in any individual, and both pathways should be assessed in the evaluation of underlying contributors to overeating behaviour so that targeted treatment approaches can be considered (Yu et al., 2015).

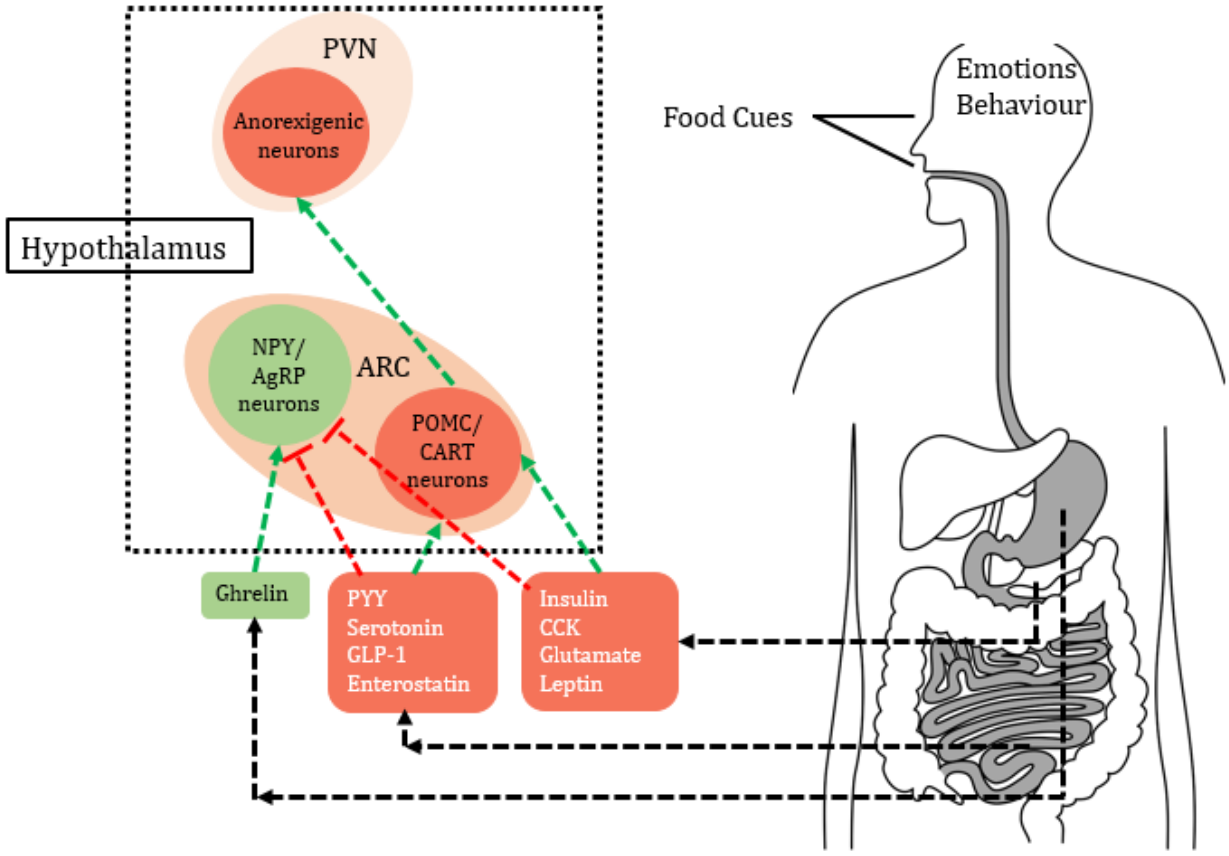

Figure 1. Physiological, environmental, and behavioural control of appetite. The hypothalamus in the central nervous system integrates input from various sources, including food properties, receptors in the gastrointestinal tract, the autonomic nervous system, metabolites in the circulatory system, and gut hormones. In anticipation of a meal, ghrelin is secreted from the stomach to promote energy intake. Following food consumption, pancreatic (e.g. insulin, CCK, and glutamate) and gut (e.g. PYY, serotonin, GLP-1, and enterostatin) peptides activate receptors in the vagus nerve that communicate with the hypothalamus to

inhibit feeding. Leptin and insulin control long-term regulators of energy intake and body weight, and are released by adipose tissue and the pancreas, respectively. Within the hypothalamus, the arcuate nucleus integrates hormonal input; its orexigenic neurons express AgRP and NPY and its anorexigenic neurons express POMC and CART. These neurons release neurotransmitters that send signals further downstream to other hypothalamic nuclei (including in the PVN) to modulate appetite. Figure adapted from Coles et al. (2016). CCK = cholecystokinin; PYY = peptide YY; GLP-1 = glucagon-like peptide-1; AgRP = agouti-related protein; NPY = neuropeptide Y; POMC = pro-opiomelanocortin; CART = cocaine- and amphetamine-regulated transcript; PVN = paraventricular nucleus

1.3 The Developmental Aspects of Appetite Regulation Throughout Childhood

Increasing evidence suggests that prenatal, perinatal, and postnatal environments influence the development of energy balance mechanisms in childhood. Studies show that the *in utero* maternal environment can have an indelible effect on fetal programming of homeostatic and hedonic regulatory systems (Dalle Molle et al., 2015; Gali Ramamoorthy et al., 2015; Schellong et al., 2013; Franke et al., 2005). Postnatally, the composition and quantity of food delivered to the infant influences their own development of appetite and satiety control (Birch, Savage, and Ventura, 2007; Fomon, 1993). Additionally, the feeding environment, including parental feeding practices, cultural beliefs, parental eating behaviours, and household structure, affect the development of children's eating habits and weight (Reicks et al., 2015; Birch, Savage, and Ventura, 2007; Savage, Fisher, and Birch, 2007). During this time period, the child also transitions from phases of complete dependence on caregivers for nourishment, to independence

in food selection and quantity consumed. Factors related to developmental aspects of appetite regulation are discussed in this section.

Nutritional imbalances *in utero* can lead to hormonal dysregulation. Animal studies indicate that reduced prenatal or perinatal nutrition leads to increased activation of orexigenic factors and reduced anorexigenic hormone activity; alterations in these hormone levels impact appetite (Dalle Molle et al., 2015; Schellong et al., 2013). Similarly, untreated maternal gestational diabetes in rodents leads to dysregulation of appetite regulation systems in the hypothalamus of the offspring causing later development of hyperphagia, overweight, and metabolic disorders (Gali Ramamoorthy et al., 2015; Franke et al., 2005). Furthermore, a recent study found epigenetic modifications caused by neonatal overnutrition that are presumed to decrease POMC activity, thus contributing to possible increased energy intake and obesity (Gali Ramamoorthy et al., 2015). Therefore, there appear to be numerous prenatal and perinatal factors related to early development of appetite regulation, with causal pathways only beginning to be understood.

In early postnatal life, empirical evidence clearly demonstrates that internal satiety cues are recognized in infants and toddlers and that young children can self-regulate quantity and selection of food intake (Birch and Fisher, 1998; Birch and Deysher, 1986). Breastfeeding is important in developing the infant's response to internal satiety and hunger cues (Birch, Savage, and Ventura, 2007); however, parental feeding practices can override these cues in infants and children. For example, the decision to breastfeed versus bottle-feed can impact energy intake in the infant, as mothers exert greater control over volume of formula consumed by encouraging the child to finish the amount available in the bottle (Fomon, 1993). Interestingly, in an

experimental situation with infants fed by bottle without maternal influence, infants adjusted their formula intake based on the energy content such that they consumed more energy-dilute formula, highlighting that maternal influence may be a more important factor linking formula feeding to altered satiety (Fomon, 1993). Finally, a very recent study examining observed infant responsiveness to food cues demonstrated that a history of exclusive formula-feeding was associated with a greater affinity for food cues in infants 6-12 months of age (Buvinger et al., 2017). In sum, these studies indicate formula feeding may be a risk-factor for altered appetite regulation, but it is not clear how much of the contribution is nutrient-mediated (i.e. formula versus breast milk), environment-mediated (e.g. maternal influence over bottle) or a combination of both.

In young children, parental feeding practices play a significant role in the child's own development of eating behaviours. At this age, parents control quantity and type of foods eaten and may employ particular feeding practices in an effort to modify or instill certain eating behaviours based on perceived social or societal norms (Birch, Savage, and Ventura, 2007). Parents who subscribe to the "bigger is better" belief may pressure their child to eat beyond energy requirements (Birch, Savage, and Ventura, 2007), which may lead to the child overeating in response to external food cues (van Strien and Bazelier, 2007; Birch, Fisher, and Davison, 2003; Carper, Orlet Fisher, and Birch, 2000). In contrast, parents perceiving their child to be on an unhealthy weight trajectory may restrict foods, which may lead to the internalization of what, how much, and when to eat and thus, diminished self-control and decreased sensitivity to internal hunger and satiety cues (Birch, Savage, and Ventura, 2007). Restricted children may then overeat in an environment with palatable food or due to negative emotions (van Strien and Bazelier, 2007; Birch, Fisher, and Davison, 2003; Carper, Orlet Fisher, and Birch, 2000). In

older children with overweight or obesity, both parental pressure to eat and restriction of eating are linked to feelings of loss of control while eating (Matheson et al., 2015). Parental use of food as a reward or restriction of food for perceived health consequences in children between the ages of 2-5 years has been associated with later emotional eating during stress in young children aged 5-7 years, possibly indicating that these parental feeding practices teach children to use high calorie foods as a means of soothing negative emotions (Farrow, Haycraft, and Blissett, 2015). These studies show that parental feeding practices may undermine the ability of children to learn appropriate responses to internal hunger and satiety signals, which may lead to the development of disordered eating behaviours.

For children and adolescents, the home environment and family structure may impact their development of eating behaviours since most food intake occurs in the home (Reicks et al., 2015). Studies have shown that children observe eating behaviours modeled by parents (Savage, Fisher, and Birch, 2007) and adopt eating behaviours of their parents and other family members, including restrained and disinhibited eating (Zocca et al., 2011; Birch and Fisher, 1998); this is especially common in families with several obese members (Birch and Fisher, 1998). However, for older children and particularly among adolescent girls, frequent family meals in a positive home environment have protective effects against loss of control eating as well as extreme weight control behaviour, including dieting (Haines, Gillman, et al., 2010; Haines, Kleinman, et al., 2010; Neumark-Sztainer et al., 2007). This association may be a result of family meal times being more regular and structured and therefore discourage disordered eating (Haines, Gillman, et al., 2010). Parental modeling and encouragement of structured eating, including eating breakfast, affects their adolescent's decision making regarding food choices when at school (Reicks et al., 2015). Children and adolescents rely on internal behavioural mechanisms to

control food intake when away from parental control and those with poor behavioural regulation may therefore lack the inhibitory control to prevent emotions or food cues from leading to unplanned food intake (Reicks et al., 2015). Family structure is also important; longitudinal research suggests that young children of single mothers are more likely to gain weight or become overweight/obese than children whose mothers are with a partner (Schmeer, 2012). This finding may be due to many single-parent families having lower incomes, increased stress, and the child spending less time with a parental figure present in the home, which increases the chance of fewer family meals together (Reicks et al., 2015). In lower income families, parents have been shown to apply higher rates of both food restriction and pressure to eat on the children (Reicks et al., 2015). These parenting styles lead to the disordered eating behaviours noted above including eating in response to food cues and negative emotions and the feeling of loss of control while eating. Taken together, there are numerous factors related to the home and family environment that may contribute to appetite regulation and disordered eating throughout childhood and adolescence.

1.4 Drivers of Eating

Recent evidence has shown contrasting features of eating behaviours and appetitive traits between children with and without obesity (Croker, Cooke, and Wardle, 2011; Bruce et al., 2010; Webber et al., 2009; Jansen et al., 2003), suggesting physiological and psychological variations corresponding to weight. Common eating traits and behaviours or "drivers of eating" that have been associated with overeating and obesity include loss of control eating, emotional eating, response to external cues/external eating, hyperphagia, impulsivity, and inattention.

Some traits have been found to co-occur in children, including loss of control eating and restrained eating (Goldschmidt et al., 2008), loss of control eating and emotional eating (Stojek et al., 2017), and loss of control eating, emotional eating, and external eating (Goossens, Braet, and Decaluwe, 2007).

1.4.1 *Loss of Control Eating*

Loss of control eating (LOCE) is the subjective feeling of being unable to stop or control one's eating irrespective of the amount of food in question (Tanofsky-Kraff et al., 2004). LOCE is the central component of binge eating, a well-recognized eating behaviour in adults and children (Fairburn and Wilson, 1993). Binge eating can be categorized in two ways: 1) Objective binge eating, which is the consumption of a larger quantity of food than most people would consume in a similar time with the sense of loss of control over eating, and 2) Subjective binge eating, defined as the feeling that one has consumed a large quantity of food that most people would not consider to be large with accompanied loss of control (Fairburn and Cooper, 1993). Studies in children have identified that LOCE, regardless of the quantity of food consumed, is the most significant aspect of identifying disordered eating and its associated psychological distress (Shomaker et al., 2010; Goossens, Braet, and Decaluwe, 2007; Tanofsky-Kraff et al., 2004; Morgan et al., 2002). Children and adolescents in particular may experience LOCE without having eaten large amounts of food, especially since their portion size may still be controlled by the parent or other eating environment (Goossens, Braet, and Decaluwe, 2007) and it may be difficult for them to quantify a large amount of food due to their changing nutritional requirements (Decaluwe and Braet, 2004). When cognitive-behavioural therapy was applied to a

sample of adult female binge eaters with obesity, those with objective binge eating fully recovered from their symptomatology but those with subjective binge eating had a poorer response to treatment (Smith, Marcus, and Kaye, 1992). As suggested by these results, the underlying feeling of loss of control common to both groups may be more resistant to treatment than reducing the quantity of food intake (Goossens, Braet, and Decaluwe, 2007).

LOCE is the focus of increasingly more studies in children and adolescents with overweight and obesity and has been described as the most common disordered eating behaviour in this population (Tanofsky-Kraff et al., 2007). A recent meta-analysis reported on 36 studies, found prevalence rates of binge eating/LOCE in children and adolescents with overweight and obesity to be 60% (mean = 26.3%; 95% CI: 23.1%, 29.7%) (He, Cai, and Fan, 2017). Tanofsky-Kraff and colleagues (2005) report that 30% of overweight children as young as eight years old have experienced LOCE at least once and some studies have found that children with obesity can recall first experiencing this eating behaviour from as young as 6 years old (Decaluwe and Braet, 2003). The mean age of the onset of overweight in the latter study occurred at 6.8 ± 3.3 years with objective overeating and LOCE onset at a mean age of 10.9 ± 2.6 years (Decaluwe and Braet, 2003). Meta-analysis data suggest there may be a slightly higher prevalence in binge eating/LOCE rates among female children and adolescents with obesity, but future studies are needed to further explore this trend (He, Cai, and Fan, 2017).

The experience of LOCE is particularly prominent in youth seeking treatment for obesity, with 9-18% attesting to have had an episode within three months of enrolling in treatment (Goossens, Braet, and Decaluwe, 2007; Decaluwe and Braet, 2003) and 20-33% of adolescents reporting moderate to severe binge eating (Pasold, McCracken, and Ward-

Begnoche, 2014; Isnard et al., 2003). Overall, a significant positive correlation has been found between binge eating symptoms and body mass index (BMI) in adolescents seeking treatment for obesity (Pasold, McCracken, and Ward-Begnoche, 2014). However, there is controversy as to whether degree of obesity is correlated with LOCE. In fact, studies from the same group have shown higher or no different BMI in LOCE versus those not affected (Goossens, Braet, and Decaluwe, 2007; Decaluwe and Braet, 2003). Finally, approximately one-quarter of adolescents with severe obesity undergoing bariatric surgery report LOCE (Utzinger et al., 2016). These statistics are especially concerning as surgical treatment outcomes may be poorer if underlying eating behaviours are not addressed (Utzinger et al., 2016).

Types of food eaten during LOCE episodes have been explored in two studies (Vannucci et al., 2014; Theim et al., 2007). One study in overweight/obese and normal weight children between 6-18 years old found that those endorsing LOCE consumed more calories from carbohydrates, including snacks and desserts, than those who did not report LOCE (Theim et al., 2007). Furthermore, adolescents with LOCE in late puberty consume significantly greater energy from carbohydrates and less from protein than their peers without LOCE; however, no difference between groups is observed in pre-pubertal or early-to-mid pubertal youth (Vannucci et al., 2014). It is plausible that the loss of control overeating episodes may occur in unrestricted environments, such as at school or restaurants where parents cannot control the nutritional environment, with foods that may be otherwise restricted by parents (Theim et al., 2007). These carbohydrate-dense foods may result in the greater BMI scores observed in children with LOCE (Theim et al., 2007).

1.4.2 *Emotional Eating*

Emotional eating is characterized as a coping method to deal with negative emotions, such as depression, loneliness, worrying, anxiety, and anger. Hilde Bruch, a psychoanalyst who studied children with eating disorders and obesity in the 1970's, suggested that children with obesity do not correctly identify negative affect and are unable to distinguish it from hunger, and thus attribute these emotions as a need to eat (Bruch, 1975). Furthermore, other research has shown individuals with obesity may routinely overeat to reduce episodic negative affect by stimulating higher cortical reward/pleasure centres with food (Ganley, 1989). Although positive emotions may potentially trigger overeating, this has been less well studied. A recent study in adult women found the association between overweight and emotional eating pertains to negative emotions and not a desire to eat in response to positive emotions (van Strien, Donker, and Ouwens, 2016), however, further research is needed.

Findings from observational research are mixed concerning the relationship of eating due to negative affect and weight status in youth. One study found a significant positive correlation between body weight and emotional overeating in children and young adolescents aged 7-12 years, signifying that heavier children overeat in response to negative affect (Webber et al., 2009). Surprisingly however, other correlational studies in children across the weight spectrum have found a significant negative relationship between emotional eating and weight in pre-adolescent girls, but no association in pre-adolescent boys or older adolescents of both sexes (Ledoux et al., 2011; Lluch et al., 2000). In a study comparing children and adolescents aged 9 to 14 years of age with obesity to their non-obese peers, the children with obesity scored significantly higher on the emotional eating subscale of the parent-report version of the Dutch Eating Behaviour Questionnaire (Braet and Van Strien, 1997). However, on a self-report version

of the measure, adolescents with overweight did not score differently than their normal-weight peers on emotional eating (Braet et al., 2008). It appears these inconsistent results may be due to the self-report versus parent-report nature of the assessments used. Studies showing a relationship between emotional eating and obesity used parent raters, and those with no significant results or a negative correlation used the child-report measures. This may be related to a tendency to underreport eating activities on self-report measures or may be due to a decreased ability of children and adolescents with obesity to link negative emotion and eating due to them perceiving negative mood as hunger. While few studies have investigated the prevalence of emotional eating in children and adolescents with obesity, several do suggest that it is a significant issue in youth with weight issues. Emotional eating is therefore an important consideration in measuring factors related to increased energy intake.

1.4.3 *Responsivity to External Cues*

Responsivity to external cues, or external eating, describes a heightened stimulation of senses to environmental food cues, thus leading to an eating episode. In the late 1960's, Schachter developed the Externality Theory of Obesity that suggests that individuals with obesity are more sensitive to palatable food cues in the environment, such as sight and smell, and less sensitive to internal satiety and hunger signals than those with normal weight (Schachter, 1968). More recent findings have suggested biological differences in food cue reactivity leading to increased food consumption in certain individuals. Studies have shown that exposure to food cues such as sight or smell can lead to spontaneous eating as well as eating a larger amount than initially planned (Ferriday and Brunstrom, 2008). Cravings have also been found to increase in response

to sights and smells of food (Ferriday and Brunstrom, 2008; Nederkoorn, Smulders, and Jansen, 2000). Additionally, physiological changes to food cues have been reported, including insulin release and increased heart rate, gastric activity, and blood pressure (Nederkoorn et al., 2004; Nederkoorn, Smulders, and Jansen, 2000; Overduin, Jansen, and Eilkes, 1997; Nirenberg and Miller, 1982), which prepare the body for planned or unplanned eating.

Food cue reactivity can be measured in a laboratory controlled setting or via self-report questionnaire without the presence of an observer and has been investigated in children and adolescents. In children, Jansen et al (2003) found that overweight was associated with no decrease in caloric intake compared to normal weight controls who decreased their intake significantly after exposure to the smell of palatable food. Thus, in normal-weight individuals, exposure to food cues such as smell and taste before eating induces some satiety and decreases food intake, whereas overweight individuals may have delayed satiety due to an attenuation of the sensory-specific decrease in neural activity in the orbitofrontal cortex (O'Doherty et al., 2000). Furthermore, results have been mixed with regards to the measurement of food cue reactivity in functional magnetic resonance imaging studies using normal-weight subjects and subjects with overweight or obesity. Both positive and negative correlations have been found between BMI and the activation of the dorsolateral prefrontal cortex, a brain region involved in response inhibition, self-control and planning, indicating that food cues may elicit an increased or decreased inhibitory response (van Meer et al., 2016; Davids et al., 2010; Stice et al., 2008). However, studies varied in methodology, such as using food versus non-food cues or unhealthy versus healthy food cues. Studies have shown either a positive or no relationship between self-reported external eating and weight in adolescents, with no influence of age or sex (Ledoux et

al., 2011; Braet et al., 2008; Lluch et al., 2000). In sum, there are mixed results as to the influence of external cues on weight status in children and adolescents.

1.4.4 *Restrained Eating*

Restrained eating is a cognitive method of setting limits and boundaries to food intake for the purpose of weight loss. However, restrained eaters may lose control and overeat when faced with certain stimuli. Restraint Theory posits that chronic diets are unsustainable in certain individuals and eventually lead to disinhibited eating caused by internal or external appetitive cues (Herman and Mack, 1975). Longitudinal research in adolescents has suggested that overweight in adolescence commonly leads to dieting, including restrained eating behaviour, in attempts to achieve weight loss (Snoek et al., 2008).

Studies in various adolescent populations have consistently found that restrained eating is common in those with elevated body weight. Cross-sectional research has demonstrated a significant positive relationship between restrained eating and BMI in pre-adolescent boys and both male and female 17-18 year old adolescents; these significant results were not affected by age, sex or ethnicity (Ledoux et al., 2011). Furthermore, in French populations of adolescents over 10 years of age (Lluch et al., 2000), and Dutch adolescents (Rutters et al., 2011; Snoek et al., 2007), weight and restrained eating were positively related; results were similar for both sexes. A longitudinal study in a community sample of adolescents aged 16-19 showed that self-reported restrained eating behaviour correlated significantly with increased body weight over a 9-month period (Stice, 1998). One study specifically designed to compare adolescents with and without obesity, demonstrated that 49% of females and 27% of males with obesity endorsed

above-average restrained eating versus 15% of females and 2% of males in the normal-weight group (Lluch et al., 2000). Additionally, adolescents with overweight scored significantly higher on restrained eating compared to their normal-weight peers and 37% of all study participants scored 3 or more on a frequency range of 1-5 (Braet et al., 2008), demonstrating that this behaviour is quite prominent in adolescents. Thus, these several studies indicate universal agreement of restrained eating behaviour in children and adolescents with obesity, and therefore, the importance of studying this eating driver in this pediatric population.

1.4.5 *Hyperphagia*

Hyperphagia describes a constant state of excessive hunger and associated preoccupation of food-seeking. The hypothalamus is a brain region implicated in food-searching behaviour and regulates body weight via nuclei that act as homeostatic centres controlling hunger and satiety. Hypothalamic dysfunction is characteristic of many rare genetic conditions that lead to severe obesity onset in childhood (Coles, Birken, and Hamilton, 2016). Hyperphagia, as a driver of eating, has rarely been studied objectively in the literature apart from in individuals with PWS for whom it is a characteristic clinical feature (Coles, Birken, and Hamilton, 2016). In studies where hyperphagic behaviour has been assessed, researchers have used a binary response (yes/no) parent question, "Does your child/teen seem excessively hungry and eat very large amounts of food?" (Anderson et al., 2016) or a laboratory method where children have access to food following an *ad libitum* meal and additional energy intake is quantified (Fisher et al., 2007).

Some studies examining eating tendencies and weight in children have indicated that indeed, in some cases, there exist deficits in internal satiety cues leading to relentless food-seeking (Anderson et al., 2016; Webber et al., 2009; Fisher et al., 2007). One group of researchers evaluated responses to parent questions related to food-seeking behaviour, including frequency of asking for food and time spent eating if allowed, and found a significant positive correlation between food responsiveness and weight (Webber et al., 2009). Another group studying Hispanic children and adolescents specifically found that those with obesity show increased hyperphagic behaviours and consume significantly more energy after a full meal than those without overweight; notably, no difference was found based on age or sex (Fisher et al., 2007). A study in young people with obesity in New Zealand found that 67% of parents report their child eats excessive amounts of food (Anderson et al., 2016). These few studies suggest that in some cases, excess weight gain may be related to dysregulated satiety cues causing hunger and food-seeking behaviour.

1.4.6 *Impulsivity*

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder that includes both hyperactive-impulsive traits and inattention. A study first linking obesity and ADHD was published in 2002 (Altfas, 2002), and shortly afterwards this association was described in children (Agranat-Meged et al., 2005; Holtkamp et al., 2004). In adults with obesity, there is an abnormally increased prevalence of ADHD relative to the general population (Cortese et al., 2008; Altfas, 2002), which complicates weight-loss success relative to those who are asymptomatic for ADHD (Altfas, 2002). The prevalence of ADHD in an in-patient pediatric

population with obesity was almost 60%, which was found to be significantly elevated ($p<0.0001$) compared to 10% in the general pediatric population without obesity (Agranat-Meged et al., 2005).

Impulsivity characterizes the propensity towards rash decision-making and decreased planned actions, with lack of consideration to negative consequences. Impulsivity can be considered and measured as a stand-alone construct using behavioural measures or self-report or parent report-for-child questionnaires. Interest in examining impulsivity in obese pediatric populations is relatively new, with the majority of studies on the subject published since 2010 (Thamotharan et al., 2013). In female adolescents, on a food-specific go/no-go paradigm task used to assess impulsivity and inhibition, higher BMI was associated with faster reaction time to food images and greater failure to inhibit responses to images of desserts (Batterink, Yokum, and Stice, 2010). In this study, this finding was supported by functional magnetic resonance imaging analyses which showed that compared to lean individuals, adolescents with greater adiposity do not effectively utilize brain regions involved in inhibitory responses and over-activate regions involved with food reward (Batterink, Yokum, and Stice, 2010). Using similar tasks measuring sensitivity to reward and inhibitory control, an additional study demonstrated that treatment-seeking adolescents with obesity showed greater impulsive reactions in comparison with their normal weight peers (Nederkoorn et al., 2006). Likewise, on a diagnostic interview, children and adolescents with overweight showed significantly higher impulsivity than those in the control group and the between-group significance was especially prominent in boys (Braet et al., 2007). Finally, a recent meta-analysis examining impulsivity as it relates to overweight/obesity in children aged 2 to adults aged 21 found a significant positive relationship between the two factors, indicating important considerations must be made in obesity treatment

strategies (Thamotharan et al., 2013). This conclusion is supported by a study of obesity treatment outcomes where adolescents without impulsive behaviour achieved significantly greater weight loss compared to those who exhibited impulsivity (Nederkoorn et al., 2006). Overall, there appears to be good evidence suggesting correlation between obesity and impulsive behaviours. Impulsivity and difficulties with inhibition may alter decision-making about food choices and should be considered in the context of weight-loss treatment.

1.4.7 *Inattention*

Inattention is another key component of ADHD, though not often considered exclusively in studies of the co-occurrence of ADHD and obesity. A select few studies, however, point to the importance of considering inattention in children and adolescents with obesity. In one study of youth seeking treatment for obesity, among the nearly 60% of patients diagnosed with ADHD, 40% were found to have predominantly inattentive symptoms while the remainder had a combination of impulsivity-hyperactivity and inattention (Agranat-Meged et al., 2005). The authors suggest that children with mostly inattentive symptoms may not demonstrate the noticeable hyperactive characteristics of ADHD and consequently, may be less likely to seek or receive treatment (Agranat-Meged et al., 2005). The literature to support the specific association of inattention and obesity shows mixed results. In one study of overweight and obese children and adolescents, a higher BMI correlated to more variable and slower performance on an inhibitory control Go/No-Go with Interference task, which indicated poor attention (Pauli-Pott et al., 2010). In another study, compared to a normal weight control group, children and adolescents with overweight had significantly more attention deficits; this difference was most

notable in boys (Braet et al., 2007). In contrast, no difference in sustained attention was found between adolescents with normal weight and obesity (Moreno-Lopez et al., 2012). Additionally, in a recent meta-analysis of ADHD features and obesity, no significant correlation was found in studies measuring inattention and obesity (Thamotharan et al., 2013). It should be noted that there are fewer studies included that had specifically examined this behaviour, and further research is required.

1.5 Psychological Indices and Eating Drivers

Mental health diagnoses are common among children and adolescents with obesity (Rankin et al., 2016). A growing literature has examined associations between various psychological indices and eating drivers in youth. Once again, LOCE is the most commonly researched eating driver in relation to mental health. Children and adolescents with LOCE score significantly higher on measures of depression and anxiety, but not body esteem, compared to those without LOCE (Goossens, Braet, and Decaluwe, 2007; Isnard et al., 2003). In a long-term study, compared to unaffected children, those with persistent LOCE were significantly associated with having depressive symptoms and had a non-significant but trend-level association with anxiety after an average of five years from the initial assessment for LOCE (Tanofsky-Kraff et al., 2011). In youth with overweight, a positive significant relationship has also been found between frequency of being teased by peers or family members and number of LOCE episodes (Libbey et al., 2008). One proposed method for the development of LOCE in youth is the interpersonal model of LOCE, which suggests that social functioning issues cause poor self-esteem and negative affect, which in turn leads to binge eating as a coping mechanism (Elliott et al., 2010).

This model has been supported by findings that negative affect (including symptoms of depression and anxiety) mediates the positive association between social problems and LOCE (Elliott et al., 2010). A direct positive correlation has also been found between social problems and LOCE (Elliott et al., 2010) and a negative correlation between social functioning and LOCE behaviour (Pasold, McCracken, and Ward-Begnoche, 2014). These findings show that social problems, depression, and anxiety are positively associated with LOCE in children and adolescents with obesity.

Emotional, external, and restrained eating are other eating drivers that have been examined with regards to their association with psychological indices. In children and adolescents with obesity, a significant relationship has been found between depressive symptoms and emotional eating, as well as between depressive symptoms and external eating (Pauli-Pott et al., 2013; Goossens et al., 2009). Furthermore, among this population, patients with symptoms of anxiety also report more emotional eating (Pauli-Pott et al., 2013; Goossens et al., 2009). Restrained eating is also more frequently reported in girls with depressive symptoms and who are anxious relative to boys and girls without these symptoms (Pauli-Pott et al., 2013). Thus, these recent findings indicate that young people with obesity may be driven to eat as a means of coping with negative mood states.

Very limited research has examined the relationship between components of ADHD, namely impulsivity and inattention, and psychological indices. Recent evidence in a large pediatric cohort points to an increased odds of developing depression in youth with ADHD who have a co-morbid diagnosis of obesity (aOR = 1.29; 95% CI: 1.08, 1.54) (Jerrell, McIntyre, and

Park, 2015). Further research is needed in this area to explore other mental health outcomes in similar populations.

1.6 Literature Gap: Clustering of Eating Drivers

The current literature on "eating drivers" in children and adolescents with obesity has focused mostly on describing the prevalence of a single driver or the relationship between drivers scored on the same measure. Nevertheless, a few groups of researchers have explored multiple behaviours simultaneously.

The majority of work has been in the area of LOCE. Polivy and Herman (1985) proposed that for people who binge eat it would be logical to subsequently restrict eating to compensate for the excess consumption, but that empirical research indicates the relationship between the two traits is the opposite such that restricting food intake leads to disinhibited eating. Several years later, Goldschmidt and colleagues (2008) found that similar to findings in adults, youth aged 8-18 with LOCE can be divided into two subgroups based on cluster analysis: those with moderate dietary restraint and those with both moderate dietary restraint and high negative affect. The sample had equal representation of overweight and normal weight youth, but results were not impacted by body weight. The authors suggest that since dietary restraint was found across subgroups, it may be a key component of LOCE in this population (Goldschmidt et al., 2008). Furthermore, the 30% of individuals who endorsed both dietary restraint and negative affect were also more likely to be in the treatment-seeking portion of the study population and may represent a subgroup with more severe disordered eating behaviour (Goldschmidt et al., 2008). In a longitudinal study, Stojek and colleagues (2017) found that non-

treatment seeking adolescents (38% overweight) who endorsed both LOCE and emotional eating at baseline, were more likely to present with a significant increase in BMI at 1-year follow up than those without LOCE at baseline, suggesting that LOCE mediated the BMI increase in youth with emotional eating. Another study found that children and adolescents with obesity who were seeking treatment and reported LOCE had increased emotional eating and external eating compared to patients with no LOCE, however their restrained eating scores did not differ (Goossens, Braet, and Decaluwe, 2007). More recent research in children and adolescents with overweight/obesity has shown that those with LOCE had a seven times greater chance of having a co-morbid ADHD diagnosis and scored significantly higher on measures for inattention and hyperactivity-impulsivity compared to those without LOCE (Reinblatt, Mahone, et al., 2015). Furthermore, LOCE was found to mediate the relationship between ADHD diagnosis and BMI (Reinblatt, Mahone, et al., 2015). Overall, these results show that indeed, LOCE is a significant eating behaviour that may co-occur with other eating drivers in overweight and obesity.

Apart from the studies above, which focus on the co-occurrence of two eating drivers in children and adolescents, there is limited research examining multifactorial phenotypes of eating behaviour in the pediatric population. One study in youth across the weight spectrum examined the clustering of eating behaviours and found five unique groups characterized primarily by one or two distinguishable eating drivers, including 1) objective binge eating, 2) subjective binge eating, 3) emotional eating, 4) emotional eating with eating in the absence of hunger, and 5) no prominent eating drivers (Vannucci et al., 2013). Further analysis revealed that groups differed in BMI z-scores with those in the objective and subjective binge eating groups exhibiting higher BMI, and, along with the emotional eating group, had more psychological symptoms of anxiety.

Only one study has specifically included children with overweight and obesity to examine various behavioural and psychological variables related to eating and response to food and found three significant clusters, namely 1) high satiety responsiveness (low response to food cues, sensitive to satiation), 2) high food responsiveness (eating in the absence of hunger, sensitive to food cues, low satiation), and 3) moderate satiety and food responsiveness (Boutelle et al., 2014). BMI was highest in group 2 and lowest in group 1, as would be expected from the cluster characteristics. Despite the fact that these studies provide intriguing preliminary results regarding the identification of eating behaviour subgroups within pediatric populations, there are some important limitations. First, only children of a narrow age range (8-12 years) were included in the study that involved obese participants. Secondly, neither study included restrained eating as one of the eating behaviours of primary interest, though, in the first study it was found to be significant in both LOCE eating phenotypes. Furthermore, components of ADHD were not considered in either study, though it has recently been found to affect a large percentage of children and adolescents with obesity and may influence eating behaviour. Considering the complexities of the underlying factors contributing to excess weight gain, and the limited number of eating drivers explored in combination, further research is needed to improve treatment strategies in obese pediatric populations. Greater understanding of how drivers cluster together into phenotypes of eating behaviours and traits will allow for more sophisticated and targeted interventions to address the underlying factors contributing to excess weight gain in children and adolescents.

Chapter 2 Research Aim, Objectives, and Hypotheses

2.1 AIM

The aim of this study was to examine whether eating drivers of interest cluster into specific phenotypes in a population of children and adolescents with obesity and whether phenotypes could be distinguished based on clinical characteristics.

2.2 OBJECTIVES

The **primary objective** of this study was to determine how eating drivers (loss of control, emotional eating, external cues, restrained eating, hyperphagia (excessive hunger), impulsivity, and inattention) cluster into specific phenotypes among children and adolescents with obesity.

The **secondary objective** of this study was to examine how identified eating phenotypes relate to clinically measured and reported individual (e.g. age, sex, BMI), family (e.g. socioeconomic status, family structure), and eating environment (e.g. frequency of meals with family, meals in front of television) characteristics.

An **exploratory analysis** was conducted to examine how identified eating phenotypes relate to other mental health outcomes, such as social functioning, mental health diagnoses, and body esteem.

Figure 2 presents a model of the eating behaviours and appetitive traits ("eating drivers") which may drive our population to overeat. Shown as potential influential factors are the clinical characteristics and mental health outcomes of interest (individual, family, behavioural/environmental, psychological), which may influence how these eating drivers cluster in participants.

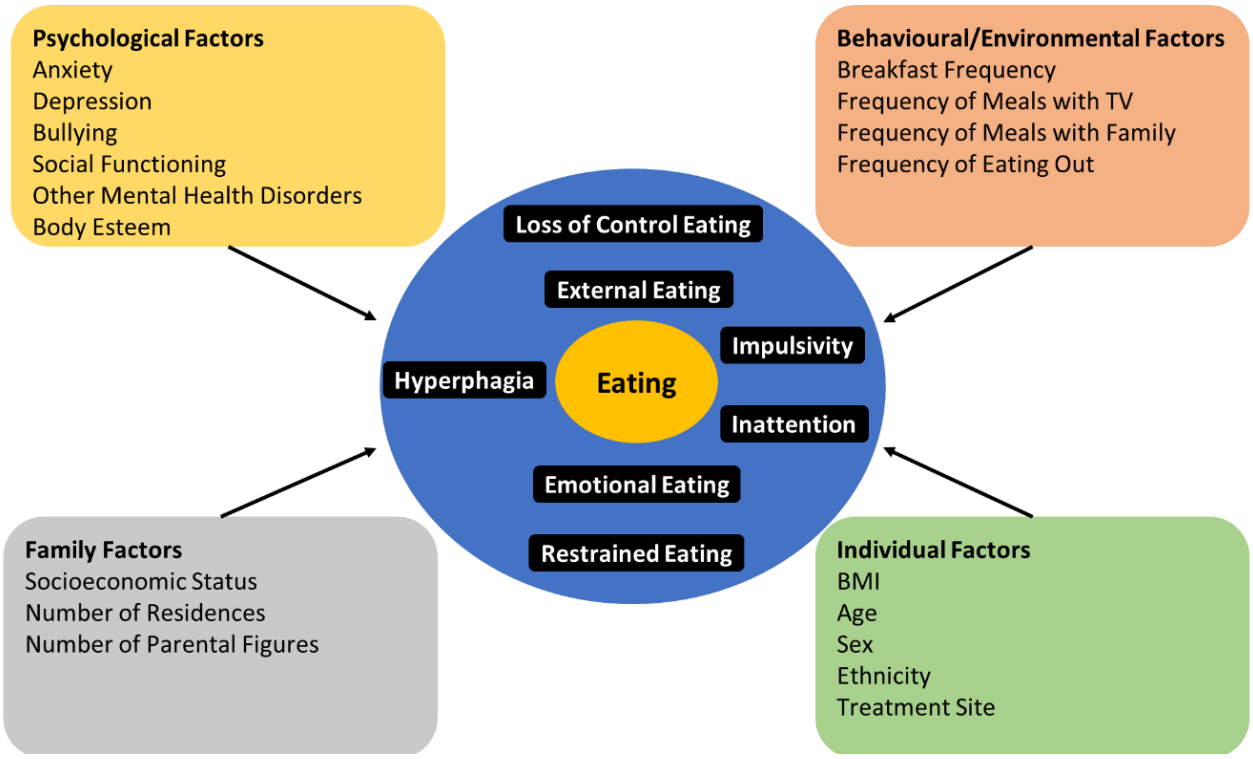

Figure 2. A model of *Pathways to Eating* in children and adolescents with obesity. Illustrated are eating drivers and individual, family, and eating environment factors which have been shown in the literature to influence certain eating drivers.

2.3 HYPOTHESES

1) Research Question: How do eating drivers, including loss of control, emotions, external cues, restrained eating, hyperphagia, impulsivity, and inattention, cluster together into specific phenotypes in children and adolescents with obesity?

2) Research Question: What are the clinical characteristics (listed in Appendix A) that best define/describe the identified eating phenotypes? How do the identified eating phenotypes relate to clinically measured and reported characteristics, including individual, family, and eating environment characteristics of children and adolescents with obesity?

Hypothesis for Research Question 1: We expected that eating drivers would cluster into several eating phenotypes in children and adolescent with obesity. We hypothesized four predominant clusters would appear, based on previous literature and clinical experience. They are: 1) loss of control eating, restrained eating, and emotional eating, 2) loss of control eating, restrained eating, and external eating, 3) impulsivity and external eating, 4) impulsivity and hyperphagia.

Hypothesis for Research Question 2: We anticipated that phenotypes with LOCE would comprise children who eat fewer meals with family, live with one parent, and live in a lower income household. The phenotype with emotional eating was predicted to include a higher percentage of females. Phenotypes with impulsivity were expected to include a greater portion of males. Finally, impulsivity and external eating were thought to be related to the family eating

environment, such as decreased frequency of eating together as a family and increased eating while watching television.

Summary rationale for hypothesis (Research Question 1):

1) LOCE, restrained eating, external eating

LOCE has been extensively studied in the literature and is prominent in children and adolescents with obesity. Goldschmidt and colleagues (2008), among others, have examined the co-occurrence of dietary restraint with LOCE. However, lacking from the literature is investigation into the trigger that causes restrained eaters to lose control over their eating. While the trigger may be an internal physiological component, the smells and sights of food in the modern obesogenic environment may override internal hunger and satiety cues to activate LOCE. Indeed, LOCE and external eating have been found to co-occur in youth with obesity (Goossens, Braet, and Decaluwe, 2007). Therefore, we hypothesized that one prominent cluster would include LOCE and restrained eating, with external cues as the eating trigger.

2) LOCE, restrained eating, emotional eating

Furthermore, other studies have found a co-occurrence of LOCE and emotional eating in adolescents with significantly increased BMI (Stojek et al., 2017; Goossens, Braet, and Decaluwe, 2007). Although these studies did not consider restrained eating, their results seem to suggest that negative emotions may be another missing link from Goldschmidt and colleagues' (2008) findings of the co-occurrence of dietary restraint and LOCE. Research has shown that children may eat as a coping mechanism to compensate for negative emotions (Farrow, Haycraft, and Blissett, 2015; Webber et al., 2009). A high prevalence of negative affect,

including depression and anxiety, in children and adolescents with obesity is associated with emotional eating either to increase positive mood or distract from negative emotions and may mediate the relationship between emotional eating to cope with these symptoms and LOCE (Goossens et al., 2009). Thus, another prominent cluster was hypothesized to include LOCE and restrained eating, with emotional eating as the eating trigger.

3) Impulsivity, external eating

Recently, it has also been found that there exists an increased prevalence of ADHD in children and adolescents with obesity compared to the general pediatric population (Agranat-Meged et al., 2005). Individuals with ADHD have difficulty with self-regulation and inhibitory control. Children with impulsivity may therefore not be able to inhibit their response to food triggers in an obesogenic environment. It has been shown that children and adolescents with obesity show both greater impulsivity and heightened response to reward compared to normal weight peers and this association was related to increased overeating in the former group (van den Berg et al., 2011). Overeating due to behavioural traits may also depend on context. Previous research has found that children with overweight or obesity only differed from normal weight children in ability to delay gratification from a reward when it was food as opposed to the non-food reward (Nederkoorn et al., 2012; Bonato and Boland, 1983). Therefore, the sight or smell of palatable food cues may trigger children and adolescents with impulsive behaviour to disregard internal satiation signals and overeat.

4) Impulsivity, hyperphagia

We also hypothesized that there would be a co-occurrence of both homeostatic and hedonic eating drivers. Little work has been done to measure hyperphagia and its associations in children with non-syndromic obesity, though it has also been suggested that the increased prevalence of obesity in children with ADHD may be attributed to the greater cognitive effort required for conducting mental tasks leading to the constant pursuit of caloric sustenance to fulfill their energy requirements (Riverin and Tremblay, 2009). However, the prevalence of hyperphagia in these children has not been empirically measured.

Chapter 3 Methods

3.1 Overview of Participants

3.1.1 *CANadian Pediatric Weight-management Registry*

Participants for the *Pathways to Eating* study were recruited from the CIHR-funded CANadian Pediatric Weight-management Registry (CANPWR) study, a prospective cohort, multi-centre study that collects cross-sectional and longitudinal anthropometric, lifestyle, and behavioural measures from consenting patients and parents attending interdisciplinary Canadian weight management programs. The overall aim of CANPWR is to evaluate anthropometrics and obesity-related co-morbidities at baseline and their change over time in overweight and obese children and youth. Patients are enrolled in a pediatric-focused weight-management program at one of ten secondary or tertiary care sites in seven cities located throughout Canada. CANPWR participants are 2-17 years old and have a BMI $\geq 85^{th}$ percentile for age and sex according to growth charts from the WHO (Morrison et al., 2014).

Pathways to Eating is a sub-study of CANPWR, funded by a CIHR team grant (Team to Address Bariatric Care in Canadian Children, 2015-2020).

3.1.2 *Pathways participants*

Inclusion criteria for *Pathways* included (i) enrolment in a participating CANPWR centre, (ii) 10-18 years of age with a BMI $\geq$ 85% percentile for age and sex, and (iii) English-speaking. This age range was chosen based on the developmental appropriateness of children and

adolescents to answer self-reflective questions included in the selected and validated questionnaires. Patients who were 17 years old at the time of CANPWR enrolment were eligible for this sub-study at their 12-month CANPWR visit, which is when they would be 18 years of age. As not all questionnaires chosen for this study have a French version available (i.e. Dutch Eating Behaviours Questionnaire and Hyperphagia Questionnaire), proficiency in understanding written English was made a requirement to participate.

Exclusion criteria included significant developmental delay, learning disability, or mental disorder (e.g. acute psychosis) precluding completion of the self-report questionnaires. This was determined by research staff based on the physician's clinical notes or from a verbal recommendation from clinical staff, when patient chart information was unclear.

3.2 Study Design and Plan

The *Pathways to Eating Study* is a cross-sectional examination of eating drivers in children and youth attending weight-management programs in Canada.

a) CANPWR recruitment and visits: Eligible families were approached prior to commencing a treatment program at one of the participating weight management centres. After obtaining informed consent, data were collected from interview- and self-report questionnaires and from the medical chart. Data were collected at a baseline visit, and at 6, 12, 24, and 36-month follow-up time points. These visits were timed for regular clinic visits, or booked as separate research visits if the patient was no longer participating in the clinic program. At each visit, a case report form (CRF) was completed by research staff which consists of

questions asked to the patient and parent related to demographics and eating and exercise habits, as well as information obtained from the medical chart concerning physical measurements and medical diagnoses.

b) *Pathways* recruitment and visits: All of the *Pathways* participants were also CANPWR participants. Patients approached for enrolment in CANPWR who also met the *Pathways* eligibility criteria were consented for *Pathways* at the same time in one of two ways depending on each treatment site's protocol: either *Pathways* was embedded in the CANPWR consent or *Pathways* participation was presented as an optional sub-study (Please see Appendix B for sample *Pathways* section of the consent form). Patients who only became eligible to participate in *Pathways* at their 12-month CANPWR visit because either *Pathways* recruitment had not yet begun at their baseline CANPWR visit or they were below 10 years of age at that visit, were then either automatically enrolled or approached for enrolment at that visit. Each site maintained an enrolment log to ensure each patient was enrolled in *Pathways* once. A portion of the data collected from the CANPWR CRFs was used in the *Pathways* analysis (variables used are described below). Participants enrolled in *Pathways* completed additional questionnaires (described in *Eating Driver Measures* section) at one of the following time points: 1) CANPWR Baseline appointment (i.e. prior to commencing treatment), or 2) 12-month CANPWR follow up appointment (i.e. a research visit approximately 12 months after the initial CANPWR Baseline assessment). Patients were enrolled at both time points for pragmatic reasons, in order to recruit an adequate number of participants over a period of approximately 16 months. Longitudinal research, as well as pilot data from our own program, indicates that overall BMI changes over 6-12

months in pediatric obesity treatment programs are very modest (Luca et al., 2015; Danielsson et al., 2012; Ho et al., 2012; Oude Luttikhuis et al., 2009). For participants enrolled in the sub-study at the 12-month CANPWR visit, time point-dependent data (e.g. BMI, medical diagnoses) were taken from the 12-month CANPWR follow up CRF and additional data were taken from the Baseline CANPWR CRF (e.g. sex, ethnicity). The additional CRF added for patients enrolled in *Pathways* included questionnaires to capture eating drivers of interest. Patients completed two self-report questionnaires which took approximately 8-10 minutes and one parent or guardian completed two parent for-child report questionnaires which took approximately 5-8 minutes. Patients and parents were asked to interpret the questions to the best of their ability without help from research staff. If a word was not understood, research staff were instructed to help the respondent understand the word in an effort to make sure the full questionnaire was completed. Research staff confirmed the completeness of responses.

3.3 Ethics Approval and Confidentiality

Research ethics approval had been previously obtained for CANPWR. The *Pathways* substudy was approved at each site as an amendment to the main CANPWR study. Consent/assent from patients and consent from parents were obtained either from enrolment in CANPWR or, at some sites, as an optional additional substudy. CRFs were anonymized using a unique identification number and data were inputted into a secure centralized data repository system.

3.4 Overview of Canadian Pediatric Weight Management Registry Clinics

The CANPWR sites that participated in *Pathways* include: BC Children's Hospital (Vancouver, British Columbia), Stollery Children's Hospital (Edmonton, Alberta), Alberta Children's Hospital (Calgary, Alberta), McMaster Children's Hospital (Hamilton, Ontario), The Hospital for Sick Children (SickKids; Toronto, Ontario), Credit Valley Hospital (Mississauga, Ontario), Children's Hospital of Eastern Ontario (CHEO; Ottawa, Ontario), and Montreal Children's Hospital (Montreal, Quebec). Programs follow clinical guidelines for obesity management and focus on small, sustainable goal-oriented approaches to diet and exercise. Treatment includes a family-centred approach by a multi-disciplinary team comprising some or all of the following specialties: pediatrics, pediatric endocrinology, nursing, psychology, social work, dietetics, exercise therapy, and behavioural therapy. Some sites also offer group sessions with children/adolescents and parents. Programs range from 6 months in duration (BC Children's Hospital) to indefinite, but most cover a 2-year period.

3.5 Variables Collected

Variables collected as part of the main CANPWR study are described in this section. Of note, a strength of these measures is that they align with measures taken in the Canadian Health Measures Survey (Tremblay, Wolfson, and Connor Gorber, 2007), so comparison with national representative data is possible. See Appendix A for a list of variables.

3.5.1 *Child Demographics*

Child's age, sex, ethnicity, and geographical location were collected. Age was considered based on recruitment time point (Baseline CANPWR or 12-month follow-up CANPWR time point). Child's ethnicity was considered based on the Baseline CANPWR interview, which required the child or family to select all relevant cultural and racial backgrounds from a list provided or to specify an alternative not listed. The most prevalent three ethnicities are reported, while the remaining options are clustered into "other". Geographical location was recorded based on recruitment site.

3.5.2 *Body Mass Index*

BMI is a calculation used clinically to assess weight status and is defined in terms of a weight-to-height (kg/m^2) ratio. The WHO definition of overweight and obesity based on BMI was used to determine eligibility for study participation (Canadian Paediatric Society, 2010). For children and adolescents 5-19 years of age, the WHO defines overweight and obesity as a BMI of greater than the 85^{th} or 97^{th} percentiles or greater than one or two standard deviations above the mean for age and sex, respectively. In the present analysis, BMI and BMI z-scores based on recruitment time point were used as outcome measures of interest.

3.5.3 *Family Demographics*

Household demographic characteristics of interest for the present analysis were socioeconomic status (SES) and living arrangement. SES of the family was based on parent report of total

annual household income. This is expressed as a check box of 5 different income ranges. This variable was time-dependent based on changing family circumstances. Living arrangement included two factors that were recorded based on the child or family's report. The first component was whether the child lives in one primary residence or in multiple households and the second was whether the child lives with one or more than one parental figure. Parental figures could include mother, father, step-mother, step-father, aunt, uncle, or another adult. Living arrangement was also time-dependent as its factors may have changed due to various family circumstances.

3.5.4 *Eating Environment*

Indices related to location and timing of meals were collected, including self-reported frequency of occurrences for each of the following: eating out or ordering in meals, having meals with family, having meals in front of the television, and eating breakfast.

3.5.5 *Psychological Factors*

The social functioning subscale of the Pediatric Quality of Life child self-report questionnaire was used in the present analysis. The subscale has good internal consistency (0.79) and has been found to be valid in distinguishing between healthy children and those with a chronic mental or physical illness (Varni, Burwinkle, and Seid, 2006; Varni, Seid, and Kurtin, 2001). Questions capture self-reported problems over the previous month with getting along with other kids, difficulty with friendships, getting teased, and having trouble keeping up with peers and doing

things peers can do. Patient mental health diagnoses were available from the medical chart. Such diagnoses included depression, anxiety, ADHD, other mental health disorders (e.g. obsessive compulsive disorder, post-traumatic stress disorder, bipolar, schizophrenia, phobias, night terrors), and bullying. The Body Esteem Scale for Adolescents and Adults (BESAA) – shortened version is a 10-item self-report questionnaire that was also administered to obtain information related to weight and shape concerns. Items were selected based on the five most valid items from each subscale (Appearance and Weight) of a confirmatory factor analysis completed by Cragun and colleagues on the original BESAA (Cragun et al., 2013; Mendelson, Mendelson, and White, 2001). Finally, the use of specific medication associated with increased appetite as a side effect was noted; particular medications included 1) CNS psychiatry (i.e. SSRI anti-depressants, other anti-depressants, anti-psychotics) and 2) Medications for ADHD.

3.6 Eating Driver Measures

For *Pathways*, eating drivers of interest included loss of control eating, emotional eating, response to external cues, restrained eating, hyperphagia, impulsivity, and inattention. Measures to capture these eating drivers were chosen on the basis of clinical utility in any treatment setting (i.e. in the presence or absence of a mental health practitioner), quality of measure (validation, previously applied in similar populations), time considerations for participant to fill out, and practicality for clinical research at several participating centres. The selected questionnaires were not meant for diagnostic or screening purposes as part of a clinical assessment. Measures are described in detail in this section. Table 1 outlines the eating drivers being measured, the measurement scale used to assess the specific eating driver, and validity of

the measures employed. Please see Appendix C for the *Pathways* CRF which captured eating drivers.

3.6.1 *Eating Disorders Examination Questionnaire: Loss of Control Eating*

Tools for measuring LOCE are limited. However, the Eating Disorders Examination Questionnaire (EDE-Q) is a commonly used self-report questionnaire which measures an array of eating behaviours and attitudes including dietary restraint, eating concerns, weight concerns, and shape concerns (Fairburn and Beglin, 1994). The EDE-Q was developed as a cost-effective and time-saving alternative to the Eating Disorders Examination (EDE) semi-structured interview which can only be conducted by an extensively trained administrator (Fairburn and Beglin, 1994). Importantly, EDE-Q can be used in clinical and research settings when economic and time considerations are of the essence (Binford, Le Grange, and Jellar, 2005) and its validity in comparison to the interview has been repeatedly demonstrated in the literature (Black and Wilson, 1996; Fairburn and Beglin, 1994), including in children and adolescents ages 9-19 with eating disorders (Binford, Le Grange, and Jellar, 2005).

As neither the EDE nor EDE-Q have a LOCE scale, we adapted the method used by Goossens, Braet, and Decaluwe (2007) with the EDE to capture LOCE from the EDE-Q. A more recent study used strictly the questions related to LOCE from the EDE-Q in adolescents aged 12-20 years (Schluter et al., 2016). The questionnaire asks respondents five sequential questions about the occurrence and frequency of objective and subjective overeating episodes and whether LOCE was experienced. Similar to other studies using this measure, we used a behaviour recall period of 14 days instead of 28 days (Hansson, Daukantaite, and Johnsson,

2015; Carter, Stewart, and Fairburn, 2001), due to the greater ability of our participants being able to estimate frequency over a shorter time frame, and simplified the question wording (e.g. "circumstances" was changed to "situation") (Carter, Stewart, and Fairburn, 2001). LOCE was used as a continuous variable as sum of number of events (subjective and objective LOCE) over the preceding two weeks.

3.6.2 *Dutch Eating Behaviours Questionnaire: Emotional Eating, External Eating, Restrained Eating*

The Dutch Eating Behaviours Questionnaire (DEBQ) (van Strien et al., 1986) is a frequently utilized and validated self-report questionnaire in adults that measures emotional eating, external eating (eating in response to external cues), and restrained eating. It was originally developed and validated using samples with overweight and obese individuals and is internally consistent across weight groups (Bohrer, Forbush, and Hunt, 2015). An abbreviated and simplified version of the DEBQ has also been utilized to assess similar disordered eating behaviours in children (van Strien and Oosterveld, 2008). The Dutch Eating Behaviours Questionnaire for Children (DEBQ-C) is a 20-item, self-report questionnaire that provides scores for emotional, external, and restrained eating. Emotional eating questions pertain to eating as a coping method for negative feelings such as depression and worry, external eating concerns eating in response to sight or smells in the surrounding environment, and restrained eating captures restrictive behaviour towards food quantity or temporality of eating. This adapted version of the questionnaire has been validated in children ages 7 to 14 years (Banos et al., 2011; van Strien and Oosterveld, 2008). The original adaptation for children scored items on a 3-point Likert

scale (1 (no), 2 (sometimes), and 3 (yes)) (van Strien and Oosterveld, 2008), whereas a more recent adaptation scores items on a 5-point Likert scale (0 = never to 4 = always) (Wagner et al., 2015). Higher numbers represent worse symptoms. The increased number of increments allows for more variation to be detected in our population and for easier assessment of change or improvement in future longitudinal studies (Krosnick and Presser, 2010). In the present analysis, 7 items are summed to obtain an emotional eating score, 6 for external eating, and 7 for restrained eating.

The DEBQ-C was chosen over other possible measures because of its use in pediatric populations, feasibility, and inclusion of multiple eating drivers of interest. Other measures that have been used to assess restrained eating and emotional eating include the Three-Factor Eating Questionnaire (TFEQ) and the Emotional Eating Scale. As previously mentioned, the DEBQ-C has been validated in and the wording tailored for children, whereas the TFEQ has not been modified for use in children. The DEBQ-C also encompasses three of our eating drivers of interest and was therefore chosen over the use of multiple assessment tools in order to reduce the questionnaire burden for our study participants. Finally, the DEBQ-C had previously been incorporated into the clinical assessments at multiple recruitment sites for this study, which allowed for greater ease of study initiation in those clinics.

3.6.3 *Hyperphagia Questionnaire: Hyperphagia*

The Hyperphagia Questionnaire (HQ) is a parent for-child report questionnaire that measures hyperphagic behaviour, drive, and severity. Dykens and colleagues initially designed the HQ for the PWS population to measure food-related preoccupation and behaviour and severity of these

concerns (Dykens et al., 2007). Typical approaches to measuring hyperphagia in PWS include monitoring food intake in a laboratory setting, which leads to overconsumption of food quantity and associated medical risks or the absence of concealed behaviour otherwise reported by parents perhaps due to the unnatural environment (Dykens et al., 2007). Additionally, other measures do not allow for the measurement of symptom severity (Dykens et al., 2007), which may be important in considering treatment approaches. The HQ was developed due to the lack of reliable measures to accurately evaluate hyperphagia, including the range of unique food-seeking behaviours that individuals with insatiable hunger may exhibit such as nighttime food seeking and foraging through the trash (Dykens et al., 2007). There currently exists no other self-report measure for hyperphagic behaviour. The HQ has previously been used to assess hyperphagic symptoms in populations with syndromic obesity in relation to suspected hyperphagia, including Bardet-Biedl Syndrome, Trisomy 21, pseudohypoparathyroidism type 1a, WAGR syndrome, and Smith-Magenis syndrome (Foerste et al., 2016; Wang and Shoemaker, 2014; Sherafat-Kazemzadeh et al., 2013; Crain, 2010; Han et al., 2008). Participants in the aforementioned studies included children, adolescents, and adults from ages 2-25 and were diagnosed with one of the syndromes in question or were in a comparison group that constituted normal-weight individuals or those with lifestyle-related obesity. Original factor analysis of HQ items by Dykens and colleagues (2007) in patients with PWS revealed three subscales accounting for 57% of the variance within hyperphagia. Eleven of thirteen of items from the HQ clustered into one of: hyperphagic behaviour (e.g. frequency of seeking food outside of mealtimes), drive (e.g. focus on food-seeking), and severity (e.g. time focused on food). Parents rate their child on 13 behaviours relating to food using a 5-point scale from never/rarely a problem to severe/always a problem. Scoring based on 11 items yields a score for

behaviour, drive, and severity. A total score can also be calculated and ranges between 11 and 55, with higher scores representing a severe or frequent hunger and lower scores meaning few or no hyperphagic symptoms are exhibited. In case a parent reports his/her child never exhibits a certain behaviour but "never" is not an answer choice, the least frequent answer choice is selected (e.g. "a few times a year"). In the present study, the total hyperphagic score was used.

3.6.4 *Strengths and Weaknesses of ADHD Symptoms and Normal Behaviour Scale: Impulsivity, Inattention*

The Strengths and Weaknesses of ADHD Symptoms and Normal Behaviour Scale (SWAN) is administered to parents and asks them to rate their child in comparison to similar-aged children on 18 symptoms related to ADHD. Swanson and colleagues developed the SWAN based on the Swanson, Nolan, and Pelham-IV scale (SNAP-IV) for evaluating ADHD symptoms (Swanson, Schuck, et al., 2012). The SNAP-IV requested categorical responses to statements based on the 18 symptoms of ADHD in the *Diagnostic and Statistical Manual of Mental Disorders* using a 4-point scale, with 0 representing the absence of the symptom and 1-3 representing the increasing prevalence of the symptom (Brites et al., 2015). Further analysis of the SNAP-IV revealed that the prevalence of ADHD symptoms in a normal population were over-estimated because of a right-ward skewness of the rating scale (Swanson, Schuck, et al., 2012). Therefore, the SWAN was developed to capture the full array of strengths and weaknesses of ADHD symptoms within a population (Swanson, Schuck, et al., 2012). Modifications from the SNAP-IV include the addition of 3-points to the left side of the scale that measure increasing strengths above average, as well as wording adjustments to reflect neutrality or strengths in behaviours. Using a scale

with gradual increases towards both severity ends in a normal distribution decreases the risk of obtaining a false positive or negative from using binary ratings (Brites et al., 2015). In contrast to other scales which strictly screen for hyperactivity/impulsivity, inattention, or both, the SWAN provides a wider range of scores and the ability to assess a continuous distribution of abilities (Swanson, Schuck, et al., 2012; Hay et al., 2007; Polderman et al., 2007). The SWAN has been used by parents to assess ADHD symptoms in a range of studies on preschool-aged children to adults (Brites et al., 2015) and several studies on children and adolescents aged 6-20 (Crosbie et al., 2013; Hurtig et al., 2011; Ramtekkar et al., 2010; Hay et al., 2007). Items on the SWAN are rated on a 7-point scale (-3 to +3), with average behaviour rated zero. Positive scores indicate the child is worse than average in ADHD symptoms and negative scores signify above average strengths. Scoring the SWAN provides a subscale for inattention (items 1 to 9) and for hyperactive-impulsive (items 10 to 18), as well as a total abilities score. Thus, higher positive scores on each subscale represent worsening symptoms, while increasing negative scores represent strengths and fewer symptoms. For the purpose of the present analysis, both the inattention and hyperactive-impulsive subscales are used.

Table 1. Questionnaires used to measure eating drivers in pathways study

Driver	Questionnaire	Scoring of Items	Scoring of Scale	Validity Scores
Loss of control eating	EDE-Q	0 (No) → 1 (Yes)	0 → 1	Not available
Emotional eating	DEBQ-C	1 (Never) → 5 (Very Often)	7 → 35	Cronbach's alpha = 0.80 (van Strien and Oosterveld, 2008); = 0.88 (overweight group; (Banos et al., 2011))
External eating	DEBQ-C	1 (Never) → 5 (Very Often)	6 → 30	Cronbach's alpha = 0.74 (van Strien and Oosterveld, 2008); = 0.73 (overweight group; (Banos et al., 2011))
Restrained eating	DEBQ-C	1 (Never) → 5 (Very Often)	7 → 35	Cronbach's alpha = 0.81 (van Strien and Oosterveld, 2008); = 0.66 (overweight group; (Banos et al., 2011))
Hyperphagia	HQ	1 (Never a problem) → 5 (Always a problem)	11 → 55	Hyperphagic Behavior: Cronbach's alpha = 0.76; Hyperphagic Drive: Cronbach's alpha = 0.80; Hyperphagic Severity: Cronbach's alpha = 0.60 (Dykens et al., 2007)
Impulsivity	SWAN	-3 (Far above average) → +3 (Far above average)	-27 → +27	Not available

Inattention	SWAN	-3 (Far above average) → +3 (Far above average)	-27 → +27	Not available

3.7 Data Analytic Plan

3.7.1.1 *Primary Objective*

Latent Profile Analysis (LPA) was used to detect the most appropriate number of 'phenotypes' that can be derived from the eating drivers, or indicator variables, under consideration. LPA assigns membership to a 'latent' class from patterns of interrelationships among indicator variables. The number of classes set is based on maximizing similarity within a class while maximizing dissimilarity between classes. For this study, LPA analysis was used to determine how variables cluster together to reveal hidden subtypes of eating drivers in an obese pediatric population. The indicator variables were eating drivers of interest.

A number of modeling methods have been used to identify the number of latent groups present among a set of variables. Most studies using LPA determine the number of classes using multiple modeling methods. Most commonly, the Bayesian Information Criterion (BIC), sample size adjusted BIC (aBIC), Akaike Information Criterion (AIC), bootstrap likelihood ratio test (BLRT), and entropy are used. Though commonly employed, AIC and entropy are the least reliable methods in selecting the most appropriate model. A review of various LPA modeling methods concluded that while the BIC is most commonly used, BLRT outperformed all other methods tested in accurately predicting the number of classes (Nylund, Asparouhov, and

Muthén, 2007). This method uses bootstrap resampling to provide a *p* value that can be used to determine the number of classes, or phenotypes, that provides the best model of fit for the data. However, often multiple modeling methods are used and compared to determine the best-fitting model. For present purposes, BLRT, BIC, and, aBIC were used to determine how many classes fit the data most appropriately. For BIC and aBIC, the lowest value of each index indicates the number of classes that best fit the data.

3.7.1.2 *LPA Sample Size Justification*

It is important to have a high degree of certainty when identifying the number of classes present in a population and assigning each population member to the class to which they belong. However, it is difficult to determine a priori the sample size needed to detect the correct number of classes because the highest determinant of power in LPA is inter-class separation distance, rather than sample size or number of variables (Tein, Coxe, and Cham, 2013). Inter-class distance is analogous to effect size such that it is the difference between the variable means of two populations divided by the groups' average standard deviation. A recent study in normal weight and overweight children and adolescents examining some of the eating behaviours included in this study found that the traits clustered into 5 classes using data collected from 411 children (Vannucci et al., 2013). A second paper using LPA to analyze satiety and food responsiveness found 3 significant classes in 117 obese children (Boutelle et al., 2014). A simulation study based on previous research in eating disorders found that at least 300 participants is recommended for similar studies (Swanson, Lindenberg, et al., 2012). Thus, a

sample size of 300 children and adolescents was determined to be sufficient for significantly identifying distinct eating phenotypes.

3.7.2 *Secondary Objective*

Once the best fitting model was identified, participants were assigned to a latent class phenotype of eating based on posterior probabilities. In other words, subjects were assigned to the phenotype that most closely resembles their eating driver scores. Subsequently, clinical characteristics were compared between phenotypes. Continuous variables were assessed using an analysis of variance (ANOVA), categorical variables were tested using chi square or Fisher's exact test, and non-normal variables were analyzed based on their medians using Kruskal-Wallis test. The independent variable in all cases was the LPA class assignment. Dependent variables of interest fell into one of three categories: 1) Demographic: age, sex, ethnicity, treatment site, SES (household income), living arrangement (number of residences; number of parental figures), 2) Anthropometric: BMI, BMI z-score, and 3) Eating Environment: frequencies of eating out or ordering in meals, having meals with family, eating meals in front of the television, and eating breakfast.

Additionally, multinomial logistic regression was used to determine the relative risk between phenotypes on clinical characteristics that were significant at $p < 0.2$ in the ANOVA. The cluster with the most participants was used as a reference cluster against the other clusters (dependent variables) to determine relative risk based on each clinical characteristic (independent variables) of belonging to a certain group.

3.7.3 *Exploratory Analysis*

An exploratory analysis was also performed using ANOVA to determine whether identified phenotypes relate to other mental health outcomes, such as social functioning, psychiatric or ADHD medication use, mental health diagnoses, and body esteem. Relevant mental health outcome variables (i.e. $p < 0.2$ for the ANOVA) were included in the multinomial logistic regression conducted for the secondary objective.

R version 3.2.5 was used for LPA. For all other analyses, SAS version 9.4 (SAS Institute, Cary, NC, USA) was used. For omnibus tests, significance was determined for $p \leq 0.05$. Tukey's or Mann-Whitney post-hoc test was used to determine pair-wise significance for mean or median scores when omnibus tests showed significance. Pair-wise significance was determined for $p \leq 0.05$.

Chapter 4 Results

4.1 Demographic Characteristics of Pathways Participants

Demographic characteristics of participants and their families are presented in Table 2. Data collection for *Pathways* occurred between November 2015 and March 2017. In total, 309 children and adolescents (46.0% male) between 10.05 and 19.17 years of age (mean age = 14.08 ± 2.17) were included in the *Pathways* analysis. The self-identified ethnic/cultural background of the population was 68.9% White. Participants' mean BMI was 35.9 ± 8.0, with a z-score of 3.40 ± 1.02, which indicates severe obesity (severe obesity > +3) (de Onis et al., 2007). Household income, measuring SES, was less than $49,999 for 25.3% of families, $50,000 to $79,999 for 22.7%, $80,000 to $99,999 for 15.3%, and $100,000 and above for 30.8%; responses to this question were not available for 5.8% of participants. Regarding living arrangement, 86.4% of the sample lived in one residence, while the remaining 13.6%, in multiple households. Additionally, 75% lived with more than one parental figure in the home and 25% lived with only one parental figure. Overall, demographic information was available for the entire sample except in one case where questions on the CRF related to SES, living arrangement, and BMI were not completed.

Eight out of ten CANPWR sites, located in seven cities throughout Canada, participated in the *Pathways to Eating* study: BC Children's Hospital (Vancouver, BC), Stollery Children's Hospital (Edmonton, AB), Alberta Children's Hospital (Calgary, AB), McMaster Children's Hospital (Hamilton, ON), SickKids (Toronto, ON), Credit Valley Hospital (Mississauga, ON), CHEO (Ottawa, ON), and Montreal Children's Hospital (Montreal, QC). Two CANPWR sites were unable to participate in *Pathways* for the following reasons: 1) Primarily francophone

patients and inability to validate French translation of the questionnaires administered in *Pathways* (Centre hospitalier universitaire Sainte-Justine, Montreal, QC) and 2) Program discontinuation (North York General Hospital, Toronto, ON). In all, the distribution of participants was 0.3% from BC Children's Hospital, 7.1% from Stollery Children's Hospital, 15.2% from Alberta Children's Hospital, 26.2% from McMaster Children's Hospital, 21.7% from SickKids, 12.9% from Credit Valley Hospital, and 16.5% from CHEO. Montreal Children's Hospital did not enrol any participants over the recruitment period.

Table 2. Demographic characteristics of participants and their families

Characteristic	**Mean ± SD or N (of 309 participants; %)**
Age (y)	14.08 ± 2.17
Age range (min, max)	10.05, 19.17
Sex (Male)	142 (46.0)
Ethnicity	
White	213 (68.9)
Black	22 (7.1)
Latin American	10 (3.2)
Other	77 (24.9)
Socioeconomic Status*	
Less than $49,999	78 (25.3)
$50,000 to $79,999	70 (22.7)
$80,000 to $99,999	47 (15.3)
$100,000 and above	95 (30.8)
Not available	18 (5.8)

Characteristic	Mean ± SD or N (of 309 participants; %)
Living Arrangement*	
One Residence	266 (86.4)
Multiple Households	42 (13.6)
One Parental Figure	77 (25.0)
> 1 Parental Figure	231 (75.0)
BMI (kg/m^2)*	35.9 ± 8.0
BMI z-score**	3.4 ± 1.0
Site	
McMaster CH	81 (26.2)
CHEO	51 (16.5)
SickKids	67 (21.7)
Credit Valley	40 (12.9)
BC CH	1 (0.3)
Stollery CH	22 (7.1)
Alberta CH	47 (15.2)

* N=308; **N=307; CH=Children's Hospital

4.2 Latent Profile Analysis: Determining Eating Phenotypes

Participant scores from the seven eating drivers of interest were used in LPA to determine the clustering properties of these variables. Scoring ranges, mean, and median scores from the population of interest are provided in Table 3.

Table 3. Descriptive statistics for eating drivers in *Pathways* population

Eating driver	Possible scoring range	Mean	SD	Median	Interquartile range (p 25, p 75)	Range (min, max)
Loss of control eating	0 → ∞	1.74	4.13	0	(0, 2)	(0, 43)
Emotional eating	7 → 35	13.28	5.99	12	(8, 16)	(7, 35)
External eating	6 → 30	15.83	4.91	16	(12, 19)	(6, 30)
Restrained eating	7 → 35	17.56	5.14	17	(14, 21)	(7, 34)
Hyperphagia	11 → 55	21.96	8.07	21	(15, 27)	(6, 51)
Impulsivity	-27 → +27	-2.20	9.86	0	(-9, 3)	(-27, 25)
Inattention	-27 → +27	0.69	9.96	1	(-5, 7)	(-27, 27)

The distribution of scores for each eating driver is displayed in Figures 3-9. Non-normally distributed data (e.g. for LOCE, emotional eating, and hyperphagia) were not adjusted or log transformed. The distribution of LOCE scores may represent a mixture of platykurtic (wide tails) and leptokurtic (high peak) distributions. This kurtosis is expected and contributes to determining latent classes in LPA analysis (McLachlan and Peel, 2000).

The majority of participants (60.2%) were asymptomatic for LOCE. A further approximately 30% of participants reported between one and five episodes of LOCE over the previous 14 days. Most participants scored low on emotional eating, whereas the scores for external eating and restrained eating were evenly distributed across the scoring range (never to very often). Scores for hyperphagia mostly ranged from never/not a problem to sometimes/sometimes a problem. Parents generally rated their children as normal for impulsivity and approximately 35% of children exhibit above average impulse control. Finally,

the distribution for inattention was normal, with some children having above normal attention and an approximately equal number having below average attention.

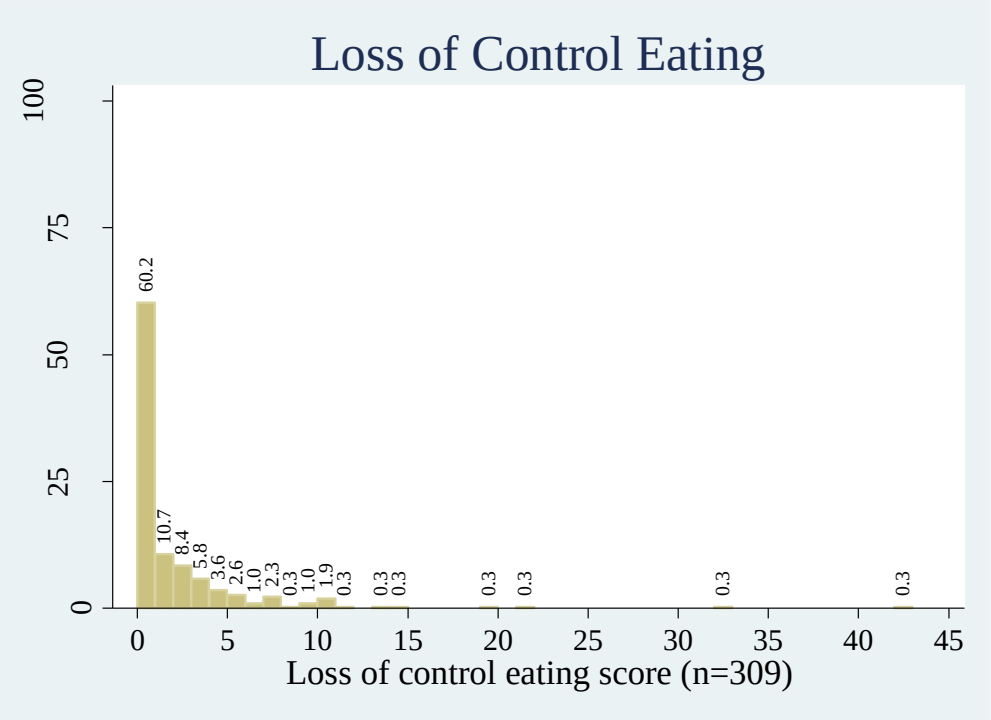

Figure 3. Distribution of loss of control eating scores for the full sample (n=309)

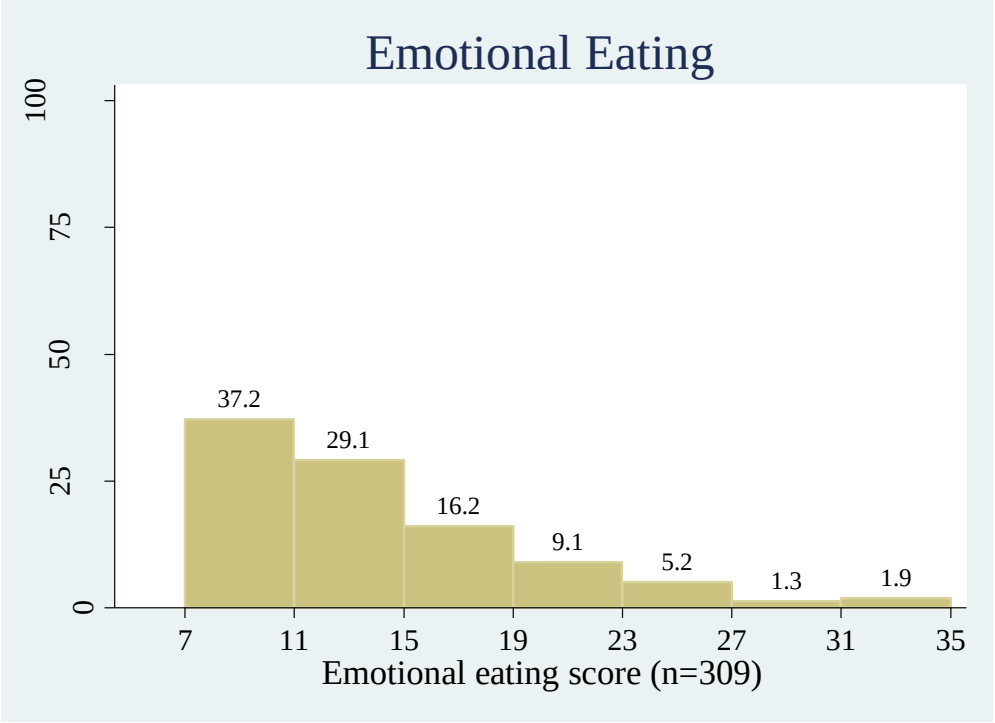

Figure 4. Distribution of emotional eating scores for the full sample (n=309)

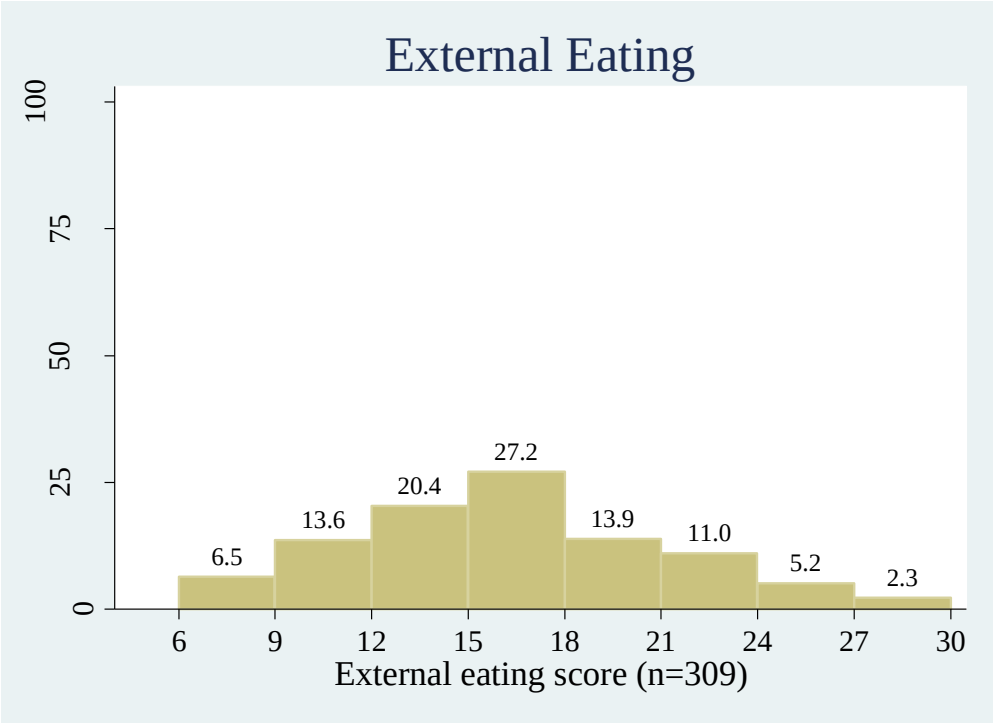

Figure 5. Distribution of external eating scores for the full sample (n=309)

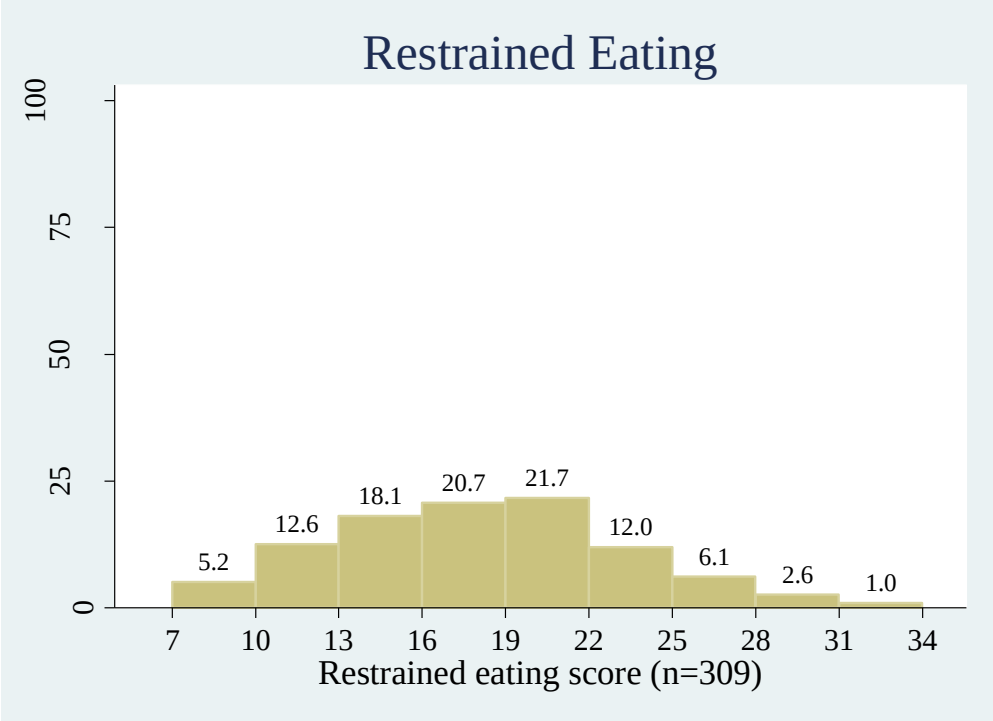

Figure 6. Distribution of restrained eating scores for the full sample (n=309)

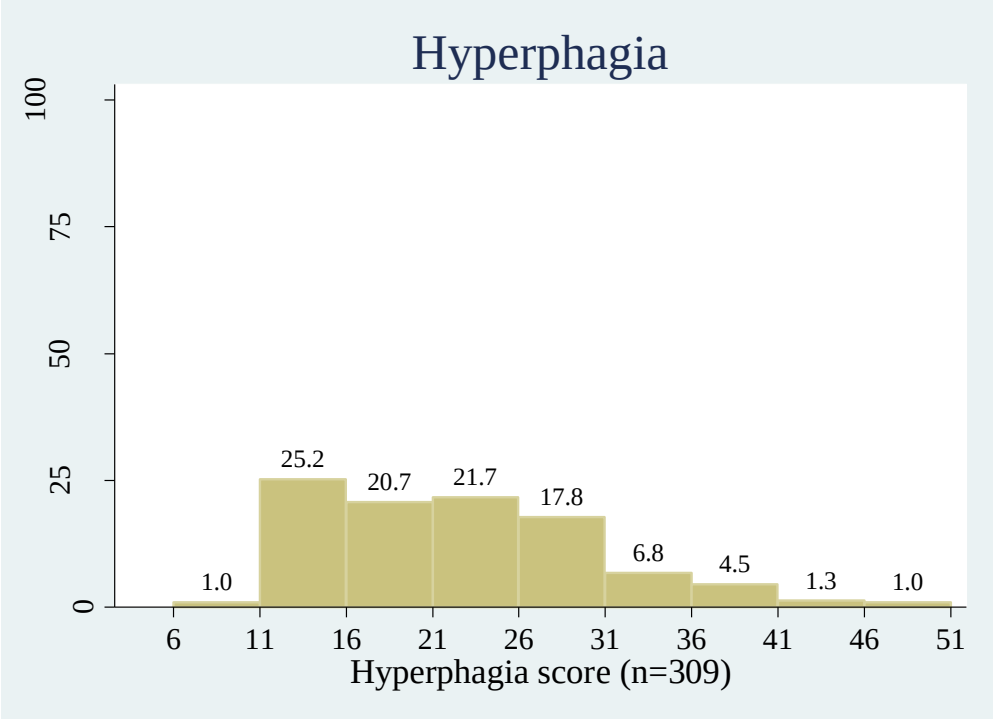

Figure 7. Distribution of hyperphagia eating scores for the full sample (n=309)

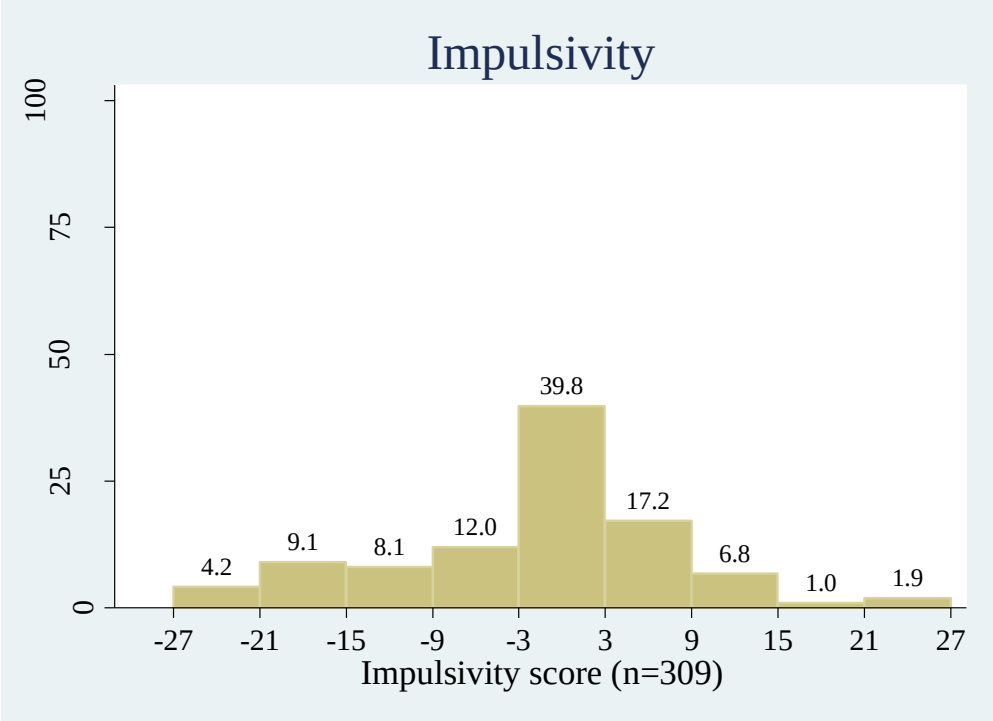

Figure 8. Distribution of impulsivity scores for the full sample (n=309)

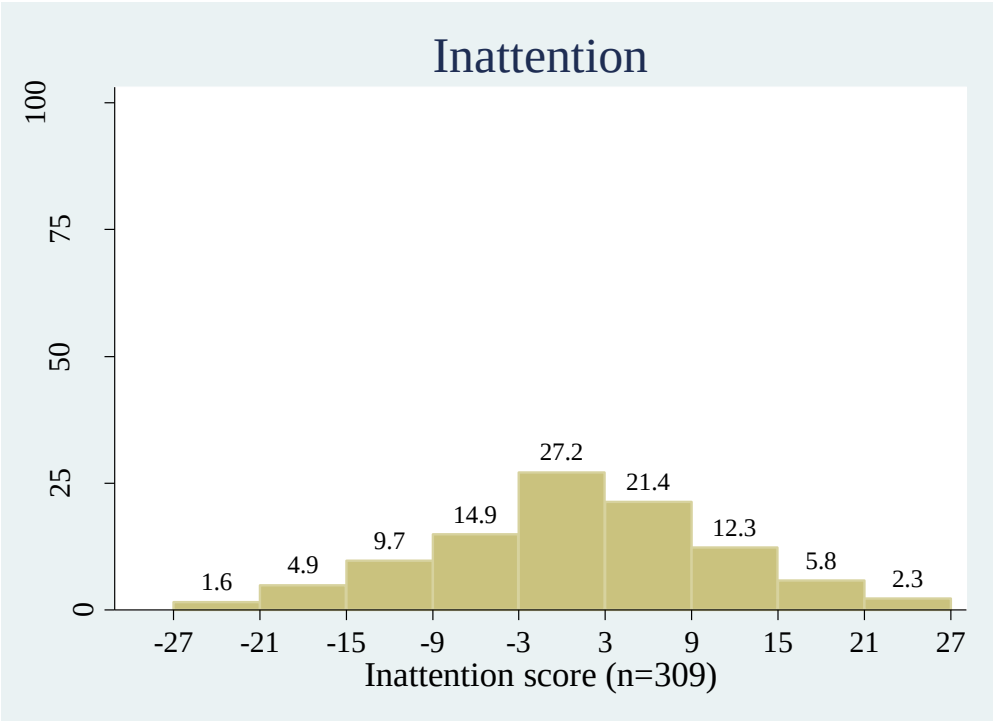

Figure 9. Distribution of inattention scores for the full sample (n=309)

Latent profile analysis was conducted and model fit was assigned using three recommended indices (Table 4). For BIC and aBIC, lower values indicate better model fit. For BLRT, which is the index most recommended for proper selection of model fit (Nylund, Asparouhov, and Muthén, 2007), model significance is indicated by the lowest *p* value. Overall model was chosen based on a combination of model fit indices and number of individuals in each phenotype.

Table 4. Model fit indices for latent profile analysis performed using 7 eating drivers

Number of latent classes	BIC	aBIC	BLRT
1	13940.07	14029.73	
2	13496.91	13622.43	0.001
3	13168.58	13329.97	0.001
4	13416.20	13613.45	0.988
5	13128.64	13361.76	0.001
6	12530.77	12799.75	0.495
7	13189.80	13494.65	0.001
8	13203.50	13544.21	0.567
9	12792.18	13168.76	0.001

Upon examination of the results from the LPA, it was determined that a model including three phenotypes was most appropriate interpretation of the data. As illustrated in Table 4, two of three model fit indices, namely BIC and aBIC, were lowest for a 6-class solution. However, BLRT was not significant for this model. The second lowest BIC and aBIC values were for the

9-class solution and BLRT is statistically significant. However, due to the large number of classes in this model, the number of participants within multiple phenotypes would be limited and secondary analysis results between groups would be difficult to interpret. The next choice for all model fit indices would be either the 3-class or 5-class model, as aBIC is third lowest for the 3-class model and BIC is third lowest for the 5-class model. BLRT is significant for both models. However, the distribution of participants in the 5 classes was discrepant with the largest group having 185 members and the smallest having 8 members. Since secondary comparisons between groups would be difficult to analyze statistically and interpret clinically because of this discordance in cluster size, the 3-class model was determined to best represent the overall data. The 3-phenotype model has robust group sizes that are more comparable in number of participants. The eating driver profile for the 3-phenotype solution is displayed in Table 5.

Table 5. Mean (± SD) or median (interquartile range) eating driver scores for each phenotype in the 3-class model

Eating driver	Phenotype 1	Phenotype 2	Phenotype 3	p-value
N	44	186	79	
Loss of control eating[1]	3.0 (1.5, 9.5)	0.0 (0.0, 0.0)	2.0 (1.0, 4.0)	< 0.001
Emotional eating[1]	10.5 (7.5, 14.0)	11.0 (7.0, 14.0)	17.0 (13.0, 22.0)	< 0.001
External eating[2]	15.95 ± 4.66	14.85 ± 4.49	18.08 ± 5.30	< 0.001
Restrained eating[2]	18.45 ± 5.13	16.63 ± 5.17	19.24 ± 4.59	< 0.001
Hyperphagia[2]	22.59 ± 6.39	20.69 ± 8.03	24.62 ± 8.40	0.001
Impulsivity[1]	1.0 (0.0, 6.0)	0.0 (-8.0, 3.0)	-3.0 (-13.0, 3.0)	0.001
Inattention[1]	5.0 (1.0, 9.0)	0.0 (-5.0, 6.0)	-3.0 (-9.0, 5.0)	< 0.001

[1]Kruskal-Wallis test
[2]F-test (ANOVA)

To name and define the phenotypes by their features the following approach was used. An ANOVA of eating drivers between eating phenotypes was performed (Table 5). For drivers with a normal distribution within the phenotype, an F-test ANOVA was used and for drivers without a normal distribution, a Kruskal-Wallis non-parametric test was used. Results from these tests are displayed in Table 5 and indicate that all eating drivers are significantly different between phenotypes. To determine which eating drivers were significant to each phenotype we used post-hoc testing and each phenotype was compared to each of the other two phenotypes (see Table 6). In a significant comparison, the phenotype with the higher mean or median eating driver score was determined to include that eating driver in the phenotype's eating profile.

Table 6. Pairwise comparisons of means or medians of eating drivers between phenotypes

	p-values for pairwise comparisons		
Eating driver	Phenotype 1 vs Phenotype 2	Phenotype 1 vs Phenotype 3	Phenotype 2 vs Phenotype 3
Loss of control eating[2]	**< 0.001**	**0.037**	**< 0.001**
Emotional eating[2]	0.689	**< 0.001**	**< 0.001**
External eating[1]	0.349	**0.047**	**< 0.001**
Restrained eating[1]	0.080	0.684	**< 0.001**
Hyperphagia[1]	0.325	0.362	**0.001**
Impulsivity[2]	**0.004**	**< 0.001**	0.146
Inattention[2]	**0.001**	**< 0.001**	**0.031**

[1]Tukey's test
[2]Mann-Whitney test

Once the highest scoring eating drivers were identified for each phenotype, their severity scores were calculated. Severity score is the percentage of one hundred of the rounded mean or median score divided by the highest score in the scoring range. Each severity score was then adjusted based on the total severity out of one hundred. Using this approach, the 3 phenotypes were: 1) LOCE-ADHD (LOCE, impulsivity, inattention), 2) No-ED (no elevated eating drivers compared to the other phenotypes), and 3) Restrained-Triggered (LOCE, emotional eating, external eating, restrained eating, hyperphagia). Figure 10 illustrates the result of these calculations graphically for each of the 3 phenotypes.

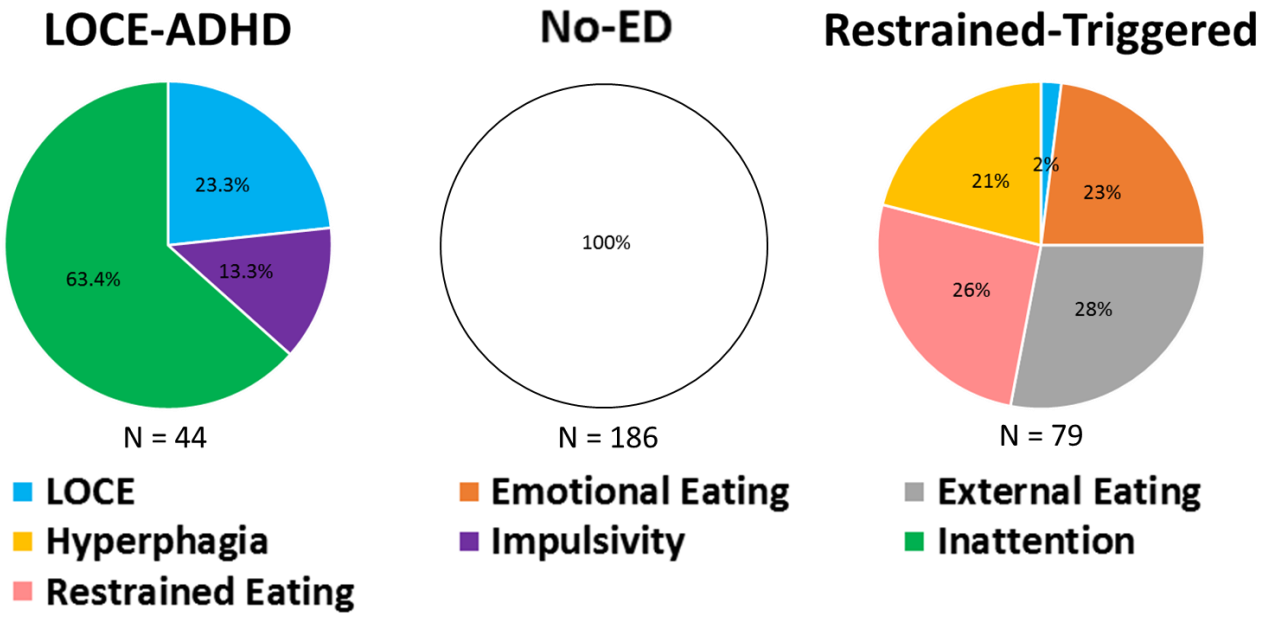

Figure 10. Visual representation of phenotypes. Phenotypes include the following eating drivers: 1) LOCE-ADHD (LOCE, impulsivity, inattention), 2) No-ED (no elevated eating drivers compared to the other phenotypes), and 3) Restrained-Triggered (LOCE, emotional eating, external eating, restrained eating, hyperphagia). Percentage severity of each eating driver was calculated based on the percentage of one hundred of the rounded mean or median eating

driver score divided by the highest score in the scoring range. Each severity score was then adjusted based on the total severity of all drivers out of one hundred.

A significant majority of participants (60.0%, n = 186) reported and were characterized as having no eating drivers with scores significantly greater than the other phenotypes (Phenotype "No-ED"). In this No-ED group, there were no reported LOCE episodes, low levels of emotional, external, restrained eating, and hyperphagia, and normal impulse control and attention. The rest of the sample clustered into two symptomatic phenotypes. LOCE-ADHD included 14.2% (n = 44) of participants who are exclusively characterized by their LOCE symptoms which occurred on average three times over a two-week period. This group also had below average characteristics of impulsivity and inattention. Finally, Restrained-Triggered comprised 25.6% (n = 79) of the sample. Affected participants in this group had high levels of emotional, external, and restrained eating, moderate hyperphagia, and on average, one LOCE episode per week.

4.3 Secondary Analysis: Eating Phenotypes and Clinical Characteristics

The three phenotypes were compared across various demographic, anthropometric, and eating environment measures. As shown in Table 7, phenotypes were significantly different for age and BMI. LOCE-ADHD was associated with younger age, being almost a full year younger than the other two groups, and was also associated with a lower mean BMI value. At a non-

significant but trend level, the LOCE-ADHD phenotype also had the highest non-White ethnicities and had the lowest frequency of eating out or ordering in meals on a weekly basis. No significant associations were found for sex, SES, living arrangement, treatment site, BMI z-score, or other eating environment measures.

Table 7. Comparison of clinical characteristics between the three phenotypes. Values displayed as mean (± SD), N (%), or median (interquartile range)

Variable	LOCE-ADHD	No-ED	Restrained-Triggered	p-value
N	44	186	79	
Child Demographics				
Age (y)[1]	13.31 ± 2.30	14.19 ± 2.12	14.24 ± 2.13	**0.040**
Sex (Male)[3]	22 (50.00)	82 (44.09)	38 (48.10)	0.705
Ethnicity (White)[3]	25 (56.82)	136 (73.12)	52 (65.82)	0.087
Site[2]				0.206
McMaster CH	15 (34.09)	48 (25.81)	18 (22.78)	
CHEO	7 (15.91)	35 (18.82)	9 (11.39)	
SickKids	5 (11.36)	39 (20.97)	23 (29.11)	
Credit Valley	4 (9.09)	24 (12.90)	12 (15.19)	
BC CH	0 (0.00)	1 (0.54)	0 (0.00)	
Stollery CH	6 (13.64)	8 (4.30)	8 (10.13)	
Alberta CH	7 (15.91)	31 (16.67)	9 (11.39)	
Anthropometrics				

Variable	LOCE-ADHD	No-ED	Restrained-Triggered	p-value
BMI (kg/m^2)[1]	32.99 ± 7.82	36.63 ± 8.18	35.69 ± 7.52	**0.026**
BMI z-score[1]	3.16 ± 1.01	3.47 ± 1.03	3.35 ± 1.00	0.168
Family Characteristics				
Socioeconomic Status[3]				0.351
Below $80,000	24 (60.00)	85 (48.02)	39 (53.42)	
$80,000 and above	16 (40.00)	92 (51.98)	34 (46.58)	
Living Arrangement				
Number of Residences[3]				0.152
One Residence	42 (95.45)	158 (85.41)	66 (83.54)	
Multiple Households	2 (4.55)	27 (14.59)	13 (16.46)	
Number of Parental Figures[3]				0.690
One Parental Figure	9 (20.45)	49 (26.49)	19 (24.05)	
> 1 Parental Figure	35 (79.55)	136 (73.51)	60 (75.95)	
Eating Environment				
Frequency of eating out or ordering in meals (Weekly)[4]	0.5 (0.5, 1.0)	1.0 (0.5, 3.0)	1.0 (0.5, 3.0)	0.082

Variable	LOCE-ADHD	No-ED	Restrained-Triggered	p-value
Frequency of having meals with the family (Weekly)[4]	7.0 (5.5, 7.0)	7.0 (3.0, 7.0)	7.0 (3.0, 7.0)	0.258
Frequency of meals in front of the television (Weekly)[4]	3.0 (0.0, 7.0)	1.0 (0.0, 7.0)	3.0 (0.0, 7.0)	0.897
Frequency of having breakfast (Weekly)[4]	7.0 (3.0, 7.0)	5.5 (3.0, 7.0)	5.5 (2.0, 7.0)	0.141

[1]F-test (ANOVA)
[2]Chi-square test
[3]Fisher's exact test
[4]Kruskal-Wallis test

4.4 Exploratory Analysis: Eating Phenotypes and Mental Health Outcomes

The phenotypes were also compared across mental health indices, including social functioning, medication use (medications for psychiatric diagnoses, medications for ADHD), obesity-related health issues (depression, anxiety, ADHD, other mental health issues, bullying), and body esteem. As displayed in Table 8, phenotypes were significantly different for social functioning and body esteem. LOCE-ADHD was associated with greater social functioning difficulties, while Restrained-Triggered was associated with lower body esteem. LOCE-ADHD was also associated at a trend-level with fewer diagnoses of depression. No significant associations were observed for medication use and other obesity-related health issues.

Table 8. Comparison of mental health outcomes between the three phenotypes. Values displayed as mean (± SD), N (%)

Mental Health Outcome	LOCE-ADHD	No-ED	Restrained-Triggered	p-value
N	44	186	79	
Social Functioning[1]	1.47 ± 1.02	0.95 ± 0.83	1.18 ± 0.85	**0.001**
Medication Use[3]				
CNS psychiatry	5 (11.36)	28 (15.05)	13 (16.46)	0.745
Medications for ADHD	8 (18.18)	19 (10.22)	10 (12.66)	0.335
Obesity related health issues[3]				
Depression	3 (6.82)	29 (15.59)	18 (22.78)	0.066
Anxiety	9 (20.45)	55 (29.57)	26 (32.91)	0.338
ADHD	10 (22.73)	30 (16.13)	15 (18.99)	0.560
Other mental health disorders	4 (9.09)	13 (6.99)	10 (12.66)	0.309
Bullying	12 (27.27)	48 (25.81)	20 (25.32)	0.971
Body esteem[1]	27.00 ± 10.23	29.38 ± 9.33	23.97 ± 8.36	< **0.001**

[1]F-test (ANOVA)
[2]Chi-square test
[3]Fisher's exact test
[4]Kruskal-Wallis test

4.5 Multinomial Logistic Regression for Measurement of Relative Risk

To determine the risk profile of the two symptomatic phenotypes compared to the No-ED phenotype on clinical characteristics and mental health outcomes, we used a multinomial logistic regression. Variables of interest were ones with a *p* value of < 0.2 in the ANOVA performed between phenotypes and included age, ethnicity, BMI z-score, frequency of eating out or ordering in meals, frequency of having breakfast, social functioning, depression, and body esteem. Also included in the model was enrolment timepoint (Baseline CANPWR versus 12-month CANPWR follow up) to determine whether there was an association between length of time in the program and phenotype.

Results showed that being ethnically White resulted in a 69% lower risk of being in the LOCE-ADHD group, eating out or ordering in meals more often resulted in a 36% lower risk of being in the LOCE-ADHD group, having good body esteem resulted in a 5% lower risk of being in the LOCE-ADHD group, and having poor social function resulted in a 222% greater risk of being in the LOCE-ADHD group than the No-ED reference group (see Table 9). Having good body esteem also resulted in a 7% lower risk of being in the Restrained-Triggered group in relation to the No-ED group (see Table 9). No difference was found between enrolment timepoints in risk for either model.

Table 9. Risk profile for all phenotypes compared to No-ED phenotype

Clinical Characteristic	Relative Risk Ratio (95% CI)	p-value
MODEL 1 – Phenotype 2 (No-ED) versus Phenotype 1 (LOCE-ADHD)		
Age (y)	0.87 (0.70, 1.08)	0.202
Ethnicity: White	0.31 (0.14, 0.70)	**0.004**
BMI z-score	0.75 (0.48, 1.17)	0.210
Frequency of eating out or ordering in meals (Weekly)	0.64 (0.45, 0.92)	**0.016**
Frequency of having breakfast (Weekly)	1.11 (0.93, 1.34)	0.250
Social Functioning	2.23 (1.37, 3.64)	**0.001**
Depression	0.46 (0.11, 2.00)	0.299
Body esteem	0.95 (0.91, 1.00)	**0.037**
Enrolment timepoint: Baseline	1.13 (0.39, 3.29)	0.821
MODEL 2 – Phenotype 2 (No-ED) versus Phenotype 3 (Restrained-Triggered)		
Age (y)	0.92 (0.78, 1.07)	0.273
Ethnicity: White	0.63 (0.34, 1.17)	0.140
BMI z-score	0.81 (0.59, 1.10)	0.181
Frequency of eating out or ordering in meals (Weekly)	1.06 (0.96, 1.17)	0.244
Frequency of having breakfast (Weekly)	0.97 (0.86, 1.09)	0.633
Social Functioning	1.01 (0.70, 1.46)	0.957
Depression	1.25 (0.55, 2.82)	0.591
Body esteem	0.93 (0.89, 0.97)	< **0.001**
Enrolment timepoint: Baseline	0.99 (0.45, 2.17)	0.976

Chapter 5 Discussion

The primary aim of this study was to characterize whether children and adolescents with obesity can be classified into latent groups based on reported eating drivers. Based on latent profile analysis of 7 eating drivers of interest (loss of control eating, emotional eating, external eating, restrained eating, hyperphagia, impulsivity, and inattention), results show that a large sample of treatment-seeking youth cluster into 3 distinct phenotypes. These phenotypes included: 1) LOCE-ADHD (LOCE, impulsivity, inattention, 2) No-ED (no elevated eating driver scores), and 3) Restrained-Triggered (LOCE, emotional eating, external eating, restrained eating, hyperphagia). Notably, LOCE was the only driver which appeared in more than one group.

The secondary objective aimed to examine whether certain measures of demographics, anthropometrics, and eating environment were significantly different between identified phenotypes. The exploratory analysis sought to determine if mental health outcomes differed between phenotypes. We found that age, BMI, social functioning, and body esteem were significantly different across the phenotypes. The LOCE-ADHD phenotype was generally younger in age, non-White, had lower BMI, ate out or ordered in meals less frequently, had decreased social functioning, and had fewer diagnoses of depression than the other two groups. The Restrained-Triggered phenotype had the lowest body esteem amongst the three groups.

5.1 Latent Profile Analysis

5.1.1 *Latent Profile Analysis: Phenotype 1) LOCE-ADHD*

Almost 15% of the population were classified into the LOCE-ADHD phenotype, which was composed of mostly inattention, with impulsivity and LOCE. Together, impulsivity and inattention comprise the criteria for the diagnosis of ADHD. Though we did not hypothesize the clustering of these drivers, there exists preliminary evidence in the literature of the co-occurrence of LOCE with both a diagnosis of ADHD and high impulsivity scores in children and adolescents with obesity (Reinblatt, Mahone, et al., 2015). In a population of children attending mental health clinics, children with ADHD were 16 times more likely to have binge eating behaviour, including LOCE episodes, than those without ADHD (Reinblatt, Leoutsakos, et al., 2015). Longitudinal analysis has shown that symptoms of hyperactivity/inattention in late childhood indirectly predict LOCE behaviour in adolescence mediated by overeating in late childhood; higher BMI was also associated with an ADHD diagnosis in late childhood (Sonneville et al., 2015). Therefore, it is possible that in a subset of individuals, the development of ADHD in childhood may lead to LOCE episodes in late childhood and adolescents. Perhaps there are underlying developmental or neurobiological pathways that are similar to both ADHD and LOCE, thus causing their co-occurrence in some individuals with obesity (as suggested by Reinblatt, (2015)). Recent evidence in a twin study shows that a shared genetic pathway could explain the association between ADHD and binge eating behaviours, particularly among females (Capusan et al., 2017). In the current *Pathways* study, assessment of longitudinal and genetic associations between eating drivers was not possible but may assist in understanding the eating profile of this group of patients.

Another possible explanation for the significant proportion of inattention and LOCE in this subgroup is their tendency towards eating as a compensatory method for the frustrations associated with poor attention (Cortese et al., 2007). Participants who are inattentive may also have more difficulty adhering to a meal schedule and may experience LOCE episodes because of the decreased ability to plan or follow structured meal times (Cortese et al., 2007). Unfortunately, these factors were not presently assessed.

5.1.2 *Latent Profile Analysis: Phenotype 2) No-ED*

More than half of the participants (n = 186) did not report or were not associated with any concerning eating drivers. All eating driver scores in the No-ED group were on the low end of each driver's rating scale, indicating that the behaviours were exhibited or experienced never or rarely. Considering that over half of the eating drivers of interest in this study were self-reported, it is possible that results were confounded by the participants' underreporting of problematic eating behaviour. Since the measures were administered during the patients' initial visit to the weight management programs, perhaps participants were reluctant to divulge sensitive behavioural information. However, measures used for these drivers have been previously used and/or validated in children with overweight and obesity (Banos et al., 2011; van Strien and Oosterveld, 2008; Goossens, Braet, and Decaluwe, 2007).

We may also consider other explanations for obesity in the group without apparent eating drivers. Living in the current obesogenic environment with decreased physical activity, poor choices for low-cost nutritious foods, and high stress lifestyles are only a few factors that may contribute to excess weight gain in children (Chang and Neu, 2015). Child abuse is an

additional environmental factor that may increase risk for obesity later in life (Hemmingsson, Johansson, and Reynisdottir, 2014). Along with these environmental factors implicated in the development of obesity, new evidence has proposed a role in early life for the human microbiome in epigenetic modifications leading to obesity and other health problems (Chang and Neu, 2015). Therefore, a genetic predisposition, genetic modifications, and/or environmental factors may be the more predominant contributors to obesity in the No-ED group but were not evaluated in this study. Future studies may explore early childhood factors or measures related to current lifestyle (e.g. diet, physical activity, stress) in secondary analyses to determine relative prominence between eating phenotypes.

It is possible that, compared to the other groups, the No-ED group consists of children and adolescents who may be more likely to benefit from education related to healthy food choices and exercise, with less of a focus on eating drivers. In this group, poor nutrition and exercise practices may have more of an effect on weight status than external or internal factors that may be driving overeating. Longitudinal analysis would allow for the assessment of the weight outcomes and change in eating driver profile of this group following participation in current weight management programs.

The low eating driver severity profile of the No-ED group is quite robust in our population, as observed from the reclassification of phenotypes from a 6-class model to a 5-class model and then again, from a 5-class model to a 3-class model (Tables 10 and 11). Participants from the No-ED group are not re-classified to other phenotypes.

Table 10. Reclassification of participants from the 6-class model to the 5-class model

Five class	Six class						Total
	1	2	3	4	5	6	
1	8	0	15	2	0	4	29
2	0	185	0	0	0	0	185
3	40	0	1	26	1	6	74
4	0	1	1	3	2	1	8
5	0	0	2	1	1	9	13
Total	48	186	19	32	4	20	309

Table 11. Reclassification of participants from the 5-class model to the 3-class model

Three class	Five class					Total
	1	2	3	4	5	
1	16	0	26	0	2	44
2	0	185	0	1	0	186
3	13	0	48	7	11	79
Total	29	185	74	8	13	309

5.1.3 *Latent Profile Analysis: Phenotype 3) Restrained-Triggered*

The second largest subgroup (n = 79), namely Restrained-Triggered, had the most complex eating profile compared to the other groups. Members had nearly equal amounts of emotional eating, external eating, restrained eating, and hyperphagia, as well as LOCE. This group seems to be the most disordered in their eating, as members are affected by five of seven eating drivers of interest.

Our first and second hypotheses, that LOCE and restrained eating would cluster with emotional eating and external eating, respectively, were partially based on the findings of Goossens, Braet, and Decaluwe (2007) and Goldschmidt et al (2008), who identified the co-occurrence of LOCE, emotional eating, and external eating, and LOCE and restrained eating, respectively, in an adolescent population with obesity. We found that indeed, the Restrained-Triggered group did consist of restrained eating and LOCE. Both emotions and external cues also clustered into this group and seem to trigger this repeated cycle of dieting and binging (as discussed by Ackard et al., (2003)). It is known that chronic overweight in adolescents leads to restrictive eating behaviour to achieve weight loss (Snoek et al., 2008), and anecdotally, a majority of patients in Toronto's SickKids Team Obesity Management Program (STOMP) have reported past weight loss efforts. The Restraint-Triggered phenotype therefore may be explained by Restraint Theory, such that chronic dieting behaviours lead to disinhibited eating caused by internal or external triggers (Herman and Mack, 1975). In this case, internal factors may include emotions and hyperphagic drive and external factors may include sights and smells in the environment measured using the external eating subscale. Thus, this subgroup with a high prevalence of disordered and disinhibited eating has features similar to a number of previous findings in the literature.

Furthermore, studies in children across the weight spectrum, including those seeking weight management treatment, have found that negative emotions and psychological disorders correlate with both emotional eating and LOCE (Eddy et al., 2007; Glasofer et al., 2007; Braet and Van Strien, 1997). As the Affect Regulation Model suggests, loss of control over eating may act as a self-soothing method to relieve negative mood states (Goossens et al., 2009). Experimental evidence for this theory is found in a systematic review which found that in adults

with obesity and binge eating disorder, negative emotions trigger binge eating behaviour as a coping mechanism (Leehr et al., 2015). Previous research suggests that in overweight children and adolescents, emotional eating may mediate the relationship between certain dysregulated mood states, such as anxiety, and LOCE (Goossens et al., 2009). For example, children with anxiety may use emotional eating as a coping method for their nervous symptomatology (Goossens et al., 2009). While not directly investigated in this study, the proposed mediation effect of emotional eating may be reflected in the Restrained-Triggered group's eating profile, which includes both emotional eating and LOCE.

5.1.4 *Latent Profile Analysis: General Discussion*

Overall, LOCE, emotional eating, impulsivity, and inattention scores did not represent a normal distribution. For LOCE, the high peak and wide tail can be partially attributed to there being no upper end to the scoring range in the measure that was used. As previously mentioned, non-normal distributions may also represent a combination of two or more distributions which contribute to determining the number of latent classes, including one (or more) with wide tails (platykurtic) and one (or more) with a high peak (leptokurtic) (McLachlan and Peel, 2000). Our results seem to indicate that for LOCE, the high peak corresponded to the No-ED phenotype and the wide tails were indicative of the other two phenotypes. Similar observations can be made for the skewness in the other eating driver scores.

Interestingly, LOCE affected all problematic eating phenotypes to varying extents. This finding is perhaps not surprising, as the literature indicates up to 60% of adolescents with overweight or obesity have experienced LOCE (He, Cai, and Fan, 2017) with children as young

as 6 years of age having experienced a LOCE episode (Tanofsky-Kraff et al., 2005). The pervasiveness of LOCE in this population is important for treatment considerations. Although we did not consider all criteria for a diagnosis of binge eating disorder, including at least one episode of LOCE per week for at least three months, feeling distress over the binge, and feeling shame and guilt about the binge (American Psychiatric Association, 2013), a large portion of participants in this study may have met the frequency of LOCE episode criterion since they indicated at least two episodes of LOCE over a two-week period. Also related to binge eating disorder is compensatory behaviours to prevent weight gain, such as purging. Prior to a more recent focus on obesity and eating disorders, eating disorder research on bulimia nervosa included both binge eating and inappropriate compensatory behaviours (Chao, 2014). In this study, we also were unable to measure purging behaviours in association with binge eating, as this information is not assessed in CANPWR and we were limited by the types of eating behaviour measures which could be used due to a lack of psychological support at some study sites. Therefore, though many participants endorsed LOCE, we were unable to determine what percentage met criteria for an eating disorder diagnosis.

While scores for emotional eating were generally not high, this eating trigger affected a significant portion of participants in our sample. Most scores ranged from rarely to sometimes on the scoring scale. We expected that emotional eating would appear in about one quarter of participants, and indeed, the Restrained-Triggered group was characterized by emotional eating and represented approximately one quarter of the sample.

Most of the sample scored in the “sometimes” range for external eating. However, unlike emotional eating, a greater percentage of participants scored above the median scoring range.

We hypothesized that a sizeable portion of our population would be affected by external food cues, including those with impulsive tendencies who would be triggered to eat by sights and smells due to their impulsivity. However, the clustering of these eating drivers was not observed. Nevertheless, we did correctly predict the clustering of external eating and LOCE with restrained eating.

More than 20% of participants scored between sometimes and very often on the DEBQ-C restrained eating scale. Although the DEBQ was originally validated in obese populations and a modified version has been used for children and adolescents, a careful evaluation of the questions asked on this scale seems to indicate questions relate to non-harmful behaviours. For example, questions were posed pertaining to monitoring food consumption, not eating between meals, avoiding food consumption after the evening meal. Although the questions associate these behaviours with the intention of losing weight, these are potentially healthy lifestyle behaviours that would be learned in a weight management program. Therefore, perhaps in our current population and especially in the Restrained-Triggered subgroups, higher restrained eating scores may indicate conscious attempts of changing eating behaviours in an effort to lose weight. However, because of the predominant influence of internal and external eating triggers these efforts may be unsuccessful.

A unique distinction between the present study and other studies that have assessed eating drivers in youth is that others have used the Eating in the Absence of Hunger (EAH) questionnaire to capture emotional eating, external eating, and eating during boredom when the subject is not hungry or already satiated (Boutelle et al., 2014; Vannucci et al., 2013). Although the EAH questionnaire has been found to be reliable in capturing these eating behaviours (Zocca

et al., 2011; Tanofsky-Kraff et al., 2008), the questions and subscales overlap with the DEBQ-C. The EAH measures eating during states of sadness or depression, anger or frustration, and anxiousness or nervousness on its emotional eating subscale, while the DEBQ-C measures eating while depressed, lonely, restless, afraid and if things go wrong, when worried, and when feeling sorry to also capture emotional eating. The EAH assesses eating if food looks or smells good and when others are still eating to measure external eating, while the DEBQ-C includes these scenarios in addition to eating due to walking by a candy store or restaurant, because someone prepares food, and because it is difficult to stay away from delicious foods. Therefore, the obvious difference between the two measures is eating while bored (EAH) and restrained eating (DEBQ-C). We chose to only administer the DEBQ-C to participants in order to avoid redundancy of questions, reduce patient burden, and to capture restrained eating based on our hypothesis of the interaction between this eating behaviour and other eating drivers (e.g. LOCE, emotional eating, and external eating).

While hyperphagia generally characterizes individuals with obesity secondary to a genetic syndrome, we found that a significant portion of parents endorse hyperphagic behaviour in their children and adolescents without syndromic obesity. Over 10% of our sample scored between sometimes a problem to always/significant problem on questions related to preoccupation with food and food-seeking behaviour. Since hyperphagia is relatively unstudied in non-syndromic obese populations, this finding indicates that future research should not disregard this behaviour which is shown to be significant in a sizable portion of this population.

We did not find the prevalence of ADHD to be near 60% as indicated by previous research in in-patient youth with obesity (Agranat-Meged et al., 2005), however, a significant

portion of cases had below average impulsivity (>25%) and inattention (>40%) scores. We also found that in approximately 15% of participants these traits cluster together with LOCE which could drive overeating. Since the presently used SWAN questionnaire is based on the *Diagnostic and Statistical Manual of Mental Disorders* criteria for diagnosing ADHD, our findings may indicate that some patients have gone undiagnosed before attending weight management programs. Future research could aim to determine whether prior diagnoses in our population correspond to scores of impulsivity and inattention collected for this study.

5.2 Differences in Clinical Characteristics and Mental Health Outcomes Between Phenotypes

Between all three phenotypes, significant differences were found in age, BMI, social functioning, and body esteem. LOCE-ADHD participants were found to be younger, of lower BMI, and had poorer social functioning. Restrained-Triggered individuals had low body esteem. Along with these characteristics, variables with *p* values greater than the cut off for significance but less than 0.2 that were also of interest to further explore were included in a multinomial logistic regression. Such variables included: ethnicity, BMI z-score, frequency of eating out or ordering in meals, frequency of having breakfast, and depression. Regression analysis revealed that among these variables, compared to No-ED, the LOCE-ADHD group were less likely to be ethnically White and to eat out or order in meals, had worse social functioning, and lower body esteem. The regression also determined that compared to No-ED, the Restrained-Triggered group had significantly lower body esteem. Finally, contrary to our hypotheses, we did not find that results were affected by sex, living arrangement (i.e. residence stability versus moving

between households or single-parent versus multiple parent households), eating meals with family, or eating meals in front of the television.

There exist other notable observations regarding the secondary and exploratory analyses. Although BMI was significantly lower in the LOCE-ADHD group, the BMI z-score was not. However, BMI z-score was entered into the regression model, as this is the recommended measurement for pediatric populations, but was not significant in the fully adjusted model. We found that those of the LOCE-ADHD phenotype were less likely to be White, which could be influenced by cultural influences of parental perception of impulsivity and inattention. In the United States, a study found that African American parents are less likely to rate their children as having traits consistent with ADHD compared to White parents (Hillemeier et al., 2007). Our non-White parent group was quite heterogeneous, so it is impossible to know how parenting and cultural factors may influence parent-for-child ratings on this measurement tool. In addition, this group was less likely to eat out or order in meals. There is a paucity of literature relating to this topic, however, it is not implausible that cultural practices may be different between White and non-White groups in this regard. Our finding of lower social functioning in this group is consistent with the interpersonal model of LOCE, such that poor social functioning leads to LOCE behaviour (Reinblatt, 2015; Elliott et al., 2010). As well, lower body esteem in the two problematic phenotypes compared to the reference (No-ED) phenotype is reflected in the more significant disordered eating behaviours clustered in these two groups, and especially notable within the Restrained-Triggered group. Though the secondary analysis did not indicate a significant difference between all groups in having ADHD diagnosis or being on medication for ADHD, this group had an overall greater percentage of participants with a diagnosis and on related medication. As indicated in the methods above, the information for these questions is

obtained through medical chart review of clinic notes. Since this information for the majority of participants in this study was obtained from the baseline visit to the weight management clinic, patients may not as yet have had a formal diagnosis of ADHD available at the time of the medical visit. As suggested by Reinblatt, Leoutsakos, et al. (2015), medications for ADHD may initially suppress appetite and therefore limit the propensity towards LOCE but reverse this inhibition when the appetite-suppression side effect is attenuated. This medication effect may be an explanation for the observed clustering of eating drivers in the LOCE-ADHD group. Furthermore, the literature on weight-altering side effects of psychotropic medications suggests that they have various effects on appetite, with some more expected to cause weight loss and others, weight gain (Hasnain and Vieweg, 2013). These medications influence the homeostatic and hedonic appetite regulation system through their affinity for its receptors (Werneke, Taylor, and Sanders, 2013). Although we did not find any significant differences, we should note that 15% of our participants were taking psychiatric medication and 12%, medication for ADHD. Thus, it is necessary to mention that despite finding no differences in taking psychotropic medications between groups, appetite-altering effects were possible in those taking stimulant medication.

Another important finding is that based on the multinomial logistic regression, there was no significant risk of belonging to a disordered eating depending on enrolment time point. The second entry point of 12 months after initial CANPWR enrolment was used for feasibility in order to achieve an appropriate sample size within the time constraints of a Master's thesis. As 80% of participants were enrolled at the baseline CANPWR time point, our population was very reflective of patients entering a weight management program. In reality, however, a majority of patients entering the treatment programs have previously sought treatment in other treatment

programs or are receiving treatment from multiple sources. Moreover, attrition rates of pediatric weight management programs are between 27-73%, which is considerably high (Skelton et al., 2011), thus at 12 months we would expect considerable heterogeneity regarding duration of treatment. We ultimately could not determine if this factor had an influence on the results, as we could not control for treatment received to date. Hence, as we continue to collect data from participants enrolled at the baseline CANPWR visit, confirmatory cross-sectional analysis and further longitudinal analysis to assess changes in eating drivers and phenotypes will be possible.

Finally, to distinguish phenotypes we examined 22 clinical or mental health variables using either F-test ANOVA, chi-square test, Fisher's exact test or Kruskal-Wallis test. Since our total number of participants (309) exceeded the standard 10 data points per variable, we can be confident that there was enough power in the analysis. As well, the *p*-values that were significant were fairly low, thus limiting the chance of accepting false positive values.

5.3 Strengths and Limitations

This study had several strengths and limitations based on the methodological approaches used to evaluate eating drivers in children and adolescents with obesity. Our findings contribute to the limited available research on the clustering of appetitive traits and eating behaviours in children and adolescents, and is the only study to examine several drivers in a clinical population with obesity. We investigated several common eating drivers, including components of attention deficit hyperactivity disorder which is highly co-morbid in our population of interest. Strengths

and limitations for the clinical population chosen, data collection, study design, and data analysis will be discussed.

Population: A strength of this study is that participants spanned a wide age range and were of diverse socio-economic status, ethnicity, and living arrangements from across Canada. With access to a national database we were able to compare results across treatment sites to determine if geography influenced eating characteristics of our population. Recruitment rates were high with only 7% declining participation. However, our sample included exclusively treatment-seeking participants, which may represent a more severely affected subgroup of youth with obesity. Therefore, results may not be fully generalizable to children and adolescents with obesity in the community.

Data Collection: Data for this study were collected using an approach that could easily be incorporated into a fast-paced clinical setting, as is the case at the CANPWR clinics. As such, the concise package of 25 item patient self-report (approximately 8-10 minutes) and 31 item parent for-child questions (approximately 5-8 minutes) could be easily administered in a similar clinic setting for participants to complete between clinician appointments. The questionnaire format allows for several eating drivers to be captured in a short amount of time with low patient burden.

However, despite these strengths in the data collection format, there exists some limitations that should considered. First, since the measures of interest did not have questionnaires available exclusively for children or for parents, it was necessary to use a combination of patient self-report and parent for-child report questionnaires. Therefore, we had to rely on reported behaviour from two different sources, which may have confounded results.

Parents may not have been aware of, for example, their child's food-seeking tendencies captured by the Hyperphagia Questionnaire before starting the treatment program. Additionally, parents may have found it difficult to compare their child's self-regulation and attentive behaviour to similar-aged children if they are not often in the presence of their child's peers. Ideally, the SWAN would have also been administered to teachers who would have reported on impulsive and inattentive tendencies in comparison to an *average* student. However, we feel that the questionnaires used for either self-report or parent-report were the best available for the measure of interest, such that patients themselves would be able to self-identify emotional eating, loss of control eating, restrained eating, and external eating, while their parents would be able to more accurately evaluate their child's food-seeking, impulsive, or inattentive behaviour.

A further potential limitation regarding the questionnaires used to capture eating drivers of interest is that modifications that were applied to the EDE-Q and DEBQ-C. Due to the limited available self-report questionnaire measures to capture LOCE, we used five questions from the EDE-Q (adapted from the methods described in Schluter et al., (2016) and Goossens, Braet, and Decaluwe, (2007)). Using a portion of a full questionnaire can alter validity, however since the EDE-Q maintains all five LOCE questions in sequence, this reduces the possibility of change in validity. We also changed the period of behaviour recall from 28 days to 14 days to ease our patients' ability to estimate number of episodes, as has been done previously (Hansson, Daukantaite, and Johnsson, 2015; Carter, Stewart, and Fairburn, 2001). We adjusted the Likert scale to include five points in the DEBQ-C from the original 3-point scale, similar to a previous study (Wagner et al., 2015).

Lastly, based on expert clinical opinion (STOMP clinical health psychologists and physician) some small changes were made to simplify or clarify specific words on the questionnaires. Input was also provided by reviewing with a few adolescents and parents with agreement on changes. Specifically, on the EDE-Q, 'circumstances' was changed to 'situation' and on the Hyperphagia Questionnaire two words were changed in favour of more colloquial language, such as 'forage' to 'search' and 'clever' to 'sneaky'.

It is difficult to discern the 'most ideal' method to capture all eating drivers of interest under unrestricted conditions. The Eating Disorders Examination interview is often used to capture LOCE and provides an opportunity for patients to clarify questions and for the interviewer to make sure the questions are understood and answered most accurately. Self-report measures for emotional eating, external eating, and restrained eating may be the best method to examine these eating drivers, since feelings of shame or unease may prevent an interviewer from accurately assessing the occurrence of related behaviours during an initial encounter with a patient. There is currently no alternative to the HQ available to measure hyperphagia, and therefore, further research is needed to validate this questionnaire in children and adolescents with obesity unrelated to PWS or another syndrome. Additionally, anecdotally, parents found the HQ questions somewhat challenging as several did not include *never* or *not a problem* as an answer choice. Parents were instructed to select the least frequent answer choice (e.g. "a few times a year") if the behaviour was untrue for their child, thus some behaviours may have been overestimated for some participants. Finally, as previously indicated, a teacher report on the SWAN may be an appropriate tool to assess impulsivity and inattention, since average child or adolescent behaviour may be difficult for a parent to assess.

Through the CANPWR study we also had access to several questionnaires related to other health behaviours. CANPWR utilized validated questionnaires from the Canadian Health Measures Survey (Tremblay, Wolfson, and Connor Gorber, 2007), which allowed for the potential to compare results to those of a national sample. However, some measures, such as those related to nutritional intake, did not reflect the depth of information that would be obtained in a typical dietetics assessment. Furthermore, the CANPWR dataset also provided access to anthropometric, demographic, medical, and behavioural information collected from patient interviews, questionnaires, and the medical chart. Therefore, the medical data used in this study was limited to the information available in the participant's medical chart. Finally, although in our introduction we presented a brief discussion of the known associations between family relationships and eating drivers, we were limited to the specific family-related variables that were available in the CANPWR study. Attachment theory describes the development of the emotional bond between infant and primary caregiver and how this connection influences the child's behavioural and emotional development (Bowlby, 1970). Indeed, research has shown that strong relationships between caregivers and children are fundamental for the development of positive relationships through life, which help to build strategies for emotion regulation and play a role in the physiological regulation of hunger and satiety (Maras et al., 2016). A recent study has found a significant relationship between insecure attachment and BMI z-scores in adolescents, which was mediated by eating behaviours measured by the DEBQ, including restrained eating (Maras et al., 2016). In future studies, it would be beneficial to measure quality of family relationships, including measures of attachment, to explore whether there are identifiable protective or harmful family factors in the development of eating drivers in children with obesity.

Study Design: The present study is also limited by the cross-sectional design. Longitudinal investigation into treatment effects on eating drivers would assist in determining whether certain phenotypes better respond to existing lifestyle treatment approaches (see future directions). Furthermore, study design does not allow for the determination of whether eating phenotypes are a cause or consequence of their distinguishing characteristics.

Data Analysis: A further strength of this study is the consistency in how study procedures were applied. The data were also considerably clean, as complete eating driver questionnaires were available for 90% of participants. A centralized study coordinator also efficiently alerted research staff at participating research centres to data entry discrepancies to ensure high fidelity data. This highlights how research can be effectively conducted within a clinical setting.

Latent Profile Analysis has been extensively used in research, however, there remain several limitations to its use. Since there is no ideal or standard model fit index for LPA, researchers resort to using multiple criteria to determine the most appropriate number of latent classes that fit the data. We chose to use BLRT, aBIC, and BIC, which have been shown to more reliably identify the correct number of latent groups (Tein, Coxe, and Cham, 2013; Nylund, Asparouhov, and Muthén, 2007). Despite this more objective method to interpret LPA results, a more subjective clinically-oriented approach is also required. Although the 9-class model seemed agreeable between all model fit indices employed, we chose to reject this model in favour of the next best solution since the small number of participants in some cells would render inaccurate the secondary analyses evaluating associated clinical features. This rationale led us to choose a 3-class model which included a high number of cases in each phenotype cell,

and thus, perhaps some rarer phenotypes were grouped together. Therefore, there is an unavoidable risk of either choosing too many or too few phenotypes when examining the data subjectively. To mitigate this risk, we strengthened the analysis by confirming statistically significant differences between drivers in the three phenotypes. In conclusion, despite the increasing utility of LPA to determine latent phenotypes, there remains a necessity to also rely on subjective interpretation methods.

Chapter 6 Implications, Summary and Future Directions

6.1 Implications

Based on available literature, we hypothesized the clustering of eating drivers of interest into four discrete groups with some overlapping drivers. However, we found that in our population, the latent eating phenotypes were distinct from each other but quite different in their complexity. A large portion of children did not display any significant eating triggers or behaviours. This suggests that for a proportion of patients seeking weight management, more standard counselling approaches can be used to modify behaviour. One group was driven by three drivers, including loss of control eating and features of ADHD. The third group had multiple drivers that contributed to their phenotype, displaying a complex array of triggers, such as emotional, external, and restrained eating patterns, as well as hyperphagia and loss of control eating. This group could be hypothesized to require a more tailored approach to management to address the underlying root causes of overeating. As we continue to collect data from a larger cohort, it is possible that further analysis with a larger dataset may produce additional phenotypes. In particular, the complex Restrained-Triggered phenotype may separate into more distinct groupings. This hypothesis is based on the latent profile analysis modeling in this study, which found small group sizes in the 9-class and 5-class solutions. With data from more participants, smaller phenotypes may be teased out. Overall, these findings support the idea that treatment strategies need to be individualized to promote behaviour change by targeting the underlying triggers to overeating.

An important finding from our secondary analysis is that the two groups with disordered eating both had lower body esteem. It has been previously shown that low body esteem is associated with eating disorders, but causality is unclear (Evans et al., 2017). It is possible that in our population, low body esteem leads to some of the eating drivers such as restrained or emotional eating; however, the eating drivers may also cause lower body esteem. The fact that body esteem was not a factor in the No-ED group supports the association between disordered eating and low body esteem.

Further specialized treatment for the two disordered eating subgroups can be considered. For example, in the LOCE-ADHD group, patients may benefit from both traditional treatment for ADHD as well as specific therapy for LOCE. As for the impulsivity and inattention in this group, a physician could prescribe appropriate medication based on a complete ADHD assessment and diagnosis. Adolescents with obesity and LOCE are positively associated with having anxiety and depression (Glasofer et al., 2007; Isnard et al., 2003) and are also associated with having low self-esteem and body image issues (Glasofer et al., 2007; Decaluwe, Braet, and Fairburn, 2003; Isnard et al., 2003). In our cohort, this group did not have significantly greater depression and anxiety diagnoses than the other groups, but did exhibit significant social functioning deficits, including not getting along with other kids and being teased by other kids, and low body esteem. Nevertheless, Tanofsky-Kraff, Wilfley et al (2007) propose the use of interpersonal psychotherapy (IPT) for the treatment of LOCE and has been used in adolescents with depression. IPT is designed to reduce depressive symptoms and interpersonal problems, which then leads to an increase in self-esteem and improved mood resulting in reduced reliance on food and associated LOCE as a coping mechanism (Tanofsky-Kraff et al., 2007). Therefore, the use of IPT for this subgroup may improve their social functioning and in turn, decrease their

reliance on food to cope with low affect. Thus, in addition to healthy lifestyle counselling, the combination of medication for ADHD symptoms and IPT for LOCE may lead to better weight management outcomes in the LOCE-ADHD group.

The Restrained-Triggered group displayed a more complex phenotype with several eating drivers affecting individuals. Soetens et al (2008) found that disinhibited restrained overweight adolescents (i.e. those who scored high on restrained eating and either emotional eating, external eating, or both) scored significantly higher on a measure of thought suppression tendencies and having intrusive thoughts than did inhibited restrained eaters. This scoring indicates that the disinhibited restrained eaters may become preoccupied with thoughts about not eating that are overbearing and interfere with their attempts of self-control. Failure at suppression of thoughts about food may then lead to overconsumption of food in the presence of food cues or negative emotional states. Treatment, such as cognitive-behavioural therapy may be employed to aid in reframing the distorted thoughts leading to restrictive eating behaviour and subsequent overeating. Furthermore, mindfulness-based therapy is another treatment option studied in the context of external eating, emotional eating, and hyperphagic characteristics belonging to the Restrained-Triggered group (Dalen et al., 2015). Mindfulness encourages judgement-free awareness of emotional, mental, and physical states, and therefore, could aid in channeling appropriate awareness to appetite cues. A recent meta-analysis on mindfulness-based interventions in adults for overweight and obesity has shown that while BMI changes are modest, there are significant effects on eating drivers including emotional eating, external eating, and binge eating (Rogers et al., 2017). Thus, treatments options for members of Restrained-Triggered group may include a combination of cognitive behavioural therapy and

mindfulness approaches due to their effects on changing intrusive and destructive thoughts and re-focusing attention to internal hunger and satiety cues.

Standard diet and exercise counselling offered in weight management programs leads to modest reductions in BMI of 1.5 kg/m^2 (Styne et al., 2017). However, these programs do not typically account for specific eating triggers or behaviours which lead to overeating. This study provides evidence that new paradigms are necessary in the consideration of treatment for obese populations.

6.2 Summary and Future Directions

In summary, seven common eating drivers have been found to cluster into three distinct phenotypes in a population of children and adolescents seeking obesity treatment. Most subjects did not identify any eating drivers to be problematic, while the most pervasive eating driver of issue was loss of control eating. In addition to standard healthy lifestyle education, treatment options for identified phenotypes may include ADHD medication, interpersonal psychotherapy, cognitive-behavioural therapy, and mindfulness approaches. Further investigation into targeted therapies for these distinct eating groups is required in order to assess whether outcomes may be improved.

While the present study provides foundational knowledge in considering the development of individualized treatment protocols, further research is necessary to understand how various eating phenotypes may respond to existing treatment programs (i.e. mostly diet and exercise counseling) and whether outcomes can be predicted based on phenotype. Moreover,

longitudinal research is needed to investigate whether eating drivers change over time and how treatment outcomes correspond to changes in eating drivers. These questions may be answered within the scope of the planned *Pathways* longitudinal study, which includes cross-sectional participants completing the same measures at yearly visits for an additional two years after baseline. We will have means of analyzing whether an individual's phenotype changes during treatment, and if so, which factors are associated with or predict this phenotype change. The association found between body esteem and disordered eating phenotypes can also be analyzed to determine if change in body esteem is associated with changes in eating drivers. We will be able to determine whether baseline eating phenotype is more predictive of BMI at 2 years than change in phenotype over time, in addition to how phenotypes relate to trajectories of eating drivers and weight change over time. Additionally, with these data we can analyze whether changes in particular eating drivers mediate change in BMI for certain phenotypes.

Furthermore, the breadth of data collected for the CANPWR study allows for the evaluation of how other nutritional, exercise, or psychological measures may associate with identified phenotypes. In addition, since patients participate in programs which vary slightly in their curriculum and scope, we will also be able to determine if certain phenotypes respond differently to variation in treatment across programs.

In addition to the longitudinal *Pathways* analysis, further studies are required to replicate present study objectives and methodology in other populations. Furthermore, to our knowledge, only one study has been performed in a general adult population to determine the clustering of eating behaviours into phenotypes with correlation to weight status (Bouhlal et al., 2017). Another population of interest is youth undergoing bariatric surgical procedures. Recently,

Utzinger et al. (2016) found that in the United States over a quarter of pre-operative adolescents had LOCE, which predicts decreased weight loss following bariatric surgery (Sysko et al., 2012). These findings indicate that the presence of eating drivers in adolescents with obesity undergoing weight loss surgery may contraindicate this type of treatment.

Treatment programs currently offer a "one size fits all" approach to pediatric weight management and outcomes are slim to modest. Evaluation of targetable phenotypes will aid in the development of more tailored intervention strategies to improve short-term and longer-term health outcomes for patients.

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Appendix A

Variables collected for *Pathways* from the CANPWR Case Report Form

Variable	Case Report Form (CRF) Question	Collection Method
Child Demographics (*Indicates variable is dependent on CANPWR time point when participant was enrolled in *Pathways*, i.e. Baseline or 12-month follow up)		
Age*	Visit Date (YYYY/MM/DD) - Child's date of birth (YYYY/MM)	Date of visit on the *Pathways* CRF minus participant's date of birth (YYYY/MM only) from Baseline CRF
Sex	Child's sex: F/M	Baseline CRF
Ethnicity	"People living in Canada come from many different cultural and racial backgrounds. Is the child: (mark all that apply)"; choices include "White, Black, Latin American, Other"	Baseline CRF
Treatment site	Not applicable	CANPWR site where the participant was recruited
Anthropometrics (*Indicates variable is dependent on CANPWR time point when participant was enrolled in *Pathways*, i.e. Baseline or 12-month follow up)		
BMI*	Height (in cm); Weight (in kg)	Calculated as weight/height^2 from Baseline or Follow-up CRF
BMI z-score (based on WHO)*	Not applicable	Calculated using BMI score (calculation above)
Family Characteristics		

(*Indicates variable is dependent on CANPWR time point when participant was enrolled in *Pathways*, i.e. Baseline or 12-month follow up)		
Socioeconomic status (SES)*	"Please indicate which category best represents the total annual household income from all sources: (Canadian currency)"; choices include "Less than $49,999, $50,000-79,999, $80,000-99,000, $100,000 and above, N/A"	Household income expressed as a check box of 5 ranges as a measure of SES from Baseline or Follow-up CRF
Living arrangement*	1) "Does this child live in one primary residence or multiple household?" 2) "Who else lives in the same household as this child's primary residence?" ▪ Parental figures were listed and could include mother, father, step-parent, aunt, uncle, or another adult	1) Number of residences ▪ Baseline or Follow-up CRF 2) Number of parental figures in the primary residence ▪ Baseline or Follow-up CRF
Eating Environment (*Indicates variable is dependent on CANPWR time point when participant was enrolled in *Pathways*, i.e. Baseline or 12-month follow up)		
Eating out or ordering in meals*	"How often does your child usually eat the following foods?"; choices include "Never/less than once per month, 1-3/mo, 1/wk, 2-4/wk, 5-6/wk, 1/day, 2-3/day, 4-5/day, >6/day"	Frequency expressed as a check box from 9 ranges on Baseline or Follow-up CRF
Meals with Family*	"How often does your child usually eat the following foods?"; choices include "Never/less than once per	Frequency expressed as a check box from 9 ranges on Baseline or Follow-up CRF

	month, 1-3/mo, 1/wk, 2-4/wk, 5-6/wk, 1/day, 2-3/day, 4-5/day, >6/day"	
Meals in Front of Television*	"How often does your child usually eat the following foods?"; choices include "Never/less than once per month, 1-3/mo, 1/wk, 2-4/wk, 5-6/wk, 1/day, 2-3/day, 4-5/day, >6/day"	Frequency expressed as a check box from 9 ranges on Baseline or Follow-up CRF
Eating Breakfast*	"How often does your child usually eat the following foods?"; choices include "Never/less than once per month, 1-3/mo, 1/wk, 2-4/wk, 5-6/wk, 1/day, 2-3/day, 4-5/day, >6/day"	Frequency expressed as a check box from 9 ranges on Baseline or Follow-up CRF
Psychological Factors (Exploratory) (*Indicates variable is dependent on CANPWR time point when participant was enrolled in *Pathways*, i.e. Baseline or 12-month follow up)		
Quality of Life – Social Functioning*	"In the past ONE month, how much of a problem have the following been for you. There are no right or wrong answers. a) I have trouble getting along with other kids b) Other kids do not want to be my friend c) Other kids tease me d) I cannot do things that other kids my age can do e) It is hard to keep up with other kids/teens"	Obtained from child self-report Pediatric Quality of Life questionnaire on Baseline or Follow-up CRF; Items are scored from 0 (Never) to 4 (Almost Always) and the sum of all 5 items is divided by 5 to obtain a Social Functioning domain score

Medication Use*	"The patient takes the following medications (mark all that apply)" ▪ Of interest: CNS psychiatry (SSRI anti-depressants, other anti-depressants, anti-psychotics), Meds for ADHD	Listed in chart review section on Baseline or Follow-up CRF
Obesity related health issues*	"Obesity related health issues (check all that apply)" ▪ Of interest: Depression, Anxiety, ADHD, Other mental health disorders, Bullying	Listed in chart review section on Baseline or Follow-up CRF
Body Esteem	"Indicate how often you agree with the following statement about yourself by checking the appropriate box" (see *Pathways* CRF for statements)	10 items taken from the Body Esteem Scale for Adolescents and Adults (BESAA) on the *Pathways* CRF; Items are scored from 1 (Never) to 5 (Always) and the sum of all 10 items produces a body esteem total score. Items a, c, e, g, h, and j are reversed scored (i.e. scored from 5 (Never) to 1 (Always)).

Appendix B

Sample *Pathways*-related section of CANPWR consent form

Eating Pathways Sub Study

Your child over 10 years of age is invited to participate in a sub study called Eating Pathways. Researchers are interested in better understanding the factors that impact eating behaviors including cravings, emotions, and hunger. Many teens and kids may also feel self-conscious about their bodies at times, which may influence how and when they eat.
Your child will be asked to fill out a questionnaire once a year for 3 years, at your regular CANPWR visit. These questionnaires will take about 10 minutes extra to complete each time. You will receive $10 each time you complete the questionnaires as a thank you for your participation.

Please check YES or NO for participation in the sub-study

☐ YES, I agree to participate in the sub-study **Initials: _____**

☐ NO, I decline participation **Initials: _____**

Appendix C

Pathways Case Report Form

Pathways **CHILD SELF ADMINISTERED QUESTIONS** **Page 1**

Pathways184 Plate #301

☐ Baseline ☐ 1 year ☐ 2 year

ID: ☐☐☐ ☐☐☐☐ *Centre #* *Participant#*

ONLY CHILDREN >10 YEARS OLD

Subject Initials ☐☐☐ *F M L*

Visit Date: 20☐☐ ☐☐ ☐☐ *year month day*

1. Instructions: Below you'll find 20 questions about eating. Please read each question carefully and tick the answer that suits you best. Only one answer is allowed. Don't skip any answers. There are no wrong answers; it's your opinion that counts.

	Never	Rarely	Sometimes	Often	Very Often
a) Do you feel like eating whenever you see or smell good food?	☐	☐	☐	☐	☐
b) If you feel depressed, do you get a desire for food?	☐	☐	☐	☐	☐
c) If you feel lonely, do you get a desire for food?	☐	☐	☐	☐	☐
d) Do you keep an eye on exactly what you eat?	☐	☐	☐	☐	☐
e) Does walking past a candy store make you feel like eating?	☐	☐	☐	☐	☐
f) Do you intentionally eat food that helps you lose weight?	☐	☐	☐	☐	☐
g) Does watching others eat make you feel like eating too?	☐	☐	☐	☐	☐
h) If you have eaten too much, do you eat less than usual the next day?	☐	☐	☐	☐	☐
i) Does worrying make you feel like eating?	☐	☐	☐	☐	☐
j) Do you find it difficult to stay away from delicious foods?	☐	☐	☐	☐	☐
k) Do you intentionally eat less to avoid gaining weight?	☐	☐	☐	☐	☐
l) If things go wrong, do you get a desire for food?	☐	☐	☐	☐	☐
m) Do you feel like eating when you walk past a restaurant or fast food restaurant?	☐	☐	☐	☐	☐
n) Have you ever tried not to eat in between meals to lose weight?	☐	☐	☐	☐	☐
o) Do you have a desire to eat when you feel restless?	☐	☐	☐	☐	☐
p) Have you ever tried to avoid eating after your evening meal to lose weight?	☐	☐	☐	☐	☐
q) Do you have a desire for food when you are afraid?	☐	☐	☐	☐	☐
r) Do you ever think that food will be fattening or slimming when you eat?	☐	☐	☐	☐	☐
s) If you feel sorry, do you feel like eating?	☐	☐	☐	☐	☐
t) If somebody prepares food, do you get an appetite?	☐	☐	☐	☐	☐

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Pathways184 Plate #302

☐ Baseline ☐ 1 year ☐ 2 year

ID: ☐☐☐ ☐☐☐☐ *Centre #* *Participant#*

ONLY CHILDREN >10 YEARS OLD

Subject Initials ☐☐☐ *F M L*

2. Instructions: These questions are about the **PAST TWO WEEKS ONLY (14 DAYS)**.

a) Over the past two weeks (14 days), have there been any times when you have felt that you ate what other people would think was a very large amount of food given the situation?

☐ No ☐ Yes

If yes, i) How many such times have you done this over the past two weeks? ☐☐

ii) During how many of these episodes of overeating did you have a sense of having lost control? ☐☐

b) Have there been other times when you felt that you lost control and felt you ate too much, but did NOT eat a very large amount of food given the situation?

☐ No ☐ Yes

If yes, i) How many times has this happened over the past two weeks? ☐☐

3. Indicate HOW OFTEN YOU AGREE with the following statement ABOUT YOURSELF by checking the appropriate box.

	Never	Not often	Sometimes	Often	Always
a) I wish I looked better.	☐	☐	☐	☐	☐
b) I really like what I weigh.	☐	☐	☐	☐	☐
c) There are lots of things I'd change about my looks if I could	☐	☐	☐	☐	☐
d) I'm pretty happy about the way I look.	☐	☐	☐	☐	☐
e) My weight makes me unhappy.	☐	☐	☐	☐	☐
f) I am satisfied with my weight.	☐	☐	☐	☐	☐
g) My looks upset me.	☐	☐	☐	☐	☐
h) Weighing myself depresses me.	☐	☐	☐	☐	☐
i) I'm looking as nice as I'd like to.	☐	☐	☐	☐	☐
j) I am preoccupied with changing my body weight.	☐	☐	☐	☐	☐

Pathways184 Plate #303

☐ Baseline ☐ 1 year ☐ 2 year

ID: Centre # Participant# **ONLY CHILDREN >10 YEARS OLD** **Subject Initials** F M L

4. Instructions: Please read each question carefully and choose the option that best describes your child's behaviour. Please answer ALL of the questions.

a) How upset does your child generally become when denied a desired food?

- ☐ Not particularly upset at all
- ☐ A little upset
- ☐ Somewhat upset
- ☐ Very upset
- ☐ Extremely upset

b) How often does your child try to bargain or manipulate to get more food at meals?

- ☐ A few times a year
- ☐ A few times a month
- ☐ A few times a week
- ☐ Several times a week
- ☐ Several times a day

c) Once your child has food on their mind, how easy is it for you or others to re-direct your child away from food to other things?

- ☐ Extremely easy, takes minimal effort to do so
- ☐ Very easy, takes just a little effort to do so
- ☐ Somewhat hard, takes some effort to do so
- ☐ Very hard, takes a lot of work to do so
- ☐ Extremely hard, takes sustained and hard work to do so

d) How often does your child search through the trash for food?

- ☐ Never
- ☐ A few times a year
- ☐ 1-2 times a month
- ☐ 1-3 times a week
- ☐ 4-7 times a week

Pathways184 Plate #304

☐ Baseline ☐ 1 year ☐ 2 year

ID: ☐☐☐ *Centre #* ☐☐☐☐ *Participant#*

ONLY CHILDREN >10 YEARS OLD

Subject Initials ☐☐☐ *F M L*

e) How often does your child get up at night to food seek?

- ☐ Never
- ☐ A few nights a year
- ☐ 1-2 nights a month
- ☐ 1-3 nights a week
- ☐ 4-7 nights a week

f) How persistent is your child in asking or looking for food after being told "no" or "no more"?

- ☐ Lets go of food ideas quickly and easily
- ☐ Lets go of food ideas pretty quickly and easily
- ☐ Somewhat persistent with food ideas
- ☐ Very persistent with food ideas
- ☐ Extremely persistent with food ideas

g) Outside of normal meal times, how much time does your child spend talking about food or engaging in food-related behaviours?

- ☐ Less than 15 minutes a day
- ☐ 15-30 minutes a day
- ☐ 30 minutes to an hour
- ☐ 1-3 hours a day
- ☐ More than 3 hours a day

h) How often does your child try to steal food (that you are aware of)?

- ☐ A few times a year
- ☐ A few times a month
- ☐ A few times a week
- ☐ Several times a week
- ☐ Several times a day

Pathways184 Plate #305

☐ Baseline ☐ 1 year ☐ 2 year

ID: Centre # Participant# **ONLY CHILDREN >10 YEARS OLD** **Subject Initials** F M L

i) When others try to stop your child from talking about food or engaging in food-related behaviours, it generally leads to:

- ☐ No distress or upset
- ☐ Mild distress or upset
- ☐ Moderate distress or upset
- ☐ Severe distress or upset
- ☐ Extreme distress, behaviours can't usually be stopped

j) How sneaky or fast is your child in obtaining food?

- ☐ Not particularly sneaky or fast
- ☐ A little sneaky or fast
- ☐ Somewhat sneaky or fast
- ☐ Very sneaky or fast
- ☐ Extremely sneaky or fast

k) To what extant do food-related thoughts, talk, or behaviour interfere with your child's normal daily routines, self-care, school, or work?

- ☐ No interference
- ☐ Mild interference; occasional food-related interference in completing school, work, or hygiene tasks
- ☐ Moderate interference; frequent food-related interference in completing school, work, or hygiene tasks
- ☐ Severe interference; almost daily food-related interference in completing school, work, or hygiene tasks
- ☐ Extreme interference; often unable to participate in hygiene tasks or to get to school or work due to food-related difficulties

l) How old was your child when they first showed an increased interest in food? ☐☐

m) How variable is your child's preoccupation or interest in food?

- ☐ Hardly ever varies
- ☐ Usually stays about the same
- ☐ Goes up and down occasionally
- ☐ Goes up and down quite a lot
- ☐ Goes up and down all the time

Pathways184 Plate #306

☐ Baseline ☐ 1 year ☐ 2 year

ID: ☐☐☐ *Centre #* ☐☐☐☐ *Participant#*

ONLY CHILDREN >10 YEARS OLD

Subject Initials ☐☐☐ *F M L*

5. Children differ in their abilities to focus attention, control activity, and inhibit impulses. For each item listed below, how does this child compare to other children of the same age? Please select the best rating based on your observation over the past month.

	Far below average	Below average	Slightly below average	Average	Slightly above average	Above average	Far above average
a) Give close attention to detail and avoid careless mistakes	☐	☐	☐	☐	☐	☐	☐
b) Sustain attention on tasks or play activities	☐	☐	☐	☐	☐	☐	☐
c) Listen when spoken to directly	☐	☐	☐	☐	☐	☐	☐
d) Follow through on instructions and finish school work or chores	☐	☐	☐	☐	☐	☐	☐
e) Organize tasks and activities	☐	☐	☐	☐	☐	☐	☐
f) Engage in tasks that require sustained mental effort	☐	☐	☐	☐	☐	☐	☐
g) Keep track of things necessary for activities	☐	☐	☐	☐	☐	☐	☐
h) Ignore extraneous stimuli	☐	☐	☐	☐	☐	☐	☐
i) Remember daily activities	☐	☐	☐	☐	☐	☐	☐
j) Sit still (control movement of hands or feet or control squirming)	☐	☐	☐	☐	☐	☐	☐
k) Stay seated (when required by class rules or social conventions)	☐	☐	☐	☐	☐	☐	☐
l) Modulate motor activity (inhibit inappropriate running or climbing)	☐	☐	☐	☐	☐	☐	☐
m) Play quietly (keep noise level reasonable)	☐	☐	☐	☐	☐	☐	☐
n) Settle down and rest (control constant activity)	☐	☐	☐	☐	☐	☐	☐
o) Modulate verbal activity (control excess talking)	☐	☐	☐	☐	☐	☐	☐
p) Reflect on questions (control blurting out answers)	☐	☐	☐	☐	☐	☐	☐
q) Await turn (stand in line and take turns)	☐	☐	☐	☐	☐	☐	☐
r) Enter into conversations and games (control interrupting/intruding)	☐	☐	☐	☐	☐	☐	☐