Original Article
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Obesity

Working Memory-Related Brain Activity Is Associated with Outcome of Lifestyle Intervention

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Objective: Lifestyle interventions including reduction of caloric intake are still the most pursued option to treat obesity. However, their outcome in terms of weight loss strongly differs between participants. In our study, we hypothesized that initial differences in brain activation in a food specific memory task are associated with weight change during a lifestyle intervention.

Design and Methods: Magnetic brain activity was recorded during a one-back visual memory task with food and nonfood pictures in 33 overweight and obese subjects before they underwent a lifestyle intervention. The intervention lasted 6 months and aimed for a reduction in daily caloric intake by 400 kcal. Body mass index (BMI) was determined before and after the intervention.

Results: Differences between outer tertiles representing people who increased their BMI by 1.4% ± 1.1% (non-responders) and who reduced their BMI by −6.9% ± 2.6% (responders) are reported. Neuronal activity was related to BMI change in sensor and source space. Non-responders showed higher activation in right inferior frontal and left occipital visual areas, whereas responders showed increased activation in right temporal areas including hippocampus and fusiform gyrus.

Conclusions: Differences in the cerebral response during a food specific memory task indicate an altered cognitive control over food intake. These differences might determine the ability to eat less and successfully lose weight.

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Introduction

Excess body weight is associated with diseases like diabetes, hypertension, and heart disease and is considered to reduce average life expectancy (1,2). Lifestyle interventions to reduce and maintain body weight are still the most pursued options and are successful both in reduction of weight and reduction of prospective health risks (3,4). However, the outcome of most lifestyle interventions concerning weight loss and especially the ability to maintain obtained weight loss over a longer period strongly differ between participants (5,6). This difference in treatment response cannot be explained exclusively by genetic predispositions and simple lifestyle factors and it was suggested that brain processes might be of fundamental importance for weight loss and maintenance (7-9).

So far, studies mostly investigated differences in brain activations between successful and nonsuccessful weight losers or nondieting controls after diet (10-12). In a functional magnetic resonance imaging study (fMRI), McCaffery et al. (10) compared neuronal responses to visually presented food pictures between successful weight-loss maintainers with normal weight and obese controls. They observed increased activation in frontal regions and primary and secondary visual cortices in those who lost weight and suggested that this may be related to increased inhibitory control in response to food cues and greater visual attention. In addition, Del-Parigi et al. (11) showed with positron emission tomography (PET) that in response to meal consumption successful dieters in comparison to nondieting controls showed increased activation in regions related to executive functions like dorsal prefrontal cortex. Furthermore, several studies showed that weight gain is also associated

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with specific activations in prefrontal cortical areas (13-15). Kishinevsky et al. (13) investigated obese women on a delay discounting task and observed that activation patterns in putative executive function areas of the brain like inferior, middle and superior frontal gyri were predictive for weight gain over the subsequent 1-3 years. Furthermore, Yokum et al. (14) showed for adolescent girls that BMI (body mass index) correlated positively with activation in a number of brain regions related to attention and food reward and orbitofrontal cortex activation predicted future increases in BMI. Finally, Batterink et al. (15) studied adolescent girls with a visual go-nogo task and observed a negative correlation between brain activation in temporal operculum on nogo trials displaying high caloric food pictures and weight gain after 1-year follow-up. In summary, recent neuroimaging studies indicate that executive functions are important for successful weight control. This is in accordance with the general concept of executive functions to control impulses and to enable goal-directed behavior. To our knowledge, so far only Murdaugh et al. (16) investigated prospectively whether the brain response to visual food cues predicts successful weight loss in a dietary lifestyle intervention program. They reported positive correlations between weight change during the diet and initial brain activation to food stimuli in areas involved in visual, reward and attentional processing.

However, they used a passive viewing task. In recent magnetoencephalography (MEG) studies, we developed a food-specific working memory task with the potential to explore the relation between food processing and executive functions (17,18). Besides general information related to the processing of food stimuli, we also reported differences in executive functions between lean and obese subjects with differential neuronal activation in visual and prefrontal areas (18). We used the same task to examine overweight and obese subjects before a diet intervention of 6 months. We hypothesized that those participants with the capability to lose weight (responders) and those without (non-responders) would show differential activation patterns mainly in prefrontal areas related to executive functions.

Methods

Study population

We studied a subgroup of an ongoing diet lifestyle intervention program of 6 month. Details on the program are given below. At baseline and after 6 months subjects' weight was determined and they underwent a continuous, incremental exercise test to volitional exhaustion on a cycle ergometer with simultaneous measurement of oxygen consumption (19), which was used as a proxy measure of physical fitness. The value of change in oxygen consumption during the diet was not available for seven subjects. In addition, all subjects participated at baseline and follow-up in a measurement of total adipose tissue using magnetic resonance techniques as described previously in Machann et al. (20). Values of two subjects were not available. Furthermore, subjects completed the German version of the three factor eating questionnaire (TFEQ) with factors cognitive restraint, disinhibition, and hunger at baseline. Scores of one subject were not available (21).

Forty subjects (out of 150) of the lifestyle intervention participated in an additional MEG recording, which was performed before the start of the lifestyle intervention.

MEG-recordings were excluded from further analysis when performance or the number of artifact free trials was too low (below 65% per condition). Therefore, 33 subjects entered the next analyses steps. These subjects had a BMI between 26 and 40 kg m^{-2} and were between 24 and 69 years old. For further analysis, subjects were separated into three tertiles according to their change in BMI with 11 subjects in each tertile (R—responders, MR—medium-responders, NR—non-responders). We decided on this approach as the overall weight loss was rather low. The separation into tertiles allowed us to focus on differences between subjects that lost a considerable amount of weight and those that didn't lose any or even gained weight.

The protocol was approved by the ethics committees of the medical faculty of the University of Tübingen and informed written consent was obtained from all subjects.

Diet regime

All subjects underwent a lifestyle intervention with the instruction to reduce their daily caloric intake by 400 kcal. Furthermore, all subjects were randomly assigned to one of three arms with additional instructions, as to no further instructions (diet 1), no consumption of red meat (diet 2) or to increase the intake of dietary fiber (diet 3). As BMI change didn't reveal to be statistically significant different between the three diet branches (BMI change (%): diet 1: -1.6 ± 1.9; diet 2: -3.7 ± 3.3, diet 3: -2.1 ± 5.2; $F(2,30) = 0.81$, $P = 0.454$), all subjects were analyzed as one cohort independently of their diet regime (for anthropometric characteristics of the three diet groups refer to Supporting Information Table S1 online). Before and during the intervention subjects were asked to fill in a food consumption questionnaire to determine their caloric intake. The information on caloric intake change during the diet was not available for two subjects.

Stimulus material

The subjects had to perform a one-back visual memory task in which each picture was presented for 1,000 ms with an interstimulus interval of 2,500 ms. During the task 64 food and 64 nonfood pictures, matched for color, size, and complexity, were presented in randomized order. Subjects had to determine whether the currently seen picture belonged to the same category as the previous one (one-back task). If the second picture belonged to the same object category subjects had to push the button with their right index finger (''same'' category—e.g., food–food: FF, and nonfood–nonfood: NN). If the picture did not belong to the same category, subjects had to push the button with their right middle finger (''different'' category—e.g., food–nonfood: FN and nonfood–food: NF) [for a detailed description of the protocol and stimulus material see Stingl et al. (17)]. Stimulus presentation was controlled with Presentation® (Neurobehavioral Systems, Albany, CA).

Data acquisition and analysis

After an overnight fast, MEG recordings started at $\sim$ 8 am. Before the recording, subjects rated their current feeling of hunger on a 10 cm visual analogue scale (VAS). All subjects were normal sighted or had corrected-to-normal vision. MEG signals were recorded using a 275-sensor whole head system (VSM, Medtech, Vancouver, Canada). Three coils generating magnetic fields were attached at three fiducial points (nasion, preauricular points on each side) of the subjects' head to continuously record the head position in relation to the MEG

sensor array. Only recordings with a maximum movement below 1 cm were further analyzed. The continuous recording was filtered offline with a 40 Hz low-pass and a 1 Hz high pass filter and separated into trials of 550 ms length (from -100 ms to 450 ms) according to the stimuli (FF, FN, NF, NN). The baseline of each trial was defined based on the activity during the prestimulus interval of 100 ms. All trials with eye movement artifacts (detected by threshold criteria) were excluded from further analysis. The number of trials per study condition was between 42 and 64. The trials were averaged for each subject and an average over all subjects per group was calculated for each experimental condition. In addition, an average of all conditions was calculated for each subject and again averaged over all subjects per group. For sensor analysis the responses were quantified by the root mean square values (RMS) of all channels of the evoked potentials in the time window between 0 and 450 ms. The MEG response was determined by the average RMS value of a 20-ms time interval at four magnetic evoked components: M1-A, M1-B, M2, and M3 (Stingl et al. (17); 123 ms, 162 ms, 251 ms, 355 ms).

Neuronal sources generating activation differences between responders and non-responders were localized with SPM8. A standard template cortical surface was transformed to match the fiducials of the MEG data (22). The sensor locations were registered to source space and a single shell head model was used to compute the gain matrix. For the inversion algorithm we used a minimum norm solution (23). The time window of the source reconstruction included the entire 450 ms after stimulus onset. The source activation was calculated for all conditions and each subject independently. For the second level analysis we applied a spatial filter of 12 mm.

Statistical analysis

Task-related group effects report differences between responders (R) and non-responders (NR). All dependent variables, including accuracy of response, reaction times (RT) and magnetic evoked components (independent analysis for each component) were analyzed using a three-way repeated measure analysis of variance (ANOVA). Two within factors, which were ''preceding stimulus'' (levels food and nonfood) and ''current stimulus'' (levels food and nonfood), and one between factor ''BMI change'' (levels: R and NR) were included. To evaluate the correlation between neuromagnetic responses and BMI change, we performed a two-sided Pearson correlation between RMS values averaged over all conditions and BMI change in percent of the initial BMI including all subjects at time points that were significantly different between responders and non-responders. Statistical analysis was performed with SPSS 20.0 (SPSS, IL) and Matlab (2008b, Mathworks, Natic, MA), results with $P < 0.05$ were considered significant.

For source space, we calculated statistical parametrical maps in a full factorial design for the entire 450 ms after stimulus onset with two within factors ''preceding'' stimulus (levels: food and nonfood) and ''current stimulus'' (levels: food and nonfood) and one between factor ''BMI change'' (levels: R and NR) to extract the source of the difference in neuronal activity between responders and non-responders. We only report activations significant at a level of $P < 0.01$ (uncorrected).

Results

Subject characteristics and BMI change

The lifestyle intervention program led to an average BMI decrease of −2.47% after 6 months (range: −11.2% to +4.2%), which corresponds to an average weight loss of −2.31 kg (range: −12.0 kg to +3.7 kg). For further analysis, subjects were separated into three tertiles according to their change in BMI. These represent people who gained weight (NR—non-responders, BMI change: 0.2 to 4.2%), who lost very few weight (MR—medium-responders, BMI change: −3.1 to −0.4%) and who reduced their BMI by at least 3.5% (R—responders, BMI change: −11.2 to −3.5%). The characteristics of these groups are displayed in Table 1. There were no significant differences in age, baseline BMI, or gender. However, change in total adipose tissue mass was significantly different between all groups and was positively correlated with change in BMI ($r = 0.849$, $P < 0.001$, corrected for age and baseline BMI: $r = 0.847$, $P < 0.001$; $n = 31$). In addition, change in BMI was significantly correlated with change in total caloric intake during the 6 month of lifestyle intervention ($r = 0.449$, $P = 0.011$, corrected for age and baseline BMI: $r = 0.510$, $P = 0.005$; $n = 31$), with a reduction of caloric intake by 26% for responders and by only 15% for non-responders and medium-responders. Whereas, the TFEQ factors disinhibition and hunger weren't significantly different between groups, cognitive restraint revealed a trend for statistical significant difference ($F(2,29) = 2.81$, $P = 0.077$) with responders and medium-responders showing higher scores than non-responders. Furthermore, change in BMI was not significantly correlated with change in maximal oxygen consumption ($r = -0.129$, $P = 0.530$, corrected for age and baseline BMI: $r = -0.083$, $P = 0.699$; $n = 26$). In addition, there was no significant difference in BMI change between genders ($t(31) = 0.41$, $P = 0.69$; mean man: −2.16%, mean women: −2.73%) nor was it significantly related to age ($r = -0.23$, $P = 0.2$; $n = 33$). In the following, for group effects, we focused on the difference between responders and non-responders.

MEG data—behavioral results and RMS

There were no significant group differences in performance for accuracy of response ($F(1,20) = 0.14$, $P = 0.71$) and reaction time ($F(1,20) = 0.4$, $P = 0.54$). However, we observed a sustained difference in the root mean square values of the evoked magnetic components over time in all conditions between weight loss responders and non-responders. A three way repeated measure ANOVA (between factor: BMI change, within factors: preceding and current stimulus) revealed significant main effects for BMI change for M2 ($F(1,20) = 6.08$, $P = 0.023$) and M3 ($F(1,20) = 5.17$, $P = 0.034$). There was no significant interaction between BMI change and the within conditions at any component. Therefore, we combined all four stimulus conditions (FF, FN, NF, NN) for further analyses on sensor level. Figure 1A and B display the root mean square values of the combined conditions for responders and non-responders. Non-responders showed significantly higher RMS values at M2 and M3. A regression analyses with all 33 subjects showed a significant positive correlation between change in BMI and RMS at M2 ($r = 0.384$, $P = 0.027$; corrected for age and baseline BMI: $r = 0.37$, $P = 0.042$; Figure 1C), but, not at M3 ($r = 0.288$, $P = 0.104$). The same correlation with RMS at M2 was obtained on trend level for change in total adipose tissue mass measured by whole body MRI ($r = 0.359$, $P = 0.053$, corrected for age: $r = 0.346$, $P = 0.061$; $n = 31$).

MEG source analysis

For investigation of differences at the source level between responders and non-responders, we calculated statistical parametrical maps with a full factorial design. The factor BMI change revealed higher

TABLE 1 Subjects' characteristics

	Responders	Medium-responders	Non-responders	*P* value[a]
N (f m^{-1})	11 (6/5)	11 (7/4)	11 (5/6)	0.91
Age (years)	45.5 ± 10.4[b]	39.1 ± 10.3	40.4 ± 13	0.39
BMI baseline (kg m^{-2})[c]	31.2 ± 2.6	32.2 ± 3.8	29.6 ± 2.1	0.12
BMI change (%)	−6.9 ± 2.6	−1.9 ± 1.0	1.4 ± 1.1	<0.001[d]
Total adipose tissue mass baseline (kg)	33.9 ± 9.7	36.4 ± 9.2	28.9 ± 4.0	0.11
Change in total adipose tissue mass (%)	−15.1 ± 10.0	−4.6 ± 4.8	2.3 ± 3.9	<0.001[d]
Caloric intake baseline (kcal)	2679.7 ± 437.8	2388.2 ± 579.7	2429.5 ± 502.6	0.42
Caloric intake change (%)	−26.0 ± 13.3	−14.9 ± 18.7	−15.4 ± 17.7	0.26
Hunger rating (cm)	3.5 ± 3.1	2.9 ± 2.1	2.2 ± 1.8	0.46
TFEQ cognitive restraint[e]	7.5 ± 1.7	8.1 ± 4.2	5.2 ± 2.5	0.08
TFEQ disinhibition	8.0 ± 2.7	7.8 ± 2.7	7.3 ± 3.1	0.83
TFEQ hunger	4.9 ± 2.3	6.4 ± 3.1	5.0 ± 3.1	0.43

[a]A one-factorial ANOVA was used for statistical analyses of continuous data and a chi-square analysis for categorical data.
[b]Data are presented as mean ± SD (all such values).
[c]BMI: body mass index.
[d]Post hoc tests showing significant differences between all groups, $P < 0.05$ (two-tailed *t* test).
[e]TFEQ: Three factor eating questionnaire.

activity in left occipital visual areas and right inferior frontal gyrus for non-responders and higher activity in right temporal regions for responders (Table 2, Figure 2). Increased activation in right inferior frontal gyrus for non-responders was also observed in regression analysis including all 33 subjects (for detailed information about source regression analysis refer to Supporting Information Figure S1 online).

Discussion

In this study, we investigated how successful (responders) and unsuccessful weight losers (non-responders) during a lifestyle intervention differ in their neuronal activity during a food specific working memory task before the start of this intervention program. As expected, neuronal activity prior to the intervention was significantly associated with change in BMI during the following 6 months program. We detected this association on the sensor as well as on the source level. Areas on the source level included left occipital visual, right inferior frontal and right temporal regions.

At the sensor level, the RMS values were higher for non-responders over the investigated time and reached statistical significance at the later components (>200 ms after stimulus presentation). The source analysis revealed that this increased activity on sensor level was generated by increased activity in right inferior frontal gyrus (rIFG) in the prefrontal cortex (PFC) and left occipital visual areas in non-responders.

Different subregions of the PFC are considered to be crucial for executive functions (24). The rIFG is involved in cognitive control mechanisms like response inhibition and attentional control (25). rIFG activity is necessary for successful inhibition of motor responses which require the detection of salient or task relevant cues for an adequate response selection (26). This indicates a role for the rIFG in monitoring target or cue events and the subsequent updating of the following action plan/response selection. This mechanism might also be important in working memory to keep target/object representations active (27).

The present results imply that non-responders have to recruit rIFG and visual areas to a greater extent than responders to adjust their monitoring capacity and to reach the same level of cognitive control and performance during the task. This might be related to a decreased ability in implementing cognitive control over their food intake. This is supported by the observation that responders show a tendency for higher scores on the TFEQ scale cognitive restraint. High scores on this scale characterize individuals with strong cognitive control over their eating behavior. Further support is provided by our finding that BMI change was correlated to change in food intake and not to change in maximal oxygen consumption as a proxy for physical fitness. In addition, change in total adipose tissue mass was correlated with BMI change and both measures showed the same correlation with brain activity at the magnetic component M2. This argues for BMI change being mostly due to loss of adipose tissue by restriction in caloric intake and thus, by control over food intake and not due to increased muscle mass. The observation that food monitoring is important for successful maintenance of weight loss has been reported by other studies (28).

Furthermore, we observed increased activity for successful dieters in mainly right medial and inferior temporal regions including hippocampus and fusiform gyrus. Inferior temporal regions are part of the ventral visual processing pathway, which is important for the perception of object identity (29). In the visual working memory task these regions are suited for processing and representation of information about perceived objects and in addition, have been shown to be critical for short-term maintenance of information about these objects (30). In the traditional view, the hippocampus is crucial for formation of long-term memories, as patients with lesion in the temporal lobe

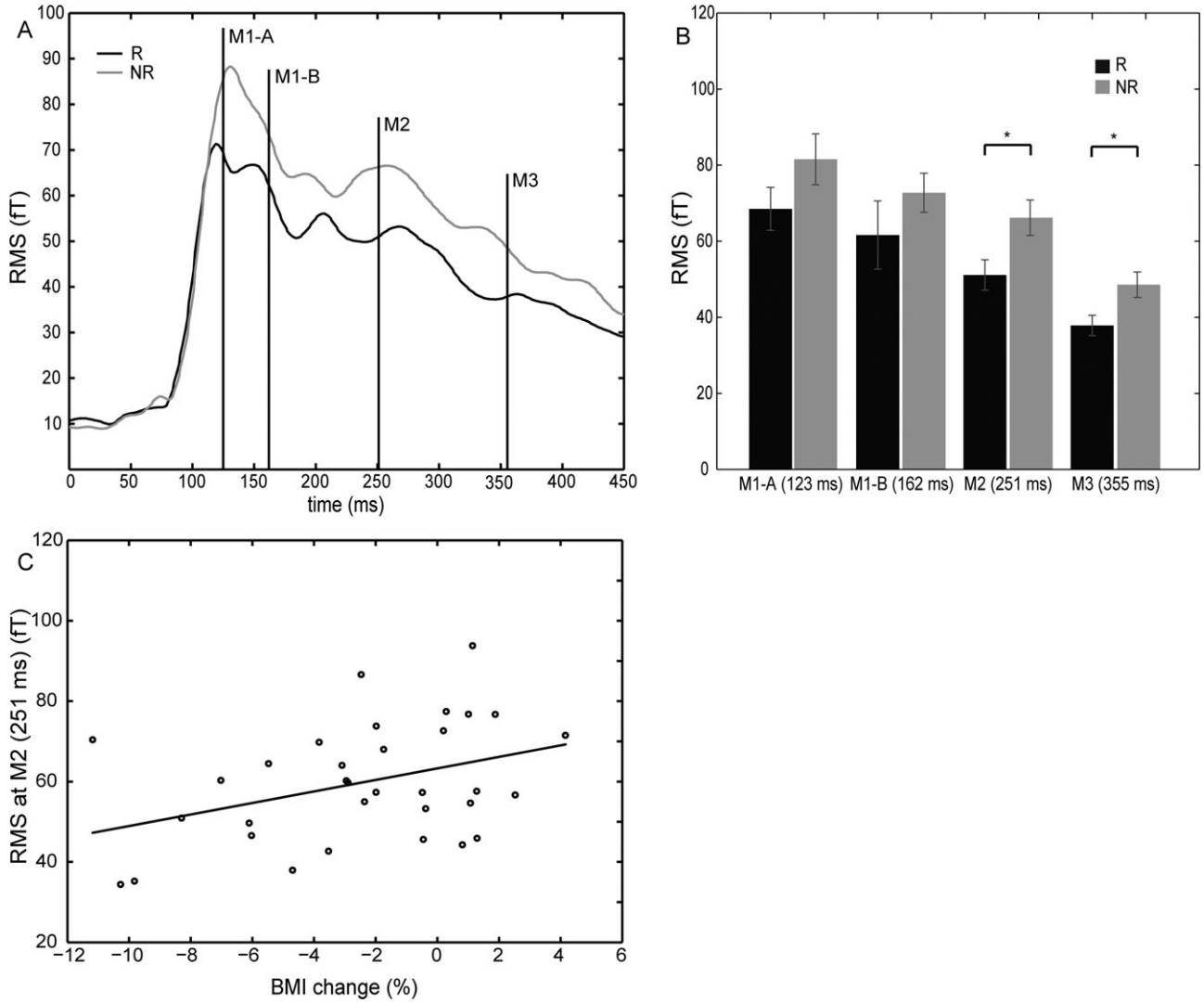

FIGURE 1 Differences between RMS (root mean square) values on sensor level between responders (R) and non-responders (NR) during the lifestyle intervention (**A**,**B**) and significant correlation between RMS values and percentage in BMI change over all participating subjects (**C**). **A**: Waveforms of the grand average magnetic field including all conditions for R-black and NR-grey. M: magnetic evoked component. **B**: Mean and standard error for R-black and NR-grey of the magnetic evoked components marked in A including all conditions. **C**: Correlation between RMS at 251 ms and BMI change ($r = 0.384$, $P = 0.027$). (*$P < 0.05$).

show impaired performance on tasks of long-term, but not of working memory (31,32). Furthermore, responders showed higher activity in right temporal operculum. This is in accordance with Batterink et al. (15), who observed a correlation between stronger activation in left temporal operculum and decreased weight gain after 1 year.

For a successful weight loss response, monitoring of food cues for subsequent action selection regarding food intake and keeping track of the consumed calories to ensure compliance to an eating schedule are of crucial importance. Responders seem to recruit more memory resources, thus, they might have a stronger representation of what they already ate. It has been observed that amnesic patients with lesions in their temporal lobe including hippocampus are susceptible to hyperphagia (33). If presented a second meal just minutes after the first one, both of them will be consumed without changes in the rating of hunger. Furthermore, hyperphagia is reported in some patients suffering from dementia (34). For normal weight subjects it has been shown that manipulation of the most recent meal affects subsequent food intake, suggesting that information about recent eating in memory is considered in current decisions about food consumption (35). Therefore, food intake in the short-term is decreased by enhancing memories of a prior meal and increased by disruption of encoding or retrieval of these memories via distraction or damage to important brain structures. The individuals' ability to encode or retrieve memories of recent food intake are probably also related to long-term energy consumption and might thus, contribute to their capability to restrict caloric intake.

In a recent study, we showed that individuals with high sensitivity of the brain for the postprandial hormone insulin before the start of a lifestyle intervention lost more weight during the following intervention program compared to participants who were less insulin

TABLE 2 Clusters of significant different activations between responders and non-responders (shown in Figure 2)

Brain region	Side	Coordinates			Cluster size (in voxels)	*Z*	*P* (uncorr.)
		x	*y*	*z*			
Non-responder > Responder							
Middle occipital gyrus	L	−40	−82	18	1210	3.20	0.001
Inferior frontal gyrus	R	54	4	20	362	2.93	0.002
Responder > Non-responder							
Superior temporal gyrus	R	54	−10	−10	474	3.27	0.001
Fusiform gyrus	R	52	−14	−28	144	2.89	0.002
Hippocampus	R	36	−20	−14	142	2.77	0.003
Inferior temporal gyrus	R	42	−54	−12	299	2.75	0.004
Insula	R	38	−12	−4	50	2.73	0.004
Heschl gyrus	R	42	−22	10	57	2.71	0.004
Fusiform gyrus	L	−36	−20	−28	146	2.59	0.006
Insula	R	38	−28	20	16	2.51	0.007

sensitive or even insulin resistant in the brain (36). In the current study, we did not assess cerebral insulin sensitivity, but the subjects' brain response in a working memory task. However, there is a strong connection between insulin action and memory pointing to improved memory formation by insulin (37). This makes it tempting to speculate that increased insulin action enhances memory representations that lead to a reduction in subsequent caloric intake.

Finally, several other studies showed that differences on the behavioral and neuronal level between lean and obese or between people who lost and gained weight were mostly food specific in the sense that they were observed when participants viewed food pictures and not when they viewed neutral pictures (14,16). In our study, we could not replicate this food specific group difference. One reason might be that in a memory task, as used in the current study, subjects need to remember in every trial the previous trial. This implies that in almost all trials either the previous or the current stimulus is a food stimulus. Therefore, the subject continuously is confronted with food related stimulation. This means that the cognitive control and memory mechanisms, which we showed to differ in this task, constantly have to deal with food. Furthermore, it might be argued that our finding is not food specific per se, but rather, that non-responders show changes in executive function in general and that these manifest themselves in reduced control over food intake. In this context, a one-back memory task might also have been too easy to elicit differences between food and nonfood trials. In addition, it should be considered that this study includes a rather small sample size that might have reduced the power to see specific food effects. Finally, we neither controlled for the menstrual cycle, although it has been suggested to influence neuronal responses to food stimuli

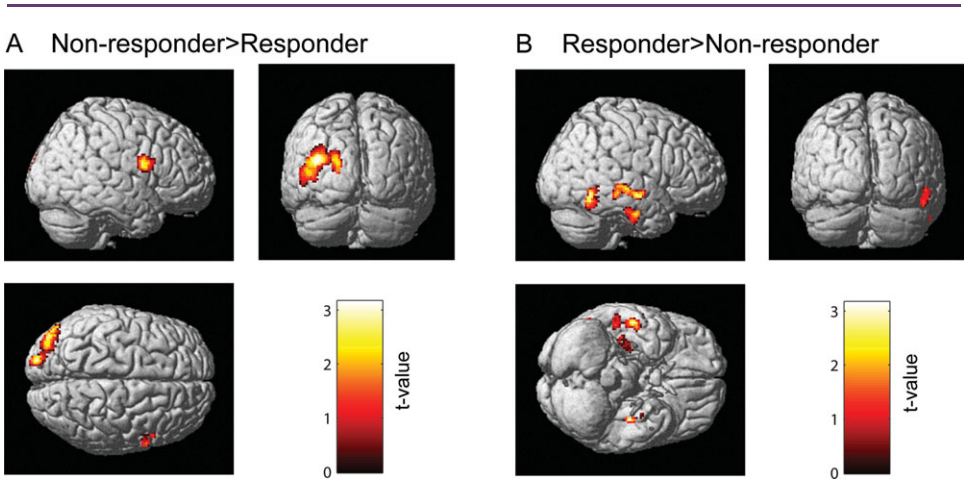

FIGURE 2 Main effect of BMI (body mass index) change for the period 0–450 ms. **A**: Areas showing stronger activity for non-responders, including left occipital visual areas and right inferior frontal gyrus; **B**: Areas showing stronger activity for responders, including right temporal regions. Cortical activity was rendered onto the surface of a standard anatomical brain volume (Montreal Neurological Institute). All regional activations above initial significance threshold $P < 0.01$ (uncorrected).

(38), nor for handedness in our subjects. These limitations should be considered and taken into account in future studies.

In summary, the results of this study are in line with the finding of Murdaugh et al. (16) that initial differences in brain activation can predict change in weight during a lifestyle intervention. However, they extend the findings by indicating that not only visual processing of food stimuli per se, but also cognitive control mechanisms possibly related to control over food intake are already different before the start of a lifestyle intervention. So far, indications for a crucial role of executive functions in weight control were mainly obtained by comparisons between lean and obese individuals as a group, by the comparison of successful weight losers and nondieting controls, or by prediction of weight gain (10-15). We now showed that equally obese individuals differ among each other in their recruitment extent of executive function and memory related areas and that these differences might determine their ability to successfully participate in lifestyle interventions and eat less. Furthermore, our results point out mechanisms in the brain that could explain why some individuals fail to respond to such programs. In a next step, these findings have to be replicated in a larger cohort and changes of brain responses during the diet have to be investigated. In the current study, a small number ($n = 25$) of subjects was available for a post diet investigation. These data showed a more pronounced change in brain response for responders. However, due to the small sample size, validity is limited and further exploration of these changes is required in future studies. As a final step, the major issue will be whether brain activation provides valid biomarkers for successful weight reduction in obese and whether strategies to alter brain activation can support weight loss (39). In particular, future studies should explore whether executive function training as for example training of memory performance prior to a lifestyle intervention can improve cognitive control over food intake and therefore, weight loss. So far, Staiano et al. (40) showed for overweight and obese adolescents that improvement of executive function skills was significantly correlated with weight loss during a lifestyle intervention. However, this has to be explored in greater detail and investigations of an adult population have to follow. O

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