# Biochemical and neurological effects of obesity on primary school girls

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The prevalence of childhood obesity has increased considerably worldwide. As with adults, obesity in childhood is strongly related to hypertension, dyslipidemia, type II diabetes, and insulin resistance. Also, obese children are at increased risk of becoming obese adults. Therefore, obese children tend to develop serious medical and psychosocial complications, and have a greater risk of adult morbidity and mortality. The principal goal of this study was to investigate the effects of obesity on the levels of some biomarkers and their relation to the cognitive function in elementary school obese girls. The current study was conducted on 45 obese girls (mean age 10.53 ± 1.29 years; mean BMI 28.43 ± 4.62 kg/m$^2$) and 45 normal age-matched girls (mean age 10.36 ± 1.53 years; mean BMI 19.07 ± 3.47 kg/m$^2$). Estimation of serum adrenomedullin (AM) and substance P (SP), and plasma noradrenaline (NA) and acetylcholine (ACh) were carried out. Cognitive function tests (auditory vigilance, digit span, coding and visual memory) were done for all subjects. The levels of serum AM and SP as well as plasma NA were highly significantly increased ($P<0.01$) in the obese group as compared with the control group. The total right response of auditory vigilance (TR) showed insignificant decrease while the total wrong response to auditory vigilance test (TW) showed a significant increase ($P<0.05$) in the obese group as compared with the control group. Digit span and visual memory classification showed a highly significant decrease ($P<0.01$) while coding showed a significant increase ($P<0.05$). Our study showed that obesity affected the measured biomarkers and, to some extent, has an adverse effect on cognitive function in primary school girls. [Nature and Science 2010;8(4):33-43]. (ISSN: 1545-0740)]

**Key words**: obesity- adrenomedullin -substance *P* - noradrenaline - acetylcholine – cognition – girls

## Introduction

Obesity is well-known to result from the disturbance of the homeostasis between food intake and energy expenditure (Gura, 2003). It is a major risk factor for the development of type II diabetes and its complications such as the metabolic syndrome, coronary heart disease and peripheral neuropathy (Lazar, 2005). It also increases the risk for insulin resistance (Formiguera and Canton, 2004), high blood pressure, and other medical problems (Sothern *et al*., 2000). Obesity may also disturb cognition, as deficits in learning, memory, and executive functioning were reported in obese when compared to non-obese subjects (Waldstein and Katzel, 2006). A recent study suggested that obesity and its consequences, including midlife hypertension, diabetes, and cerebrovascular disease, contribute significantly to cognitive decline and accelerate the development of dementia (Qiu *et al*., 2007).

Adrenomedullin (AM) belongs to the family of adipokines (Nambu *et al*., 2005). This 52-amino acid peptide was first isolated from phaeochromocytoma tissue as a vasoactive and cardioprotective factor (Shimosawa *et al*., 2002). AM has been also found in the hypothalamus-pituitary-adrenal axis (Letizia *et al*., 2003) and produced largely by mature adipocytes and stromal vascular cells (Fukai *et al*., 2005). AM has local paracrine or autocrine effects on the tissue so that it can trigger many physiologic events by remaining in the plasma like the circulating hormone (Letizia *et al*., 2005). AM elicits a long-lasting vasodilatation and diuresis. Its action is mainly mediated by the intracellular adenylate cyclase coupled with cyclic adenosine monophosphate (cAMP) and nitric oxide (NO)-cyclic guanosine monophosphate (cGMP) pathway through its specific receptor (Eto, 2001).

Substance P (SP), an undecapeptide, was first discovered in crude form in 1931 by von Euler and Gaddum (von Euler and Gaddum, 1931) but its study was limited until its isolation by Leeman and colleagues in 1971 (Hokfelt *et al*., 2001). SP belongs to the tachykinin family, which also includes neurokinin A and neurokinin B (Stout *et al*., 2001). Upon its release, SP binds to a family of neurokinin (NK) receptors, preferentially acting on the metabotropic NK1 receptor (Harrison and Geppetti, 2001).

SP is abundant in the stomach, duodenum, and jejunum, all important areas for digestion and nutrient uptake, as well as in hypothalamic areas concerned with feeding behavior, such as the arcuate and ventromedial nuclei, along with the presence of NK-1R in the hypothalamus (Mantyh *et al*., 1984) and in adipose tissue (Karagiannides *et al*., 2006). The orexigenic effect of SP has been demonstrated in mice and the administration of the NK-1R pharmacologic inhibitor (CJ 012,255) counteracts the increase in feeding, ameliorates the weight gain induced by feeding with high fat/high caloric content diets, and improves their ability to remove glucose from the blood and respond to insulin (Karagiannides *et al*., 2008). It has been found that SP has also neurotrophic as well as memory-promoting effects and when applied peripherally (i.p.), it promotes memory and is reinforcing. These effects of SP seemed to be encoded by different SP-sequences, since the N-terminal SP1-7 enhanced memory, whereas C-terminal hepta- and hexapeptide sequences of SP proved to be reinforcing in a dose equimolar to SP. Also, direct application of SP into the region of the nucleus basalis magnocellularis (NBM) has memory-promoting and reinforcing effects (Huston and Hasenöhrl, 1995).

The sympathetic nervous system (SNS) is an important contributor to energy expenditure, and is widely assumed to play a major role in the pathophysiology of obesity (Reaven *et al.*, 1996). Noradrenaline (NA) is synthesized and stored in sympathetic nerve endings and is the neurotransmitter involved in SNS signal transmission. Although most of NA released from sympathetic postganglionic neurons is cleared locally by neuronal reuptake and effector cell metabolism, a portion of released NA spills over into the bloodstream. Therefore, whole body NA spillover rate into plasma has been used as an index of SNS activity (Coppack *et al*., 1998). The noradrenergic system plays a role in appetite regulation, with activation of $\alpha_1$- and $\beta_2$-adrenergic receptors inhibiting food intake. Phentermine acts as an NA reuptake inhibitor, thereby increasing synaptic NA to reduce appetite and weight gain (Bays and Dujovne, 2002). In contrast, activation of $\alpha_2$-adrenergic receptors increases food intake (Stanley *et al*., 2005).

Forebrain ACh modulates several cognitive functions (Sarter and Bruno, 2000). There's a considerable evidence suggesting that loss of cholinergic functions may be a major contributor to the severe cognitive deficits evident in individuals with Alzheimer's disease (Winkler *et al*., 1998).

**Objective:** The main goal of the current study is to investigate the effects of obesity on the levels of some biomarkers (SP, AM, NA and ACh) and their relation to the cognitive function in primary school obese girls.

## SUBJECTS AND METHODS

### Research Design and Methods:

Forty-five Egyptian girls with simple obesity and Forty-five lean age-matched girls, as controls, were recruited from 4 primary schools in Dokki region, Giza governorate, Egypt, between September 2008 to Jan 2009. Their ages ranged from 8 to 12 years. Anthropometric measurements, body composition, cognitive tests and biochemical analysis were done to every subject. A questionnaire for the social information was answered by parents.

### *1. Study Population*

To determine whether subjects presented previous diseases, an appropriate questionnaire was administered. Also, clinical diagnosis was done in the National Research Centre Clinic to ensure that subjects recruited were in good health and with no known diseases. None was anemic and none had a chronic illness, such as hypertension, diabetes mellitus, heart failure or chronic hepatic failure (none of the girls had any overt disease other than obesity). None of the girls was taking medication. Informed consent was signed by parents before taking part in the study. The protocol was approved by the Ethical Committee of the National Research Centre, Egypt. All examinations were performed during fasting and after emptying the urinary bladder.

### *2- Anthropometry and Body Composition*

Body mass index (BMI) was calculated as

weight (Wt) in kilograms divided by squared height ($Ht^2$) in meters squared ($Kg/m^2$). BMI for age and sex was calculated. Normal weight children were defined as having a BMI for age and sex < $85^{th}$ percentile and obese children as having BMI for age and sex ≥$95^{th}$ percentile (Ogden et al., 2002).

Ht was measured to the nearest 0.5cm on a wall-mounted Harpenden's stadiometer. Wt was measured to the nearest 0.1kg on a standard medical balance scale, with the subject dressed only in light underwear and no shoes. Waist (midway between the $10^{th}$ rib and the iliac crest) and hip (greater femoral trochanter) circumferences (WC and HC) were measured using a non-stretchable tape measure in a standing position. Waist to hip ratio (WHR) and waist to Ht were calculated. Also, Wt for age [percent median (%median), Z-score and percentile] and Ht for age (%median, Z-score and percentile) were calculated (McCarthy *et* al., 2001). Body composition was determined by a bioelectrical impedance analyzer using a formula provided by the manufacturers and fat mass percent (FM%) was calculated.

**3- Cognitive Tests:**

*a- The Digit Span Test*

The digit span memory task is a verbal measure of immediate memory and working memory maintenance and manipulation (subtest of the WAIS-III, Wechsler, 1997). The subjects were asked to repeat a number of digits after having been presented orally by the examiner, and this measures immediate memory. The list length began with two digits and increased sequentially until recall errors were made on at least one of two trials. The increasing set of numbers' backward recall can assess working memory. Performance of participants was calculated from the numbers of digits they could repeat without mistakes (Cserjési *et al.*, 2007).

*b- Coding*

In the coding test, children had to substitute symbols for numbers as quickly as possible. The score represents the total number of correct symbols written during a fixed time. The coding test primarily assesses visual-motor coordination, visual encoding, and short-term memory, concentration, and sustained attention.

*c- The Auditory Vigilance Test*

This test measures the attention ability. It's a measure of the efficiency of identifying figural stimulation in the context of non-signal stimuli. The subjects were asked to pay attention while listening to many words from different categories like key, ball, school, etc., and they were asked to give a sign, like raising their hands, when they hear certain words, chosen by the administrator. The scores of the test were calculated as total right and total wrong.

*d- The Visual Memory Test*

This test is a measure of free recall of visual object. It also taps some aspects of classification ability. The subjects were shown a group of different photos like animals, cars, plants, etc., and then were asked to mention as many photos as they can. The results of the test are categorized into classification- of photos according to their groups- and recall of photos shown. The score is calculated from the right results.

**4- Biochemical Measurements:**

Fasting blood samples were withdrawn from patients and controls in the morning and plasma as well as sera were separated using cooling centrifuge (4˚C) and then stored at -80˚C till analysis. AM was measured by an enzyme-linked immunosorbent assay kit (ELISA kit) purchased from DRG International Inc., USA according to the method of Porstmann and Kiessig (1992). SP was measured by an ELISA kit purchased from Cayman Chemical Company, Ellsworth, Ann Arbor according to the method of Renzi *et al*. (1987). NA was measured by an ELISA kit, purchased from Labor Diagnostika Nord GmbH & Co. KG. ACh was measured colorimetrically using the kit purchased from BioVision Research Products, Linda Vista Avenue, Mountain View, USA.

**Statistical Analysis:**

All statistical analyses were performed using SPSS for PC version 14. Student *t*-test and Pearson's correlation were performed to compare groups and detect the possible relationships among measurements. Also, stepwise regression analysis was done considering BMI as the dependent variable.

**RESULTS**

Table (1) shows descriptive statistics with mean (±SE) and *P* values of the anthropometric measurements in the control and obese girls. All of these measurements revealed highly significant increase ($P<0.01$) in the obese group as compared

with the control group, except for Ht which showed significant increase ($P<0.05$) and both of Ht-for-age parameters (% median, Z-score, percentile) and WHR which showed insignificant increase ($P>0.05$).

Table (2) represents the levels of serum AM and SP and plasma NA and Ach of control and obese girls. The levels of serum AM and SP and plasma NA showed highly significant increase ($P<0.01$) in the obese group as compared with the control group.

The data in table (3) illustrate the cognitive tests for control and obese groups. In the obese group, TW showed significant increase ($P<0.05$). Digit span and visual memory classification showed highly significant decrease ($P<0.01$) while coding score showed significant increase ($P<0.05$) in the obese group as compared with the control group.

Table (4) depicts the results of Pearson's correlation between the biochemical markers and anthropometric measurements in the obese group. Serum AM showed highly significant positive correlation ($P<0.01$) with Wt, BMI, WC, HC, waist/Ht, and Z-score and percentile of Wt-for-age and significant positive correlation ($P<0.05$) with %median of Wt-for-age.

The results in table (5) represent Pearson's correlation among the biochemical markers under study in the control and obese groups. In the control group, only significant positive correlation was recorded between levels of NA and ACh ($P<0.05$). In the obese group, only SP showed significant positive correlation with NA ($P<0.05$).

Table (6) depicts Pearson's correlation between cognitive tests and anthropometric measurements in the control group. TR showed highly significant negative correlation ($P<0.01$) while TW showed highly significant positive correlation ($P<0.01$) with FM%. Also, coding score showed significant negative correlation ($P<0.05$) with Waist/Ht ($P<0.01$) and parameters of Wt-for-age (%median, Z-score and percentile). Visual memory recall showed highly significant positive correlation ($P<0.01$) with Wt, Ht, BMI, WC and HC, but highly significant negative correlation ($P<0.01$) with Ht-for-age parameters (%median, Z-score and percentile). Visual memory classification showed significant negative correlation ($P<0.05$) with Waist/Ht and highly (2Bdeleted) significant negative correlation ($P<0.01$) with Wt-for-age parameters (%median, Z-score and percentile).

The data in table (7) illustrate Pearson's correlation between cognitive tests and anthropometric measurements in the obese group. There was significant negative correlation between TW and Wt ($P<0.05$). Also, coding score showed highly significant negative correlation ($P<0.01$) with Wt, WC and HC and significant negative correlation ($P<0.05$) with Ht. Digit span showed highly significant positive correlation ($P<0.01$) with FM%.

**Table (1): Anthropometric and body composition measurements for control and obese girls**

| Parameters | Control (n = 45) Mean ± SE | Obese (n = 45) Mean ± SE |
|---|---|---|
| Wt (Kg) | 39.211 ± 1.414 | 61.333 ± 1.977** |
| Ht (cm) | 142.618 ± 1.352 | 147.778 ± 1.554* |
| BMI ($Kg/m^2$) | 19.065 ± 0.518 | 28.430 ± 0.689** |
| FM % | 21.194 ± 1.520 | 33.144 ± 1.011** |
| Waist (cm) | 69.711 ± 0.960 | 83.133 ± 1.325** |
| Hip (cm) | 82.200 ± 0.829 | 98.231 ± 1.806** |

| | | | | | | |
|---|---|---|---|---|---|---|
| Waist/Ht | 0.490 | ± | 0.007 | 0.563 | ± | 0.008** |
| WHR | 0.847 | ± | 0.005 | 0.850 | ± | 0.010 |
| Wt for age (% median) | 107.891 | ± | 1.457 | 184.296 | ± | 18.863** |
| Wt for age (z-score) | 0.294 | ± | 0.061 | 2.733 | ± | 0.216** |
| Wt for age (percentile) | 60.776 | ± | 2.217 | 98.013 | ± | 0.343** |
| Ht for age (% median) | 99.642 | ± | 0.663 | 101.296 | ± | 0.580 |
| Ht for age (z-score) | -0.091 | ± | 0.146 | 0.263 | ± | 0.126 |
| Ht for age (percentile) | 48.998 | ± | 3.940 | 58.758 | ± | 4.012 |

Asterisks indicate significant differences between the two groups (*) $P<0.05$, (**) $P<0.01$

Wt= weight, Ht= height, BMI= body mass index, FM%= fat mass percent, WC= waist circumference, HC= hip circumference, WHR= waist to hip ratio.

Table (2): Levels of adrenomedullin (AM), substance P (SP), noradrenaline (NA) and acetylcholine (ACh) in control and obese girls

| Parameter | Control (n = 45) Mean ± SE | | | Obese (n = 45) Mean ± SE | | |
|---|---|---|---|---|---|---|
| AM (ng/ml) | 0.896 | ± | 0.011 | 5.547 | ± | 0.275** |
| SP (pg/ml) | 35.311 | ± | 0.784 | 40.9 | ± | 0.596** |
| NA (ng/L) | 189.72 | ± | 7.209 | 237.159 | ± | 6.104** |
| ACh (nmol/ml) | 2.371 | ± | 0.107 | 2.711 | ± | 0.149 |

Asterisks indicate the significant differences between the two groups, (**) $p<0.01$

Table (3): Cognitive tests for control and obese groups

| Parameters | Control (n = 45) Mean ± SE | Obese (n = 45) Mean ± SE |
|---|---|---|
| TR | 40.489 ± 0.269 | 39.711 ± 0.421 |
| TW | 1.511 ± 0.269 | 2.511 ± 0.416* |
| Digit span | 13.867 ± 0.689 | 10.822 ± 0.724** |
| Coding | 12.089 ± 0.256 | 13.244 ± 0.372* |
| Recall | 10.600 ± 0.630 | 10.489 ± 0.362 |
| Classification | 8.111 ± 0.264 | 6.222 ± 0.246** |

Asterisks indicate the significant differences between the two groups (*) $p<0.05$, (**) $p<0.01$

TR= total right response to auditory vigilance test, TW= total wrong response to auditory vigilance test

Table (4): Pearson's correlation between biochemical markers and anthropometric measurements in the obese group

| | Wt | BMI | WC | HC | Waste/Ht | Wt for age %median | Wt for age Z-score | Wt for age Percentile |
|---|---|---|---|---|---|---|---|---|
| AM | 0.698** | 0.771** | 0.614** | 0.647** | 0.501** | 0.294* | 0.492** | 0.509** |
| SP | 0.016 | 0.151 | -0.071 | -0.042 | 0.046 | 0.222 | 0.160 | -0.240 |
| NA | 0.034 | 0.170 | 0.077 | 0.023 | 0.186 | 0.109 | 0.125 | -0.048 |
| Ach | 0.015 | 0.075 | 0.030 | -0.107 | 0.045 | 0.107 | 0.037 | -0.109 |

Data are expressed as correlation coefficient (r) values, asterisks indicate significant correlation (*) $P<0.05$, (**) $P<0.01$

Table (5): Pearson's correlation among the biochemical markers in the control and obese groups

| | AM | | SP | | NA | | Ach | |
|---|---|---|---|---|---|---|---|---|
| Group | Control | Obese | Control | Obese | Control | Obese | Control | Obese |
| AM | 1.000 | 1.000 | 0.238 | 0.076 | 0.073 | 0.113 | 0.050 | 0.038 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| SP | 0.238 | 0.076 | 1.000 | 1.000 | 0.053 | 0.331* | 0.007 | 0.089 |
| NA | 0.073 | 0.113 | 0.053 | 0.331* | 1.000 | 1.000 | 0.320* | 0.058 |
| Ach | 0.050 | 0.038 | 0.007 | 0.089 | 0.320* | 0.058 | 1.000 | 1.000 |

Data are expressed as r values, asterisks indicate significant correlation (*) *P<0.05*

Table (6): Pearson's correlation between cognitive tests and anthropometric measurements in the control group

| | Wt | Ht | BMI | WC | HC | FM% | Waste / Ht | Wt for age % median | Wt for age Z-score | Wt for age Percentile | Ht for age % median | Ht for age Z-score | Ht for age Percentile |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| TR | -0.075 | -0.094 | -0.034 | -0.166 | -0.239 | -0.500** | -0.088 | -0.143 | -0.091 | -0.085 | -0.068 | -0.073 | -0.013 |
| TW | 0.075 | 0.094 | 0.034 | 0.166 | 0.239 | 0.500** | 0.088 | 0.143 | 0.091 | 0.085 | 0.068 | 0.073 | 0.013 |
| Digit span | 0.037 | -0.019 | 0.068 | 0.069 | 0.017 | 0.058 | 0.068 | 0.201 | 0.200 | 0.205 | 0.052 | 0.044 | 0.094 |
| Coding | 0.035 | 0.234 | -0.088 | -0.250 | -0.247 | 0.067 | -0.388** | -0.307* | -0.355* | -0.364* | -0.074 | -0.065 | -0.042 |
| Recall | 0.600** | 0.460** | 0.528** | 0.420** | 0.424** | 0.106 | 0.105 | 0.215 | 0.139 | 0.123 | -0.460** | -0.446** | -0.438** |
| Classification | -0.076 | 0.190 | -0.185 | -0.290 | -0.224 | 0.124 | -0.377* | -0.522** | -0.559** | -0.560** | -0.062 | -0.052 | -0.065 |

Data are expressed as r values, asterisks indicate significant correlation (*) *P*<0.05, (**) *P*<0.01

Table (7): Pearson's correlation between cognitive tests and anthropometric measurements in the obese group

| | Wt | Ht | BMI | WC | HC | FM% |
|---|---|---|---|---|---|---|
| TR | 0.260 | 0.229 | 0.163 | 0.270 | 0.252 | 0.151 |
| TW | -0.314* | -0.275 | -0.204 | -0.283 | -0.276 | -0.151 |
| Digit span | 0.189 | 0.261 | 0.237 | 0.167 | 0.287 | 0.447** |
| Coding | -0.484** | -0.304* | -0.290 | -0.445** | -0.439** | -0.077 |
| Recall | 0.081 | 0.181 | -0.023 | -0.014 | 0.192 | 0.280 |
| Classification | -0.006 | 0.062 | -0.036 | -0.115 | -0.045 | 0.024 |

Data are expressed as r values, asterisks indicate significant correlation (*) $P<0.05$, (**) $P<0.01$

## DISCUSSION

The results of the current study revealed that plasma AM level showed a significant increase in obese girls as compared to the controls. This finding is in agreement with those of previous studies (Letizia *et al*., 2001; Kato *et al*., 2002 and Fukai *et al*., 2005). Because AM expression in the adipose tissue is increased in obesity, the source of elevated plasma AM in obese subjects is likely to be the adipose tissue (Li *et al*., 2007). In addition, pancreatic islets may also be a source of AM (Letizia *et al*., 2001) as AM causes a decrease in insulin secretion and the increased level of plasma AM may be an adaptive mechanism to decrease hyperinsulinemia (Letizia *et al*., 2005). It has been found that endogenous AM acts against insulin resistance via its vasodilator and anti-oxidant actions (Li *et al*., 2007).

Although AM showed insignificant correlation with all of the anthropometric measurements in the control group, it showed significant positive correlation with Wt, BMI, WC and HC in the obese group. These results agree with those of Kato *et al*. (2002). The relationship between AM and BMI can reflect the dysfunction of glucose and lipid metabolism (Kato *et al*., 2002).

In the present study, serum SP level was significantly higher in obese girls as compared to the control. In the intestine, SP produced by several cell types may circulate in the blood as a hormone or act locally in a paracrine fashion (Severini *et al*., 2002). SP has been found to have a role in promoting appetite and weight gain (Karagiannides *et al*., 2008). Also, there is potentially a direct physiological effect of SP on fat cells, which is mediated by NK-1R, and this is supported by the expression of the functional NK-1R on the surface of human preadipocytes (Karagiannides *et al*., 2008). These authors discovered a role for SP in appetite regulation and metabolism, in addition to the already established effects of this peptide in gastric motility and digestion (Nicholl *et al*., 1985). Most importantly, the effects of NK-1R blockade on appetite, body weight and adiposity point to a novel approach for treating obesity and insulin resistance (Karagiannides *et al*., 2008). Because of the orexigenic effect of SP, its increase in obese subjects may be a factor contributing to increased appetite and weight gain.

Our results showed insignificant correlation between SP level and all of the cognitive tests. However, Krappmann *et al*. (1994) reported that there is evidence that SP plays a role in learning and reinforcement processes and that reinforcing effects of SP were found upon injection into several parts of the brain. Also, Tomaz and Nogueira (1997) stated that peripheral (i.p.) post-training SP administration in rats enhances memory in a dose- and time-dependent way. The memory-enhancing effects are long-lasting and are mediated, at least in part, via interactions with the endogenous opioid system. The mnemotropic effects of peripherally administered SP are sensitive to the functional integrity of the vagus, suggesting that the vagus nerve may be one pathway by which systemic SP influences memory storage processes in the brain. Furthermore, these effects seemed to be encoded by different SP sequences, the N-terminal SP1–7, but not the C-terminal hepta- and hexapeptide sequences being responsible for the memory -promoting effects. Moreover, SP showed memory-promoting, reinforcing and anxiolytic-like effects when administered systemically or into the nucleus basalis of the ventral pallidum. In addition, SP injection into the ventral pallidum can lead to increases of ACh in frontal cortex and dopamine in nucleus accumbens, suggesting that the hypermnestic, positively reinforcing and anxiolytic effects observed upon basal forebrain injection of SP are mediated by activation of the nucleus accumbens-ventral pallidum circuitry (Hasenöhrl *et al*., 2000). The lack of correlation between SP level and any of the cognitive tests may be due to the small number of cases studied.

Our study showed that plasma NA level was significantly increased in the obese group as compared with the control group. However, plasma NA level showed insignificant correlation with all of the anthropometric measurements and FM% in both the obese and control group. Studies based on catecholamine levels in obese individuals produced conflicting results (Peterson *et al.*, 1988 and Young *et al.*, 1992), some of the variability in these studies may be related to confounding variables that influence SNS activity (Coppack *et al*., 1998) but the consensus favors increased NA levels in obese humans (Goldstein, 1995). Our finding of increased NA levels in obese girls is supported by that of Søndergaard *et al*. (1999). More recently, other studies reported that trend (Eikelis *et al.* 2004), thereby supporting the hypotheses attributable to

Landsberg and Young (Landsberg and Young, 1978) which supposed sympathetic activation as an adaptive response to overeating that helps to stabilize body weight but contributes to complications of obesity such as hypertension (Eikelis and Esler, 2005). Several mechanisms have been proposed to explain the sympathetic activation in obesity. It has been suggested that increases in sympathetic tone are due to the state of insulin resistance, as it has been documented that high levels of insulin may increase sympathetic nerve traffic in man (Blum *et al.* 1997).

In the current study, plasma ACh level in the obese group showed an insignificant increase as compared with the control group. Also, there were insignificant correlation between ACh and the cognitive tests and this may be due to small sample size. Many evidences that supported an important role for ACh in modulating cognitive functions include findings from a host of pharmacological studies that showed that interfering with cholinergic function generally impairs learning and memory, and that augmenting cholinergic functions generally results in an enhancement (Warburton *et al*., 2003). It was found that direct injections of cholinergic agonists and antagonists into the amygdala, striatum, and hippocampus generally enhance and impair, respectively, learning and memory for tasks associated with those neural systems (Wallenstein and Vago, 2001).

Our results showed that obesity affected digit span adversely and this is in accord with Gunstad *et al*. (2006) and Malter-Cohen (2007). Also, total wrong response to auditory vigilance test (TW) and visual memory classification were adversely affected, however, obesity had no effect on either total right response to auditory vigilance test (TR) or visual memory recall. Although coding was better in obese than control, it showed significant negative correlation with Wt, WC, HC and Ht.

When applying BMI as dependent variable, stepwise multiple regression analysis showed that AM was the most significant independent determinant of obesity ($r^2 = 0.594$, $P > 0.001$).

In conclusion, our study showed that obesity affected the levels of the measured biomarkers and, to some extent, had an adverse effect on cognitive function in girls. The lack of effect of obesity on some cognitive tests may be a result of increased levels of SP which has memory-promoting and reinforcing effects and as a result of the high levels of NA and the normal level of ACh which have roles in memory processing.

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Submission date: 31-1-2010