



Contents lists available at ScienceDirect

Physiology &amp; Behavior

journal homepage: [www.elsevier.com/locate/phb](http://www.elsevier.com/locate/phb)

## Modulation of attentional networks by food-related disinhibition

Maike A. Hege<sup>a,\*</sup>, Krunoslav T. Stingl<sup>b</sup>, Ralf Veit<sup>a,f</sup>, Hubert Preissl<sup>a,c,d,e</sup>

<sup>a</sup> Institute for Diabetes Research and Metabolic Diseases of the Helmholtz Center Munich at the University of Tübingen, German Center for Diabetes Research (DZD e.V.), Tübingen, Germany

<sup>b</sup> Pupil Research Group at the Centre for Ophthalmology, University of Tübingen, Tübingen, Germany

<sup>c</sup> Institute for Diabetes and Obesity, Helmholtz Diabetes Center, Helmholtz Zentrum München, German Research Center for Environmental Health (GmbH), Neuherberg, Germany

<sup>d</sup> Department of Internal Medicine, Division of Endocrinology, Diabetology, Angiology, Nephrology and Clinical Chemistry, Eberhard Karls University Tübingen, Tübingen, Germany

<sup>e</sup> Institute of Pharmaceutical Sciences, Department of Pharmacy and Biochemistry, Interfaculty Centre for Pharmacogenomics and Pharma Research, Eberhard Karls University Tübingen, Tübingen, Germany

<sup>f</sup> Institute of Medical Psychology and Behavioural Neurobiology, University of Tübingen, Tübingen, Germany

### HIGHLIGHTS

- A food-related version of the attention network task is introduced.
- Higher disinhibition was associated with rapid reorienting and an enhanced alerting effect.
- Activation of right-lateralized ventral attention network during reorientation
- Disinhibition was related to activation strength of this ventral attention network.
- Alerting contrast showed activation in visual, temporo-parietal and anterior sites.

### ARTICLE INFO

#### Article history:

Received 7 November 2016

Received in revised form 16 February 2017

Accepted 17 February 2017

Available online xxxx

#### Keywords:

fMRI

Disinhibition

Food

Reorienting

Alerting

### ABSTRACT

The risk of weight gain is especially related to disinhibition, which indicates the responsiveness to external food stimuli with associated disruptions in eating control. We adapted a food-related version of the attention network task and used functional magnetic resonance imaging to study the effects of disinhibition on attentional networks in 19 normal-weight participants. High disinhibition scores were associated with a rapid reorienting response to food pictures after invalid cueing and with an enhanced alerting effect of a warning cue signaling the upcoming appearance of a food picture. Imaging data revealed activation of a right-lateralized ventral attention network during reorienting. The faster the reorienting and the higher the disinhibition score, the less activation of this network was observed. The alerting contrast showed activation in visual, temporo-parietal and anterior sites. These modulations of attentional networks by food-related disinhibition might be related to an attentional bias to energy dense and palatable food and increased intake of food in disinhibited individuals.

© 2017 Elsevier Inc. All rights reserved.

### 1. Introduction

Attentional control is crucial for rapid selection of sensory information relevant for current goals and to redirect the attentional focus when novel stimuli are potentially threatening or rewarding. Of special importance from an evolutionary approach are the detection, evaluation and consumption of food. Visual food stimuli interact with the brain's reward system and trigger attentional capture and motivated behavior to secure food intake. With the increased exposure to energy dense and palatable food over the last decades, these basic cognitive

processes probably contributed to the increased prevalence of obesity. Consumption of palatable food is associated with reward and pleasure, which is mediated by the mesocorticolimbic dopamine system [1]. According to the incentive sensitization theory originally developed for drug addiction, frequent pairings of reward from food intake and cues predicting food intake lead to a hyper-responsivity of this system to food cues, resulting in an attention bias, craving, and over-eating [2].

In line with this theory, several studies provide evidence for an increased attentional bias to food words and pictures in obese individuals [3–6], while others fail to do so (for reviews refer to Nijs and Franken [7], Doolan et al. [8], and Hendrikse et al. [9]). In this regard, it should be considered that attention is a heterogeneous concept and has thus been separated into different subdomains. Therefore, possible causes for the different findings may relate to methodological differences of

\* Corresponding author at: IDM, University of Tübingen, Otfried-Müller-Straße 47, 72076 Tübingen, Germany.

E-mail address: [maike.hege@med.uni-tuebingen.de](mailto:maike.hege@med.uni-tuebingen.de) (M.A. Hege).

the studies like the investigation of different components of attention. They may, however, also relate to individual differences in traits describing eating behavior and food responsiveness.

The factor disinhibition of the three factor eating questionnaire (TFEQ) [10] is considered to measure responsiveness to food stimuli such as the sight or smell of food and associated vulnerability to disruptions in eating control especially in response to environmental cues in combination with a weak satiety response and emotion-based eating [11,12]. The factor is strongly related to BMI, energy intake, and prospective weight gain and might thus be very important not only in the maintenance, but also in the development of overweight [11–15]. Consequently, disinhibition is not only related to over-eating in overweight populations, but already affects eating behavior in normal-weight individuals. For instance, it was shown that normal-weight participants with high disinhibition scores consumed more food (ice cream) than those with low disinhibition scores [16,17]. Disinhibition might thus be considered a risk factor for increased food intake and associated future weight gain already in a normal-weight population. Therefore, investigating the relationship between food-related disinhibition and attentional networks in normal-weight individuals can contribute to the understanding of the development of obesity.

It is conceivable that this increased responsiveness to external food cues leading to increased food intake is associated with an attentional bias to food cues observed in some individuals. In this context, it was reported that individuals scoring higher on the factor 'external eating' from the Dutch eating behavior questionnaire (DEBQ) [18], which is also considered to be associated with overeating in response to external food cues, showed an increased attentional bias to visual food stimuli as assessed by a pictorial version of the visual probe task [19,20]. In a recent study, a similar task was used in combination with the TFEQ disinhibition scale and an attentional bias to energy dense food was again reported to be largest in the group high in disinhibition [21]. Furthermore, it was shown that the tendency towards disinhibited eating was associated with greater attention to food versus non-food pictures in a priming and working memory task [22]. The aim of our study was to explore how individual disinhibition scores modulate attentional networks in the presence of food stimuli not only on the behavioral, but also on the neural level. Furthermore, we aimed to investigate whether different components of attention would be affected differently by disinhibition.

Literature exploring the neural correlates of attentional modulation by food-related cues is rather limited. The largest part represents studies that reported modulation of attention related brain areas when participants were presented with palatable food (e.g. [23–27]). Apart from that, Yokum et al. [28] employed a task that was specifically designed to extract different attentional networks and investigated the neural correlates of attentional bias to food cues in adolescent girls. They showed by using a food-related version of the attention network task (ANT) that during initial orientation to food cues, body mass index (BMI) correlated positively with activation in brain regions related to food reward and attention.

The ANT is designed to assess neural networks of different aspects of visuospatial attention simultaneously [29]. Evidence for different components of attention that perform different but interrelated functions with specific contributing brain networks has also been provided by several other studies. These components include alerting, orienting and executive control of attention [29–33]. In the current study, we focused on the investigation of the alerting and orienting components of attention in a food-related context. We designed a functional magnetic resonance imaging study with a food ANT based on designs by Yokum et al. [28] and Fan et al. [34]. We were interested in the question which specific subcomponents of attention would relate to food-related disinhibition in a sample of healthy, normal-weight individuals. This might help in understanding the increased responsiveness to food cues of individuals with high disinhibition, which is probably related to

the increased energy intake and the risk for future weight gain associated with this trait.

In particular, we aimed to disentangle the specific influence of disinhibition on goal-directed (top-down) and stimulus-driven (bottom-up) aspects of attentional control and brain networks.

In this regard, it has been suggested that orienting of attention to external stimuli mainly involves two brain systems [30]. When a spatially informative cue is given, activation of a dorsal system including the frontal eye fields (FEF) and the intraparietal sulcus (IPS) redirects attention in a goal-directed (top-down) manner to the respective location in space [35–37]. A more ventral, mostly right-lateralized system involving the temporo-parietal junction (TPJ) and the ventral frontal cortex is activated when the target was mislocated and allows reorientation and detection of behaviorally relevant salient sensory events (bottom-up) [35,38–40]. This ventral reorienting network is considered to interact with the dorsal orienting system to interrupt and reset ongoing activity to redirect the focus of attention to salient events [30,31]. In the ANT, goal-directed orienting can be induced by providing the participants with a spatially informative cue indicating the location where the target stimulus will appear. Providing an invalid spatial cue that wrongly indicates the target location will require interruption of the dorsal orienting system and stimulus-driven reorienting of attention to the actual position of the target.

As disinhibition measures reward responsiveness to food and the tendency to eat opportunistically in response to food cues in the environment, it rather assesses the impact of exogenous cues on eating behavior control than volitional control on eating behavior. Consequently, we hypothesized on the behavioral level that disinhibition would modulate the stimulus-driven reorienting response time by increasing the reorienting speed to the presented appetizing food stimuli and not the top-down controlled orienting response time. We expected this behavioral effect of faster reorienting to be associated with changes in the activity level of the ventral attention network.

Finally, we aimed to investigate whether disinhibition could modulate the alerting system. Alerting is defined as achieving and maintaining a state of high sensitivity to incoming stimuli and is strongly associated with activity in the locus coeruleus and the neuromodulator norepinephrine with projections to the frontal cortex and parietal areas related to the dorsal visual pathway [41,42]. In the ANT, a spatially uninformative cue is used as a warning signal prior to the target event to induce a phasic increase in alertness. We hypothesized that individuals with increased disinhibition scores would have a higher level of alertness to food cues and thus show a stronger alerting effect, which would be related to changes in the activity level of brain areas associated with the alerting system.

## 2. Material and methods

### 2.1. Participants

21 young, healthy adults with no self-reported eating disorder or diabetes participated in the study. One participant had to be excluded due to head movements and one participant due to invalid responses. The mean age of the remaining 19 participants (10 women/9 men) was 27 (range: 22–34) years and the mean self-reported BMI was 22 (range: 19–25) kg/m<sup>2</sup>. All participants were right-handed and had normal or corrected-to-normal vision (contact lenses, MR compatible glasses). Recordings started between 2 and 6 pm. Participants were asked to either have breakfast or lunch and afterwards refrain from eating for 4 h before the start of the recordings. Before the recording, participants indicated their current hunger on a 10 cm visual analog scale (0: not hungry at all, 10: very hungry). Furthermore, participants filled in a German version of the three factor eating questionnaire (TFEQ), which measures the factors disinhibition, cognitive restraint and hunger for subjective evaluation of eating behavior [43]. All participants gave written consent

prior to the study. The study was approved by the Ethics Committee of the Medical Faculty of the University of Tübingen.

## 2.2. Study design

Participants rated the stimulus set of 84 food pictures for current wanting ('How much would you want to eat this food right now?') on a scale from 1 to 5 to reduce novelty effects during the scanning. The rating was performed on a laptop. For the fMRI recording, we adapted the ANT reported in Fan et al. [34] and Yokum et al. [28]. The ANT is designed to provide a measure of different attentional networks within a single task. In the present study, attention networks were analyzed with respect to alerting, orienting and reorienting to food pictures. Details of the paradigm are shown in Fig. 1. One trial included a fixation cross, a cue (spatial indicator where the target will appear), another fixation cross and a target food picture. After the initial fixation cross (variable duration of 2000–4000 ms), participants were presented in 70% of the trials with a single arrow (fixed duration of 250 ms) at the position of the fixation cross pointing to the left or to the right side. The direction of the arrows indicated on which side the target would appear. In 15% of the trials, a double arrow indicated that the two sides are equally likely and in 15% of the trials the target appeared without a preceding cue. The cue period followed a second fixation cross (variable duration of 250–1000 ms) before the target image appeared. On single arrow trials, the target image appeared on the side of the arrow (congruent) in 70% and on the opposite side (incongruent) in 30% of the cases. This ratio was chosen to ensure that participants would still expect the target on and orient their attention to the congruent side, but to simultaneously allow for a sufficient number of incongruent trials. On double arrow and no cue trials the target image appeared 50% on each side. To ensure that participants attended to the stimuli, they had to determine whether the picture seen was high (42 pictures including e.g. French fries, pizza, muffins) or low (42 pictures including e.g. salad, vegetables, fruits) caloric, using their thumb and pressing a left button for low and a right button for high caloric pictures. In all pictures, the food was displayed on a white background, they all had the same image dimensions and high and low caloric food images were similar in spatial spectral power (calculated as in Knebel et al. [44]). Our main outcome measure was reaction time; correctness was only evaluated to control for task adherence. We regarded participants with an error rate (also included omissions) below 20% as attentive and included them in further analysis. This resulted in the exclusion of only one participant, who

showed accumulated omissions of responses. The mean error rate for all included participants was 6%. The target was presented for 2000 ms. The experiment consisted of two runs lasting 10 min each and with a combined total of 168 trials with fixed trial order. The order of the runs was randomized across participants. An additional amount of 20% of the trials was included as null events to allow deconvolution of the hemodynamic response function (HRF) [45] and to improve design efficiency for both main and differential effects [46]. During these events no cue or target appeared.

Prior to scanning, participants were familiarized with the fMRI paradigm through practice on a laptop including a separate set of high and low caloric pictures not presented during the main task. During scanning, stimuli were presented visually using Presentation® (Neurobehavioural Systems, Inc., Albany, CA.) and were displayed using a video projector that illuminates a rear projection screen at the end of the head-bore. Participants viewed the stimuli through an adjustable mirror attached to the head coil.

## 2.3. Behavioral analysis

For each participant and condition median reaction times (RT) were calculated for correct responses. For calculation of the respective attention effects, we subtracted the reaction times according to the contrasts described below. For the alerting effect, we subtracted the RTs of the double arrow (bidirectional) cue condition from the RTs of the no cue condition ( $RT_{\text{alerting}} = RT_{\text{no cue condition}} - RT_{\text{bidirectional cue condition}}$ ). Participants exhibiting high values for this contrast (indicating a major difference in RTs between the two conditions) were considered to be more strongly alerted by the warning cue and thus their response speed benefited more strongly from the warning cue in comparison to the no cue condition. Subtraction of the RTs of the congruent directional cue condition from the RTs of the double arrow condition provided the RTs for the orienting contrast ( $RT_{\text{orienting}} = RT_{\text{bidirectional cue condition}} - RT_{\text{congruent directional cue condition}}$ ). Participants with increased spatial orienting of attention in response to the informative directional cue in comparison to the uninformative bidirectional cue should thus exhibit higher values for this contrast. Finally, for the reorienting contrast we subtracted the RTs of the incongruent directional cue condition from the congruent directional cue condition ( $RT_{\text{reorienting}} = RT_{\text{incongruent directional cue condition}} - RT_{\text{congruent directional cue condition}}$ ). Consequently, lower scores for this contrast would indicate a lower reorienting cost (faster reorienting response)

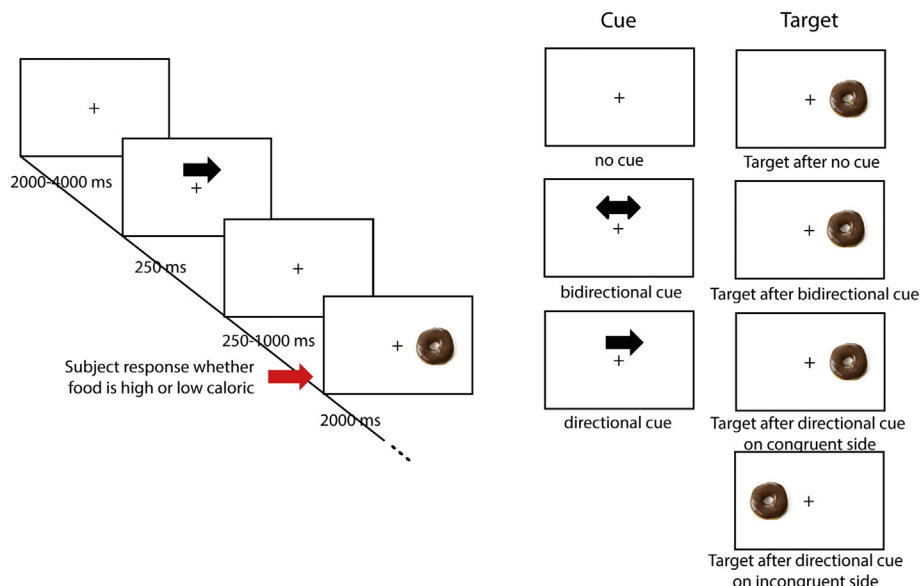


Fig. 1. Illustration of the experimental design.

in response to the wrongly cued position. Participants with short reorienting RTs are considered to need less time to redirect their attention to the actual position of the target.

Behavioral data was analyzed with the software package spss 20.0 (SPSS Inc., Illinois; USA). All data are presented as unadjusted mean  $\pm$  standard error of the mean. Alerting, orienting and reorienting effects were evaluated with two-sided one-sample *t*-tests to test if the average of all the values was different from zero. For correlation analysis between reaction time effects and TFEQ scores two-sided spearman rho correlations were calculated and a *p*-value  $< 0.05$  was considered to be statistically significant. We did not include a correction for multiple testing due to strong a priori hypotheses. Based on our aim to disentangle the influence of disinhibition on brain networks, fMRI data was analyzed only for those specific contrasts that showed a significant correlation with TFEQ-disinhibition scores on the behavioral level (which were the alerting and the reorienting contrast).

#### 2.4. Imaging protocol

Whole brain fMRI data were obtained by using a 3.0 T scanner (Siemens Tim Trio, Erlangen, Germany). Each of the two runs consisted of 300 scans (repetition time = 2 s, echo time = 30 ms, matrix  $64 \times 64$ , flip angle  $90^\circ$ , voxel size  $3 \times 3 \times 3.75 \text{ mm}^3$ , 30 slices), and the images were acquired in ascending order. Furthermore, a high-resolution T1-weighted anatomical image (magnetization-prepared rapid gradient echo (MPRage): 176 slices, matrix  $256 \times 256$ ,  $1 \times 1 \times 1 \text{ mm}^3$ ) of the brain was obtained. In addition, we acquired a static field map to unwarp geometrically distorted functional scans. Participants were scanned while lying in a supine position with their head stabilized by foam padding around their head within the head coil.

#### 2.5. Image processing

Preprocessing and statistical analysis of the fMRI data were performed using SPM8 (Wellcome Trust Centre for Neuroimaging, London, UK). Images were realigned and resliced to the first image after unwarping in the phase-encoding direction (anterior-posterior) to account for susceptibility by movement artifacts using the pre-calculated voxel displacement map for phase correction. A mean image was created and co-registered to the T1 structural image. The anatomical image was normalized to Montreal Neurological Institute (MNI) space, and the resulting parameter file was used to normalize the functional images (voxel size  $3 \times 3 \times 3 \text{ mm}^3$ ): Finally, the normalized images were smoothed with a 3-dimensional isotropic Gaussian kernel [full width at half maximum (FWHM): 10 mm]. fMRI data were highpass filtered (cutoff period 128 s) and global AR (1) auto correlation correction was performed. Participants with movement  $> 1.2 \text{ mm}$  or  $0.5^\circ$  in the residual motion plots were excluded.

#### 2.6. Independent component analysis

ICA is a data-driven method to separate statistically independent brain networks. In some cases, this method has been shown to be more sensitive to differences between participants than standard general linear model (GLM) approaches [47,48] and to isolate activation patterns that cannot be detected by GLM [49]. Group spatial ICA [49] was used to decompose the smoothed, normalized fMRI images into 30 components using the GIFT software (<http://icatb.sourceforge.net>) as follows. To determine the number of components, the dimensionality of the data was estimated using the minimum description length criterion, modified to account for spatial correlation [50]. Data from all participants were then concatenated, and this aggregated data set was reduced to 30 temporal dimensions using principal component analysis, followed by an independent component (IC) estimation using infomax algorithm [51]. A time course for each component and its corresponding spatial map, which represent a real contribution to this component time

course, was obtained. Finally, for each participant, spatial maps were reconstructed and converted to *z*-values. The *z*-values of the spatial maps represent the fit of a specific voxel blood oxygen level-dependent time course to the group-averaged component's time course.

#### 2.7. Component selection

For the Selection of the ICs, fMRI data were analyzed in an event-related design using the GLM approach in a two-level procedure to create masks for spatial sorting. On the first level in the single participant models, responses to stimuli were modeled as events and convolved with canonical hemodynamic response function to account for the lag between event onset and expected increase of the blood oxygenation level-dependent (BOLD) signal. The base functions were a synthetic hemodynamic response function composed of two gamma functions (Friston et al., 1998). To account for variance caused by head movement, six realignment parameters were included as additional regressors in the model. The data from each participant were analyzed by using linear regression between the observed event-related EPI signals and regressors that represent the individual trial events (fixation with no cue, congruent directional cue, incongruent directional cue, bidirectional cue, target after no cue, target on congruent side, target on incongruent side, target after bidirectional cue). The individual contrast images from each participant (alerting: bidirectional cue minus no cue, reorienting: target on incongruent side minus target on congruent side) were then entered into a second level analysis using separate one-sample *t*-tests. Effects were considered significant using a primary threshold at peak level of  $p < 0.001$  uncorrected and a whole-brain family wise error correction (FWE) of  $p < 0.05$  at cluster level for multiple comparisons. Statistical *t*-maps were used as masks for spatial sorting in the Independent Component Analysis (ICA).

Before sorting, we discarded noise-related components that showed spatial correlation  $r^2 > 0.02$  for white matter or  $r^2 > 0.05$  for cerebrospinal fluid. We further ran group ICA 50 times using ICASSO [52] and used the cluster quality index ( $I_q$ ) to validate ICA reliability. In order to examine the relationship between the ICs and the experimental paradigm, a regression was performed on the ICA time courses with the GLM design matrix (in SPM8), which contained 8 regressors (see above). This is referred to as temporal sorting in GIFT. The regression analysis resulted in a set of beta-weights, which represent the degree of synchrony between component and reference time course. Thus, the beta-weights indicate the extent of modulation of a specific component in a given task condition [53]. Positive and negative beta-weights indicate that the network was either positively or negatively modulated by the task. Beta-weights were averaged across the 2 runs for each participant and each regressor. Finally, components were selected by using spatial sorting in GIFT to constrain our analysis to task-relevant components. To achieve this, we used masks determined from the GLM for the alerting and reorienting contrast, respectively.

#### 2.8. Statistical analysis of functional networks

For those contrasts that showed a significant correlation with TFEQ-disinhibition scores on the behavioral level (including the alerting and the reorienting contrast), we selected two components that showed the highest spatial correlation with the masks. For each component, the difference in beta-weights between respective task conditions (reorienting: target on incongruent side-target on congruent side; alerting: double cue- no cue) was calculated. Correlation analysis was performed between the respective delta beta-weights, RT reorienting and RT alerting, and TFEQ factor disinhibition, respectively. For correlation analysis two-sided spearman rho correlations were calculated and a *p*-value  $< 0.05$  was considered to be statistically significant.



### 3. Results

#### 3.1. Behavioral results

There was no significant difference in reaction times between high and low caloric food pictures; therefore, we did not separate between conditions for further analysis. Reaction times for the contrasts alerting (no cue condition-double cue condition), orienting (valid cue condition-double cue condition), and reorienting (incongruent cue condition-congruent cue condition) are displayed in Fig. 2. All of them revealed to be significantly larger than zero ( $t(18) = 2.098, p = 0.05$ ;  $t(18) = 2.929, p = 0.009$ ;  $t(17) = 2.540, p = 0.021$ ). For the reorienting condition one participant was identified as an outlier ( $>3$  standard deviations apart from the mean) and excluded from further correlation analyses for this contrast. Participants stated a medium hunger level (mean:  $5.2 \pm 3.2$  (SD) cm). There were no significant correlations between reaction time contrasts and age, hunger, or BMI measures, respectively.

Regarding the three factor eating questionnaire, we only observed significant correlations between the factor disinhibition and reaction times of the alerting and reorienting contrasts. The scale of the TFEQ factor disinhibition ranges from 0 to 16. Participants included in this study scored from 1 to 14 with a mean score of  $5.7 \pm 4.0$  SD. 10 out of 19 participants scored 4 or lower and thus, exhibited low and very low disinhibition levels. The remaining 9 scored on a medium to very high level of the scale. The alerting contrast showed a positive significant correlation ( $r = 0.582, p = 0.011, n = 18$  (one of the participants was excluded as an outlier due to distance based criteria)) and the reorienting contrast a negative correlation ( $r = -0.585, p = 0.011, n = 18$ ) between delta reaction time and disinhibition score (Fig. 3). Consequently, in the following, we only report findings for the contrasts of reorienting and alerting.

#### 3.2. Imaging results

##### 3.2.1. Reorienting

Reorientation after target presentation on the incongruent side elicited activations in left and right temporo-parietal junction (TPJ) and right lateral medial frontal cortex (Fig. 4, Table 1). These activations were used as a mask for spatial sorting of the ICA components. Components that showed the strongest spatial correlation are displayed in Fig. 7 (A,B). These components involve a right attention and a temporo-parietal attention network [54–56]. In addition, beta-weights indicating the extent of modulation of the ICA components by the different task conditions were calculated as described above.

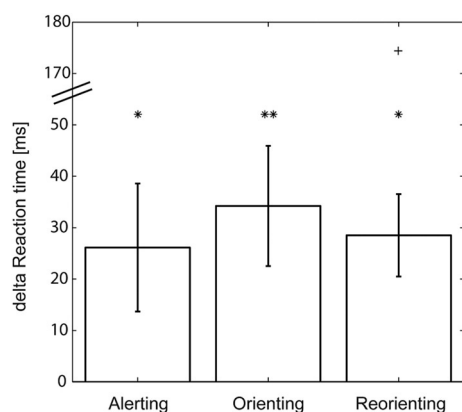


Fig. 2. Reaction times for contrasts alerting, orienting, and reorienting with mean and standard error of the mean. \* $p \leq 0.05$ , \*\* $p \leq 0.01$ , + outlier.

Only the difference between the beta-weights for the target on the incongruent side minus the target on the congruent side of the right attention network was positively correlated with the reaction time for this reorienting contrast ( $r = 0.509, p = 0.031, n = 18$ , Fig. 5A). Furthermore, this difference in beta-weights was negatively correlated with individual TFEQ-disinhibition scores ( $r = -0.482, p = 0.043, n = 18$ , Fig. 5B).

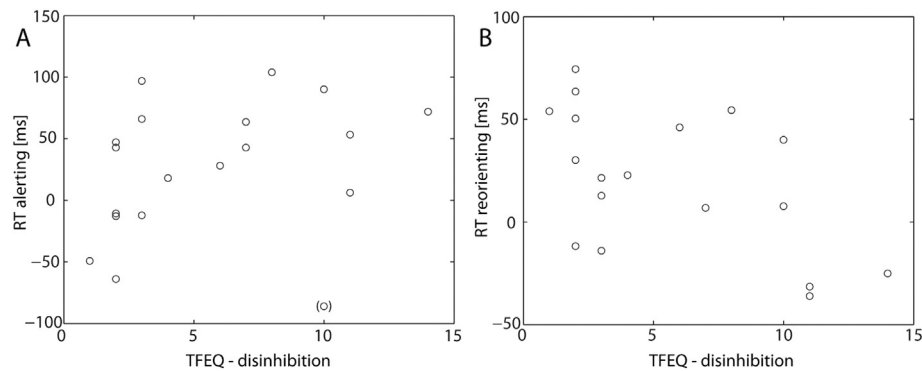
##### 3.2.2. Alerting

A double cue in comparison to the no cue condition elicited activations in right TPJ, left and right precentral/inferior frontal gyrus, and left and right occipital areas (Fig. 6, Table 1). Again, this contrast was used for spatial sorting of the ICA components. In Fig. 7(B,C) the components with the strongest spatial correlation are shown, including a temporo-parietal attention network and a visual network [54,55].

### 4. Discussion

In this study, we investigated the modulation of attentional networks on the behavioral and neural level by food-related disinhibition with an adaptation of the attention network task including food stimuli. For all three investigated attentional components we replicated the behavioral findings reported in the literature, indicating that the attentional manipulation during the different tasks was successful. Furthermore, the alerting and the reorienting contrast, but not the orienting contrast correlated with TFEQ-disinhibition scores. In the ANT, orienting is manipulated by presenting a spatially informative cue that indicates, prior to the presentation of the target, where the participants should direct their attention to. Most spatial cues were valid, randomly interleaved with a low percentage of infrequent invalid ones incorrectly indicating the target location and resulting in reorientation to the new location. As reported previously, participants responded faster when given a spatially informative cue that correctly indicated the location of the upcoming food stimulus in comparison to when given only a spatially uninformative cue. This indicates that they indeed oriented their attention to the cued location. In addition, orienting to the cued location resulted in a behavioral cost when the target appeared on the incongruent side. Thus, participants responded slower after invalid cuing in comparison to valid cuing. Orienting is considered as a top-down controlled, goal-directed behavior and is mediated by the dorsal attention network. Reorienting on the other hand requires the activity of the bottom-up, stimulus-driven ventral attention network that interacts with the dorsal network to interrupt and reset ongoing activity to redirect the focus of attention to relevant but unexpected stimuli [30,31]. In accordance with our hypothesis, disinhibition, which rather assesses the impact of exogenous cues on eating behavior control than volitional controls on eating behavior, only modulated the efficiency of stimulus-driven reorienting and not of top-down controlled orienting. Individuals with higher disinhibition scores took less time to reorient than did individuals with lower scores. Analysis of the reorienting contrast on the brain level showed activation of a right-lateralized network including left and right TPJ and right frontal areas. Activated areas resemble those reported for the ventral attention network involved in reorienting [31,33,56]. The time course of this network was modulated stronger by invalidly than validly cued targets. As expected, the individual differences in this modulation and thus, the strength of the activation of this network in response to reorienting was related to reaction time and the disinhibition score.

These results support the hypothesis that participants with higher disinhibition scores show a faster reorienting response and indicate that this is related to less activation of the attentional reorienting network. This might be related to altered interaction between the dorsal and the ventral attention network. At rest, each network is distinct and internally correlated, however, when attention is focused, the ventral network is suppressed by the dorsal network to prevent redirecting attention to distracting stimuli [57,58]. However, when orientation to



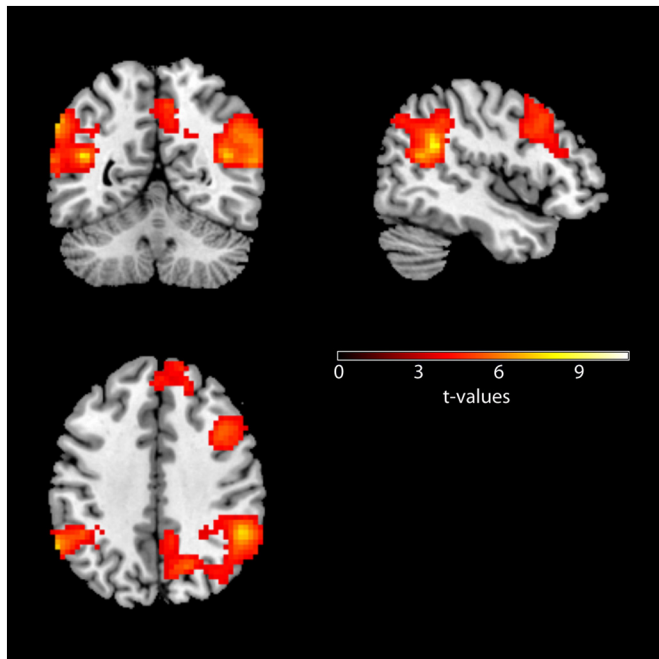
**Fig. 3.** Correlation analyses between three factor eating questionnaire (TFEQ)-disinhibition score and reaction time (RT) of A alerting ( $r = 0.582$ ,  $p = 0.011$ ,  $n = 18$ ) and B reorienting contrast ( $r = -0.585$ ,  $p = 0.011$ ,  $n = 18$ ). (○) outlier.

new salient, behaviorally relevant stimuli is required, the ventral system has been suggested to serve as a circuit-breaker to interrupt and reset ongoing activity to break the current attentional set and adopt a new one [30]. This suggests that individuals with lower disinhibition have a strong attentional focus possibly mediated by the dorsal goal-directed system and therefore, a stronger activation of the ventral stimulus-driven network is required to overcome this control. Consequently, their reorienting response is slower and in real life food stimuli might be less likely to capture their attention.

Besides reorientation to food stimuli, also the reaction time of the alerting contrast was related to disinhibition. A warning cue prior to the target signaled the appearance of a food cue in close temporal proximity. In accordance with our hypothesis, reaction time to the target decreased following the warning cue and the benefit of this cue for the response speed was positively related to high disinhibition. Alerting refers to the ability to prepare and sustain alertness to process incoming stimuli with high priority. As soon as a warning cue is presented, the resting state is replaced with a state which involves preparation for

detecting and responding to the expected target [33]. Brain activations observed in the current study during this preparation were in line with previous findings. Increased activation in both left and right extrastriate areas was also reported by Thiel et al. [59] for a similar alerting contrast. This can be considered as attentional modulation of extrastriate activity by top-down control to prepare for incoming visual information. Furthermore, we observed activation in left and right clusters in precentral gyrus with the right cluster extending to the inferior frontal gyrus and activation of the right temporo-parietal junction. Activation of similar fronto-parietal areas was reported by Fan et al. [34]. Frontal activations particularly of the left side also included areas of the premotor cortex that are involved in planning movements. As participants were required to respond with the right hand this might be related to response preparation. It should, however, also be considered that, although participants were instructed to fixate, the appearance of the cue in comparison to the no cue condition might have resulted in an increase in eye movements. As we did not record eye tracking data, we cannot rule out that the reported activations might be contaminated by eye movements.

Nonetheless, activation of the reported areas has been associated with the alerting system before, as tasks which require different levels of alertness activate frontal and parietal areas predominantly of the right hemisphere [60]. In mediating these activations, the norepinephrine system may play an important role. The norepinephrine pathway has important nodes in the frontal and parietal cortex and acts strongly on the posterior attention system of the right hemisphere [32,42]. This interaction can facilitate the selection of high priority visual information for further processing. In our study, participants expected and prepared for the appearance of the target stimuli with presumable stronger preparation in case of high disinhibition. It is possible that individuals who scored higher on the disinhibition factor assessing food sensitivity

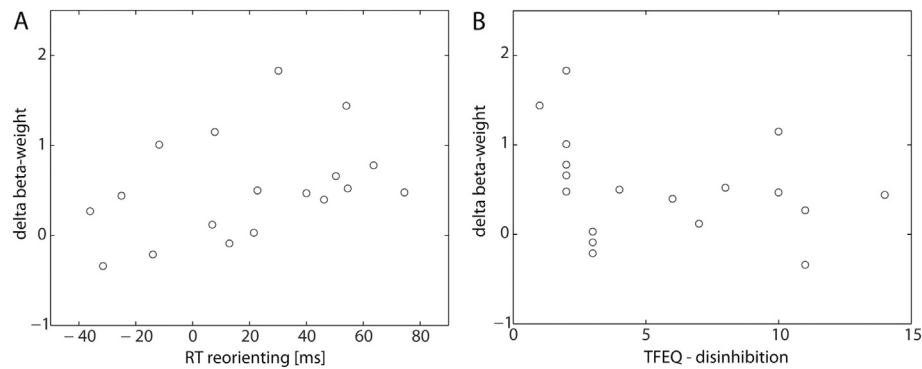


**Fig. 4.** Main effect of the reorienting contrast showing increased activation for targets on the incongruent side in temporo-parietal junction and right middle and lateral frontal areas (color-coded  $t$ -value map;  $p < 0.05$  FWE corrected). This statistical  $t$ -map was used as a mask for spatial sorting in the independent component analysis. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

**Table 1**

Clusters of significant activations for alerting and reorienting contrast.

Brain region	Side	Coordinates			Cluster size (in voxels)	Z	p Value (FWE corr.)
		x	y	z			
<i>Alerting</i>							
Superior temporal gyrus	R	57	−46	16	793	5.22	<0.001
Inferior frontal gyrus	R	45	5	31	288	4.72	<0.001
Inferior occipital gyrus	L	−30	−85	−8	557	4.44	<0.001
Precentral gyrus	L	−45	−1	37	120	4.40	0.012
<i>Reorienting</i>							
Inferior parietal lobule	R	51	−46	28	1109	5.96	<0.001
Superior temporal gyrus	L	−45	−58	19	445	5.16	<0.001
Middle frontal gyrus	R	39	17	40	738	4.50	<0.001



**Fig. 5.** Correlation analysis of the difference between beta-weights of the right attention network for targets on the incongruent minus targets on the congruent side with A showing a positive correlation between delta beta-weights and reaction time (RT) for the reorienting contrast ( $r = 0.509$ ,  $p = 0.031$ ,  $n = 18$ ) and B showing negative correlation between delta beta-weights and the three factor eating questionnaire (TFEQ)-disinhibition score ( $r = -0.482$ ,  $p = 0.043$ ,  $n = 18$ ).

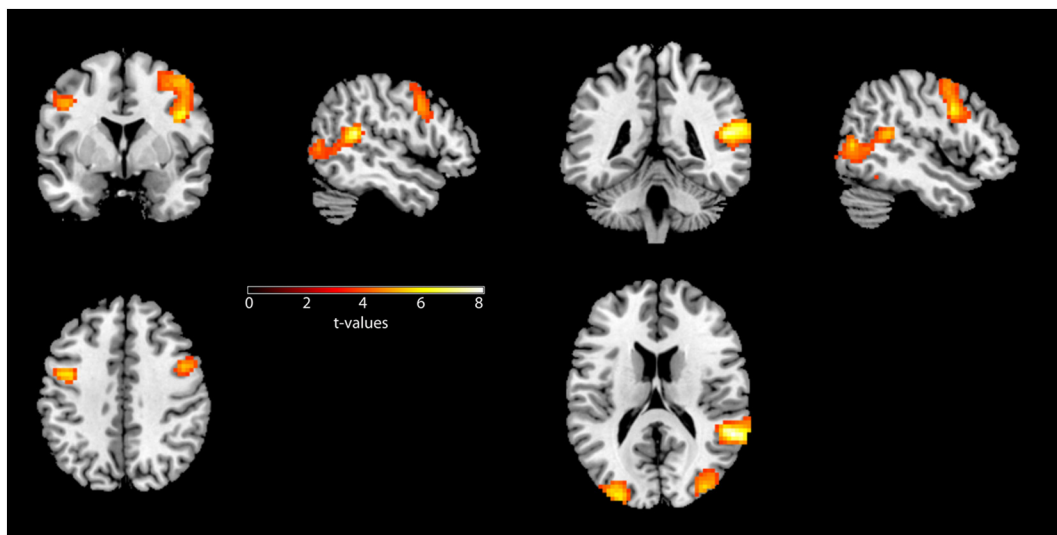
attributed higher value to food cues, which resulted in higher levels of alertness and thus, faster responding to food cues after a warning cue.

However, contrary to our hypothesis we did not observe brain-behavior correlations for this contrast. Thus, further research is needed to elucidate the network interactions that result in the reported behavioral modulations. Furthermore, future research should also include a non-food contrast to compare with. The absence of such a contrast in our study limits the interpretation of our results in the sense that we cannot conclude whether the observed effects are due to interactions with the specific motivational salience of the food stimuli or are due to general changes in attentional networks in disinhibited individuals. That there might actually also be a food specific effect is suggested by some studies using the visual dot probe task [19–21]. In this task, stimulus-driven orienting to a probe replacing a food or a neutral stimulus is measured. Faster responding to a probe replacing a food stimulus in comparison to a neutral stimulus is considered as an attentional bias to food and was reported to be related to higher disinhibition.

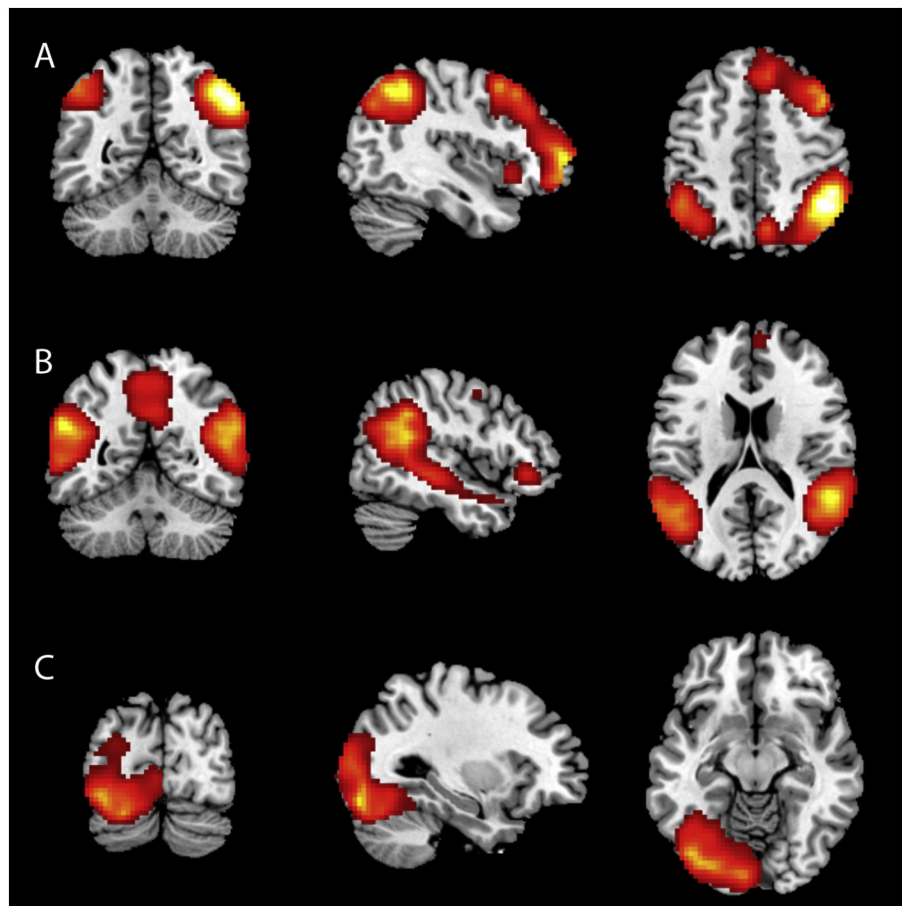
An open question also remains of how the modulation of the attentional networks by disinhibition might be mediated. One possibility is that alterations in the reward system interact with the salience attribution of food stimuli and thus, alter the response of the attention networks. In another study, modulation of areas involved in selective attention by the motivational value of the food target was shown [61].

They further suggested the posterior cingulate cortex to be involved in the interaction between motivation and spatial attention by biasing spatial attention to motivationally relevant events [61,62]. An alternative explanation could be based on the suggestion that an attentional bias to food does not result from increased craving for desired food but from eating-related worries like fear of losing control of eating [4]. These considerations should be addressed in future studies. Furthermore, it would be interesting to investigate in more detail how food specific these effects really are. This relates to the general attempt to explain obesity in the context of personality characteristics and a recent review showing that food-related behavioral tendencies like the disinhibition score are associated with more general personality characteristics like the factor neuroticism of the five factor model ('Big Five') [63,64].

Another limitation of our study is that it only included normal-weight participants with half of them having low disinhibition scores. Investigating whether the results can also be observed in an obese population with higher disinhibition scores might be a better indicator for the significance of the observed effects for actual eating behavior and weight consequences. Finally, we did not include eye tracking in our paradigm, which could have provided a more direct and sensitive measure of attention than indirect inferences of reaction times. Furthermore, it would have allowed us to monitor fixation of the participants to



**Fig. 6.** Main effect of the alerting contrast showing increased activation in the double cue condition in right temporo-parietal junction, in left and right precentral/inferior frontal gyrus and inferior occipital gyrus (color-coded  $t$ -value map;  $p < 0.05$  FWE corrected). This statistical  $t$ -map was used as a mask for spatial sorting in the independent component analysis. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)



**Fig. 7.** ICA components selected by spatial regression showing highest similarity with alerting and reorienting contrast, respectively, with  $p < 0.05$  FWE corrected. A right attention network (reorienting contrast), B temporo-parietal attention network (alerting and reorienting contrast), and C visual network (alerting contrast).

better control for possible contamination of our fMRI results by differences in eye movements between conditions.

In summary, we observed specific modulations of attentional networks by the factor disinhibition that is strongly associated with unhealthy food choices and increased weight. High food-related disinhibition resulted in a rapid reorienting response that was associated with less activation of the ventral attention network involved in redirecting the focus of attention. In addition, it enhanced the alerting effect of a warning cue signaling the upcoming appearance of the target stimulus. These results indicate that individual differences in traits influencing eating behavior interact with the heterogeneous concept of attention, which might explain the contradictory findings concerning attentional biases to food stimuli in the obese population. Detailed knowledge about influencing factors of human eating behavior on different subcomponents of attention might contribute to better control strategies in the prevention of weight gain and in the obese population.

#### Conflict of interest

The authors declare no conflict of interest.

#### Acknowledgments

We thank Maike Borutta for her assistance during the measurements. This study was supported by the Fortune program of the University of Tübingen (grant number F1561120) and by the European Union Seventh Framework Programme (FP7/2007–2013) under Grant Agreement 607310 (Nudge-it).

#### References

- [1] A.E. Kelley, K.C. Berridge, The neuroscience of natural rewards: relevance to addictive drugs, *J. Neurosci.* 22 (2002) 3306–3311.
- [2] K.C. Berridge, 'Liking' and 'wanting' food rewards: brain substrates and roles in eating disorders, *Physiol. Behav.* 97 (2009) 537–550.
- [3] E.H. Castellanos, E. Charboneau, M.S. Dietrich, S. Park, B.P. Bradley, K. Mogg, et al., Obese adults have visual attention bias for food cue images: evidence for altered reward system function, *Int. J. Obes.* 33 (2009) 1063–1073.
- [4] J. Werthmann, A. Roefs, C. Nederkoorn, K. Mogg, B.P. Bradley, A. Jansen, Can(not) take my eyes off it: attention bias for food in overweight participants, *Health Psychol.* 30 (2011) 561–569.
- [5] I.M. Nijs, I.H. Franken, P. Muris, Food-related Stroop interference in obese and normal-weight individuals: behavioral and electrophysiological indices, *Eat. Behav.* 11 (2010) 258–265.
- [6] I.M. Nijs, P. Muris, A.S. Euser, I.H. Franken, Differences in attention to food and food intake between overweight/obese and normal-weight females under conditions of hunger and satiety, *Appetite* 54 (2010) 243–254.
- [7] I.M. Nijs, I.H. Franken, Attentional processing of food cues in overweight and obese individuals, *Curr. Obes. Rep.* 1 (2012) 106–113.
- [8] K.J. Doolan, G. Breslin, D. Hanna, A.M. Gallagher, Attentional bias to food-related visual cues: is there a role in obesity? *Proc. Nutr. Soc.* 74 (2015) 37–45.
- [9] J.J. Hendrikse, R.L. Cachia, E.J. Kothe, S. McPhie, H. Skouteris, M.J. Hayden, Attentional biases for food cues in overweight and individuals with obesity: a systematic review of the literature, *Obes. Rev.* 16 (2015) 424–432.
- [10] A.J. Stunkard, S. Messick, The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger, *J. Psychosom. Res.* 29 (1985) 71–83.
- [11] S.A. French, L.H. Epstein, R.W. Jeffery, J.E. Blundell, J. Wardle, Eating behavior dimensions. Associations with energy intake and body weight. A review, *Appetite* 59 (2012) 541–549.
- [12] E.J. Bryant, N.A. King, J.E. Blundell, Disinhibition: its effects on appetite and weight regulation, *Obes. Rev.* 9 (2008) 409–419.
- [13] V. Boschi, D. Iorio, N. Margiotta, P. D'Orsi, C. Falconi, The three-factor eating questionnaire in the evaluation of eating behaviour in subjects seeking participation in a dietotherapy programme, *Ann. Nutr. Metab.* 45 (2001) 72–77.



- [14] V. Provencher, V. Drapeau, A. Tremblay, J.P. Despres, S. Lemieux, Eating behaviors and indexes of body composition in men and women from the Quebec family study, *Obes. Res.* 11 (2003) 783–792.
- [15] N.P. Hays, S.B. Roberts, Aspects of eating behaviors “disinhibition” and “restraint” are related to weight gain and BMI in women, *Obesity* 16 (2008) 52–58.
- [16] T. Van Strien, A. Cleven, G. Schippers, Restraint, tendency toward overeating and ice cream consumption, *Int. J. Eat. Disord.* 28 (2000) 333–338.
- [17] J. Westenhoefer, P. Broeckmann, A.K. Munch, V. Pudel, Cognitive control of eating behaviour and the disinhibition effect, *Appetite* 23 (1994) 27–41.
- [18] T. Vanstrien, J.E.R. Frijters, G.P.A. Bergers, P.B. Defares, The Dutch Eating Behavior Questionnaire (Debq) for assessment of restrained, emotional, and external eating behavior, *Int. J. Eat. Disord.* 5 (1986) 295–315.
- [19] C. Brignell, T. Griffiths, B.P. Bradley, K. Mogg, Attentional and approach biases for pictorial food cues. Influence of external eating, *Appetite* 52 (2009) 299–306.
- [20] R. Hou, K. Mogg, B.P. Bradley, R. Moss-Morris, R. Peveler, A. Roefs, External eating, impulsivity and attentional bias to food cues, *Appetite* 56 (2011) 424–427.
- [21] C.H. Seage, M. Lee, Do disinhibited eaters pay increased attention to food cues? *Appetite* 108 (2017) 151–155.
- [22] S. Higgs, D. Dolmans, G.W. Humphreys, F. Rutters, Dietary self-control influences top-down guidance of attention to food cues, *Front. Psychol.* 6 (2015) 427.
- [23] K.S. Burger, E. Stice, Elevated energy intake is correlated with hyperresponsivity in attentional, gustatory, and reward brain regions while anticipating palatable food receipt, *Am. J. Clin. Nutr.* 97 (2013) 1188–1194.
- [24] L.E. Stoeckel, R.E. Weller, E.W. Cook 3rd, D.B. Twieg, R.C. Knowlton, J.E. Cox, Widespread reward-system activation in obese women in response to pictures of high-calorie foods, *NeuroImage* 41 (2008) 636–647.
- [25] L.E. Martin, L.M. Holsen, R.J. Chambers, A.S. Bruce, W.M. Brooks, J.R. Zarcone, et al., Neural mechanisms associated with food motivation in obese and healthy weight adults, *Obesity* 18 (2010) 254–260.
- [26] K.T. Stingl, S. Kullmann, C. Ketterer, M. Heni, H.U. Haring, A. Fritsche, et al., Neuronal correlates of reduced memory performance in overweight subjects, *NeuroImage* 60 (2012) 362–369.
- [27] I. Garcia-Garcia, A. Narberhaus, I. Marques-Iturria, M. Garolera, A. Radoi, B. Segura, et al., Neural responses to visual food cues: insights from functional magnetic resonance imaging, *Eur. Eat. Disord. Rev.* 21 (2013) 89–98.
- [28] S. Yokum, J. Ng, E. Stice, Attentional bias to food images associated with elevated weight and future weight gain: an fMRI study, *Obesity* 19 (2011) 1775–1783.
- [29] J. Fan, B.D. McCandliss, T. Sommer, A. Raz, M.I. Posner, Testing the efficiency and independence of attentional networks, *J. Cogn. Neurosci.* 14 (2002) 340–347.
- [30] M. Corbetta, G.L. Shulman, Control of goal-directed and stimulus-driven attention in the brain, *Nat. Rev. Neurosci.* 3 (2002) 201–215.
- [31] M. Corbetta, G. Patel, G.L. Shulman, The reorienting system of the human brain: from environment to theory of mind, *Neuron* 58 (2008) 306–324.
- [32] M.I. Posner, S.E. Petersen, The attention system of the human brain, *Annu. Rev. Neurosci.* 13 (1990) 25–42.
- [33] S.E. Petersen, M.I. Posner, The attention system of the human brain: 20 years after, *Annu. Rev. Neurosci.* 35 (2012) 73–89.
- [34] J. Fan, B.D. McCandliss, J. Fossella, J.I. Flombaum, M.I. Posner, The activation of attentional networks, *NeuroImage* 26 (2005) 471–479.
- [35] M. Corbetta, J.M. Kincade, J.M. Ollinger, M.P. McAvoy, G.L. Shulman, Voluntary orienting is dissociated from target detection in human posterior parietal cortex, *Nat. Neurosci.* 3 (2000) 292–297.
- [36] S. Kastner, M.A. Pinsk, P. De Weerd, R. Desimone, L.G. Ungerleider, Increased activity in human visual cortex during directed attention in the absence of visual stimulation, *Neuron* 22 (1999) 751–761.
- [37] J.B. Hopfinger, M.H. Buonocore, G.R. Mangun, The neural mechanisms of top-down attentional control, *Nat. Neurosci.* 3 (2000) 284–291.
- [38] C.M. Arrington, T.H. Carr, A.R. Mayer, S.M. Rao, Neural mechanisms of visual attention: object-based selection of a region in space, *J. Cogn. Neurosci.* 2 (2000) 106–117.
- [39] J.M. Kincade, R.A. Abrams, S.V. Astafiev, G.L. Shulman, M. Corbetta, An event-related functional magnetic resonance imaging study of voluntary and stimulus-driven orienting of attention, *J. Neurosci.* 25 (2005) 4593–4604.
- [40] S. Vossel, C.M. Thiel, G.R. Fink, Cue validity modulates the neural correlates of covert endogenous orienting of attention in parietal and frontal cortex, *NeuroImage* 32 (2006) 1257–1264.
- [41] G. Aston-Jones, J.D. Cohen, An integrative theory of locus coeruleus-norepinephrine function: adaptive gain and optimal performance, *Annu. Rev. Neurosci.* 28 (2005) 403–450.
- [42] J.H. Morrison, S.L. Foote, Noradrenergic and serotonergic innervation of cortical, thalamic, and tectal visual structures in Old and New World monkeys, *J. Comp. Neurol.* 243 (1986) 117–138.
- [43] D. Pudel, J. Westenhöfer, Fragebogen zum Eßverhalten (FEV). Handanweisung, Hogrefe, Göttingen, 1989.
- [44] J.F. Knebel, U. Toepel, J. Hudry, J. le Coutre, M.M. Murray, Generating controlled image sets in cognitive neuroscience research, *Brain Topogr.* 20 (2008) 284–289.
- [45] M.A. Burock, R.L. Buckner, M.G. Woldorff, B.R. Rosen, A.M. Dale, Randomized event-related experimental designs allow for extremely rapid presentation rates using functional MRI, *Neuroreport* 9 (1998) 3735–3739.
- [46] R.N. Henson, Efficient experimental design for fMRI, in: K.J. Friston, J.T. Ashburner, S.T. Kiebel, T.E. Nichols, W.D. Penny (Eds.), *Statistical Parametric Mapping: the Analysis of Functional Brain Images*, Academic Press, London 2006, pp. 193–210.
- [47] S.A. Rombouts, J.S. Damoiseaux, R. Goekoop, F. Barkhof, P. Scheltens, S.M. Smith, et al., Model-free group analysis shows altered BOLD fMRI networks in dementia, *Hum. Brain Mapp.* 30 (2009) 256–266.
- [48] N. Ibarretxe-Bilbao, M. Zarei, C. Junque, M.J. Martí, B. Segura, P. Vendrell, et al., Dysfunctions of cerebral networks precede recognition memory deficits in early Parkinson's disease, *NeuroImage* 57 (2011) 589–597.
- [49] V.D. Calhoun, T. Adali, G.D. Pearson, J.J. Pekar, A method for making group inferences from functional MRI data using independent component analysis, *Hum. Brain Mapp.* 14 (2001) 140–151.
- [50] Y.O. Li, T. Adali, V.D. Calhoun, Estimating the number of independent components for functional magnetic resonance imaging data, *Hum. Brain Mapp.* 28 (2007) 1251–1266.
- [51] A.J. Bell, T.J. Sejnowski, An information-maximization approach to blind separation and blind deconvolution, *Neural Comput.* 7 (1995) 1129–1159.
- [52] J. Himberg, A. Hyvarinen, F. Esposito, Validating the independent components of neuroimaging time series via clustering and visualization, *NeuroImage* 22 (2004) 1214–1222.
- [53] S.A. Meda, M.C. Stevens, B.S. Folley, V.D. Calhoun, G.D. Pearson, Evidence for anomalous network connectivity during working memory encoding in schizophrenia: an ICA based analysis, *PLoS One* 4 (2009), e7911.
- [54] E.A. Allen, E.B. Erhardt, E. Damaraju, W. Gruner, J.M. Segall, R.F. Silva, et al., A baseline for the multivariate comparison of resting-state networks, *Front. Syst. Neurosci.* 5 (2011) 2.
- [55] S.M. Smith, P.T. Fox, K.L. Miller, D.C. Glahn, P.M. Fox, C.E. Mackay, et al., Correspondence of the brain's functional architecture during activation and rest, *Proc. Natl. Acad. Sci. U. S. A.* 106 (2009) 13040–13045.
- [56] M.D. Fox, M. Corbetta, A.Z. Snyder, J.L. Vincent, M.E. Raichle, Spontaneous neuronal activity distinguishes human dorsal and ventral attention systems, *Proc. Natl. Acad. Sci. U. S. A.* 103 (2006) 10046–10051.
- [57] G.L. Shulman, M.P. McAvoy, M.C. Cowan, S.V. Astafiev, A.P. Tansy, G. d'Avossa, et al., Quantitative analysis of attention and detection signals during visual search, *J. Neurophysiol.* 90 (2003) 3384–3397.
- [58] J.J. Todd, D. Fougny, R. Marois, Visual short-term memory load suppresses temporoparietal junction activity and induces inattention blindness, *Psychol. Sci.* 16 (2005) 965–972.
- [59] C.M. Thiel, K. Zilles, G.R. Fink, Cerebral correlates of alerting, orienting and reorienting of visuospatial attention: an event-related fMRI study, *NeuroImage* 21 (2004) 318–328.
- [60] J.T. Coull, C.D. Frith, R.S. Frackowiak, P.M. Grasby, A fronto-parietal network for rapid visual information processing: a PET study of sustained attention and working memory, *Neuropsychologia* 34 (1996) 1085–1095.
- [61] A. Mohanty, D.R. Gitelman, D.M. Small, M.M. Mesulam, The spatial attention network interacts with limbic and monoaminergic systems to modulate motivation-induced attention shifts, *Cereb. Cortex* 18 (2008) 2604–2613.
- [62] D.M. Small, D. Gitelman, K. Simmons, S.M. Bloise, T. Parrish, M.M. Mesulam, Monetary incentives enhance processing in brain regions mediating top-down control of attention, *Cereb. Cortex* 15 (2005) 1855–1865.
- [63] U. Vainik, A. Dagher, L. Dube, L.K. Fellows, Neurobehavioural correlates of body mass index and eating behaviours in adults: a systematic review, *Neurosci. Biobehav. Rev.* 37 (2013) 279–299.
- [64] G. Gerlach, S. Herpertz, S. Loeber, Personality traits and obesity: a systematic review, *Obes. Rev.* 16 (2015) 32–63.