Associations between elevated body mass index and cognitive functioning in adolescents

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Associations between elevated body mass index and cognitive functioning in adolescents

Abstract

In 2012, the Centers for Disease Control estimated that 18% of adolescents in the United States are obese. Emerging research has shown reduced neurocognitive functioning in adults with high body mass index (BMI) compared to normal-weight individuals, particularly in the areas of executive function and memory. Studies examining children and adolescents have also suggested reduced visual-spatial and executive functioning in those with high BMI; however, results have been somewhat equivocal. Adolescence is a critical period of brain development, such that adolescents with high BMI may show a unique pattern of neurocognitive impairment that differs from other stages of life. This study examined neurocognitive performance in obese (n = 31, BMI above 95th percentile) versus normal-weight adolescents (n = 31, BMI between 30th and 70th percentiles) on a brief battery of neuropsychological tasks, including tests of executive functioning (Delis-Kaplan Color-Word Inhibition and Switching tasks, Paced Auditory Serial Addition Task), speed of processing (Delis-Kaplan Color-Word Naming and Reading tasks), verbal memory (Rey Auditory Verbal Learning Test), and estimated intelligence (Wechsler Abbreviated Scale of Intelligence, 2-subscale). Independent samples t-tests confirmed no group differences in age, gender, ethnicity, or socio-economic status. Multivariate analysis of variance showed significant differences between groups on this battery (Wilks’ λ = .65, F_{8,62} = 3.55, p < .05, partial η^2 = 0.35). A significant univariate main effect for verbal memory was found (F_{1,62} = 10.15, p < .006, partial η^2 = 0.15). No other significant univariate main effects were observed. These results suggest obesity may be related to decreased verbal memory retrieval in adolescents. It is possible that obesity may impact frontal regions necessary for efficient memory retrieval – a finding not present until this critical stage of development.

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ASSOCIATIONS BETWEEN ELEVATED BODY MASS INDEX AND COGNITIVE FUNCTIONING IN ADOLESCENTS

A DISSERTATION

SUBMITTED TO THE FACULTY

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Abstract
In 2012, the Centers for Disease Control estimated that 18% of adolescents in the United States are obese. Emerging research has shown reduced neurocognitive functioning in adults with high body mass index (BMI) compared to normal-weight individuals, particularly in the areas of executive function and memory. Studies examining children and adolescents have also suggested reduced visual-spatial and executive functioning in those with high BMI; however, results have been somewhat equivocal. Adolescence is a critical period of brain development, such that adolescents with high BMI may show a unique pattern of neurocognitive impairment that differs from other stages of life. This study examined neurocognitive performance in obese (n = 31, BMI above 95th percentile) versus normal-weight adolescents (n = 31, BMI between 30th and 70th percentiles) on a brief battery of neuropsychological tasks, including tests of executive functioning (Delis-Kaplan Color-Word Inhibition and Switching tasks, Paced Auditory Serial Addition Task), speed of processing (Delis-Kaplan Color-Word Naming and Reading tasks), verbal memory (Rey Auditory Verbal Learning Test), and estimated intelligence (Wechsler Abbreviated Scale of Intelligence, 2-subscale). Independent samples t-tests confirmed no group differences in age, gender, ethnicity, or socio-economic status. Multivariate analysis of variance showed significant differences between groups on this battery (Wilks’ $\lambda = .65$, $F_{8,62} = 3.55$, $p < .05$, partial $\eta^2 = 0.35$). A significant univariate main effect for verbal memory was found ($F_{1,62} = 10.15$, $p < .006$, partial $\eta^2 = 0.15$). No other significant univariate main effects were observed. These results suggest obesity may be related to decreased verbal memory retrieval in adolescents. It is possible that obesity may impact frontal regions necessary for efficient memory retrieval – a finding not present until this critical stage of development.

Keywords: Adolescence, BMI, Neuropsychological Function, Verbal Memory
Introduction

Obesity has become a major health problem in the United States, with rates significantly increasing over the past 30 years. Data collected between 1999 and 2002 via the National Health and Nutrition Examination Survey by the Centers for Disease Control indicate that approximately 30% of adults are obese, and 16% of children between the ages of 6 and 19 are overweight (Baskin, Ard, Franklin, & Allison, 2005). Within the period of time between 1976 and 2002, the number of adolescents between the ages of 12 and 19 considered to be overweight has more than tripled to reach 16.1% based on the Centers for Disease Control survey (Baskin et al., 2005). Further, gender differences may be important given that between 1999-2000 and 2009-2010, adolescent males showed a significant trend for increasing BMI, while female adolescents did not (Ogden, Carroll, Kit, & Flegal, 2010).

Obesity in youth has received significant attention, as being overweight or obese as a child or adolescent predicts being overweight or obese later in life (Duckelbaum & Williams, 2001). Further, childhood and adult obesity have been associated with a number of long-term negative outcomes. Obesity has been determined to be a risk factor for several medical conditions, including hypertension, Type 2 diabetes, heart disease, sleep apnea, and cancer (Bray, 2004). In addition, increased Body Mass Index (BMI) has been linked to increased risk for development of both dementia and Alzheimer’s disease (Gustafson, Rothenberg, Blennow, Steen, & Skoog, 2003; Hassing et al., 2009; Whitmer, Gunderson, Quesenberry, Zhou, & Yaffe, 2007). A growing body of literature is finding that being overweight or obese also has an effect on cognitive, as well as physical, functioning. Even more startling, not all of these effects appear to be the result of prolonged obesity.
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Given that being overweight is associated with medical and cognitive risks across the lifespan, obesity during childhood represents a significant public health concern. Therefore, it is important to understand how obesity affects development in greater detail. Specifically, the current study is interested in investigating the effects of obesity on neurocognitive development. While some general literature exists regarding the relationship between cognition and obesity, there is modest literature that particularly addresses neurocognitive functioning and obesity in adolescence – a time during which both the brain and neurocognitive functioning are actively developing. To this end, this literature review begins with an overview of research related to adult obesity or high BMI and neurocognitive functioning deficits, followed by structural brain differences. A review of typical adolescent brain development and cognitive processes developing during adolescence is provided to elucidate typical and atypical development. This review also provides the backdrop and context for developmental changes across adolescence, and establishes a context for what should be expected to take place during typical adolescent development. Research on obesity-related differences is then contrasted with neurocognitive functioning deficits and structural brain differences in adolescents. Finally, a rationale for the current proposed study will be provided along with research hypotheses.

Literature Review

Obesity related cognitive deficits in adults

There is a growing body of research indicating that increased BMI is associated with both cognitive deficits, as well as structural brain differences, in adults. While the presence of cognitive deficits in adults with elevated BMI has been consistently shown, it is challenging to parse the unique contribution of elevated body mass to the cognitive and structural brain
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differences observed in adults. This is due, in part, to the fact that obesity is known to correlate with several medical conditions which also impact cognitive functioning. However, several studies have attempted to look at cognitive functioning in overweight and obese adults who have yet to develop secondary medical conditions. While these studies often make reference to the fact that their findings may underrepresent the magnitude of cognitive deficits in the general population of obese individuals, they provide valuable insights into the possible unique contribution of increased body mass to cognitive functioning.

There have been multiple studies which have attempted to examine the relationship between BMI and cognition in adults. These studies have produced mixed results, with multiple aspects of functioning implicated in study findings. Early research focused on several aspects of neuropsychological functioning and found associations between elevated BMI and decreased word-list learning (Cournot et al., 2006) and impaired executive functioning (Fergenbaum et al., 2009; Gunstad et al., 2007). In addition, increased body mass has been found to be associated with poorer performance on verbal fluency tasks, tasks of visual memory, and prospective memory tasks (Gunstad, Lhotsky, Wendell, Ferrucci, & Zonderman, 2010).

While some areas of cognitive functioning appear to have negative associations with BMI, there are specific domains that have been shown to be unaffected in adults. Multiple studies have found no association between BMI and performance on tasks of attention (Gunstad et al., 2010; Gunstad et al., 2007). In addition, performance on language tasks, verbal memory tasks, and measures of global cognitive ability do not appear to be associated with increased BMI (Gunstad et al., 2010; Gunstad et al., 2007; Stanek et al., 2013). In contrast, however, a recent study by Stanek and colleagues (2013) examined the relationship between BMI and cognitive functions across the adult lifespan and found that BMI was independently associated with
decreased attention, processing speed, and fine motor speed across the adult life span. They did not find that executive functioning was independently related to BMI; however, they did find a significant age by BMI interaction, suggesting that obesity-related cognitive deficits in the executive domain may increase with age. Notably, some of the tasks that were defined as tasks of attention for the purpose of this study were included as tasks of executive functioning in other studies. This may indicate that there are certain types of executive functions which are more susceptible to the influence of BMI. The authors of this study stated that these findings provide support for a frontal-subcortical pattern of cognitive dysfunction in obese individuals, which suggests a possible impact on signaling loops between prefrontal cortical areas and deeper brain structures (Stanek et al., 2013). As initial evidence of obesity-related neurocognitive differences has emerged, a parallel body of work has examined possible structural and functional brain differences which may be present in individuals with elevated BMI and may help to explain neurocognitive dysfunction.

**Obesity related structural brain differences in adults**

Research indicating that cognitive differences exist between adults with varying BMI suggests that underlying brain differences are likely also present. Neuroimaging studies have found evidence that obesity is related to global reductions in brain volume, as well as to reductions in gray matter in frontal and temporal regions in adults (Gunstad et al., 2008; Taki et al., 2008). Specifically, high BMI has been found to be associated with cerebral atrophy of temporal regions in a study of elderly women (Gustafson, Lissner, Bengtsson, Bjorkelund, & Skoog, 2004). In addition, in a voxel-based morphometric study, obese subjects were found to have lower gray matter density in the post-central gyrus, frontal operculum, putamen, and middle frontal gyrus when compared to lean individuals (Pannacciulli et al., 2006). A study of middle-
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Aged Japanese males demonstrated reduced gray matter volumes in the medial temporal lobes, hippocampus, and precuneus when compared to individuals with normal BMI (Taki et al., 2008). Raji and colleagues (2010) conducted a tensor-based morphometry (TBM) study examining gray matter and white matter differences in cognitively intact elderly individuals with varying levels of BMI. Their results showed atrophy in the frontal lobes, anterior cingulate gyrus, hippocampus, and thalamus compared with individuals who had normal BMI. In the studies mentioned above, BMI was associated with smaller volumes in several cortical and subcortical regions, with convergent evidence for reduced volume in frontal and temporal lobes.

Another line of research has focused on examining white matter microstructure, specifically whether the white matter tracts connecting the multiple brain regions implicated in the previously mentioned studies may be impacted by increased BMI. White matter facilitates communication in the brain and is critical for intact brain functioning. Therefore, it makes sense to examine whether differences in microstructure may be related to the functional impairment observed in obese adults.

Current research utilizing diffusion tensor imaging (DTI) has revealed important information about white matter integrity in individuals with elevated BMI. Fractional anisotropy (FA) is used as an index of white matter health. In its basic sense, FA describes the degree of restriction in the diffusion of water molecules (Basser & Pierpaoli, 1996). Higher FA values, where diffusion is more restricted, are associated with highly myelinated white matter tracts (Basser & Peirpaoli, 1996). In other types of tissue, such as gray matter, water content is less and diffusion is more random. Thus, examination of FA is specifically helpful in examining white matter tracts. FA is often associated with white matter integrity, as higher levels of FA are related to highly myelinated tracts with high levels of integrity, axonal coherence, and
organization. By this reasoning, if the myelin sheath is less robust, water molecules will diffuse more freely, resulting in lower FA. Thus, reduction in white matter integrity is analogous with lower levels of FA.

Generally, researchers have concluded that increased BMI is globally associated with a reduction in white matter integrity independent of age (Stanek et al., 2011; Verstynen et al., 2012). Specific areas which appear to be most impacted are the corpus collosum, fornix, midbrain tract, and brainstem tract (Stanek et al., 2011; Verstynen et al., 2012; Xu et al., 2013). While the mechanism as to why these white matter tracts are impacted by high BMI is unclear, seeing the apparent insult to these tracts gives evidence to support possible hypotheses suggesting cognitive dysfunction in individuals with increased BMI.

As discussed, BMI has been linked to several types of neurocognitive functioning deficits in adult populations. Specifically, deficits in executive functions in adults with elevated BMI have been most consistently demonstrated across studies, with additional evidence for impairment in word-list learning, visual memory, and prospective memory. Imaging studies have consistently shown smaller volumes in several cortical and subcortical regions, with convergent evidence for reduced volume in frontal and temporal lobes in obese adults. Additionally, decreases in white matter integrity have been observed, with the corpus collosum, fornix, midbrain tract, and brainstem tract being especially implicated. One challenge to understanding the cause of these cognitive deficits is the potentially confounding factor of age. While some studies have attempted to statistically control for the impact of age, this approach is limited. Possible causes for obesity-related cognitive dysfunction may be revealed further by examining children and adolescents as several macro- and micro-structural brain regions are maturing during this period, which are associated with refinement of several cognitive skills.
The discussion will now shift to the course of typical brain development, with a specific emphasis on the developmental changes that take place during adolescence. This review is included to provide context for the types of neurocognitive skills which are developing during childhood and adolescence, as well as an overview of the brain regions which are developing during the same period. Understanding typical development is crucial for creating hypotheses as to how elevated BMI may be impacting adolescents at a neurocognitive and brain anatomical level.

**Typical brain development**

While the current study is focused on the period of adolescence, brain development begins much earlier in life. A large portion of the brain’s development takes place during the gestational period and the first few years of a child’s life (Lenroot & Giedd, 2006). An individual’s brain has just about reached its full volume by 5 years of age (Dekaban & Sadowsky, 1978). While much of the brain’s growth takes place during these early years, total cerebral brain volume does not peak until 14.5 years of age in males and 11.5 years of age in females (Giedd et al., 1999). Though total brain volume stays relatively stable over the course of development, the cortical gray matter and white matter volumes change dramatically over the course of development.

Cortical gray matter volume tends to follow an “inverted U” developmental course, with peak volumes being reached in different lobes at different points in time followed by periods of decrease (Lenroot & Giedd, 2006). These periods of decreasing gray matter density have been attributed to synaptic pruning (Giedd et al., 1999; Sowell, Thompson, Tessner, & Toga, 2001). Gray matter in the parietal lobe peaks at 10.2 years in girls and 11.8 years in boys; frontal lobe gray matter reaches its maximum volume at 11.0 years in girls and 12.1 years in boys; and
temporal lobe gray matter volumes peak at 16.7 years in girls and 16.2 years in boys (Giedd et al., 1999). Thus, there are several areas of gray matter which continue refinement during adolescence and do not reach maturity until early adulthood. The last areas to reach adult levels of cortical thickness are the dorsolateral prefrontal cortex and portions of the temporal lobe (Gogtay et al., 2004; Sowell et al., 2001), as well as the striatum and other subcortical structures (Sowell et al., 2002). These are areas implicated in executive functioning, including the control of impulses, judgment, and decision-making (Lenroot & Giedd, 2006), functions which are also developing during the adolescent years (Hooper, Luciana, Conklin & Yarger, 2004; Leon-Carrion, Garcia-Orza, & Perez-Santamaria, 2004; Luciana, Conklin, Cooper, & Yarger, 2005).

In contrast to the developmental course of gray matter, white matter tends to follow a more linear developmental course. White matter volume generally increases throughout childhood and adolescence (Lenroot & Giedd, 2006). A large part of white matter development involves the process of myelination. Myelination occurs regionally, starting with the brain stem beginning at 29 weeks gestation and generally proceeds from inferior to superior and posterior to anterior (Inder & Huppi, 2000). It is generally observed that proximal pathways tend to myelinate before distal, sensory before motor, and projection before association. The majority of myelination in the brain is completed by the age of 5 (Nakagawa et al., 1998); however, white matter maturation continues through late childhood, adolescence, and into the third decade of life (Pfefferbaum et al., 1994; Sowell et al., 2003).

Adolescence has also been shown to be a critical time point in the development of white matter. The regions which experience the greatest volumetric white matter growth during adolescence are the frontal and parietal cortices (Sowell et al., 2003). This has been consistently
interpreted as reflecting continued axonal myelination during adolescence (Giedd et al., 1999; Marsh, Gerber, & Peterson, 2008).

As previously discussed, diffusion tensor imaging (DTI) allows for the study of the microstructural components of white matter which include myelination and axonal organization (Asato, Terwilliger, Woo, & Luna, 2010). Fractional anisotropy (FA) values have been found to increase in the prefrontal regions, the internal capsule, basal ganglia, thalamic pathways, ventral visual pathways, and the corpus collosum with age (Barnea-Goraly et al., 2005); regions which are important for attention, motor skills, and memory (Cummings, 1993; Herrero, Barcia, & Navarro, 2002; Packard & Knowlton, 2002). In addition, DTI studies have demonstrated that white matter microstructure continues to develop during adolescence in the cortical and subcortical tracts (Asato et al., 2010). There are several tracts which appear to reach maturity during the period of adolescence. These include the association tracts related to the fronto-occipital/temporal-occipital regions and the fronto-temporal region, as well as projection tracks within the fronto-subcortical region (Asato et al., 2010).

The maturation of several macro and microstructural brain regions and increased plasticity observed during adolescence result in a critical period for development. As such, this critical period suggests that the systems developing may be vulnerable to insult. If these developing systems are impacted, one would expect to see differences in cognitive performance on tasks implicated by brain regions which are developing during adolescence.

**Cognitive development during adolescence**

The changes in brain development and maturation described in the previous section are related to the refinement of multiple cognitive skills during adolescence. This section will review the cognitive processes known to show marked development during the adolescent
period. Specifically, executive functioning, working memory, and processing speed are generally considered to undergo significant refinement during this period.

The term executive functioning is generally used to refer to higher-order cognitive processes involved in goal-oriented behavior (DeLuca & Leventer, 2008; Lezak, 1995). Many executive functions are present in basic, fundamental forms during childhood and then undergo refinement during adolescence (Davies & Rose, 1998; Levin, Culhane, Hartmann, Evankovich, & Mattson, 1991). During the period of adolescence, individuals develop a greater capacity for abstract thought, experience an increase in cognitive flexibility, and engage in rule-guided behavior (Luna, 2009). Response inhibition is a key executive function which, while present from early childhood, becomes refined during adolescence; specifically, the rate of correct inhibitory responses increases during adolescence (Bedard et al., 2002; Luna et al., 2004; Vandenberg & Van der Molen, 2004; Williams et al., 1999). In addition to response inhibition, selective attention (Stinson, 2009) and response planning (Asato, Sweeny, & Luna, 2006) also continue to be refined during this period.

Working memory is another subset of executive functioning which undergoes refinement during adolescence. Working memory refers to the system which allows for temporary storage of information and the manipulation of said information, which is necessary for tasks such as comprehension, learning, and reasoning (Baddeley, 2000). Working memory tasks tend to involve the presentation of information, which must be remembered over a delayed period while either an interfering stimulus is presented or there is a manipulation requirement placed on the information initially presented (Luna, 2009). While working memory capabilities are present early in development (Diamond & Goldman-Rakic, 1989), the adolescent period is notable for increase in ability to perform complex tasks, demonstrate increased precision, and control
distraction (Luna et al., 2004; Zald & Icono, 1998). These developmental changes allow for a more efficient working memory process. It can be difficult to parse working memory from other processes of executive function previously mentioned, such as response inhibition, selective attention, and response planning. This is due to the fact that it appears that all of these processes interact in a way which contributes to the development of efficient higher-level cognitive processes (Asato et al., 2006). Therefore, working memory is often included as an executive function along with inhibition, attention, and planning.

Executive functions are thought to develop across the lifespan, with different types of executive functions following unique developmental trajectories (Davies & Rose, 1999; DeLuca & Leventer, 2008; Levin et al., 1991). It is believed that the development of executive functions maps onto brain development, with the later development of these functions being related to delayed maturation of the prefrontal cortex. The prefrontal cortex is the region of the brain which mediates executive functions including planning, impulse control, and internally guided behavior (Casey et al., 1997), and is one of the last regions of the brain to mature (Giedd et al., 1999; Gotay et al., 2004). Therefore, skills implicated by this region do not reach their full functional capacity until mid to late adolescence (Luna, Garver, Urban, Lazar, & Sweeny, 2004).

Along with development of the prefrontal cortex, connectivity between different association areas continues to become refined during adolescence (Gogtay et al., 2004; Pfefferbaum et al., 1994). Frontostriatal connectivity is known to support cognitive skills, such as spatial working memory and response inhibition mentioned previously (Luna et al., 2004). These connections have been noted to continue to develop into late adolescence and early adulthood (Asato et al., 2010). The development in these regions is related to pruning of synapses, which allows for more efficient local neuronal computations (Huttenlocher, 1990), and
myelination, which speeds neuronal transmission (Pfefferbaum et al., 1994; Schmithorst, Wilke, Darzinski, & Holland, 2005).

In addition to the executive functions previously discussed, speed of processing also undergoes refinement during the second decade of life. Processing speed, the time it takes one to execute basic cognitive processes in order to produce a response, is another cognitive process which is still immature in late childhood (Hale, 1990). Increased speed of processing has been found to be associated with enhancement in other cognitive processes, including capacity of working memory, response inhibition, and accuracy in solving arithmetic and word problems (Fry & Hale, 1996; Kail & Ferrer, 2007; Kail & Hall, 1999; Luna et al., 2004).

Similar to the cognitive processes discussed previously, processing speed also undergoes development during late childhood and adolescence. Specifically, processing speed increases throughout childhood and adolescence, reaching its peak during the third decade of life and then slowly decreasing thereafter (Hale, 1990; Kail, 1993). Decreases in reaction time, indicating faster speed of processing, have been found during adolescence using simple visual reaction time tasks (Fischer, Biscaldi, & Gezeck, 1997; Fukushima et al., 2000) as well using tasks that place additional cognitive demands (Luna et al., 2004; Munoz et al., 1998).

As discussed earlier, white matter organization and development continues during the adolescent period into early adulthood. The strengthening of white matter tracts enables distal brain regions to communicate more quickly and efficiently. Increasing coherence and organization, as well as the degree of myelination of white matter tracts, affect action potential conduction speed which is viewed behaviorally as processing speed (Gutierrez, Boison, Heinemann & Stoffel, 1995; Tolhurst & Lewis, 1992). Significant correlations have been found between speed of processing and white matter organization in the parietal and temporal lobes, as
well as in the connections between posterior brain regions and the lateral prefrontal cortex (Turken et al., 2008). As previously discussed, several white matter tracts involving the temporal lobe, including the temporo-occipital and fronto-temporal tracts, show increased white matter integrity across adolescents (Asato et al., 2010). As such, it stands to reason that this increase in white matter integrity plays an important role in the development of processing speed during adolescence.

An understanding of the course of typical adolescent brain development, as well as typical adolescent neurocognitive development, is necessary to formulate hypotheses about the possible associations between elevated BMI and neurocognitive functioning during the adolescent period. It is important to understand the linkage between areas of insult and areas of expected development in the brain in order to begin to understand how BMI may affect this development and subsequent neurocognitive functioning. As adult literature suggests that these neurocognitive deficits persist across the lifespan, tracing the trajectory of these deficits back through adolescence may provide a more holistic picture of the brain-behavior relationship associated with elevated BMI.

**Body mass index and cognitive functioning in children and adolescents**

Limited research has begun to emerge examining whether group differences for children and adolescents in normal, overweight, and obese groups exist for varying dimensions of neurocognitive functioning. Overall, it appears that some differences may exist, although some contradictory evidence is also present. In a large study of children between the ages of 8 and 16, a significant inverse association between performance on the Wechsler Intelligence Scale for Children, Revised (WISC-R) Block Design task and BMI was observed (Li, Dai, Jackson, & Zhang, 2008). This finding held true even after parent/family characteristics, sports
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participation, physical activity, hours spent watching television, blood pressure, and serum-lipid profile was controlled for. The authors suggested that their findings indicate a possible association between high BMI and impairment in visuospatial organization. Along similar lines, a study of school children (ages 6 to 13) revealed a significant relationship between increased BMI and lower Performance IQ scores on the WISC-R (Parisi et al., 2010). Neither of these studies measured attention or executive functions above and beyond abilities assessed by a general assessment of intellectual functioning.

Another group of neurocognitive studies involving adolescents have demonstrated that BMI negatively correlates with performance on a broad range of tasks of executive functioning. Specifically, adolescents with high BMI have been found to perform more poorly on tasks of inhibition (Maayan et al., 2011), working memory (Maayan et al., 2011), and set-shifting (Delgado-Rico, Rio-Valle, Gonzalez-Jimenez, Campoy, & Garcia, 2012; Verdejo-Garcia et al., 2010). These deficits in executive functioning align with previously mentioned research that demonstrated similar executive deficits in adult obese populations.

In contrast, some studies have found no differences between normal weight, overweight, and obese children and adolescents with regard to neurocognitive functioning. A multi-site National Institute of Health (NIH) study examining children ages 6 to 18 over a period of four years found no relationship between BMI and performance on any tests within their neuropsychological test battery (Waber et al., 2012). Notably, this battery did not include tests of inhibition or set-shifting similar to those tasks found in previous studies to highlight differences in performance between BMI groups. Thus, while there are multiple possible reasons as to why significant differences were not found in the NIH study, one possible reason is
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that the battery used varied from tasks typically included in studies that have found significant differences.

Gunstad and colleagues (2008) conducted a study which included 478 children and adolescents between the ages of 6 and 19. The results, which were adjusted for age and intellectual function, did not support a significant relationship between BMI and cognitive test performance in the full sample. Cognitive tests utilized in this study included a computerized digit span backwards task assessing working memory, a computerized adaptation of the Trails Making Test B assessing executive set-shifting, a verbal recall task assessing verbal memory, a semantic fluency task assessing executive functioning, and a finger tapping task assessing motor speed. It is possible that by controlling for IQ that some of the variance in performance on the tasks between these groups was eliminated.

In summary, the modest body of literature related to cognitive differences between children and adolescents with high BMI and their average weight peers has found contradicting results. Most notably, some studies have found no effects (Gunstead et al., 2008; Waber et al., 2012), whereas other studies have found differences primarily in inhibition, set-shifting, and working memory (Delgado-Rico, Rio-Valle, Gonzalez-Jimenez, Campoy, & Garcia, 2012; Maayan et al., 2010; Verdejo-Garcia et al., 2010). This may be related to methodological differences between studies, including varying test batteries measuring different components of executive functions, as well as the inclusion of covariates, such as IQ, in certain studies. The fact that some studies have found group differences suggests the presence of possible neurobiological differences between children with elevated BMI and average weight counterparts, perhaps similar to those in seen in adults.
Brain structural differences in children and adolescents with elevated BMI

An emerging body of research has noted subtle structural differences between the brains of obese children and adolescents when compared to their typical weight counterparts. In a structural MRI study of participants ages 14-21, increased BMI was significantly related to less gray matter volumes in the orbito-frontal region, with a trend for global gray matter reductions across the frontal lobes (Maayan, Hogendoorn, Weat, & Convit, 2011). In a large, multi-site National Institutes of Health (NIH) MRI study of normal brain development, higher BMI was associated with decreased whole-brain and lobar occipital gray matter volumes and increased whole-brain and lobar white matter volumes, with no net effect on total brain volume and no effect on subcortical gray matter structures, cerebellum, or brainstem (Waber et al., 2012).

Alosco and colleagues (2014) conducted a study which examined 120 typically developing children ages 6 to 18. They found that increased BMI was associated with decreased frontal lobe gray matter volume, as well as decreased gray matter volume in the limbic region, with a trend toward decreased gray matter volume in the parietal lobe. This study found no significant associations between elevated BMI and white matter FA, suggesting that no significant differences in white matter integrity were observed. This study suggests that there is a direct association between BMI and frontal-subcortical brain structure independent of demographic, medical, and global gray matter changes related to maturation (Alosco et al., 2014).

In addition to the differences in gray matter volume mentioned above, reductions in cortical thickness were observed in the orbitofrontal cortex and anterior cingulate cortex in adolescents with uncomplicated obesity (Yau, Kang, Javier, & Convit, 2014). FA reductions were also observed in major fiber tracts involved in cortico-subcortical and interhemisphereic
signal transmission. Similarly to the study by Alosco et al. (2014), no decrease in white matter integrity, as measured by FA, was observed in the frontal lobes.

The previous sections have highlighted deficits in neurocognitive functioning and structural brain differences observed in both children and adults with elevated BMI. If indeed elevated BMI is related to insult on brain structure and function, having elevated BMI during periods of brain development may result in specific deficits.

**Summary and Rationale for Proposed Study**

The literature reviewed highlighted several key issues related to BMI, structural brain differences, and neurocognitive differences in both adults and children/adolescents. In adults across the lifespan, an increase in BMI has been associated with a number of neurocognitive deficits including executive functioning and working memory. In addition to the observed neurocognitive deficits, brain imaging studies have revealed both macro- and micro-structural differences in adults with high BMI. Preliminary studies on neurocognitive differences between children and adolescents with varying BMI have been contradictory, with some finding significant BMI effects and others failing to find any associations. Recent imaging studies on typical brain development in children and adolescents have found structural differences in temporal gray matter in children and adolescents who have high BMI.

The period of adolescence is considered to be a developmental period during which changes in cognition and behavior take place. During this period, there is a marked refinement of higher-level cognitive processes which continues into early adulthood. Multiple structural regions and association tracts are known to develop significantly during adolescence, including the prefrontal cortex and frontostraialatal connectivity. The development in these regions is related to pruning of synapses, which allows for more efficient local neuronal computations, and
myelination, which speeds neuronal transmission. Myelination that takes place during adolescence results in white matter development of regions implicated in executive functioning, including attention, inhibition, and mental flexibility. As such, any insult to the development of these regions during adolescence may impact refinement of cognitive skills which are associated with those brain regions. It stands to reason that insult sustained during this critical period of development would have a greater impact on subsequent cognitive skills, such as executive functioning, as compared to other periods across the lifespan as more change is taking place during this time.

The adult literature examining associations between brain microstructure and body mass finds that individuals with elevated BMI also have poorer white matter integrity in frontal regions, as well as white matter association tracts. As previously mentioned, many of these areas which appear to suffer insult in adults with elevated BMI are developing during adolescence. Though the mechanism by which white matter integrity becomes compromised in obese adults is unknown, if elevated body mass does play a role in the observed insult to white matter, one might expect that the effects of this would be especially prominent in adolescents with high BMI. As the adolescent period is a critical time for development of white matter in the prefrontal cortex and association tracts, it is possible that differences in cognitive processes, such as executive functions including set-shifting, inhibition, and working memory mediated by these regions, would be observable in adolescents with varying body mass.

**Proposed Study**

The proposed study will examine several cognitive processes in typically developing adolescents to see if differences exist between adolescents with normal weight and adolescents with elevated BMI. Of specific interest are executive functions, including response inhibition and
BMI AND COGNITIVE FUNCTIONING IN ADOLESCENTS

... set-shifting, attention, working memory, and processing speed – all shown to be compromised in obese adults (Fergenbaum et al., 2009; Gunstad et al., 2007) and known to be maturing during the adolescent years (Casey et al., 1997; Hale, 1990; Luna et al., 2004; ).

The aim of the proposed study is to add to the current body of literature related to the possible associations between BMI and neurocognitive functioning. While the proposed study will not have the ability to determine any mechanism by which possible differences exist, if significant neurocognitive differences are found, knowing which skills are most impacted will allow for hypotheses to be developed as to possible mechanisms of differences which could be tested in future research.

Hypotheses

Based on reviewed literature and the rationale for the present study, the following hypotheses are proposed:

1. Given the abundance of literature suggesting various structural brain differences as well as differences in performance on cognitive measures by both adults and adolescents with elevated BMI, it is hypothesized that a group difference will be observed between normal weight and obese adolescents on a neuropsychological battery including measures of intelligence, executive functioning, speed of processing, and verbal memory.

2. Given previous demonstration of deficits in executive functioning among obese adults, decreased frontal lobe volumes in adults, inconsistent demonstration of impairment on tasks of inhibition, set-shifting, and working memory in adolescents, as well as literature supporting gray matter reductions in the frontal lobes and orbito-frontal regions and evidence for differences in fronto-subcortical structure in obese adolescents, it is hypothesized that the group of obese adolescents will perform more poorly than their
normal weight counterparts on measures of executive functioning such as set-shifting, inhibition, and working memory.

3. Given literature suggesting decreased processing speed in obese adults, decreased white matter integrity across several brain tracts in obese adults, and modest emerging evidence for decreased white matter integrity in association tracts among obese adolescents, it is hypothesized that the group of obese adolescents will perform more poorly than their normal weight counterparts on measures of processing speed.

4. Given the evidence across the literature that global intellectual functioning is not significantly different between obese and normal weight adults or adolescents, it is hypothesized that there will be no significant differences between the obese group of adolescents and their normal weight counterparts in IQ.

Method

Participants

Participants were 62 typically-developing, right-handed adolescents between the ages of 12 and 16 (Mean = 14.63 years; SD = 1.47). Right-handedness was confirmed using the Edinburgh Handedness Inventory (Oldfield, 1971). Participants were drawn from three larger, ongoing and completed, grant-funded studies conducted by Principal Investigator: Bonnie Nagel, Ph.D. These larger studies were carried out through the Developmental Brain Imaging Laboratory (DBIL) at Oregon Health and Science University (OHSU) and were designed to investigate typical neural development in adolescents. The data used to conduct the present study is a compilation of participants from these three larger studies and was not collected for the sole purpose of the current study. Therefore, there were variations in the study protocols in terms of
the specific measures given. All participants were recruited for these studies through mailings, newspaper advertisements, fliers, online advertisements, and notices at Portland area schools.

As per the individual study protocols, exclusionary criteria included a lifetime history of psychiatric or substance use disorders as defined by the *Diagnostic and Statistical Manual of Mental Health Disorders* (DSM-IV-TR; American Psychiatric Association, 1994), history of significant substance use not meeting criteria for disorder (e.g., 10 lifetime alcoholic drinks or 2 drinks per occasion, more than 5 experiences with marijuana, smoking more than 4 cigarettes per day, or any other illicit drug use), neurological illness, significant head trauma, major medical problems, intellectual disability, learning disability, current use of medication affecting the central nervous system, reported history of bipolar I disorder in biological parents, history of psychotic disorders in biological parents, non-fluency in the English language, sensory problems, and left-handedness. These exclusionary criteria were used in an attempt to create a sample absent of abnormal neuropsychological performance.

All participants from the three larger studies who met study criteria were collapsed together into one larger dataset, which contained a total of 243 adolescents. Adolescents were then categorized into one of four groups based on body mass index (BMI) percentile by age according to the guidelines set forth the by Centers for Disease Control (CDC). In congruence with the CDC guidelines, participants were placed in the “underweight” group if their BMI was below the 5th percentile for their age, in the “normal weight” group if their BMI fell between the 5th and 85th percentile for their age, in the “overweight” group if their BMI fell between the 85th and 94th percentile for their age, and in the “obese” group if their BMI was at or above the 95th percentile for their age. As the current study aimed to examine group differences between normal weight adolescents and obese adolescents, further group dichotomization was necessary.
Therefore, participants falling in the “underweight” and “overweight” groups were both eliminated from the sample. This left a sample consisting of 119 adolescents who belonged to either the “normal weight” or “obese” group. Of this remaining sample, 20 participants were eliminated due to missing data.

Of the remaining sample, 31 “obese” adolescents remained. These 31 adolescents were then each matched to a “normal weight” adolescent based on age, gender, ethnicity, and socioeconomic status (SES) as measured by the Hollingshead Index of Social Position (Hollingshead, 1975). As previously mentioned, it was desired to have as much dichotomization in BMI as possible between groups. For this reason, normal weight controls were restricted to those in the normal weight group who had BMI between the 30\textsuperscript{th} and 70\textsuperscript{th} percentile for age so that, on average, the normal weight group mean would approximate the 50\textsuperscript{th} percentile ($Mean = 48; SD = 12.12$). The confidence interval of plus or minus 20 percent was chosen such that participant BMI fell closer to the mean than to either the overweight or underweight extremes. Following this matching process, the final dataset consisted of 62 adolescents. Independent samples T-tests were performed to confirm group equivalency across demographic domains. As expected, there were no differences found. See Table 1 for complete demographic information for the sample.

Table 1

<table>
<thead>
<tr>
<th>Participant Demographic Information</th>
<th>Normal Weight Group</th>
<th>Obese Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>$M = 14.7; SD = 1.48$</td>
<td>$M = 14.7; SD = 1.47$</td>
</tr>
<tr>
<td>SES</td>
<td>$M = 26.5; SD = 12.65$</td>
<td>$M = 31.1; SD = 12.9$</td>
</tr>
<tr>
<td>Gender</td>
<td>65% Male</td>
<td>65% Male</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>87% Caucasian</td>
<td>87% Caucasian</td>
</tr>
</tbody>
</table>

Following the creation of groups, the sample was further characterized across multiple behavioral variables including self-reported levels of depression, self-reported levels of anxiety,
self-reported sleepiness and sleep/wake problems, and self-reported levels of physical activity. It should be noted that due to the nature of participant selection in this study not all of these behavioral measures were available for the entirety of the sample. Independent samples t-tests were conducted to determine whether any significant group differences were present across any of these variables.

Self-reported level of depression was measured using the Children’s Depression Inventory (CDI; Kovacs, 1985). An independent samples t-test was conducted to evaluate whether levels of self-reported depression were significantly different between obese and normal weight adolescents. The test was not significant, t(60) = .09, p = .93. Adolescents in the obese group (M = 41.90, SD = 6.8) did not significantly differ in levels of self-reported depression as compared to normal weight adolescents (M = 42.06, SD = 6.69).

Self-reported level of anxiety was measured using the State Trait Anxiety Inventory (STAI; Spielberger, 1989). An independent samples t-test was conducted to evaluate whether levels of self-reported anxiety were significantly different between obese and normal weight adolescents. The test was not significant, t(52) = 1.91, p = .06. Adolescents in the obese group (M = 39.55, SD = 6.46) did not significantly differ in levels of self-reported anxiety as compared to normal weight adolescents (M = 42.89, SD = 6.33).

Self-reported level of sleepiness was measured using the Sleepiness Scale of the Sleep Habits Questionnaire (SHQ). An independent samples t-test was conducted to evaluate whether amount of sleepiness was significantly different between obese and normal weight adolescents. The test was not significant, t(43) = .37, p = .72. Adolescents in the obese group (M = 12.68, SD = 2.64) did not significantly differ in levels of self-reported sleepiness as compared to normal weight adolescents (M = 13.0, SD = 3.13).
Self-reported level of problems related to falling asleep and waking from sleep were measured using the Sleep/Wake Problems Behavior Scale Score of the Sleep Habits Questionnaire (SHQ). An independent samples t-test was conducted to evaluate whether amount of sleep/wake problems was significantly different between obese and normal weight adolescents. The test was not significant, $t(42) = .28, p = .78$. Adolescents in the obese group ($M = 14.68, SD = 3.76$) did not significantly differ in amount of sleep/wake problems as compared to normal weight adolescents ($M = 15.05, SD = 4.89$).

Self-reported level of physical activity was measured using the hours per week of physical activity question, which is part of the Youth Risk Behavior Survey (YRBS; Centers for Disease Control, 2011). An independent samples t-test was conducted to evaluate whether the amount of physical activity engaged in per week was significantly different between obese and normal weight adolescents. The test was significant, $t(44) = 2.18, p < .05$. Adolescents in the obese group ($M = 5.36, SD = 4.19$) engaged in significantly fewer hours of physical activity per week as compared to normal weight adolescents ($M = 8.00, SD = 4.00$). The 95% confidence interval for the difference in means ranged from .20 to 5.07. The eta-squared ($\eta^2$) index was moderate and indicated that 10% of the variance in amount of physical activity engaged in per week was accounted for by whether a participant was in the obese versus normal weight group. See Table 2 for a summary of mean differences between obese and normal weight adolescents for behavioral measures.
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Table 2

<table>
<thead>
<tr>
<th></th>
<th>Mean Obese (SD)</th>
<th>Mean Normal Weight (SD)</th>
<th>Sig</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children’s Depression Inventory</td>
<td>41.90 (6.80)</td>
<td>42.06 (6.69)</td>
<td>.92</td>
<td></td>
</tr>
<tr>
<td>State Trait Anxiety Inventory</td>
<td>39.55 (6.4)</td>
<td>42.87 (6.33)</td>
<td>.06</td>
<td></td>
</tr>
<tr>
<td>SHQ Sleepiness Scale</td>
<td>12.68 (2.64)</td>
<td>13.00 (3.13)</td>
<td>.72</td>
<td></td>
</tr>
<tr>
<td>SHQ Sleep/Wake Problems Scale</td>
<td>14.68 (3.76)</td>
<td>15.04 (4.89)</td>
<td>.78</td>
<td></td>
</tr>
<tr>
<td>YRBS Physical Activity per Week</td>
<td>5.36 (4.19)</td>
<td>8.00 (4.00)</td>
<td>.03*</td>
<td>.10</td>
</tr>
</tbody>
</table>

* p < .05

Procedure

A battery of neuropsychological tests was administered to each participant by trained research assistants and volunteers at the OHSU DBIL. Though the exact protocols differed by study, participants completed a testing session approximately 2-3 hours in length which included administration of neuropsychological assessments, as well as completion of personality inventories and behavior checklists. A subset of assessment instruments measuring the domains of intelligence, executive functioning, and memory were utilized for the present study.

Measures

Intelligence. The Wechsler Abbreviated Scale of Intelligence (WASI) was used as an estimate of intellectual functioning. The WASI was developed in 1999 as an abbreviated measure of intelligence which can be administered in either a two subtest or four subtest version (WASI; Wechsler, 1999). For the purposes of the current study, the two-scale intelligence quotient (2-Scale IQ) was used. The 2-Scale IQ includes the Vocabulary and Matrix Reasoning Subtests. The Vocabulary subtest is designed to measure verbal expression of word knowledge
and represents an estimate of ability to articulate crystalized knowledge. The Matrix Reasoning subtest is designed to measure non-verbal abstract reasoning and represents an estimate of non-verbal fluid reasoning.

**Executive Functions.** The domain of executive functioning is complex, therefore, multiple measures were used to assess the various domains of this construct. The Color Word Interference Test, a subtest of the Delis-Kaplan Executive Function System (D-KEFS; Delis et al., 2001) was administered to each participant. The Color Word Interference Test has four conditions: Color Naming, Word Reading, Inhibition, and Inhibition/Switching. Both the Color Naming and Word Reading conditions provide estimates of speed of processing as they require the participant to either quickly name patches of color or quickly read color words aloud (e.g., “red”). The Inhibition task is a measure of speed and accuracy of dominant response inhibition. On this task the participant is asked to name the color of the ink that different color words are printed in (e.g., the word “red” may be printed in green ink requiring the correct response of green). The Inhibition/Switching task measures both speed and accuracy of dominant response inhibition paired with a cognitive flexibility and set-shifting component. As in the previous condition, the participant is required to name the color of the ink that different color words are printed in; however, if a word is surrounded by a box they are to read the word, disregarding the color of the ink. In this way, participants are required to cognitively shift between two separate rule-sets while also inhibiting dominant responding for one rule-set.

The D-KEFS Color Word Interference Test provides scoring for both task completion time, as well as for accuracy. For the purposes of the study, only scores for completion time were used for the Color Naming and Word Reading conditions. For the Inhibition and Inhibition/Switching conditions, a composite variable was created using both speed of task
completion as well as accuracy as measured by total errors. Creation of these composite variables is described below.

A modified version of the Paced Auditory Serial Addition Test (PASAT; Gronwall & Sampson, 1974) was administered as a measure of attention, working memory, and speed of information processing. The PASAT was initially developed as a means to monitor recovery in patients who had sustained mild head injuries. The task is administered via an audio recording which controls the rate at which stimuli are presented. Single digits are presented at a rate of either one every 3 seconds (3s PASAT) or one every 2 seconds (2s PASAT). The participant must listen for two consecutive numbers, calculate the sum of the numbers in their head, and provide the answer to the administrator. The participant continues in this manner, adding each new number to the one preceding it, for a total of 60 trials per condition. There is a 10 digit practice trial which precedes both the 3s PASAT and 2s PASAT trials. This is a very challenging task which requires the simultaneous utilization of several executive functions.

The PASAT is scored by calculating the percentage of correct responses out of 60 possible trials for the 3s and 2s conditions respectively. For the purpose of the present study, a composite variable was created which combined performance on both the PASAT 3s and PASAT 2s conditions. The PASAT composite score was an average of the percentage of correct trials on each condition.

**Verbal Memory.** The Rey Auditory Verbal Learning Test (RAVLT) was administered as a measure of verbal learning and memory, both encoding and retrieval (Rey, 1941). The RAVLT was initially developed in French in 1941 and has subsequently been translated into English as well as four other languages. The RAVLT consists of four components: the learning trials, an interference list, the recall trials, and the recognition trial. The test begins with five learning
trials. For each learning trial, the participant is read the same list of 15 words, presented in the same order, which are read at a rate of approximately one per second. Following each presentation of the word list, the participant is asked to recall as many words from the list as possible, regardless of word order. Following the fifth learning trial, the participant is read an interference list which consists of 15 new words not on the first list. The participant is then asked to recall as many words as possible from this new list regardless of word order. After the interference trial, the participant is asked to recall as many words as they can from the initial 15-word list. A delayed recall trial takes place 30 minutes after the interference trial. After the delayed recall trial, the participant completes a recognition trial where they are asked to identify the words they previously learned from a larger list of words which includes words from the initial word list, words from the interference list, and novel words.

For the purposes of the present study, only performance on the delayed recall trial and the recognition trial were used. Performance on the 30-minute recall condition was used as a measure of verbal memory retrieval. Performance on the recognition trial was measured by number of words from the initial word-list correctly identified from a list of words containing words from the initial word list, the interference list, as well as novel words. This score was used to account for possible discrepancies between retrieval and encoding.

**Variables**

Prior to analyses being completed, three composite variables were created from the data set. For the Color-Word: Inhibition task a composite variable was created utilizing speed at which the task was completed and errors made while completing the test. The composite was created by taking the average of the scaled score for time of completion and the scaled score for total errors made. A similar composite variable for speed and errors made was created for the
Color-Word: Inhibition/Switching task. This composite variable was created by taking the average of the scaled score for time of completion and the scaled score for total errors made. A final composite variable was created for performance on the PASAT 3s and PASAT 2s conditions. Performance on the PASAT is measured by percentage of trials answered correctly out of 60 possible trials. The composite variable was an average of the percentage of trials answered correctly for each of the PASAT conditions respectively. Notably, unlike the other variables utilized in this study, the PASAT composite does not take into account age-related variance in performance.

Multiple types of neuropsychological measures were used in the analyses. As such, performance on each measure is quantified using a different type of score (e.g., standard score, scaled score, z-score, percentile). Therefore, scores on each of these measures were standardized so that performance could be compared using the same metric. Z-score transformation was utilized for each of the measures. The participant’s age adjusted score was transformed rather than the raw score in order to account for the effect of age on performance, with the exception of performance on the PASAT which does not have age-adjusted norms available. These age-adjusted scores were then z-normalized compared to the sample mean to create standardized dependent variables.

**Pre-analysis data screening**

A one-way multivariate analysis of variance (MANOVA) was conducted to evaluate group differences between normal weight and obese adolescents in performances on the various neuropsychological measures. MANOVA requires that several assumptions be met in order to control for Type 1 and Type 2 errors. When indicated, pre-analysis data screening was completed to ensure that necessary statistical assumptions were met prior to analysis.
The assumption of independence requires that participants’ performance on each of the dependent measures are not influenced by or related to the scores of other participants on the same dependent measure. This assumption is met due to study design in which all subjects were assessed independent of one another and no participant’s score influenced another participant’s score. The linearity assumption holds that the relationships between all pairs of dependent variables are linear. To test this assumption scatter plots of each pair of dependent variables were created for each level of the independent variable. No curvilinear relationships nor outliers were observed. Therefore, it can be assumed that the assumption of linearity was met.

There are several assumptions of normality which must be met for MANOVA. Univariate normality holds that all of the dependent variables must be distributed normally for each level of the independent variable. This was assessed for by examining skewness and kurtosis coefficients for each of the dependent variables. Bivariate normality holds that for every combination of two dependent variables, each is normally distributed at all levels of the other variable. Bivariate normality was assessed using the Shapiro-Wilk test. It was determined that both assumptions of univariate normality and bivariate normality were met.

Multivariate normality holds that all of the dependent variables must have multivariate normal distribution for each level of the independent variable. Mahalanobis D² was used to assess for multivariate normality by examining for multivariate outliers. A critical value was determined based on an alpha of \( p < .001 \). For this sample, the critical value of \( \chi^2 \) at \( p < .001 \) and \( df = 8 \) was 26.12. None of the participants had a Mahalanobis distance greater than 26.12. Therefore, no multivariate outliers were present in the current sample and the multivariate normality assumption was met.
Finally, the assumption of homoscedasticity requires that the covariance matrices be homogeneous. This assumption was tested using Box’s $M$ test and was significant ($p<.001$) in this sample. However, due to the fact that the sample sizes were equal in both of the groups, the robustness of the significance tests reported below is expected. Therefore, the significant Box’s $M$ test is assumed to not have a significant adverse effect on the analyses.

Results

Once it was confirmed that all assumptions had been met, a MANOVA was conducted. The MANOVA results indicated a significant multivariate main effect for group performance on this battery of assessments, Wilks’ $\Lambda = 0.65$, $F(8, 62) = 3.55$, $p < .01$. The multivariate partial eta squared ($\eta_p^2$) of .35 indicated a moderate relationship between adolescent weight class (e.g., obese versus normal weight) and performance on neuropsychological outcome variables.

Given the significance of the multivariate test, the univariate main effects were examined. To control for Type I error across the eight univariate tests, alpha was set at .006 (.05/8) for each. A significant univariate main effect of group for RAVLT Delayed Recall was observed, $F(1, 62) = 10.15$, $p = .002$, partial eta squared ($\eta_p^2$) = .15. However, significant univariate main effects of group were not found for WASI 2-scale IQ, $F(1, 62) = 5.28$, $p > .006$, partial eta squared ($\eta_p^2$) = .08, Color-Word: Color Naming, $F(1, 62) = .75$, $p > .006$, partial eta squared ($\eta_p^2$) = .01, Color-Word: Word Reading, $F(1, 62) = 2.25$, $p > .006$, partial eta squared ($\eta_p^2$) = .04, Color Word: Inhibition plus errors, $F(1, 62) = .70$, $p > .006$, partial eta squared ($\eta_p^2$) = .01, Color Word: Inhibition/Switching plus errors, $F(1, 62) = 1.99$, $p > .006$, partial eta squared ($\eta_p^2$) = .03, PASAT, $F(1, 62) = .01$, $p > .006$, partial eta squared ($\eta_p^2$) = .00, or RAVLT Recognition, $F(1, 62) = .08$, $p > .006$, partial eta squared ($\eta_p^2$) = .00. The means and standard deviations for each...
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dependent variable for the normal weight and obese groups are presented in Table 3. A summary of the univariate main effects is presented in Table 4.

Table 3
Means and Standard Deviations for Dependent Variables

<table>
<thead>
<tr>
<th>Dependent Variables</th>
<th>Normal Weight</th>
<th></th>
<th>Obese</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
</tr>
<tr>
<td>WASI 2-Scale IQ(^a)</td>
<td>114.39</td>
<td>8.1</td>
<td>108.13</td>
<td>12.8</td>
</tr>
<tr>
<td>Color-Word: Color Naming(^b)</td>
<td>10.32</td>
<td>2.51</td>
<td>9.29</td>
<td>3.08</td>
</tr>
<tr>
<td>Color-Word: Word Reading(^b)</td>
<td>10.87</td>
<td>2.03</td>
<td>9.23</td>
<td>5.77</td>
</tr>
<tr>
<td>Color-Word: Inhibition + Errors(^b)</td>
<td>10.06</td>
<td>2.38</td>
<td>9.50</td>
<td>2.91</td>
</tr>
<tr>
<td>Color-Word: Inhibition/Switching + Errors(^b)</td>
<td>10.22</td>
<td>2.25</td>
<td>9.26</td>
<td>3.08</td>
</tr>
<tr>
<td>PASAT(^c)</td>
<td>60.89</td>
<td>13.5</td>
<td>60.36</td>
<td>17.00</td>
</tr>
<tr>
<td>RAVLT – Delayed Recall(^d)</td>
<td>1.44</td>
<td>.83</td>
<td>.49</td>
<td>1.43</td>
</tr>
<tr>
<td>RAVLT – Recognition(^d)</td>
<td>.09</td>
<td>.97</td>
<td>.02</td>
<td>1.21</td>
</tr>
</tbody>
</table>

Note. Scores are represented as: (a) Standard Score; (b) Scaled Score; (c) Percentage; (d) z-score

Table 4
Table of Univariate Main Effects

<table>
<thead>
<tr>
<th></th>
<th>F</th>
<th>p</th>
<th>(\eta^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WASI 2-Scale IQ</td>
<td>5.28</td>
<td>.025</td>
<td>.08</td>
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<tr>
<td>Color-Word: Color Naming</td>
<td>.75</td>
<td>.391</td>
<td>.01</td>
</tr>
<tr>
<td>Color-Word: Word Reading</td>
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<td>.139</td>
<td>.04</td>
</tr>
<tr>
<td>Color-Word: Inhibition + Errors</td>
<td>.70</td>
<td>.406</td>
<td>.01</td>
</tr>
<tr>
<td>Color-Word: Inhibition/Switching + Errors</td>
<td>1.99</td>
<td>.163</td>
<td>.03</td>
</tr>
<tr>
<td>PASAT</td>
<td>.02</td>
<td>.892</td>
<td>.00</td>
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<tr>
<td>RAVLT – Delayed Recall</td>
<td>10.15</td>
<td>.002*</td>
<td>.15</td>
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<tr>
<td>RAVLT – Recognition</td>
<td>.80</td>
<td>.779</td>
<td>.001</td>
</tr>
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</table>

* Significant at \(p < .01\)

Hypotheses

Each of the hypotheses in the current study was tested using the MANOVA previously reported. The first hypothesis was that there would be a significant difference in performance on a brief neuropsychological battery between a group of obese adolescents and a group of normal weight adolescents. This hypothesis was tested by examining the multivariate main effect of the MANOVA. The multivariate main effect was significant, suggesting that the hypothesis was
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supported. This effect was primarily due to differences in performance on the RAVLT delay task.

The second hypothesis was that adolescents with elevated body mass would demonstrate significantly poorer performance on tasks of executive functioning, including set-shifting inhibition, and working memory, when compared to their normal weight counterparts. This hypothesis was not supported by the results of the MANOVA. Examination of univariate effects for Color-Word: Inhibition, Color-Word: Inhibition/Switching, and PASAT composite were all non-significant.

The third hypothesis was that the obese group would demonstrate slower processing speed as compared to the normal weight group. This hypothesis was also not supported by the results of the MANOVA. Examination of univariate main effects for Color-Word: Color Naming and Color-Word: Word Reading; both were non-significant.

The fourth hypothesis was that the obese group would not differ from the normal weight group on IQ. This was tested for by examining the univariate main effect for WASI 2-Scale IQ. This main effect was non-significant, indicating that the hypothesis was supported. However, it should be noted that trend-level differences between the groups were observed ($p < .05$, with the obese group demonstrating lower average IQ compared to their normal weight counterparts.

**Exploratory analyses**

As previously reported, the results of the MANOVA indicated that a group difference between normal weight and obese adolescents was present in this sample, with a significant main effect for performance on the RAVLT Delay condition. Further analyses of the main effects indicated trend level significance in WASI 2-scale IQ, with normal weight adolescents performing better than their obese counterparts. A one-way analysis of covariance (ANCOVA)
was conducted to evaluate the effect of BMI category (i.e., normal weight or obese) on performance on the RAVLT Delay, while controlling for WASI 2-scale IQ.

A preliminary test to evaluate the homogeneity of regression (slopes) assumption was conducted and indicated that there was not a significant interaction between BMI category and WASI 2-scale IQ scores. That is, a preliminary analysis evaluating the homogeneity of slopes assumption indicated that the relationship between the covariate and the dependent variable did not differ significantly as a function of the independent variable, $F(1, 58) = .17, MSE = .84, p = .68$, partial eta squared ($\eta^2_p$) = .003. Thus, the results indicate that the homogeneity assumption was met.

The ANCOVA was significant, $F(1, 59) = 6.60, MSE = .83, p < .05$, partial eta squared ($\eta^2_p$) = .10. The strength of relationship between the independent variable and dependent variable was moderate ($\eta^2_p$), with BMI category accounting for 10% of the variance in RAVLT Delay scores, holding constant WASI 2-scale IQ scores. The Bonferroni adjusted t-test was used to control for Type I error across the two pairwise comparisons. Adolescents who were in the obese group ($M = -.31, SE = .17$) on average had significantly lower RAVLT Delay scores when compared to adolescents in the normal weight group ($M = .30, SE = .17$), after controlling for WASI 2-scale IQ scores. The 95% confidence interval for the difference in adjusted means ranged from -.65 to .02.

As mentioned in the Participants section, there was a significant difference between number of hours of physical activity engaged in per week between the obese and normal weight groups. A multivariate analysis of covariance (MANCOVA) was conducted to determine whether or not amount of physical activity mediated group difference in performance on the neurocognitive battery. It should be noted that information on amount of physical activity
engaged in each week was not available for the entire sample. As such, the MANCOVA which will be reported is from a subset of 46 of the original 61 participants. The MANCOVA results indicated a significant multivariate main effect of group for performance on this battery of assessments, Wilks’ \( \Lambda = 0.50 \), \( F(8, 45) = 4.30, p = .001 \). The multivariate partial eta squared (\( \eta_{p}^2 \)) of .50 indicated a strong relationship between adolescent weight class (e.g., obese versus normal weight) and performance on neuropsychological outcome variables when amount of physical activity per week was controlled for.

Given the significance of the multivariate test, the univariate main effects were examined. To control for Type I error across the eight univariate tests, alpha was set at .006 (.05/8) for each. A significant univariate main effect of group for RAVLT Delayed Recall was observed, \( F(1, 46) = 16.30, p < .001 \), partial eta squared (\( \eta_{p}^2 \)) = .28. However, significant univariate main effects of group were not found for WASI 2-scale IQ, \( F(1, 46) = 4.27, p > .006 \), partial eta squared (\( \eta_{p}^2 \)) = .09, Color-Word: Color Naming, \( F(1, 46) = 1.29, p > .006 \), partial eta squared (\( \eta_{p}^2 \)) = .03, Color-Word: Word Reading, \( F(1, 46) = 3.20, p > .006 \), partial eta squared (\( \eta_{p}^2 \)) = .07, Color Word: Inhibition plus errors, \( F(1, 46) = .13, p > .006 \), partial eta squared (\( \eta_{p}^2 \)) = .003, Color Word: Inhibition/Switching plus errors, \( F(1, 46) = 1.56, p > .006 \), partial eta squared (\( \eta_{p}^2 \)) = .04, PASAT, \( F(1, 46) = .03, p > .006 \), partial eta squared (\( \eta_{p}^2 \)) = .00, or RAVLT Recognition, \( F(1, 46) = 3.71, p > .006 \), partial eta squared (\( \eta_{p}^2 \)) = .08. A summary of the univariate main effects is presented in Table 5.
Table 5

<table>
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<th>Table of Univariate Main Effects for MANCOVA</th>
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<td>.09</td>
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<td>.081</td>
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* Significant at $p < .006$

Discussion

The purpose of this study was to examine possible cognitive differences between obese adolescents and their normal weight counterparts. As the incidence of childhood obesity has risen over the past 20 years in the United States, it is important to understand the implications this has across various domains of functioning. It was hypothesized that a significant difference in performance on a neuropsychological battery would be observed, with normal weight adolescents performing significantly better than their obese counterparts, particularly on measures of executive functioning (e.g., set-shifting, inhibition, working memory) and processing speed. As expected, there was a significant difference between obese and normal BMI group performance on this neuropsychological battery; however, contrary to hypotheses, this difference was driven by performance on a verbal memory task, rather than on tasks of executive functioning or processing speed.

While the overall hypothesis of observable BMI group differences held true, the major skill area driving the difference was not the one which had been anticipated. It was not expected that performance on a verbal recall task would be significantly different between groups, as few studies have examined word-list learning and memory in obese adolescents. Most studies which
have reported on memory performance in obese adolescents used working memory paradigms, such as digit span tasks, which really are measures of executive functioning, as opposed to memory functioning. Some studies of working memory reported no relationship between BMI and performance on these measures (Cserjesi, Molnar, Luminet, & Lenard, 2007; Verdejo-Garcia et al., 2010), and others found working memory to be impaired in adolescents with elevated BMI (Maayan et al., 2011). Only two studies were found which assessed verbal recall specifically in adolescents, and no relationship was found between elevated BMI and performance on a delayed verbal recall task in these studies (Gunstead et al., 2008; Waber et al., 2012); however, IQ was controlled for in the study conducted by Gunstead and colleagues (2008), which may have accounted for some of the variance in memory performance given demonstrated associations between these two constructs in individuals with average IQ (Bornstein, Chelune, & Prifitera, 1989; Tremont, Hoffman, Scott, & Adams, 1998). In the adult literature, there is evidence that elevated BMI is related to decreased word-list learning and verbal recall (Cournot et al., 2006; Gunstead, Paul, Cohen, Tate, & Gordon, 2006; Sabia et al., 2009); however, as this had not been demonstrated in adolescent populations, it was thought that perhaps obesity’s impact on word-list learning and memory was a result of prolonged obesity over the course of the lifespan.

It is unclear as to the mechanisms behind the discrepancy between the adult and adolescent literature regarding the relationship between elevated BMI and poor verbal recall and memory. It has been suggested that the discrepancy between memory impairment in adults and adolescents with elevated BMI may be related to complications of obesity, such as insulin-resistance, with complications related to more severe BMI possibly being predictive of memory impairment (Yau, Kang, Javier & Convit, 2014). It has been noted that for adults, significant
differences in verbal memory performance are only observed in groups of individuals with BMI within the highest quartile (Sabia et al., 2009). However, verbal recall deficits have not shown an age by BMI interaction, suggesting that chronicity may not be necessary for verbal memory deficits to be seen (Gustead et al., 2006). This suggests that high levels of BMI are necessary for deficits in verbal memory to be observed. It is possible that high BMI has a particular impact on brain regions involved in verbal memory.

Studies of typically developing children and adolescents have examined the brain-behavior relationship between verbal memory and maturation of different brain regions. There are multiple brain regions which are involved in both the encoding and retrieval processes necessary for verbal memory. Both temporal and frontal cortical regions are implicated in the process of encoding novel information and retrieving it at a later time. Throughout childhood, neural interaction increases between these two regions, thought to aide in memory development (de Haan et al., 2006; Menon et al., 2005; Nelson, 1995). Further, involvement of the frontal cortex supports strategy use and retrieval in memory recall (Nyberg et al., 1995; Takahashi et al., 2007). In typically developing children, gray matter density predicts memory performance, with maturational thinning (i.e., decreased density) of the frontal cortex being predictive of better delayed verbal retrieval (Sowell et al., 2001). During the process of typical brain development, maturation of frontal and temporal cortical regions is thought to be related to refinement of memory processes during the period between childhood and adolescence.

Beyond changes in gray matter density, it is thought that increased integrity that takes place during typical development between white matter pathways within and between the temporal and prefrontal cortical regions, such as the uncinate fasciculus, are key in refining the memory process (Schmahmann et al., 2007). There is evidence that shows increased functional
connectivity within the temporal cortex and between the temporal and prefrontal cortex is related to increased efficiency of memory processes in older children (Menon et al., 2005). Further, performance on auditory verbal memory tasks has been shown to be related to white matter integrity of the left uncinate fasciculus in typical adolescents (Mabbott, Rovet, Noseworthy, Smith, & Rockel, 2009). Taken together, cortical maturation in both the frontal and temporal regions, as well as increases in white matter integrity between temporal and prefrontal regions, especially the uncinate fasciculus, during typical development is related to improved efficiency in memory.

Given the known relationship between maturation of frontal and temporal regions and memory performance, it is important to examine whether there is any known insult to these regions in children with elevated BMI. Obesity in children and adolescents is associated with decreased gray matter volume in both frontal and limbic regions, independent of global gray matter changes associated with brain maturation (Alosco et al., 2014). Another brain region that is often implicated in memory function is the fornix, the major fiber tract which connects the medial temporal lobe and the medial diencephalon. Reduction in volume of the fornix has been associated with decreased memory recall (Tsivilis et al., 2008). In the adult literature, obesity has been shown to be related to decreased white matter integrity in the fornix (Stanek et al., 2011; Verstynen et al., 2012; Xu et al., 2013), suggesting another potential neurobiological mechanism underlying observed memory deficits. Findings from DTI studies with adolescents suggest that obesity may be associated with frontal-subcortical neuropathology (Alosco et al., 2014; Yau et al., 2014). As far as white matter integrity and FA, results are not as conclusive. Some research suggests no differences are present in white matter FA (Alosco et al., 2014), while others have
found FA reductions in major fiber tracts involved in cortio-subcortical signal transmission, including the uncinate fasciculus (Yau et al., 2014).

While there is limited research corroborating the findings of the present study (i.e., delayed verbal memory being significantly poorer in obese adolescents compared to normal weight adolescents), the evidence from functional and structural imaging studies provide support for this result. Both frontal and temporal regions are implicated in typical memory function. During the period between childhood and adolescence, maturation in this region aids in memory refinement. Emerging evidence suggests that it is possible that the frontal regions, as well as white matter tracts which connect fronto-temporal regions, may be adversely impacted by elevated BMI. It is possible that insult to these regions adversely impacts memory retrieval due to interference with typically developing memory processes. Studies should examine this possible relationship by examining both behavioral and imaging data in obese and normal weight adolescents, as this may provide evidence of a correlation between insult to these regions and impaired performance on verbal memory tasks.

While verbal memory has been tested in several studies involving obese adults, few studies of obese adolescents have examined this domain. The only studies found which examined verbal memory in obese adolescents did not find any group differences in performance (Gunstead et al., 2008; Waber et al., 2012). It is unknown as to why poorer verbal memory among obese adolescents was observed in this sample when it was not observed in other studies of obese adolescents. It is possible that the duration of elevated BMI plays a role in its impact on neurological functioning and development. As this study did not track weight over time, it is impossible to know the chronicity of obesity in the sample at hand. This study also aimed to dichotomize obese and normal weight adolescents, creating two groups which varied greatly in
BMI composition. It is possible that this dichotomization allowed for the discrepancy in verbal memory to be more apparent between groups than it may otherwise have been in other studies. The role of IQ and its association with verbal memory performance was taken into consideration as a possible mediating factor, as one of the studies which found no group differences in memory performance controlled for IQ (Gunstead et al., 2008). Exploratory analyses were conducted examining IQ as a covariate for verbal memory performance. The groups remained significantly different on verbal memory performance, even after controlling for IQ, suggesting that verbal memory performance is significantly different in obese and normal weight adolescents independent of the influence of IQ.

Environmental enrichment is a factor which has been shown to be related to increased memory performance in animal models. In rodent studies, exposure to enriched environments have led to improved long-term recognition memory (Brue-Jungerman et al., 2005) and improved spatial memory (Williams et al., 2001). This enhancement in behavioral performance on memory tasks has been attributed to increased neurogenesis in the hippocampal regions. Results from several animal studies seem to suggest that exposure to more enriched environments stimulates processes in the brain which lead to improved memory functioning. Many children and adolescents who are obese tend to engage in more sedentary lifestyles, limiting the type of enrichment which they can receive from their environment. Therefore, it is possible that differences observed in memory performance are not related to direct insult to the brain due to obesity; rather, the lack of environmental enrichment which often accompanies the sedentary lifestyles of obese adolescents may be having a negative impact on their memory performance. Notably, however, though the current sample differed on a measure of physical activity, this difference did not explain the observed group difference in verbal memory.
Another factor to consider in attempting to explain observed differences in neurocognitive performance is heredity. High heritability of gray matter volume in several cortical regions has been found, especially in Broca’s and Wernicke’s language areas as well as frontal brain regions (Posthuma et al., 2002; Thomas et al., 2001). In addition, high levels of heritability and total white matter volume have been observed (Posthuma et al., 2002). Results of monozygotic and dizygotic twin studies suggest that the frontal, sensorimotor, and anterior temporal cortices are under significant genetic control (Thomas et al., 2001; Toga & Thompson, 2005). This is important for the purposes of this study, as the brain regions discussed as being implicated in verbal memory retrieval are also structures which are known to be most influenced by heritability. Obesity tends to run in families (Perusse & Bouchard, 1999). As such, it is conceivable that any genetic difference that parents of obese children may have is passed along. The current study is limited in that information about participants’ parents was not collected as a means of comparison. However, results from previous studies suggest that heritability likely plays a role in verbal memory retrieval, suggesting this be considered in future studies.

It was expected that differences in performance on measures of executive functioning, such as set-shifting, inhibition, and working memory, would have been observed between the two groups in this sample. While numerous studies of obese adolescents report inverse relationships between BMI and performance on tasks of inhibition (Maayan et al., 2011), set-shifting (Delgado-Rico, Rio-Valle, Gonzalez-Jimenez, Campoy, & Garcia, 2012; Verdejo-Garcia et al., 2010), and working memory (Maayan et al., 2011; Verdejo-Garcia et al., 2010), other studies have failed to observe significant differences between obese and normal weight adolescents (Gunstad et al., 2008; Waber et al., 2012). Methodological differences between studies are often cited as possible reasons for discrepancy between results. Of note, performance
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on the Wisconsin Card Sort Test (WCST) is often cited as significantly different in obese and normal weight adolescents. The WCST is a measure of executive functioning and set-shifting which was not utilized in the present study. It is possible that the behavioral measures used to assess inhibition, set-shifting, and working memory (i.e., D-KEFS Color-Word and PASAT) were not sensitive enough to detect differences in the present sample of typically developing adolescents.

It was hypothesized that differences would be observed in processing speed based on the fact that white matter refinement, which takes place during adolescence, is associated with increased processing speed (Turken et al., 2008). The existing literature on neurocognitive functioning in obese adolescents has generally failed to measure processing speed as a construct of interest. The current study failed to discern any significant difference in processing speed between obese and normal weight adolescents. While this may be related to the specific tasks used to measure processing speed in the current study, it may also be reflective of the fact that speed of processing is not impacted by elevated BMI in adolescence.

Finally, it was hypothesized and demonstrated that overall IQ would not be significantly different between normal weight and obese adolescents; however, there was a trend toward group difference in IQ. Literature suggests that global intellectual functioning as represented by intelligence quotient is not significantly different in obese and normal weight adolescents (Gunstead, 2008; Waber et al., 2012). It stands to reason that global intellectual functioning would be preserved, as areas of the brain hypothesized to be impacted by obesity tend to be restricted to the frontal region and associated tracts, and areas implicated in general intelligence tend to be more global. It is possible that the trend toward significance is reflective of the fact that certain cognitive skill areas included in IQ are impacted by BMI differences while other skill
areas remain unaffected. Alternatively, it is possible that the trend toward group differences in IQ is reflective of unique characteristics of the present sample.

**Limitations**

There were multiple limitations to the current study. While the initial group of participants available to the study was quite large, several participants were eliminated based on missing data and study criteria for BMI ranges. As a result, the final sample size of 61 was much smaller than initially anticipated. The smaller sample size made it more difficult to detect significant group differences across the battery of neuropsychological assessments and prevented analyses of sex-differences. It is possible that insult to neuroanatomical and cognitive development related to obesity has different effects on the male and female brain, due to differences in rate of development and interaction with hormones. Understanding whether or not sex differences are present would add valuable information as to possible mechanisms by which insult due to obesity may take place. Additionally, the smaller sample size impacts the generalizability of the results to the general population of adolescents.

Specific characteristics of the study sample also limited the generalizability of the results. The study sample was 87% Caucasian, which while consistent with Portland demographics, is discrepant from the ethnic diversity of the general population. In addition, the socioeconomic status (SES) of the study sample was higher than would be found in a community sample. Thus, SES should also be considered when interpreting the results. The Hollingshead Index scores for the groups of participants had a mean of 26.5 for the normal weight group and a mean of 31.1 for the obese group. These scores are generally commensurate with middle class individuals. However, in the United States, obesity is often present at higher rates among people of lower
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socioeconomic status as well as among particular ethnic groups (Wang, 2001). It is possible that this group of middle class obese adolescents receives greater protective benefit that positively impacts cognitive development (e.g., access to less energy-dense foods such as vegetables; regular medical care) in comparison to their lower class counterparts.

The current study included individuals between the ages of 12 and 16. While each of the groups were matched on age, there were not equal numbers of participants in each age category across the age range of participants. Adolescence is an important period of brain development in which several systems are being refined. As such, individuals who are in varying stages of adolescence are in varying stages of typical brain development. An individual who is 12 is unlikely to have reached a similar level of refinement as compared to a 16 year old. As such, having unequal numbers of participants in each age designation across the adolescent period may have decreased sensitivity to changes that are not observable until a certain age is reached.

In creating the sample for this study, normal weight controls were matched to obese adolescents based on age, gender, ethnicity, and socioeconomic status. The study was designed so that the control group BMI would be as close to the 50th percentile as possible. While the study sample did have a mean close to the 50th percentile, due to the nature of the participants available to the study, the BMI percentiles for the normal weight group ranged from the 30th to the 70th percentile. It was necessary to expand the range of controls in order to ensure matching across the demographic variables. Expanding the range to include individuals from the 30th to the 70th percentile may have decreased sensitivity to detecting differences between groups as it made the control group more heterogeneous in terms of BMI range.

This study was conducted utilizing data collected for three larger studies, each of which had different aims than the present study. As such, limitations on the types of assessment
measures available to analyze were present. For example, while literature suggests a possible difference in visual spatial construction between obese and normal weight children, a measure of this skill was not available to be utilized for the present study. While the measures included in the present study tapped into several important domains, it is possible that other measures may have been able to detect group differences in skill areas such as inhibition.

Behavioral factors are also known to be associated with obesity. Increased physical activity is known to have a positive impact on cognition (Ruiz et al., 2010); however, children and adolescents who are obese engage in significantly fewer hours of physical activity each week (Janssen et al., 2005). In this study, self-reported amount of physical activity per week was examined for a subset of the sample for which it was available. Consistent with literature, the group of obese adolescents engaged in fewer hours per week of physical activity as compared to their normal weight counterparts. Due to this observed difference, further analysis of group differences on measures of neurocognitive functioning were performed with amount of physical activity being introduced as a covariate. With this sample of adolescents, group differences continued to be seen between obese and normal weight adolescents, even when physical activity was controlled for. Due to the fact that information about physical activity was not available for all participants, understanding of the true impact of physical activity is limited.

Children who are obese are more likely to suffer from disturbances in sleep (Mitchel et al., 2013). Further, sleep disturbance can have an adverse impact on cognition (Dewald-Kauffman, 2013). Differences in sleep were examined on a subset of the current sample for which data was available. Of this subset, there were no significant differences in self-reported levels of sleepiness or sleep/waking problems between normal weight and obese adolescents. As such, differences in sleep are unlikely to account for the neurocognitive group differences.
observed in the present sample. Again, limited information about sleep was available for the current study. Future studies may benefit from a more thorough examination of sleep and sleep disturbance to understand possible impact on cognitive functioning in obese adolescents.

Mood is also known to have some relationship to neurocognitive functioning. Depression in adolescents has been shown to be related to decreased visual memory (Matthews, Coghill, & Rhodes, 2008), executive functions including planning and impulsivity (Maalouli et al., 2011), and verbal memory (Gunther, Jolles, Herper-Dahlmann, & Konrad, 2004). Anxiety has also been related to decreased verbal memory in adolescents (Gunther et al., 2004) and both visual (Boldrini et al., 2005; Cohen et al., 1996) and verbal memory (Asmundson et al., 1995) in young adults. Some research suggests that adolescents who are obese experience higher rates of psychopathology, such as depression and anxiety (Anderson et al., 2007; Erermis et al., 2004), especially in females. It is therefore important to determine whether or not symptoms of anxiety and depression may be contributing to group differences observed in the current sample. Independent samples t-tests confirmed that there were no group differences between obese and normal weight adolescents on either measures of depression or anxiety. As such, it is unlikely that psychopathology contributed to group differences observed in the present sample; however, due to the nature of recruitment for this study and unique sample characteristics, scores for both groups on measures of anxiety and depression were far below the clinical level. This limits the representativeness of the sample to the general population of obese and normal weight adolescents.

**Future directions**

While the present study contributed information regarding the impact of elevated BMI on cognitive functioning, further studies are necessary to clarify the nature of this relationship. One
of the greatest challenges to researchers in this field is to disentangle whether obesity creates an insult to the brain resulting in the macro and micro-structural differences and neurocognitive differences which are observed, or whether macro and/or micro-structural brain differences result in behavioral differences which lead to obesity. Current literature fails to provide a real answer to this question, as present studies examine individuals who are already considered to be obese, making it impossible to know which preceded which. While there are many barriers to research, including financial and temporal, longitudinal studies designed to follow children before the onset of obesity through emergence of obesity would provide the best information as to the directionality of mechanism by which the observed differences between normal weight and obese individuals come to be. These longitudinal studies would ideally incorporate not only brain imaging and neurocognitive measures, but also examine the behavioral factors mentioned previously such as mood, sleep, and physical activity, as well as factors such as heredity and environmental enrichment.

As previously mentioned, the present study did not have equal numbers of participants in each age group across the age range. Future studies should examine cohorts of adolescents at varying ages throughout the adolescent period. Having a sample that consists of a large cohort at the earlier and later ends of adolescent development may lend itself to identification of skill differences emerging and possibly diverging during adolescence between obese and normal weight groups within the context of typical skill development during this period. In this way, it may be possible to further identify the brain structures and systems adversely affected by elevated BMI.

Inferences about brain regions and systems impacted by elevated BMI were made based on results obtained in this study. Future MRI studies examining brain structure are warranted in
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order to determine whether group differences exist structurally, and if so, where they are located. As previously discussed, white matter continues to mature throughout adolescence and into early adulthood. Diffusion tensor imaging (DTI) studies are warranted to examine white matter integrity, specifically in association tracts known to be developing during this period. If differences in white matter integrity exist between normal weight and obese adolescents, inferences may be drawn about the mechanisms by which elevated BMI insults cognitive functions.

Should future studies continue to find differences either structurally or functionally between normal weight adolescents and their counterparts with elevated BMI, studies examining the permanency of these effects are warranted. The plasticity of the brain, paired with the continuing development that takes place during adolescence, leads to hope that differences observed in this and other studies may be able to be addressed and lessened. It may be possible that interventions aimed at increasing physical activity and changing diet could improve areas of cognitive skill difference observed in obese adolescents.

Despite the limitations previously discussed, the present study had multiple strengths. By utilizing a matching strategy as part of the study design, group differences in gender, age, ethnicity, and socioeconomic status were able to be accounted for. As such, confounds on those demographic variables were reduced as no significant group differences on those variables were present. In addition, the utilization of rigorous pre-screening of participants eliminated additional confounds such psychiatric disorders, history of head trauma, major medical problems, or learning disability, all of which could impact neurocognitive performance.

Another strength of this study was the dichotomization of BMI between groups. In creating the groups, the obese group consisted of individuals with BMI at or above the 95th
percentile for age, and the normal weight group consisted of individuals with BMI between the 30\(^{th}\) and 70\(^{th}\) percentiles with the mean being the 48\(^{th}\) percentile. Creating a greater difference in BMI range between the groups increases the sensitivity with which differences in performance can be observed. In this way, the current study may have been more sensitive to differences in performance related to elevated BMI as compared to studies which include individuals with BMI percentiles up to the 85\(^{th}\) percentile for age in the normal weight group.

In conclusion, the current study added to the body of literature regarding neuropsychological differences between normal weight and obese adolescents. While the findings of the study were discrepant from those often found in the literature, newer imaging studies are revealing possible neuroanatomical differences in obese adolescents which may relate to the poorer verbal memory performance observed in this study. Insult to frontal regions, as well as frontal-temporal and cortical-subcortical tracts, may have an adverse effect on memory retrieval leading to the observed results. It will be important for future studies to combine neuropsychological and imaging data in order to better understand the brain behavior relationship between neuropsychological performance and anatomical and functional brain differences.
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