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TEMPTED BY THE EYES: BEHAVIORAL AND BRAIN RESPONSES TO FOOD SHAPED BY APPRECIATION, PREFERENCES AND FOOD-EXTRINSIC INFORMATION

Notter Marie-Laure

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Département des Neurosciences Cliniques et Département de Radiologie

TEMPTED BY THE EYES: BEHAVIORAL AND BRAIN RESPONSES TO FOOD SHAPED BY APPRECIATION, PREFERENCES AND FOOD-EXTRINSIC INFORMATION

Thèse de doctorat en Neurosciences

présentée à la

Faculté de Biologie et de Médecine
de l'Université de Lausanne

par

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TEMPTED BY THE EYES: BEHAVIORAL AND BRAIN RESPONSES TO FOOD SHAPED BY APPRECIATION, PREFERENCES AND FOOD-EXTRINSIC INFORMATION

Lausanne, le 7 octobre 2016

pour Le Doyen
de la Faculté de Biologie et de Médecine

Prof. Jardena Puder

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ABSTRACT (ENGLISH)

Obesity has become a major public health issue as it has reached pandemic proportions over the last decades. This increasing prevalence of obesity and overweight in industrialized countries is to a large part explained by the abundance of tempting foods promoting overeating and subsequent weight gain. Resisting food temptations has thus become a necessity in order to maintain a healthy body weight. The thesis at hand provides a better understanding of behavioral and brain responses involved in sensory food perception, reward and control.

The first study (study A) assessed how food liking influences subsequent choice between two food alternatives, and how, in turn, these factors modulate brain responses to the viewing of high- and low-energy foods (published manuscript: “ Does my brain want what my eyes like? – How food liking influences choice and impacts spatio-temporal brain dynamics to food viewing” (Bielser & Crézé et al., 2015)). In this study, we found that strongly like foods were chosen more often and faster than less liked foods. Further, the level of liking and subsequent choice influenced brain responses in areas involved in reward attribution as well as decision-making processes, likely influencing prospective food intake.

The second study (study B) investigated the neural representation of meal images varying in portion size in the context of prospective food intake and expected satiety (published manuscript: “Brain dynamics of meal selection in humans” (Toepel, Bielser et al., 2015)). In this study, our results showed that brain regions involved in visual processing and reward attribution trace physical portion size increases during early stages of perception, likely reflective of the quantification of the amount of food available for subsequent intake. During a later stage of information processing, brain regions involved in attention and adaptive behaviors responded to “ideal” portion sizes, likely reflecting control over food intake to select portions to achieve adequate satiety.

The third study (study C) assessed how encountering traffic light labeling (as used on food packages) preceding food images influenced behavioral and brain responses to high- and low-energy foods (“Biasing behavioral decisions and brain responses to food with traffic light labeling” (Bielser et al., in preparation)). In this study, we found that traffic light labeling and energetic content of viewed foods modulated neural activity in a network of regions known to be involved in reward valuation, inhibitory control, attention and object categorization. These findings support traffic light labeling as a potentially effective means to guide food choices and ameliorate body weight long-term management.

Together, the studies comprised in this thesis showed that modulations of neural activity in response to food perception occur already at early stages of visual processing and can be influenced by the level of appreciation, the amount of food presented as well as food-extrinsic information. These findings contribute to a better understanding of factors shaping food-related behavior and, in extension, food intake.

RESUME (FRENCH)

L'obésité est devenue un problème majeur de santé publique qui a atteint des proportions pandémiques au cours des dernières décennies. L'augmentation de la prévalence du surpoids et de l'obésité dans les pays industrialisés s'explique en grande partie par l'abondance de nourriture dont le degré d'attirance incite à une consommation en excès et engendre une prise de poids. Cette thèse avait pour but une meilleure compréhension des réponses comportementales et cérébrales impliquées dans la perception sensorielle de nourriture, la récompense et le contrôle.

La première étude (étude A) a investigué la façon dont l'appréciation de la nourriture influence un choix subséquent entre deux alternatives alimentaires, et comment, par extension, ces facteurs modulent les réponses cérébrales à la vue de nourriture à haute et basse teneur énergétique (manuscrit publié : " Does my brain want what my eyes like? – How food liking influences choice and impacts spatio-temporal brain dynamics to food viewing" (Bielser & Crézé et al., 2015)). Dans cette étude, nous avons montré que la nourriture hautement appréciée est choisie plus souvent que les aliments moins bien notés. De plus, le niveau d'appréciation et le choix subséquent influencent les réponses cérébrales d'aires impliquées dans l'attribution de récompense ainsi que dans les processus de prise de décision et par la même, un impact probable sur la prise alimentaire prospective.

La deuxième étude (étude B) a investigué les représentations cérébrales d'images de repas dont la taille des portions varient, dans le contexte d'une prise alimentaire prospective et de la satiété en résultant (manuscrit publié : "Brain dynamics of meal selection in humans" (Toepel, Bielser et al., 2015)). Dans cette étude, nos résultats ont montré que des régions cérébrales impliquées dans les processus visuels, ainsi que dans l'attribution de récompense tracent les augmentations physiques de portion durant les premières étapes de perception, représentant probablement une quantification de la nourriture disponible pour une prise alimentaire subséquente. Durant une étape plus tardive du décodage d'information, des régions cérébrales impliquées dans l'attention et dans les comportements adaptatifs présentent une forte réactivité pour les portions jugées de taille « idéale », reflétant sans doute un contrôle sur la prise alimentaire afin de sélectionner une portion permettant d'atteindre une satiété adéquate.

La troisième étude (étude C) a investigué comment la rencontre fortuite de feux de circulation, comme ceux utilisés actuellement sur les labels d'étiquetage alimentaire, influence les réponses comportementales et cérébrales à la vue de nourriture à haute et basse teneur énergétique ("Biasing behavioral decisions and brain responses to food with traffic light labeling" (Bielser et al., en préparation)). Dans cette étude, nous avons montré que ces labels modulent les réponses cérébrales dans un réseau d'aires impliquées dans l'attribution de récompense, le contrôle inhibiteur, l'attention et la catégorisation d'objets. Ces résultats démontrent l'efficacité des labels reproduisant les feux de circulation comme moyen de guidage des choix alimentaires et d'amélioration de la gestion du poids à long terme.

Ensemble, les études comprises dans cette thèse ont démontré que les modulations de l'activité cérébrale en réponse à la perception de nourriture ont lieu à des étapes très précoces du décodage d'information visuelle et qu'elles peuvent être influencées par le niveau d'appréciation, la quantité de nourriture disponible ainsi que par des informations contextuelles.

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LIST OF ABBREVIATIONS

ACC : Accuracy

ANOVA : Analysis of Variance

BDI: Beck Depression Inventory

BMI: Body Mass Index

CCK: Cholecystokinin

CER-VD: Cantonal Human Research Ethics Commission of Vaud

DLPFC: Dorsolateral Prefrontal Cortex

EEG: Electroencephalography

ERP: Event-Related Potential

fMRI: Functional Magnetic Resonance Imaging

G: Green Traffic Light

GCG: Glucagon

GDA: Guideline Daily Amount

GFP: Global Field Power

G-O: Green Relative to Off Traffic Light

HiFat: High-Fat Food

HPA: Hypothalamic-Pituitary-Adrenal Axis

Hz: Hertz

INS: Insula

ISI: Inter-Stimuli Interval

ITI: Inter-Trial Interval

latPFC: Lateral Prefrontal Cortex

LAURA: Local Autoregressive Average

LINE: Laboratory for Investigative Neurophysiology

LoFat: Low-Fat Food

medPFC: Medial Prefrontal Cortex

MFG: Middle Frontal Gyrus

MNI: Montreal Neurological Institute

ms: Millisecond

MTG: Middle Temporal Gyrus

N170: Negative voltage occurring around 170ms post-stimulus onset

O: Off Traffic Light

OCC: Occipital Lobe

OFC: Orbitofrontal Cortex

OB: Olfactory Bulb

P1: Positive voltage occurring around 100ms post-stimulus onset

P300: Positive voltage occurring around 300ms post-stimulus onset

PAR: Parietal Lobe

PET: Positron Emission Tomography

PYY : Peptide YY

R: Red Traffic Light

R-O: Red Relative to Off Traffic Light

ROI: Region of Interest

RT: Reaction Time

SEDM-CHUV: Endocrinology, Diabetology and Metabolism Service of the Vaudois University Hospital Center

s.e.m.: standard error of the mean

SMAC: Spherical Model with Anatomical Constraints

STG: Superior Temporal Gyrus

TEMP: Temporal Lobe

TFEQ: Three-Factor Eating Questionnaire

TMS: Transcranial Magnetic Stimulation

TW: Time Window

VAS: Visual Analogue Scale

VEP: Visual-evoked potential

µA/mm3: Microampere per millimeter cube

µV: Microvolt

CHAPTER 1 GENERAL INTRODUCTION

1.1 Food intake behavior and body weight management

The human body is evolutionary designed to store fat in periods of food availability to ensure survival in moments of famine (Heitmann et al., 2012). However, over the past decades, the dietary environment of Western countries has drastically changed. The development of industrial agriculture, leading to massive production, has created a world of overabundant food availability in many countries. As a consequence, readily available energy-dense foods have spread in stores and markets, tempting consumers by low prices and practical aspects (Westerterp and Speakman, 2008). Further, sugar-sweetened beverage (i.e. soda) consumption has severely increased, adding numerous liquid calories to one's diet (Tappy et al., 2010). In parallel to the food industry, new technologies have also changed our daily work and habits. The amount of energy expenditure required to survive and function has decreased, as physical effort is no longer a necessity to forage food (Popkin and Gordon-Larsen, 2004). In combination, excessive food intake driven by maladaptive food options and choices as well as the increasingly sedentary lifestyle promote caloric intake beyond energy needs, creating an obesogenic environment (Prentice and Jebb, 2004). Obesity has reached pandemic proportions over the last thirty years, affecting 400 million people worldwide, in addition to one billion suffering from overweight (Finucane et al., 2011; Flegal et al., 2012). In Europe, 50% of the population is today overweight and 20% is obese (WHO, 2016) (See Figure 1). Obesity is defined as excessive body fat mass and can be measured by means of body mass index (BMI, overweight ≥ 25; obese ≥ 30 kg/m^2) (WHO, 2000). The accumulation of body fat is detrimental for health and associated with morbid pathologies, such as cardiovascular diseases, type II diabetes mellitus, stroke, cancer and respiratory diseases (Formiguera and Cantón, 2004). Obesity has thus become one of the leading causes of death in Western societies and, by extension, a major public health issue by its impact on health care management and costs. Appropriate food choices and intake are thus of crucial importance to maintain a healthy body weight. Yet, the complex mechanisms involved in food drives and intake regulations are still not fully understood, therefore preventing the development of efficient strategies for long-term management of weight.

Figure 1: Prevalence of obesity worldwide, ages 18+, 2014, both sexes (WHO).

Food intake behavior is mainly regulated by two key players, the gut and the brain, via the so-called gut-brain axis (Berthoud, 2011; Hussain and Bloom, 2013; Mercer, 2016). This regulation already occurs during pre-ingestive stages of food perception. Gastrointestinal physiological signals such as digestive hormones, as well as gastric distension and emptying are conveyed to the central nervous system, where they are integrated and valued, regulating the short-term control of food intake according to the current energy needs (Horner et al., 2011; Jimura et al., 2010; Suzuki et al., 2012). However, as food is a biologically salient stimulus, survival instincts drive feeding behavior towards the consumption of foods with higher amounts of calories and fat as they are better palatable and attributed greater rewarding properties (de Araujo, 2004; Heitmann et al., 2012). Rewarding stimuli induce hedonic responses from the dopaminergic mesolimbic reward system (Haber and Knutson, 2010; McCutcheon, 2015). This reward network includes the ventral tegmental area, the nucleus accumbens, the amygdala, the striatum, and the hippocampus, whose activities are overall controlled by the prefrontal cortex (Kelley and Berridge, 2002; Tomasi and Volkow, 2013; Volkow et al., 2011, 2013). Furthermore, the ventral prefrontal cortex, the insula, the cingulate gyrus, and the thalamus play a key role in attributing salience to a stimulus as a function of the current homeostatic needs and the rewarding properties of a stimulus and modulate the motivation and attention towards this stimulus (Downar et al., 2001; Menon and Uddin, 2010; Seeley et al., 2007). The hedonic control of food intake is thus associated with drives towards food that are mostly independent of body energetic needs (Lutter and Nestler, 2009; Meye and Adan, 2014; Saper et al., 2002), leading to maladaptive food choices and consumption, and subsequent weight gain. In turn, the increase in adipose tissue leads to imbalances along the gut-brain axis, further deregulating control over food intake and favoring hedonic processes in food choices (Alonso-Alonso et al., 2015; Blundell et al., 2000). In the recent literature, the debate on an addiction-like model to palatable energy-dense food consumption is still ongoing (Davis and Carter, 2009). Shared neural substrates for food and drug reward processes have been identified by Pelchat (2002) and further research showed that food, as addictive drugs, is capable of increasing dopamine levels in the reward network, facilitates Pavlovian incentive learning and favors a tolerance to reward properties by the top-down regulation of dopamine receptors in the striatum (Grigson, 2002; Hajnal et al., 2008).

Food intake behavior is influenced by factors inherent to the body (e.g. gender, motivation to eat, body weight), by sensory, as well as by contextual information (e.g. smell and taste of the food, labeling, portion size). For further details, please refer to section 1.3. An integrative view on food perception and intake behavior thus requires the consideration of many different aspects. The thesis at hand aims at adding complementary pieces to this mosaic.

1.2 Neural signatures of human food perception

Several sensory features are intrinsic to food, i.e. visual, olfactory and gustatory. These sensory aspects often interact and shape food perception, including brain responses to food. In this section, we shortly discuss the brain mechanisms underlying taste perception and food viewing.

1.2.1 Brain responses to food tasting

Taste is the result of an interaction between gustatory and olfactory food properties. Gustatory components are detected by taste buds localized on the tongue, the soft palate, the larynx, the pharynx and the upper esophagus. Taste buds possess various receptors allowing for the discrimination of five basic taste qualities: sweet, salty, bitter, sour and umami. Current research is also debating the possible existence of additional taste bud receptors dedicated to fat detection (Laugerette et al., 2007; Mattes, 2005). Taste signals are then conveyed via the nucleus of the solitary tract and the thalamus to the primary gustatory cortex, located in the postcentral gyrus and the insula. In parallel, food odorants, i.e. volatile chemicals, are transported by the air from the mouth to the nasal cavity, where they reach the olfactory mucosa. There, the combined activity of receptor neurons arising from the olfactory nerve discriminates the various odorant molecules. The olfactory nerve then relays the information via the cribriform plate to the olfactory bulb in the forebrain. Taste quality seems to be one of the first features processed in the central gustatory system. Previous electrical neuroimaging studies have reported that modulations of brain activity in response to taste occurred as early as 130-150ms for salty, sweet and electric taste in the left insula, the middle temporal gyrus, the ventromedial orbitofrontal gyrus and the anterior cingulate cortex (Ohla et al., 2010, 2012). The multisensory gustatory and olfactory information are further processed in the frontal operculum, the anterior insula and the orbitofrontal cortex, allowing for a “taste” representation (Crouzet et al., 2015; Okamoto and Dan, 2013). For a complete review, please refer to Rolls (2015). Contextual information can further modulate the pleasantness and the intensity of the perceived taste. For more information on the influence of context information on taste perception, please refer to section 1.3.2.

1.2.2 Brain responses to food viewing

Food is a highly salient biological stimulus inherently rewarding and hedonic (LaBar et al., 2001), and its foraging is necessary for survival. Food perception does not only rely on gustatory and olfactory features, but is greatly influenced by visual properties upon pre-ingestive viewing. In daily life, most food choices are based on visual presentation, i.e. when selecting food packages in a supermarket or by looking at cafeteria displays.

The sight of food, as opposed to non-food objects, was shown in many previous functional neuroimaging studies over the last decade to modulate neural activity in distributed brain areas. For example, regions of the dopaminergic mesolimbic reward network including the orbitofrontal cortex, lateral prefrontal cortex, amygdala, left caudate nucleus, striatum, ventral tegmental area as well as the anterior cingulate cortex showed differential responses to food as compared to non-food object viewing (Blechert et al., 2016; Killgore et al., 2003; Schur et al., 2009). In particular, these regions known to be involved in reward attribution and valuation, revealed greater neural activity to food than to non-food viewing. Moreover, changes in activity over temporo-parietal and occipital brain regions have been reported by several studies (Killgore et al., 2003; LaBar et al., 2001; Rothemund et al., 2007; Santel et al., 2006; Uher et al., 2004), suggesting a greater attentional and motivational salience of food than non-food objects, even during pre-ingestive viewing. In line, increased neural activity in response to food viewing was also found in regions involved in homeostatic integration, such as the hypothalamus, and the insula (Schur et al., 2009). A recent meta-analysis on the most commonly reported neural correlates of food perception (van der Laan et al., 2011) summarized that the viewing of food (vs. non-food) most consistently yields alterations in the activity of the lateral occipital cortex, the lateral orbitofrontal cortex and the middle insula. The authors proposed that visual food perception as investigated in human neuroimaging studies thus involves object recognition processes (occipital cortex), processes related to the valuation of the expected pleasantness of prospective food ingestion (orbitofrontal cortex) and processes related to the memory retrieval of the expected taste (insular cortex). The sight of food thus leads to modulated activity in sensory and somatosensory brain regions, but also reward and association cortices.

In addition to the categorization of food from non-food objects, the brain also readily traces the energetic content of foods during pre-ingestive viewing. Previous functional neuroimaging studies reported neural correlates of the distinction between high- and low-energy foods based on their visual features. A study by Killgore and colleagues (2003) was the first to investigate how energy density modulates neural activity in response to food viewing. They reported that low-energy (vs. high-energy) foods elicited an increased activity in the superior temporal gyrus, the medial orbitofrontal cortex, the postcentral gyrus and the parahippocampal gyrus, regions involved in object categorization, somatosensory representation and taste perception. In contrast, high-energy (vs. low-energy) foods elicited higher activation in the medial and lateral prefrontal cortex, the thalamus and the hypothalamus. These regions are involved in homeostatic integration (i.e. hypothalamus), as well as in reward valuation and reward value signal encoding (i.e. medial prefrontal cortex). Moreover, especially the lateral prefrontal cortex has been associated with inhibitory processes, decision-making and food intake termination (Cornier et al., 2010; Hare et al., 2009; Hutcherson et al., 2012; Plassmann et al., 2010) indicating that food perception in humans is not only driven by the reward and hedonic values attributed to perceived foods, but also subject to, possibly top-down, control processes. Several studies over the recent years have accordingly shown that in particular the viewing of high-energy, as opposed to low-energy, foods consistently leads to increased activity in reward-related brain regions, but also to modulations of neural activity in areas associated with cognitive control (Gautier et al., 2001; van der Laan et al., 2011; Stoeckel et al., 2008; Toepel et al., 2009). In line, the meta-analysis of van der Laan and colleagues (2011) previously mentioned reported that the most concurrent brain region modulated as a function of energy density across functional neuroimaging studies was a region stretching from the hypothalamus to the ventral striatum, always showing increased activity to the viewing of high-, as opposed to low-energy foods. Energetic content, as one major food-intrinsic determinant of palatability and contribution to the energetic homeostasis of the human body, thus consistently modulates activity in a brain region involved in food intake regulation as a function of homeostatic needs and reward valuation. In the section 1.3, we will detail a number of other food- but also body-intrinsic, as well as extrinsic factors that have been found to influence food perception.

While the previously mentioned functional neuroimaging studies well described the neural networks underlying sensory processing of food, reward valuation and control processes, still few studies investigated the timing of food perception. A study by Toepel and colleagues (2009) was the first to provide insights on the timing of food's energetic content discrimination. In the study, normal-weight participants were presented with images of high- and low-energy food while undergoing electroencephalographic (EEG) recordings. Head-surface visual-evoked potentials (VEPs) were found to be modulated as a function of the energetic content of the viewed food at two distinct temporal stages of the discrimination, i.e. ~165ms and ~300ms post-image onset. Estimation of neural sources underlying the first head-surface modulation (~165ms) showed an increased activity in response to high-energy (vs. low-) in the superior temporal cortex and the postcentral gyrus. Over the second time period (~300ms), the viewing of high-, as opposed to low-energy foods, modulated the activity in the occipito-temporal cortex, the inferior parietal cortex, the dorsal frontal cortex, and the ventromedial prefrontal cortex. Energetic content of food was thus found to modulate brain areas involved in object categorization, decision-making and reward valuation already at early stages of information processing. A recent VEP study reported similar modulations of responses to high- vs. low-energy food viewing (Meule et al., 2013). In this study, normal-weight women viewed color images of food and had to imagine either immediate or long-term consequences of the ingestion of the food item on screen. While early head-surface visual responses around ~150ms after image onset (no neural sources were estimated in this study) were only sensitive to the type of food viewed, later responses were additionally influenced by the imagined consequences of food intake. That is, the study of Meule and colleagues (2013) shows that reward valuation processes are succeeded by regulation and control processes during pre-ingestive food viewing.

Taken together, previous studies on food perception in humans show that the sight of food leads to modulations of activity in brain areas involved in homeostatic and somatosensory integration reward valuation, goal-directed behavior, decision-making and inhibitory control. Accumulating evidence also gave rise to the assumption that the consumption of pleasurable food increases the sensitivity to visual food cues and in turn elicits greater activity in the reward network in response to food viewing, leading to an overriding of homeostatic needs and excessive energy intake on the long run (Volkow et al., 2012).

1.3 Food perception and eating behavior

Several factors have been shown to influence food perception. These factors can be roughly divided into such that are intrinsic to the body and food-extrinsic context information, e.g. the environment in which food is perceived.

1.3.1 Body-intrinsic factors influencing food perception

Body weight: Although cause and consequence are strongly debated, body weight is one of the most well known factors influencing food perception and intake. To account for weight-induced alterations in eating behavior, a dual model has been developed by Alonso-Alonso and Pascual-Leone (2007). In this model, a switch from “reflective” to “reflexive” food intake as a function of body weight increase is proposed. While healthy body weight maintenance is characterized by reflective food intake and regulated by cognitive, physiological as well as societal factors, the corruption of reflective eating by weight gain leads to a reflexive food intake mode. This reflexive eating behavior is characterized by uncontrolled drives towards food intake, overriding homeostatic needs in energy, in extension leading to overweight and obesity. As mentioned in section 1.1, mounting evidence on addiction-like behavior towards foods containing high amounts of fat and sugar has been reported in animal as well as human literature (Grigson, 2002; Hajnal et al., 2008). Another recent model explaining excessive food intake (Davis, 2013) proposed, in line with the model of Alonso-Alonso and Pascual-Leone, that normal-weight individuals starting to show signs of unconscious passive overeating might develop binge-like craving attitudes over time. In turn, these cravings result in active addiction-like food intake leading to weight gain and possibly obesity. Modulations by body weight are also reflected in neural responses to food viewing. For example, obese individuals were found to show higher activation in temporal and parietal lobes in response to viewed food, especially to high-fat food cues, reflecting a greater responsiveness and attention to food cues (Doolan et al., 2014, 2015; Hume et al., 2015). Further, obese individuals tend to show lower activation of the dorsal prefrontal cortex when viewing food as compared to lean individuals, i.e. in a brain region involved in food intake termination and inhibitory control (Cornier et al., 2010; Hutcherson et al., 2012). These findings suggest possible impairments in the capacity to exert self-control over food intake (Harris et al., 2013; Hume et al., 2015; Stoeckel et al., 2008; Tuulari et al., 2015). High body weight has also been associated with greater activity in the medial prefrontal cortex, the insula, the amygdala, the anterior cingulate cortex as well as the ventral striatum (Rothemund et al., 2007; Stoeckel et al., 2008). These regions are known to be part of a network involved in reward valuation and salience attribution (Hare et al., 2009; Menon and Uddin, 2010; Seeley et al., 2007). That is, previous studies have found consistent evidence that obesity influences the visual perception of food in distributed brain areas and in particular alters responses in reward- and control-related brain regions.

Food intake motivation: A second body-intrinsic factor influencing food perception and intake is motivation towards food intake varying as a function of hunger and satiety. Hunger is a physiological state signaling energy depletion of the body. This information is conveyed to the brain via digestive hormones secreted by the gut along the gut-brain axis. Once integrated, this information will lead to increased drives towards food intake. Several neuroimaging studies have confirmed the modulation of brain responses to visual food cues by hunger, in both homeostatic and hedonic regions. A positron emission tomography (PET) study of Del Parigi and colleagues (2006) reported that hunger, as compared to satiety, increases the activity in the hypothalamus, the thalamus, the insula and the orbitofrontal cortex in resting state. Another PET study assessing the neural responses to visual food cues found an increase in activity in the postcentral gyrus, the superior temporal gyrus, the insula and the orbitofrontal cortex in fasted as compared to fed participants (Wang et al., 2004a). Further, a study by Goldstone and colleagues (2009) showed that hunger selectively increases neural activity in response to high-energy, as opposed to low-energy, foods in the ventral striatum, the amygdala, the insula and the orbitofrontal cortex. Altogether, previous findings revealed that hunger alters brain responses to food viewing, in areas involved in homeostatic integration, goal-directed attention, reward valuation and salience attribution, likely favoring the intake of high-energy foods. In contrast, satiety was found to be associated with an increase in activity of the dorsal prefrontal cortex (Gautier et al., 2001; Del Parigi et al., 2006), i.e. a brain region involved in food termination, inhibition and decision-making. When investigating the spatio-temporal dynamics to food viewing as a function of food intake motivation, a study by Nijs and colleagues (2010) using electroencephalography showed that hunger modulates visual response to food around 300ms after food image encounter in lean participants, interpreted as an enhancement in the allocation of attention to food pictures prior as opposed to post food intake. This modulation was however not observed in overweight and obese individuals.

Gender: Previous studies have shown substantial differences in behavioral and brain responses to food in women vs. men. In women, the menstrual cycle is known to greatly influence circadian rhythm (Baker and Driver, 2007), as well as cognitive, sensory, emotional and eating behaviors (Dye and Blundell, 1997; Farage et al., 2008). In a review, Dye and Blundell (1997) reported changes in hunger, cravings for certain foods and alteration in meal size selection across menstrual cycle. A functional neuroimaging study of Horstmann and colleagues (2011) showed that women, as opposed to men, prefer salient immediate rewards independent of negative long-term consequences during a behavioral task. The authors attributed these gender effects to structural differences. In women, they found that the grey matter volume in the dorsal striatum and dorsolateral prefrontal cortex (DLPFC), i.e. two regions involved in goal-directed behavior and inhibitory control, was associated with measures of obesity (i.e. BMI and leptin), whereas these associations were not present in men. In line, a study by Cornier and colleagues (2010) showed that in women, the activity in the DLPFC and in the parietal cortex was higher in response to visual food cues than in men. In women, the activity of the DLPFC was further found to be negatively correlated with subsequent energy intake. When assessing the differences in spatio-temporal brain dynamics to food viewing in men vs. women, a study by Toepel and colleagues (2012) revealed that gender influenced viewing responses as early as 170ms after food cue onset, related to modulations of neural activity in prefrontal and temporo-parietal brain regions. Therein, neural activity in the ventral prefrontal cortex when viewing food (as compared to kitchen utensil images) negatively correlated with body weight in women, but not in men. Thus, gender shapes brain responses to food viewing in early stages of visual processing related to object categorization and reward valuation.

Several other body-intrinsic factors (although often induced by external factors), such as mood, stress level and sleep deprivation are known to influence food perception and intake.

Mood: Several studies reported a strong association between negative affect and abnormal eating patterns. For example, the study of Yeomans and Coughlan (2009) assessed the influence of positive and negative mood on snacking, and found that women with high restraint and disinhibition scores on the three-factor eating questionnaire (TFEQ) consumed more snacks when presented with a negative movie, as compared to neutral or positive movies. The authors thus proposed that emotional valence (negative vs. positive), rather than arousal imposed by the movies was responsible for greater food intake. In a study of Goldschmidt and colleagues (2014), individuals suffering from depression self-reported greater emotional eating tendencies and had a higher body weight than individuals with no depression symptoms. The authors proposed that emotional eating could thus be a coping strategy for depressed mood, in turn leading to weight gain. In a review, Macht (2008) supported this hypothesis by reporting that individuals showing high depression scores tended to like and eat energy-dense foods to compensate for their negative emotions. So far, studies on mood-modulated brain mechanisms to food in humans quite sparse. However, as the dopamine level in the reward neural circuitry affects and is affected by both mood and eating behaviors, negative mood (synonym of a decreased dopamine level) could lead to a more compulsive consumption of rewarding palatable foods as means to re-equilibrate the dopaminergic balance in the brain (Singh, 2014). For complete review on the relation between mood and food intake behavior, please refer to (Cardi et al., 2015).

Stress: Stress levels have also been reported as important modulators of food intake. The impact of stress on eating behavior seems to greatly vary between individuals. A review of Torres and Nowson (2007) reported that stress may lead to both increased or decreased food intake, depending on its severity and duration. Chronic stress leads to the intake of more energy-dense foods, whereas the effects of acute stress seem to be more susceptible to inter-individual variations. In line, a study of Haynes and colleagues (2003) assessing the effect of acute stress in women with different degrees of restraint and disinhibition revealed that participants with low restriction and high disinhibition tend to reduce their food intake in stressful as opposed to relaxed situations. In contrast, participants with high restraint and/or low disinhibition ate more when stressed. In the brain, stress is known to trigger the release of cortisol via the stimulation of the hypothalamic-pituitary-adrenal axis (HPA) (Tsigos and Chrousos, 2002). Excessive levels of cortisol in turn modulate gastric hormone secretion, as well as the reward value attributed to foods, and stimulate hunger (Epel et al., 2001). This excess in cortisol also plays a key role in the development of visceral obesity via the increase in glucocorticoid receptor density in the intra-abdominal adipose tissue, favoring fat accumulation and modifying the overall lipid metabolism (Adam and Epel, 2007; Lundholm et al., 1985). Stress might thus well be factor contributing to the dysregulation of eating behavior and weight fluctuations across life span.

Sleep: Sleeping patterns were also shown to greatly influence food intake behavior. Sleep restriction has been linked to maladaptive food intake and weight gain. Sleep deprivation is believed to alter glucose metabolism, increase food intake and decrease energy expenditure (Brondel et al., 2010; Knutson et al., 2007). Lack of sleep dysregulates the secretion of growth hormones and cortisol, creating a “stress-like” situation for the body and the brain (Knutson et al., 2007). A study of Brondel and colleagues (2010) assessing the influence of partial sleep deprivation on food intake behavior showed that after a 4h-long night (as compared to 8h), participants increased their food intake by more than 20%, without changing the liking attributed to the food or the desire to eat. This strong increase in food intake by sleep deprivation can lead, on the long run, to dramatic weight gain and eventually obesity.

1.3.2 Food-extrinsic factors influencing food perception

Extrinsic environmental and contextual information accompanying food choice and intake play an important role in pre-ingestive perception. In this section, some of the most relevant factors shaping the context of food intake are described. For a review on food-extrinsic factors influencing food perception, please refer to (Okamoto and Dan, 2013).

Colors: colors substantially influence food taste and odor perception. From an early age, western individuals learn that the color red is an implicit “stop” or warning signal, whereas the color green is an implicit “go” signal. Red and green increase arousal and modulate the perception of the environment (Mehta and Zhu, 2009; Shi, 2013). Color incentive meanings in a food context in our daily life are likewise acquired (Spence et al., 2010). For example, in food marketing, green is often linked to a notion of "healthiness" of a product and is used for the packaging of "organic" or low-energy foods (Schuldt, 2013; Shi, 2013). The influence of color on taste perception and on the amount of food consumed has been extensively investigated over the last decades. In a study where naive participants were asked to perform orthogonal tasks (i.e. taste evaluation and questionnaire filling) while offered to snack freely on soft drinks and pretzels presented in red, white or blue cutlery, it was found that consumption decreased when snacks and drinks were presented in plates or cups that were red as compared to blue or white (Genschow et al., 2012). Colors yet not only have an influence on actual food intake, but also strongly modulate perceived odor and taste. For example, in a study of Harrar and colleagues (2011), salty popcorn eaten out of red bowl was rated by participants as sweeter than when eaten out of a white bowl. Further, the color of a beverage was found to be used as a strong indicator of post-absorptive refreshment feeling by participants (Zellner and Durlach, 2003). Further, the intensity of a color seems to modulate the perceived odor intensity of a beverage in an incremental manner (Zellner and Whitten, 1999). These modulations of food perception point to a decisive role of colors as an indicator of edibility and of their association with particular flavors (Clydesdale, 1993; Velasco et al., 2015).

Labels: Over the last years, an increasing number of food label formats have been implemented in several countries in order to guide consumers towards healthier food choices. These formats comprise front-pack labels, Guideline Daily Amount (GDA), verbal labels, organic labels and traffic light labels (Borgmeier and Westenhoefer, 2009). Their efficacy in terms of shaping food preferences and purchase is still debated, but previous research has reported an impact of traffic light, brand and organic labels format on food perception and choice (Baltas, 2001; Grabenhorst et al., 2013; Linder et al., 2010; Temple and Fraser, 2014). Traffic light labeling has overall been shown to be the most effective label format, helping individuals to identify better and faster healthy vs. unhealthy food items (Borgmeier and Westenhoefer, 2009; Enax et al., 2015; Siegrist et al., 2015). The effectiveness of traffic light labeling likely relies on influences exerted by colors on physiological, behavioral and cognitive processes (Meier et al., 2015), as discussed in the previous paragraph. A functional neuroimaging study by Enax and colleagues (2015) was the first to investigate the influence of traffic light labels on food valuation and neural responses to food viewing. Results showed that the presentation of traffic light labeling, as compared to GDA labels, increased participants' willingness to pay for healthy foods and was reflected by an increased activity in the medial prefrontal cortex (medPFC), i.e. a reward-valuation area. When participants were presented with visual cues of unhealthy foods, traffic light labels, as compared to GDA, lead to an increased activity in the lateral prefrontal cortex (latPFC), i.e. a region involved in self-control and decision-making. Therein, when viewing red (vs. green) traffic lights, the activity of the latPFC showed an increased functional coupling with the activity of the medPFC, suggesting reward-signal value encoding with the exertion of inhibitory control. In contrast, green (vs. red) labels lead to an increased functional coupling between the activity of the posterior cingulate gyrus and the medPFC, likely reflecting an increase in reward expectation. This study provided first evidence of the influence of traffic light labeling on neural processes involved in food valuation and cognitive control. The impact of traffic light labeling on behavioral and spatio-temporal brain dynamics to food viewing has further been investigated in the study C of the thesis at hand (chapter 5).

Another type of labeling, brand-naming, has also been shown to strongly influence appreciation as well as brain responses to food cues. In a study of McClure and colleagues (2004), Coca-Cola and Pepsi were presented to participants with and without brand labels. In the absence of labels, both drinks were equally appreciated, whereas in the presence of labels the Coca-Cola was significantly more liked. Further, the presentation of brand labels was shown to modulate brain responses in the hippocampus and in the dorsolateral prefrontal cortex, interpreted as a retrieval of information linked to a particular brand and its assimilation on affective experience of flavor.

Lately, also labels referring to manufacturing mode were shown to modulate behavioral and brain responses to the viewing of food items. A study by Linder and colleagues (2010) reported than when typical daily consumed foods were presented with the label “organic”, participants were willing to pay more for them, as compared to food presented with conventional manufacturing labels. This increased preference for organic foods was also reflected by an increased activation in the ventral striatum, a region involved in reward processing. That is, organic labels seem to be associated with a greater reward attribution, likely due to the positive anticipation of healthy foods conveyed by this label.

Packaging: Another extrinsic factor influencing food perception and choice behavior is the packaging aesthetics. The notion of aesthetics strongly diverges across cultures and each country shows preferences for different features of packaging. For example, in western countries particularly sensitized to ecology and environmental preservation such as Finland, individuals show a greater preference for packaging containing recyclable elements (Rokka and Uusitalo, 2008). However, it seems that consumers across the world tend to purchase a product based on the overall visual aesthetics of the packaging rather than on the products details and nutrient information (Silayoi and Speece, 2007). A neuroimaging study of Van der Laan and colleagues (2012) assessed brain modulations in response to preferred packages. When participants chose their favorite packaging between to alternatives, they showed stronger activation in the inferior parietal and in the middle temporal gyri. These activations likely reflected the valuation of the two alternatives as a function of the anticipated reward. Further, the study showed that the level of activity in the superior frontal gyrus and the middle occipital gyrus to package viewing was predictive of the subsequent choice. The aesthetics in packaging design thus plays a non-negligible role in food choice behavior.

Portion size: Portion size is another key determinant of eating behavior and body weight management. Over the last decades, the standard amount per serving has been multiplied by five (Brehm and D'Alessio, 2000). It has been demonstrated that larger portion sizes increase the energy intake by favoring the override of homeostatic needs (Rolls et al., 2002). In a study of Rolls and colleagues (2006), participants were given varying portion sizes of food and beverages over two consecutive days. The amount per serving varied from 100% to 200% of the baseline amounts. Results showed that even though participants did not eat the full amount proposed, their energy intake increased by up to 26% when presented with larger portion sizes, leading to overeating beyond physiological needs. Further, this increase in energy intake seems be independent of gender, body weight or eating traits (Rolls et al., 2002). The study B of the thesis at hand further investigated the spatio-temporal brain dynamics to meal images varying in portion size in the context of prospective food intake and expected satiety (chapter 4).

Product price: Finally, the price of a food product has a major impact on choice and purchase behavior. In western countries, the increasing rate of obesity is strongly associated with low and moderate household income (Popkin and Gordon-Larsen, 2004). Food is often purchased from convenience stores, offering mostly cheap ready-meals and energy-dense foods and favoring the development of obesity (Cummins, 2014). In general, marketing strategies favor the purchase of food product by lowering their price (French, 2003). A study lead by Hannan and colleagues (2002) showed that lowering the price of low-fat foods by 20% while increasing the price of high-fat foods by 10% in a high-school cafeteria lead to an increased purchase of low-energy foods by students. In some countries, the governmental implementation of a tax on high-sugar food and beverages is currently discussed, as a means to discourage the purchase of such unhealthy foods (Encarnação et al., 2016). Price was also found to play a role in food taste and quality perception (Veale and Quester, 2009). This study assessed the relative influence of price and country of origin as extrinsic factors on wine quality and taste evaluation, as compared to wine's intrinsic factors, i.e. acidity. Results showed that, when aiming at identifying a "good" wine, participants let the price information override the intrinsic taste 72% of the time during quality assignment phase. Price is thus an important determinant in choice and purchase behavior.

1.4 Aim of the thesis

The thesis at hand aimed at investigating how behavioral and spatio-temporal brain responses to food perception and choice are shaped by food-intrinsic and extrinsic factors. Three studies are reported in the following experimental approaches.

The first study investigated how food liking influences subsequent choice between two food alternatives, and how, in turn, these factors modulate brain responses to the viewing of high- and low-energy foods. This experiment is further referred to as Study A and led to the publication of *"Does my brain want what my eyes like? – How food liking influences choice and impacts spatio-temporal brain dynamics of food viewing"* in Brain and Cognition (Bielser & Crézé et al., 2015). Please refer to chapter 3 for a summary, and to annex 1 for the published article.

The second study assessed spatio-temporal brain responses to meal images varying in portion size in light of prospective food intake and expected satiety. This study is further referred to as Study B and led to the publication of "*Brain dynamics of meal selection in humans*" in NeuroImage (Toepel, Bielser et al., 2015). Please refer to chapter 4 for a summary, and to annex 2 for the published article.

The third study examined how the incidental encounter of traffic light labeling of different colors (i.e. green, red, off) as used on food packages impacted behavioral and brain responses to foods varying in energetic content. This study is further referred to as Study C and is entitled "*Biasing behavioral decisions and brain responses to food with traffic light labeling*". Study C composes the chapter 5 of this thesis.

All three studies made use of electroencephalography (EEG) to assess neural modulations to food viewing. High-density EEG is a neuroimaging technique allowing for investigating spatio-temporal brain dynamics. This method offers the advantage of being non-invasive and provides very high temporal (millisecond) and good spatial resolution of the assessed neural processes at both head-surface and neural source level (Michel and Murray, 2012; Murray et al., 2008). For further details on the EEG methodology, please refer to chapter 2.

CHAPTER 2 METHODOLOGY

2.1 From Electroencephalography (EEG) to Event-related potentials (ERPs)

In the thesis at hand, continuous electroencephalography (EEG) was used as a means to investigate spatio-temporal brain dynamics to food's visual perception. The electrodes at the scalp-surface record the summation of the momentary post-synaptic activity of the neurons of the brain (Michel and Murray, 2012). Neural responses to particular stimuli (in our case, food and object images) can be isolated from the global ongoing brain activity. As these responses have rather small amplitudes as compared to basal neural activity and surrounding electrical noise, each stimulus has to be repeated many times to differentiate stimulus-specific neural activity from the ongoing brain activity. The neural response is time-locked to the visual stimulation, allowing the averaging of the peri-stimulus epoch across many repetitions for each stimulus category. This peri-stimulus averaging provides a replicable waveform with a high signal-to-noise ratio for each stimulus category, so-called event-related potential (ERP) (Luck, 2005). These averaged ERPs waveforms are characterized by their discrete timing as well as the polarity of their voltage, positive (P) or negative (N). In the case of salient visual stimuli, such as food, resulting ERPs typically comprise positive early latency P1 (~80-130ms), negative N170 (~150-200ms) and positive P300 (~250-280ms) late latency peaks (Haider et al., 1964; Mangun, 1995; Sutton et al., 1967). Figure 2 displays the computation of ERPs, resulting from the averaging of peri-stimulus epochs at each electrode, for each experimental condition. ERPs can thus provide information on "how" and "when" experimental conditions differ (Murray et al., 2008, 2009). However, analyses of "local" ERP components (i.e. electrode by electrode modulations) to assess differences between experimental conditions are debated: as each measure obtained at an individual electrode is calculated against a chosen reference to obtain an event-related potential, the arbitrary choice of the reference location inherently influences the resulting EEG waveforms in terms of amplitude and scalp-position. This reference-dependence of local ERP component analysis has been shown to influence the interpretation of EEG data in the literature (Michel and Murray, 2012). To thwart this reference-dependence, a "global" analysis approach for ERP data has been developed. This analysis approach provides information on changes in global measures of the electric field, such as the global response strength and topography, and is independent of the chosen reference electrode(s). Further, this approach allows for the estimation of neural source activity underlying the head-surface electrical modulations (Brunet et al., 2011; Michel and Murray, 2012; Michel et al., 2004; Murray et al., 2008). Global response strength, global topography dissimilarity as well as neural source estimation analyses are further detailed in sections 2.2 – 2.4. Figure 3 displays local and global analyses on continuous EEG recordings. In all three studies of the thesis at hand, we mainly concentrated on the global electric strength (i.e. global field power) in terms of amplitude and peaks as a means of data reduction. Global field power peaks reflect periods of topographic stability and maximal synchronously active neural sources. We further conducted neural source estimations over the time windows of global field power peaks (see sections 2.2 and 2.4). Further methodological and analysis details are reported in the methodology section of each of the three studies comprised in this thesis (see chapters 3, 4, and 5).

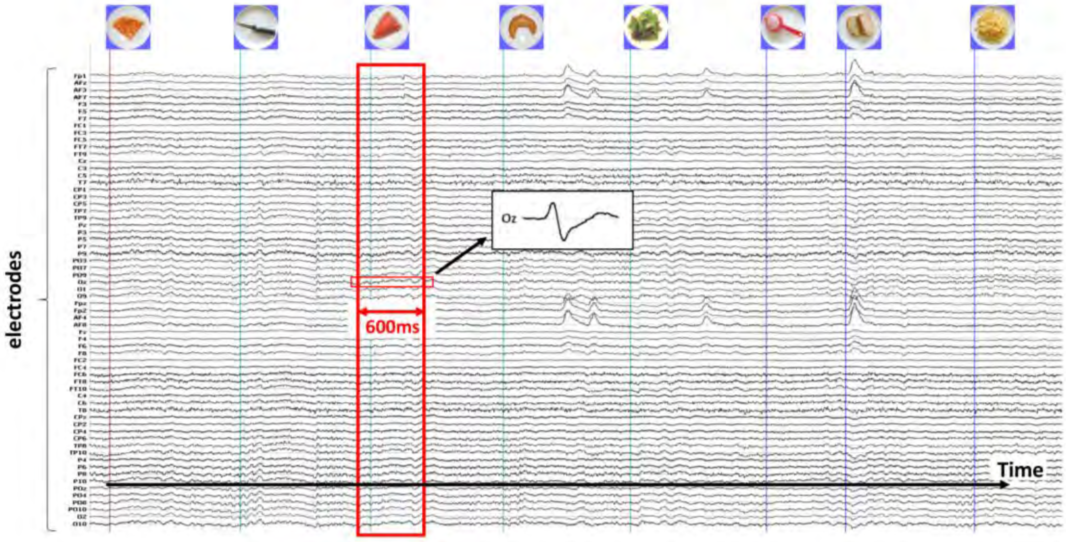

Figure 2: From electroencephalography to event-related potentials: display of continuous EEG (y axis) over time (x axis). Visual stimuli trigger time-locked neural responses, allowing the averaging of the peri-stimulus time period (red box) and over trials for each condition and electrode, resulting in event-related potentials.

2.2 Global Field Power

A quantitative measure of the electric field strength at the head-surface is the Global Field Power (GFP) (Lehmann and Skrandies, 1980). As previously mentioned, GFP analyses provide the advantage of a reference-free measure reflecting synchronized activity of underlying neural sources by quantifying the average power of the electrical signal across the electrode montage expressed in microvolts (µV). GFP provides no information about the spatial distribution of the ERPs across the scalp and, by extension, no information about the spatial configuration of the underlying brain generators. Mathematically, GFP equals to the standard deviation of all electrodes at a given moment of time (Brunet et al., 2011; Lehmann and Skrandies, 1980; Murray et al., 2008). Periods of GFP peaks reflect periods of topographic stability and correspond to moments during which the largest amount of underlying neural sources are synchronously active. Modulations of GFP across different experimental conditions can be assessed time point by time point on a given data set. However, in the three studies of the thesis at hand, as a means for data reduction and to define time windows of interest for further analyses, GFP was averaged over time periods of GFP peaks (i.e. periods of maximal synchronously active neural sources). This provided us with the mean GFP amplitude for each participant to each experimental condition separately, and served for further analyses described in the respective methodological section of each study (see chapters 3, 4, and 5).

2.3 Global topographic dissimilarity

Topographic measures provide qualitative spatial information on the electric field topographic configuration at the head-surface. Global topographic dissimilarity is, as GFP, a reference-independent measure. This measure identifies time periods of changes in the neural generator configuration (Brunet et al., 2011; Michel and Murray, 2012; Murray et al., 2008). In turn, topographic analyses also determine when the neural generator configuration differs between varying experimental conditions (Murray et al., 2008). Further, this measure is independent from the electric field strength (i.e. GFP). Only a short description of global topographic dissimilarity is given here, as we focused on analyses of GFP peak time windows in this thesis (For details, see Michel and Murray, 2012)).

2.4 Estimation of active neural sources underlying head-surface modulations

High-density electrode montages in EEG recordings allow for the estimation of active neural sources underlying electric signal modulations recorded at the head-surface. Neural source estimations for the thesis at hand are realized by means of a mathematical model called “inverse solution model”, based on the electric potentials measured at the scalp surface (Brunet et al., 2011; Spinelli et al., 2000). These neural source estimations provide information on the location and level of activity of the brain generators, with a high temporal resolution (millisecond range) and a relatively good spatial precision (Michel and Murray, 2012). However, as a given electric potential recorded at the scalp can arise from various configurations of intracranial sources at a specific time point, neural source estimations cannot provide unique solutions. For the three studies reported, we used a distributed linear inverse solution applying a local autoregressive average (LAURA) algorithm (Brunet et al., 2011; Grave de Peralta Menendez et al., 2001, 2004; Michel and Murray, 2012; Michel et al., 2004). LAURA provides a 3D head model of the brain containing 3005 nodes selected from a 6x6x6mm grid and equally arranged within the gray matter of the Montreal Neurological Institute’s (MNI) average brain. The version of the LAURA inverse solution applied here was created with the Spherical Model with Anatomical constraints (SMAC) (Spinelli et al., 2000). The output of the source estimation algorithm provides current density values (in µA/mm3) for each node of the solution point matrix. In the thesis at hand, inverse solutions were conducted for each participant's responses to experimental conditions over time periods of interest as previously defined based on the head-surface response modulations (i.e. global field power peaks). Further analyses conducted on source estimations are described in the respective methodological section of each study (see chapters 3, 4, and 5).

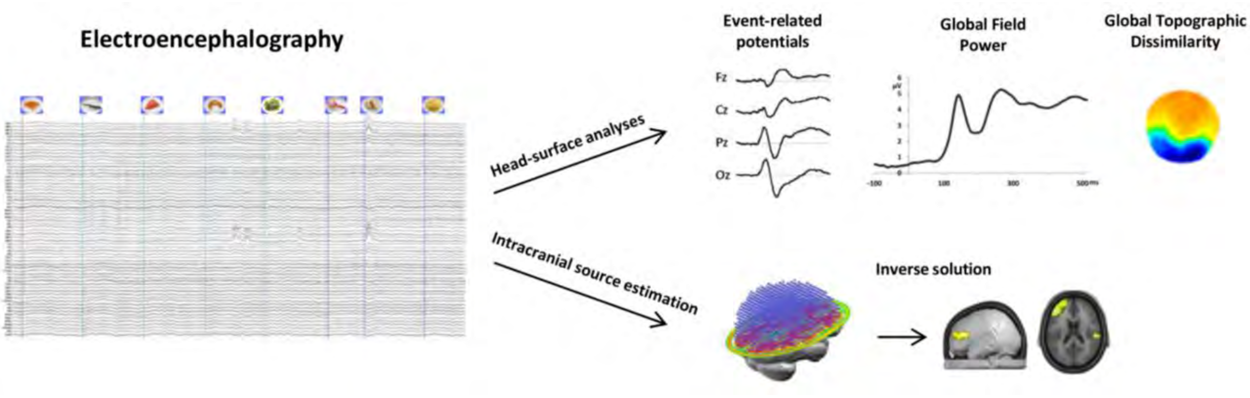

Figure 3 : Illustration of the global analysis approach of electroencephalographic data. Electroencephalographic traces can be analyzed at both head-surface (i.e. event-related potentials (ERP), Global Field Power (GFP); Global Topographic Dissimilarity) and intracranial level (i.e. source estimation). (Adapted from Murray et al., 2012).

CHAPTER 3 STUDY A – Does my brain want what my eyes like? - How food liking and choice influence spatio-temporal brain dynamics of food viewing

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(* equal contribution)

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Contribution: The candidate analyzed the data and prepared the manuscript for submission.

This study investigated whether food valuation influences subsequent decision-making and how, in turn, both modulate behavioral responses as well as spatio-temporal brain dynamics to food viewing. Twenty-two normal-weight participants partook in the study and were presented with pairs of food photographs while undergoing electroencephalographic (EEG) recordings. Image pairs always comprised two foods from the same product category (e.g. deserts, fruits, meat, milk products). Participants were asked to rate their appreciation of each individual food image by button press during a “valuation phase” (1-5 Likert scale). Following each image pair, they were asked to decide which of the two alternative foods per pair they preferred (“choice period”). Analyses of the valuation responses showed that strongly liked foods were rated faster as compared to mildly liked and disliked foods, irrespective of the subsequent choice. Strongly liked foods were also chosen most often and this choice was made faster than for less appreciated foods. Analyses on brain responses to food viewing were conducted by means of visual evoked potentials (VEPs). Both food liking and subsequent choice were found to modulate VEPs as early as 135-180ms after food image onset. Analyses on neural source activity over this time period of interest revealed an interaction between liking and the subsequent choice in the insula, the dorsal frontal and the superior parietal region. The level of liking attributed by participants was found to modulate neural responses to food viewing when foods were subsequently chosen, but not when dismissed for an alternative. When subsequently chosen, responses to disliked food were overall higher than those to mildly and strongly liked foods. Our findings indicate that spatio-temporal brain dynamics to the viewing of foods are influenced by valuation of the food (attributed liking), but also by the subsequent preference decisions. These processes of valuation and choice occur in brain areas known to be involved in salience attribution as well as in decision-making processes, likely influencing prospective food intake.

CHAPTER 4 STUDY B – Brain dynamics of meal size selection in humans

Authors: Ulrike Toepel, Marie-Laure Bielser, Ciaran Forde, Nathalie Martin, Alexandre Voirin, Johannes le Coutre, Micah M. Murray, Julie Hudry – (2015)

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Contribution: The candidate contributed to the data acquisition, data analyses and manuscript preparation.

This study investigated the spatio-temporal brain dynamics to the viewing of meal images varying in portion size. Twenty-one normal-weight women partook in the study and were asked to perform a task of ideal portion selection for prospective lunch intake and expected satiety while undergoing electroencephalographic recordings. Neural responses to meal portion sizes judged as “too small”, “ideal”, and “too big” were assessed by means of visual evoked potentials (VEPs). Head-surface modulations of the global electric field strength (i.e. global field power) showed an incremental increase with the portion ratings from “too small” to “too big” as early as 105-145ms post-image onset. Neural source estimations conducted over this time window of interest showed that the judgment on portion size also resulted in modulated activity in brain regions like the insula, the middle frontal and middle temporal gyrus. In contrast, over a later time window of interest from 230-270ms, head-surface global field power was maximal for the “ideal” as compared to “non-ideal” portion sizes. Neural source estimations over this later time period revealed greater activity to “ideal” relative to “non-ideal” portion sizes in the inferior parietal lobule, the superior temporal gyrus, and the mid-posterior cingulate gyrus. Our results provide first evidence that brain regions involved in visual processing, salience and reward attribution trace “physical” portion size increases during early stages of perception, likely reflecting a quantitative evaluation of the amount of food available for prospective ingestion. During a later information processing stage, brain regions involved in attention and adaptive behaviors show greater responsiveness to portions judged as “ideal”, likely reflecting control over food intake, thus leading to the selection of an ideal portion to reach adequate satiety.

CHAPTER 5 STUDY C – Biasing behavioral decisions and brain responses to food with traffic light labeling

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Contribution: The candidate prepared and conducted data recording, did the data analyses and is currently preparing the manuscript for submission.

5.1 Abstract

Our study investigated the influence of traffic light labeling (as used for nutrient information on food packages) on behavioral and brain responses to food viewing. Multichannel electroencephalography (EEG) served to assess visual evoked potentials (VEPs) to the viewing of color images of low-fat and high-fat foods in 16 healthy, non-dieting, and normal-weight participants. Food image viewing was preceded by either 'green', 'red' or 'off' traffic light labels. Participants performed an online food/non-food categorization task and additionally rated the liking of food items offline. Analyses focused on the influence of 'green' and 'red' relative to 'off' traffic lights on food viewing. In the online behavioral categorization task, participant's accuracy was decreased when HiFat foods were preceded by 'green' or 'red' as compared to 'off' labels. VEP analyses showed that color labels affected responses to food viewing over two time windows (i.e. 115-155ms (TW1) and 240-280ms (TW2) post-image onset). Neural source estimations over both intervals showed interactions of traffic light labeling and food category viewed in lateral prefrontal cortex and superior temporal gyrus (TW1) and medial prefrontal cortex (TW2). Neural activity in the latPFC and medPFC, regions involved in cognitive control and reward valuation, respectively, were higher when low-energy foods were combined with a red label and when high-energy foods were paired with a green traffic light. In the STG, a region involved in memory and learned associations, the activity was higher for low-energy foods preceded by a green label and for high-energy foods preceded by a red label. Our results show the potential of traffic light labeling as means to influence food perception at both behavioral and neural levels. These findings support previous evidence that traffic light labeling influences behavioral and brain responses to food upon incidental encounter. In extension, traffic light labeling could thus be an effective tool for benefit of body weight management.

5.2 Introduction

Obesity has reached pandemic proportions over the last decades, notably due to the over-abundance of tempting foods encouraging overeating and subsequent weight gain. Since hedonic properties of food tend to override homeostatic energetic needs, new means to attain healthier food choices and resistance to tempting foods are needed. Given that energy-dense foods are constantly and immediately available in Western countries, poorly-guided food purchase and intake decisions are identified as leading causes of the increasing prevalence of obesity (Finucane et al., 2011; Morris et al., 2015; Ogden et al., 2015; Stevens et al., 2012). That is, resisting food temptations has become a necessity in order to maintain healthy body weight. Research on human food perception has already identified alterations in the perception of food by overweight and heightened body mass index and as a function of whether high- or low-energy foods are perceived (Rothemund et al., 2007; Stoeckel et al., 2008; Toepel et al., 2012; Uher et al., 2004). Little is known on how to influence food perception, and in turn choices, for the benefit of a sustainable body weight management. Food is usually not perceived in isolation, and its perception can be influenced by external contexts. Here, we tested traffic light labeling as contextual means to impact food perception. A better understanding of the modulations of brain responses to food viewing by food traffic light color labeling are of interest to assess the effectiveness of such means to guide food choices and intake.

Contexts in which foods are encountered (such as food packaging, pricing and plating) exert a strong influence on food perception and subsequent intake. The packaging aesthetics, rather than its nutritive information, is a strong neural predictor of further purchase (Van der Laan et al., 2012). For example, food presented with organic labeling increases the willingness to pay for it and is reflected by a higher activation the reward neural network as compared to equal food presented in conventional form (Linder et al., 2010). In line, verbal-emotional labeling decreases neural responses to food viewing, specifically to high-energy foods, notably in brain areas involved in cognitive control and adaptive behavior, such as the posterior dorsal frontal cortex, the posterior cingulate cortex, the posterior insula as well as the occipital cortex (Toepel et al., 2014).

In several countries, food labeling (i.e. front-pack labels, verbal labels, traffic light labels, Guideline Daily Amount (GDA)) has been implemented in order to encourage healthier choices (Borgmeier and Westenhoefer, 2009). However, evidence as to the efficacy of these labels on guiding food purchase decisions remains controversial (Baltas, 2001; Drichoutis et al., 2006; Padberg, 1992; Temple and Fraser, 2014). In particular, the impact of nutritional labeling on food preferences, choices, and attention attenuation are still strongly debated (Baltas, 2001; Borgmeier and Westenhoefer, 2009). Within the existing labeling formats, traffic light labeling was found to be the most effective one. Behavioral as well as eye-tracking studies showed that, in comparison to other formats (i.e. GDAs;

nutrition table; “healthy choice” tick), traffic lights labels help to identify better and faster healthy food items (Borgmeier and Westenhoefer, 2009; Siegrist et al., 2015). The success of traffic light labeling is likely due to the fact that colors induce physiological, behavioral and cognitive changes, notably through learned associations (Elliot and Maier, 2007, 2014; Mehta and Zhu, 2009; Meier et al., 2015). Typically, red is often used as a stop or warning signal, whereas green is perceived as a go signal (Elliot et al., 2009). That is, colors increase arousal, in turn modulating perception of the environment in general (Mehta and Zhu, 2009; Shi, 2013), but also food in particular (Spence et al., 2010 for review). A study of Genschow and colleagues (2012) showed that the red coloring of serving plates/cups reduces amounts of snacks/soft drink consumption. Further, it was demonstrated that perceived taste and sweetness were modulated by color information provided with the food. For example, salty popcorn was rated as sweeter when eaten out of a red as compared to white bowl (Harrar et al., 2011). In line, chocolates were judged more “chocolaty” when presented in a brown as opposed to green color coating (Shankar et al., 2009). However, to date, still little is known on whether and how the incidental encounter of color labeling influences behavioral and brain responses when foods differing in energy density are viewed.

We investigated the impact of encountering traffic light labeling preceding food images on behavioral and brain responses to food viewing and whether these traffic labels differentially influence the viewing of high- vs. low-energy foods. Multichannel electroencephalographic (EEG) recordings were conducted while normal-weight participants viewed images of foods varying in energetic content preceded by off (i.e. baseline), green and red traffic lights. Features of the global properties of head-surface electric field (i.e. Global Field Power) and neural source activity to food viewing were analyzed to assess the influence of green and red traffic light labels relative to off labels. Moreover, regression analyses tested associations of neural responses modulations by color label with the like ratings of high- and low-energy foods.

5.3 Materials and methods

5.3.1 Participants

Sixteen remunerated volunteers (nine males) aged 19-40 years (mean ± SEM = 25.5 ± 1.3) partook in our study. Their BMIs were within normal range (mean ± SEM = 21.3 ± 0.6 kg/m^2). All participants were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971), with normal or corrected-to-normal vision and with no neurological pathologies or psychiatric illnesses. Exclusion criteria were color blindness, history of eating disorders, crurrent diet or dietary restraints (i.e. vegetarianism), food intolerance (e.g. lactose, gluten), recreational drug taking, pregnancy or breastfeeding. Female participants were tested between day 3 and 15 of their menstrual cycle and 6 out of 7 used contraceptive medication. All volunteers signed written, informed consent to the procedures, which were previously approved by the Cantonal Human Research Ethics Commission of Vaud (CER-VD).

5.3.2 Experimental protocol: EEG recording set-up, stimuli and task

Participants arrived to the lab at 10am or at 3pm to control for circadian regulation of hunger. They were instructed and self-reported to have eaten a usual portion of breakfast or lunch ~2h30 before the experiment. Upon arrival, participants filled out psychometric questionnaires, i.e. the Three-Factor Eating Questionnaire (TFEQ) (Karlsson et al., 2000) and the Beck Depression Inventory (BDI) (Beck and Beck, 1972). Before and after the experiment, they rated their level of hunger as well as their will to eat on visual analogue scales (VAS). A Biosemi ActiveTwo system (Biosemi, Amsterdam, Netherlands) electrode cap was placed on the volunteers' head for electroencephalographic (EEG) recordings. EEG data were acquired at a sampling frequency of 512Hz from 128-channels referenced to a ground circuitry (CMS-DRL). Participants completed a ~1 hour EEG recording session comprising the viewing of 240 color photographs of food images and 120 nonfood items (i.e. kitchen utensils), in a dark lit, sound-proof booth in a sitting position facing a computer screen. Each of the 360 images appeared once preceded by each traffic light color (i.e. off (O), green (G), red (R)) in a pseudo-randomized order. The food images were subdivided into two categories: 120 pictures of high-energy foods (henceforth: HiFat) and 120 pictures of low-energy foods (henceforth: LoFat). The division into HiFat/LoFat was based on the Swiss nutritional database (Swiss Federal Office of Health and Swiss Federal Institute of Technology in Zürich). LoFat items had a fat content comprised between 0 and 5g/100g (mean ± s.e.m. = 0.89g ± 0.13) and HiFat items a fat content between 12 and 81.10g/100g (mean ± s.e.m. = 27.12 ± 1.39). The mean energy density for LoFat pictures was 142.98 kCal/100g (s.e.m. ± 12.36) and 384.77 kCal/100g (s.e.m. ± 13.05) for the HiFat images. All images measured 300x300 pixels and were taken from an identical top-view angle with an identical background (Toepel et al., 2009). Images were controlled for low-level visual features, and the luminance and spatial frequency were adapted between LoFat and HiFat images (Knebel et al., 2008). Moreover, a pre-test in 24 subjects made sure that valence and arousal of LoFat and HiFat images did not differ between food categories. During the EEG recording sessions, traffic light labels as well as food and non-food pictures appeared for 500ms on the computer screen, separated by a random inter-stimulus interval (ISI) of 250-500ms. The inter-trial interval (ITI) varied randomly between 250 and 750ms. Each recording session was composed of 9 consecutive blocks, containing 120 pseudo-randomized pictures each. Any particular traffic light – image combination appeared only once per block. To avoid eye movement artifacts, a fixation cross was displayed on the screen whenever no traffic light label or photograph was presented. During EEG recordings, participants were asked to categorize photographs "online" into food and non-food items via button press as fast as possible and received no explicit instruction regarding the preceding traffic lights labels or the varying energetic content of the food images. Data analyses focused on the behavioral and neural changes in response to LoFat and HiFat foods as a function of the preceding traffic light color (i.e. the impact of the incidental encounter of color labels on food perception). Exemplary stimuli and the experimental trial set-up are displayed in Figure 4.

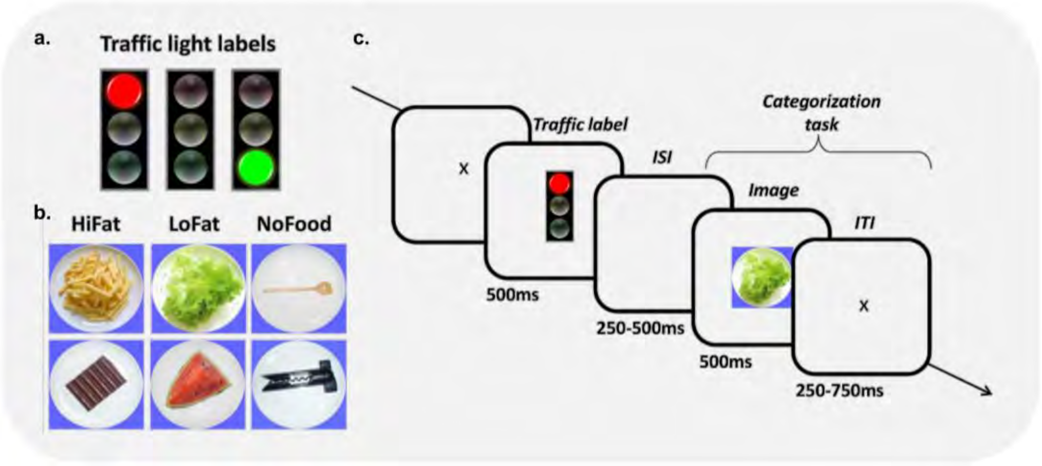

Figure 4 : Experimental design. a. Traffic light labels (red, off, green)**; b.** Examples of HiFat and LoFat food, as well as non-food images (i.e. kitchen utensils, solely serving the behavioral task)**; c.** Trial structure. Participants were asked to categorize images into food and non-food items by button press. Each image was presented once preceded by each traffic light label color.

After EEG recordings, the electrode cap was removed from participants' head. Volunteers were once more presented randomly with all food images and asked to rate how much they liked each on a 1-5 Likert scale (offline food like rating). Each food image appeared for 500ms on the computer screen with a random ISI of 250 to 1000ms. The control of stimulus display and the recording of behavioral responses were done by E-prime software (Psychology Software Tools Inc., Pittsburgh, USA).

5.3.3 Behavioral data analyses

Responses in the online categorization task were analyzed with respect to response accuracy (ACC) and reaction times (RT). For each participant, the relative differences (in %) in responses to LoFat and HiFat foods preceded by a color label (green; red) as compared to "off" traffic light (as baseline) were computed (henceforth: G-O_LoFat; G-O_HiFat; R-O_LoFat; R-O_HiFat). The resulting data provides differences between responses to color-food combinations with respect to a baseline (off-food combination) and accounts for inter-individual baseline response differences. Response modulations by color label and food category were assessed by means of two-way ANOVAs with the factors of label color (G-O and R-O) and food category (LoFat and HiFat). Post-hoc paired t-tests (two-tailed) were applied when appropriate. Further, one-sample t-tests (two-tailed) were conducted to detect whether particular color-food combination revealed response patterns that significantly differed from the response to off-food (i.e. baseline) combination.

For the analyses of offline food like ratings, weighted mean scores were computed for each food category (LoFat, HiFat) in each participant. A paired t-test (two-tailed) was conducted to assess differences in liking between the two food categories. For all statistical tests, only results with p-values ≤0.05 are reported.

5.3.4 EEG pre-processing steps

Visual evoked potentials (VEPs) to the viewing of LoFat and HiFat foods were epoched over the peri-stimulus period from -100ms to 500ms of food image onset. During epoching, band-pass filtering (0.1-40Hz), a 50Hz Notch filter, and a semi-automatic artifact rejection criterion of 80µV were applied. EEG epochs were then first averaged for each participant, and each food category preceded by each color label (O_LoFat; O_HiFat; G_LoFat; G_HiFat; R_LoFat; R_HiFat) separately. Electrodes with artifacts were interpolated (Perrin et al., 1987). Group-average VEPs were then computed for each food viewing condition; pre-stimulus baseline-correction was applied over the period from -100 to 0ms before image onset. These group-average VEPs were then recalculated against the average reference. All pre-processing steps were done with the CARTOOL software (http://www.fbmlab.com/cartool-software/), the STEN toolbox (http://www.unil.ch/line/home/menuinst/about-the-line/software--analysis-tools.html), and customized MATLAB and Python scripts.

5.3.5 VEP analyses and associations between neural responses to food viewing with food liking and psychometric assessments

Head-surface VEP analyses to the viewing of food focused in particular on global strength of the electric field, i.e. Global Field Power (GFP) (Lehmann and Skrandies, 1980). GFP equals the standard deviation of the electric field amplitude at a given moment of time (Brunet et al., 2011; Murray et al., 2008). That is, GFP provides quantitative information on the momentary electrical potentials across the head surface, corresponding to the synchronized activity of the neural sources and reflecting the strongest VEP topography (Brunet et al., 2011). GFP peaks are time periods of strongest synchronization in neural generators but least modulations in the topography of responses (Michel and Murray, 2012). First, single and group-average GFP waveforms were computed over peri-stimulus epoch for each viewing condition (i.e. O_LoFat; O_HiFat; G_LoFat; G_HiFat; R_LoFat; R_HiFat). Then, GFP peak time windows for further analyses were defined in group-average data and cross-checked in individual data. Within each time window of interest (±20ms of absolute peak value in group average data), instantaneous GFP values in each individual were averaged for each of the 6 conditions. Then, the relative differences between responses to food images preceded by a color label (red; green) as opposed to off traffic light were computed in terms of %difference. The resulting data reflect changes in response to each color-food combination from baseline (i.e. off-food combination) resulting in 4 conditions (i.e. G-O_LoFat; G-O_HiFat; R-O_LoFat; R-O_HiFat), also accounting for inter-individual baseline differences (i.e. off-food combinations). Two-way ANOVAs with the factors of label color (G-O; R-O) and food category (LoFat; HiFat) were conducted over each GFP peak window to assess significant modulations of head-surface responses by these factors. Post-hoc paired t-tests (two-tailed) were applied when appropriate. Further, one-sample t-tests (two-tailed) were conducted to detect whether a particular color-food combination revealed activity patterns that significantly differed from the response to off-food (i.e. baseline) combination. For all statistical tests, only results with p-values ≤0.05 are reported.

In a second step, analyses consisted of estimations of intracranial sources underlying the head-surface GFP peak responses and modulations. As input, data were averaged over the time windows of interest (GFP peak TW), resulting in a single data point per electrode for each participant and each condition to increase the signal-to-noise ratio. Intracranial source estimations were computed using the local autoregressive average (LAURA) distributed linear inverse solution (Grave de Peralta Menendez et al., 2001, 2004; Michel et al., 2004). LAURA uses a 3D head model, containing 3005 nodes equally arranged within the gray matter of the Montreal Neurological Institute’s (MNI) average brain. The particular inverse solution was generated with the Spherical Model with Anatomical constraints (SMAC) (Spinelli et al., 2000). The output of the source estimation by LAURA is given in terms of current density (in µA/mm3) for each of the 3005 nodes of the model. In order to assess whether color labels influenced neural responses to food viewing, we again calculated the relative difference (in %) between color-food combinations as opposed to off-food combinations (as baseline). This was computed as the difference of activity in one node between color-food combinations (i.e. G_LoFat; G_HiFat; R_LoFat; R_HiFat) relative to the average activity across all sources nodes in the off light condition (i.e. O_LoFat; O_HiFat). To assess modulations in neural source activity by label color and food category within each time window, whole-brain statistical analyses were conducted by means of two-way ANOVAs with the factors of label color (G-O; R-O) and food category (LoFat; HiFat). Only clusters revealing a significant interaction (p-values ≤0.05) in >10 nodes were retained for consecutive region of interest (ROI) analyses. For ROI analyses, the averaged neural activity (in $\mu A/mm^3$) of the source node with the lowest p-value (plus its immediate 6 neighbors) entered post-hoc and correlation analyses. Further, one-sample t-tests (two-tailed) within each ROI served to detect whether the response to a particular color-food combination significantly differed from the responses to off-food combination (i.e. baseline). In each of these ROIs, post-hoc paired t-tests (two-tailed) were conducted to assess whether the activity to the viewing of food significantly differed as a function of food category or preceding traffic light. Additional Spearman correlation analyses served to detect associations between changes in neural activity to color-food combinations relative to off-food combinations, and the food liking scores. For all post-hoc analyses, only results with p-values ≤0.05 are reported.

5.4 Results

5.4.1 Behavioral data and psychometric assessments

In the online behavioral food/non-food categorization task during EEG recording, participants overall response accuracy was 95.14% (± s.e.m. = 1.42). The average response accuracy was 90.14% (± s.e.m. = 1.73) for Non-Food, 97.60% (± s.e.m. = 1.81) for LoFat, and 97.67% (± s.e.m. = 1.46) for HiFat. The overall mean response time was 514.46ms (± s.e.m. = 15.11). The average response time was 546.74ms (± s.e.m. = 14.78) for Non-Food, 496.80ms (± s.e.m. = 15.26) for LoFat, and 499.85ms (± s.e.m. = 15.20) for HiFat.

In Figure 5a, the relative difference in accuracy is plotted when LoFat and HiFat foods were coupled with color traffic labels (i.e. green or red) relative to the respective off-food combination. Descriptively, the viewing of color-food combinations led to a decrease in accuracy relative to off-food combinations. ANOVAs on accuracy and reaction times revealed no main effect or interaction of traffic label color or food category. One-sample t-tests, on the other hand, revealed a significant decrease in accuracy only when participants had to categorize HiFat foods preceded by either green (t_{15}=-3.13, p=0.01; r^2=0.39) or red (t_{15}=-2.13, p=0.05; r^2=0.23) labels, as compared to off-food combinations.

Weighted scores of food liking as assessed offline after the EEG recording were found to be significantly higher for HiFat (mean ± s.e.m. = 3.47 ± 0.10) than for LoFat (mean ± s.e.m. = 3.17 ± 0.07) foods (t_{15}=-2.45; p=0.03; r^2=0.30) (Figure 5b).

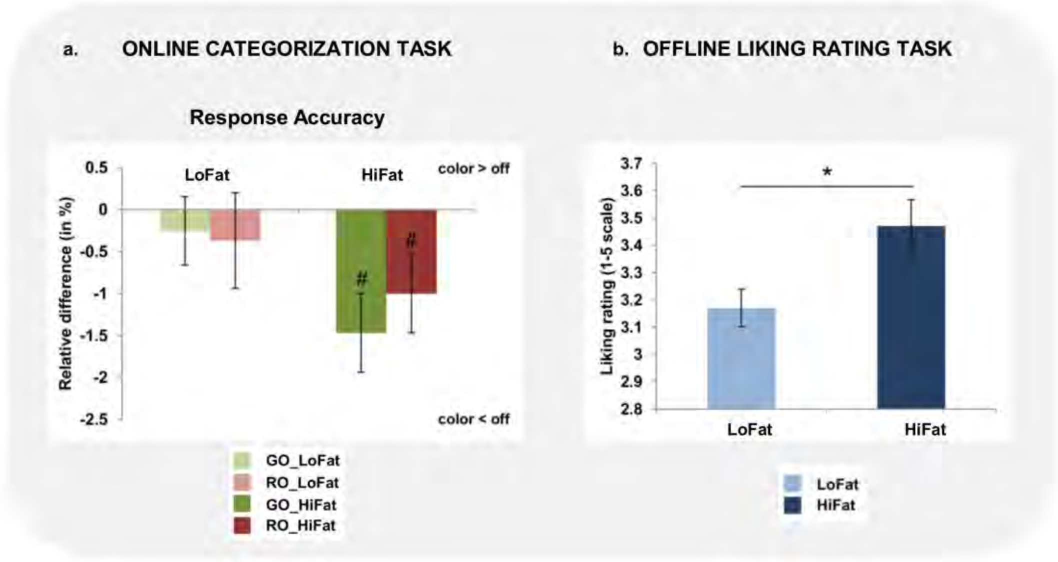

Figure 5: Behavioral results of the online food/non-food categorization task. Relative difference in % (±s.e.m.) in accuracy for each color-food relative to off-food combination (as baseline). #p≤0.05 (one-sample t-tests) **; b. Behavioral results of the offline food like rating task ;** Mean liking ratings (±s.e.m.) weighed by the scale for HiFat and LoFat foods on a 1-5 Likert scale.*p≤0.05 (paired t-tests).

5.4.2 Head surface global electric field strength

In the GFP waveform over time, two GFP peaks were identified, motivating the choice of time intervals from 115-155ms and 240-280ms following food image onset for further analyses (Figure 6a). ANOVAs on the GFP over both time windows revealed no main effect or interaction of traffic label color and viewed food category. Also, one-sample t-tests over both time windows showed no significant difference within conditions when food images were preceded by a color relative to off label.

5.4.3 Modulations of neural source activity to food viewing

Neural source estimations were computed over both time windows of interest (i.e. 115-155ms and 240-280ms). Figures 6b and 6c visualize brain regions that showed a significant interaction of traffic label color and food category in the whole-brain analyses. Coordinates of the source node showing the lowest p-value by region are given by means of the Talairach system (Talairach and Tournoux, 1988) and visualized on the MNI template brain.

Over the time interval from 115-155ms, whole-brain analyses showed an interaction of traffic label color and food category in the left lateral prefrontal cortex (latPFC; Max: -47; 32; 19) and in the right superior temporal gyrus (STG; Max: 60; -21; 14). ROI analyses showed that in the latPFC, the perception of color-food combinations relative to off-food combinations resulted in higher neural activity when viewing LoFat foods preceded by a red label (t_{15}=2.43; p=0.03; r^2=0.28) and when viewing HiFat foods preceded by a green label (t_{15}=2.58; p=0.02; r^2=0.31). In the STG, solely the activity to HiFat foods preceded by a red label was significantly higher than for the off-food combinations (t_{15}=2.37; p=0.03; r^2=0.27). Post-hoc analyses in each region showed that in the latPFC, neural activity was significantly higher when viewing HiFat foods preceded by a green as opposed to a red traffic label (t_{15}=2.46; p=0.03; r^2=0.29). In contrast, post-hoc analyses in the STG showed higher activity when HiFat foods were viewed preceded by a red as opposed to a green label (t_{15}=-2.14; p=0.05; r^2=0.24) (Figure 6d).

Over the 240-280ms time interval, whole-brain analyses showed an interaction of label color and food category in the right medial PFC (medPFC; Max: 26; 24; 53). In this ROI, only the viewing of LoFat preceded by a red label revealed a greater activity than the off-food combination (t_{15}=2.18; p=0.05; r^2=0.24). Post-hoc analyses in this region showed that the activity was significantly higher when viewing LoFat foods preceded by a red as compared to a green label (t_{15}=-2.63; p=0.02; r^2=0.32) (Figure 6e).

5.4.4 *Associations of neural source activity with individual food likes*

Figure 6f displays the associations of neural source activity with food like ratings. Over the time interval 115-155ms, only for responses of the lateral prefrontal cortex, correlation analyses revealed a negative association between the food viewing activity when viewing HiFat foods preceded by a red label and the respective offline food like scores (r_{s14}=-0.55; p=0.03). That is, the more an individual indicates to like HiFat foods, the less prefrontal brain responses to HiFat food are modulated by a red traffic light label.

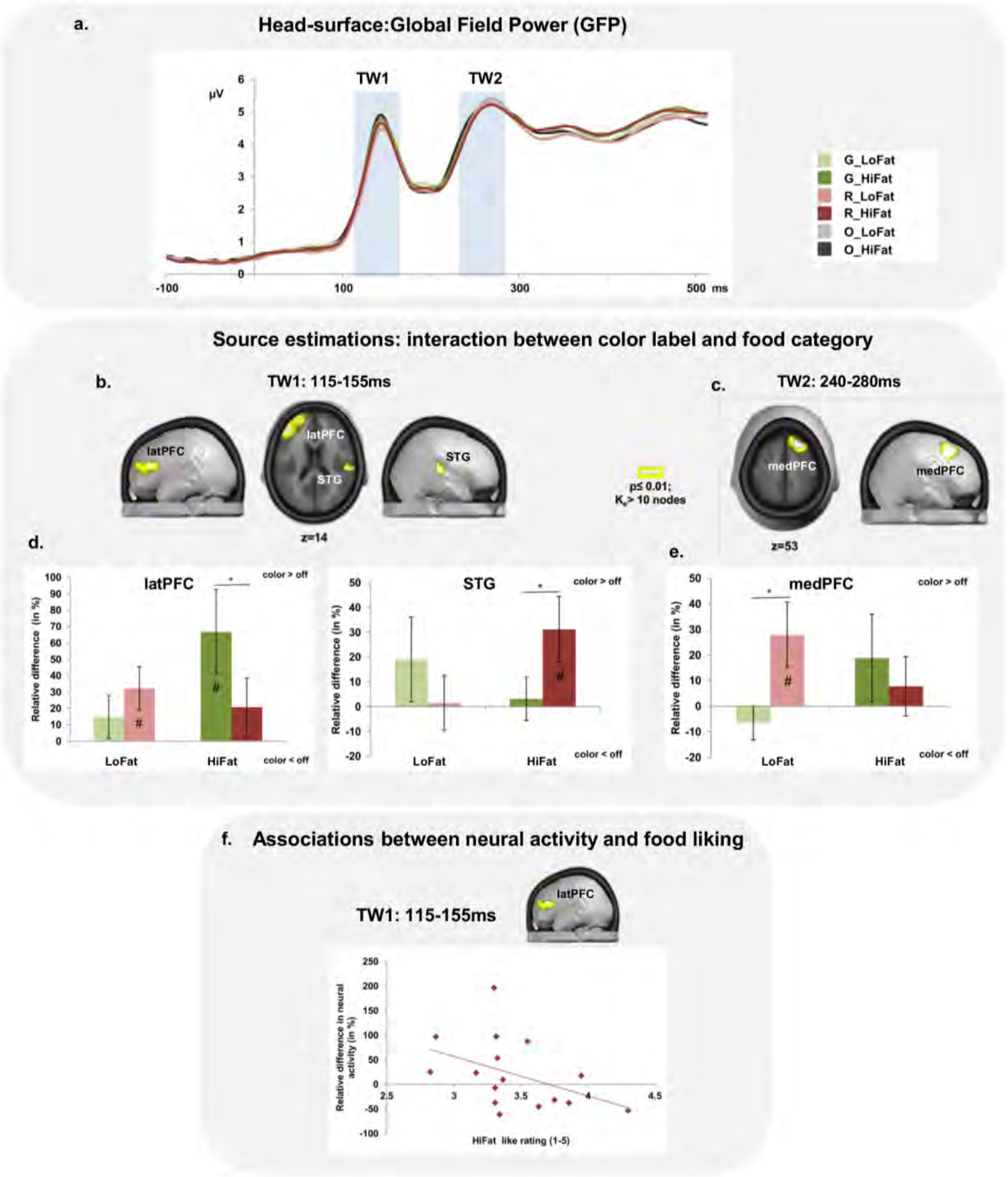

Figure 6 : a. Results of the head-surface VEP analyses: Global Field Power (GFP) waveforms to the viewing of each food category (LoFat and HiFat) preceded by each traffic light (green, off, red). Time windows of interest were two GFP peaks (i.e. TW1=115-155ms and TW2=240-280ms post-image onset) ; **b. and c. Source estimations** : Whole-brain modulations by color label and food category over TW1 (115-155ms) and TW2 (240-280ms) respectively ; **d. and e. relative differences (in %) (±s.e.m.) in neural activity** within each region of interest in response to each color-food combination relative to off-food combination over TW1 and TW2 respectively. #p≤0.05 (one-sample t-tests), *p≤0.05 (paired t-tests) ; **f. Association** between the relative difference in neural activity in the lateral prefrontal cortex to the viewing of red-HiFat combination relative to off-HiFat combination, and the offline food like rating of HiFat foods.

5.5 Discussion

Our study shows that traffic light labeling modulates behavioral accuracy during a categorization task, as well as spatio-temporal brain dynamics to the viewing of food images varying in energetic content.

During the online food/non-food categorization task, color-food combinations led to a general decrease in accuracy of participants relative to off-food combinations, in particular when viewing high-energy foods. Most studies so far assessed the influence of the color red on task performance only. For example, in line with our results, a study testing the influence of the colors red, green and black on intellectual performance found that the color red was perceived as negative contextual information. Performance of participants was also shown to decrease when the color red was present during the achievement of anagram completion (Elliot et al., 2007). In this study, the color green did not influence the performance of participants. In a review, Elliot and Maier (2014) reported that the color red in particular affects tasks of intermediate difficulty for participants, such as categorization tasks, but has less effects on cognitively more challenging tasks. Another study (Genschow et al., 2012) assessing the influence of colors on soft drink and food consumption showed that the color red effectively reduced the amounts consumed. In this study, naive participants were asked to evaluate the taste of soft drinks while drinking out of cups labeled with either red or blue stickers. In addition, participants were asked to fill questionnaires while being invited to snack freely on pretzels presented on red, blue or white plates. In both cases, participants' snack consumption decreased when the cutlery was red. Therefore, the impact of color traffic lights on the behavioral responses of our participants could reflect a change in the allocated attention to foods, in turn impacting psychological and motor responses.

In terms of spatio-temporal brain dynamics to food viewing, we determined two periods of peaks in global field power, i.e. 115-155ms and 240-280ms post-image onset. The timing of these modulations is in line with previous literature on brain responses to the viewing of food varying in energetic content as well as the impact of verbal labeling on the viewing of such foods. Previous studies showed that images of high-energy foods are discriminated from object images as early as ~100ms in temporal and parietal cortices and that a subsequent categorization between high- and low-energy food images occurs at ~165ms and ~300ms post-image onset in ventral and dorsal prefrontal cortices (Toepel et al., 2009, 2010). Further, the study from Toepel and colleagues (2014) on the influence of verbal-emotional labeling on behavioral and brain responses to the viewing of food showed a selective impact of positive verbal (vs. neutral and negative) labels on spatio-temporal brain dynamics to the viewing of high-energy (vs. low-energy) foods. Labels with a positive emotional valence specifically modulated neural activity to high-energy foods in occipital, posterior, frontal, insular and cingulate brain areas over 260-300ms post-image onset.

Statistical analyses on neural source activity over the earlier time window (i.e. 115-155ms) revealed an interaction of traffic light labels and viewed food category in the lateral prefrontal cortex (latPFC) and the superior temporal gyrus (STG). In the latPFC, the relative difference of the activity when color-food combinations were viewed relative to off-food combinations was greater for high-energy foods preceded by a green compared to a red label. Only responses to low-energy foods preceded by a red and high-energy foods preceded by a green label differed from their respective off-food combinations. The neural activity in the STG presented an inverse pattern of modulation by traffic light label and the viewed food category. Only responses to high-energy foods preceded by a red label differed from those to off-food combinations and were higher than high-energy foods preceded by a green label. Neural source estimations over the later time window of interest (240-280ms) showed an interaction of traffic light labels and viewed food category in the medial prefrontal cortex (medPFC). Only neural responses to low-energy foods preceded by a red label differed from off-food combinations and were additionally higher than responses to low-energy foods preceded by a green label. Taken together, these results show that modulations in neural activity to the viewing of food as a function of both traffic light labels and the type of food viewed comprised a network of regions known to be involved in salience valuation, inhibitory control, attention, and object categorization.

The latPFC was previously described in the literature as being related to cognitive and food intake control, as well as decision-making. For example, a study from Cornier and colleagues (2010) showed that women show greater dorsolateral prefrontal activity than men in response to salient food cues and that this increased activity was in turn related to higher inhibitory cognitive control exerted towards these visual food cues. Further, a study in which participants were asked to actively down-regulate their food cravings showed a modulation of the activity of the latPFC, likely indicating top-down control of reward valuation (Hutcherson et al., 2012). In line, in a study of Harris and colleagues (2013) in which participants were presented with appetizing food images and were asked to choose healthy food options for subsequent intake, the modulation of latPFC activity was associated with the voluntary exertion of dietary self-control, therefore confirming the presence of top-down attentional filtering and value modulation at a timing similar to our findings (i.e. 150-200ms post-image onset). The medPFC, another region modulated by traffic light labels and food category in our study, is known to be involved in reward-valuation processes and goal-value signal encoding. In a neuroimaging study from Hare and colleagues (2009), self-reported dieters were asked to make decision about which food to subsequently eat. They found that activity in the medPFC reflected goal-directed value signal encoding. Further, as the activity of the latPFC was associated with the activity in the medPFC, the authors postulated that the various factors influencing a choice between different options are integrated in the medPFC and that the latPFC exerts self-control to modulate the value signal according to higher cognitive factors and needs. In line, a study of Plassmann and colleagues (2010) showed that when participants had to bid for the right to eat liked or disliked food, the computation of goal values for both appetitive and aversive options at the time of decision modulated the activity in the medPFC as well as in the latPFC. Finally, the medPFC as well as the temporal cortex were found to be involved when judgments on whether a portion size is ideal (vs. too big or too small) for prospective lunch are required (Toepel et al., 2015). Our results showed that response modulations in the prefrontal region by traffic light labels and viewed food category showed consistent patterns. Neural activity in latPFC and medPFC were higher when low-energy foods were combined with a red traffic light and when high-energy foods were combined with a green label. In line with previous findings, our results might thus reflect the computation of values as a function of the food-color combination viewed. A green label, i.e. an implicit "go" signal, in combination with high-energy foods likely represents a very salient pairing, therefore increasing the activity of brain regions involved in salience attribution. Further, the arousal and implicit "stop" signaling of the red color might be linked with an automatic initiation of cognitive control involving the prefrontal cortex, in particular modulating brain responses to low-energy foods.

The superior temporal gyrus, a third region modulated in our study, is known to be related to object categorization and its activity is influenced by attentional as well as affective relevance of visual stimuli (Vuilleumier et al., 2001). With respect to food perception, a study of Toepel and colleagues (2009) showed that the activity of the STG was higher when viewing high-energy as compared to low-energy foods around 160-230ms post-image onset. Moreover, the activity of the STG was found to be particularly modulated by images of ideal plating size for subsequent lunch (as compared to too big or too small portions) ~230-270ms after image onset (Toepel et al., 2015). The STG region is also known for its important role in memory processes. A study in patients with lesions of the temporal lobe highlighted its involvement in semantic memory (Mummery et al., 2000). This finding was supported by the study of Davey and colleagues (2015) showing the crucial role of the temporal lobe in semantic retrieval and learned-associations by means of transcranial magnetic stimulation (TMS). In this study, participants were asked to identify matching words and pictures to assess their performance in object identification and in retrieval of thematic associations while undergoing TMS on their temporal lobe. The inhibition of this brain area resulted in the disruption of participants' performance. Our results showed higher activity in the STG when combinations of low-energy foods preceded by a green and high-energy foods preceded by a red traffic light were viewed. These findings could reflect learned associations between, on the one hand, the implicit "go" signaling function of the color green, frequently linked to healthiness in food marketing and low-energy content of foods often promoted as healthy. On the other hand, the implicit "stop" or warning signal function of the color red is often associated with unhealthiness and high-energy foods (Schuldt, 2013; Shi, 2013). That is, participants might have learned associations between specific color meanings in a food context in their daily life, influencing their perception of food when incidentally encountered with color labels.

With respect to the associations between the changes in neural activity over the 115-155ms interval and the food like rating scores, an inverse association was found between the activity in the latPFC when participants viewed HiFat foods preceded by a red relative to an off label and the like rating of the respective foods. That is, participants showing less modulation in responses to HiFat by a red label liked HiFat foods more. This finding indicates that the more high-energy foods are appreciated, the less the neural responses in a brain region exerting self-control to these foods are influenced by “stop” signals. The study of Hare and colleagues (2009) has shown that the ability of the latPFC to exert influence on the medPFC during decision-making also reflects individual’s success in diet attempts. Therefore, the participants of our study showing the lowest modulation of the latPFC by a stop signal when perceiving strongly liked high-energy foods might thus be less sensitive to food intake guidance by means of traffic light labeling. However, whether participants who appreciate energy-dense foods more and show less modulation in the activity of the latPFC when encountering a stop signal finally exert lower self-control during actual food choice and intake remains to be tested.

5.6 Conclusion

Taken together, our results provide new insights on the influence of food-extrinsic factors (labels) on the behavioral and spatio-temporal brain dynamics to food viewing. Our findings suggest that traffic light labeling might be an efficient means to guide food choices upon incidental encounter, in extension being a potential means to interfere with everyday food choices in invidiuals for the benefit of health and body weight.

CHAPTER 6 GENERAL DISCUSSION AND CONCLUSION

The thesis at hand provides insights on behavioral and brain responses to food perception as a function of food appreciation, preferences and food-extrinsic information, assessed by means of behavioral and electroencephalographic (EEG) data.

The first study (study A) investigated how food appreciation (i.e. liking) influences subsequent choice between two food alternatives, and how, in turn, these factors modulate spatio-temporal brain dynamics to the viewing of food varying in energetic content. Foods rated as strongly liked by participants were found to be more often chosen than dismissed and to be rated faster than less appreciated foods. Strong appreciation thus seems to facilitate food choices over an alternative. Previous literature reported similar findings. A study by Kahnt and colleagues (2014) showed that participants were faster at responding to strongly (vs. low) valued visual stimuli during an outcome prediction task involving appetitive and aversive outcomes. In our study, both food liking and subsequent choice were found to modulate neural source activity as early as 135-180ms post-image onset, in brain areas comprising the insula, the dorsal frontal cortex and the superior parietal cortex. Therein, the level of appreciation modulated neural responses to food viewing when foods were subsequently chosen but not when dismissed for an alternative. An overall higher neural activity was found in response to disliked but nevertheless chosen foods. The timing of these neural modulations corresponds to previously described spatio-temporal brain dynamics to food viewing, in relation with the discrimination of food’s energetic content (Toepel et al., 2009). Our study thus provided evidence that food liking and choice further modulate neural activity to food perception in brain areas associated with reward valuation and cognitive control (Menon and Uddin, 2010; Mitchell, 2011).

The second study (study B) assessed the spatio-temporal brain dynamics of meal size selection while participants were asked to judge whether the viewed portion size was “too small”, “ideal” or “too big” for prospective food intake and expected satiety. Our participants rated portion sizes judged as “ideal” faster than “non-ideal ones” and did not systematically rate the largest portion available as “ideal”. These findings are in line with previous literature showing that the portion chosen for ideal expected satiety is rarely the biggest one available and that incremental increases in food quantity are not key drivers in portion size decisions (Brunstrom et al., 2010). When investigating the influence of portion size on neural responses to meal images, we found head-surface modulations at 105-145ms post-image onset, with an incremental increase of the head-surface global electric strength with portion size judgment from “too small” to “too big”, and at 230-270ms post-image onset, with a maximal global field power for “ideal” portion sizes. Over the earlier time window (105-145ms after image onset), portion size judgment also resulted in modulated activity in the insula, the middle frontal gyrus and the middle temporal gyrus. Over the later period of meal image viewing (230-270ms after image onset), greater activity to “ideal” as opposed to “non-ideal” portion sizes was found in the inferior parietal lobule, the superior temporal gyrus and the mid-posterior cingulate gyrus. The timing of these modulations is in line with previously reported spatio-temporal brain dynamics to food viewing (Toepel et al., 2009). Our study provided first evidence that brain areas involved in visual processing and reward attribution trace “physical” portion size increases during early stages of visual perception (Killgore et al., 2003; Menon and Uddin, 2010; Plassmann et al., 2010), likely reflecting an evaluation of the quantity of food available for subsequent intake, and that during a later stage of information processing, brain areas involved in attention and adaptive behaviors showed greater responsiveness to portions judged as “ideal” as compared to “non-ideal” (Corbetta and Shulman, 2002; Hagemann et al., 2003; Leech et al., 2011), likely reflecting control over food intake, to allow the selection of an ideal portion for adequate expected satiety.

The third study (study C) investigated how traffic light labels, as used on food packages for nutrient content information, modulate behavioral responses and spatio-temporal brain dynamics to the viewing of food varying in energetic content. When participants were asked to perform a food/non-food categorization task while undergoing EEG recording, their accuracy decreased when viewing high-energy foods preceded by a green or a red label, as compared to an off label. The presence of color traffic lights thus seems to have changed the allocated attention to foods, in turn impacting psychological and motor responses ((Elliot and Maier, 2014; Elliot et al., 2007; Genschow et al., 2012). Traffic light labels as well as energy density of the viewed food were found to modulate neural responses to food over two time windows, from 115-155ms and 240-280ms post-image onset. The timing of these modulations is in line with previous literature on spatio-temporal brain dynamics to food viewing and to verbal-emotional labeling (Toepel et al., 2009, 2014). Traffic light labels and type of food viewed modulated neural activity in the lateral prefrontal cortex (latPFC) and in the superior temporal gyrus (STG) over the earlier time interval (115-155ms) and in the medial prefrontal cortex (medPFC) over the later time period (240-270ms). Neural activity in the latPFC and medPFC, regions involved in cognitive control and reward valuation respectively, were higher when low-energy foods were combined with a red label and when high-energy foods were paired with a green traffic light. These results likely reflect the computation of values as a function of perceived food-color combination, as the implicit go signal of green color combined with high-energy food represent a highly salient pairing, and as the implicit stop signal of red likely triggered an automatic initiation of cognitive control from the prefrontal cortex (Cornier et al., 2010; Hare et al., 2009; Harris et al., 2013; Hutcherson et al., 2012). In the STG, a region known to be related to memory and learned associations in addition to object categorization (Davey et al., 2015; Vuilleumier et al., 2001), higher activity was found when viewing low-fat foods paired with a green light and high-fat foods paired with a red light. These modulations are thus likely to reflect learned associations between specific color meanings in the context of food perception. Our results complement behavioral results observed in previous studies assessing the influence of traffic light labeling on food perception and choice behavior. A study from Borgmeier and Westenhoefer (2009) reported that when presented with various format labels (i.e. healthy choice tick, traffic light label, and GDA), participants were better and faster at identifying healthy food items when those were accompanied by traffic lights, as opposed to other label formats. Our study thus highlighted the potentials of traffic light labeling as means to influence food perception via the modulation of reward valuation and cognitive control processes both at the behavioral and neural level upon incidental encounter.

Altogether, the thesis at hand provided new insights on how preferences, and food's intrinsic (i.e. energy density), as well as extrinsic (i.e. portion size, labeling) factors modulate spatio-temporal brain dynamics to food perception and associated food intake behavior. Food appreciation and subsequent choice, adequate portion size selection for prospective intake and traffic light labels were found to generally modulate brain responses in areas involved in reward valuation and cognitive control. A neurobiological integrative model on how body-intrinsic, food-intrinsic and food-extrinsic factors modulate brain responses to food perception is proposed in Figure 7. Primary senses underlying food perception, such as the taste, smell and sight have been shown to be influenced by body-intrinsic factors, such as body weight, motivation to eat and gender, food-intrinsic (energy density, taste quality, palatability and portion size), but also food-extrinsic factors such as colors and labels. The model aims at a more integrative view on how brain responses are modulated as a function of some of these key determinants described in previous studies and those comprised in the thesis at hand.

For example, body weight has been reported to lead to alterations in neural activity to food viewing in temporal and parietal lobes, and in dorsal and medial prefrontal cortex, i.e. regions involved in reward valuation and inhibitory control (Cornier et al., 2010; Hume et al., 2015; Stoeckel et al., 2008). Hunger, and thus motivation towards food intake, has been shown to influence brain responses to food viewing in the superior temporal gyrus, the insula and the orbitofrontal cortex, i.e. areas involved in homeostatic integration, goal-directed attention and reward valuation (Del Parigi et al., 2006; Wang et al., 2004a). Moreover, individual's gender influences how food is perceived, shaping spatio-temporal brain in lateral and medial prefrontal cortex, regions linked to reward valuation and inhibitory control

(Horstmann et al., 2011; Toepel et al., 2012). Body-intrinsic factors thus seem to shape reward valuation and inhibitory control processes in particular during food perception.

Food-extrinsic factors such as colors and labels were found to modulate neural activity in temporal lobe as well as in medial and lateral prefrontal cortex (Enax et al., 2015; Study C of the thesis at hand), i.e. regions involved in reward valuation and cognitive control. Finally, food-intrinsic factors such as portion size and energy density influence neural responses to food viewing in the parietal and temporal lobes, as well as in the insula and the prefrontal cortex, regions involved in visual processing, reward attribution and adaptive behavior (Study B and C of this thesis). The model in Figure 7 aims to summarize neural modulations by these factors in studies A, B, and C comprised in the thesis at hand and roughly represents areas modulated by body-intrinsic, food-intrinsic and food-extrinsic factors, as well as brain areas involved in food sensory perception. Neural modulations due to body-intrinsic factors are represented in shades of green. For food-intrinsic factors, neural modulations are represented in shades of pink and for body-extrinsic factors, modulations are represented in shades of blue.

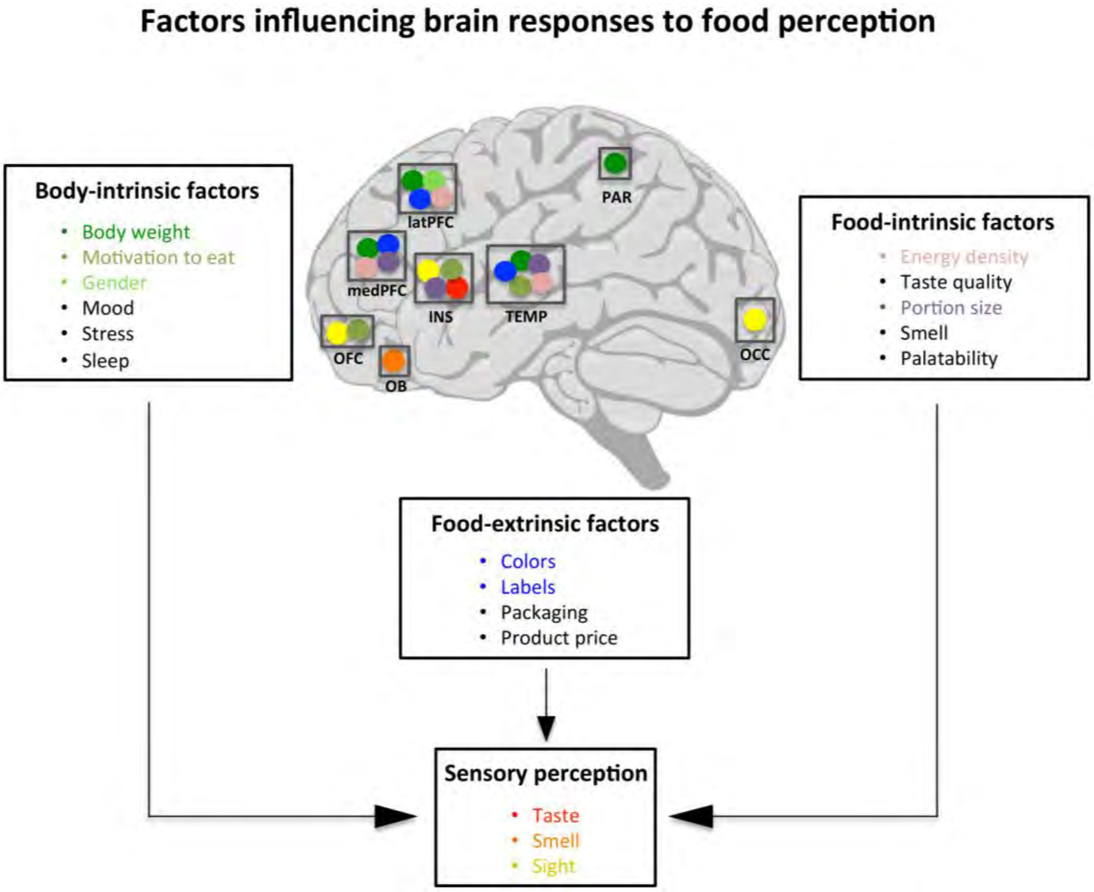

Figure 7: A neurobiological model on how body-intrinsic, food-intrinsic and food-extrinsic modulate neuro-sensory responses to food perception. Color blubs summarizing brain areas modulated by these factors: shades of green for body-intrinsic, shades of pink for food-intrinsic and shades of blue for food-extrinsic factors. Brain areas: Lateral prefrontal cortex (latPFC); medial prefrontal cortex (medPFC); orbitofrontal cortex (OFC); olfactory bulb (OB); insula (INS); temporal lobe (TEMP); parietal lobe (PAR); occipital lobe (OCC).

As detailed in the model, studies comprised in the current thesis as well as previous ones showed that contextual (i.e. food-extrinsic) information as well as factors intrinsic to body and food concurrently modulate neural responses to food perception in brain areas involved in reward valuation and cognitive control. By extension, they are likely to exert influences on food intake behavior, and by extension, on body weight management. Our results complement previous findings on reward and inhibitory control processes.

A functional neuroimaging study by Seeley and colleagues (2007) showed that two dissociable networks were critical for the guidance of behavior, namely the salience network and the executive control network. Functions of the salience network (Menon and Uddin 2010) consist in integrating various aspects of reward processing, such as reward valuation, motivation and attention, allowing for the segregation of the most salient stimulus and supporting goal-adapted behavior. Menon and Uddin (2010) reported several brain regions to be involved in this salience network, including the thalamus, the cingulate cortex, the amygdala, the substantia nigra, the ventral tegmental area and the insula. The latter was further described as the "integration" center of the salience network, receiving enteroceptive inputs and mediating physiological and psychological states in accordance. The cingulate gyrus and the thalamus allow for adaptive behavior and appropriate allocation of attentional resources. In contrast, the executive control network exerts influence on the attention directed towards salient stimuli, choice options and takes into account physiological, semantic and contextual information (Seeley et al., 2007). This control network includes the lateral prefrontal cortex, the pre-SMA and the lateral and parietal cortex (Curtis and D'Esposito, 2003; Lau et al., 2006).

In the context of food perception, a meta-analysis of functional neuroimaging by Brooks and colleagues (2013) showed that the imbalance between food reward valuation and food intake control mechanisms is strongly associated to maladaptive choices and subsequent weight gain. Increased activity to food viewing was found in obese, as compared to lean individuals, in regions involved in salience attribution, motor response and explicit memory, i.e. medial prefrontal cortex, pre-central gyrus, parahippocampal gyrus, superior and inferior frontal gyrus and anterior cingulate. In addition, a consistent decrease in neural activity in response to food cues was reported in the lateral prefrontal cortex and insula in obese participants, a region involved in inhibitory control. The authors thus proposed that an increased body weight is associated with an increased salience attribution and a decreased cognitive control in anticipation of food, i.e. an imbalance between reward and control processes. These findings are in line with the neural modulations in reward and control-related brain areas by food-intrinsic and food-extrinsic factors in response to food perception as observed in studies A, B and C reported in the thesis at hand.

Accumulating evidence also points towards an addiction-like model to palatable high-energy food intake behavior (Davis and Carter, 2009). Drug addiction and food addiction-like behaviors were reported to share the same clinical aspects and neural substrates (Pelchat, 2002). Food's micronutrient such as sugar and fat were found to elevate mood by the release of neuropeptides, thus reinforcing selective preference for high-energy foods through the activation of the dopaminergic system (Ifland et al., 2009; Kelley et al., 2005; Wang et al., 2004b). For example, patients suffering from binge eating disorder were found to show higher activity in the medial prefrontal cortex, the amygdala and the ventral striatum in response to food cues as compared to healthy controls (Schienle et al., 2009; Weygandt et al., 2012). That is, patients suffering from compulsive overeating show greater motivational sensitivity and attribute higher reward values during food perception. Recent models in drug addiction also conclude that drug consumption results in increased motivation towards drug intake and decreased executive control, via modulations of the dopaminergic system, in turn impairing the ability to resist cravings (Koob, 2013; Longo et al., 2016; Volkow and Morales, 2015). Since drug addiction and food-like addiction were shown to share common neural substrates, it is likely that similar phenomena take place during repetitive maladaptive food intake on the long run.

The current thesis, providing insights into behavioral and brain responses to food as a function of appreciation, preferences and extrinsic factors in normal weight participants can certainly only be viewed as proofs of concepts. In order to further elaborate on imbalances in reward and control processes, further studies are needed. For example, investigations in overweight individuals or persons undergoing non-mechanical (i.e. diet) and mechanical weight loss (i.e. bariatric surgery) procedures are necessary to for further detail these processes. Moreover, food perception and intake is not explained by cerebral functions alone but also by its interaction with peripheral signals, i.e. digestive hormones, via the gut-brain axis. Digestive hormones are known for their ability to cross the blood-brain barrier and for their influence on the activity in brain regions involved in homeostatic as well as hedonic processes in response to food perception (Gibson et al., 2010; Schloegl et al., 2011). Digestive hormones convey satiety and hunger signals to the hypothalamus, a region involved in homeostatic integration (Asarian and Bächler, 2014). In addition, many digestive hormones have been shown to modulate responses in brain areas involved in reward processes and salience attribution. For example, the administration of peptide YY (PYY) during satiety was found to increase neural activity in the orbitofrontal cortex (Batterham et al., 2007). Animal studies also showed that leptin and ghrelin receptors in the mesolimbic dopaminergic reward system can modulate food appreciation and drives (Leinninger et al., 2009; Sáinz et al., 2015).

First insights on the links between spatio-temporal brain responses and gut hormone secretion release were also part of my thesis, although not described in the manuscript at hand. An interdisciplinary study was carried out as a collaboration between the Laboratory for Investigative Neurophysiology (LINE), the group of Professor Luc Tappy from the Institute of Physiology of the University of Lausanne and PD. Dr. Vittorio Giusti from the Endocrinology, Diabetology and Metabolism Service of the Vaudois University Hospital Center (SEDM-CHUV). This study assessed the impact of body weight (19-36kg/m^2) on gastrointestinal hormone secretion, and how, in turn, these factors were associated with brain responses to the viewing of foods varying in energetic content as a function of the motivation to eat (Bielser et al., manuscript in preparation). For this purpose, 16 women underwent a day-long experimental protocol comprising EEG recordings conducted pre- and post-prandially while participants were presented with images of high- and low-energy foods. Additionally, blood samples were collected at regular time intervals to allow for the measurement of digestive hormone plasma levels. EEG data analyses were conducted as in study C of this thesis. In this study, we found that relative differences in neural responses to food viewing were modulated by the energetic content of foods (HiFat vs. LoFat) as early as 110-150ms and 230-270ms post-image onset. Over the earlier time interval of visual processing, greater changes after food intake in the secretion of digestive hormones promoting satiety (i.e. pancreatic peptide YY (PYY) and cholecystokinin (CCK)) were related to greater neural modulations in brain areas implicated in object categorization as a function of their attentional relevance (i.e. MTG and STG) (Martin et al., 1996; Vuilleumier et al., 2001). Over the later time interval, smaller changes in the secretion of a pancreatic hormone promoting the termination of food intake (i.e. glucagon) are related to greater neural modulations in a brain area known to be involved in reward valuation and goal-value signal encoding (i.e. MFG) (Hare et al., 2009). Further, a higher BMI was associated with greater change in PYY secretion level relative to food intake. Altogether, these findings show that body weight influences peripheral signals conveying information about the internal state of the body to the brain, and that in turn, these latter are associated with modulations of brain responses to the viewing of food in areas involved in visual processing, attention allocation and reward valuation. This study extended knowledge on body-intrinsic factors (i.e. body weight and peripheral hormone secretion) and food-extrinsic factors (i.e. energetic content) influence on spatio-temporal brain dynamics to food viewing and will help to complement the neurobiological model of brain responses to food perception.

Only few studies have so far investigated how variations in body-weight, i.e. by weight loss, impact brain responsiveness to food viewing and hormonal secretion. The model will thus also need to incorporate changes in body-intrinsic factors as shaping food perception and intake. Therein, further work is needed, also focusing on the effects of non-mechanical (i.e. alimentary diet) and mechanical (i.e. bariatric surgery) weight loss on food responsiveness. Both non-mechanical and mechanical-surgical weight loss are not effective alike in humans and factors determining success are still largely under-explored. For example, hypocaloric diets are known to be efficient on the short-term, but most dieters fail to stabilize their weight loss and consecutively regain weight, sometimes reaching a higher body-weight than prior to the diet (Brownell, 1994; Hennecke and Freund, 2014; Mann et al., 2007; Meckling et al., 2004).

A functional neuroimaging study by Murdaugh and colleagues (2012) was the first to assess short- and long-term non-mechanical weight loss outcomes and their neural correlates. In this study, obese and overweight (BMI range: 28-44kg/m^2) participants were enrolled in a 12-weeks weight loss program, and their brain responses to food were assessed before and after the diet. During fMRI, participants were presented with images of high- and low-energy foods, and control images of cars. They were asked to complete a memory task after the scan to ensure they attended to the images. Obese and overweight participants came again to the lab 9 months later for body-weight measures. Before the weight-loss intervention, the obese/overweight group showed higher activity when viewing high-energy food as opposed to control images in the insula, the amygdala, the cingulate cortex, the postcentral gyrus, the inferior temporal and frontal gyrus, and the middle occipital cortex. Obese/overweight individuals thus showed greater reactivity to high-food images in brain areas involved in reward attribution than normal-weight participants before undergoing a diet. After the 12 weeks diet, obese/overweight individuals had lost on average 3,5% of their original body weight, and showed a decreased activity in response to high-energy foods in the medial prefrontal cortex, the inferior parietal lobule, the posterior cingulate cortex and the angular gyrus, as compared to before the diet. In the obese/overweight group, weight loss had stabilized in 17% of the participants 9 months after the diet. Additional weight loss was found in 18% of them, whereas 46% regained weight. When investigating relationships between neural activity after the diet and weight maintenance in obese/overweight participants, the authors found a positive correlation between the 9 months weight changes and the activity in the ventral tegmental area, the putamen, the insula, the hippocampus (i.e. regions involved in reward valuation) as well as in the superior occipital gyrus, and the fusiform gyrus (i.e. areas of visual processing) and in the inferior parietal lobule (i.e. region involved in attention modulation). In addition, when assessing the relationship between changes in neural activity from pre- to post-diet and body weight maintenance, they found that the activity in the insula and the inferior frontal gyrus was negatively correlated with body weight maintenance capacities. Altogether, this study provides first insights on how non-mechanical body-weight loss affects neural responses to food viewing, and how, in turn, these neural changes can predict successful weight maintenance. Weight loss modulates neural activity in brain regions involved in reward processing, vision and attention, and the change in activity of the insula and the inferior frontal gyrus resulting from a diet seems to be good predictor body-weight maintenance.

In both non-mechanical and mechanical weight loss interventions, individuals show variable susceptibility for long-run success or failure in the maintenance of weight-loss. A project in our group is currently investigating “Gut-brain interactions during visual food perception following gastric bypass intervention” (Bielser et al., manuscript in preparation) to gain further insights on how mechanical-weight loss impacts brain responses to food viewing and digestive hormone secretion. However, weight loss success of failure and determinants of weight loss maintenance and weight regain remain largely unknown. Genetic markers have been identified by genome-wide association studies as predictors of bariatric surgery weight loss outcome, such as the obesity genes MC4R and FTO (Mirshahi et al., 2011; Sarzynski et al., 2011). Some clinical predictors, such as social context, eating patterns, physical activity, and psychological traits have also been shown to influence the outcome of non-mechanical weight loss intervention (Elfhag and Rossner, 2005 for review). First insights on neural predictors of long-term successful and unsuccessful non-mechanical weight loss attempts have been provided by previous studies. As the outcome of weight loss interventions seems to be multifactorial and to include physiological, metabolic, genetic, and neural determinants, further interdisciplinary studies integrating these various key factors are needed to develop a predictive model of successful approach. Given the relatively low success rate of hypocaloric diets and bariatric surgery, the development of a more individualized health care, integrating individual risk factors and susceptibilities for the benefit of body weight management would allow to predict which intervention is the most suitable for individual’s benefit to better tackle overweight and obesity.

Such (preferentially longitudinal) studies would further benefit from task settings including more direct measures of reward and control processes, given that maladaptive food intake is likely to be caused by an imbalance between reward attribution and cognitive control processes. The study designs of the current thesis involved categorization, valuation and choice tasks and showed differences as a function of food reward viewed (i.e. high- vs. low-energy foods). In terms of measuring control processes, these are yet only indirect means. For this reason, future studies would benefit from more ecologically valid tasks to assess imbalance in reward and cognitive control in individuals. For example, Go-NoGo tasks have been shown effective to train inhibitory control in response to salient cues in the context of drug addiction. A study by Houben and colleagues (2011) demonstrated that the training of inhibitory responses to alcohol-related cues decreased alcohol intake in heavy drinkers. In their task, Go and NoGo responses were attributed to beer- or water-related pictures. Participants were asked to refrain from responding when NoGo conditions were presented, and to respond as fast as possible when Go signals were shown. The authors report that participants undergoing the NoGo-beer condition showed decreased alcohol consumption in weekly alcohol intake post-training as compared to prior training. When translating this inhibitory Go-NoGo task to food intake behavior, Houben and Jansen (2011) showed that temptation towards high-energy foods can also be modulated by this training. Participants, chocolate cravers this time, were divided in three groups. The first group always had a NoGo responses associated to chocolate stimuli, the second always a Go responses to chocolate stimuli, and the third group had Go and NoGo half of the time. The authors measured chocolate consumption after the training, pretexting a taste test, and found that participants who were trained to inhibit responses to chocolate consumed less chocolate than the other groups. That is, training inhibitory control by repeated response inhibition to one particular stimulus seems to be an effective strategy to decrease drives towards the latter. Integrating a Go-NoGo task to future electrical neuroimaging studies would thus allow for the examination of explicit signs of inhibitory control at the behavioral level, and implicit modulations in the reward network and cognitive control processes in the brain by the training. Individual capacities to inhibit their responses could provide a first marker to target people at risk for failure in diet attempts. Therein, it might well be that in some individuals food responses are more prone to be influenced by food-extrinsic cues (e.g. color labels). That is, comprehensive investigations are needed to assess individuals' responsivity to food inhibitory means and their training.

The thesis at hand provided insights on how appreciation, preferences and food-extrinsic information modulate behavioral and brain responses to the viewing of food. These studies reported in detail (studies A, B, C) involved normal-weight participants and show that food-intrinsic and food-extrinsic factors shape behavioral and brain responses to food. In addition, a study sketched as additional thesis work showed how body-intrinsic factors (weight and digestive hormone secretion) alter food responsiveness along the gut-brain axis. Future research needs to further address means to interfere with food perception, and in extension, food intake, for the benefit of body weight and long-term health.

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Annex 1

STUDY A – Does my brain want what my eyes like? - How food liking and choice influence spatio-temporal brain dynamics of food viewing

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Does my brain want what my eyes like? – How food liking and choice influence spatio-temporal brain dynamics of food viewing

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ABSTRACT

How food valuation and decision-making influence the perception of food is of major interest to better understand food intake behavior and, by extension, body weight management. Our study investigated behavioral responses and spatio-temporal brain dynamics by means of visual evoked potentials (VEPs) in twenty-two normal-weight participants when viewing pairs of food photographs. Participants rated how much they liked each food item (valuation) and subsequently chose between the two alternative food images.

Unsurprisingly, strongly liked foods were also chosen most often. Foods were rated faster as strongly liked than as mildly liked or disliked irrespective of whether they were subsequently chosen over an alternative. Moreover, strongly liked foods were subsequently also chosen faster than the less liked alternatives. Response times during valuation and choice were positively correlated, but only when foods were liked; the faster participants rated foods as strongly liked, the faster they were in choosing the food item over an alternative.

VEP modulations by the level of liking attributed as well as the subsequent choice were found as early as 135–180 ms after food image onset. Analyses of neural source activity patterns over this time interval revealed an interaction between liking and the subsequent choice within the insula, dorsal frontal and superior parietal regions. The neural responses to food viewing were found to be modulated by the attributed level of liking only when foods were chosen, not when they were dismissed for an alternative. Therein, the responses to disliked foods were generally greater than those to foods that were liked more. Moreover, the responses to disliked but chosen foods were greater than responses to disliked foods which were subsequently dismissed for an alternative offer. Our findings show that the spatio-temporal brain dynamics to food viewing are immediately influenced both by how much foods are liked and by choices taken on them. These valuation and choice processes are subserved by brain regions involved in salience and reward attribution as well as in decision-making processes, which are likely to influence prospective dietary choices in everyday life.

1. Introduction

A better understanding of how humans evaluate foods and make choices about them, particularly if associated with objective brain markers underlying decision-making processes, are of great interest because eating-related disorders and especially obesity figures are still increasing world-wide. In daily life, decisions on what to eat are determined by hunger (homeostatic needs), and also by hedonic drives that can even override homeostatic needs (Berthoud, 2011; Kenny, 2011). The latter have been strongly associated with the propensity of food indulgence, leading to overweight and detrimental health consequences like cardiovascular disease and diabetes. In light of such developments, it is critical to better understand how food choice decisions are shaped as well as the underlying neural mechanisms, with the long-term

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goal to potentially being able to affect maladaptive choices in favor of health-beneficial ones.

A core concept in research on human economic and food-related decisions states that when several choice options are present at the same time, they are assigned abstract and often subjective values. These values, and especially between-value weighing, serves to enable decisions in favor of a (more highly valued) choice option (Economides, Guitart-Masip, Kurth-Nelson, & Dolan, 2015; Hare, Camerer, & Rangel, 2009; Kable & Glimcher, 2009). Several functional neuroimaging studies have revealed that in particular the ventromedial prefrontal cortex (vmPFC) subserves the computation of an overall subjective value of choice options and thereby biases decisions (Kable & Glimcher, 2009). Dorsal and ventrolateral PFC (dlPFC and vlPFC, respectively) have been shown to modulate vmPFC activity and are involved in inhibitory control processes (Hare et al., 2009; Hutcherson, Plassmann, Gross, & Rangel, 2012) as well as emotional self-regulation (Ochsner & Gross, 2008). For example, activity of the vmPFC was found to be modulated by lateral PFC activity in individuals who are successful (self-) controllers of their dietary choices (Hare et al., 2009). In the study of Hare et al. (2009), the success of self-control on dietary choices (meaning that study participants successfully considered the health aspects of food in their dietary choices) was positively associated with the activity in the dlPFC, subsequently influencing food value attribution as reflected by vmPFC modulations. Other neuroimaging studies have further shown that the brain tracks the energy content of foods (García-García et al., 2013; Killgore et al., 2003; Van der Laan, de Ridder, Viergever, & Smeets, 2011). Responses to varying food types (Toepel, Knebel, Hudry, le Coutre, & Murray, 2009) and food portion sizes (Toepel et al., 2015) have been shown to differ already within 200 ms after image exposure; reflected by activity modulations in temporo-occipital and frontal brain regions (e.g. orbitofrontal cortex, anterior cingulate cortex, lateral prefrontal cortex, and the insula).

To date, only few neuroimaging studies have investigated modulations in brain responses during food viewing according to valuation or liking, respectively, including the impact of valuation on subsequent food choices. In nutrition sciences and research on human food choice behavior, a prominent concept posits a dissociation of processes related to food 'liking' as opposed to 'wanting', as well as how 'liking' and 'wanting' impact food choices and intake (Berridge, 2009). Consequently, foods that are not necessarily 'liked' can nevertheless trigger implicit 'wanting' mechanisms (e.g. when adequate alternatives are lacking) and thus impact food choices and intake (Berridge, 2009; Finlayson, King, & Blundell, 2007). By contrast, 'liking' is not necessarily coupled with 'wanting' since this would be maladaptive for dietary choices given the abundance of foods with strong hedonic impact in everyday life.

Our study aimed to determine how food liking and successive choices shape the spatio-temporal brain dynamics during food image viewing. Visual evoked potentials (VEPs) were analyzed within an electrical neuroimaging framework (Koenig, Stein, Grieder, & Kottlow, 2014; Murray, Brunet, & Michel, 2008). This approach not only includes the analysis of VEPs at the head-surface, but also intracranial source estimations. We have successfully employed this method when investigating uni- and multisensory responses to food (Lietti, Murray, Hudry, le Coutre, & Toepel, 2012; Ohla, Toepel, le Coutre, & Hudry, 2012; Toepel, Knebel, Hudry, le Coutre, & Murray, 2012; Toepel, Ohla, Hudry, le Coutre, & Murray, 2014; Toepel et al., 2009, 2015). We hypothesized that the level of liking attributed to foods directly impacts VEPs and neural source activity during food viewing. Moreover, we questioned whether participants' successive choices (i.e. whether food items were subsequently chosen or dismissed for an alternative offer) would differentially impact brain responses during food viewing, given that choices between alternatives only had to be taken subsequent to, but not during, food viewing.

2. Materials and methods

2.1. Participants in the EEG study

Twenty-two (11 female) normal-weighted volunteers, aged 21–38 yrs (mean ± s.e.m. = 27.23 ± 0.98 yrs; mean BMI ± s.e.m. = 22.72 ± 0.61 kg/m^2), participated in the study. Twenty of these participants were right-handed, and two were ambidextrous according to the Edinburgh Handedness Inventory (Oldfield, 1971). None of the participants reported current or prior neurological or psychiatric illnesses or self-reported eating disorders, and all participants had normal or corrected-to-normal vision. All participants completed the Three-Factor-Eating questionnaire TFEQ-R 18 (Karlsson, Persson, Sjöström, & Sullivan, 2000) and the momentary craving state questionnaire (FCQ-S) (Nijs, Franken, & Muris, 2007). The EEG recording sessions started between 15:00 and 16:00 h to control for circadian modulations of hunger. Furthermore, participants were instructed (and also themselves reported) to have eaten lunch ~2 h before the recording sessions. The volunteers provided written, informed consent to the procedures, which were approved by the Ethics Committee of the Faculty of Biology and Medicine of the University of Lausanne and the Vaudois University Hospital Center (CHUV).

2.2. Procedure of the EEG study

Participants sat comfortably inside a dimly lit, sound-attenuated booth and completed 704 trials (structure as schematized in Fig. 1). Images were presented on a 21″ CRT monitor. On each trial, participants were successively presented with two food items and rated each during a 'valuation phase' on a 5-point Likert according to how much they liked each food item presented (Literal translation from French: 1 = The item does not seem pleasant to me.; 5 = The item seems very pleasant to me.). Following each image pair, participants were presented with a question mark indicating the 'choice period'. They were told to decide by button press whether they preferred the first (button press 1) or the second food (button press 2) viewed. All behavioral responses were given by button-presses on a serial response box using the index finger. Responses were allowed during the presentation of the food image and 2000 ms after image/question mark offset. Participants were instructed not to respond at all in case they encountered unknown food items. Stimulus presentation and response recordings were controlled by E-Prime (Psychology Software Tools Inc., Pittsburgh, USA; www.pstnet.com/eprime).

Image pairs consisted of foods from a similar product category (e.g. milk products, meat products, desserts, salty snacks, fruits, vegetables) and were adapted in energy content (Toepel et al., 2009) to prevent effects from general preferences for e.g. only sweet or high-energy foods. Each food image pair was presented twice to each participant with inversed image order to avoid position effects of foods within a trial. Images were controlled for low-level visual features, including luminance and spatial frequency (Knebel, Toepel, Hudry, le Coutre, & Murray, 2008).

2.3. Behavioral data analyses

First, we analyzed participants' behavioral responses to each food item given during the valuation phase. By using customized MATLAB scripts, individuals' responses to each food were sorted by the level of liking participants had attributed, as well as by whether the food items were subsequently "chosen" vs.

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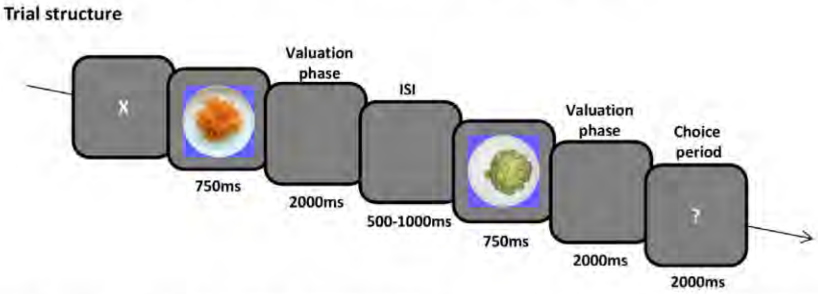

Fig. 1. Trial structure. Participants were asked to rate how much they liked each of two presented food items per trial on a 1–5 Likert scale during the valuation phase. Over the choice period participants had to choose whether they prefered the first or second presented food item.

"dismissed". Since extreme ratings were low in number, food items scored with "1" and "2" were pooled together, as well as those rated with "4" and "5". That is, overall six conditions entered the analyses, i.e. chosen food items that had been rated as rather disliked, as mildly liked and strongly liked, as well as dismissed food items which had been rated as rather disliked, as mildly liked and strongly liked. For each condition, the frequency of responses and reaction times were first averaged within and then across subjects. 2 × 3 ANOVAs with the factors of choice (chosen vs. dismissed) and liking (rather disliked, mildly and strongly liked) were conducted on response frequencies as well as response times. When appropriate, separate one-way ANOVAs for each choice option as well as paired post-hoc *t*-tests (two-tailed) were conducted.

Second, we analyzed participants' response times to the chosen food item during the 'choice period' of each trial. Therein, responses to chosen foods were (this time retrospectively) sorted depending on whether the respective food item had been rated as rather disliked, mildly liked or strongly liked. A one-way ANOVA including the three liking levels was conducted to investigate liking-related differences in food choices, as well as paired post-hoc *t*-tests when appropriate.

Third, we conducted Pearson correlation analyses (two-tailed) between individuals' response times in the valuation and choice period to investigate whether decisions about food liking (as assessed by response times) are linked to food choice decisions. The outcomes of all performed analyses were only considered significant when $p \leqslant 0.05$.

2.4. Electroencephalography (EEG) acquisition and preprocessing

Continuous EEG was acquired at 512 Hz through a 128-channel Biosemi ActiveTwo system (Biosemi, Amsterdam, The Netherlands) referenced to a ground circuitry (common mode sense and driven right leg electrodes or CMS–DRL). This circuitry functions as a feedback loop driving the average potential across the montage as close as possible to the amplifier zero. Details of this circuitry, including a diagram, can be found on the Biosemi website (http://www.biosemi.com/pics/zero_ref1_big.gif). All data pre-processing steps and VEP averaging were done using the Cartool software (http://sites.google.com/site/fbmlab/cartool; (Brunet, Murray, & Michel, 2011). All statistical analyses were conducted using the Statistical Toolbox for Electrical Neuroimaging (STEN) developed by Jean-François Knebel (http://www.unil.ch/line/home/menuinst/about-the-line/software-analysis-tools.html).

To calculate VEPs, epochs of EEG from 98 ms pre- to 488 ms post-food image onset (i.e. 50 data points before and 250 data points after stimulus onset) were separately averaged for each response condition and each participant. In addition to an automatic ±80 μV artifact rejection criterion, EEG epochs containing eye blinks or other noise transients were removed by trial-to-trial inspection of the data. Data were high-pass and low-pass filtered during single-subject averaging (second order Butterworth with −12db/octave roll-off; 0.1 Hz high-pass; 40 Hz low-pass; 50 Hz notch) and baseline corrected using the 98 ms pre-stimulus period. Data from artifact electrodes of each participant were interpolated using 3-D splines (Perrin, Pernier, Bertrand, Giard, & Echallier, 1987), and single-subject EEG epochs were averaged into VEPs depending on the behavioral response of each participant on each trial (see above). EEG responses were thus sorted into six conditions, i.e. responses to (subsequently) chosen food that had been rated as rather disliked, as mildly liked and strongly liked, as well as responses to (subsequently) dismissed foods that had been rated as rather disliked, as mildly liked and strongly liked. Single subject's responses were then group-averaged and recalculated against the average reference. The average number of accepted VEP epochs ranged from 60 (s.e.m. ± 12) to 175 (s.e.m. ± 16) per condition. Due to the differing number of epochs per condition, VEP epochs were normalized by the mean instantaneous Global Field Power (GFP) at each sampling point (Lehmann & Skrandies, 1980) during group averaging. GFP is calculated as the square root of the mean of the squared amplitude value recorded at each electrode of the 128-channel montage we used (vs. the average reference) and represents the spatial standard deviation of the electric field measured on the head surface (Koenig & Melie-Garcia, 2010).

2.5. Analyses of VEP data

The influence of liking and choice on brain responses was quantified by assessments of modulations in the VEPs at the head-surface and in estimations of the underlying neural activity (Brunet et al., 2011; Murray et al., 2008). Periods of interest were determined by a time-point and electrode-wise 2 × 3 ANOVA with the factors of choice (chosen vs. dismissed) and liking (disliked, mildly and strongly liked). Only periods showing a significant interaction of liking × choice ($p \leqslant 0.05$) for longer than 20 ms on more than 10% of all channels were considered significant, so as to account for temporal and spatial auto-correlation (e.g. Guthrie & Buchwald, 1991).

In parallel, we assessed the electric field strength at the scalp surface for each response condition, viz. Global Field Power (GFP; (Lehmann & Skrandies, 1980) in the VEP responses. GFP is calculated as the square root of the mean of the squared amplitude value recorded at each electrode of the 128-channel montage (vs. the average reference) and represents the spatial standard deviation of the electric field at the scalp. That is, GFP yields larger amplitudes for stronger electric fields, and GFP peaks are indicative of maximally synchronized neural sources underlying the scalp-recorded activity (Michel & Murray, 2012). Over the periods of interest (i.e. showing an interaction between the factors of choice

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and liking at the VEP level), mean GFP values were computed for individuals and used for statistical analyses. First, 2 × 3 ANOVAs with the factors of choice (chosen vs. dismissed) and liking (rather disliked, mildly and strongly liked) were conducted. When appropriate, separate one-way ANOVAs for each choice option condition as well as *t*-tests (two-tailed) were conducted to detail the impact of each level of liking attributed on subsequent food choice. All these results were only considered significant when $p \leqslant 0.05$.

To assess whether and which neural sources (i.e. brain regions) revealed activity patterns modulated by liking and choice, we then estimated the active sources over the GFP maxima in each condition using the local autoregressive average (LAURA) distributed linear inverse solution (Grave de Peralta Menendez, Gonzalez Andino, Lantz, Michel, & Landis, 2001; Grave de Peralta Menendez, Murray, Michel, Martuzzi, & Gonzalez Andino, 2004). As input for these estimations, single subject VEP responses at each electrode were averaged over the (overlapping) interval of the GFP maxima and electrode-wise VEP differences, by this generating a single value for each participant and each response condition to increase the signal to noise ratio. The LAURA algorithm then serves to estimate the neural sources of the electric signal recorded at the 128 head-surface sensors by using an inverse solution matrix consisting of 3005 nodes equally distributed within the grey matter of the Montreal Neurological Institute (MNI) average brain. This implementation of LAURA was generated with the Spherical Model with Anatomical Constraints (SMAC; (Spinelli, Andino, Lantz, Seeck, & Michel, 2000). As output, LAURA provides current density values (in mA/mm^3) at each node. The spatial accuracy attained, which is on the order of the grid size (here: 6 × 6 × 6 mm; (Gonzalez Andino, Michel, Thut, Landis, & Grave de Peralta, 2005; Gonzalez Andino, Murray, Foxe, & de Peralta Menendez, 2005; Michel et al., 2004), has been documented and discussed in detail in prior fundamental and clinical research.

Modulations in neural source activity over each GFP maximum were assessed by means of 2 × 3 ANOVAs on each node of the solution point matrix with the factors of choice (chosen vs. dismissed) and liking (rather disliked, mildly and strongly liked). Activity in brain regions where a significant interaction of both factors was found served as regions of interest for post-hoc analyses. These regions of interest were considered significant when the statistical threshold of $p \leqslant 0.05$ (two-tailed) was exceeded within a cluster of $\geqslant 10$ contiguous nodes of the inverse solution matrix. This spatial extension criterion was based on AlphaSim randomizations (http://afni.nimh.nih.gov) and also used in previous publications of our group (Lietti et al., 2012; Toepel et al., 2009, 2012, 2014). Post-hoc comparisons (separate one-way ANOVAs for responses to chosen and dismissed foods as well as *t*-tests between) were conducted on the averaged scalar values (in $\mu\text{A/mm}^3$) of the node revealing the minimal *p*-value within a region of interest plus its six immediate neighbors. The results analyses were rendered on the MNI template brain with the Talairach and Tournoux (1988) coordinates of the maximal statistical differences indicated.

3. Results

3.1. Behavioral results

Fig. 2a shows the mean response frequencies (in percent) to chosen and dismissed food items as a function of the liking level attributed. A 2 × 3 ANOVA revealed an interaction of liking and choice ($F_{2,42} = 46.93$; $p \leqslant 0.01$; $\eta_p^2 = 0.69$) indicating that the number of food items rated as rather disliked, mildly or strongly liked substantially differed depending on whether they were subsequently chosen over an alternative or dismissed. Separate one-way ANOVAs for each choice condition revealed an effect of liking for chosen ($F_{2,42} = 17{,}88$; $p \leqslant 0.01$; $\eta_p^2 = 0.46$), but not for dismissed food items. Within the chosen foods items, paired *t*-tests showed that strongly liked ones were preferred more often over an alternative than mildly liked ($t_{21} = 3.57$; $p \leqslant 0.01$) and disliked ones ($t_{21} = 4.54$; $p \leqslant 0.01$). Also, food items rated as mildly liked were chosen more often than disliked ones ($t_{21} = 2.09$; $p \leqslant 0.05$). Paired *t*-tests between the two choice options (chosen vs. dismissed) revealed that rather disliked foods were chosen less often than dismissed ($t_{21} = 6.30$; $p \leqslant 0.01$), but that strongly liked foods were indeed more often chosen than dismissed ($t_{21} = 8.12$; $p \leqslant 0.01$). Fig. 2b displays mean reaction times of participants (in milliseconds) to food items as a function of how much they were liked. A 2 × 3 ANOVA with the factors of choice (chosen vs. dismissed food items) and liking (rather disliked, mildly or strongly liked) only revealed a main effect of liking ($F_{2,42} = 307.62$; $p \leqslant 0.01$; $\eta_p^2 = 0.94$). For post-hoc comparisons, responses were thus collapsed across choices (chosen and dismissed). Paired *t*-tests between liking levels showed that food items rated as strongly liked were rated faster than mildly liked ($t_{21} = 25.08$; $p \leqslant 0.01$) and disliked ones ($t_{21} = 14.20$; $p \leqslant 0.01$).

Fig. 2c illustrates reaction times of participants over the period of choice between the two presented food alternatives in each trial. A one-way ANOVA revealed a main effect of liking ($F_{2,42} = 5.883$; $p \leqslant 0.01$; $\eta_p^2 = 0.22$). Post-hoc paired *t*-tests between liking levels revealed that participants were faster when choosing food images that had previously been rated as strongly liked as compared to mildly liked ($t_{21} = 2.26$; $p \leqslant 0.05$) and rather disliked ($t_{21} = 3.25$; $p \leqslant 0.01$). Fig. 2d illustrates the associations between participants' response times in the food valuation phase and the subsequent food choice period. When participants were fast in rating foods as mildly or strongly liked, they were likewise faster in making a decision in favor of these foods over the choice period (mildly liked foods: $r_{20} = 0.46$; $p \leqslant 0.05$; strongly liked foods: $r_{20} = 0.54$; $p \leqslant 0.01$). Supplementary table provides a comprehensive numerical overview of participants' responses given during the valuation phase and the food choice period.

3.2. Modulations of head-surface responses to food viewing by liking and choice

The electrode-wise 2 × 3 ANOVA on the head-surface VEPs over time revealed an interaction between liking and subsequent choice over the 135–180 ms post-image onset interval (Fig. 3a). The effect was particularly prominent at frontal electrodes, though we would remind the reader that analyses of voltage waveforms are dependent on the choice of the reference electrode, including also when the average reference is used. We therefore also analyzed a reference-independent measure – GFP – taking a mean value over the time window identified above (i.e. 135–180 ms; bar graph in Fig. 3b). The 2 × 3 ANOVA conducted revealed an interaction of liking and choice ($F_{2,20} = 4.84$; $p \leqslant 0.05$; $\eta_p^2 = 0.33$). Separate one-way ANOVAs for each choice condition (chosen and dismissed) revealed that the GFP was only modulated by the level of liking attributed when later chosen foods were viewed ($F_{2,20} = 3.72$; $p \leqslant 0.05$; $\eta_p^2 = 0.27$), but not when later dismissed foods were viewed ($p = 0.09$; $\eta_p^2 = 0.21$). Within chosen foods, post-hoc *t*-tests then showed that the electric field strength when viewing strongly liked foods was higher than when mildly liked foods were viewed ($t_{21} = 2.78$; $p \leqslant 0.01$). Paired *t*-tests between responses to equally liked chosen and dismissed foods showed that the GFP was higher for successively chosen strongly liked foods as opposed to their dismissed counterparts ($t_{21} = 3.19$; $p \leqslant 0.01$).[2]

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[2] Note: We did not find correlations between participants' behavioral data, anthropometric characteristics or food intake attitudes with the GFP responses.

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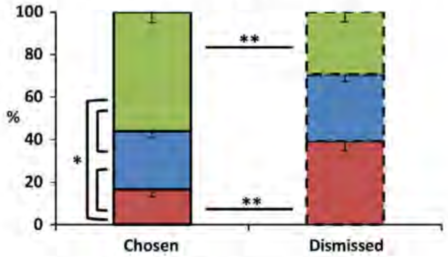
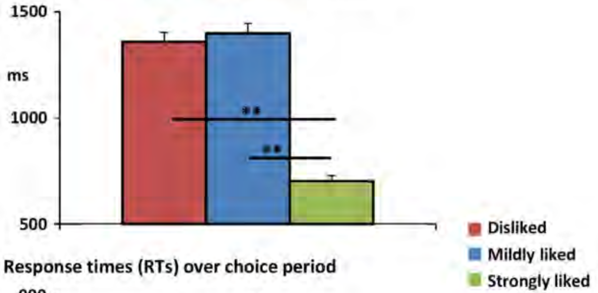
Behavioral results

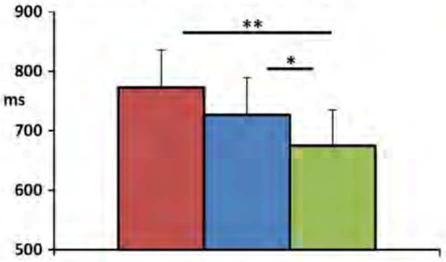
(a) Response frequencies during valuation phase



(b) Response times (RTs) during valuation phase



(c) Response times (RTs) over choice period



(d) Associations between valuation and choice RTs: chosen foods

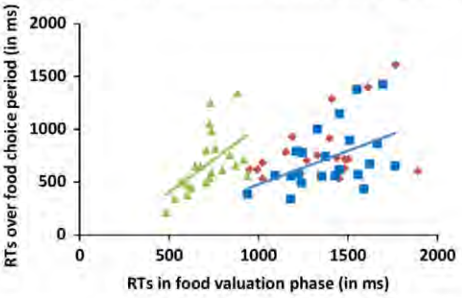


Fig. 2. Behavioral results. (a) Mean response frequencies (±s.e.m.) and (b) mean response times to disliked (red), mildly liked (blue) and strongly liked food items (green) during the valuation phase. (c) Response times (±s.e.m.) over the choice period where participants had to choose in each trial one of two food alternatives. (d) Associations between response times during the food valuation phase and the choice period. $^{*}p \leqslant 0.05$, $^{**}p \leqslant 0.01$.

3.3. Modulations in neural source activity to food viewing by liking and choice

A whole-head 2 × 3 ANOVA with the factors of liking (rather disliked, mildly and strongly liked) and choice (chosen vs. dismissed) served to define regions of interest for post-hoc contrasts (Fig. 4). An interaction of the factors liking and choice (visualized in Fig. 3a) was observed in the right dorsolateral PFC (dlPFC; Max: 57, −5, 35), the insula of the left hemisphere (INS; Max: $x = -34$, $y = -11$, $z = 14$), and in the right superior parietal cortex (SPC; Max: $x = 22$, $y = -40$, $z = 65$). Neural activity in these regions was modulated by whether foods are liked and whether they are successively chosen or dismissed for an alternative.

Separate one-way ANOVAs on neural activity in the abovementioned areas to foods that were either chosen or dismissed revealed modulations only when subsequently chosen foods were viewed, but not when later dismissed foods had been encountered (dlPFC: $F_{2,42} = 3.25$; $p = 0.05$; INS: $F_{2,42} = 5.42$; $p \leqslant 0.01$; SPC: $F_{2,42} = 3.28$;

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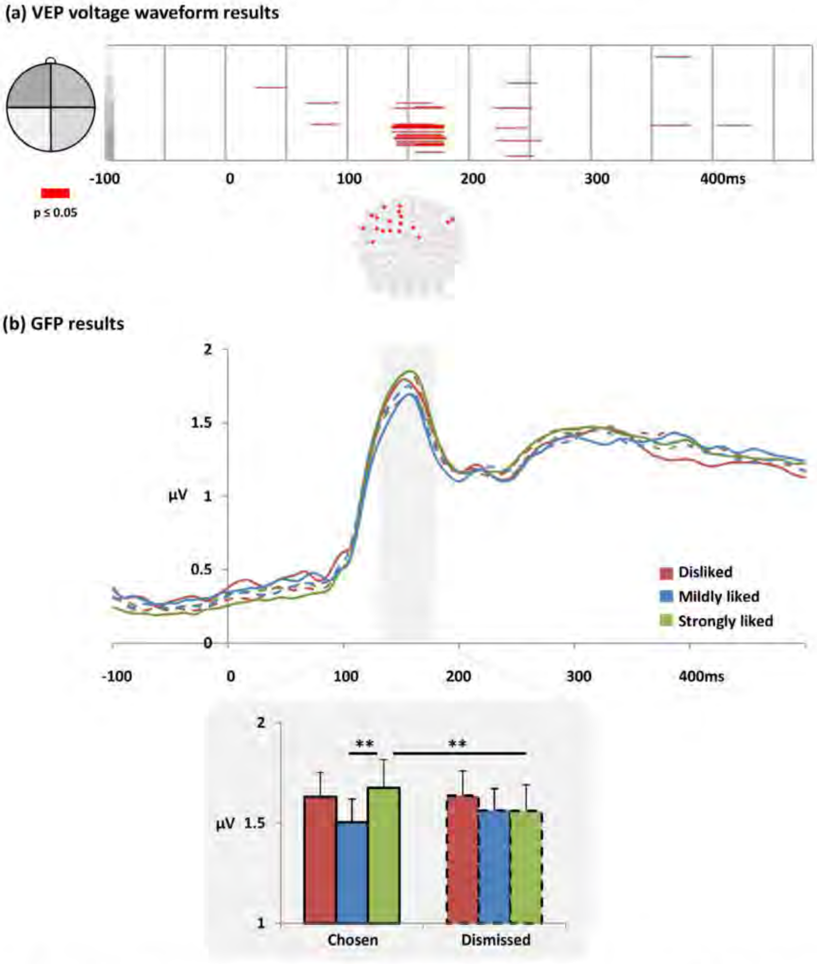

Fig. 3. Results of head-surface VEP analyses. (a) Interaction obtained by an electrode and time-point-wise 2 × 3 ANOVA with the factors of liking and choice, (b) GFP waveforms to food viewing as modulated by liking and subsequent food choices as well as bar graphs visualizing the mean GFP to each food viewing condition over the time window 135–180 ms. $^{**}p \leqslant 0.01$.

$p \leqslant 0.05$). Post-hoc *t*-tests on the neural activity pattern in these regions showed the following results. In the dlPFC, the difference in neural activity was most pronounced when subsequently chosen mildly liked foods were viewed as opposed to their dismissed counterparts ($t_{21} = 2.67$; $p \leqslant 0.05$). Moreover, the activity when viewing mildly liked subsequently chosen foods was higher than when strongly liked later chosen foods were viewed ($t_{21} = 2.49$; $p \leqslant 0.05$). In the insula, neural activity when viewing rather disliked foods was higher when they were subsequently chosen as when they were later dismissed for an alternative ($t_{21} = 3.00$; $p \leqslant 0.01$), and also greater as when mildly liked foods were viewed that were later chosen ($t_{21} = 3.29$; $p \leqslant 0.01$). In the superior parietal region, neural activity was found greater when rather disliked foods were viewed that were subsequently chosen as compared to when disliked foods were later dismissed for an alternative ($t_{21} = 3.71$; $p \leqslant 0.01$). Activity was also greater when comparing the neural responses to disliked subsequently chosen foods and strongly liked chosen foods ($t_{21} = 2.48$; $p \leqslant 0.05$).

The whole-head 2 × 3 ANOVA we conducted additionally revealed a main effect of liking (visualized in Fig. 4b) in the dorsomedial prefrontal region (Max: $x = -20$, $y = 30$, $z = 42$) indicating that this region's responsiveness is modulated by food liking rather independent of whether foods are subsequently chosen or dismissed for an alternative. For post-hoc comparisons, data points for chosen and dismissed foods were thus collapsed, and revealed stronger activity to the viewing of rather disliked as opposed to mildly ($t_{21} = 2.33$; $p \leqslant 0.05$) and strongly liked foods ($t_{21} = 2.17$; $p \leqslant 0.05$).

Moreover, the whole-head 2 × 3 ANOVA showed an additional main effect of choice (visualized in Fig. 4c) in the right dorsolateral prefrontal cortex (Max: $x = 27$, $y = 49$, $z = 20$) indicating that activity in this region is in particular modulated by food choices, independent of how much the viewed foods were liked. For post-hoc comparisons, data points were thus collapsed across liking levels, and revealed stronger activity to the viewing of subsequently chosen as opposed to dismissed foods ($t_{21} = 2.37$; $p \leqslant 0.05$).[3]

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[3] Note: We did not find correlations between participants' behavioral data, anthropometric characteristics or food intake attitudes with the neural source estimation measures.

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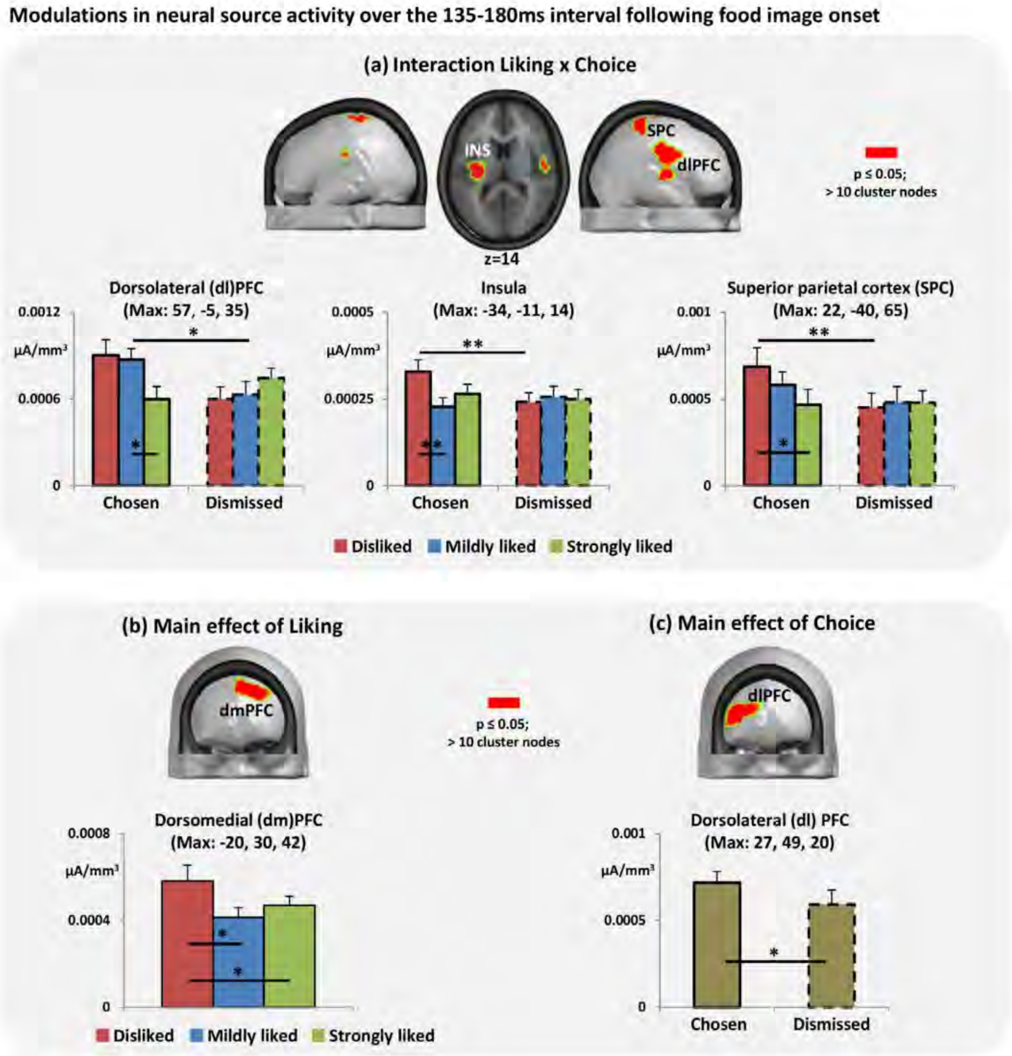

Fig. 4. Neural source modulations by liking and subsequent food choice over the 135–180 ms interval following food image onset. (a) Brain areas showing an interaction of the factors Liking and Choice (b) main effect of Liking. (c) Main effect of Choice. $^{*}p \leqslant 0.05$, $^{**}p \leqslant 0.01$.

4. Discussion

Our study identified the impact of food liking and successive choices on the spatio-temporal brain dynamics during food viewing in normal-weight participants. Behaviorally, our results showed (unsurprisingly) that strongly liked food items were more frequently chosen than dismissed, and that disliked items were more frequently dismissed than chosen. Nonetheless and regardless of the subsequent choice (i.e. whether food items were chosen or dismissed), participants were faster in rating food items as strongly liked (vs. disliked or mildly liked). Moreover, they were faster in making a choice in favor of foods that had been rated as strongly liked as opposed to mildly liked and disliked ones. Response times in both behavioral tasks, food valuation and food choice, were positively correlated when foods had been rated as mildly or strongly liked, showing that a fast food valuation response goes along with a fast decision in favor of a food item, but only when foods are liked. In other words, liking a food facilitates its choice over an alternative, but our study design cannot elucidate whether a similar relation in reaction times is apparent when foods are disliked and consecutively dismissed for an alternative.

These findings are in line with previous literature reporting decreased response times to highly valued visual items (Kahnt, Park, Haynes, & Tobler, 2014). Given that in our study liked items were also more often chosen by participants in general, this association is likely due to the inherent parallel assessment of 'liking' and 'wanting' aspects during preference building (Finlayson, King, & Blundell, 2008). We would nonetheless note that the food choice task we employed in our study is not appropriate to investigate deliberate 'wanting' (Berridge, 2009) and to thus enable assertions on a clear dissociation of 'liking' and 'wanting' processes. Participants were not given the opportunity of 'free' choices between food options, but they had to perform forced decisions between two alternatives. We will further refer to this point in the discussion on elevated brain responses to disliked foods that were still chosen over an alternative.

With respect to spatio-temporal brain dynamics, VEP modulations during food viewing as a function of liking and subsequent

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choice were apparent within the first 150 ms after image onset. The timing of these modulations converges with previously reported effects of food categorization in terms of energy content (Toepel et al., 2009) and effects of judging meal portion sizes for expected satiety (Toepel et al., 2015). Estimations of neural source activity over the time interval from 135 to 180 ms showed an interaction of liking and choice in the neural activity patterns of the dorsolateral PFC, the insula and the superior parietal lobe. Only brain responses to foods that were successively chosen were modulated by the level of liking, whereas no modulation was observed for responses to foods that were later dismissed for an alternative. Within the responses to chosen foods, strongest neural activity was often associated with the viewing of disliked foods that were nevertheless preferred over an alternative. Moreover, we identified two brain areas whose activity was either modulated by food liking only, independent of whether the viewed foods were subsequently chosen or dismissed for an alternative (i.e. dorsomedial PFC), or was altered by choice only, independent of how much the viewed foods had been rated as liked (i.e. lateral PFC).

Modulations in neural activity during food viewing by the level of liking attributed and subsequent choices thus involved a network of regions associated with salience-related attentional and cognitive control processes (Menon & Uddin, 2010; Mitchell, 2011). Harris, Hare, & Rangel, 2013 showed that the dlPFC is involved in the early top-down modulation of attention when participants had to perform a decision-making task and exercise self-control while viewing appetizing food images. This electrical neuroimaging study reported higher neural activity over the time interval between 150 and 200 ms when participants successfully chose healthy foods for prospective consumption while dismissing unhealthy food alternatives. These effects temporally converge with the time interval over which we observed pronounced modulations of neural activity by the level of liking attributed to foods that were successively chosen over an alternative. Therein, the viewing of disliked foods that were nevertheless chosen over an alternative elicited the greatest activity.

The prefrontal cortex has consistently been found to be involved in decision-making and emotion regulation in different experimental paradigms and modalities (Mitchell, 2011; Shenhav & Buckner, 2014). Whereas the dorsomedial PFC is involved in the encoding of reward-related information, i.e. stimulus values, in the context of decision-making (Camus et al., 2009), the dorsolateral prefrontal cortex is particularly recruited when choice options have to be weighed and self-control has to be exerted (Hare et al., 2009; Kober et al., 2010; McClure, Ericson, Laibson, Loewenstein, & Cohen, 2007). When facing conflicts between choice options, the activity of the dmPFC and dlPFC often increases in parallel, allowing for an adjustment of cognitive control and rendering of most relevant stimulus features as salient in order to guide choice behavior (Egner & Hirsch, 2005; Mitchell, 2011; Mitchell et al., 2009; Walton, Rudebeck, Bannerman, & Rushworth, 2007). Directly related to decisions on food options, increased dlPFC activity was reported in successful rather than in unsuccessful dieters (Hare et al., 2009).

Insula modulations, on the other hand, have been associated with task-related signaling in the context of food valuation (Born et al., 2011). In particular middle-to-posterior insular regions are involved in the exertion of self-control over food intake (Harris et al., 2013) and the integration of interoceptive sensations (Craig, 2002). Due to its high connectivity with the dlPFC and the vmPFC (Carmichael & Price, 1996; Craig, 2002), the insula is thought to be a key player enabling interactions between regions for stimulus valuation and choice (Harris et al., 2013). Prior electrical neuroimaging studies have shown that insular activity is elevated within 150 ms when participants view meal portion sizes judged as inappropriate for prospective intake (Toepel et al., 2015) further indicating its role in the integration of homeostatic and hedonic information.

The superior parietal cortex (SPC), another region showing modulations by liking and choices in our data, has been ascribed a role in attentional processes (Bisley & Goldberg, 2010), e.g. when non-food objects are viewed (Levy, Lazzaro, Rutledge, & Glimcher, 2011). Moreover, the superior parietal cortex was also found to be involved in the abstract coding of stimulus values in order to mediate goal-directed behaviors (Kahnt et al., 2014) and decisions between choice alternatives (Kable & Glimcher, 2009; McClure et al., 2007). Electrical neuroimaging results have shown SPC modulations within 200 ms when visual cues require an abstract value coding to enable decisions between choice options (Harris, Adolphs, Camerer, & Rangel, 2011).

In our study, both the insula and the posterior parietal region showed elevated responses especially when viewing foods rated as disliked, but subsequently chosen; likely since the alternative food option was not considered more tempting. That is, an increased stimulus valuation mediating decisions between two choice options cannot account for the obtained results. An alternative explanation of the observed patterns might be a particularly strong choice conflict when both food alternatives presented in one experimental trial were rated as rather disliked, but a choice had to nonetheless be indicated despite of the low liking level attributed to both images. In order to address this question, we computed indices of choice coherence in individuals (Supplementary figure), and also investigated whether individuals' choice coherence was associated with neural source activity.

First, we calculated for each participant the %response to foods that were chosen among the two alternatives presented per experimental trial *and* had been attributed the highest level of liking (coherent choice). In addition, individuals' %response to foods chosen although *not* attributed the highest level of liking in the respective experimental trials were computed (incoherent choice). Moreover, neutral choices were defined as instances were both food items had been attributed the identical level of liking. In a next step, the percentage of incoherent choices was subtracted from the percentage of coherent choices in each participant and for each level of liking to obtain 'choice coherence indices'. A one-way ANOVA on participants' choice coherence including the three levels of liking (disliked, mildly liked and strongly liked) revealed an effect of liking. For highly liked foods, choices were more coherent than for mildly liked than for disliked foods. However, choice coherence was not correlated with neural source activity during the viewing of disliked but chosen food items in any of the previously discussed brain regions. The additional analysis thus could not provide evidence for a relation between a strong choice conflict (assumed for disliked yet chosen foods) and elevated neural responses when foods were viewed that were rated as disliked, yet subsequently chosen over an alternative option. We would like to point out that we attempted further analyses (i.e. reaction times as a function of choice coherence; impact of difference in liking levels attributed to food alternative 1 and 2 per trial on our findings), but it should become clear from Supplementary figure that there were only very few data points for some conditions hindering these efforts. That is, we cannot fully exclude the possibility of a strong choice conflict for disliked food items induced by the forced-choice task in our design.

However, in a recent EEG study top-down attentional influences on food viewing responses were found within 200 ms when controlled decisions need to be taken (Harris et al., 2013). In this study, participants viewed appetizing food products under varying tasks. In one part of the experiment, participants were asked to make random food choices without constraints. In a second part they had to exert self-control during food viewing with the goal to receive monetary incentives for longitudinal body weight loss.

Over the 150–200 ms interval during food viewing, successful self-control trials (which were defined as accepting healthy, but disliked foods or rejecting unhealthy, but liked foods) elicited stronger activity in the insula, the dorsolateral PFC and the ventrolateral PFC. Harris and colleagues proposed that this result pattern is due to attentional filtering mechanisms serving to mediate self-control when needed, i.e. in order to adjust food choice behavior.

Although our study design differs from the one of Harris et al. (2013) in task instructions (food choices without vs. with exertion of self-control to support body weight management) and visual food 'valuation conditions' (self-attributed liking vs. taste/health ratings), results of both studies converge on the timing of early response modulations, and partially on the brain network involved. That is, we have reason to believe that in our study responses to foods rated as disliked, but nonetheless chosen, are influenced by attentional modulations of brain regions involved in salience attribution and decision-making. Notably, our study design does not permit the comparison of responses to disliked-chosen with strongly liked-rejected food items to further strengthen parallels with the study of Harris et al. (2013). Moreover, valuation and choice were highly intertwined in our study as they are in everyday dietary behavior, and future research still needs to disentangle the influences of valuation and choice on the spatio-temporal brain dynamics to food viewing. Yet, further investigations of choice conflicts between food alternatives (similar or differing in attributes like perceived pleasantness, health impact and tastiness) are certainly needed to complete insights in human food intake behavior and their role in body weight management and its health consequences.

Acknowledgments

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.bandc.2015.10.005.

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Annex 2

STUDY B – Brain dynamics of meal size selection in humans

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Brain dynamics of meal size selection in humans

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ABSTRACT

Although neuroimaging research has evidenced specific responses to visual food stimuli based on their nutritional quality (e.g., energy density, fat content), brain processes underlying portion size selection remain largely unexplored. We identified spatio-temporal brain dynamics in response to meal images varying in portion size during a task of ideal portion selection for prospective lunch intake and expected satiety. Brain responses to meal portions judged by the participants as 'too small', 'ideal' and 'too big' were measured by means of electro-encephalographic (EEG) recordings in 21 normal-weight women. During an early stage of meal viewing (105–145 ms), data showed an incremental increase of the head-surface global electric field strength (quantified via global field power; GFP) as portion judgments ranged from 'too small' to 'too big'. Estimations of neural source activity revealed that brain regions underlying this effect were located in the insula, middle frontal gyrus and middle temporal gyrus, and are similar to those reported in previous studies investigating responses to changes in food nutritional content. In contrast, during a later stage (230–270 ms), GFP was maximal for the 'ideal' relative to the 'non-ideal' portion sizes. Greater neural source activity to 'ideal' vs. 'non-ideal' portion sizes was observed in the inferior parietal lobule, superior temporal gyrus and mid-posterior cingulate gyrus. Collectively, our results provide evidence that several brain regions involved in attention and adaptive behavior track 'ideal' meal portion sizes as early as 230 ms during visual encounter. That is, responses do not show an increase paralleling the amount of food viewed (and, in extension, the amount of reward), but are shaped by regulatory mechanisms.

1. Introduction

The sight of food triggers a range of physiological and psychological anticipatory responses based on knowledge acquired through past experiences. These responses not only prepare the body for ingestion but serve to guide food choice and intake with little conscious effort. At the neural level, the simple viewing of energy-dense foods elicits strong activations in visual, homeostatic and reward-related areas in comparison to low-energy foods (Frank et al., 2010; Killgore et al., 2003; Siep et al., 2009; Toepel et al., 2009). The most consistent activations across functional magnetic resonance imaging (fMRI) studies are found in the middle occipital gyrus, inferior temporal gyrus, hypothalamus, ventral striatum and middle frontal gyrus (van der Laan et al., 2011). These activations were obtained in normal-weight individuals while viewing food items with high vs. low caloric content with no explicit evaluation of foods requested. Detecting foods rich in energy is essential to ensure nutrition as those foods help to achieve satiety faster and for longer periods than foods poor in energy (Drewnowski and Almiron-Roig, 2010). Responses to the sight of energy-dense foods, especially in the prefrontal region, may further reflect the expected pleasantness of these foods because this brain region is highly responsive to the pleasant taste or flavor of foods (Kringelbach et al., 2003; Kringelbach, 2005; Ohla et al., 2012; Small et al., 2003b; Tzieropoulos et al., 2013). Yet, the practical implications of the greater activations to energy-dense foods on food intake control and in particular on portion size selection remain so far elusive. For example, the abovementioned neuroimaging studies (Frank et al., 2010; Killgore

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Abbreviations: CG, cingulate gyrus; EEG, electro-encephalographic; fMRI, functional magnetic resonance imaging; GFP, global field power; IOG, inferior occipital gyrus; IPL, inferior parietal lobe; INS, insula; LAURA, local autoregressive average; MFG, middle frontal gyrus; MTG, middle temporal gyrus; FCQ-S, momentary craving state questionnaires; SPL, superior parietal lobule; STG, superior temporal gyrus; TFEQ-R 18, Three-Factor-Eating questionnaire; VEPs, visual evoked potentials.

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et al., 2003; Siep et al., 2009; Toepel et al., 2009; van der Laan et al., 2011) did not systematically control food portion sizes (Frank et al., 2010; Killgore et al., 2003; Siep et al., 2009; Toepel et al., 2009; van der Laan et al., 2011).

Portion size is yet a crucial determinant of energy balance and weight management (Rolls et al., 2002; Wansink et al., 2005; Wansink and Kim, 2005). Using computer-based tasks with food pictures, a number of studies showed that decisions on portion size are not driven by food energy density or food liking as such, and that participants do not necessarily select the largest portion sizes as their ideal ones (Brogden and Almiron-Roig, 2010; Brunstrom et al., 2010; Brunstrom and Rogers, 2009; Brunstrom and Shakeshaft, 2009; Forde et al., 2011). In other words, it seems that individuals do not select meal portion sizes only for calories or for pleasure. Instead, other factors related to expected post-ingestive effects appear to be key motivators for meal size selection, namely 'expected satiation' (anticipated fullness after consumption) and 'expected satiety' (anticipated fullness between meals). Along these lines, Wilkinson et al. (2012) showed that portion size selection and expected satiety are good predictors of energy intake, thus establishing the practical relevance of computer-based assessments to food intake behavior.

The primary objective of the current study was to identify the spatio-temporal brain dynamics mediating portion size judgment to gain further insight into food intake behavior and control. Responses to visually presented meals of varying portion size were assessed by means of electro-encephalographic (EEG) recordings in 24 normal-weight women during a task of portion size judgment for expected satiety. Stimuli were pictures of 19 meals presented on a computer screen in a range of 11 different portion sizes. EEG data were analyzed using an electrical neuroimaging approach (Michel and Murray, 2012) as a function of individuals' judgments on the presented portion size among the three following forced-choice options: 'too small', 'ideal' and 'too big'. Under an assumption that only the increasing quantity of food viewed modulates brain responsiveness, one would expect to find an incremental increase of responses in the temporo-occipital brain regions involved in visual analysis and categorization within 200 ms after image onset (Busch et al., 2004; Puce et al., 2013), likely paralleled by similar response directions in prefrontal regions due to the reward value to food (Frank et al., 2010; Killgore et al., 2003; Siep et al., 2009; Toepel et al., 2009; van der Laan et al., 2011). In contrast, we hypothesized that an at least partially distinct network of brain regions would be involved in adaptive portion size selections (i.e., greatest responses to the portions judged as 'ideal' relative to those judged as 'non-ideal'). Due to the high temporal resolution of EEG, such response dissociations might not only be observed along a spatial dimension as in functional neuroimaging studies, but also along a temporal dimension with EEG modulations differing in the time domain for the expected effects (i.e., incremental increase vs. highest response to the portions judged as 'ideal'). Secondary objectives of the study were to explore associations between individual's responses to self-selected portion sizes with food intake attitudes such as dietary restraint and tendencies to overeat in emotionally challenging situations. These factors, known to influence brain responses to visual food cues (Meule et al., 2013; Toepel et al., 2012) and decisions on portion size (Brunstrom et al., 2008) in normal-weight individuals may reveal further insights into the brain mechanisms mediating portion size selection.

2. Material and methods

2.1. Study participants

Twenty-four normal-weight women participated in the study. Women were chosen to avoid confounding factors linked to gender differences in eating behavior and neural responses to food cues (Cornier et al., 2010; Rolls et al., 1991; Toepel et al., 2012). They completed the Three-Factor-Eating questionnaire (TFEQ-R 18) (Karlsson et al., 2000) and momentary craving state questionnaires (FCQ-S) (Nijs et al., 2007). Data from the standardized questionnaires were used for secondary data analyses as factors relating to food intake attitudes. All participants were healthy, with no prior history of self-reported head trauma, neurological disorder or diabetes, and were not under medication. All reported not having any history of eating disorders, current diet attempts, food allergies or intolerances and food restriction such as vegetarianism. Other exclusion criteria were pregnancy, breast-feeding, illicit drug consumption and the consumption of more than one alcoholic drink per day. Due to low EEG signal quality of three participants, only the data of 21 women entered the final analyses and their characteristics are summarized in Table 1. The study was approved by the Ethics Committee of the Faculty of Biology and Medicine of the University of Lausanne. All subjects gave written informed consent and received financial compensation for their participation.

2.2. Stimuli

Stimuli were pictures of 19 test meals commercially available and used previously in a consumer study (Forde et al., 2011). Each stimulus was photographed on a standard white plate. Fifty-one color pictures of different 'physical' portions for each meal were used during a prior familiarization session during which pictures were presented with a description label. A subset of 11 pictures for each meal was used for the subsequent EEG session (Fig. 1A). For a given meal, the central picture #25 corresponds to 100% of the portion size as sold. Picture #1 and picture #50 respectively represent 33% and 300% the kcal content of picture #25. Across this range, the portion size and, by extension, the caloric content of pictures, increase in equal logarithmic steps (0.3 log series) based on the originally published method for quantifying expectations of satiety and satiation (Brunstrom and Shakeshaft, 2009).

2.3. Study design and procedure

Participants completed two experimental sessions on different days. They were instructed to have their usual breakfast between 7:00 and 8:00 am and to refrain from eating any food and drinking caffeinated beverages until they arrived in the laboratory between 9:00 and 10:00. Participants were tested individually in a sound-attenuated booth.

During the prior familiarization session, participants performed a computer-based task comprising sequentially: Thirst and hunger ratings, matched fullness task (expected satiation), selection of portion size to stop feeling hungry until an evening meal (expected fullness), food consumption frequency (times per day/week/month/year), food familiarity and expected liking ratings. The exclusive purpose of this session was to familiarize participants with the views of the 19 meals used in the subsequent EEG session. A report on the outcome data is not in the scope of the current report.

During the EEG session, participants first received the following instructions: "You will be presented with a number of food pictures.

Table 1
Participants' BMI and food intake attitudes (N = 21).

		Mean (±s.e.m.)	Range
BMI (in kg/m^2)		21.3 (±0.4)	17.5–26
TFEQ-R 18	Uncontrolled eating score	40.4 (±3.1)	19–67
	Emotional eating score	42.3 (±5.1)	0–78
	Restrained eating score	27.0 (±4.1)	0–56
FCQ-S score		31.8 (±2.0)	16–49

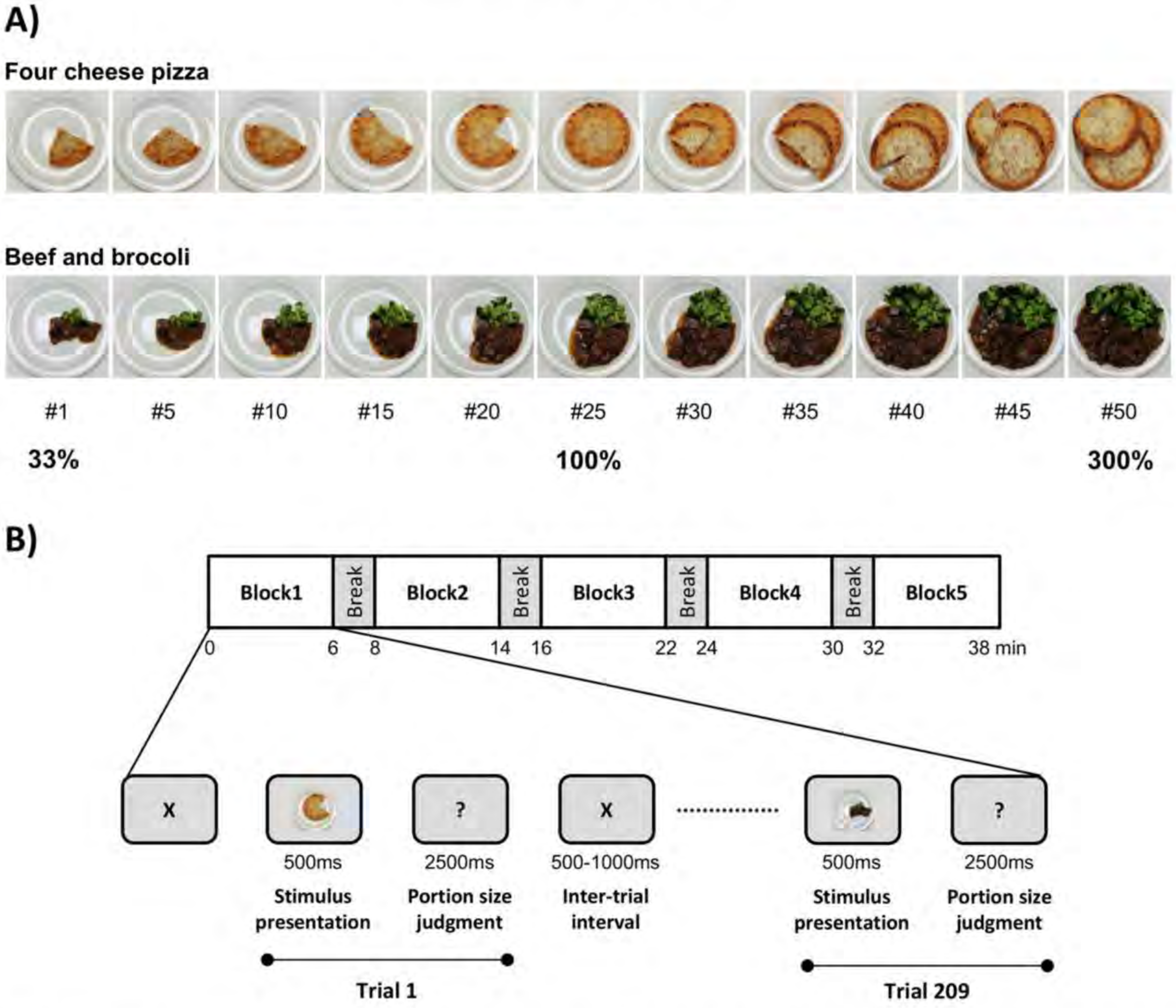

Fig. 1. Exemplar stimuli and study design. A) Portion size range of two test meals used in the EEG session. For each meal, every fifth portion size was chosen out of the full picture set with #25 being current portion of the meal as sold (100%), #1 being the smallest (33%) and #50 the largest (300%). B) Experimental design of the EEG session. The 209 stimuli (19 meals * 11 portion sizes) were presented once during each experimental block in a pseudo-random order. For each stimulus participants had to judge the size of the meal portion presented relative to their expected satiety for prospective lunch intake by choosing between 'too small', 'ideal' and 'too big'.

Imagine you are about to eat that food at lunchtime. No other foods are available. Judge the size of the portion relative to the size that you would select yourself for lunch today to stop feeling hungry until an evening meal." They were further instructed not to respond in cases where they completely disliked a meal so that the related data did not enter the subsequent analysis. They then completed five blocks of trials of approximately 6 min each and separated by a 2 min break (Fig. 1B). One block of trials consisted of the presentation of all 209 stimuli (19 meals × 11 portion sizes) in a pseudo-random order, differently arranged in each block. The order of blocks was counter-balanced across participants to avoid position effects. During one trial, a meal picture was presented for 500 ms in the center of a 21″ CRT monitor screen with a gray background, which was followed by a question mark presented for 2500 ms. Starting from stimulus presentation onset, participants had 3000 ms for judging the size of the meal portion relative to expected satiety according to a 3-alternative forced-choice: 'too small', 'ideal' or 'too big'. Behavioral responses and response times were recorded via a response box controlled by E-Prime with stimulus presentation (Psychology Software Tools Inc., Pittsburgh, USA; www.pstnet.com/eprime). Inter-trial intervals varied between 500 and 1000 ms during which participants had to fixate a central cross to avoid eye movements. The EEG session lasted between 60 and 75 min including electrode preparation.

EEG was continuously recorded at a 512 Hz digitization rate using a Biosemi ActiveTwo system (Biosemi, Amsterdam, The Netherlands) from 64 head-surface electrodes, arranged according to the expanded 10–20 positions. This system uses a pair of electrodes (common mode sense and driven right leg) as a feedback loop driving the average potential across the montage as close as possible to the amplifier zero. Details of this circuitry, including a diagram can be found on the Biosemi website (http://www.biosemi.com/pics/zero_ref1_big.gif). In the beginning and at the end of the session, participants rated their hunger level using 100 mm rating scales anchored from 'not hungry at all' to 'extremely hungry' to check for changes in food motivation along the procedure. Overall, hunger level increased in all participants (mean change ± s.e.m. $= 42.8 \pm 5.5$), indicating that the task did not have a detrimental impact on food motivation due to repeated exposure to visual food cues.

2.4. Data analysis

2.4.1. Behavioral data analysis

In a first descriptive step, the distribution of portion size judgments ('too small', 'ideal', 'too big') for the 11 physical portion sizes was assessed by averaging response frequency across meals and participants. In a second step, the frequency of portion size judgments and related reaction times were averaged across meals, physical portion sizes and participants. These data were submitted to one-way ANOVAs with the factor of portion judgment ('too small', 'ideal', 'too big'). Post-hoc paired t-tests were computed when justified by the ANOVAs. Results were considered significant when $p \leq 0.05$.

2.4.2. EEG data analysis

Visual evoked potentials (VEPs) were computed by averaging EEG epochs from -100 ms to 500 ms relative to stimulus onset, separately for each participant as a function of individual portion judgment ('too small', 'ideal', 'too big'). The number of trials obtained for each portion judgment was examined individually and adjusted when necessary by randomly removing trials. As a result, the final number of trials for VEP analyses did not statistically differ between portion judgment conditions ($F_{2,60} = 0.55$; $p = 0.58$; mean ± s.e.m.: 'too small' $= 312 \pm 4$, 'ideal' $= 290 \pm 10$, 'too big' $= 300 \pm 16$). To avoid data contamination by artifacts such as eye blinks and drifts, an automatic trial rejection criterion of $\pm 80\ \mu V$ was applied and followed by a trial-by-trial visual inspection. The EEG was filtered (2nd order Butterworth with -12 dB/octave roll-off; 0.1 Hz high-pass; 30 Hz low-pass; 50 Hz notch). The filters were computed linearly in both the forward and backward directions to eliminate phase shifts. Artifact-corrupted electrodes were interpolated using 3-D splines (Perrin et al., 1987). Group average VEPs were next computed against the average reference.

The impact of portion size judgments on the spatio-temporal brain dynamics was then quantified by assessing modulations in the strength of the global electric field amplitude at the scalp (global field power, GFP) and in the underlying activity of neural sources using the CarTool (http://sites.google.com/site/fbmlab/cartool) and the STEN software packages (http://unil.ch/line/home/menuinst/about-the-line/software-analysis-tools.html). GFP was derived from VEP responses and calculated as the square root of the mean of the squared amplitude values recorded at each electrode (vs. the average reference),representing by definition the spatial standard deviation of the electric field (Brunet et al., 2011; Murray et al., 2008). That is, GFP yields larger amplitudes for stronger electric fields, and GFP maxima are indicative of maximally synchronous neural sources underlying the scalp-recorded activity (Michel and Murray, 2012; Skrandies, 1990). We identified GFP maxima from the group-averaged VEPs and verified their occurrence in single-subject data. These GFP maxima (spanning 40 or 60 ms, respectively, to encompass the latencies of GFP peaks in each individual's data) delineated time windows of interest for further analyses. Mean GFP amplitudes were calculated in each time window, for each participant and portion judgment condition separately, resulting in one data-point per subject and condition. Mean amplitude values were submitted to one-way ANOVAs with the factor of portion judgment ('too small', 'ideal', 'too big'). Post-hoc paired t-tests were conducted when a main effect had been attested by the ANOVA. Results were considered significant when $p \leq 0.05$.

The same averages across time windows of GFP maxima were the basis for neural source estimations using the local autoregressive average (LAURA) distributed linear inverse solution (Grave de Peralta et al., 2001, 2004). The solution matrix consists of 3005 nodes equally distributed within the gray matter of the Montreal Neurological Institute average brain. This implementation of LAURA was generated with the Spherical Model with Anatomical Constraints (SMAC; Spinelli et al., 2000). As output, LAURA provides current density values (in $\mu A/mm^3$) at each solution point (node). Mean current density values at each node and over each time window were submitted to one-way ANOVAs with the factors of portion judgment ('too small', 'ideal', 'too big'). The effect of portion judgment was considered significant when the statistical threshold of $p \leq 0.05$ was exceeded within a cluster of ≥ 10 contiguous nodes of the inverse solution matrix to correct for multiple measures. This spatial extension criterion was based on AlphaSim randomizations (http://afni.nimh.nih.gov) which has been similarly applied in prior works from our group (Lietti et al., 2012; Toepel et al., 2009, 2012). Prior basic and clinical researches have documented and discussed in detail the spatial accuracy of this inverse solution, which is in the order of the grid size of the solution points (here $\sim 6 \times 6 \times 6$ mm) (Gonzalez Andino et al., 2005a, 2005b; Grave de Peralta et al., 2004; Michel et al., 2004). Within the statistically defined regions of interest based on whole-brain analyses, post-hoc paired t-tests (two-tailed) and correlation analyses were conducted, i.e., on the mean value of the node (plus its six immediate neighbors) for which the ANOVA had revealed the maximal F-value. Results were considered significant when p-values ≤ 0.05.

2.4.3. Correlation analysis

Pearson's correlation coefficients were computed to explore associations between neural source activity elicited by portion size judgments and food intake attitudes (cognitive restraint of eating score, emotional eating score and uncontrolled eating score from the subscales of the TFEQ-R18 and food craving score from FCQ-S) and BMI. Results were considered significant when $|r19| \geq 0.433$; $p \leq 0.05$ (two-sided).

3. Results

3.1. Behavioral responses to meal portion sizes

Fig. 2A displays the distribution of portion size judgments ('too small', 'ideal', 'too big') for the 11 physical portion sizes across meals and participants. The frequency of portions judged as 'too small' progressively decreases from pictures #1 to #50; that is from the smallest to the largest portion size presented (see Fig. 1). Portions judged as 'too big' follow the opposite pattern. After plotting the behavioral data across portion sizes, the statistical analysis on response frequencies revealed a significant effect of portion judgment ($F_{2,40} = 6.58$; $p \leq 0.01$). Meal portions were more often judged as 'too small' (40.8%) relative to 'ideal' (28.4%; $t_{20} = 4.27$; $p \leq 0.01$) and 'too big' (30.6%; $t_{20} = 4.27$; $p \leq 0.05$) for expected satiety. Portion judgment also had a significant effect on response times ($F_{2,40} = 8.83$; $p \leq 0.01$). Participants responded significantly faster when portions were judged as 'ideal' (942 ms ± 49 s.e.m.) than 'too small' (998 ms ± 50 s.e.m.; $t_{20} = 2.08$; $p \leq 0.05$) or 'too big' (1038 ms ± 48 s.e.m.; $t_{20} = 5.08$; $p \leq 0.01$) (Fig. 2B).

3.2. GFP modulations by portion size judgment

In the group-averaged data, the GFP waveform showed three maxima, in turn delineating three time intervals of interest for statistical analyses on single-subject responses (Fig. 3A). Over the first time interval (105–145 ms), the ANOVA revealed an effect of judgment ($F_{2,40} = 30.19$; $p \leq 0.01$) driven by a significant increase of the GFP as portion size increases (Fig. 3B, left panel). Over the second time interval (230–270 ms), portion size judgment had a significant effect on mean GFP ($F_{2,40} = 4.33$; $p \leq 0.05$), with larger responses for the 'ideal' than for the 'too small' and 'too big' portion sizes (Fig. 3B, middle panel). Over the third time-interval (350–410 ms), the effect of portion size judgment ($F_{2,40} = 4.33$; $p \leq 0.05$) was due to a linear decrease of the GFP while portion size increased (Fig. 3B, right panel).

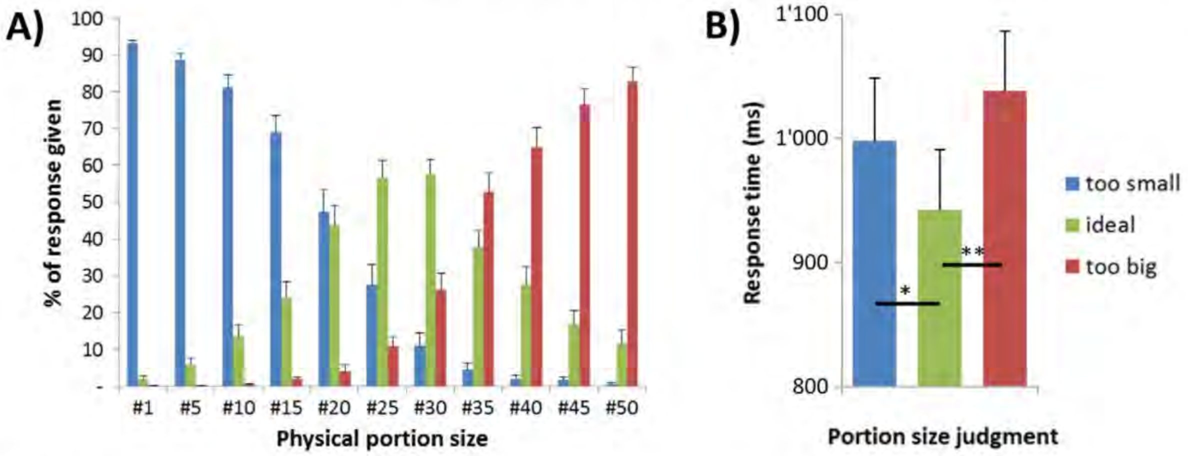

Fig. 2. Behavioral data collected during the EEG session. A) Distribution of the behavioral responses given to the different portion sizes across meals. B) Mean response times for portion size judgments. Error bars, standard error of the mean; $^{*}p \leq 0.05$; $^{**}p \leq 0.01$.

3.3. Neural source modulations by portion size judgment

Over the first time interval (105–145 ms), the ANOVA revealed a distributed impact of portion judgment on neural source activity in the right middle frontal gyrus (MFG), right insula (INS) and bilaterally in the middle temporal gyrus (MTG) (Fig. 4A). Within these regions of interest, post-hoc t-tests showed that this effect was due to an incremental increase of neural activity as portion size increases (Fig. 4B).

The ANOVA on neural source activity over the second time interval (230–270 ms) revealed effects of portion judgment on responses in the frontal, temporal, parietal, and occipital regions (Fig. 5A). Two directions of responses were found therein (Fig. 5B): (1) incremental increases of activity in the MFG and inferior occipital gyrus (IOG) as portion size increases, and (2) maximal activity in response to portions judged as 'ideal' compared to 'non-ideal' (i.e., 'too small' and 'too big') in the inferior parietal lobe (IPL), cingulate gyrus (CG) and superior temporal gyrus (STG).

Over the last time interval (350–410 ms), portion size judgment was found to modulate neural activity in the temporal, parietal and occipital regions (Fig. 6A) with mixed effects (Fig. 6B). On the one hand, portions judged as 'ideal' induced higher neural activity in the STG and superior parietal lobule (SPL) relative to 'too small' portions. On the other hand, portions judged as 'too small' went along with lower neural activity in the IOG and higher neural activity in the MTG than portions judged as 'ideal' or 'too big'.

3.4. Associations between neural activity and food intake attitudes

Significant correlations between neural source activity and food intake attitudes as assessed by the TFEQ-R18 scores were observed over the second (Fig. 7A) and third (Fig. 7B) time intervals (i.e., 230–270 ms and 350–410 ms during meal viewing). Neural activity in the cingulate gyrus was negatively associated with cognitive eating restraint when portion sizes were judged as 'too big' ($r_{19} = -0.44$;

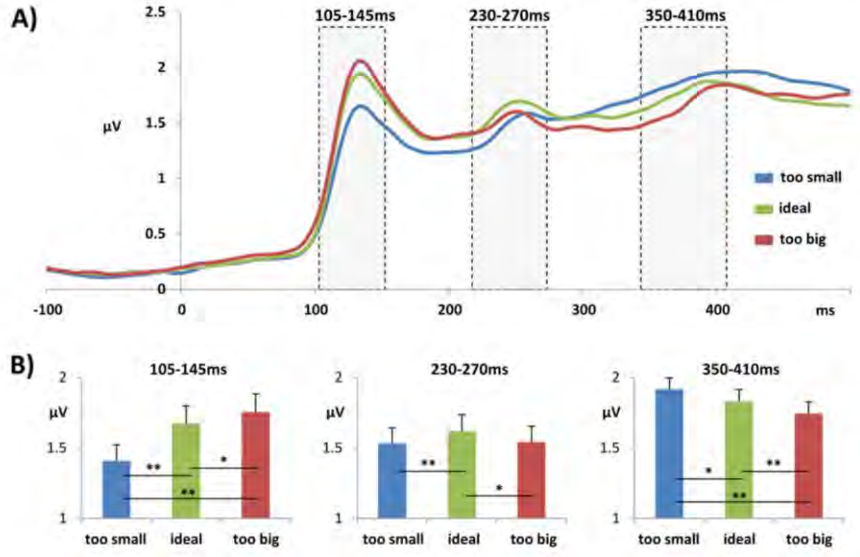

Fig. 3. GFP analysis as a function of portion size judgment over time. A) GFP waveform with three time intervals of maxima highlighted by a gray frame with dotted lines. B) Mean GFP computed for the three time intervals. 0, stimulus presentation onset; $^{*}p \leq 0.05$; $^{**}p \leq 0.01$; error bar, standard error of the mean.

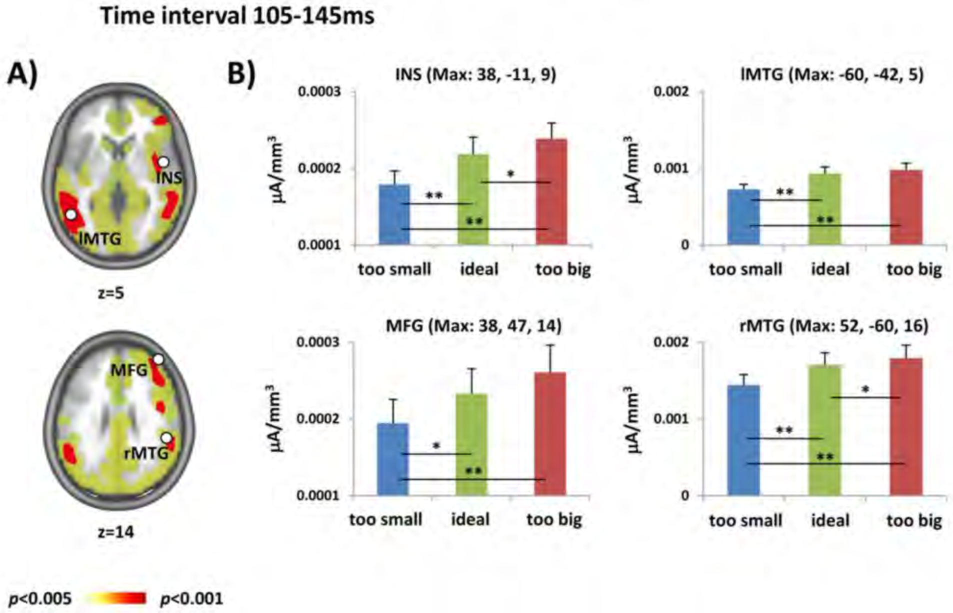

Fig. 4. Differences in neural source activity as a function of portion size judgment during 105–145 ms post-stimulus onset. A) Color-coded p-values of the ANOVA on portion size judgment plotted on axial brain sections with maxima indicated. B) Results of post-hoc t-tests in brain regions showing the portion judgment effect with Talairach coordinates of maxima (x,y,z). *p ≤ 0.05; **p ≤ 0.01; error bar, standard error of the mean; INS, insula; MFG, Middle frontal gyrus; l/rMTG, left/right middle temporal gyrus.

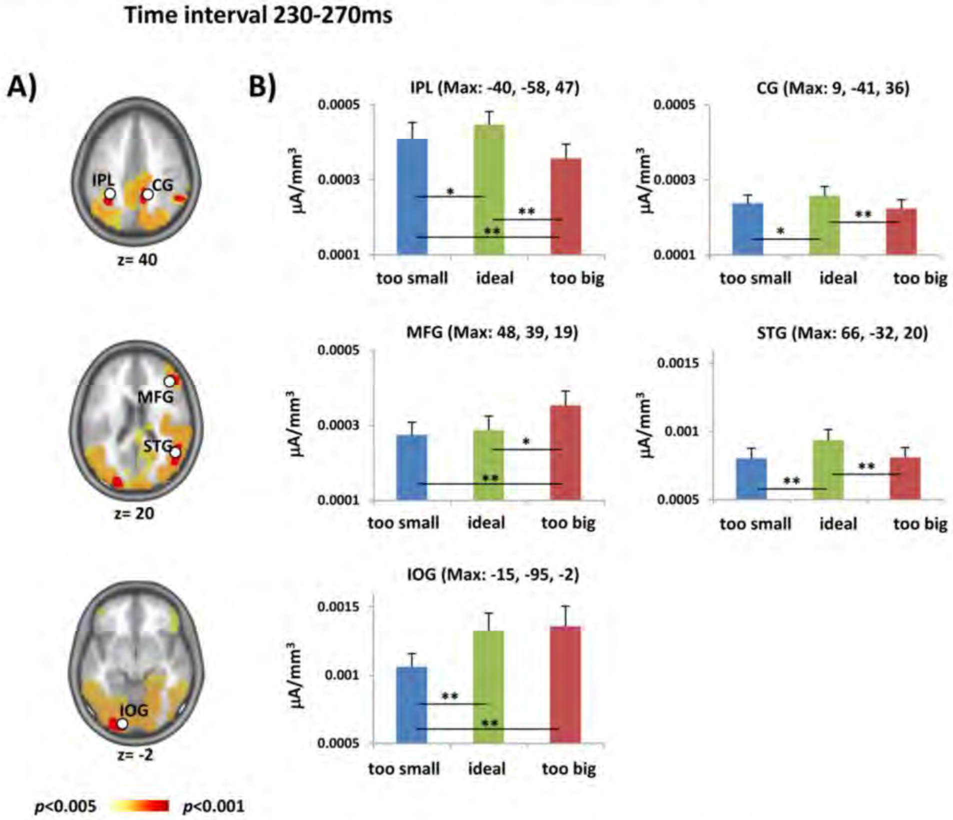

Fig. 5. Differences in neural source activity as a function of portion size category during 230–270 ms post-stimulus onset. A) Color-coded p-values of the ANOVA on portion size judgment plotted on axial brain sections with maxima indicated. B) Results of post-hoc t-tests in brain regions showing the portion judgment effect with Talairach coordinates of maxima (x,y,z). *p ≤ 0.05; **p ≤ 0.01; error bar, standard error of the mean; CG, cingulate gyrus; IOG, inferior occipital gyrus; IPL, inferior parietal lobe; MFG, middle frontal gyrus; STG, superior temporal gyrus.

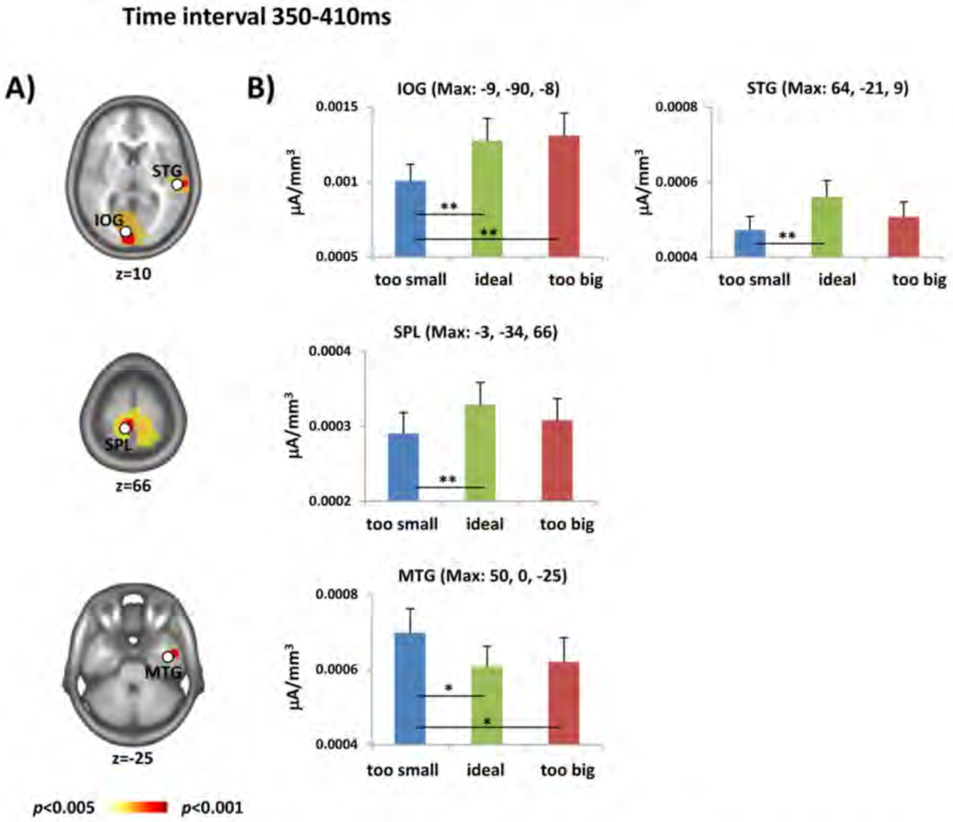

Fig. 6. Differences in neural source activity as a function of portion size category during 350–410 ms post-stimulus onset. A) Color-coded p-values of the ANOVA on portion size judgment plotted on axial brain sections with maxima indicated. B) Results of post-hoc t-tests in brain regions showing the portion judgment effect with Talairach coordinates of maxima (x,y,z). $^{*}p \leq 0.05$; $^{**}p \leq 0.01$; error bar, standard error of the mean; IOG, inferior occipital gyrus; MTG, medial temporal gyrus; SPL, superior parietal lobule; STG, superior temporal gyrus.

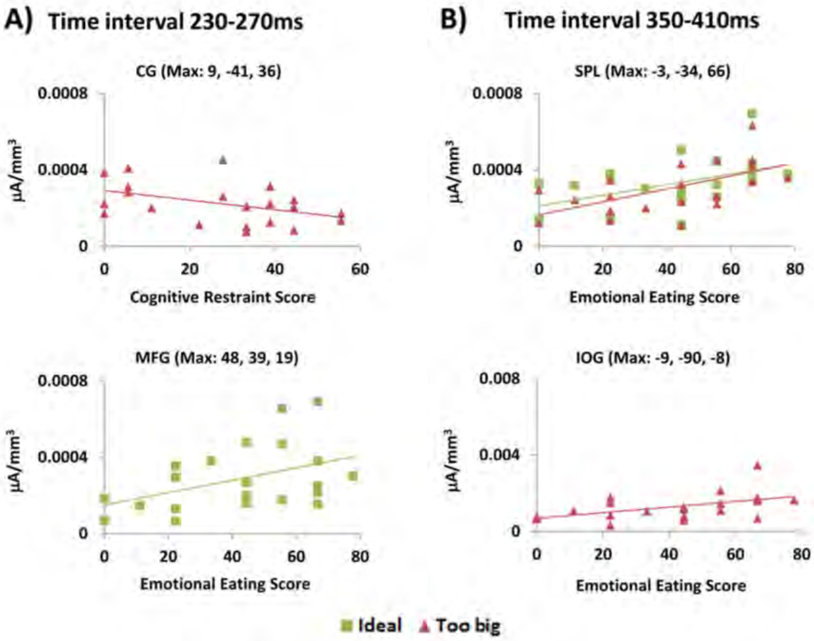

Fig. 7. Correlations between neural response and factors relating to eating style. Significant correlations obtained during A) 230–270 ms and B) 350–410 ms post-stimulus onset in response to meal portions judged as 'ideal' or 'too big'. CG, cingulate gyrus; IOG, inferior occipital gyrus; MFG, middle frontal gyrus; MTG, middle temporal gyrus; SPL, superior parietal lobule.

$p \leq 0.05$). Activity in the ventral prefrontal MFG, SPL and IOG was positively linked with emotional eating. The later associations were obtained in the MFG in response to 'ideal' portions ($r_{19} = 0.44$; $p \leq 0.05$), in the SPL to both 'ideal' ($r_{19} = 0.49$; $p \leq 0.05$) and 'too big' ($r_{19} = 0.60$; $p \leq 0.01$) portions, and in the IOG to 'too big' portions ($r_{19} = -0.50$; $p \leq 0.05$).

4. Discussion

This is the first study to investigate brain responses to meal images presented in different portion sizes. While female participants were judging the size of the foods presented relative to their expected satiety, we identified spatio-temporal brain dynamics underlying ideal portion selection and disentangled effects due to the increase in food quantity (i.e., from portions judged as 'too small' to 'too big').

4.1. Portion size judgments

The distribution of response frequencies across physical portion sizes shows that portions judged as 'too small', 'ideal' and 'too big' largely overlap with the smallest, intermediate and largest portions, respectively. This result is well aligned with previous work showing that the portion chosen as ideal for satiety is not necessarily the largest portion available (Brunstrom et al., 2010; Brunstrom and Rogers, 2009; Brunstrom and Shakeshaft, 2009; Forde et al., 2011). Response times show that portions considered as 'ideal' for prospective lunch intake and satiety were judged faster than 'non-ideal' meal portions. This result confirms that incremental increases in food quantity and/or visual complexity are not the key drivers in portion size decisions and are in line with those previous results on portion selection (Brunstrom et al., 2010; Brunstrom and Rogers, 2009; Brunstrom and Shakeshaft, 2009; Forde et al., 2011). Studies on the visual perception of non-food objects have established that the higher the reaction times the more complex the stimuli and task requirements are (O'Shea and Bashore, 2012). In contrast, our study shows longer reaction times for both 'too small' and 'too big' portion sizes as compared to 'ideal' ones, likely indicating the influence of additional variables in these judgments like the weighing between energetic needs and hedonic drives for food intake control.

4.2. Dissociable brain dynamics to meal portions and ideal portion selection

EEG responses to the meal portion sizes presented were quantified by assessing modulations in the GFP which is derived from the visually evoked potentials and which represents the strength of electric potentials concurrently recorded at all electrodes (Michel and Murray, 2012; Skrandies, 1990). Three periods of GFP maxima were identified and results revealed differential modulations of the GFP within these periods as a function of portion size judgment (see Fig. 3). Over the first time interval (105–145 ms), GFP increased incrementally from viewing portions judged as 'too small', 'ideal', and 'too big'. The opposite effect was observed over the late time interval (350–410 ms) as GFP decreased from viewing meal portions judged as 'too small', 'ideal' and 'too big'. In contrast, over the second time interval (230–270 ms), the largest electric field strength was observed in response to portions judged as 'ideal'. Because global GFP maxima are indicative of greatest synchronization of underlying neural sources (Michel and Murray, 2012), not excluding the contemporaneous possibility of differences between conditions (here: responses to selected portion sizes), we conducted neural source estimations over these three time intervals of interest.

4.3. Brain regions showing incremental increase with meal portions

Over the earliest time interval, we observed incremental increases of activity in the insula, MFG and the MTG from portions judged as 'too small', 'ideal' and 'too big'. Over the later time windows, similar modulations in neural activity were observed in the MFG (230–270 ms) and IOG (230–270 ms and 350–410 ms). These findings resemble previous results from EEG and fMRI studies comparing brain responses to pictures of high- versus low-caloric foods (Asmaro and Liotti, 2014; Garcia-Garcia et al., 2013; van der Laan et al., 2011). Changes in the physical size or number of non-food visual stimuli have been shown to induce similar incremental increases in neural activity, yet confined to occipito-temporal and intraparietal regions as observed for instance with numbers/letters (Pinel et al., 2004), cubes (Kornmeier et al., 2011) or faces (Puce et al., 2013). However, our data show food portion size-related increases also in the insula and lateral prefrontal areas. The insula is involved in the detection of stimulus salience and serves to integrate information provided by varying functional systems (Kurth et al., 2010; Menon and Uddin, 2010). Lateral prefrontal regions are usually associated with cognitive influences on sensory processes and reward valuation, such as pricing information on product preferences and choices (Knutson et al., 2007), and control over food intake (see review of Garcia-Garcia et al., 2013). Yet, other studies have also shown that the lateral prefrontal cortex is positively associated with the evaluation of appetitive rewarding goals (Plassmann et al., 2008). Current data thus suggest that responses to food quantity (as reflected by incremental increase in activity in response to portions judged as 'too small', 'ideal' and 'too big') are mediated by brain regions involved in visual analysis and categorization as well as in salience attribution and reward valuation.

4.4. Brain regions showing greatest responsiveness to 'ideal' meal portions

Higher neural activity to 'ideal' meal portion as compared to 'non-ideal' portions was observed during the later stages of responses to meal viewing, with the largest effects at 230–270 ms post-stimulus onset and residual effects at 350–410 ms post-stimulus onset. GFP responses to meal images judged as 'ideal' portion sizes were significantly stronger than those to images judged as 'too small' or 'too big' over the 230–270 ms time interval. In particular, three brain regions showed an 'ideal'-preferring response pattern: the inferior-to-posterior parietal region, the superior temporal gyrus and the mid-posterior cingulate cortex, suggesting that these areas are influenced by cognitive processes in order to weigh adaptive food choices (i.e., 'ideal' portion sizes) against non-adaptive ones.

The temporo-parietal junction is a key region in attentional processes mediating the selection of behaviorally relevant stimuli (Corbetta and Shulman, 2002). In the context of food perception, responses to high-caloric foods in a network of brain regions encompassing the parietal lobule have been for instance associated with weight management success (Murdaugh et al., 2012). The posterior cingulate cortex is a region believed to act as a hub integrating diverse types of information through a dense connectivity pattern with prominent connections to the frontal and limbic regions (Hagemann et al., 2003). This region has been associated with a large number of functions in relation to conscious awareness, cognitive control and adaptive behavior (Leech and Sharp, 2014; Pearson et al., 2011; Vogt and Laureys, 2005). In particular, it is involved in the allocation of attentional resources to relevant stimuli (Leech et al., 2011, 2012; Small et al., 2003a) and in the subjective valuation of a selected option relative to the outcomes of a choice (Kable and Glimcher, 2007). In a task of visual spatial attention, activity in the posterior cingulate was found to be higher for the detection of food cues when participants were hungry compared to being sated (Mohanty et al., 2008). In the same study, this effect was not observed for non-food cues, thus highlighting a role of this region in the motivational modulation of attention to food stimuli based on homeostatic needs. Taken together, a distributed network of brain regions likely mediating the motivational and attentional relevance of complex food cues subserves the elevated responsiveness to 'ideal' as opposed to 'non-ideal' portion sizes.

4.5. Associations between meal portion responses and food intake attitudes

With respect to the second objective of our study, we found several associations between individuals' food intake attitudes (as assessed by the subscales of the TFEQ-R18; Karlsson et al., 2000) and the neural activity patterns in the brain regions discussed above. Neural responses to meal portions judged as 'ideal' or as 'too big' for prospective lunch intake in the middle frontal gyrus (interval 230–270 ms), as well as in the superior parietal lobule and the inferior occipital gyrus (350–410 ms) co-varied with emotional eating scores. A similar correlation was found by Meule et al. (2013) between emotional eating and the amplitude of the late ERP component (350–550 ms). Emotional eating can be defined by the inability to resist emotional cues where eating is triggered by feelings of anxiety, sadness or loneliness. As a consequence, emotional eaters indulge more snack foods rich in energy and have a higher energy intake than other individuals (de Lauzon et al., 2004; Lahteenmaki and Tuorila, 1995). Our current data indicate that the responsiveness to food in lateral prefrontal to occipital regions is influenced by tendencies to overeat in emotionally challenging situations, but further research is certainly needed to investigate such links in more detail. Results of the current study revealed an inverse relationship between neural activity level in the CG and cognitive restraint scores when meal size was judged as 'too big' (see Fig. 7A). Dietary restraint is defined by the cognitive effort made to consciously limit food intake to avoid weight gain or promote weight loss (Karlsson et al., 2000). This self-regulation leads to the selection of low- over high-energy foods and to a lower energy intake in restrained than non-restrained eaters (de Castro, 1995; de Lauzon et al., 2004; Sunday et al., 1992). The motivational value of food modulated by cognitive control for weight management is mediated by a set of brain regions encompassing the posterior cingulate cortex (Harris et al., 2013; Yokum and Stice, 2013). From this, the diminished neural activity level in the CG by cognitive restraint when large portions are presented may reflect a lessened cognitive load engaged for self-regulation by participants with already high dietary restraint to reject those inadequate 'too big' meal portion sizes.

4.6. Conclusion

In conclusion, results of the present study provide the first evidence that the selection of the ideal portion size relies on specific spatio-temporal brain dynamics. We propose that incremental increases in early brain response – in visual, salience and reward-related regions – to portion size increases (from portions judged as 'too small' to 'too big') likely reflect an assessment of the general amount of food available for ingestion (i.e., a quantitative evaluation). Only during a subsequent information processing stage, marked by greatest responsiveness to the portions judged as 'ideal', brain regions involved in attention and adaptive behaviors subserve the choice of a meal size portion assumed by the individual as adequate to reach satiety. Future studies investigating the impact of food intake attitudes and also other factors like hunger state, gender or weight status on the neural dynamics of portion size selection would certainly help gain further insight in the neural processes associated with portion selection and ultimately food intake regulation.

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