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Central Adiposity Is Negatively Associated with Hippocampal-Dependent Relational Memory among Overweight and Obese Children

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Objective To assess associations between adiposity and hippocampal-dependent and hippocampal-independent memory forms among prepubertal children.

Study design Prepubertal children (age 7-9 years; n = 126), classified as non-overweight (<85th percentile body mass index [BMI]-for-age [n = 73]) or overweight/obese (≥85th percentile BMI-for-age [n = 53]), completed relational (hippocampal-dependent) and item (hippocampal-independent) memory tasks. Performance was assessed with both direct (behavioral accuracy) and indirect (preferential disproportionate viewing [PDV]) measures. Adiposity (ie, percent whole-body fat mass, subcutaneous abdominal adipose tissue, visceral adipose tissue, and total abdominal adipose tissue) was assessed by dual-energy X-ray absorptiometry. Backward regression identified significant ($P < .05$) predictive models of memory performance. Covariates included age, sex, pubertal timing, socioeconomic status (SES), IQ, oxygen consumption, and BMI *z*-score.

Results Among overweight/obese children, total abdominal adipose tissue was a significant negative predictor of relational memory behavioral accuracy, and pubertal timing together with SES jointly predicted the PDV measure of relational memory. In contrast, among non-overweight children, male sex predicted item memory behavioral accuracy, and a model consisting of SES and BMI *z*-score jointly predicted the PDV measure of relational memory.

Conclusion Regional, but not whole-body, fat deposition was selectively and negatively associated with hippocampal-dependent relational memory among overweight/obese prepubertal children. *(J Pediatr 2015;166:302-8)*.

Converging evidence now suggests that poor cognitive function may be yet another complication of obesity.[1] Obesity is an independent risk factor for developing dementia and Alzheimer disease later in life.[2] In addition, the complications of obesity are becoming evident in obese children.[3] Nonetheless, there has been only limited research connecting obesity to cognitive function in childhood. Central adiposity in particular is implicated in the progression of insulin resistance.[4] Fat around the abdominal viscera in the mesentery and omentum, known as visceral fat, is functionally different from fat in the abdominal subcutaneous areas (subcutaneous fat); however, the implications of these fat depositions or their sum (total abdominal adiposity) on pediatric cognitive function remain unknown.[5] Furthermore, as in adults, different fat compartments in children may have differential functional effects based on weight status.[6] Increased waist-to-hip ratio is negatively correlated with memory and hippocampal volume in adults.[7,8]

The hippocampus is critical for relational (associative) memory, which supports representation of the relationships between items, such as the relationships among the constituent elements of events and their subsequent flexible expression.[9] It is likely that acquisition of relational knowledge provides a foundation for scholastic achievement, and its flexible expression enables successful handling of novel challenges. Therefore, changes in the development of this system in childhood would have wide-ranging impacts. In contrast, memory for individual items (item memory) relies on the perirhinal cortex, the anterior region of the parahippocampal gyrus.[9] The dependence of these 2 memory processes on distinct neural substrates provides an opportunity to study their differential sensitivity to adiposity.

Consequently, in the present study, we examined whether relational and/or item memory are related to whole-body and central adiposity in prepubertal

BMI	Body mass index
CT	Computed tomography
DXA	Dual-energy X-ray absorptiometry
PDV	Preferential disproportionate viewing
SAAT	Subcutaneous abdominal adipose tissue
SES	Socioeconomic status
TAAT	Total abdominal adipose tissue
VAT	Visceral adipose tissue
VO_{2max}	Maximal oxygen consumption

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children, and whether these associations varied by weight status. We hypothesized that central adiposity would be selectively and negatively associated with relational memory, and that this association would vary based on weight status.

Methods

A total of 126 prepubertal children aged 7-9 years provided written assent, and each child's legal guardian provided written informed consent in accordance with the regulations of the University of Illinois Institutional Review Board. Children were screened for neurologic disorders, physical disabilities, psychoactive medication status, and normal or corrected-to-normal vision. Data were also collected on IQ, using the Kaufman Brief Intelligence Test[10] or the Woodcock-Johnson Tests of Cognitive Abilities[11]; socioeconomic status (SES), estimated based on household income, participation in a school meal-assistance program, maternal and paternal education levels, and number of parents working full-time; and pubertal status.[12]

Anthropometrics and Body Composition

Height and weight were measured using a stadiometer (model 240; Seca, Hamburg, Germany) and a digital scale (WB-300 Plus; Tanita, Tokyo, Japan). The Centers for Disease Control and Prevention's 2000 growth charts were used to determine body mass index (BMI)-for-age percentile and BMI *z*-score.[13] Classification of children as non-overweight or overweight/obese was based on the 85th percentile BMI-for-age cutoff.[13]

Adiposity was assessed by dual-energy X-ray absorptiometry (DXA) using a Hologic QDR 4500A bone densitometer (software version 13.4.2; Hologic, Bedford, Massachusetts). Percent whole-body fat mass was expressed using the standard software measure. The estimation of central adiposity variables has been described previously.[14] In brief, the abdominal region of interest was a 5-cm-wide section placed across the entire abdomen just above the iliac crest at a level approximately coinciding with the fourth lumbar vertebrae on the whole-body DXA scan. Total abdominal adipose tissue (TAAT) was defined as the total adipose tissue area within this region. Subcutaneous abdominal adipose tissue (SAAT) was determined using an algorithm that composites the adipose tissue on the sides of the abdominal cavity and estimated amount of subcutaneous fat overlying the abdominal cavity. This estimated SAAT was subtracted from the TAAT to determine the visceral adipose tissue (VAT) value. This estimated VAT has been shown to correlate ($r = 0.92$; $P < .01$) with computed tomography (CT)-determined VAT values.[14]

Cardiorespiratory Fitness Assessment

Maximal oxygen consumption (VO_{2max}) was measured using a modified Balke treadmill protocol.[15] Oxygen consumption was measured with a computerized indirect calorimetry system (True Max 2400; ParvoMedics, Sandy, Utah) with averages for oxygen consumption and respiratory exchange ratio assessed every 20 seconds. VO_{2max} was based on maximal effort, as evidenced by: (1) a peak heart rate ≥185 bpm[15] and a heart rate plateau[16]; (2) a respiratory exchange ratio >1.0[17]; (3) a score of >8 on the children's OMNI rating of perceived exertion scale[18]; and/or (4) a plateau in oxygen consumption corresponding to an increase of <2 mL/kg/min despite an increase in workload.[15] The absolute VO_{2max} was then adjusted for fat-free mass (derived by DXA) to calculate the measure of fat-free VO_{2max}.[19]

Memory Tasks

Children completed a task adapted from Monti et al,[20] but with child-friendly creatures (Electronic Arts, XXX, California) rather than faces (**Figure 1**; available at www.jpeds.com).[21] In separate study test blocks, children studied individual creatures (item condition) or uniquely paired associations between creatures and backgrounds ("habitats"; relational condition). During the test, participants were instructed to find the creature originally studied with that scene from an array of 3 creatures. One of the creatures had been studied with that scene (target), and the other 2 had been studied with other scenes (foils). Thus, familiarity across the 3 creatures was matched, necessitating the use of hippocampal-dependent relational memory.[22] In the item condition, the background scene was the same for all creature–scene pairings within each block. During the test, participants were instructed to find the previously viewed creature. In each test display, 2 creatures were novel and 1 creature had been studied, allowing for discrimination on the basis of familiarity, an ability independent of the hippocampus.[23] Lists of stimuli were counterbalanced across conditions between participants, and target locations on test trials were counterbalanced within participant such that the target was equally likely to appear in any of the 3 possible locations. The order of study test blocks was counterbalanced across participants such that one-half of the participants began with the relational condition and the other one-half began with the item condition.

An Eyelink 1000 eye-tracker (SR Research, XXX, Ontario, Canada) was used remotely to record eye-movements at 500 Hz. Time courses were quantified using preferential disproportionate viewing (PDV), defined as the difference in proportion of time spent viewing correctly selected matching creatures relative to proportion of time spent viewing incorrectly selected creatures before a behavioral response. This measure corrects for the fact that individuals look longer at the stimulus that they will behaviorally select, independent of previous experience. In this way, the magnitude of PDV provides a measure of memory for previous experience, with greater PDV indicating a greater degree of memory accuracy, an effect that has been shown to manifest even before the viewer's behavioral awareness.[24]

Statistical Analyses

Differences between the non-overweight and overweight/obese participants in memory measures were assessed using an independent-samples *t* test. Initially, Pearson correlations were used to assess bivariate relationships between adiposity