

Original Article



Visual Hyper-vigilance But Insufficient Mental Representation in Children with Overweight/Obesity: Event-related Potential Study with Visual Go/NoGo Test

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OPEN ACCESS

Received: Aug 7, 2018

Revised: Sep 1, 2018

Accepted: Sep 3, 2018

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Funding

This work was supported by the research fund of Hanyang University (HY-2016).

Conflict of Interest

None of the authors have any conflicts of interest to declare.

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ABSTRACT

Purpose: The neural processing of children with overweight/obesity (CWO), may affect their eating behavior. We investigated the visual information processing of CWO under response control condition, by event-related potential (ERP) study, an electrophysiologic study for cognitive mechanism.

Methods: Seventeen CWO (mean age: 10.6±1.9), and 17 age-matched non-obese children (NOC), participated in the study. Neurocognitive function tests and visual ERP under Go/NoGo conditions, were implemented. Area amplitudes of major ERP components (P1, N1, P2, N2, and P3) from four scalp locations (frontal, central, parietal, and occipital), were analyzed.

Results: For Go and NoGo conditions, CWO had significantly greater occipital P1, fronto-central N1, and P2 amplitudes compared with NOC. P2 amplitude was significantly greater in CWO, than in NOC, at the frontal location. N2 amplitude was not significantly different, between CWO and NOC. For CWO and NOC, Go P3 amplitude was highest at the parietal location, and NoGo P3 amplitude was highest at the frontal location. In Go and NoGo conditions, P3 amplitude of CWO was significantly less than in NOC.

Conclusion: The greater P1, N1, and P2 suggested hyper-vigilance to visual stimuli of CWO, but the smaller P3 suggested insufficient mental representation of them. Such altered visual processing, may affect the eating behavior of CWO.

Keywords: Children; Obesity; Event-related potential; Go/NoGo; Visual

INTRODUCTION

The importance of controlling obesity in childhood, cannot be overemphasized due to its impact on lifelong health conditions, and its negative effects on physical and mental development [1]. However, unlike known metabolic complications, cognitive problems associated with obesity are not widely recognized. Cognitive performance can be modified by nutrition and systemic energy

balance, and can also influence eating behavior and excessive calorie gain [2-4]. In a recent study with elementary school students in Korea, obese children showed higher rates of consuming soft drinks, insufficient sleep, bullying experiences, and runaway impulses [5].

Previous studies indicated that inhibitory control, was associated with overweight/obesity [2,4]. The more obese the children, the higher the extent of inattention. Early-life inhibitory control and cognitive flexibility, were linked to prediction of body weight [6,7]. After adjusting for covariates, children with attention-deficit hyperactivity disorder (ADHD), showed an odd ratio of 1.9 for being overweight/obese [8]. The study conducted by Deux et al. [9] using overweight adolescent psychiatric patients and a Go/NoGo paradigm, showed that overweight adolescents had more difficulties with inhibition, in response to food and neutral stimuli. Therefore, reduced inhibitory performance of obese patients, may be a general response rather than food-specific.

Cognitive controls can be measured by neuropsychological tests such as Go/NoGo tasks, the continuous performance test, and the Stroop and Flanker test. These tests measure frontal executive function using reaction time, and the number of correct or omitted responses. Further neural bases for cognitive control scan be investigated using neurophysiological and neuroimaging methods [10-12]. Event-related potential (ERP) study is an electrophysiological method using electroencephalography (EEG), which reveals elapsed time of cognitive processing in milliseconds (ms). In various clinical disorders such as ADHD, schizophrenia, epilepsy, dementia, and depression, ERP showed different electrophysiologic patterns, reflecting altered brain function [13-16].

ERP means the time-locked brain response, to experimental stimuli. It is an averaged waveform, and consists of prominent positive and negative peaks called components. Major components are named according to polarity and sequence, and each component reflects certain cognitive processes. P1 and N1 are positive and negative components, around 100 ms, after the stimuli. P1 is best visualized at an occipital location to visual stimuli, while N1 is best visualized at fronto-central location, to auditory stimuli. These components are related, to automatic vigilance and orientation. Recently, the P1-N1 complex was suggested to act as an inhibitory filter, for attentional control and early categorization [17,18]. N2 is the second major negative peak around 200 ms, and is commonly related to response inhibition. From the Go/NoGo paradigm, NoGo N2 is largest when the Go stimuli are more common, than NoGo stimuli [19]. P3 is the most prominent component of the ERP wave, and occurs around 300 ms after stimulation. It is best visualized in centro-parietal locations. P3 reflects mental representation, attentional resource allocation, and context update [15,19,20]. In general, decrease in amplitude of components means cognitive deterioration, and latency of components, is associated with mental speed [20].

Go/NoGo paradigms are frequently used, in experiments investigating response control. Typically, the specific response of participants is required for the Go condition (response activation), and suppression of prepared action is required for the NoGo condition (response inhibition). In a study by Gao et al. [21], the No/Go condition showed greater frontal P3 than the Go condition, implying that response inhibition, was more cognitively demanding than response activation.

Although neurophysiological studies are considerably informative, such studies on children with overweight/obesity (CWO) issues are relatively scarce. P300 studies by Tascilar et al. [22] reported longer latency and decreased amplitude of P300, in children with obesity. Longer

reaction times in executive function tests and decreased P300 (P3) amplitudes at Go/NoGo tests, were revealed in a recent test, in otherwise healthy overweight children [23]. Those results suggested altered inhibitory control, and neuronal networks in CWO.

In this study, we investigated characteristics of brain information processing, in CWO during visual tasks requiring response control. We hypothesized that early automatized ERP components and later components for conceptualization of CWO, may differ from that of non-obese children (NOC). Since most stimuli associated with eating behavior are visually presented, we used a visual Go/NoGo paradigm. The stimuli we used were not food specific images, but instead general stimuli, to reflect general visual processing. In this study, the amplitudes of ERP components were calculated using the area amplitude method, which we believe is a more feasible and objective method, for overcoming ambiguity of peak delineation in childhood ERP [19]. In addition to the results of ERP study, complementary neuropsychological data were also analyzed.

MATERIALS AND METHODS

Participants

This study was performed at the Hanyang University Hospital in the Republic of Korea from November 2015 to June 2017. Seventeen CWO (mean±standard deviation [SD]: 10.7±2.0 years old, male 13, female 4) and 17 age-matched NOC were recruited (mean±SD: 10.9±2.0 years, male 11, female 6).

Overweight and obesity were defined according to the WHO reference, for children age 5–19 [24]. Inclusion criteria were overweight or obese children age 7–13, with otherwise normal development: overweight $\geq +1$ SD, obesity $\geq +2$ SD of body mass index (BMI). Children with intellectual disabilities, severe physical diseases, neurological or neuropsychological disease, or difficulties in hand or visual functions were excluded. All research protocols were approved by the institutional review board at Hanyang University Guri Hospital (IRB No. 2015-11-005). Written informed consent was received from subjects and the parents.

Laboratory tests

Baseline blood samples were drawn from CWO for complete blood tests, as well as total protein, albumin, glucose, aspartate amino-transferase, alanine amino-transferase, triglyceride, free fatty acid, cholesterol, high density cholesterol and low density cholesterol tests.

Neuropsychological test battery

All participants were given the following neurocognitive function tests by a child neuropsychologist: The Korean Wechsler intelligence scale for children-IV, Rey-Kim memory test for children, the Korean-child behavior checklist, the children's version of the Stroop color-word test, and the Children's color trails test (CCTT).

Electrophysiological tests

Visual Go/NoGo test

EEG was recorded during the visual Go/NoGo task. Stimuli were delivered using the Presentation[®] experiment control program (Neurobehavioral Systems, Inc., CA, USA). Go stimuli for targets were Os (n=50), and NoGo stimuli for non-targets were Xs (n=50). Stimuli were 3 cm² and presented in the center of the monitor, as white color on a black background.

Go and NoGo stimuli were presented, with the same probability in pseudorandom order. Stimuli duration was 70 ms, and inter-stimulus interval was 1,000 ms. The experiment consisted of two same-test blocks, with a brief intermission in between.

The children were seated in front of a monitor in a quiet room, instructed to look at the center of a black screen, and focus attention on upcoming O or X stimulus. They were asked to press the button as quickly as possible, when Os were seen, and to not to press the button when Xs were displayed. The experiment process is illustrated in **Fig. 1**.

EEG acquisition and preprocessing for ERP

A 29-channel electrode cap (Waveguard®, ANT neuro, Enschede, Netherlands) was used for EEG acquisition. Electro-oculograms were recorded at the right supraorbital, and the left infraorbital area. Reference electrodes were A1 and A2, and externally averaged as a common reference. Band pass filter was 0.1–70 Hz, and sampling rate was 500 Hz. Preprocessing was performed using EEGLAB®, an open source toolbox operating on MATLAB® (version R2015b, Math Works, Natick, MA, USA). Averaged EEG was divided into trials using the –200–800 ms time window, from stimulus onset. Large body and eye movement artifacts were removed, by visual inspection and independent component analysis.

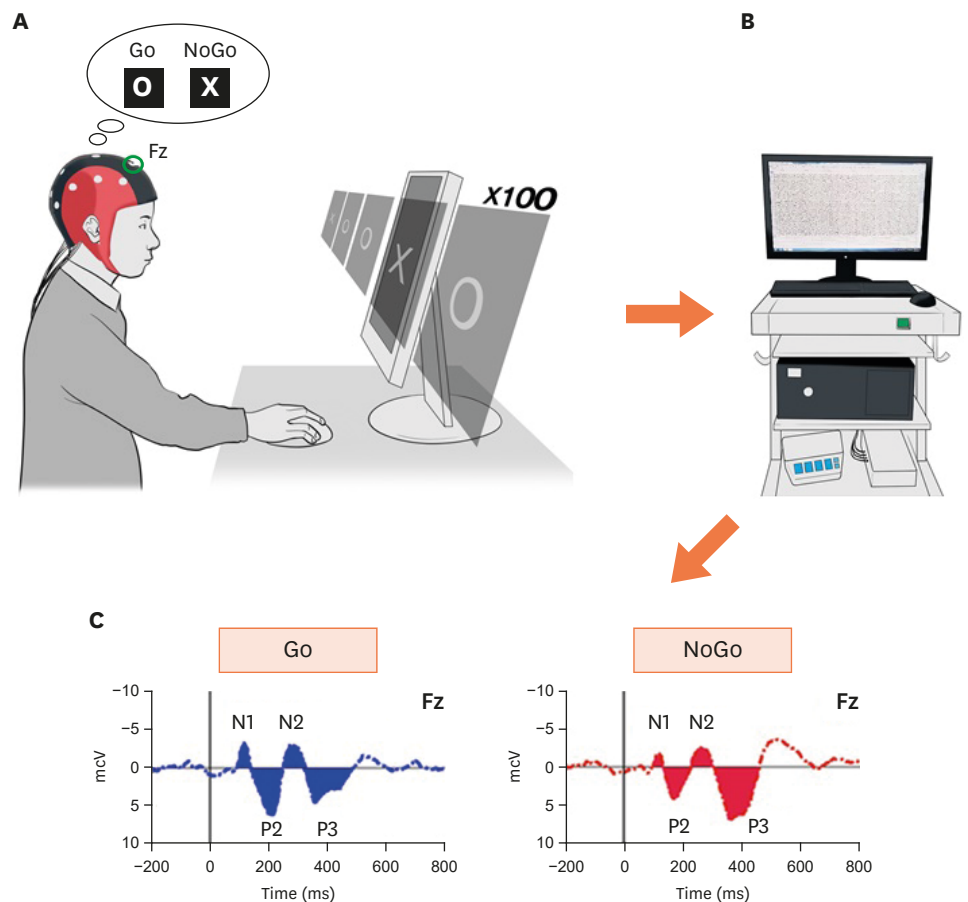


Fig. 1. The process of ERP experiment with Go/NoGo task. Detailed electrodes such as electro-oculograms and lines are omitted in this figure. The Go stimuli for targets are Os (n=50), and the NoGo stimuli for nontargets are Xs (n=50) with pseudorandom order (A). Recorded electroencephalographic data is preprocessed for ERP analysis (B). ERP graphs for area amplitudes of each Go (left figure) and NoGo (right figure) condition on Fz site (C). ERP: event related potential.

For objectively measuring the ERP component in children, we calculated the area amplitude of each component, the integral area between ERP waves and baseline, during the time windows of the component [19]. The time windows were decided by grand-averaged ERP waves, and area amplitudes were calculated by MATLAB® programming.

Statistical analysis

Baseline characteristics and neurocognitive function test data, were analyzed by Mann-Whitney nonparametric test for continuous data, and Pearson's χ^2 test for categorical data. EEG data from F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, O1, POz, and O2 electrode sites were used. These were further grouped into four locations: frontal (F3, Fz, and F4), central (C3, Cz, and C4), parietal (P3, Pz, and P4), and occipital (O1, POz, and O2).

Amplitudes of P1, N1, P2, N2, and P3 were analyzed by repeated-measures analysis of variance (RM-ANOVA). Within-subject factors were Condition (Go-target and NoGo-nontarget), Block (block1 and block2), and Location (frontal, central, parietal and occipital), while the between-subjects factor was Group (CWO and NOC). Statistical analysis was performed, using IBM SPSS version 21.0 (IBM Corp., Armonk, NY, USA). A *p*-value less than 0.05 was considered statistically significant.

RESULTS

Clinical and laboratory data

Mean BMI was significantly different between CWO and NOC (mean±SD: 25.8±3.87 vs. 17.7±1.5; *p*<0.001). Baseline clinical characteristics, and laboratory data are compared in **Table 1**.

Neurocognitive function tests

Full scale intelligence quotients (IQ), subscales of IQ, and memory quotients of subjects were within normal ranges, and were insignificantly different between CWO and NOC. However,

Table 1. Baseline characteristics and laboratory data of the CWO and HC

Categories	CWO	HC	<i>p</i> -value
Subject number	17	17	-
Sex (Male:Female)	13:4	11:6	0.708
Age	10.176±2.0	10.231±1.32	0.465
BMI	25.8±3.9	17.7±1.5	<0.001*
Overweight: obesity	5:12	-	-
Handedness (RH:LH:BH)	13:4:0	14:2:1	0.238
Blood chemistry			
Total protein	7.5±0.5 g/dL	NC	-
Albumin	4.7±0.3 g/dL	NC	-
Cholesterol	202.3±44.8 mg/dL	NC	-
Glucose	95.1±6.8 mg/dL	NC	-
AST	36.1±23.0 U/L	NC	-
ALT	54.2±56.3 U/L	NC	-
Triglyceride	144.8±76.3 mg/dL	NC	-
Free fatty acid	754.5±254.6 uEq/L	NC	-
HDL	50.1±10.4 mg/dL	NC	-
LDL	129.1±43.4 mg/dL	NC	-

The continuous data are presented as mean±standard deviation.

CWO: children with obesity/overweight, HC: healthy children, BMI: body mass index, RH: right-handedness, LH: left-handedness, BH: both-handedness, NC: not checked, AST: aspartate transaminase, ALT: alanine transaminase, HDL: High-density lipoproteins, LDL: low-density lipoproteins.

**p*<0.05.

T-scores of Stroop color-word and CCT1 in the executive function tests, were significantly lower in CWO compared with NOC (**Supplementary Table 1**).

Analysis for Go/NoGo test

Response time, correction, and omission

Mean response time of CWO was significantly longer, compared to NOC (mean±SD: 6007.8±1260.1 ms vs. 5402.3±841.3 ms; $p=0.035$). Mean numbers of correct responses (CWO, 48.9±1.7; NOC, 49.3±1.0; $p=0.127$), incorrect responses (CWO, 3.5±2.9; NOC, 2.2±1.5; $p=0.081$), and omission errors (CWO, 2.3±1.5; NOC, 1.7±1.1; $p=0.428$) per block were insignificantly different between groups.

ERP analysis

Grand-averaged ERP and component ranges

The grand-averaged ERP graphs in GO and NoGo conditions are presented in **Fig. 2**. The time window of each condition was estimated, from grand-averaged waveforms. P1 was best visible on occipital sites, and amplitude was measured from the occipital location. N1, P2,

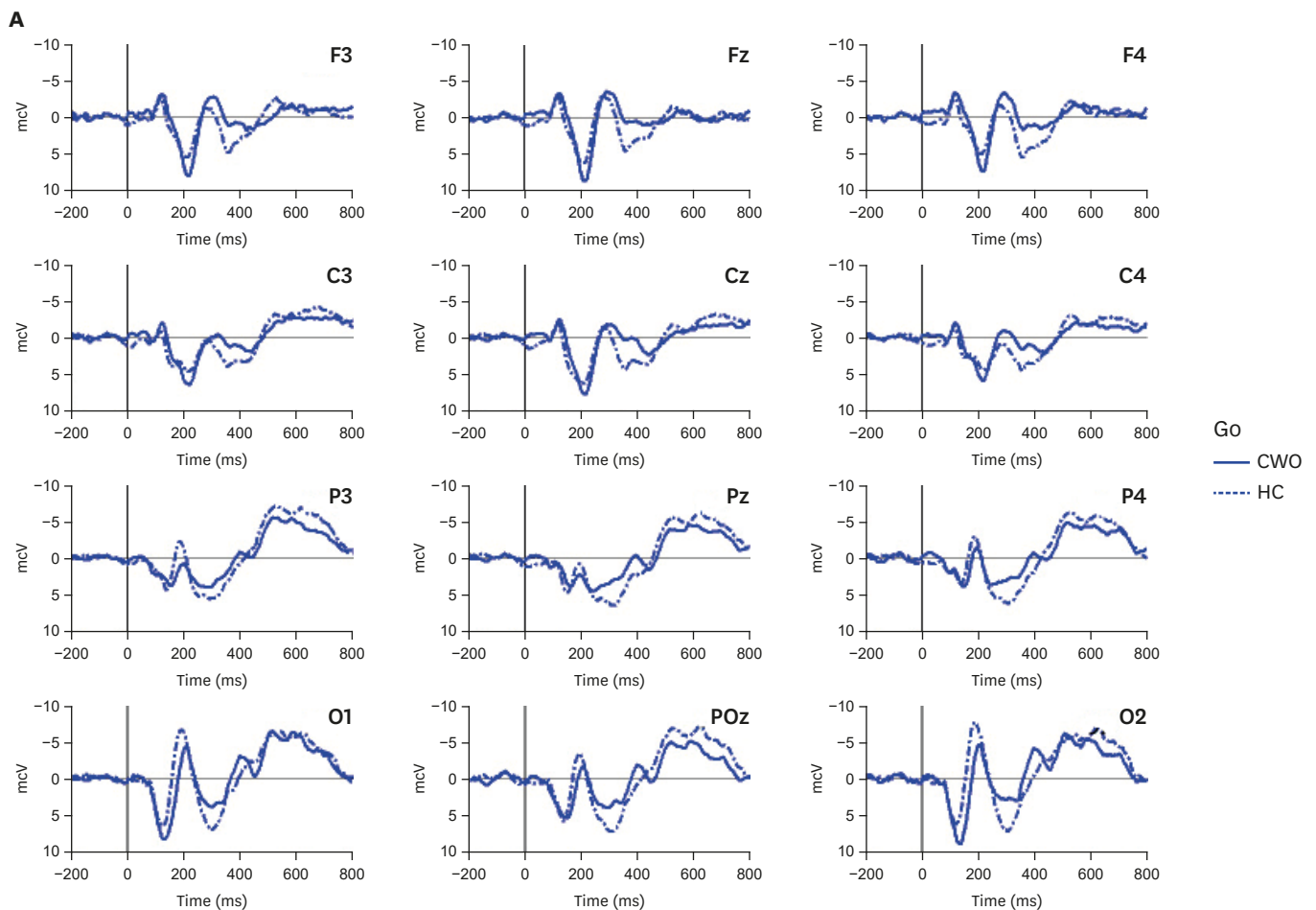


Fig. 2. The grand averaged ERP of children with overweight/obesity and healthy children in Go condition (A), and in NoGo condition (B). Blue line represents Go condition and red line represents NoGo condition. Solid line represents children with overweight/obesity and dash-dot line represents healthy children. ERP: event related potential, CWO: children with overweight/obesity, HC: healthy children. (continued to the next page)

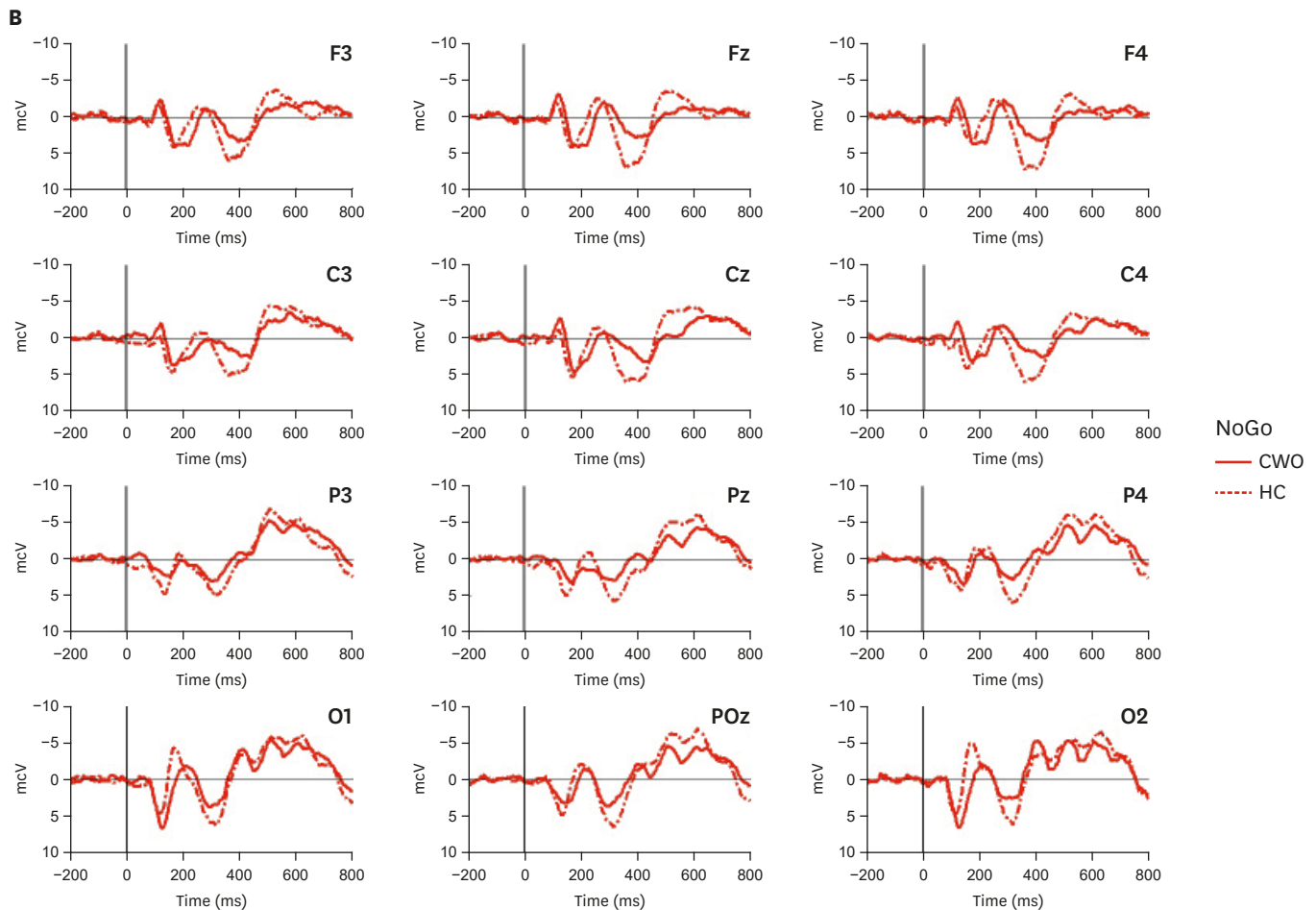


Fig. 2. (Continued) The grand averaged ERP of children with overweight/obesity and healthy children in Go condition (A), and in NoGo condition (B). Blue line represents Go condition and red line represents NoGo condition. Solid line represents children with overweight/obesity and dash-dot line represents healthy children. ERP: event related potential, CWO: children with overweight/obesity, HC: healthy children.

and N2 were evident on fronto-central locations, and amplitudes were measured from these locations. P3 was evident on all sites, and measured from all four locations. Detailed time window ranges, are presented in **Supplementary Table 2**.

P1

RM-ANOVA on P1 amplitude yielded significant main effect on Group ($F[1,100]=13.534$, $p<0.001$) and Condition ($F[1,100]=43.346$, $p<0.001$), which showed greater P1 amplitude in CWO, than in NOC (mean±standard error [SE]: 391.770 ± 33.776 μV vs. 216.043 ± 33.776 μV), and greater P1 amplitude in Go condition than in NoGo condition (mean±SE: 379.572 ± 25.305 μV vs. 228.241 ± 27.653 μV). There was no interaction between Condition and Group (**Supplementary Table 3** and **Fig. 3A**).

N1

N1 amplitude yielded significant main effect on Group ($F[1,100]=10.158$, $p=0.002$), which showed greater N1 amplitude in CWO than in NOC (mean±SE: -81.625 ± 10.572 μV vs. -33.973 ± 10.572 μV). Interaction between Condition and Location, was significant ($F[1,100]=18.021$, $p<0.001$) (**Supplementary Table 3** and **Fig. 3B**).

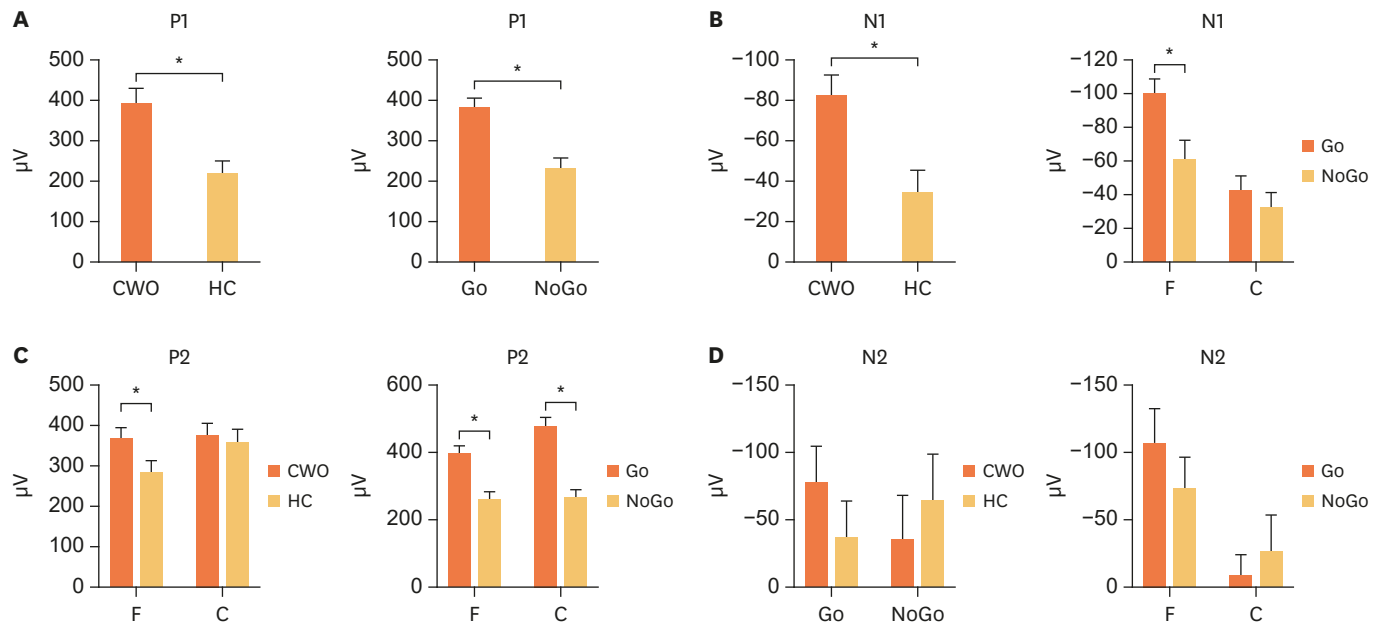


Fig. 3. Comparison of the area amplitudes of P1, N1, P2, N2 components. P1 amplitude yields significant main effect on Group (left) and Condition (right) (A). N1 amplitude yields significant main effect on Group (left) and the interaction between Condition and Location is significant (right) (B). P2 amplitude yields significant interaction between Group and Location (left) and Condition and Location (right) (C). N2 amplitude yields no significant interaction between Group and Condition (left), but significant interaction between Condition and Location (right) (D). CWO: children with overweight/obesity, HC: healthy children, F: frontal, C: central. * $p < 0.05$.

P2

P2 amplitude showed insignificant effect on Group. However, there was significant interaction between Group and Location ($F[1,100]=4.601, p=0.034$). The P2 amplitude in frontal location relative to central location, was greater in CWO than in NOC. There was also significant interaction between Condition and Location ($F[1,100]=9.710, p=0.002$) (**Supplementary Table 4** and **Fig. 3C**).

N2

N2 amplitude showed insignificant effect on Group. Although no significant interaction existed between Group and Condition, NOC showed greater N2 amplitude in NoGo than in Go condition. On the contrary, CWO showed greater N2 amplitude in the Go condition, than in the NoGo condition. There interaction between Condition and Location was significant ($F[1,100]=10.291, p=0.002$) (**Supplementary Table 4** and **Fig. 3D**).

P3

P3 amplitude showed significant main effect on Group ($F[1,100]=10.681, p=0.001$), and was consistently less in CWO, compared with NOC in Go and NoGo conditions (mean \pm SE: $268.054\pm 46.368 \mu V$ vs. $482.362\pm 46.368 \mu V$) (**Supplementary Table 5**). In addition, there was significant interaction between Condition and Location ($F[3,98]=49.378, p<0.001$), which showed greatest Go P3 amplitude in the parietal location, and greatest NoGo P3 amplitude in the frontal location in CWO and NOC. Post-hoc analysis showed that Go P3 amplitudes of CWO, were significantly less than NOC in frontal and occipital location, and NoGo P3 amplitude of CWO was significantly less than NOC in frontal location (**Fig. 4**).

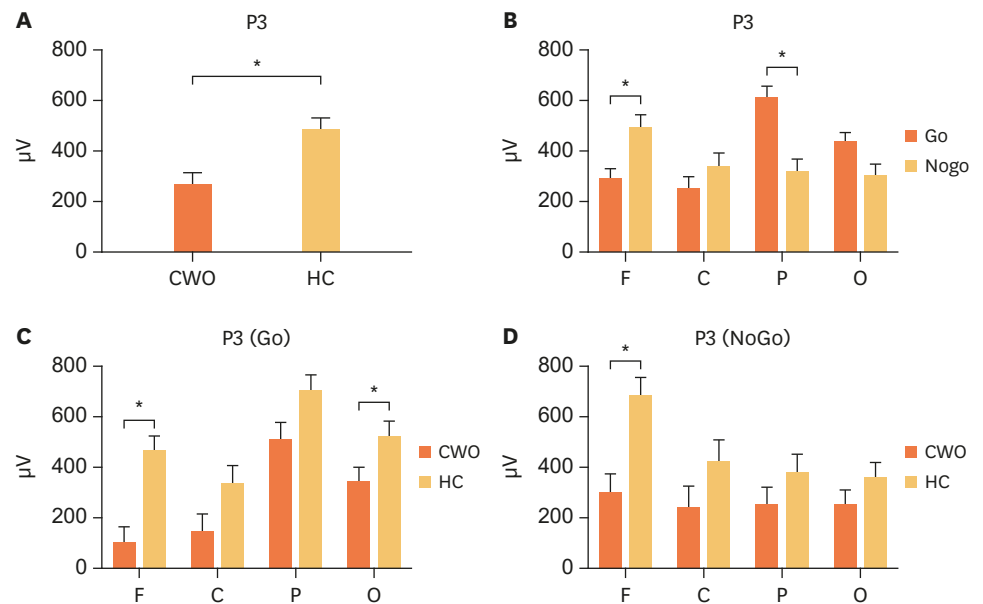


Fig. 4. Comparison of the area amplitudes of P3 component. P3 amplitude yields significant main effect on Group; P3 amplitude is always lower in children with overweight/obesity than in healthy children (A) and significant interaction between Condition and Location (B). The greatest Go P3 amplitude is in the parietal location (C), and the greatest NoGo P3 amplitude is in the frontal location (D). CWO: children with overweight/obesity, HC: healthy children. F: frontal, C: central, P: parietal, O: occipital. * $p < 0.05$.

DISCUSSION

Food images are transferred via the optic pathway to the visual cortex, wherein visual cognitive processing is initiated. Further processing in dorsal and ventral networks, is associated with memory comparison, and executive controls. In this study, we compared cortical visual processing, under response control conditions of CWO with NOC. Results revealed over-activated early ERP components from P1 to P2, and under-activated relatively later component P3 in CWO, relative to NOC. Alteration of neural processing to visual stimuli under response control condition, can be applied to eating behavior of CWO.

Although standardized electrophysiological methods for people with obesity are not established, previous studies revealed various alterations in ERP components in the people with obesity [22,25-27]. Appetizing food images triggered larger P100 and P300, relative to control images in obese and non-obese adolescents [4]. In patients with Prader-Willi syndrome, N1 amplitudes were correlated with BMI and hyperphagia scores [28]. However, few studies reported early components of brain responses such as P1, N1 or P2 in CWO.

The N2 component is associated with inhibitory control [25]. Developmental trajectory of NoGo N2 showed that amplitude and latency of NoGo N2, decreases across the normal childhood period, and that NoGo N2 amplitude was more negative than Go N2. Such findings support the interpretation of NoGo N2, as indexing response inhibition [29]. However, in a previous study, obese children had larger NoGo N2 than Go N2, which was not observed in NOC [26]. Our study showed greater NoGo N2 amplitude than Go N2 amplitude in NOC, and greater reverse Go N2 amplitude than NoGo N2 amplitude in CWO, but these

findings were statistically insignificant. As our task consisted of relatively simple stimuli, an elaborately-designed paradigm for inhibition, may reveal different N2 responses in CWO.

P3 (P300) is the most known component. Tsai et al. [30] measured behavioral performance and ERP in children with obesity, and reported less P300 amplitudes in these children, when performing visuospatial attention tasks. However, these latencies were insignificantly different. Reyes et al. [23] showed that CWO had slower reaction times on the Stroop test, and decreased P300 amplitude with Go/NoGo trials, which indicated altered inhibitory functions. Another study conducted by Nijs et al. [31] on overweight/obese and normal weight adult women, showed that P300 amplitude in response to food pictures was only enhanced, in the normal weight group. However, decreased P300 was not always consistent. Food-specific P300 amplitude paradoxically increased in the obese group with higher restraint scores, indicating that they were more vulnerable to visual food images [4]. A P300 study with simple auditory tone stimuli by Tascilar et al. [22] indicated that decreased P300 response in obese children, may be general and not specific, to visual food stimuli.

Results from our study more clearly elucidated ERP responses of CWO, than previous studies. In Go and NoGo conditions, early components such as P1, N1 and P2 responses significantly increased in CWO, suggesting hyper-activation of early visual processing, in this group. The time period before 300 ms after stimuli presentation, is usually before mental representation, meaning that hyper-activation was at subconscious level, and automatic processing. This period is associated with alertness and vigilance. Automatic comparison occurs around 200–250 ms after stimuli. On the contrary, decreased P3 amplitude observed in CWO, means that actual mental representation in this group was inefficient despite hyper-arousal to visual stimuli. Results were in line with results of executive function tests in this study, in which T-scores of Stroop color-word and CCTT-1, were significantly lower in CWO compared with NOC.

Interestingly, Go P3 was greatest in the parietal location, and NoGo P3 was greatest in the frontal location in CWO and NOC. These findings suggest that target conceptualization and response activation, were allocated to the parietal area, and response inhibition was allocated to the frontal area, as a part of executive function. In the recent study from Gao et al. [21], response inhibition was more cognitively demanding, than was response activation.

Our study used simple visual stimuli such as Os and Xs for Go/NoGo condition, instead of stimuli with food images. Such paradigm may reflect more general visual processing, and may be more easy to apply to children, as well as adults. This study used semi-automatically calculated area amplitude, instead of peak amplitude of components. Area amplitude is essentially the same as mean amplitude, a common alternative to peak amplitude [19]. In fact, ambiguity of peak detection, is one of the major obstacles of ERP study in children. We suggest that measuring area amplitude of components, is a more objective method than visual peak detection in children.

A limitation of this study, is that we did not obtain latencies of components for measuring area amplitude. In fact, reaction time was significantly lengthier, in CWO than in NOC. Other limitations are the small sample size, and that we did not analyze data, according to insulin resistance. Results of this study should be confirmed though further studies, based on larger sample sizes and classification of obesity groups.

This study suggested that hyper-vigilance to visual stimuli and insufficient mental representations, are characteristics in CWO. Such characteristic processing can be a general cognitive working pattern under response control conditions, which may influence eating behavior and behavioral problems associated with CWO. In addition to physical treatment for weight control, more work should be focused on improving the cognitive function of obese children.

SUPPLEMENTARY MATERIALS

Supplementary Table 1

Details of neurocognitive function tests in CWO and HC

[Click here to view](#)

Supplementary Table 2

Detailed time window ranges of each component

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Supplementary Table 3

Repeated-measures analysis of variance for P1 and N1 amplitudes

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Supplementary Table 4

Repeated-measures analysis of variance for P2 and N2 amplitudes

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Supplementary Table 5

Repeated-measures analysis of variance for P3 amplitudes

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