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Research report

Functional imaging in obese children responding to long-term sports therapy

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HIGHLIGHTS

- Obesity is associated with decreased psychophysiological response to emotional stimuli.
- Children with obesity might show a down-regulation of dopamine D2 receptors.
- We performed a longitudinal study using comprehensive therapy including sports in obese children.
- Therapy responders showed increased putamen activation in response to food pictures.
- Therapy responders showed increased motor network activation when observing sport pictures.

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ABSTRACT

Functional imaging studies on responders and non-responders to therapeutic interventions in obese children are rare. We applied fMRI before and after a one-year sports therapy in 14 obese or overweight children aged 7–16 years. During scanning, participants observed a set of standardized pictures from food categories, sports, and pleasant and neutral images. We were interested in alterations of the cerebral activation to food images in association with changes in the BMI-standard deviation score (BMI-SDS) after therapy and therefore separated the observation group into two outcome subgroups. One with reduction of BMI-SDS >0.2 (responder group) and one without (non-responder group). Before therapy fMRI-activation between groups did not differ. After therapy we found the following results: in response to food images, obese children of the responder group showed increased activation in the left putamen when compared with the non-responder group. Pleasant images evoked increased insula activation in the responder group. Only the responder group showed enhanced activity within areas known to store trained motor patterns in response to sports images. Both the putamen and the insula are involved in the processing of emotional valence and were only active for the therapy responders during the observation of food or pleasant stimuli. Elevated activity in these regions might possibly be seen in the context of an increase of dopaminergic response to emotional positive stimuli during intervention. In addition, sport images activated motor representations only in those subjects who profited from the sports therapy. Overall, an altered response to rewarding and pleasant images and an increased recruitment of motor engrams during observations of sports pictures indicates a more normal cerebral processing in response to these stimuli after successful sports therapy in obese children.

1. Introduction

During the last decade the prevalence of overweight and obese children has become a public health concern. In Germany the percentage of obese children continues to increase rapidly [31] and obesity causes health risk factors for orthopedic, neurological, pulmonary, gastroenterological and endocrine conditions [40].

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Excessive food intake alters dopamine D2 receptor distribution within the dopaminergic network. Hernandez and colleagues demonstrated that the anticipation of food is associated with the release of dopamine [23], and this plays a crucial role for the eating behavior of an individual. Recent studies have shown an association between obesity and the down-regulation of D2 receptors [9,62]. For normal-weighted participants, food depicts reward in a consummatory and anticipatory way [54]. These findings suggest that overweight and obese children need a larger amount of food for a sufficient dopamine release to experience a rewarding effect.

One specific region that contains dopamine receptors is the striatum, which is divided into a ventral and a dorsal part. The ventral striatum (i.e., the nucleus accumbens and ventromedial putamen) is involved in the evaluation of rewarding and emotional stimuli [26] and the dorsal striatum (i.e., the caudate nucleus and other parts of the putamen) is related to the motivation for food consumption [60] and the processing of food rewards [52,61].

Behavioral and cognitive information are processed through several cortical and subcortical circuits [7] that form a top-down control system. The prefrontal cortex (PFC), which is responsible for the processing of motor, sensory, and limbic information [39], is part of this top-down control system. The ventromedial part of the PFC (vmPFC) is predominantly associated with the processing of emotional stimuli [45] and the ventrolateral part (vlPFC) is more involved in cognitive processing and the appraisal of emotional stimuli [42].

A higher body mass index (BMI) is associated with diminished orbitofrontal cortex (OFC) activation in obese individuals seeing images of high-calorie foods [28]. Two studies have reported a negative correlation between vmPFC and vlPFC activation and BMI in obese participants in response to food stimuli [27,53]. The vlPFC has projections to sensory and reward associated regions [44]. Therefore, an increased reactivity of this area to food stimuli might be interpreted as an indicator of increased reward association with food stimuli after successful therapy. Moreover, obesity alters PFC activity and therefore attenuates deactivation in limbic and paralimbic areas, i.e., the hippocampus, hypothalamus, and amygdala, and increases activity in the insular cortex in response to food stimuli in obese adults compared with normal-weighted adults [11,20,21].

Sport plays an important role in obesity prevention and therapy. Therefore, sports therapy might affect brain regions that are associated with motion processing. Observing transitive or intransitive movement [17] or implied motion is associated with activity of the mirror neuron system (MNS) [49]. The MNS was first described in monkeys [19] as activation of the premotor area and the inferior parietal cortex (IFC) during the perception of active or implied movement [48]. In humans the rostral part of the inferior frontal gyrus (IFG), the ventral premotor cortex (vPMC) and the posterior part of the IFG are the main parts of the MNS [47]. Furthermore, the occipital lobe has shown activity during the perception of both meaningful and meaningless actions [4]. In addition, the ventral premotor area, which stores specific motor patterns [4], is active during the imitation of movements [24]. The timing and execution of movements is processed by the cerebellum [25].

We applied fMRI to detect cerebral activation changes in response to food, pleasant, sports and neutral images in obese children before and after a therapeutic intervention through sports. In a previous cross-sectional study using the same fMRI paradigm, we demonstrated that activation of the PFC in response to food pictures is highly discriminative in obese vs. normal-weighted children [8]. Longitudinal data in this patient group have not been reported.We hypothesized different brain activations in areas associated with reward and emotion in obese and overweight children with unchanged BMI-SDS vs. changed BMI-SDS. These areas include the ventral and dorsal striatum, vmPFC and vlPFC, anterior cingulate cortex (ACC) [34], insula, amygdala, thalamus, and hippocampus. Furthermore, we hypothesized an increased response in regions associated with motion processing to pictures with people practicing sports (i.e., the IFG, IPC, vPMC, and cerebellum) in responders compared to non-responders after sports therapy.

2. Materials and methods

2.1. Participants

The pediatric clinic of the University of Greifswald started an intervention program focused on children with a BMI-standard deviation score (BMI-SDS) over 1.5 resembling a BMI of 22.5.

Sixty-two obese children were recruited by newspaper, school doctors, pediatricians, general practitioners and youth welfare office. Excluding criteria were eating disorders (anorexia, bulimia) and neurologic or psychiatric disorders. Thirty-eight participants met these criteria. Eleven overweight and obese children had to be excluded because of anxiety and claustrophobia. Fifteen sessions exhibited excessive motion artifacts (cutoff: >2 mm or >2° in any direction) and therefore had to be excluded, too. Twenty-four obese and overweight children finished the first fMRI session. After the children had completed the intervention successfully, the program ended with a second fMRI session. Additionally, seven scans were excluded because of motion artifacts beyond the named cutoff. Furthermore, scans of three children who gained weight during the therapy program were excluded for matching both groups.

Subsequently, 14 obese and overweight children under pre-therapy condition (average age: 13.15, ±(standard deviation) 2.51, range: 6.68–15.50 years; 2 male, mean BMI: 28.90 ± 3.80; mean weight percentile: 98.29 ± 1.91; mean BMI-SDS: 2.31 ± 0.44, range: 1.50–3.03) and post-therapy condition (average age: 14.48 ± 2.44; range: 8.31–16.59; average BMI 28.53 ± 4.28; average weight percentile: 97.31 ± 2.41; mean BMI-SDS: 2.11 ± 0.51, range: 1.36–3.17) remained for the further analysis. All participants had normal or corrected-to-normal vision. A more detailed description of the patients is given in Table 1.

The study was approved by the Ethics Committee of the Medical Faculty of the University of Greifswald. The parents of all participants provided written informed consent.

2.2. Intervention program

The obese children took part in different therapeutic interventions twice a week for a period of 45 weeks, which included sports therapy, physical and dietary education divided in two sessions. Details of the whole program are given in the supplemental information.

2.3. fMRI

MRI was conducted on a 1.5 T scanner (Siemens Magnetom Symphony, Erlangen, Germany) using echo planar imaging and structural T1-weighted images. Details are provided in the supplemental information. All obese children were scanned twice before and after therapy. Time since the last meal was balanced between the pre and post measurement (less than 1 h time difference between the pre and post measurement in relation to the last meal consumed). During both sessions a set of pictures selected from the International Affective Picture System (IAPS) [33] was presented. During scanning, stimuli were presented in alternating blocks (twenty pictures of the same category) lasting 30 s, with a total of five blocks of each category presented in random order. Each image was shown for 1500 ms, with the order randomized within each block, minimizing the effect of habituation. A blank screen was shown during the 15 s inter-block-intervals. The beginning of a new