

Original Research

fNIRS correlates of the development of inhibitory control in young obese subjects

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Executive functions are closely related to the prefrontal cortex, and inhibitory control is an important component of executive functioning. Previous studies have found that inhibitory control continues to develop after adolescence and that obesity is associated with executive functions. However, few studies have addressed whether obesity affects the development of inhibitory control. Hence, we focused on whether inhibitory control continues to develop after adolescence in obese individuals. We used a Stroop task to measure the inhibitory control of young obese subjects, and monitored accompanying brain activation by functional near-infrared spectroscopy technology. The findings suggest that brain activation due to Stroop interference does not increase with age in obese subjects and that early prevention of executive function deficit is recommended.

Keywords

Obesity; inhibitory control; development; fNIRS; Stroop color-word task; frontal cortical function

1. Introduction

Executive functions (also known as executive control or cognitive control) are top-down psychological processes required by individuals during attention or inhibiting irrational instinctual behavior (Diamond, 2013). Executive functions are closely related to academic achievement, social functioning, and emotional control in the development of individuals (Best et al., 2009; Liang et al., 2014). Inhibitory control is one of the most important components of executive functions. Inhibitory control usually refers to the ability to suppress automatic or dominant responses, but inhibition also requires interference control, directed forgetting, emotional control, and behavioral control (Nigg, 2000). Also, inhibitory control plays an important role in the development of individuals and can predict individual growth; for example, children with good inhibitory control are mentally and physically healthier in adulthood (Moffitt et al., 2011).

The development of inhibitory control continues after puberty. Previous behavioral studies have shown that the Stroop effect decreases when adolescence begins (Ikeda et al., 2011; Ordaz et al.,

2013; Prencipe et al., 2011; Wu et al., 2011). Previous brain imaging studies have also reached relatively consistent conclusions. A study used functional magnetic resonance imaging (fMRI) techniques and the Stroop paradigm to examine 30 participants aged 7 to 22 years and found that activation in the frontal lobe increased with age; activation was significantly higher in young adults than in adolescents, who, in turn, showed significantly greater activation than children (Adleman et al., 2002). Another study used functional near-infrared spectroscopy (fNIRS) technology and the Stroop paradigm in 23 children and 14 adults to address this topic and revealed that brain activation (especially in the dorsolateral prefrontal cortex) caused by the Stroop effect increased with age from 7 to 29 years (Schroeter et al., 2004).

Executive function deficits are closely related to the prefrontal cortex. Clinical cases have shown that patients with prefrontal cortex lesions have difficulties with goal setting, planning, inhibition, and self-maintenance. Previous neuropsychological research has shown that the maturity of the frontal cortex parallels the development of executive functions (Garon et al., 2008; Luna et al., 2010; Ordaz et al., 2013; Prencipe et al., 2011; Shing et al., 2010; Wu et al., 2011). In the 1960s and 1970s, studies on human brain anatomy demonstrated that some brain regions, especially the prefrontal cortex, developed beyond childhood, and in the 1970s to 1980s, studies suggested that prefrontal cortex structure changed obviously in adolescence (Blakemore and Choudhury, 2006). In tasks that require the function of the frontal lobe, the performance of individuals followed a multi-polar developmental track, meaning that each subcomponent of the executive functions developed to maturity at a different time and in a different way. The most rapid period of development was from 6 to 8 years of age, during which abilities as concept formation, set-shifting, and rudimentary planning skills were present. Then, development tended to be more gradual from late childhood and throughout adolescence continuing to develop into early adulthood (Ordaz et al., 2013; Tanaka et al., 2012). Previous studies have almost universally reached the consistent conclusion that executive functioning and the prefrontal cortex continue to develop after adolescence (Brown et al., 2005; Buttelmann and Karbach, 2017; Hsu et al., 2014; Luna et al., 2010; Prencipe et al., 2011; Satterthwaite et al., 2013; Shing et al., 2010).

In addition to age, obesity is another factor that influences the development of executive function. Previous studies have shown that obese children (or adolescents) exhibit lower inhibitory control than overweight children (or adolescents) (Pauli-Pott et al., 2010). The decline of cognitive function in children (or adolescents) is closely related to overweight (Li et al., 2008). Previous behavioral studies have shown that obese children have worse performance on the classical experimental task that is used to measure inhibitory control (Bruce et al., 2011; Wirt et al., 2014). A large number of executive function measurements have shown that obese children have significantly less control than healthy children, and obese adolescents have significant deficits in the structure of the prefrontal cortex (Liang et al., 2014). Brain imaging studies have also come to the same conclusion. For example, one study used functional magnetic resonance imaging (fMRI) and the Stroop paradigm to compare 54 obese participants and 37 healthy participants, and the results showed that the body mass index (BMI) was negatively correlated with Stroop interference and gray matter volume (Maayan et al., 2011). However, few imaging studies have addressed whether obesity damages the development of inhibitory control; hence, we used the Stroop task and fNIRS to explore the relationship between age and inhibitory control in obese individuals.

Inhibitory control is important for the development of individuals, and age and obesity are two factors that influence the development of inhibitory control. Inhibitory control and the prefrontal cortex, whose functioning is related to being overweight, develop to maturity after adolescence. The relationship between executive function and obesity may be bidirectional, that is to say, executive function deficits may be a potential factor in individual BMI increases, while weight loss is helpful to a certain extent in executive function improvement of obese individuals (Xianlin et al., 2015).

To study the inhibitory control of obesity, we conducted experiments using fNIRS and the Stroop color-word task, which is the classic psychological task for measuring frontal cortex function (Adleman et al., 2002; Yennu et al., 2016). In the Stroop task, participants are instructed to name the color of font in which a word is printed and ignore the dominant tendency to read the meaning of the word (naming the color of the word is more difficult because it is not the habitual response); therefore, the task requires inhibitory control (Aron, 2010). Stroop interference is the difference between the congruent condition (in which the text color matches the meaning) and the incongruent condition (in which the word for one color is printed in another color) in the Stroop task. The greater the differences in reaction time and accuracy, the larger the Stroop effect was; the worse the inhibitory control ability, the lower the prefrontal cortex activation (Schroeter et al., 2007).

Brain imaging techniques like fNIRS use near-infrared light changes in living tissues to detect specific changes in the concentration of oxygen in the targeted brain regions. The advantage of fNIRS is that this technology is not very sensitive to head movement, and optical imaging is both readily accepted by participants and harmless to the human body (Timinkul et al., 2008). It also provides appropriate spatial and temporal resolution and is easily accepted even by children and obese participants.

2. Material and methods

To explore whether obesity would affect the development of inhibitory control, we used fNIRS to test 54 individuals while they performed a Stroop task. As BMI is negatively correlated with inhibitory control and its related brain region (the prefrontal cortex), we hypothesized that Stroop interference on behavioral tests would not decrease with age and that the accompanying frontal cortex brain activation would not increase with age in obese individuals.

2.1 Subjects

We enlisted 45 obese subjects with high body mass index (mean BMI in $\text{kg}/\text{m}^2 = 31.39$, $\text{SD} = 4.50$) recruited from a fitness and weight loss summer camp participated in our study. All of them or their legal guardians signed informed consent forms. For subjects aged 18 - 25, based on the BMI cut-off points for obesity in the Chinese population, overweight ($24 < \text{BMI} < 28 \text{ kg}/\text{m}^2$) and obesity ($\text{BMI} > 28 \text{ kg}/\text{m}^2$) were defined. For subjects aged < 18 , overweight and obesity were defined according to the 2004 Group of China Obesity Task Force definition (WGOC, 2004). Seven of them were excluded from the analyses because they could not complete the whole study or moved excessively during the study. Ultimately, 38 obese participants (24 male, 14 female) aged 9 to 25 old (mean age in years 16.11, $\text{SD} = 4.75$; 22 subjects aged < 18 , 16 subjects aged 18 - 25) remained in this study (mean BMI = $31.55 \text{ kg}/\text{m}^2$, $\text{SD} = 4.17$, range = $25.20 - 40.71 \text{ kg}/\text{m}^2$, median = $31.62 \text{ kg}/\text{m}^2$). Word reading plays an important role in the performance of the Stroop task; therefore, we chose subjects over the age of 8 years to ensure that reading performance would not be a confounding variable. The presence of psychological impairments was assessed using the Chinese version of Symptom Checklist-90 (SCL-90). All subjects showed standard scores compared to the national norm. Cognitive development was assessed using the Chinese version of WISC-III or WAIS-III. All participants scored higher than 80 for full-scale IQ. None of the subjects reported learning disabilities or abnormal neurological development, neither a history of developmental or psychological disorders. They were all right-handed and had a normal or corrected-to-normal vision and normal color vision. This study was approved by the Ethical Committee of Wuhan Sports University.

2.2 Stimuli and procedures

We used E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA) to present the stimuli and to record the data. This study used a modified Stroop task for visual-cognitive stimulation to evoke event-related potentials (Ehlis et al., 2005). The stimuli consisted of four words: "red", "green", "blue" and "yellow", and each word was printed in red, green, blue or yellow to produce interference between color words and their text colors. The congruent condition meant that the color of the word was congruent with the meaning of the word (e.g., the word "RED" was printed in red text); the incongruent condition meant that the color of the word was incongruent with the meaning of the word, e.g., the word "RED" was printed in blue text (see Fig. 1A). Stroop interference was measured as the difference between the incongruent and congruent conditions (the incongruent minus the congruent) (Chen et al., 2013; Xu et al., 2007). The experimental procedure is displayed in Fig. 1A. In each trial, a cross-shaped fixation point "+" was displayed for 1000 ms first, and then the stimulus was presented

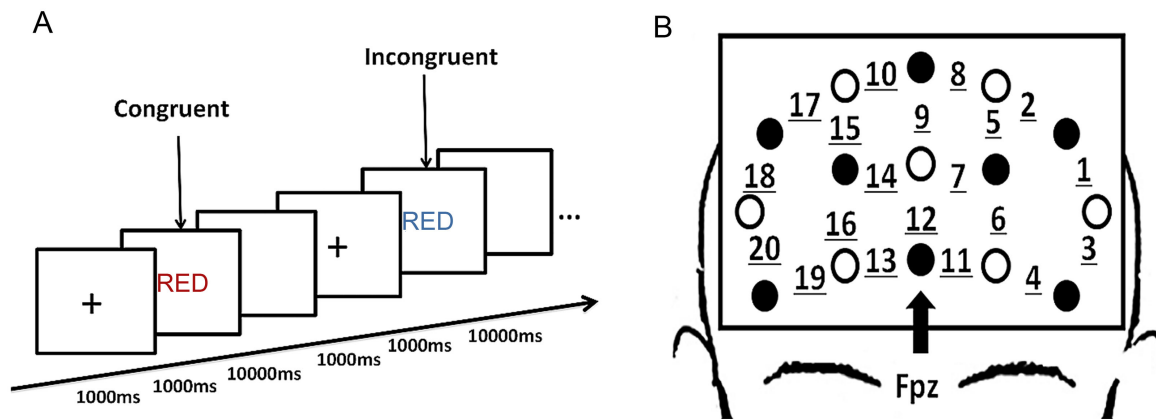


Figure 1. A. The design of the experimental runs and instance for the two conditions (congruent and incongruent conditions) of the modified Stroop task. Participants were instructed to decide whether the semantic meaning of the word corresponded to the color of the word. B. The fNIRS probe consisted of 8 dual-wavelength sources (●) and 7 optical detectors (○), and the numbers (1 to 20) indicate the fNIRS channels. Optical sources and detectors probe on the international 10-20 standard positions.

for 1000 ms, followed by a blank screen presented for 10000 ms. The participant was asked to press the button to indicate whether the meaning of the word was congruent with its printing color as quickly and accurately as possible. The order of the stimuli was random. The formal experiment consisted of 48 trials (24 congruent conditions and 24 incongruent conditions). Also, before the experiment, there was a practice session consisting of six trials to ensure that the participant understood the procedure.

2.3 Data recording and analysis

We employed a multichannel continuous-wave fNIRS instrument (NIRX Medical Technologies LLC, USA). The fNIRS probe consisted of eight dual-wavelength sources (760 and 850 nm) and seven optical detectors. These probes covered the frontal cortex, and they were placed according to the 10-20 system, with some adjustments to make sure that each emitter was 3 cm from the corresponding detector (see Fig. 1B). Previous studies have demonstrated the positional relationship between the channels of fNIRS and specific brain regions (Okamoto et al., 2009; Tsuzuki et al., 2007). The sampling rate was set to 7.8 Hz. The hemoglobin data were band-pass filtered between 0.01 Hz and 0.3 Hz to remove baseline drift and physiological noise. Based on the modified Beer-Lambert law (MBLL), we acquired signals of both oxy-hemoglobin (oxy-Hb) and deoxygenated hemoglobin (deoxy-Hb) in the monitored brain regions. As the oxy-Hb signal was more sensitive to the change of stimuli in the task, we analyzed only the oxy-Hb signal in the present study.

We used fNIRS to collect hemodynamic data from the congruent and incongruent conditions in all 20 channels during the Stroop task. Then, we analyzed the relationship between age and Stroop interference. Benjamini & Hochberg's method (Singh and Dan, 2006) was adopted for controlling the false discovery rate (FDR). Bayes factors (BF) were computed with Bayesian Pearson correlation for hypotheses testing, BF_{01} is expressed as odds for support or evidence for the H_0 over H_1 . The behavioral and fNIRS results were analyzed with SPSS 25.0 software (SPSS Inc., Chicago, IL, USA).

Table 1. Demographic characteristics and descriptive statistics (mean \pm SD)

	Male (n = 24)	Female (n = 14)	t
BMI (kg/m ²)	32.41 \pm 4.33	30.07 \pm 3.56	1.71
Age	16.88 \pm 4.92	14.79 \pm 4.28	1.32
RT Interference	94.17 \pm 116.69	102.56 \pm 61.14	0.25
ACC Interference	-0.10 \pm 0.21	-0.05 \pm 0.04	0.89

Note: Interference is the difference between the incongruent and congruent conditions in the Stroop task (the incongruent minus the congruent).

3. Results

3.1 Behavioral results

We observed significant differences between the congruent and incongruent conditions in both reaction time (RT) and accuracy (ACC). The mean RT in the incongruent condition (mean RT in ms = 1070.39, SD = 190.42) was significantly higher than in the congruent condition (mean RT in ms = 973.12, SD = 144.48). The mean ACC in the incongruent condition (mean ACC = 0.87, SD = 0.02) was significantly lower than in the congruent condition (mean ACC = 0.95, SD = 0.08). Paired-sample t-tests showed that there existed Stroop interference in both, RT ($t_{(37)} = 6.06$, $P < 0.01$) and ACC ($t_{(37)} = 3.13$, $P < 0.01$). As shown in Table 1, there was no significant difference in Stroop interference between male and female participants in RT ($t_{(36)} = 0.25$, $P = 0.81$) or ACC ($t_{(36)} = 0.89$, $P = 0.38$). Therefore, when we analyzed how age affected Stroop interference, we could ignore the factor of gender.

To test whether obesity would affect the development of inhibitory control, we assessed the relationship between Stroop interference and age. However, Pearson correlation coefficients showed no significant correlation between age and Stroop interference in RT ($r = -0.28$, $P = 0.09$) or in ACC ($r = 0.19$, $P = 0.24$). There was no significant correlation between BMI and Stroop interference in RT ($r = -0.14$, $P = 0.41$) or in ACC ($r = 0.24$, $P = 0.14$). A significant relationship between age and BMI ($r = 0.50$,

$P < 0.01$) was detected, yet no significant partial correlation between age and Stroop interference in RT ($r = -0.25$, $P = 0.14$) or in ACC ($r = 0.09$, $P = 0.62$), after controlling for BMI. Bayesian analyses revealed anecdotal or moderate evidence for the null hypothesis (RT Interference $BF_{01} = 1.84$, ACC Interference $BF_{01} = 4.03$).

3.2 fNIRS results

The hemodynamic Stroop interference effect was calculated as the difference of oxy-Hb between the incongruent and congruent conditions (the incongruent oxy-Hb minus the congruent oxy-Hb). Paired sample t-tests showed that at 8 channels a significant Stroop interference effect was captured (incongruent > congruent); these channels were ch3, ch4, ch7, ch11, ch15, ch16, ch19, and ch20 (q value of maximum FDR = 0.05, see Fig. 2). We converted all of the corresponding electrode positions to standard Montreal Neurological Institute (MNI) coordinates using a probabilistic estimation method (Cutini et al., 2011; Szűcs et al., 2012). We determined the anatomical labels according to the MNI coordinates of all the corresponding electrodes and observed that the activated channels were located above the right frontopolar area (ch16), the bilateral orbitofrontal area (ch4 and ch11 for left; ch19 for right), the bilateral dorsolateral prefrontal cortex (ch7 for left and ch15 for right) and the bilateral ventrolateral prefrontal cortex (ch3 for the left and 20 for the right). We calculated the Pearson correlation coefficient to investigate the relationship between the hemodynamic Stroop interference and BMI, but no significant correlation was found ($P > 0.05$). Also, there was no significant difference in hemodynamic Stroop interference between male and female participants ($P > 0.05$). There was no significant correlation between RT/ACC interference and hemodynamic Stroop interference ($P > 0.05$).

Next, we investigate whether age was associated with hemodynamic Stroop interference. Hemodynamic Stroop interference was not significantly negatively associated with age in these eight channels (r range = $-0.36 \sim -0.15$, q value of maximum FDR = 0.05, see Fig. 3). There was no significant partial correlation between age and hemodynamic Stroop interference (r range = $-0.34 \sim -0.11$, q value of maximum FDR = 0.05), after controlling for BMI. Bayesian analyses revealed anecdotal or moderate evidence for the null hypothesis (BF_{01} range = $0.71 \sim 4.97$). We next divided 20 of the 38 participants into two groups according to their age. The youngest ten participants represented the bottom 27% of their age (BG: mean age in years 10.70, SD = 1.06; mean BMI = 29.35 kg/m², SD = 3.40) and other ten participants represented the upper 27% of their age (UG: mean age in years 22.40, SD = 1.77; mean BMI = 33.01 kg/m², SD = 4.73). There was no significant age effect on RT interference ($t_{(18)} = 1.71$, $P = 0.11$), ACC interference ($t_{(18)} = -0.96$, $P = 0.35$), and hemodynamic interference (q value of maximum FDR = 0.05) between the BG and the UG.

4. Discussion

Our study suggested that the behavioral performance and prefrontal cortex activation of 38 obese participants in the Stroop task did not increase with age. We found that RT was significantly higher in the incongruent condition than in the congruent condition and that ACC was significantly lower in the incongruent condition than in the congruent condition. Thus, our study successfully elicited Stroop interference following previous literature

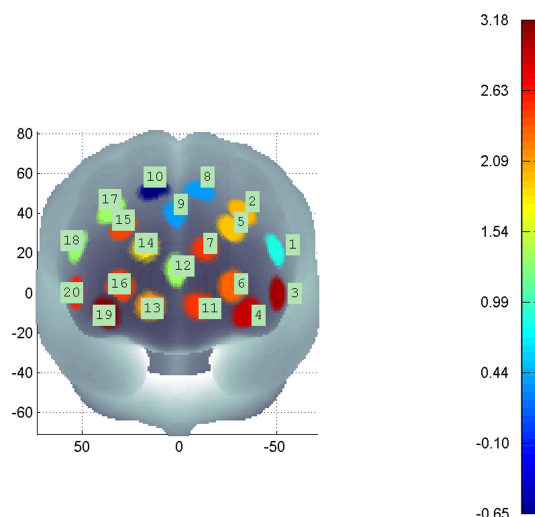


Figure 2. The figure is a t-map of oxy-Hb signal change, and it reflects the Stroop interference effect (incongruent condition minus congruent condition). The color bar showed t-values, and the color is closer to red, the Stroop interference is more likely to be significant. We observed significant Stroop interference effects in the right frontopolar area, bilateral orbitofrontal area, bilateral ventrolateral prefrontal cortex, and the bilateral dorsolateral prefrontal cortex.

(Ehlis et al., 2005). Then, we found that age was not associated with Stroop interference in RT or ACC. In other words, behavioral Stroop interference did not decrease throughout cognitive development. This result differed from those of previous research (Huizinga et al., 2006). Also, we found that prefrontal cortex activation did not increase with age. The neural result was also inconsistent with previous studies in normal-weight participants, which showed that inhibitory control developed after adolescence. For example, an fMRI study found a positive correlation between ages from 7 to 22 years and Stroop-related activation in the left lateral prefrontal cortex in normal-weight participants. They also found that Stroop-task-related functional development of the prefrontal cortex continues to develop into adulthood (Adleman et al., 2002).

Another fNIRS study (Schroeter et al., 2004) found that the brain activation due to Stroop interference significantly increased with age (from 7 to 29 years) in the DLPFC in normal-weight participants. In the present study, activation during the Stroop task did not increase with age from childhood to young adulthood, implying that the neural mechanisms used to suppress the Stroop effect did not develop in obese individuals as it does in normal-weight people. This inconsistency might be explained by the fact that we included obese individuals as our participants, unlike Schroeter et al. (2004) or others did, since obesity might affect the association between age and the Stroop interference-effect. Although not consistent with the current literature about the non-obese population, the findings of obese participants in our study can be regarded as a novel, but a meaningful phenomenon that warrants further study. As a review points out, the heavy burden of overweight and obesity during childhood and adolescence and its effects on cognitive control development (Esteban-Cornejo et al., 2018).

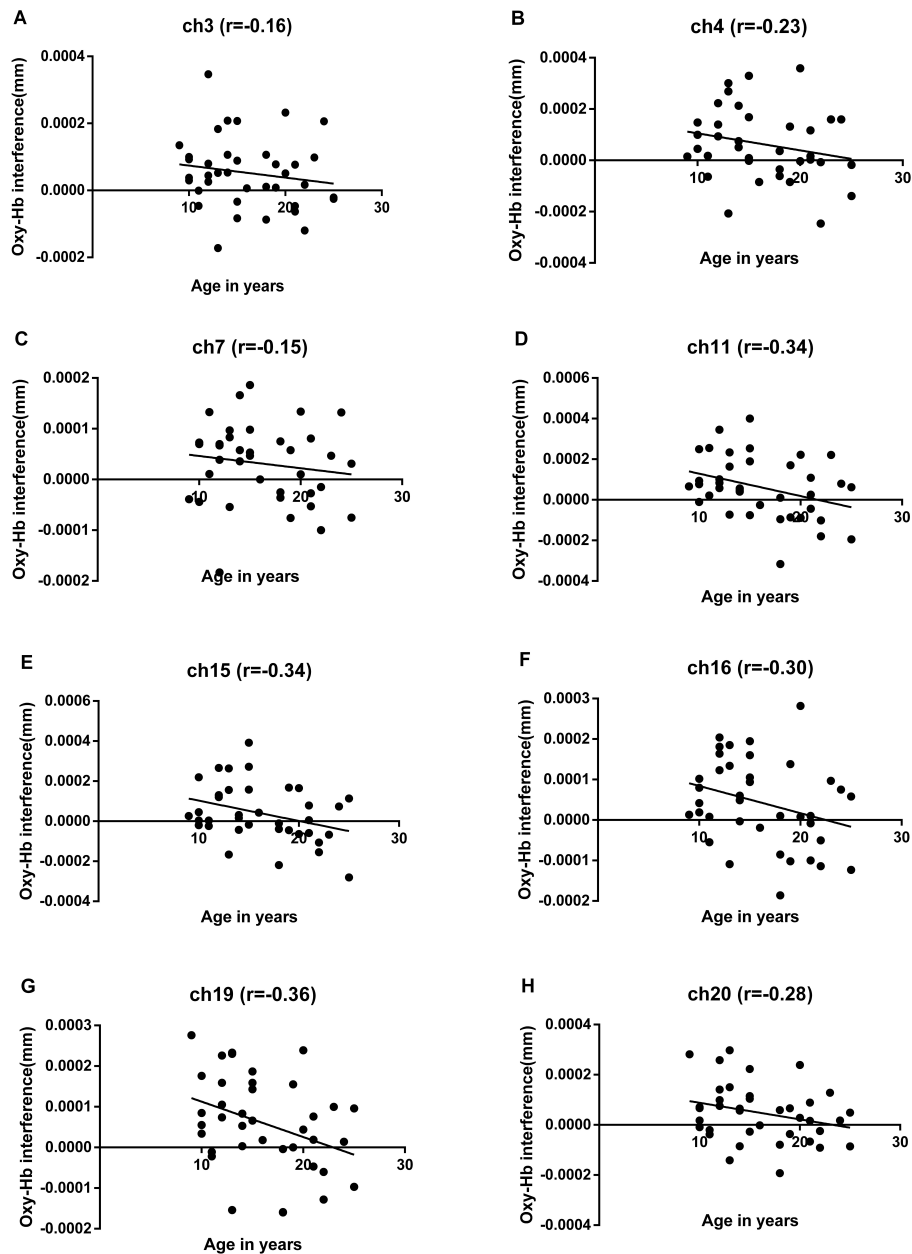


Figure 3. Oxy-Hb interference due to Stroop interference (y-axis) across age (x-axis) in ch3, ch4, ch7, ch11, ch15, ch16, ch19, and ch20. Pearson correlation coefficients showed no significantly negative correlation between age and hemodynamic Stroop interference (r range = $-0.36 \sim -0.15$, q value of maximum FDR = 0.05).

Executive function deficits are closely related to the prefrontal cortex. Clinical cases have shown that patients with prefrontal cortex lesions have difficulties with goal setting, planning, inhibition and self-maintenance, and previous neuropsychological research has shown that the maturity of the frontal cortex parallels the development of the executive functions (Leon-Carrion et al., 2004). Studies using non-invasive brain stimulation procedures have found that the DLPFC implicated in inhibitory control. One study found that repeated tDCS for 5 days over the right DLPFC may induce a more persistent decrease in self-reported craving, probably because enhancing the right DLPFC activity

may strengthen inhibitory control (Ljubisavljevic et al., 2016).

Overweight or obese individuals often show deficits in executive function compared to normal-weight individuals. In childhood, obese individuals have more difficulty in response inhibition than lean individuals (Nederkoorn et al., 2007). A systematic literature review showed that obese adolescent individuals (from 13 to 18 years of age) had poorer performance than healthy individuals in tasks that depend on inhibitory control and, furthermore, had smaller OFC volume (Reinert et al., 2013). In an adult population, Willeumier et al. (2011) found that high BMI might be a risk factor for decreased prefrontal cortex function and potentially impaired

executive function. Our study found that in obese subjects, brain activation during the Stroop task did not increase with age and decreased in the right DLPFC and the OFC, implying that obesity affected the development of those two areas.

Obesity itself has a compounding negative impact on the brain via mechanisms currently attributed to low-grade systemic inflammation, elevated lipids, and/or insulin resistance (Smith et al., 2011). Components of the immune system involved in inflammation can alter neural, cognitive, and motivational processes that lead to impaired self-regulation and poor health (Shields et al., 2017). Therefore, we recommend early prevention of impaired executive function. A previous study showed that the performance of participants on a Stroop task improved after dieting (Makris et al., 2013). Also, aerobic exercise helped improve executive functions (Kamijo et al., 2012). Furthermore, regular exercise can affect brain plasticity and increase the volumes of gray matter and white matter in the brain (Dupuy et al., 2015). Therefore, exercising to lose weight might be a good way for young people to improve their executive function ability and promote the healthy development of the prefrontal cortex.

We did not find a correlation between BMI and brain activation during the Stroop task. One possible explanation is that, although BMI is commonly used to measure obesity, it is not a very accurate predictor of cognitive processes and does not represent body fat percentage very well (Nuttall, 2015). If we could find a better index of obesity that predicted cognitive processes more accurately, then we could examine the relationship between obesity and various health risks through functional neuroimaging. For example, waist circumference is a more sensitive indicator of obesity, particularly in females, for potentially determining the adverse effects of obesity and overweight on the brain and associated risks to health (Kurth et al., 2013). Another reason might be the design of the present study procedure; the difficulty of the Stroop task was lowered to adapt the test to child participants. Research on developmental inhibitory control may be affected by the flexibility of the task, and complex cognitive tasks can reflect those small changes (Buttelmann and Karbach, 2017).

Inhibitory control plays a very important developmental role but obesity impairs its development. In healthy individuals, inhibitory control continues to develop into adulthood. However, in obese individuals, inhibitory control does not follow the same developmental trajectory, possibly because obesity impairs prefrontal cortex function (Willeumier et al., 2011). Therefore, we recommend early prevention of impaired executive function.

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Conflict of interest

The authors declare no competing interests.

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