Implicit and Explicit Appetitive Outcome-Learning in Obesity

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Table of Contents

List of Abbreviations

BED	-	Binge Eating Disorder
BMI	-	Body Mass Index
DA	-	Dopamine
fMRI	-	functional Magnetic Resonance Imaging
GDP	-	Gross Domestic Product
NAcc	-	Nucleus Accumbens
PE	-	Prediction Error
SEM	-	Standard Error of the Mean
WM	-	Working Memory

List of Figures

Introduction

Obesity: Causes, Consequences and Societal Perspectives

Prevalence rates of obesity in developed and developing societies are rising at a fast pace (World Health Organization, 2018). Through its connections to a plethora of noncommunicable diseases, obesity considerably burdens individuals and society alike.

"Obesity, also called corpulence or fatness, [is an] excessive accumulation of body fat, usually caused by the consumption of more calories than the body can use. The excess calories are then stored as fat, or adipose tissue. Overweight, if moderate, is not necessarily obesity, particularly in muscular or large-boned individuals." (Encyclopaedia Britannica, 2019).

People with obesity commonly suffer from comorbidities including metabolic syndrome, coronary heart disease, diabetes, liver disease, orthopaedic illnesses and affective disorders (A Wirth et al., 2013). Coincidental to obesity rates, Type-2 Diabetes prevalence rates have increased considerably (1980: 4.7%; 2014: 8.5%). Even in young children, higher obesity and diabetes prevalence have been reported (World Health Organization, 2014, 2018). These developments necessitate research into the current rise in obesity rates.

Clinically, overweight and obesity are identified with the help of the body-mass-index (BMI) which is calculated as relative weight for squared height (DIMDI, 2020). A BMI of more than 25 kg/m^2 and more than 30 kg/m^2, respectively define overweight and obesity. Obesity, in turn, is categorized into three subdivisions: Class 1 (30 - 34.9 kg/m^2), class 2 (35 -

39.9 kg/m^2) and class 3 (more than 40 kg/m^2), which represent the current clinical standard (Hauner, Bosy-Westphal, & Müller, 2013).

$$Body\ mass\ index = \frac{weight\ in\ kg}{height\ in\ m^2}$$

Simply put, obesity is the result of an imbalance between energy intake and expenditure (Bischoff et al., 2017) (see Figure 1). Although the aetiology of obesity depends on a multitude of factors, there is a wide consensus on the most prominent causes: Environmental factors, including food consumption, physical activity and lifestyle, have changed dramatically in the past. In societies with a high gross domestic product (GDP), an energy-dense and affluent food-environment (Bellisle, 2014; Gore, Foster, DiLillo, Kirk, & Smith West, 2003) often goes hand

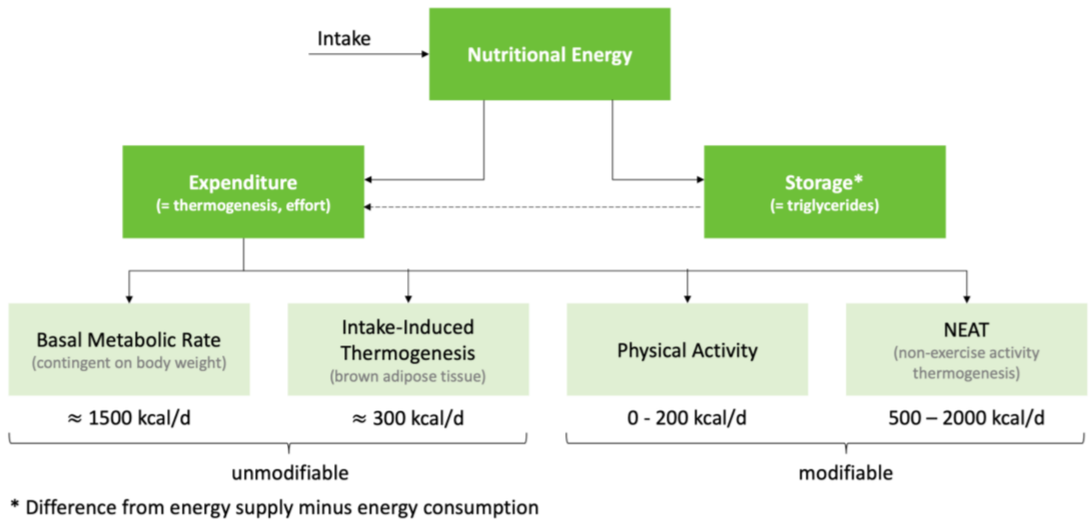

Figure 1 Transformation and storage of energy; translated schematic from *Adipositas – Neue Forschungserkenntnisse und klinische Praxis* (Bischoff et al., 2017)

in hand with modern living conditions that promote a sedentary lifestyle (Hu, Li, Colditz, Willett, & Manson, 2003; Tucker & Bagwell, 1991; Tucker, Bagwell, & Friedman, 1989). Food composition has changed substantially and needs to be addressed in the form of food policy change (Slyper, 2018). Physically inactive forms of employment and free time activities, as well as unhealthy sleeping patterns coinciding with an increased intake of processed foods and beverages are common promoters of obesity (Bischoff et al., 2017). Despite some advances in the past, profound policy changes regulating food producers' impact on environments (e.g. marketing or distribution) have not been facilitated (Sonneville & Rodgers, 2019).

Next to man-made environments, genetic predisposition is another well-researched risk factor

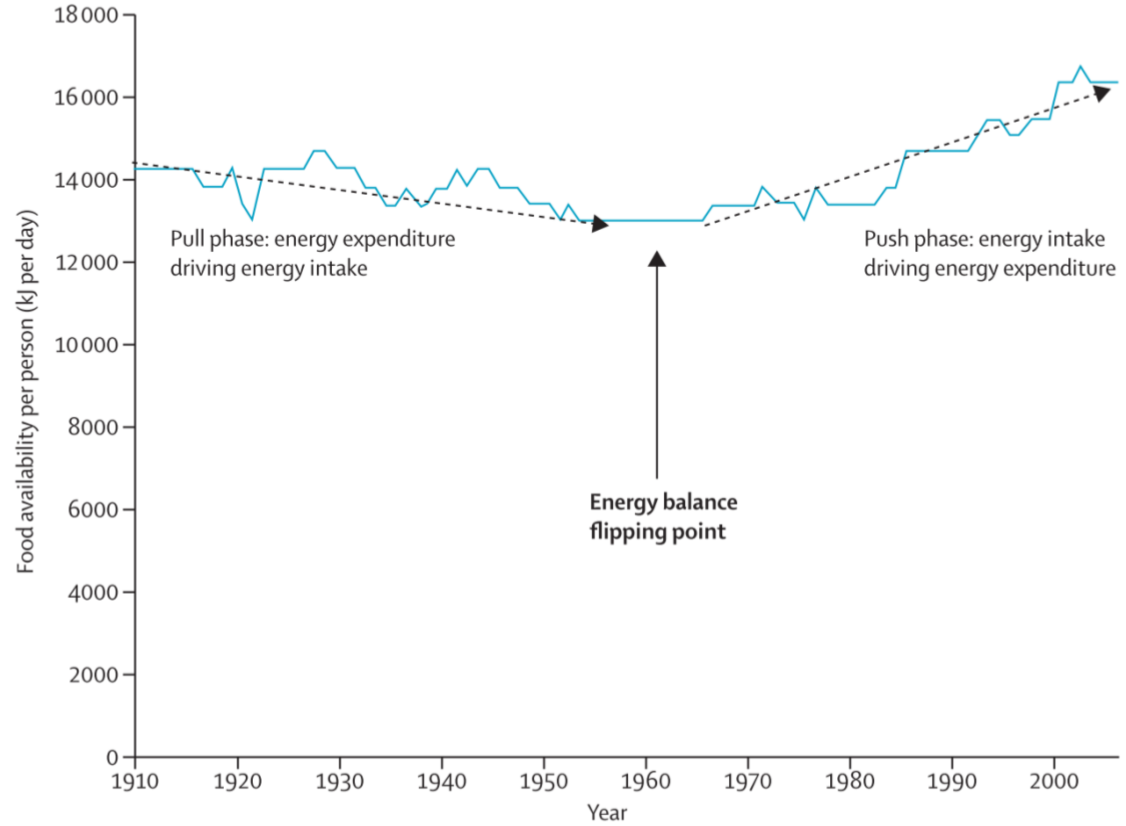

Figure 2 Food availability and energy balance strategies in the USA, 1910-2006; reproduced from *The global obesity pandemic: shaped by global drivers and local environments* (Swinburn et al., 2011)

for obesity. Even though known genetic parameters can only account for 5% of the obesity variation (Blüher et al., 2013), research consistently corroborates a heritability of obesity (Comuzzie & Allison, 1998; Hebebrand, Hinney, Knoll, Volckmar, & Scherag, 2013). Their limits as predictors for obesity are illustrated by the following facts: One being that its rates in people with the same ethnic background vary strongly along the lines of migration (Misra & Ganda, 2007). Another reason against this view being that obesity rates have risen drastically during the last decades – a timeline that makes genetic factors alone a highly unlikely culprit (Bischoff et al., 2017). These developments coincide with changes in food availability, as can be seen from the example of the USA (Swinburn et al., 2011, see Figure 2).

Integrating both approaches into one framework, environmental factors seem to be the strongest predictor for overweight and obesity, while interacting with other effects. When looking into specific societies, genetic factors can account for a large proportion of the obesity risk, identifying groups of individuals that might need specific preventative efforts to counteract their inherited risk for weight gain. It furthermore illustrates how genetic background needs to be considered when formulating the need for therapeutic interventions. Looking at this interaction from a different angle, George Bray states that

"the genetic background loads the gun, but the environment pulls the trigger"
(as cited in Swinburn et al., 2011).

In a similar fashion, other risk factors for obesity might contribute to the aetiology of obesity through interaction with the environment. For example, understanding cognitive pathways that make individuals react to an unhealthy environment might facilitate targeted prevention strategies and potent therapies against the consumption of unhealthy foods. Reasoning from a population-based point of view: Political action for the improvement of a given food system requires knowledge about these pathways – a research field that lies at the heart of market research for large food manufacturers. When entering shops and malls, we are immediately confronted with smells and oversized depictions of palatable foods. The fact that these anthropogenic environments could presently coerce whole societies to stop listening to their bodily signals of hunger or satiety and instead eat as a function of external cues makes research into its mechanisms necessary. As executive functions influence eating-behaviour (Dempsey, Dyehouse, & Schafer, 2011; Rangel, 2013) this dissertation focusses on the relationship between cognitive markers and weight.

Cognitive Performance and Reward Learning in Overweight and Obesity

Previous review articles have reported inconsistent findings on a possible relationship between BMI and executive functions (Boeka & Lokken, 2008; Dye, Boyle, Champ, & Lawton, 2017; Fitzpatrick, Gilbert, & Serpell, 2013; Gunstad, Lhotsky, Wendell, Ferrucci, & Zonderman, 2010; van den Berg, Kloppenborg, Kessels, Kappelle, & Biessels, 2009). Fitzpatrick and colleagues conclude that, while lower performance in decision-making tasks seems to be evident, high BMI alone is unlikely to be the cause for these deficits (Fitzpatrick et al., 2013). It remains to be investigated, how a high BMI and cognitive capacity are connected. Several theories have been proposed, including structural differences in the brain (R. Zhang et al., 2018) as well as BMI-dependent variation in relative tonic and phasic dopamine signalling (Horstmann, Fenske, & Hankir, 2015).

Obesity-Related Structural Changes in the Brain

Structural changes in the brain could account for a link between cognitive dissimilarities and obesity. A study with 1255 participants of a wide age range was able to show an indirect relationship between cognitive markers and higher BMI through lower structural connectivity in many bilateral regions of the brain (R. Zhang et al., 2018). Correspondingly, a recent meta-analysis revealed a possible age-dependent relationship between nucleus accumbens (NAcc) volume and BMI (García-García, Morys, & Dagher, 2019). While larger NAcc volume in young age was positively associated with obesity measures, older age predicted a flip in this relationship. This could be due to the NAcc being a risk factor for overeating and resulting weight gain, while persistent obesity over a lifetime might damage brain structure: Possible causes for this effect include neuroinflammation (Beilharz, Maniam, & Morris, 2016) or elevated blood pressure inflicting structural damage on the brain. Hypertension has been shown to reduce cognitive performance and impair brain structure especially in the elderly (Iadecola et al., 2016). Due to evidence of an association between obesity and cognitive deficits already at a young age, previous literature has concluded that the link between obesity and cognitive function cannot be explained by obesity-related cardiovascular change (Smith, Hay, Campbell, & Trollor, 2011). However, their assumption - that blood-pressure related brain-damage is unlikely in the young - has been recently invalidated by several studies showing that even young participants with subclinical blood pressure elevation show signs of brain injury, including differential white matter diffusivity as well as lower grey matter and whole brain volumes (Lane et al., 2019; Maillard et al., 2016; Schaare et al., 2019). Whether the association of hypertension and brain structure and the association of obesity and impaired executive function (Burger & Stice, 2011; Kroemer & Small, 2016) are interrelated, needs to be investigated further in future research.

Obesity-Related Differences in Tonic vs. Phasic Dopamine Levels

Another pathway has been proposed by Horstmann and colleagues (Horstmann, Fenske, et al., 2015). They argue that seemingly conflicting data on dopamine (DA) receptor availability in obesity can be reinterpreted by way of divergent DA tone. Their theoretical framework proposes that weight-dependent DA binding potential follows an inverted u-shape with lower DA tone (i.e. higher binding potential) in people with overweight and higher dopaminergic tone (i.e. lower binding potential) in people with obesity compared to the healthy BMI range (see Figure 3). Transferring this notion into the cognitive domain, it predicts differential learning from reward and punishment: Changes in tonic DA levels can in- or decrease the relative signal strength of phasic drops or rises during learning tasks. A clear picture of the underlying dynamics requires the inclusion of a wider BMI range, with continuous BMI measures comprising overweight.

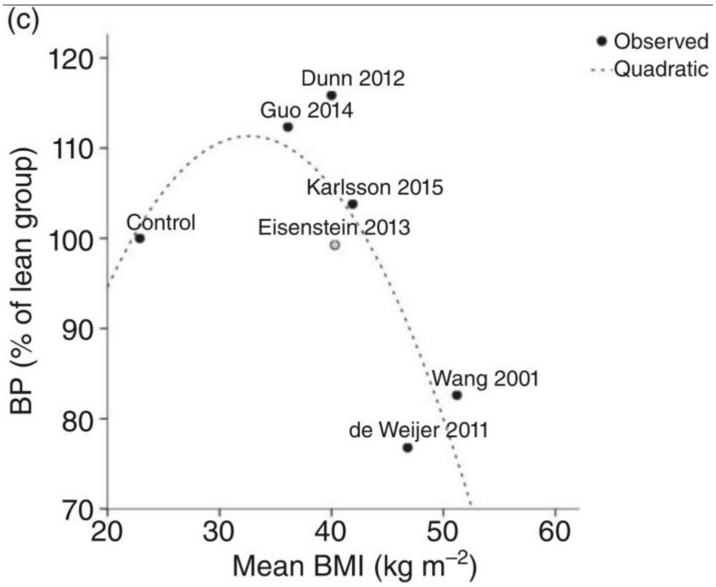

Figure 3 Relationship between mean BMI of the obese group on the relative dopaminergic binding potential suggests divergent tonic dopamine levels; reproduced from *Argument for a non-linear relationship between severity of human obesity and dopaminergic tone* (Horstmann, Fenske et al., 2015).

Cognitive Parameters in Obesity Research

Weight-specific differences in cognitive functions like working memory (WM) or decision making have been scrutinized in several studies. WM describes the ability to retain relevant information until a decision making process has been completed (Gross, 2005). It has been shown to be impaired in people with overweight and obesity (Coppin, Nolan-Poupart, Jones-Gotman, & Small, 2014; Stingl et al., 2012; van den Berg et al., 2009). A prominent theory regarding high BMI and maladaptive reward learning purports that, while reward anticipation gains increased behavioural relevance in people with obesity, reward receipt is less strongly signalled in the brain (Kroemer & Small, 2016). This could lead to a higher motivation to engage in food intake behaviours when palatability is high and a decreased ability to curb food intake behaviour when satiety is reached. Another aspect of this would be that, as reward and punishment are less strongly signalled in the brain, respective outcomes might exhibit an attenuated behavioural effectiveness. The effect of food as a natural reward can be studied with the help of reward and punishment learning paradigms. This approach allows insight into food intake as goal-directed, dynamic behaviour. However, the standardization of paradigms in terms of choosing reward and punishment stimuli is challenging. Possible *rewards* include positive outcomes as well as the omission of negative ones. Likewise, omission of positive outcomes can be used as *punishment* in much the same way as motivationally negative stimuli. This is illustrated when looking at their effect in terms of prediction errors (PEs): Sutton and Barto describe PEs in reward learning as

"*discrepancies between the expected and the received reward signal, being positive when the reward signal is greater than expected, and negative otherwise*" (Sutton & Barto, 2018)

Schultz and colleagues pioneeringly showed that PEs can be seen in terms of dips and rises in dopamine signalling (Schultz et al., 1997, see Figure 4). Thus, neuroscientific research into differential reinforcement processing needs to consider how reward and punishment act as positive and negative reinforcers on the individual. This is further complicated when looking at different reward and punishment domains. In the food domain, there have been reports of both impaired learning from reward receipt (Janssen et al., 2017), as well as lower effectiveness of omission of reward (Horstmann, Dietrich, et al., 2015; Meyer, Risbrough, Liang, & Boutelle, 2015) in people with obesity. When using monetary rewards, obesity has been connected with an attenuated effect of negative outcomes in learning tasks (Horstmann et al., 2011; Kube et al., 2017; Mathar et al., 2017). Many studies have shown less behavioural effectiveness of food or monetary reinforcers in people with obesity (Coppin et al., 2014; Kube et al., 2017; Meyer et al., 2015; van den Akker, Schyns, & Jansen, 2017). A study utilizing monetary and social reinforcers showed that women with obesity showed blunted cardiac responses during social compared to monetary outcome phases (Kube et al., 2016). Furthermore, this effect was especially strong for social punishment: Obese women who reported previous stigma experience seemed to exhibit a decreased salience and affective response toward negative social stimuli, possibly reflecting a defensive attitude to social punishments that are deemed unfair.

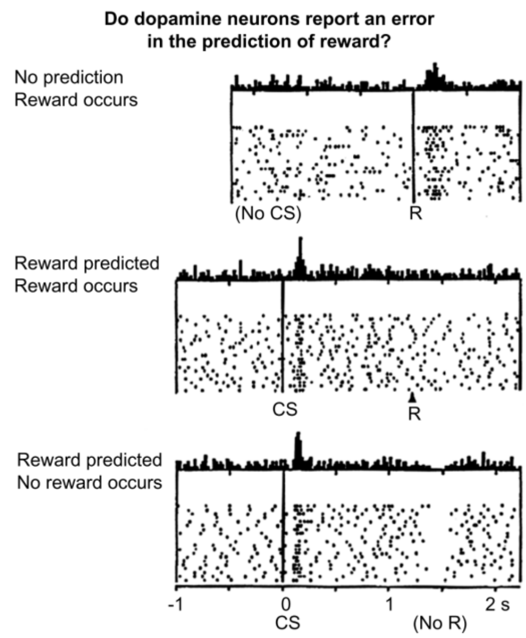

Figure 4 Relationship between the previous prediction of a reward and the firing rate of a dopaminergic neuron after a reward was presented and omitted respectively; reproduced from *A Neural Substrate of Prediction and Reward* (Schultz et al., 1997).

Reinforcement learning bears the potential to explain unhealthy eating in terms of maladaptive behaviour. An example of this is the reversal learning paradigm that has been used in various ways to test for behavioural adaption in the reinforcement context (Cools, Clark, Owen, & Robbins, 2002). Its application in obesity research has provided insight into possible reasons for inflexible eating patterns obstructing goal-directed health behaviours (van den Akker et al., 2017; Z. Zhang, Manson, Schiller, & Levy, 2014).

Research Questions

The two included studies were designed to offer insight into the basic mechanism through which our environment impacts food choices. Significant differences between people with healthy weight compared to people with overweight or obesity would identify environmental forces, like e.g. food advertising, as a promising target for preventive policy, especially in rich societies with omnipresent cues for, and an overabundance of, palatable foods.

Study 1 – Active and Passive Reward Learning in Obesity

In order to investigate how our environment shapes eating behaviour, study 1 was aimed at finding the proposed link between BMI and bias formation between visual cues and positive food outcomes. Previous research has shown that implicit visual cues in our environment can impact portion size and food composition (Berridge, 2009; Brignell, Griffiths, Bradley, & Mogg, 2009). As Boyd A. Swinburn says:

"The obvious possible drivers of the epidemic are in the food system: The increased supply of cheap, palatable, energy-dense foods; improved distribution systems to make food much more accessible and convenient; and more persuasive and pervasive food marketing"
(Swinburn et al., 2011).

How the affective load – in terms of reward or punishment during the training phase – and motivational value of these cues are learned and how they are flexibly redefined when associations change, was the subject of a paper by Zhang and colleagues that garnered some media attention. Their study showed that particularly women with obesity struggle with behavioural adjustment to previously rewarded food cues when rewards are omitted (Z. Zhang et al., 2014). However, their paper proposed that this was due to an inability to correctly integrate new knowledge in the presence of distracting food cues (Z. Zhang et al., 2014) – an interpretation that cannot be completely absolved from the suspicion of prejudice. Thus, in order to further investigate the reported interaction between obesity status and sex in basic association learning, we decided to replicate their paradigm. In addition to comparing people with and without obesity, we also included people in the range of overweight. Previous research has even indicated more distinctive behaviour in people with overweight than in obese populations – compared to people within the healthy range (Coppin et al., 2014; Davis, Strachan, & Berkson, 2004; Dietrich, Federbusch, Grellmann, Villringer, & Horstmann, 2014). As in Zhang et al., we aimed to compare learning from monetary and food rewards, which were additionally scaled to be of similar value for each participant. This was meant to achieve equal motivation to obtain both rewards.

Study 2 – Pavlovian-to-Instrumental Transfer in Obesity

Identifying the pathway of implicit environmental bias on eating behaviour was the aim of the second study. This was done following the reasoning that pervasive food marketing could drive eating behaviour with an effectiveness that is nearing homeostatic need. A stronger bias of rewarding cues on free choices in people with obesity would indicate that an affluent food environment might impact their eating behaviour more directly than people in the normal BMI range. Accordingly, we tested whether appetitive food cues have the potential to bias choices between two stimuli in a free-choice task. To this end, we modified a previously used Pavlovian-to-Instrumental Transfer (PIT) paradigm by Prévost and colleagues (Prévost, Liljeholm, Tyszka, & O'Doherty, 2012). PIT is measured as two different components: *Specific PIT* describes the ability of a pavlovian cue to bias behaviour in a way that an individual performs instrumental actions that can earn the same reward as the presented cue. *General PIT*, on the other hand, describes how pavlovian cues – that are positively associated – can bias an individual to perform instrumental actions that also earn positive rewards. Both effects could be theorized as mechanisms of environmentally biased food-seeking behaviour. We adapted the previously used PIT paradigm by including direct food rewards with the help of a gustometer: Rewards consisted of fruit juices which were placed on the participants' tongues in a direct temporal relationship with the paradigm on screen.

Experimental Work

Study 1 – Active and Passive Reward Learning in Obesity

Keeping track of promised rewards:

Obesity predicts enhanced flexibility when learning from observation

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Keeping track of promised rewards: Obesity predicts enhanced flexibility when learning from observation

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ABSTRACT

Goal-directed behaviour depends on successful association of environmental cues with reward or punishment. Obesity has been linked to diminished learning success in this domain. In contrast, here we demonstrate superior learning in obese participants independent of reward type. We tested association learning in 85 participants with a wide body-mass-index (BMI) range (lean to obese) in four probabilistic reversal-learning experiments. Experiments differed regarding learning mode (active and passive) and reward stimulus (pictures of snack food and money). Food and monetary rewards were adjusted regarding their motivational value in order to allow a direct comparison of related learning characteristics. Our results reveal enhanced associative learning in obese compared to normal-weight participants – reward-independently for expectancy updating and specifically for food-rewards for initial acquisition. When comparing the influence of continuous BMI in active and passive learning, food reward was associated with opposite effects of BMI on performance. Our data indicate generalized, weight-dependent differences in essential reward-learning, though particularly for food reward. We thereby argue that flexible updating of reward-related information may in fact be enhanced in people with obesity – and, thus, possibly promote unhealthy food choices in modern society.

1. Introduction

Obesity is a multi-faceted condition that is connected with various factors such as lifestyle, genetics and food intake (Choquet & Meyre, 2011; Hankinson et al., 2010; Tucker & Bagwell, 1991; Tucker, Bagwell, & Friedman, 1989). Contributing factors to development and maintenance of human obesity include over-consumption of highly rewarding food.

Affected individuals often struggle to behaviourally adhere to their dietary goals. Converging evidence implies that this decreased goal-directedness is caused by impairments in behavioural adaptation. For instance, obese women were found to prefer salient immediate monetary rewards despite negative long-term consequences (Horstmann et al., 2011). Similarly, in a food context, people with obesity have repeatedly been shown to be less sensitive to reward devaluation (Horstmann, Dietrich, et al., 2015; Janssen et al., 2017).

Diminished behavioural adaptation has been linked to impairments in reinforcement learning, irrespective of reward type (Coppin, Nolan-Poupart, Jones-Gotman, & Small, 2014; Kube et al., 2017; Meyer, Risbrough, Liang, & Boutelle, 2015; van den Akker, Schyns, & Jansen, 2017). For instance, Coppin and colleagues (Coppin et al., 2014) found that obesity predicted a diminished preference for rewarded over negatively associated patterns in two cue-conditioning paradigms using monetary and food reinforcement. This finding has recently been replicated in differential appetitive conditioning using chocolate as reinforcement (van den Akker et al., 2017). Other studies further highlight that obesity may be characterized by a failure to learn from negative action outcomes in monetary (Kube et al., 2017; Mathar, Neumann, Villringer, & Horstmann, 2017) as well as food reinforcement learning tasks (Meyer et al., 2015). Interestingly, people with obesity exhibited increased conditioned responses during acquisition – indicating that a reduced bias extinction cannot be solely explained by generally reduced association learning (Meyer et al., 2015). Importantly, other factors such as diminished working memory capacity most likely contribute to this alteration in reinforcement-based learning in individuals with obesity (Coppin et al., 2014).

In sum, these studies suggest generalized, obesity-related alterations in reinforcement-based learning across different types of reinforcers.

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However, recent research questions this generalized effect. Using an observational reversal learning task with one rewarded and one unrewarded visual stimulus, Zhang and colleagues (Zhang, Manson, Schiller, & Levy, 2014) showed that female obese participants exhibited impaired association learning from rewards exclusively in the food condition. However, it should be noted that their food and monetary stimuli strongly differed regarding objective monetary value. Further, participants learned to attribute reward by passive observation, similar to paradigms used in fear-conditioning studies (Schiller, Levy, Niv, LeDoux, & Phelps, 2008), while most studies in the field have employed task designs requiring active choice behaviour (Coppin et al., 2014; Horstmann et al., 2011; Kube et al., 2017). This suggests additional mechanisms that could account for seemingly contradictory findings.

One important difference between active and passive learning is the amount of positive and negative prediction errors (PE) following contingency changes. A negative PE is the response to unexpected punishment or reward omission after a conditioned stimulus (CS), while a positive PE describes the response to unexpected punishment omission or reward. Observational paradigms signal reversals by positive PEs, as participants obtain unexpected reward after the new CS^+ (the previous CS^-). Reward presentation in active learning tasks depends on the participants' choice. They are unlikely to deviate from previously successful behaviour – and thus discover the contingency change – until they become cognizant of the lack of reward after the CS^-. Thus, active learning paradigms arguably rely more on learning from negative PEs. There is a fair amount of research on the influence of dopamine in reversal learning (Cools et al., 2009; Cools, Altamirano, & D'Esposito, 2006; Smittenaar et al., 2012). Current research suggests dopaminergic signalling as a possible mechanism for behavioural alterations in obesity (Horstmann, Fenske, & Hankir, 2015). Notably, learning from negative PEs is argued to be more vulnerable in this context (Mathar, Neumann, et al., 2017). Here, we aim to compare the influence of weight-status on learning performance across different learning modes (active, passive) and reinforcement stimuli (food, money) using a within-subject design. Thus, we aim to bridge the gap between seemingly contradictory findings on association learning success in obesity.

Specifically, we tested association learning in four reversal learning experiments manipulating learning mode and reward category. First, we investigated the domain-specificity of learning alterations in obesity. To this end, we compared participants with and without obesity in passive learning tasks adapted from Zhang and colleagues (Zhang et al., 2014). Secondly, we analysed the combined influence of body-mass-index (BMI), learning mode and reinforcement stimuli by comparing performance in all four tasks. Further, due to their likely impact on learning success (Coppin et al., 2014; Zhang et al., 2014), we investigated the effect of working memory capacity and individual differences in impulsivity and disinhibited eating. In addition to comparing participants with and without obesity, we included individuals with overweight, as their learning characteristics seem to be more distinct from lean populations than those found in obesity (Coppin et al., 2014; Davis, Strachan, & Berkson, 2004; Dietrich, Federbusch, Grellmann, Villringer, & Horstmann, 2014; Lehner, Balsters, Bürgler, Hare, & Wenderoth, 2017). We hypothesize overweight and obese participants to exhibit impaired reward-based learning compared to lean participants. Since possible dopaminergic changes in obesity would impair learning from negative PEs, which arguably promote active learning tasks, we expect pronounced group differences there. Given that we ensured comparable value of monetary and food rewards to the participants, we predict learning performance to be similar across reward types.

2. Methods

2.1. Participants

97 healthy, young participants (44 women) with a wide BMI range (19.23–51.1 kg/m^2), matching in age and education, were recruited from a local participant database. An initial telephone screening evaluated inclusion and exclusion criteria (see Supplementary Information for details). The final sample of 85 participants included all individuals who completed at least one reversal in the behavioural test.

In addition to the main experiments, all participants completed a digit span (DS) working memory task from the Wechsler Memory Scale – Revised (WMS-R; Härting et al., 2000) as well as several questionnaires to evaluate personality, clinical, and eating behaviour characteristics, encompassing the German versions of the UPPS Impulsive Behaviour Scale (Schmidt, Gay, D'Acremont, & Van der Linden, 2008), Barrat Impulsiveness Scale – Short Form (BIS-15; Meule, Vögele, & Kübler, 2011), the Behavioural Inhibition System and Behavioural Activation System Scales (BIS/BAS; Strobel, Beauducel, Debener, & Brocke, 2001), the Three Factor Eating Questionnaire (TFEQ; Pudel & Westenhöfer, 1989), Yale Food Addiction Scale (YFAS; Meule, Vögele, & Kübler, 2012), as well as the Beck Depression Inventory (BDI; Hautzinger, 2006). Details are presented in Table 1.

All participants gave written informed consent prior to their participation and received a fixed reimbursement of 7€/hour with an average study duration of 2 h as well as an additional snack and monetary bonus depending on task performance. The study was carried out in accordance with the Declaration of Helsinki and was approved by the local ethics committee of the University of Leipzig.

2.2. Willingness-to-pay task

To align subjective values of food and monetary rewards used in the learning tasks, participants completed a willingness-to-pay auction immediately before the learning experiments. Here, they bid money on the opportunity to eat snack food items (See Supplementary Information for details). The food pictures with the highest average bid and its rounded monetary equivalent were subsequently used as task rewards. This resulted in individualized monetary and food rewards per participant with comparable incentive value.

2.3. Reversal learning paradigms

All participants performed four versions of a probabilistic reversal learning task in a within-subject design. The tasks were presented in pseudorandomized order and varied in response type (active, passive) and reward category (snack food, money). Trial structures and timings are displayed in Fig. 1.

In each task, participants were presented with a red and a blue square, the position of which was counterbalanced throughout the task. One colour was associated with a reward in 50% of the trials (CS^+), while the other was never followed by reward (CS^-). This reward schedule was chosen so that participants would be rewarded sufficiently often to ensure stable contingencies for CS^+ as well as CS^-. Repeatedly during the task, the stimulus-reward contingencies reversed: The former CS^- was now rewarded (new CS^+), while the previous CS^+ was no longer followed by reward (new CS^-). Participants were instructed that one stimulus would occasionally result in reward, while the other stimulus would never be rewarded and that these associations would change sporadically throughout the experiment. Thus, if participants recognized this rule change, they should adjust their responses accordingly. Rule changes were not signalled and occurred after the participant had responded correctly in four to six consecutive trials (pseudorandomized learning criterion). Each task continued until the participant achieved 11 successful rule changes (reversals) or after 40 consecutive trials without any reversals.

Two response types were employed: In the *passive learning tasks*, participants made predictions about stimulus-reward associations. Specifically, each trial required the participant to estimate the likelihood that one preselected coloured square would lead to a reward on a 9-point Likert scale ranging from −4 (very unlikely) to 0 (don't know)

Table 1
Sample characteristics.

Sample characteristics							
Variable		Lean		Overweight		Obese	
		Female	Male	Female	Male	Female	Male
N		15	14[a]	14	14	15[a]	15
Age[1]		24.07 ± 3.35	26.00 ± 3.72	27.14 ± 4.35	26.43 ± 3.03	25.93 ± 3.85	27.40 ± 3.72
Years of education		12.36 ± 0.84	12.43 ± 0.65	12.50 ± 0.52	12.29 ± 0.91	12.00 ± 1.36	12.80 ± 0.94
Anthropometrics							
BMI[2]		22.74 ± 1.72	22.83 ± 1.65	26.85 ± 1.14	26.79 ± 0.96	36.04 ± 6.66	33.73 ± 4.20
WHR[2,3]		0.76 ± 0.19	0.90 ± 0.42	0.82 ± 0.53	0.91 ± 0.33	0.90 ± 0.26	0.95 ± 0.05
Working Memory							
DS Forward		9.93 ± 2.28	9.86 ± 2.48	10.14 ± 2.32	10.21 ± 2.05	10.27 ± 1.98	10.73 ± 2.09
DS Backward		8.33 ± 1.80	7.43 ± 2.31	8.14 ± 2.41	7.64 ± 1.55	7.53 ± 1.60	7.80 ± 2.81
Individual Characteristics							
BISBAS	BIS[4]	20.07 ± 3.58	18.50 ± 3.67	21.71 ± 3.07	18.36 ± 3.18	20.40 ± 3.48	17.40 ± 2.77
	BAS[4]	42.87 ± 4.66	39.79 ± 3.87	41.21 ± 4.02	41.43 ± 4.20	41.87 ± 3.27	39.33 ± 4.67
BIS15	non-plan	12.80 ± 1.21	13.43 ± 1.56	13.36 ± 1.34	13.14 ± 1.46	13.13 ± 1.36	13.47 ± 1.85
	motor	12.00 ± 2.10	11.93 ± 1.59	12.14 ± 2.03	11.64 ± 1.95	12.60 ± 2.03	11.33 ± 2.44
	attention[1]	10.40 ± 1.24	10.00 ± 2.18	10.57 ± 2.59	9.86 ± 1.61	11.33 ± 2.55	10.80 ± 1.66
TFEQ	Dis[4,5]	6.80 ± 1.86	3.93 ± 2.37	8.93 ± 3.45	4.43 ± 1.28	6.87 ± 3.29	6.53 ± 3.29
	Restraint[1]	7.73 ± 4.70	4.14 ± 3.01	6.29 ± 5.01	5.71 ± 4.30	8.67 ± 5.55	7.87 ± 3.74
	Hunger	6.13 ± 3.38	6.07 ± 3.08	6.00 ± 2.94	5.29 ± 3.36	5.40 ± 3.56	5.93 ± 4.04
BDI		5.00 ± 4.05	4.29 ± 3.91	4.57 ± 4.57	4.50 ± 4.90	5.07 ± 4.38	5.13 ± 5.44
Hunger Levels		2.87 ± 1.73	4.07 ± 1.94	3.93 ± 2.34	4.07 ± 1.98	3.67 ± 2.23	4.07 ± 1.87
Willingness-to-pay							
Monetary value		4.48 ± 1.11	4.20 ± 1.40	4.47 ± 0.75	4.61 ± 0.82	4.64 ± 1.01	4.55 ± 1.04
Sweet food item		9	13	13	11	10	11

Years of education = years of school education, BMI = body mass index in kg/m^2, WHR = waist-to-hip-ratio, DS = digit span, BIS/BAS = Behavioural Inhibition/ Behavioural Activation Scale, BIS = Subscale Behavioural Inhibition, BAS = Subscale Behavioural Activation, BIS-15 = Barrat Impulsiveness Scale – Short Form, non-plan = Subscale non-planning, motor = Subscale motor impulsivity, attention = Subscale Attentional Impulsivity, TFEQ = Three Factor Eating Questionnaire, Dis = Subscale Disinhibition, Restraint = Subscale Restraint, Hunger = Subscale Hunger, BDI = Beck Depression Inventory, Sweet food item = # of participants who showed the highest willingness-to-pay for a sweet food item.[1] Showed significant positive correlations with BMI across all participants. [2] A univariate ANOVA revealed a significant main effect of BMI group.[3] A univariate ANOVA revealed significantly higher scores in male than female participants.[4] A univariate ANOVA revealed significantly higher scores in female than male participants.[5] A univariate ANOVA revealed a significant interaction of BMI group (lean, obese) and Sex, suggesting significantly higher TFEQ Disinhibition scores in obese than lean males, but not significant differences between obese and lean females.

[a] Please note, that one additional participant from this group was excluded from the analysis of active vs. passive learning paradigms due to no reversals in an active learning task. Values represent mean ± SD. Significant effects are defined as $p < .05$.

to +4 (very likely). Thereafter, either reward was presented or a fixation cross signalled no reward in the current trial. Participants were explicitly instructed that reward presentations depended solely on the highlighted stimulus and were independent of performance. Reversals occurred after the learning criterion was reached, that is, participants stably gave positive reward predictions for the current CS$^+$ and negative predictions for the current CS$^-$. Following each reversal, the new CS$^+$ was deterministically highlighted in the first trial and resulted in reward to facilitate reversal detection.

In the *active choice learning tasks*, participants were instructed to actively select the coloured square that was associated with a reward (CS$^+$). After choice of one colour, either reward was presented or a fixation cross signalled no reward in the current trial. Reversals occurred after stable choice of the CS$^+$ for four to six trials (pseudorandomized learning criterion). The first selection of the new CS$^+$ after a reversal was always rewarded to facilitate reversal detection.

Participants played each task twice – employing pictures of either food or the corresponding monetary rewards respectively. Before the start of the experiment, they performed 20 practice trials per response mode to familiarize with trial structure and probabilistic nature of the task. In order to keep participants motivated throughout the experiment, they were informed that they would receive a bonus payment at the end of the experiment depending on task accuracy (For more details, see Supplementary Information).

2.4. Learning indices

In a first step, we attempted to replicate findings of food-specific learning deficits in individuals with obesity reported by Zhang et al. (Zhang et al., 2014). Leaning on their proposed indices, we derived two learning measures from the reward expectancy ratings of the *passive learning tasks* for participants from the lean and obese groups only (n = 59):

ACQ (acquisition score) signals the difference between the mean CS$^+$ and CS$^-$ reward expectancy ratings during the initial acquisition phase. Thus, positive values indicate that participants correctly expressed higher reward expectancy ratings for the CS$^+$ than CS$^-$, while zero or negative *ACQ* values suggest that participants had learned no or wrong stimulus-reward-associations, respectively.

$$ACQ = CS^{+}_{Acq} - CS^{-}_{Acq}$$

ΔRating measures the average difference in reward expectancy ratings between phases in which a stimulus was CS$^+$ to phases in which the same stimulus served as CS$^-$. Consequently, positive values indicate higher reward expectancy towards CS$^+$ than CS$^-$ and thus, a better learning performance:

$$\Delta Rating = CS^{+} - CS^{-}$$

Please note that for these indices, we included all trials of the initial acquisition (*ACQ*) and the first five reversal stages (*ΔRating*), while Zhang et al. (Zhang et al., 2014) focused on the late trials during acquisition and one reversal stage, only. This was done to ensure a sufficient reliability of learning indices while excluding over-training in the last reversal stages.

While these indices summarized the evaluation of CS$^+$ and CS$^-$ over subsequent trials, we further derived an index that is more directly

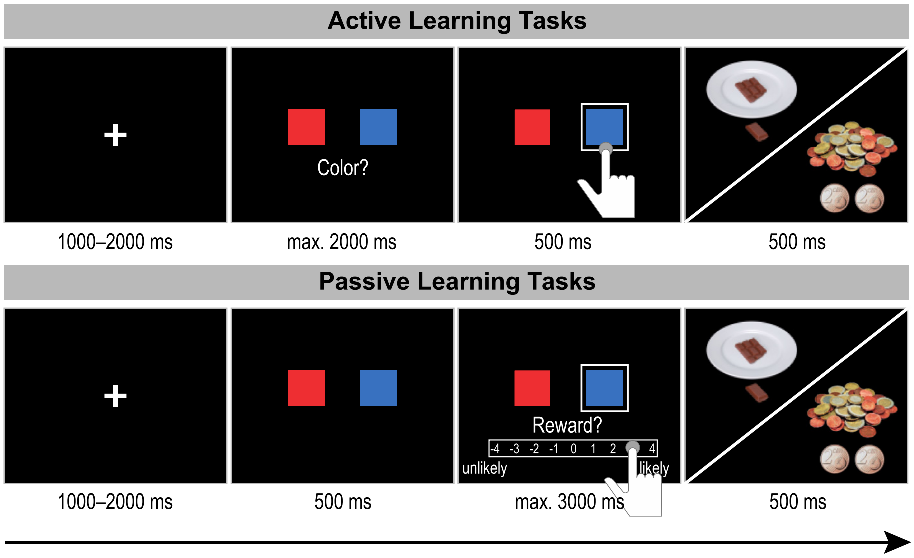

Fig. 1. *Task description.* Trial structure and timing of the active and passive reversal learning tasks. Two separate versions of each type were administered that either employed pictures of monetary or food rewards.

related to reversal learning:

Rev_rating expresses the difference in mean reward expectancy ratings between CS^+ and CS^- during the second post-reversal trial. Deterministically, the previous trial presented the new CS^+ followed by reward. Consequently, behaviour in the second post-reversal trial reflects immediate learning from positive PEs, while *ΔRating* represents an average over a whole phase of the experiment. Positive values indicate higher reward expectancy towards the new CS^+ than the new CS^- after reversal and thus reflect better learning.

$$rev\_rating = CS^{+}_{rev\_rating} - CS^{-}_{rev\_rating}$$

This index was calculated for a sub-sample of 41 participants (25 obese), for which both CS^+ and CS^- ratings were available from second post-reversal trials. Due to the pseudorandomized trial order, all other participants saw only CS^+ or CS^- in the second post-reversal trials across the experiment.

In addition, we derived measures to directly compare active and passive learning in all 85 participants during the acquisition and first five reversal stages. Specifically, we evaluated:

Accuracy as the percentage of correct responses, i.e. trials in which participants chose the current CS^+ (active) or gave correct reward expectancy ratings for the current CS^+ and CS^- (passive).

Trials-to-reversal as the average number of trials needed to reach the learning criterion and initiate a reversal (active and passive).

Reversal errors as the average number of trials after reversals until participants chose the new CS^+ for the first time (active) or gave correct reward expectancy ratings for the new CS^+ and the new CS^- (passive, See Supplementary Information for details).

2.5. Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

3. Results

3.1. Willingness-to-pay

Lean and obese participants did not significantly differ in preferred food items and corresponding monetary values, as indicated by the results of the willingness-to-pay auction. Similarly, across all participants there was no significant influence of continuous BMI on chosen food items and willingness-to-pay (see Supplementary Information for details).

3.2. Passive reversal learning

We first aimed to replicate findings of compromised learning performance for food, but not monetary rewards in women with obesity (Zhang et al., 2014). For this purpose, we focused on the passive learning experiments that measure the capacity to acquire and adapt reward expectations from observation.

ACQ and *ΔRating* were included in a repeated-measures MANCOVA employing the within-subject factor Reward Category (food, money) and the between-subject factors BMI group (lean, obese), Sex (female, male), and Age. We found a main effect of BMI group [Pillai's trace: $V = .179$, $F(2,53) = 5.785$, $p = .005$] that originated from significantly altered flexible updating scores [*ACQ*: $F(1,54) = 1.717$, $p = .196$, $\eta_p^2 = 0.031$, *ΔRating:* $F(1,54) = 11.639$, $p = .001$, $\eta_p^2 = 0.177$]. A Reward Category × BMI group interaction [$V = 0.119$, $F(2,53) = 3.594$, $p = .034$, Fig. 2] was present in both univariate follow-up analyses for *ACQ* [$F(1,54) = 5.119$, $p = .028$, $\eta_p^2 = 0.087$] and *ΔRating* [$F(1,54) = 4.346$, $p = .033$, $\eta_p^2 = 0.082$]. In contrast to Zhang et al. (Zhang et al., 2014), for *ACQ*, individuals with obesity showed a higher performance than lean participants in the food [$p = .024$], but not monetary condition [$p = .644$]. For *ΔRating*, individuals with obesity showed a reward-independent, higher performance than lean participants [food: $p < .001$, money: $p = .014$]. The interaction was thus most likely driven by the fact that obese participants had a numerically higher performance in the food [$M = 2.99$, $SD = 1.73$] than monetary condition [$M = 2.66$, $SD = 1.96$, $p = .151$], while lean participants exhibited the reversed pattern [food: $M = 1.08$, $SD = 2.54$; money: $M = 1.45$, $SD = 2.27$, $p = .099$]. We found no evidence for a modulation of learning performance by Sex [main effect of Sex: $V = 0.049$, $F(2,53) = 0.496$, $p = .611$; interaction of Sex × BMI group: $V = 0.049$, $F(2,53) = 1.374$, $p = .262$; interaction of Sex × BMI group × Reward Category: $V = 0.019$, $F(2,53) = 0.507$, $p = .605$]. This suggests that obesity-related differences in learning are independent of sex.

For a graph of performance in the passive learning tasks including overweight participants see Supplementary Information (Supplementary Fig. 1).

To examine immediate reward-related learning performance after reversal, we evaluated immediate reversal ratings using a repeated

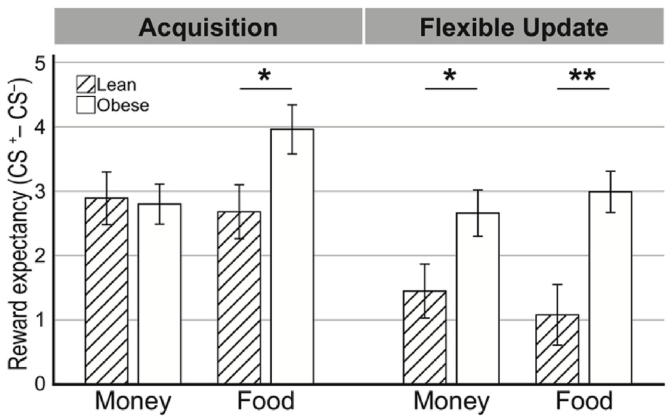

Fig. 2. *Contingency acquisition and update.* Comparison of learning performance between individuals with obesity and lean control participants in the passive reversal learning tasks. In the passive food task, individuals with obesity compared to lean control participants exhibited a higher differentiation in reward expectancy for CS^+ compared to CS^- during initial acquisition (*Acquisition*). This was not present in the passive monetary task. Furthermore, they showed stronger differences in reward expectancy between phases in which a stimulus served as CS^+ and phases in which the same stimulus served as CS^- (*Flexible Update)* in both tasks. Error bars represent the standard error of the mean. *p < .05; **p < .001.

measures ANOVA with the same factors employed in the previous analysis. We found a significant main effect of BMI group [$F(1,36) = 8.267$, $p = .007$, $\eta_p^2 = 0.187$, Fig. 3], showing a stronger differentiation in reward expectancy ratings towards CS^+ vs. CS^- in individuals with obesity. However, there was no evidence for differential effects of reward [main effect of Reward Category: $V = 0.005$, $F(1,36) = 0.171$, $p = .682$; interaction of Reward Category × BMI group: $V = 0.001$, $F(1,36) = 0.041$, $p = .842$]. This suggests a generally higher immediate reversal learning performance in obese compared to lean participants. Again, performance was not modulated by Sex [main effect of Sex: $F(1,36) = 0.087$, $p = .769$; interaction of Sex × BMI group: $F(1,36) = 0.285$, $p = .596$; interaction of Sex × BMI group × Reward Category: $V = 0.010$, $F(1,36) = 0.348$, $p = .559$].

3.3. Active vs. passive reversal learning

The analysis of learning behaviour in the passive learning tasks served to compare results with previous studies. In addition, we aimed to investigate weight-related influences on learning performance across different response types (active vs. passive) and a wider range of BMI (including overweight).

We thus subjected *accuracy*, *trials-to-reversal* as well as *reversal errors* in the active and passive learning tasks to a repeated measures MANCOVA including the within-subject factors Response Type (active, passive) and Reward Category (food, money), the between-subject factor Sex as well as the mean-centred covariates BMI and Age. We found a multivariate interaction of BMI × Response Type × Reward Category [Pillai's trace: $V = 0.198$, $F(3,78) = 6.416$, $p = .001$, $\eta_p^2 = 0.198$]. The follow-up inspection of the univariate effects revealed that this was driven by *accuracy* [$F(1,81) = 17.864$, $p < .001$]. To further disentangle the interaction, we split our analysis by BMI group (lean, overweight, obese) and separately evaluated the influence of Response Type (active, passive), Reward Category (food, money), and Age on *accuracy* in these groups. We found a significant interaction effect of Response Type × Reward Category in lean [$F(1,25) = 4.531$, $p = .043$, $\eta_p^2 = 0.153$] as well as obese individuals [$F(1,26) = 5.606$, $p = .026$, $\eta_p^2 = 0.177$]. Participants with obesity exhibited a higher accuracy in the passive than active food learning task [$p < .001$], while lean participants showed the reversed pattern [$p = .020$, Fig. 4]. Neither group exhibited differences in the monetary learning tasks.

Additional analysis of Response Times (RT) revealed significantly faster responses in obese than lean participants in the passive learning

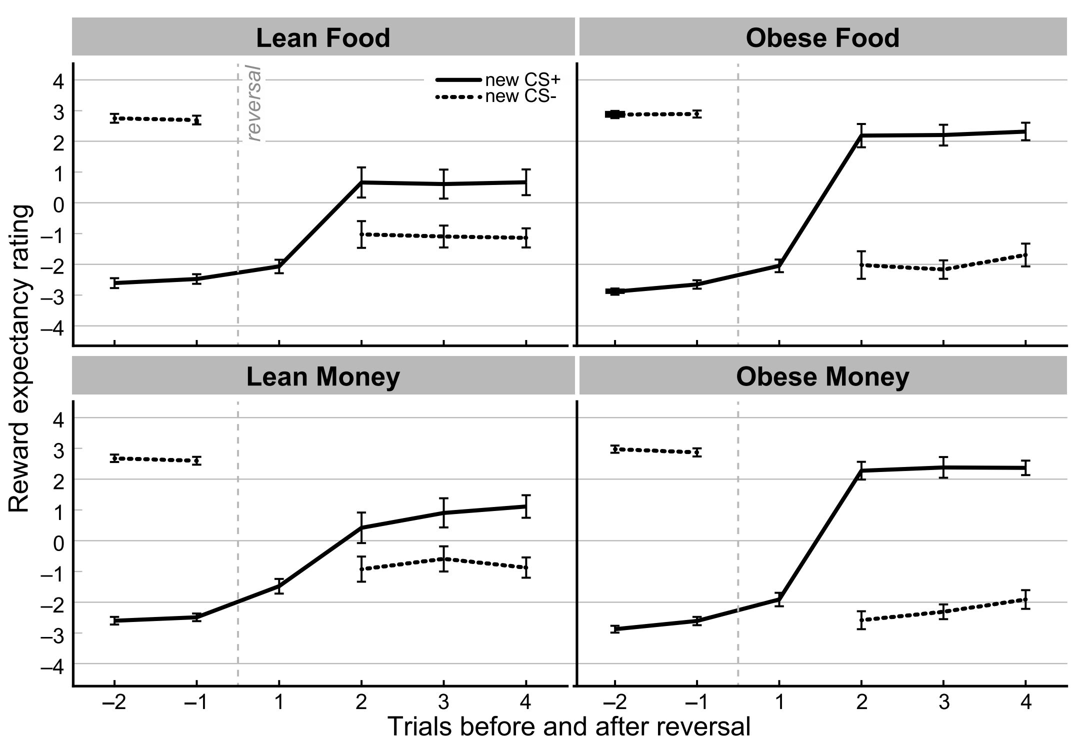

Fig. 3. *Immediate expectancy update.* Comparison of lean and obese participants' reward expectancies towards CS^+ and CS^- around the time of reversal in the passive reversal learning tasks. In both the monetary and food tasks, individuals with obesity showed a significantly stronger dynamic adaptation of reward expectancy ratings towards CS^+ than CS^- after a reversal than lean control participants. A plot including all five reversal stages separately can be found in the Supplementary Information (Supplementary Fig. 2). Error bars represent the standard error of the mean.

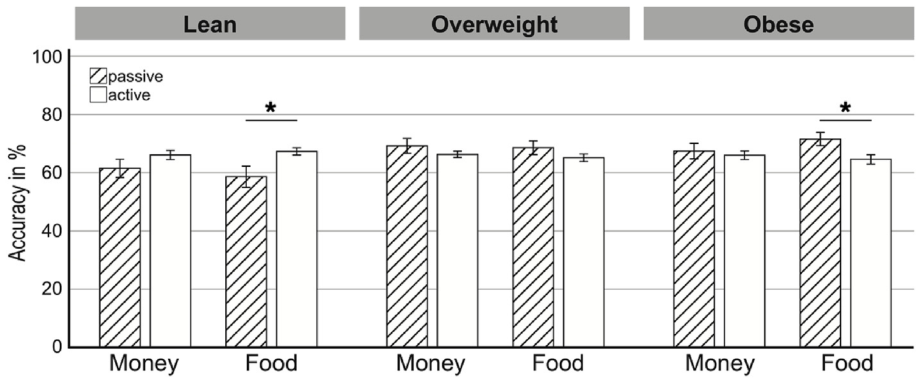

Fig. 4. *Interaction effect of BMI, response type and reward.* Percentage of correct responses in the active compared to passive learning tasks for food and monetary rewards in lean, overweight, and obese participants. The obese group exhibited higher accuracy in the passive compared to active food learning task, while lean control participants showed the reversed pattern. No differences were found in the overweight group. Error bars represent the standard error of the mean. *$p < .05$.

tasks. Learning performance was not modulated by personality and working memory (see Supplementary Information).

Please note that our data were not normally distributed. As common transformations did not improve skew and our large sample was equally distributed throughout the BMI range, we decided to continue working with the original values (see Supplementary Information for details).

4. Discussion

Here, we systematically investigated the influence of learning mode (passive, active) and offered reward (snack food, money) on association learning in the obesity setting. In contrast to previous reports of less efficacious learning from food rewards in people with obesity – particularly women – we do not find evidence supporting this hypothesis. Contrarily, our study indicates more successful learning from observation in participants with obesity – Even pronouncedly so when food rewards were presented. Furthermore, we found no sex differences or influences of impulsivity, reward- and punishment sensitivity or self-reported eating behaviour. Moreover, all participants successfully acquired and updated stimulus-reward associations independent of reward type.

Previous studies have mainly shown reduced reinforcement-based learning performance in obesity for both food and monetary reward (Coppin et al., 2014; Kube et al., 2017) and thus seemingly conflict with the current results. Recently, van den Akker and colleagues (van den Akker et al., 2017) found improved observational extinction learning in women with obesity. They suspected this to result from impaired initial acquisition. However, recruitment for the obese group was part of a weight-loss program, which may have led to socially conformed underreporting. Contrarily, in our study, obesity predicted both better acquisition learning and more flexible updating of contingencies compared to lean individuals.

However, when integrating our findings into previous research in the field, there are several factors to consider. First of all, most studies employed active trial-and-error learning, while our results mainly stem from a variation of the passive tasks that have been used less frequently (van den Akker et al., 2017; Zhang et al., 2014). The main difference between active and passive learning paradigms arguably lies in the directness of feedback. Agency drives active learning. Although probabilistically, each feedback represents the correctness of the participant's choice, while feedback in passive trials represents the correctness of a random, computer-generated choice – which might require more cognitive effort by separating reward delivery from instrumental action. This could explain our three-way interaction of better learning from the passive food tasks in people with obesity: Possibly, higher salience of food rewards led to improved focus on presented outcomes and consequently to superior learning by participants with obesity. Due to our highly-controlled reward selection, this learning advantage cannot be explained by way of differential values of food and monetary rewards between lean and obese participants. Salience, on the other hand, might be affected by weight status (Hendrikse et al., 2015) and was not controlled in our study. It might thus be speculated that participants with obesity show enhanced focus on food reward, not because of higher subjective value but because food outcomes are more attention-grabbing to them (Castellanos et al., 2009; Hendrikse et al., 2015).

Previous reports of lower learning performance in obesity were mainly based on more complex cue-outcome contingencies (Coppin et al., 2014; Kube et al., 2017; Mathar, Neumann, et al., 2017). At each time point, multiple stimuli predicted reward and punishment with variable probabilities. Such complex tasks might divert focus from salient outcomes toward highly ambiguous predictors whose effects need to be disentangled. Highly flexible behaviour of participants with obesity as observed in the current study may be detrimental in these tasks, which require immunity to distractors and stable choice behaviour. This effect might even be enhanced by the fact that participants were explicitly instructed that reward was exclusive to one variable at a time. Thus, learning of reward-associations was most likely driven by learning from the CS^+.

Notably, we found an opposing pattern of accuracy in the passive compared to active food learning tasks in obese and lean participants, but no differences in the overweight group. This emphasizes the importance of including participants with overweight, who have been rarely investigated in the past. Importantly, they might exhibit specific behavioural traits, for example through modulated dopaminergic response to rewards (Coppin et al., 2014; Dietrich, de Wit, & Horstmann, 2016; Horstmann, Fenske, et al., 2015). One previous study investigated differential responding to food and monetary rewards in a sample spanning from lean to obese body weight (Verdejo-Roman, Vilar-Lopez, Navas, Soriano-Mas, & Verdejo-Garcia, 2017). Results suggest that participants with higher weight value plain food less than lean participants and respond slower to neutral outcomes in a monetary incentive delay task. Importantly, their study did not find weight-related differences in reaction to salient rewards. Taken together, these studies suggest behaviour of participants with overweight not as a simple continuum between lean and obese, but as possibly influenced by mechanistic differences, like dopamine signalling (Horstmann, Fenske, et al., 2015).

Furthermore, to our knowledge, active and passive tasks have not been compared directly in reversal learning. Supplementary analysis of our data showed faster initiation of reversals in the passive condition. A key difference between active and passive learning might be feedback timing. In the former case, the contingency change is indicated deterministically by a presentation of the new CS^+ and reward (positive PE). We chose this approach to keep conditions as close as possible to previous passive paradigms in the field (van den Akker et al., 2017; Zhang et al., 2014). In the active condition, on the other hand, participants had to detect absence of expected reward (negative PE). Data from participants with and without Parkinsonism suggest that patients learn more efficiently from reward under observational conditions compared to trial-and-error learning (Kobza et al., 2012). Another study from our lab showed that patients with Parkinson's disease *on* compared to *off* L-DOPA medication are impaired in learning from negative PEs (Mathar, Wilkinson, et al., 2017). As overweight and obesity are argued to be associated with chronic changes in dopamine levels (Horstmann, Fenske, et al., 2015), we had speculated that obesity-related learning impairments are more likely in the active learning tasks. However, since we did not find such an interaction effect of BMI and response mode, this theory is not supported by our data. Nevertheless, we did not monitor dopamine levels in our participants. Combined observation of dopamine levels and response mode dependent reversal learning thus poses an interesting target for future research.

One additional sign of behavioural flexibility might be speeded reactions – Better learning might lead to less insecurity when choosing responses. Our data show a correlation between BMI and RTs, particularly in the passive tasks. This was significant even after controlling for age and self-reported motor impulsivity, raising the question as to whether higher accuracy in people with obesity and lower RTs might be related. *Post-hoc* analysis of our data revealed an inverted U-shaped association between RTs and accuracy in the passive learning tasks (see Supplementary Information for details). This highlights that fast RTs may reflect both excellent learning and hasty response behaviour.

One factor impacting generalizability of our findings is that the sample mainly comprised of highly educated, young people. Furthermore, age positively correlated with BMI and was consequently used as a covariate in all analyses.

Another factor to consider when interpreting our results, is the number and pace of reversal occurrences. The comparatively short reversal stages allow us to interpret our results as reflecting behavioural flexibility. Longer-term behaviour, however, would probably be better assessed with the help of longer learning phases with fewer reversals, as used in other studies (van den Akker et al., 2017; Zhang et al., 2014). Furthermore, while one reversal allows for unexpected contingency change, this is necessarily impossible with repeated reversals. Therefore, reversal updating scores are less comparable between paradigms with one or several reversals, respectively. Here, we look at flexible learning that stems from environmental awareness. The close instruction of our participants was aimed at allowing a strong focus on basic contingency learning and subsequent reversal detection in light of the complex nature and high pace of the task. Another difference to previous passive designs is that participants were aware of the exclusivity of reward to one of the stimuli, making a generalisation of reward-expectancy from the CS^+ to the CS^- very unlikely. This might partly explain the strong contrast to e.g. Zhang et al. (2014) findings. Further, it would be interesting to investigate behavioural flexibility while focusing on underlying attentional processes, e.g. with the help of eye-tracking. This would allow us to further disentangle possible influences of reward salience on learning success.

An additional limitation arguably lies in performing four similar tasks, which might have led to a training effect. However, task order was randomly assigned per participant, thus rendering within-subject training effects unlikely to impact our results.

5. Conclusions

This study sheds light onto an ongoing debate about efficacy of food reward in obesity research. At the same time, inclusion of overweight participants offers a more comprehensive picture of weight-related differences. As we controlled for individual reward preferences and minimized error variance with a within-subject design, we believe that previous reports of a BMI × Reward Type interaction in association learning might partly be due to methodological issues. It is compelling to argue that individuals with obesity are not impaired in their reinforcement-based learning performance per se, but instead show increased flexibility in reward-approach behaviour – A behaviour that arguably allowed adaptation to changing food-environments in the past but may nowadays facilitate unhealthy food choices in the constant presence of highly palatable foods. How this difference in association learning affects eating behaviour still has to be determined.

Author contribution statement

MTM, JK, CW and AH designed the study. MTM and JK collected the data. MTM, JK and AH analysed the data. MTM and JK drafted the manuscript. MTM, JK, CW and AH critically revised and approved the final manuscript.

Additional information

The authors declare no competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.appet.2018.08.029.

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Study 2 – Pavlovian-to-Instrumental Transfer in Obesity

Appetitive Pavlovian-to-Instrumental Transfer in Participants

with Normal-Weight and Obesity

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Article

Appetitive Pavlovian-to-Instrumental Transfer in Participants with Normal-Weight and Obesity

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Abstract: Altered eating behavior due to modern, food-enriched environments has a share in the recent obesity upsurge, though the exact mechanisms remain unclear. This study aims to assess whether higher weight or weight gain are related to stronger effects of external cues on motivation-driven behavior. 51 people with and without obesity completed an appetitive Pavlovian-to-Instrumental Transfer (PIT) paradigm. During training, button presses as well as presentation of fractal images resulted in three palatable and one neutral taste outcome. In the subsequent test phase, outcome-specific and general behavioral bias of the positively associated fractal images on deliberate button press were tested under extinction. While all participants showed signs of specific transfer, general transfer was not elicited. Contrary to our expectations, there was no main effect of weight group on PIT magnitude. Participants with obesity exhibited higher scores in the Three-Factor Eating Questionnaire Disinhibition scale, replicating a very robust effect from previous literature. Individual Restraint scores were able to predict body-mass index (BMI) change after a three-year period. Our data indicate that PIT is an important player in how our environment influences the initiation of food intake, but its effects alone cannot explain differences in—or future development of—individual weight.

Keywords: Pavlovian-to-Instrumental Transfer; PIT; obesity; food reward; human

1. Introduction

The prevalence of weight-related conditions has continuously risen, with 52% of adults and 18% of children worldwide being classified as overweight or obese as of 2019 [1]. This coincides with environmental changes concerning increased availability of high-caloric foods and lower energy expenditure [2–4]. While maladaptive reward-learning has been linked to over-eating in our modern, food-cue-enriched environment, the interactions are not well understood. One possibility is that basic cognitive traits such as appetitive conditioning and habit-formation guide individual behavior in everyday food intake. A thorough understanding of the mechanisms underlying the influence of environmental cues on food intake may lead to effective preventive efforts or constitute future treatment targets in disordered eating.

Eating in response to appetitive cues such as pictures of food—external eating—is related to increased awareness of food-cues [5], which can gain more behavioral relevance than homeostatic drive [6]. This attention bias to food-cues is more prominent in children from obese backgrounds [7]. Obesity has further been linked to lower homeostatic control over attention to food-cues [8] and eating behavior per se [9], as opposed to hedonic control. The strict dichotomy between homeostatic and hedonic behavioral control is currently under debate [10]. Furthermore, increased automatic approach toward food cues [11,12] and impaired reversal learning after food-reward devaluation [13] were shown in people with obesity, while higher body-mass index (BMI) predicted stronger interference of high-palatability food words in a Stroop task [14]. Together, these studies imply a strong susceptibility to food cues in obesity, making behavior less deliberate and more reliant on impulsive behavior.

These findings might be discussed in the light of habits, which is a highly controversial topic with mixed results in human samples. The introduction of inflexible behavioral biases through over-training [15,16] has not been replicated in a study including five attempts of habit-induction [17]. Though studies showing successful habit induction mainly stem from animal research, e.g., [18], theoretical models of overtrained, habit-like behavior in humans do exist [19]. In the context of food, devalued food-cues can nevertheless evoke acquired responses in human participants [20], which increases with higher caloric content of the depicted food [21]. This leads to the interpretation that especially palatable food can lead to unhealthy eating styles that become progressively more insensitive to bodily needs.

Behaviorally, eating in the absence of hunger can be seen as a result of bias-vulnerability, i.e. diminished internal homeostatic control over eating, in favor of external drivers. A widely used bias-vulnerability test is Pavlovian-to-Instrumental Transfer (PIT) [20,22–24], which measures the influence of task-irrelevant cues on behavior. Past research has resulted in mixed findings concerning food-related PIT and body weight [25–28]. Given the uncertain link between automatic behaviors, vulnerability to food-related environmental cues and weight development, we aimed to further investigate this issue. The current study tested the applicability of a previously used PIT paradigm [23] to human participants with appetitive food rewards, namely fruit juices that were delivered via a gustometer.

In addition, we obtained questionnaire scores for eating behavior, reward-drive, and behavioral inhibition [29–31] in order to relate these constructs to our participants' outcomes in the behavioral task. We were particularly interested in two subscales of the Three Factor Eating Questionnaire (TFEQ) [31]: Disinhibition measures loss of control during food intake, and Cognitive Restraint measures active cognitive effort to reduce food-intake. These subscales may capture the strength of bottom-up control of food cues and have been studied in lean and obese weight groups with varying outcomes [8,32]. It has been argued that the subscales are interconnected and bear the potential to describe eating behavior more intricately when combined [30]. However, Cognitive Restraint by itself can predict future weight gain [33], possibly through emotional eating following perceived underachievement of strict dieting goals. Thus, we were interested in investigating a possible link between Cognitive Restraint, the strength of PIT and weight change.

In this study, we wanted to assess obesity-related differences in the magnitude of PIT. Assuming that a substantial part of weight variation can be explained by unhealthy eating styles, we expected participants with obesity to exhibit stronger PIT than normal-weight controls. Moreover, we hypothesized that PIT effects would positively correlate with the TFEQ Cognitive Restraint and Disinhibition subscales as well as a questionnaire measure of Impulsivity (UPPS Urgency, [34]). In order to investigate whether extended training is involved causally, we invited half of our participants for further cue- and action-outcome learning before the test phase. Support for our hypotheses would strengthen the notion that greater action control of incidental food cues, and inflexibility of over-trained, automatic action-tendencies, can impair cognitive control over food intake [9,16,19].

2. Materials and Methods

2.1. Participants

We performed a cross-sectional study investigating group-specific PIT strength in people with and without obesity. The experiments were conducted at the Max-Planck-Institute for Human Cognitive and Brain Sciences in Leipzig, Germany. We invited 64 healthy, non-smoking participants between 18 and 35 years of age, from a local database, who took part in this study after a telephone screening. Inclusion criteria were: No acute or chronic psychological or physical illnesses, no allergies and no medication besides oral contraceptives. Participants were not actively dieting or undergoing any other change in eating behavior. Furthermore, pregnancy or breastfeeding led to exclusion from the study. Participants were asked to abstain from eating or drinking anything other than water for two hours prior to the appointment. All participants were introduced to the set-up and signed informed written consent before participation. Thirteen data sets were excluded from the final analyses (3 obese/8 female; 5 for low pleasantness ratings of the taste rewards, as explained below, 6 for missing data, 1 due to indication of depressive symptoms (BDI > 18) and 1 for significantly increased reaction times (z-scored RT > 2.5) compared to sample mean). The remaining 51 participants (27 females) were composed of four groups depending on sex and body-mass index (BMI). Obesity was defined as a BMI higher than or equal to 30.0 kg/m^2, while normal-weight participants displayed a BMI of higher than 18.5 kg/m^2 and lower than or equal to 25.5 kg/m^2. Demographic data can be found in Table 1. The study was carried out in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the University of Leipzig, Germany.

Table 1. Sample Characteristics.

		Lean		Obese	
Variable		**Female**	**Male**	**Female**	**Male**
n		14	12	13	12
Age		24.21 ± 3.07	24.67 ± 3.06	25.50 ± 2.98	26.42 ± 5.87
BMI		21.90 ± 1.96	22.16 ± 2.19	38.37 ± 5.80	35.34 ± 3.55
Self-Report Characteristics					
BIS/BAS	BIS [1]	21.43 ± 2.82	19.17 ± 2.98	19.23 ± 2.95	16.00 ± 2.22
	BAS [2]	17.29 ± 1.44	16.00 ± 1.76	16.38 ± 2.02	15.33 ± 1.44
UPPS	Urgency	26.93 ± 7.13	26.58 ± 4.98	29.31 ± 7.35	27.08 ± 3.09
TFEQ	Dis [3]	5.79 ± 2.67	5.08 ± 2.35	8.38 ± 3.12	6.50 ± 3.50
	Restraint	6.07 ± 3.22	5.08 ± 3.12	8.15 ± 5.52	5.75 ± 5.52
BDI		4.57 ± 4.33	3.42 ± 2.81	4.92 ± 3.48	5.83 ± 4.02
Hunger Levels		4.25 ± 2.02	4.21 ± 2.12	3.42 ± 1.78	4.04 ± 2.34

[1] A univariate ANOVA revealed significantly higher scores for lean than obese participants as well as higher scores for female than male participants. [2] A univariate ANOVA revealed significantly higher scores for female than male participants. [3] A univariate ANOVA revealed significantly higher scores for obese than lean participants. BMI = body mass index in kg/m^2, BIS BAS/BAS Drive = Behavioral Inhibition/Behavioral Activation Scale: Subscale Drive, UPPS Urgency = Urgency/Premeditation/Perseverance/Sensation Seeking: Subscale Urgency, TFEQ Dis = Three Factor Eating Questionnaire: Subscale Disinhibition, TFEQ Restraint = Three Factor Eating Questionnaire: Subscale Cognitive Restraint of Eating, BDI = Beck Depression Inventory, Hunger Levels = Mean of hunger ratings pre and post paradigm.

2.2. Questionnaires

During two questionnaire sessions (one before and one after the behavioral paradigm) participants were asked to fill in questionnaires concerning general health (BDI, [35]), stress exposure (TICS, [36]), reward and/or punishment sensitivity (BIS/BAS, [37]), impulsivity (UPPS, [38]) and eating behavior (TFEQ, [31,39]) in a fixed order. After 3 years, participants were again contacted to fill in the TFEQ for a second time.

2.3. Selection of Taste Rewards

Participants were asked to rate subjective hunger on a 10-point Likert scale from 1 (not hungry) to 10 (extremely hungry). Each subject chose four out of the following juices as taste rewards, which were subsequently used in the following rating procedure: Strawberry, Mango, Apple, Coconut-Pineapple, Cherry, Banana, Blackcurrant, Orange, or Grape. Per trial, 5 ml of juice was delivered centrally onto the participant's tongue via polyethylene and silicone tubes by an in-house built gustometer that was controlled via Presentation®software (Version 16.5, Neurobehavioral Systems, Inc., Berkeley, CA, USA, www.neurobs.com). Maximum trial duration was 12 seconds or until logging via button press. Each juice was presented six times (24 trials in total). Juices were initially rated on a Likert scale from 1 (frowning face) to 9 (smiling face). A positive mean rating (>4.5) and comparable pleasantness for three of the four juices qualified these as taste rewards for use in the paradigm. If all four juices were perceived as pleasant, the three juices with the closest mean ratings were used. Each juice was then assigned to a button and visual stimulus. Furthermore, a neutral taste solution, as described elsewhere [40], was used as a fourth taste stimulus and one visual stimulus was associated with this cue exclusively.

2.4. Pavlovian-to-Instrumental Transfer

In PIT, participants learn to associate neutral cues with affective outcomes such as reward or punishment. Bias vulnerability is tested by introducing these task-irrelevant cues into a free choice task. Two transfer types can be studied: Specific transfer describes the bias strength of a specific cue in a free choice between two rewarded actions. General transfer measures the bias strength an affective cue has on instrumental behavior in comparison to behavior after a neutral cue.

The task was administered with Presentation®software. A 4-button response box was placed in front of the participants who were asked to press the 3 task buttons with the fingers that were most convenient for them. After reading the standardized instructions, participants completed seven test trials including randomly selected taste feedback to make them familiar with general timing and setup of the task (following [23]; max. two test runs when required) and were allowed to ask questions if necessary.

An instrumental trial (Figure 1A) entailed a 6s display of two buttons, constituting a free choice between two trained taste rewards. Participants were instructed to deliberately press one or more of the depicted buttons during that time in order to earn taste rewards (action–outcome). The reward criterion required 5–15 button presses (BPs) per trial for reward delivery. Before each trial, the criterion was randomly drawn from a flat distribution between 5 and 15. Multiples of this minimum resulted in multiple reward deliveries per trial. The partial reinforcement schedule was intended to make responding more robust to reward extinction in the transfer phase. This has previously been shown to be effective by Cartoni and colleagues [41]. Participants were furthermore instructed that there was no correct choice and that each button was stably associated with one of the three juices. Online visual feedback about BPs was provided during trials. This consisted of a short on-screen color-change of the pressed button. The instrumental phase consisted of 30 trials (10 per button pair). During Pavlovian trials (Figure 1B), participants were presented with a fractal picture for 6s (randomized order). Three of the four fractal images were stably accompanied by one of the three taste rewards (CS+; stimulus–outcome) while one image was accompanied by the neutral taste (CS-). Taste presentation was probabilistically determined with 60 percent of trials being rewarded. The inter-trial-interval (ITI, black screen with white fixation) was presented for 2–6 s (randomized) during which neutral taste was used to rinse the tongue in case the previous trial was rewarded. The Pavlovian phase consisted of 40 trials (10 per fractal image). Transfer trials (Figure 1C) consisted of simultaneous fractal picture presentation, similar to the Pavlovian phase, and button choice between two buttons, similar to the instrumental phase. This was intended to test whether the previous training with positive reinforcement created a measurable behavioral bias on free choices between these stimuli. Participants were instructed to view the fractal cue pictures while responding as in previous instrumental trials. They were specifically instructed that there were no right or wrong button choices, no rules, and they should respond according to their impulses. Picture presentation, response window duration, and visual feedback on registered BPs was given as in previous phases. Without prior instruction, transfer trials were conducted under extinction, meaning that rewards were withheld in this part of the task. The transfer phase entailed 90 trials: 30 trials testing for specific PIT with one of the offered two buttons being associated with the same reward as the presented cue picture; 30 trials testing for a general positive bias with both buttons and the cue picture being associated with different positive rewards during training; and 30 trials testing responding after presentation of the neutral cue picture.

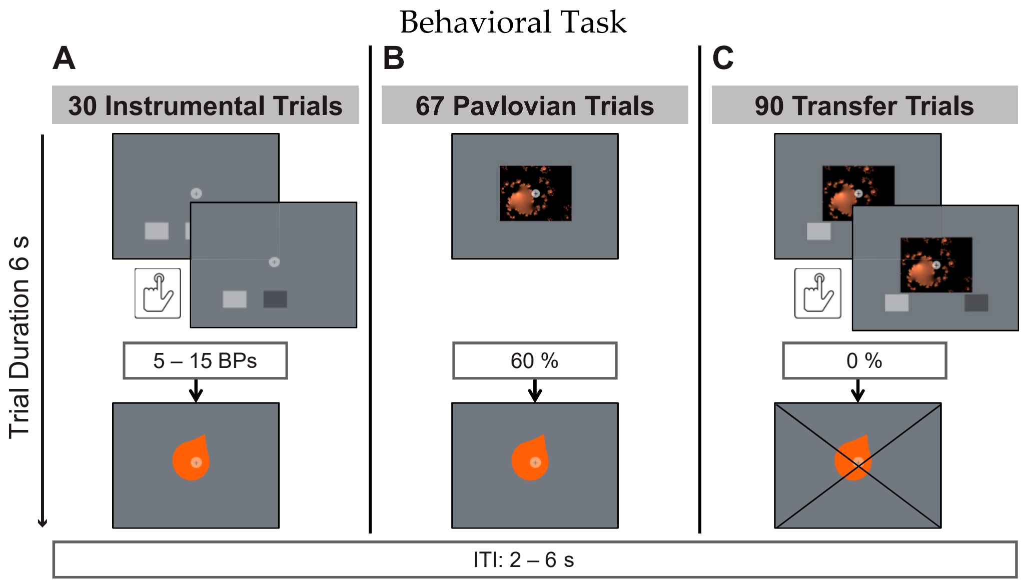

Figure 1. Example trials of the instrumental (**A**), Pavlovian (**B**) and transfer (**C**) phases with respective reward probabilities. Each button and visual cue was stably associated with one taste. The inter-trial-interval (ITI) had a pseudorandomized duration between 2-6s in all three phases.

After completion of the paradigm, participants finally provided a second subjective hunger rating and filled in the remaining questionnaires. In order to test for conditioned reward association, 43 of the 51 participants also performed a paired comparison between the four visual stimuli after completing the paradigm. They were instructed to compare, pairwise, each picture with each of the others regarding subjective pleasantness. They indicated by " $<$ / $>$ / $=$ " whether they preferred one fractal image to each of the other three images. A picture received a score of 1 if it was preferred, a 0 if it was less favorable and a 0.5, if both were rated as equally pleasant. Scores for all comparisons per picture were subsequently added, averaged over juice-related pictures and compared via t-test to the score obtained by the picture trained with the neutral taste.

In order to gain more insight into learning dynamics and to test for previously reported training effects [42], 50% of the participants were invited for two training sessions. Those participants only completed the instrumental and Pavlovian phases during session 1 and the complete paradigm during session 2, which was identical to the paradigm that the no-training group completed. Session 2 was scheduled within one week after session 1.

2.5. Data Analysis

Data were analyzed using MATLAB and Statistics Toolbox Version 8 (Release 2012b, The MathWorks, Inc., Natick, MA, USA) and SPSS Statistics Version 22.0 (Release 2013, IBM Corp., Armonk, NY, USA). Significant results were followed up by post-hoc least square difference tests.

2.6. Assessment of Data Quality and Preparatory Steps

In addition to confirming association learning and investigating possible group-related differences by univariate ANOVA, Pavlovian conditioning was tested by using a paired t-test on scored pairwise picture comparisons. We compared the mean score of juice-related pictures with the score for the neutral taste-related picture. This information was only collected for a subgroup (n = 43).

Pleasantness of taste rewards was examined for all but one subject, whose reward-button assignments could not be reconstructed. First, mean subjective pleasantness ratings of the rewards were compared to a rating of 4.5 (affectively neutral) using an independent sample *t*-test. A repeated measures analysis of variance (rmANOVA; within-factor juice) was used to further test for differences in pleasantness between the juices assigned to buttons 1, 2, and 3 as well as differences between participant groups in order to rule out any influence of unequal pleasantness on button press behavior. For some participants ($n = 24$), reward pleasantness was assessed before and after the paradigm in order to test for changes in pleasantness over time. For this, another rmANOVA with factors juice and time was used to ascertain that juices did fulfil their purpose as reward until the end of the paradigm.

Subjective hunger ratings before and after the paradigm were compared using an rmANOVA (within-subject factor time, between-subject fixed factors weight group and sex) and change in hunger was tested for correlation to the initial hunger level. All other analyses contained mean-centered hunger as a covariate of no interest in order to rule out hunger-related differences between our experimental groups. Mean-centered age was always included in order to compensate for possible effects of age on learning.

As dependent measures, response rates (RR; in z-scored number of BPs) and response times (RT; in tenths of milliseconds) were observed. Reaction time was defined as the time between stimulus onset and onset of first button response. A within-subject z-score standardization of trial-based RR was applied to compensate for between-subject disparities in baseline responding. Furthermore, RTs were examined on a trial and subject level. Z-scores of within-subject RTs and z-scores of mean RTs per subject were computed and unusually high values (z-score > 2.5) were excluded in order to minimize effects of inattentiveness or unspontaneous responding.

Variation of button pressing (RR and RT) during rewarded training and unrewarded transfer (factor experimental phase) for the different buttons (factor button) was tested using rmANOVA. This was done in order to investigate the effect of extinction on response behavior.

2.7. Hypothesis Testing

In order to interpret behavioral differences between groups in a meaningful manner, questionnaire scores were analyzed in univariate analyses of variance (ANOVA) with sex and weight group entered as fixed factors. Results can be seen in Table 1. As hypotheses were formed only for the Disinhibition and Restraint scales of the Three Factor Eating Questionnaire (TFEQ) and the Urgency scale of the UPPS, only these scale scores were entered as dependent variables in the main analysis. As both BIS and BAS-scores of the BIS/BAS questionnaire exhibited significant main effects, a post-hoc analysis with these scales was set up in addition to the a priori tests.

Specific PIT was defined as the difference in instrumental response rates between cued and uncued outcomes (i.e. congruent versus incongruent). General PIT was calculated as the difference in instrumental response rate between positive, but non-associated, and neutral cue pictures. Presence of transfer was tested using a paired TTEST for both specific and general PIT.

$$\text{Specific PIT} = \text{mean}(RR_{\text{cued CS+}}) - \text{mean}(RR_{\text{uncued CS+}}) \quad (1)$$

$$\text{General PIT} = \text{mean}(RR_{\text{uncued CS+}}) - \text{mean}(RR_{\text{CS+/-}}) \quad (2)$$

To rule out the possibility that group differences in the likelihood to choose the neutral stimulus masked possible general transfer effects, we conducted a univariate ANOVA on that variable, with between factors sex and weight group.

To test our main hypothesis, specific transfer was then investigated in a 2×2 ANOVA with sex and weight group as fixed factors. Mean-centered TFEQ Disinhibition and Restraint as well as UPPS Urgency scores were entered as covariates. Because of a non-normal distribution, general PIT was analyzed in a nonparametric Mann–Whitney-Test, including Weight group as a grouping factor.

As the transfer phase consisted of 90 unrewarded trials, continuity of response behavior was tested as a function of time during transfer. For this, a rmANOVA was set up. RR was defined as the dependent variable and time (time bins 1–5) and transfer type (specific or general PIT) were defined as within-subject factors. Magnitude of transfer effects (gPIT, sPIT) was compared between training groups via MANOVA. The influence of the BIS and BAS subscales of the BIS/BAS questionnaire on transfer was analyzed separately in an exploratory ANOVA model on specific PIT, including sex and weight group as fixed factors.

Finally, we contacted participants for a follow-up report of their BMI after 3 years (mean = 1097 days, range = 972:1229 days). Of all 31 responders, only 19 participants were available for on-site BMI measurement and therefore we first ran a correlation analysis between observed and reported BMI at both time points to determine the validity of reported BMI (i.e. a high correlation of more than r = 0.9). We set up a multivariate regression model on change of self-reported weight at follow-up as dependent variable. As independent variables, we included sex and age, specific PIT, the restraint scale of the TFEQ, as it has been connected to weight gain in the past, and BMI at time point 1. This was done in order to test the predictive power of these factors with regard to weight development.

3. Results

Participants correctly identified juice-button and juice-cue associations in 96% of cases. This did not differ between sexes ($F_{45,1} = 0.40$, $p = 0.53$, $\eta_p^2 = 0.09$) or weight groups ($F_{45,1} = 0.04$, p = 0.84, $\eta_p^2 = 0.01$ interaction: $F_{45,1} = 2.24.$, $p = 0.14$, $\eta_p^2 = 0.05$). CS+ pictures were preferred over the CS- ($t_{42} = 9.32$, $p < 0.001$). Taste ratings before the paradigm were positive (test value = 4.5, button1: mean = 7.0, SD = 1.0, $t_{49(B1)} = 16.81$, $p < 0.001$, button2: mean = 7.1, SD = 1.0, $t_{49(B2)} = 18.63$, $p < 0.001$, button3: mean = 6.8, SD = 0.9, $t_{49(B3)} = 18.49$, $p < 0.001$) and did not significantly differ by juice ($F_{47,2} = 3.08$, $p = 0.06$, $\eta_p^2 = 0.12$) or weight group (interaction juice*weight group: $F_{47,2} = 0.08$, $p = 0.93$, $\eta_p^2 = 0.00$). Repeated measures ANOVA testing for preferences between the three button-taste pairs yielded a trend ($F_{46,2} = 3.18$, $p = 0.05$, $\eta_p^2 = 0.12$) towards preference for button 2 compared to button 3. Repeated Measures ANOVA of juice liking over time revealed no significant increase or decrease of preference for the taste rewards over time ($F_{21,1} = 0.00$, $p = 1.00$, $\eta_p^2 = 0.00$). The interaction of time and juice was evaluated by Greenhouse–Geisser corrected output due to violations of sphericity (Mauchly's W = 0.56, $p < 0.05$) and showed no significant effect over time and juices ($F_{29.2,1.4} = 1.33$, $p = 0.27$, $\eta_p^2 = 0.06$). Because this data was derived from a small subsample, we did not test for group differences in this context. Hunger before the paradigm averaged at a rating of 3.6 (SD = 2.0) and after the paradigm at 4.3 (SD = 2.3). Repeated measures ANOVA indicated a significant difference between the time points (time: $F_{46,1} = 12.54$, $p = 0.001$, $\eta_p^2 = 0.21$). This was not affected by weight group ($F_{46,1} = 2.38$, $p = 0.13$, $\eta_p^2 = 0.05$) or sex ($F_{46,1} = 1.98$, $p = 0.17$, $\eta_p^2 = 0.04$; interaction: $F_{46,1} = 2.10$, $p = 0.16$, $\eta_p^2 = 0.04$). This analysis was performed without including mean-centered hunger ratings as a covariate. Initial hunger and change in hunger were not correlated ($r = -0.15$, $p = 0.31$).

As some reaction times were unusually high, we excluded outlier trials subject-wise ($z > 2.5$). We had to exclude 2.27 trials on average (SD = 0.9) from all but one participants' 90 transfer trials. We furthermore excluded one complete dataset which exhibited a mean reaction time of more than 2.5 seconds per trial ($z = 3.3$), as we suspected noncompliance in the form of inattentiveness to the task.

Repeated Measures ANOVA testing for extinction effects revealed a significantly different button press behavior between the training and transfer phases ($F_{47,2} = 19.39$, $p < 0.001$, $\eta_p^2 = 0.45$). Specifically, participants responded more frequently and slowly during the transfer phase than during training (RR: $F_{48,1} = 9.33$, $p < 0.01$, $\eta_p^2 = 0.16$; RT: $F_{48,1} = 18.72$, $p < 0.001$, $\eta_p^2 = 0.28$) with a significant univariate interaction effect on RR, as responding with button 1 and 2 as opposed to button 3 was specifically increased during transfer ($F_{96,2} = 4.31$, $p = 0.02$, $\eta_p^2 = 0.08$). It stands to reason that this is likely due to participants choosing the right ring finger for operating button 3, which is less practiced than the index and middle finger. Another reason might be a preference of tastes 1 and 2 over taste 3, although only the preference of taste 2 over 3 was statistically significant, as reported above.

MANOVA of questionnaire results testing for effects of sex and weight group revealed a significant multivariate effect of BMI on questionnaire results ($F_{43,4} = 4.97$, $p = 0.01$, $\eta_p^2 = 0.26$). This effect was driven by a univariate main effect of BMI on TFEQ Disinhibition score ($F_{45,1} = 14.70$, $p < 0.001$,

η_p^2 = 0.25) with higher values in the obese than in the control group (TFEQ Restraint: $F_{45,1}$ = 2.12, p = 0.15, η_p^2 = 0.05; UPPS Urgency: $F_{45,1}$ = 1.30, p = 0.26, η_p^2 = 0.03). There was no main multivariate effect of sex ($F_{43,4}$ = 1.39, p = 0.26, η_p^2 = 0.09) and no interaction effect ($F_{43,3}$ = 0.42, p = 0.74, η_p^2 = 0.03).

Specific transfer was observable in our sample (t_{50} = 10.88, p < 0.001, Figure 2A) while general transfer was not expressed significantly (t_{50} = 0.19, p = 0.85). Effects of sex and weight group on specific PIT were tested using a 2×2 ANOVA with mean-centered hunger, age and TFEQ Disinhibition score entered as covariates. There were no significant main (weight group: $F_{44,1}$ = 1.71, p = 0.20, η_p^2 = 0.04; sex: $F_{44,1}$ = 0.00, p = 1, η_p^2 = 0.00, Figure 2B) or interaction effects (weight group*sex: $F_{44,1}$ = 0.02, p = 0.88, η_p^2 = 0.00). Nonparametric comparison between general transfer in lean and obese participants resulted in acceptance of the null hypothesis (U = 288, p = 0.49). As a follow up to this, we nonparametrically analyzed response rates solely after presentation of the neutral stimulus. There was no significant difference in response strength between lean and obese participants (U = 277, p = 0.37).

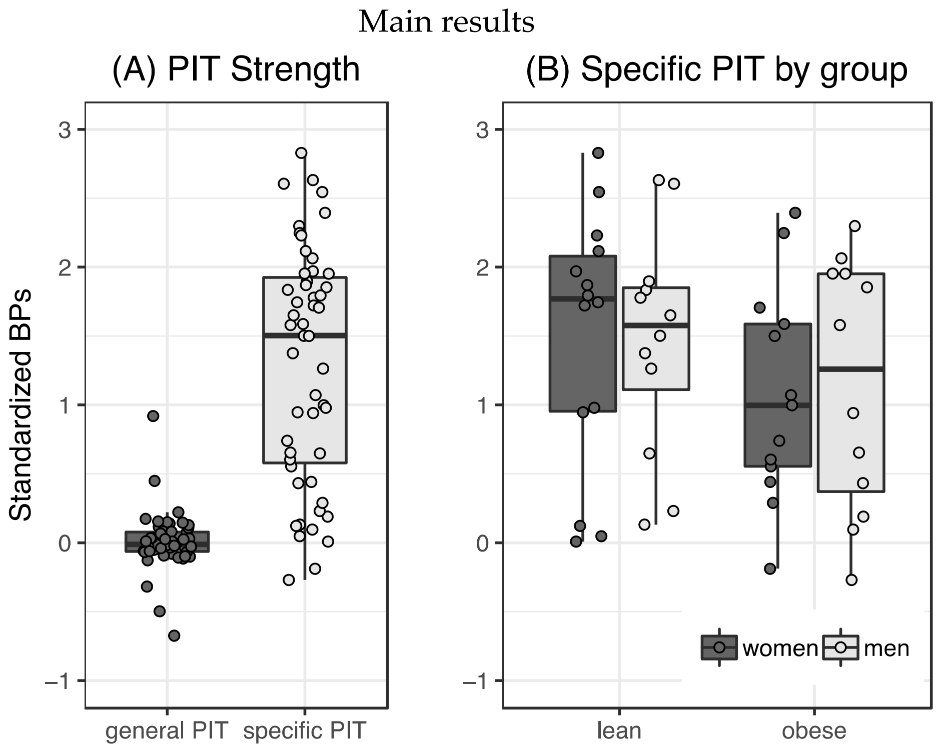

Figure 2. (**A**) While specific Pavlovian-to-Instrumental Transfer (PIT) could be significantly elicited in our sample, general PIT was not observed. (**B**) Despite a visible trend toward less specific PIT in the obese group, we did not observe a significant main effect of weight group or sex on button press behavior. (plotted with ggplot for R (R Core Team, 2015; Wickham, 2016)).

Repeated measures ANOVA of responses over five bins of transfer trials showed significant violations to the assumption of sphericity for the different time bins (Mauchly's W = 0.65, p = 0.03). We therefore used the Greenhouse–Geisser corrected F values and found no main effect of time ($F_{147.3,1}$ = 2.09, p = 0.1, η_p^2 = 0.04). Response rates were significantly different between transfer types ($F_{48,1}$ = 78.96, p < 0.001, η_p^2 = 0.62) with participants responding more to specific PIT trials (p < 0.001) as well as an interaction effect of both ($F_{192,4}$ = 3.8, p < 0.01, η_p^2 = 0.07). Participants decreased the amount of specific transfer between time bin 1 and 5, while the lack of general transfer was stable over time. Different numbers of training trials did not significantly affect PIT strength ($F_{46,2}$ = 1.63, p = 0.21, η_p^2 = 0.07). The exploratory general linear model testing for effects of BIS and BAS scores on specific transfer did not yield any significant main or interaction effects (BIS: $F_{45,1}$ = 0.693, p = 0.41, η_p^2 = 0.02; BAS: $F_{45,1}$ = 0.05, p = 0.82, η_p^2 = 0.01).

Finally, Pearson product–moment correlations were run to determine the relationship between observed and reported BMI at both time points. Neither at time point 1 ($r = 0.997$, $n = 51$, $p < 0.001$) nor at time point 2 ($r = 0.996$, $n = 19$, $p < 0.001$) did BMI measurements differ significantly. We therefore used reported BMI in the following analysis.

A multiple regression was run to predict BMI change from time point 1 to time point 2. Predictors were specific PIT, TFEQ restraint and BMI at time point 1, sex and age (Figure 3).

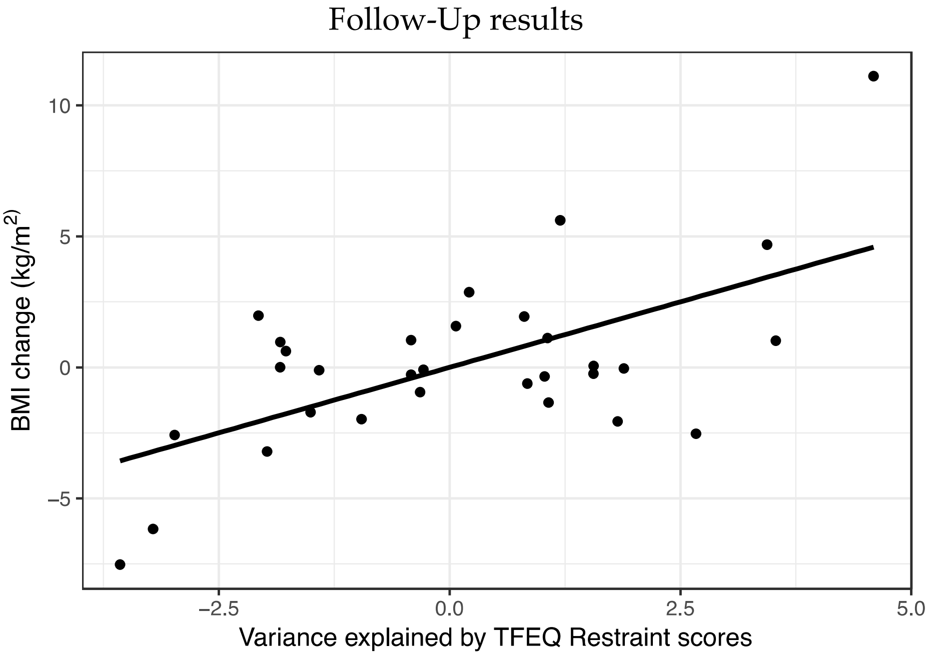

Figure 3. Three Factor Eating Questionnaire (TFEQ) Restraint scores significantly predicted BMI change after three years (plotted with ggplot for R (R Core Team, 2015; Wickham, 2016)).

Statistically, this model significantly predicted BMI ($F_{5,30} = 3.05$, $p = 0.03$, $R^2 = 0.38$). Of the five variables, only Restraint scores ($t = 3.54$, $p = 0.002$) predicted BMI change with higher weight at time point 2 in people with higher Restraint scores.

4. Discussion

Acknowledging that obesity is the consequence of a multitude of underlying processes and predispositions, we aimed at investigating whether vulnerability toward incidental priming, with appetitive stimuli, can be seen as a contributor underlying obesity. We successfully trained participants to associate previously unknown and neutral pictures with positive tastes in order to prime their subsequent instrumental behavior. Evidence of an effective environmental bias would be an increase in response behavior after exposure to positively associated cues. Of particular interest would be effects of weight group on the magnitude of general and specific PIT. Our hypothesis was that higher BMI would predict stronger transfer effects.

Replicating previous studies [23,43–51], we found evidence for specific PIT in our sample. Conditioning with immediate taste rewards was successful. Participants preferred rewarded cues to the neutrally associated picture when explicitly asked to rate them according to their subjective feeling toward them. This preference cannot be explained by aesthetic preference, as pictorial stimuli were randomized per subject. The fact that these pictures were also able to direct behavior in the subsequent transfer task implies that humans can be guided toward a response after overtly stating their freedom to choose by preference and also when reward was omitted. This points toward a mechanism that initiates reward seeking that is not solely controlled by homeostatic drive but also modulated by the environment. In the present study, transfer was prompted using appetitive food stimuli. This allows for the interpretation that specific PIT might be involved in altered eating behavior in modern, food-cue enriched environments. However, we should not forget about other possible sources of weight development that we did not measure in this study (e.g. energy expenditure). This might be why we did not detect an impact of weight group on specific transfer. The data even implies a trend for less specific transfer in the obese group than in the controls, which might be masked by the high variability of the data. Further support for this incidental finding would stand in contrast to our initial hypothesis of transfer effects contributing to diet-induced obesity.

Our null-result may, of course, indicate something different. Incidental food priming might affect everyone equally and thus, might not predict the development of overweight and obesity. Previous studies to date have produced mixed results concerning a direct relationship between BMI and strength of food PIT. While a study of Lehner et al. showed no difference in PIT strength between lean and obese participants, people with overweight showed stronger susceptibility to food PIT [26]. Watson et al. did not find differences in PIT strength per se in people with and without obesity [25]. However, low as opposed to high caloric content foods did not elicit PIT in the obese group, exclusively. In addiction research, PIT was not associated with dependence severity [46–51] and did not differ between participants with and without an addiction [45]. In addition, we might only be able to see these effects in larger samples than ours. Furthermore, PIT tasks always carry the difficulty of instructing participants to follow their instincts, even though a lab environment arguably stands in the way of natural and automatic behavior. Looking at the results from the angle of measurement choice, although weight status allows for simple analysis and comprehensible results, it is not a very direct way for understanding individual eating styles. Different bodies process incoming energy in vastly different manners. Consequently, weight groups were intended to give a first impression of possible effects, which we did not find in this study. Connecting attentional processes and PIT to energy intake per se would be a very direct way of determining the environmental validity of PIT in the context of food and should be looked at in the future. On the other hand, energy intake is difficult to measure and requires participants with very high levels of diligence and perseverance. Consequently, BMI should not be dismissed lightly. Apart from its very strong standing as a population measure, it is helpful as an indirect measure for individual health-behaviors. Finding a link between obesity and PIT might require a finer resolution of the predictor, like continuous BMI, including the less studied BMI range from 26 to 29 kg/m^2. A further approach would be longitudinal studies measuring weight development in relation to transfer strength. Toward that end we followed up on the link between personality traits and obesity, obtaining self-reported weight after three years. We were thus able to analyze the predictive power of transfer strength as well as replicate the finding of van Strien et al. [33] concerning the association between weight development and the restraint scale of the TFEQ. Despite the relatively small case number, our data indicate a strong influence of restraint on BMI development, while specific transfer did not significantly contribute to the model. It would be interesting to replicate this in a larger sample in order to include disinhibition scores. Theoretically, people with high disinhibition tendencies and low restraint could be more susceptible to incidental food priming, while people with high restraint scores and low disinhibition might be better protected from this effect [30].

In a 2011 study, exposure to remote food stimuli (i.e. sight and smell of pizza) primed individuals toward larger prospective portion sizes [27]. This effect was independent of weight group, while salivation and motivation to eat was significantly increased for overweight individuals compared to normal-weight participants. Therefore, considering this relationship between automatic, appetitive responses and weight group, it might be worthwhile to retest our hypothesis including measures of visual attention and arousal in future studies.

Another factor requiring attention when looking at our results is reward type. This study used juices as immediate taste rewards. That is a valid approach, as fruit juices are generally perceived as positive and come in diverse flavors. There are, on the other hand, indications that gustatory as well as sensory properties or caloric content differentially affect pleasantness and taste as well as influence intake in lean and obese populations [52].

An interesting approach would be to reproduce this study with the additional factor of hunger and satiety. As has been shown previously, weight group significantly modulated the influence of homeostatic state on attentional bias to food cues [9]. Unlike the control group, participants with overweight and obesity did not exhibit a decreased attentional bias to food cues when sated. In the current study, all participants performed under conditions of relative satiation, meaning that they had not eaten in the two hours prior to the experiment. Furthermore, hunger ratings increased during the task, potentially increasing the influence of this factor. A standardized meal before participation might pronounce differences between weight-groups in future studies and lead to a more thorough understanding of external drivers of appetitive responses.

Unfortunately, we did not elicit general transfer in our sample, which might be a more viable measure of transfer in the food context. General and specific PIT constitute separate behavioral pathways for environmentally driven behaviors. While specific transfer is a measure of the circumstantial bias towards a certain incentive, general transfer describes an externally elicited bias towards reward (i.e. food) in general. In humans, automatic behavior and PIT have been connected via blood-oxygenation level dependent (BOLD) signal changes in the human brain [23,24,43,53]. In rats, the nucleus accumbens (NAc), has been closely linked to PIT. Lesions of the NAc shell affected only specific transfer, while general transfer was eliminated by lesions to the NAc core [26], underlining the double dissociation between specific and general PIT. As our theoretical approach to this study centers on a universal appetitive response in the face of ubiquitous food supply and pervasive food-related environmental cues, the concept of general transfer was driving hypothesis formation. Future studies in this field might center on general transfer, as we also believe that combined testing of both transfer types—especially under extinction—might affect outcome quality negatively. The current setup might drive participants to explicitly test picture-button combinations in order to trigger reward delivery, rather than respond naturally. Participant reports after paradigm completion, as well as our data, corroborate this notion. The number of button presses was at its highest in the beginning of the transfer phase, when participants fully expected a reward. Congruent button presses, meaning specific PIT, were executed significantly more often in the first trials of the transfer phase. Button presses that were identified as markers of general PIT, on the other hand, were almost absent during the transfer phase. Several other studies [20,54,55] have focused instrumental training on two outcomes, while the paradigm included three Pavlovian outcome pairings. This way, the general PIT effect could be measured in a much clearer fashion, as both the CS+ and the neutral CS are not paired with an instrumental response, thus avoiding confusion. According to participant feedback, different strategic approaches were tried, presumably until cessation of reward delivery expectation. The exclusivity of increased BPs for buttons 1 and 2 can be explained by the fact that most participants decided to use the index and middle fingers of their right hand for the first two buttons, while they operated the third with their ring finger. This decision could have led to a relative unwillingness to press button 3 for reasons of convenience.

In order to test general PIT effects under ecologically valid conditions, future studies should consider omitting extinction during the transfer phase or introducing it gradually to avoid confusion. This has been done in other studies [46,54–57]. As our study included extinction during transfer, this might be an explanation for the absence of general transfer effects. Absence of conditioned rewards has previously been shown to substantially reduce transfer effects [58]. However, as suggested by the authors, a more sensitive measure might be the choice in itself, in contrast to the amount of button presses. The present study calculated PIT as the difference in response rate after priming. However, priming effects might be visible when looking at the pure button choice in itself. Another reason for absent general PIT might be a relative over-representation of choices for the neutral cue, as was observed by Yin, Zhuang, and Balleine [59] in a PIT task in dopamine transporter knockdown mice. We therefore checked our data set for similar influences, but did not find any evidence for this effect.

Hypothesizing that a higher amount of training may lead to more involuntary responses to the Pavlovian stimulus, we tested whether doubling operant and Pavlovian learning increased PIT strength. Contrary to our hypothesis, training had no effect on transfer magnitude in our sample.

Holmes and colleagues [42] argued that increased training of associations might lead to a competition between instrumental and Pavlovian tendencies in rats. Following their line of argument, this effect should be investigated with a specific increase of Pavlovian training. While the amount of overtraining found in rats will be difficult to replicate in human participants, this specificity might circumvent competition abolishing the transfer effects.

Obesity, indisputably, is a very heterogeneous condition. Most probably, metabolic differences and eating behavior are the primary contributors to the development of a chronic homeostatic imbalance leading to excess weight. Looking at personality and behavioral traits might prove a valuable approach to disentangling these influences on eating style from homeostatic and attentional sources. While some individuals might have a tendency toward eating in response to personal circumstances like stress, others may respond to environmental cues, or to a combination of both, like following external cues during emotionally challenging situations. In our sample, obesity status predicted differences in self-reported eating behavior. Participants with obesity showed higher levels of disinhibition, meaning that food intake was more likely to become uncontrolled and excessive. This, taken together with the fact that all participants were vulnerable to PIT, implies graver consequences from reacting to external cues when, at the same time, the intake amount is less restricted. This theoretical role of PIT in an interaction model of attentional bias and disinhibited eating is corroborated by a study in adolescents by Shank and colleagues [60]. Though our study did not find a connection between personality traits and PIT, it thus might still be an interesting target for further inquiry.

Garofalo and colleagues [61] recently confirmed the existence of goal- and sign-tracking subtypes in humans with a monetarily reinforced PIT. Sign-tracking participants focused on the CS+ before engaging in reward-seeking, while goal-trackers instantly oriented towards the predicted outcome signals. Garofalo and colleagues found that sign-tracking individuals were particularly susceptible to PIT in comparison to goal-trackers and that this effect increased with probability of reward delivery. This is especially interesting, as we found improved flexibility in people with obesity in a reversal learning task [62]. We argued that people with obesity exhibited an improved focus on the outcomes of each trial and were thus superior in keeping track of contingency changes. It has further been implied by animal data [63] that sign-trackers might be especially responsive for discrete cues while goal-trackers can be influenced by contextual cues. Thus, eye-tracking data during PIT studies might explain inter-individual differences in transfer magnitude and help in determining whether an individual might benefit from therapeutic interventions targeting susceptibility to external food cues. Additionally, the data from Garofalo and colleagues directs attention toward the concept of partial reinforcement and transfer under extinction, which might decisively affect transfer strength in a subset of participants.

In addition to capturing orientation toward rewarding cues, reactivity to those cues might pose as a valuable target for treatment. It has previously been shown that neuronal reactivity to food and sexual depictions predicts future weight gain and sexual behavior respectively [64]. In obesity, reactivity to affective cues seems to be more pronounced than in lean control participants [65], highlighting the importance of including cue reactivity in modern treatment programs. Retraining of automatic approach behavior toward food cues has been shown to be a promising target for cognitive training [11,12]. As recently implied in a paper from Verhoeven et al. [54], in addition to overriding the effect of health warnings, PIT also bears positive potential. Linking and thus supporting wholesome food intake with these health warnings, instead of competing for attention with convenience foods, might direct behavior toward healthy outcomes—bearing the potential to use already well-established advertising practices of the food industry to our benefit.

5. Conclusions

Over-eating in the presence of pervasive food-related cues can result from overtrained reward seeking behavior and subsequent translation into automatic response patterns. This study provides additional evidence for Pavlovian-to-Instrumental Transfer of appetitive cues to reward seeking behavior. Consequently, a stricter regulation of advertising strategies might contribute to a healthier lifestyle in the general population, particularly in times when children are especially targeted by food marketing. Furthermore, this finding supports therapeutic interventions targeting attentional bias towards food cues as a means to curb externally driven appetitive responses or build positive associations with healthy foods. Individual weight development was not predicted by PIT, while self-reported TFEQ-restraint scores were related inversely to weight change and explained ca. 30% thereof over three years. Further studies might focus on connecting PIT effects to the interplay of eating styles and disposition towards sign-tracking, ideally including more fine-grained measures of obesity. Another interesting addition would be the inclusion of longer-term weight development in the context of transfer strength.

Author Contributions: Conceptualization, M.M. and A.H.; methodology, M.M. and A.H.; formal analysis, M.M. and A.H.; investigation, M.M.; resources, A.H.; data curation, M.M.; writing—original draft preparation, M.M.; writing—review and editing, M.M. and A.H.; visualization, M.M.; supervision, A.H.; project administration, A.H.; funding acquisition, A.H.

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Discussion

The aim of this thesis was to investigate whether overweight and obesity are related to changes in reward driven association learning or vulnerability to incidental reward cues.

Keen Association Learning in the Food Context: Advantage or Disadvantage?

In our first study, we focussed on mechanisms impacting explicit reward learning. We were able to show that successful acquisition and reversal of reward expectancy is not dependent on weight-group. People with and without obesity were able to correctly track reward associations irrespective of reward type. This finding should have implications for all research on reward-driven behaviour and obesity, as negative findings have been reported previously (van den Akker et al., 2017; Z. Zhang et al., 2014). Our data show a clear difference in learning success between reliance on active stimulus choice in comparison to a passive outcome observation. This is also reflected in a significant interaction between BMI, reward and response type. While people in the healthy BMI-spectrum exhibit relatively lower accuracy in passive compared to active trials, people with obesity seem to profit in the passive condition. When looking at the passive tasks exclusively, we find more flexible associations between incidental cues and reward outcomes in people with obesity. Combined with our finding of faster reaction times in people with obesity, we infer improved explicit learning from highly salient food rewards to be the driver of this interaction. The idea that obesity might be the result of a behavioural adaptation (Chaput, Doucet, & Tremblay, 2012) – with disadvantages as well as advantages – rather than an illness per se, offers intriguing room for interpretation.

The second study was aimed at testing the possible influence which reward-related cues might have on subsequent food-choice behaviour. While we did not find group differences between people with and without obesity, all participants showed signs of bias vulnerability. Thus, this study suggests a possible mechanism of overeating in environments that are rich in palatable food cues. Reportedly, food system policy can potentially correct the recent undesirable trend in promoted over-nourishment in some societies as well as undernourishment in large parts of the world (Swinburn et al., 2011). However, in a subset of participants who were contacted by us two years after initial participation in our study, we found no evidence for a relationship between this bias and weight gain. A limitation of this study is the small sample size. In order to retest this hypothesis and investigate the appearance of less specific PIT in people with obesity, our study should be replicated in a larger sample. Additionally, PIT, though helpful in the animal literature, is most likely not easily brought into a human setting. Arguably, PIT paradigms might not be suitable to instil habit-like behaviour in human participants (de Wit et al., 2018). As a way to circumvent this, usage of previously strongly trained cues like advertising material by large food manufacturers should be considered. Furthermore, while some measures of personality and eating behaviour were acquired in this study, cognitive parameters like WM could give a more complete picture on the pathways of cue-triggered eating behaviour. A recent paper by Garofalo and colleagues (Garofalo, Battaglia, & di Pellegrino, 2019) has shown that WM score was positively associated with the amount of congruent button presses in the specific PIT condition, while incongruent button presses were inversely correlated to WM score. As obesity and working memory capacity have been reported to be inversely related (Coppin et al., 2014; Stingl et al., 2012; van den Berg et al., 2009), combined testing of specific PIT, WM score and obesity would seem logical for a replication study. How these findings can be translated into individual behavioural differences in a natural food setting is not clear and needs to be addressed in field studies.

Evaluation of Study Findings: Checking Stereotypes

When looking at the results of the included studies, negative biases in the interpretation of data from clinical populations need to be discussed. This applies to the first study's finding of overweight and obesity predicting higher learning flexibility. Evaluating specific behaviour as either flexibility or unsteadiness is certainly a matter of debate. Seeing obesity as a biological adaptation, findings of higher flexibility might be interpreted as a pathway of evolutionarily positive behaviour that has become maladaptive in the modern world. It would be interesting to check these behavioural mechanisms in countries where food availability is low. Following this line of argument, a flexible assignment of learned associations between reward outcomes and instrumental cues from the environment could predict a higher BMI and, thus, better health.

Comparing Protective and Risk Aspects of Higher Weight

Elevated blood pressure is similarly accompanied by seemingly positive effects in some populations: Obesity (Chaput et al., 2012) as well as hypertension (Mendlowitz, 1982) have been discussed in terms of biological adaptation.

Apart from reported risks due to comorbid diseases like Type-2 Diabetes or hypertension, positive health effects of overweight have been shown, including lower risk of osteoporosis or fractures and frailty in elderly populations (Chaput et al., 2012). The same review reports negative health effects of weight-loss, purporting that classification of obesity as an illness is debatable, since therapy is not necessarily positive for the body. Underweight and obesity have been connected to higher mortality rates, while overweight predicted lower mortality compared to the healthy weight group – an effect that did not change after 10 years of weight-stability (Flegal, Graubard, Williamson, & Gail, 2018). Besides these protective effects of higher weight, several risk aspects cannot be denied. As an example, at the age of

18, the lifetime risk of being diagnosed with Type-2 Diabetes is increased by as much as 37.2% for obese men and 37.5% for obese women (Narayan, Boyle, Thompson, Gregg, & Williamson, 2007). Notably, the increase for people with overweight is reported as 9.9% in men and 18.3% in women, showing two things: (1) how BMI classifications differ in terms of clinical applicability between the sexes. (2) The drastic increase in lifetime risk for Type-2 Diabetes between overweight and obesity – in contrast to the much lower rate change between healthy weight and overweight – illustrates how the relationship between higher weight and risk of comorbid diseases is not well reflected in the weight classification system.

Hypertension can be discussed in the same vein, while a causal relationship between hypertension and mortality rates has been stably established (Iadecola et al., 2016; World Health Organization, 2019). Although the consequential serious health decline makes prevention and therapeutic intervention necessary (The SPRINT Research Group, 2015), elevated blood pressure has also been related to better quality of life, better academic success and lower distress in young participants (Berendes, Meyer, Hulpke-Wette, & Herrmann-Lingen, 2013; Hassoun et al., 2015). A strong dependence of mortality rates on diagnosis rather than presence of the disease (Jørgensen, Langhammer, Krokstad, & Forsmo, 2017) as well as negative effects of antihypertensive treatment in elderly patients (Douros et al., 2019) have also been shown. Possibly, higher blood pressure in young age can be discussed as an advantage in terms of physical performance while its detrimental long-term consequences become visible only after longer affliction.

In sum, modest expressions of both obesity and hypertension seem to predict better quality of life, while negative clinical consequences grow with stronger manifestation. This needs to be considered in therapeutic settings. Most likely, psychological stress considerably accounts for reduced quality of life after diagnosis – especially in conditions like obesity that are perceived to be due to the individual's behaviour (Kirk et al., 2014; Sikorski et al., 2011). While hypertension therapy is well-researched and medication is successful in most cases (The

SPRINT Research Group, 2015), bariatric surgery – thereby involving all the risk that is associated with surgeries in general – is considered to be the only effective method to date for people with extreme obesity (Hauner, Wirth, et al., 2013).

The Obesity Stigma and its Relevance in Research and Therapy

Causes and views on individual weight and eating behaviour have undergone drastic changes during the past centuries. In some developing countries, overweight and obesity are still generally accepted signs of health, prosperity and – especially when looking at women – fertility (Furnham, Moutafi, & Baguma, 2002; Mavoa & McCabe, 2008; Pollock, 1995). Current wide-spread stigmatization of overweight and obesity in most developed civilizations culminates in body-shaming practices that are based on assumptions of poor health and a low socioeconomic status (McLaren, 2007; van Leeuwen, Hunt, & Park, 2015). Seemingly simple body measurements like BMI or waist circumference can thus strongly affect participants' mindsets – especially in people with obesity who report significantly more personal stigma experience than people with healthy weight, even in young childhood (Pont et al., 2017). Furthermore, inclusion and exclusion criteria or covariates like, e.g. comorbid physical or psychological illness, have the potential to distort effects of obesity on study outcomes greatly (Kube et al., 2016; Schrimpf, 2017) and need to be controlled closely. This line of argument culminates in the central difficulty of creating a considerate study environment and checking stereotypes when interpreting cognitive data from populations with stigma experience.

Illustrating potential systematic effects of these implicit forces, people with obesity reportedly receive less time and attention from medical staff and, consequently, seek less medical help (Forhan & Salas, 2013). A higher obesity risk for some demographic groups (e.g. African Americans, Comuzzie & Allison, 1998) can therefore create a systematic healthcare bias.

BMI in Research and Medical Practice

BMI definition is irrespective of body composition or sex and therefore only of limited use in individual diagnosis and therapy. Our findings rely strongly on grouped analyses. As obesity risk is determined not only by way of food intake, but also body composition, sex, basal metabolic rate, etc., grouped comparisons can only approximate an explanation of weight development. However, despite its poor resolution, BMI predicts cardiovascular risk with a grade of precision that is comparable to more sophisticated methods like skinfold measurement or X-ray absorptiometry (Steinberger et al., 2005). Another benefit of BMI as a clinical and research measure is the simplicity of its measurement – requiring only one height and weight measurement – and its comparability between different examiners (Steinberger et al., 2005). The UK Foresight programme classifies obesity as a “wicked problem” that needs to be addressed by reducing complexity – without resorting to oversimplification – in order to find solutions to the global and local obesity problem (Swinburn et al., 2011).

Conclusion

Our studies have indicated that implicit bias by way of food advertisement and omnipresence of palatable food cues offers a way of interpreting unhealthy food choices. They illustrate how higher BMI can be discussed in terms of an evolutionary adaptation. While we showed that people with obesity seem to update cue-reward associations more flexibly than people within the healthy weight range, implicit cue responsiveness by way of PIT was not systematically different between the weight groups. However, presence of specific PIT in both weight groups deems research into preventative efforts in form of food policy changes promising. Besides the facilitation of an active lifestyle, energy intake is therefore a promising target for population-based interventions.

Summary

Zusammenfassung der Arbeit

Dissertation zur Erlangung des akademischen Grades Dr. rer. med.

Implicit and Explicit Appetitive Outcome-Learning in Obesity

eingereicht von Marie-Theres Meemken, M.Sc. Neurocognitive Psychology

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Obesity and its comorbidities are key public health concerns in western societies, with prevalence rates rising sharply over the last decades (Bischoff et al., 2017; World Health Organization, 2017). Contributing factors range from genetic predisposition to socioeconomic or environmental factors like eating style or exercise, as well as the cultural background (Bischoff et al., 2017). A strong disparity between intake and expenditure promotes obesity in high-income countries with an affluent food-environment and a sedentary lifestyle (Bellisle, 2014; Gore et al., 2003; Hu et al., 2003; Tucker & Bagwell, 1991; Tucker et al., 1989).

These factors indicate that pathways of environmentally driven food intake need to be scrutinized, leading to the following research questions: how do cognitive influences shape our

appetites or behaviours? How does the decision to pursue intake of a specific food in contrast to another depend on implicit biases from our surroundings?

Previous research has connected executive functions and eating-behaviour (Dempsey et al., 2011; Rangel, 2013). At the same time, the relationship between executive functions and obesity measures is not clear – though a negative impact of obesity on test outcomes seems undeniable (Boeka & Lokken, 2008; Dye et al., 2017; Fitzpatrick et al., 2013; Gunstad et al., 2010; van den Berg et al., 2009). Several cognitive functions such as working memory capacity have been shown to differ between people with overweight and obesity, and people in the healthy weight range (Coppin et al., 2014; Stingl et al., 2012; van den Berg et al., 2009). Kroemer and Small propose a model by which obesity is accompanied by decreased goal directedness due to differential reward learning. They argue that exaggerated reward anticipation signals in the brain go hand in hand with blunted reward receipt signalling in obesity (Kroemer & Small, 2016), possibly resulting in attenuated behavioural goal-directedness and less adherence to dietary goals. In line with this, food reward receipt (Janssen et al., 2017) and omission (Horstmann, Dietrich, et al., 2015; Meyer et al., 2015) as well as negative monetary outcomes (Horstmann et al., 2011; Kube et al., 2017; Mathar et al., 2017) have been shown to be less potent reinforcers in people with obesity. Additionally, other factors such as stigma or social exclusion experience (Kube et al., 2016) might be able to explain negative findings regarding cognitive functions in obesity, but are rarely accounted for.

To cite an example for this, a study comparing learning success between people with and without obesity suggested inferior learning in women with obesity when learning from food rewards (Z. Zhang et al., 2014). In their study, coloured squares were associated with either monetary or food outcomes, the contingencies of which changed after initial acquisition. Next to other methodological concerns, their findings were based on strongly dissimilar monetary and food rewards, making interpretation of their results difficult. Their suggestion that women with obesity exhibited lower learning parameters due to difficulty to focus when being confronted with salient food rewards thus seemed premature. This consideration was the starting point of my first study.

Study 1 – In order to re-test this hypothesis and broaden its informative value, we replicated their study with the inclusion of the overweight BMI range (Meemken, Kube, Wickner, & Horstmann, 2018). With the help of four probabilistic reversal learning paradigms, we analysed data of 85 participants of both sexes between 18 and 35 years of age with a BMI range between 19 and 51 kg/m^2. Through a willingness-to-pay paradigm we individually identified food and monetary rewards of comparable value.

In addition to the replication of the two paradigms (one food, one monetary), participants performed two further learning tasks. The original paradigms relied on learning by observation, as participants passively viewed whether a certain stimulus was followed by a reward – reporting their associations through subsequent reward expectancy ratings. We additionally tested active learning: participants selected the stimulus that they believed would result in a reward – which is more often used in learning research (Coppin et al., 2014; Horstmann et al., 2011; Kube et al., 2017). When looking at the passive tasks specifically, people with obesity showed faster and more accurate learning for both food and monetary rewards (see figure S1). A comparison of active and passive tasks indicated that in the food tasks, people at the lower end of our BMI spectrum showed relatively better learning from the active than passive task. People with a high BMI, on the other hand, showed the opposite effect with higher accuracy measures in the passive than active tasks. Arguably, while feedback in the active tasks can be understood in terms of correct vs. incorrect choices, feedback in the passive tasks is more challenging. The participant is confronted with a random coloured stimulus and indicates whether they expect a reward or not. The actual feedback then confirms or rejects their reward expectation, adding one layer of complexity to the outcome phase. We therefore reasoned that the obesity-related flexibility in this context was due to improved focus on the outcome phase, possibly through higher salience of the food rewards. The fact that all participants were able to correctly learn reward associations goes against the findings of Zhang et al. (2014).

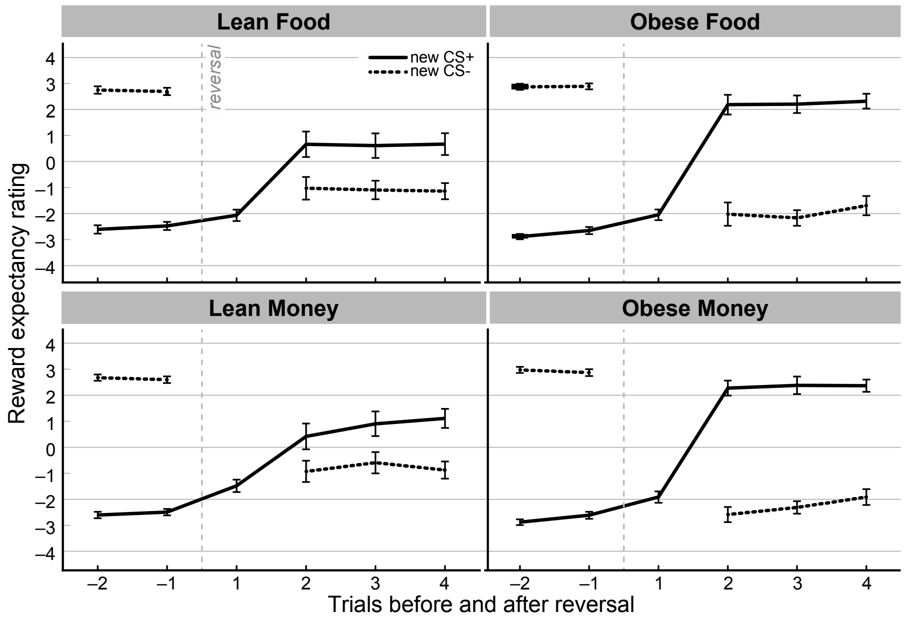

Figure S1 *Main effect of BMI group during passive reversal learning*. Error bars represent SEM. (Meemken, Kube, Wickner, & Horstmann, 2018)

Study 2 – Following this, we were interested in the mechanisms through which these learned associations impact behaviour. It has been reported that so-called external eating is related to an attentional bias towards food cues (Brignell et al., 2009), which has been found in overweight and obesity (Hendrikse et al., 2015). In our second study, 51 male and female participants from two weight groups (healthy weight, obese) between the ages of 18 and 35 completed a paradigm testing external bias on free-choice behaviour (Meemken & Horstmann, 2019) – a Pavlovian-to-Instrumental Transfer (PIT) task (Prévost et al., 2012). The task was performed with food rewards (i.e. fruit juices) that were orally delivered through a gustometer and consisted of three phases. During the first two phases, each participant consolidated two associations per taste: one with a visual cue and one with a button press. During the final test phase, participants were confronted with the choice between two buttons and instructed to choose freely based on gut instinct. Concurrently, however, one of the previously trained cue pictures was visible on screen. A PIT effect is calculated as relative response strength:

Specific PIT – How often did the participant respond with the button press that was associated with the same reward as the incidentally visible cue picture? This is reported in relation to the amount of button presses that were not associated with the same outcome.

General PIT – How often did the participant respond with a button press when the presented cue picture was previously paired with another, unrelated taste rather than a picture that was previously paired with a tasteless liquid?

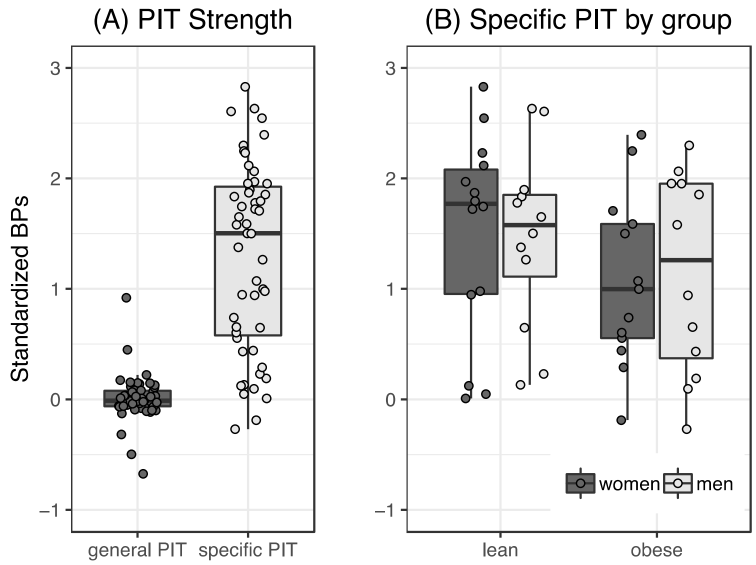

Figure S2 *Specific PIT was not associated with weight group or sex.* (Meemken & Horstmann, 2019).

Our study showed that specific PIT affects all participants, irrespective of weight group (see figure 2). Even though this is not set in a realistic food environment, our study shows that irrelevant visual cues can have a behavioural effect. Retesting as part of a field study would be necessary to gain insight into the possible efficacy of food policy changes like bans for food advertisements that promote an unhealthy lifestyle. As a test of the predictive power of this behavioural trait, we furthermore conducted a regression analysis of several factors on weight change after a follow-up period of three years. These included individual specific PIT, a subscale of the Three-Factor Eating Questionnaire (Stunkard & Messick, 1985), BMI, sex and age. Of these five factors, only the questionnaire score was able to predict BMI change.

Taken together, our studies paint a different picture than hypothesized: while obesity predicted better performance in basic association learning in study 1, once formed, associations did not bias subsequent instrumental choices differentially in the two weight groups in study 2. Apart from the fact that our findings need to be corroborated in replication studies, some methodological issues need to be addressed in order to continue this line of argument. Firstly, the four learning tasks in study 1 were highly similar, making training effects a concern. As the order of paradigm presentation was randomized individually, we do not believe that this influenced group effects. Furthermore, the PIT paradigm from study 2 is aimed at detecting implicit influences on highly habituated behaviour. Whether this behaviour can be elicited in human participants is currently under debate (de Wit et al., 2018). Finally, social influences like stigma experience often differ depending on weight group and have been shown to influence study outcomes in the reward learning context (Kube et al., 2016). Thus, we need to (1) consider social stigma experience as a hindrance during cognitive testing or (2) create an atmosphere that allows all participants to focus on the task at hand. Such factors are crucial for all future research in connection with this highly stigmatized participant group.

In conclusion our studies underline that a societies immediate food environment can impact food choice and should be protected against unhealthy influences, though the connection to weight development is not clear.

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Declaration of Authenticity

Erklärung über die eigenständige Abfassung der Arbeit

Hiermit erkläre ich, dass ich die vorliegende Arbeit selbstständig und ohne unzulässige Hilfe oder Benutzung anderer als der angegebenen Hilfsmittel angefertigt habe. Ich versichere, dass Dritte von mir weder unmittelbar noch mittelbar eine Vergütung oder geldwerte Leistungen für Arbeiten erhalten haben, die im Zusammenhang mit dem Inhalt der vorgelegten Dissertation stehen, und dass die vorgelegte Arbeit weder im Inland noch im Ausland in gleicher oder ähnlicher Form einer anderen Prüfungsbehörde zum Zweck einer Promotion oder eines anderen Prüfungsverfahrens vorgelegt wurde. Alles aus anderen Quellen und von anderen Personen übernommene Material, das in der Arbeit verwendet wurde oder auf das direkt Bezug genommen wird, wurde als solches kenntlich gemacht. Insbesondere wurden alle Personen genannt, die direkt an der Entstehung der vorliegenden Arbeit beteiligt waren. Die aktuellen gesetzlichen Vorgaben in Bezug auf die Zulassung der klinischen Studien, die Bestimmungen des Tierschutzgesetzes, die Bestimmungen des Gentechnikgesetzes und die allgemeinen Datenschutzbestimmungen wurden eingehalten. Ich versichere, dass ich die Regelungen der Satzung der Universität Leipzig zur Sicherung guter wissenschaftlicher Praxis kenne und eingehalten habe.

18.12.2019	[Marie-Theres Meemken]
Datum	Unterschrift

Appendix

Telephone Screenings

Datum:______________________ **Interviewer:**__________________
Probanden-Code:________________ **ggf. neuer Termin:**_____________

Telefonscreening – ALE-OB-Studie
Hallo Frau/Herr… Mein Name ist….und ich arbeite am Max Planck Institut für Kognitions- und Neurowissenschaften in Leipzig. Ich habe Ihre Daten in unserer Datenbank gefunden und wollte mich erkundigen, ob Sie Interesse hätten an einer Studie teilzunehmen.

Informationen zur Studie
In dieser Studie geht es um das Lernen von Zusammenhängen und darum, Vorhersagen zu treffen. Sie würden eine Aufgabe am PC bearbeiten, bei der Ihnen verschiedene Reize präsentiert werden, u. A. können Sie Geld oder Süßigkeiten gewinnen.

Im Anschluss an dieses Experiment gäbe es dann noch einige Fragebögen zu beantworten, außerdem wiegen wir Sie und messen Ihre Größe. Insgesamt würde Ihre Teilnahme damit etwa 2 bis 3 Stunden dauern.

Hätten Sie Interesse an dieser Studie teilzunehmen?

Wenn ja: Bevor ich Sie zu einem Untersuchungstermin einladen kann, gibt es zunächst noch ein paar Dinge, die wichtig sind, damit wir Sie der richtigen Versuchsgruppe zuordnen können. Dazu möchte ich Ihnen im Folgenden einige Fragen stellen. Insgesamt würde unser Gespräch damit etwa 5 min. dauern.

Bevor wir mit der Beantwortung der Fragen fortfahren, möchte ich Sie noch darauf hinweisen, dass selbstverständlich alle Informationen, die Sie uns geben, streng vertraulich behandelt werden. Sind Sie damit einverstanden?

Allgemeiner Teil	
Wie alt sind Sie?	
Wie groß sind Sie?	
Wie viel wiegen Sie derzeit?	
BMI (kg/m^2)	
Sind Sie derzeit Raucher oder Nichtraucher?	Raucher Nichtraucher Gelegenheitsraucher
Machen Sie derzeit eine Diät?	Ja Nein

Leiden Sie unter irgendwelchen körperlichen Erkrankungen?	Ja Nein Wenn ja, welche? _______________ _______________ *Nicht erlaubt:* *a) Schilddrüsenerkrankungen (u.a. adipogene Erkrankungen)* *b) Diabetes*
Leiden Sie an Allergien?	Ja Nein Wenn ja, welche? _______________ _______________ *Alle Lebensmittelallergien ausschließen!*
Waren Sie schon jemals in psycholog., psychotherap. oder psychiatrischer Behandlung?	Ja Nein
Nehmen Sie regelmäßig Medikamente ein?	Ja Nein Wenn ja, welche?: _______________ _______________ *Nicht erlaubt sind:* *Psychopharmaka, Allergiemedikamente, Medik. mit Einfluss auf das auton. Nervensystem, Kortikosteroide* *Okay sind: Kontrazeptiva*
Mögen Sie Schokolade?	Ja Nein
Mögen Sie Gummibärchen?	Ja Nein
Bei Frauen: Sind Sie zurzeit schwanger?	Ja Nein
Wenn Ausschluss: Frau/ Herr…, da wir in unserer Studie sehr strenge Einschlusskriterien haben, muss ich Ihnen leider mitteilen, dass Sie dieser Studie nicht teilnehmen können. Wenn wir aber Probanden für andere Studien suchen, würden wir sehr gern wieder auf Sie zurückkommen. Vielen Dank noch einmal für Ihr Interesse und Ihre Zeit.	

So, wir sind am Ende angekommen. Vielen Dank für Ihre Unterstützung Herr/Frau…

Soweit ich das anhand der Fragen beurteilen kann, sind Sie sehr gut für unsere Studie geeignet und ich würde Sie gern zu einem Termin einladen.

Ich möchte Sie noch bitten, vor dem Termin x Stunden nichts mehr zu essen

Ich werde Ihnen noch eine Bestätigungsemail mit unserer Anschrift und genauem Datum und Uhrzeit zuschicken.

Falls sie den Termin kurzfristig doch absagen oder verschieben möchten, rufen Sie bitte Frau Menger unter der 0341 9940-2214 an, sie wird das dann an mich weiterleiten.

Email:_______________

Termin:_______________

Datum:__________________________ **Interviewer:**___________________
Probanden-Code:_________________ **ggf. neuer Termin:**_____________

Telefonscreening – OBPIT

Hallo Frau/Herr… Mein Name ist….und ich arbeite am Max Planck Institut für Kognitions- und Neurowissenschaften in Leipzig. Ich habe Ihre Daten in unserer Datenbank gefunden und wollte mich erkundigen, ob Sie Interesse hätten an einer Studie teilzunehmen.

Informationen zur Studie

In dieser Studie geht es um das Lernen von Assoziationen zwischen Bildern, Tasten und Geschmackssorten bei normal- und übergewichtigen Probanden. Die Studie besteht im Wesentlichen aus einer Aufgabe, die am Computer zu lösen ist, während verschiedene Geschmacksstoffe probiert werden. Die Aufgabe dauert in etwa 30 Minuten und wird an **einem / zwei** Tagen bearbeitet. Vorher werden einige Fragebögen beantwortet, außerdem messen wir Ihre Größe und ihr Gewicht. Insgesamt würde Ihre Teilnahme damit 2-3 Stunden **(an zwei verschiedenen Tagen)** dauern. Wir würden außerdem gerne eine kleine Blutprobe entnehmen, um den Einfluss unserer Gene und bestimmter Stoffwechselmarker auf unser Verhalten einschätzen zu können. Hätten Sie Interesse an dieser Studie teilzunehmen?

Wenn ja: Bevor ich Sie zu einem Untersuchungstermin einladen kann, gibt es zunächst noch ein paar Dinge, die wichtig sind, damit wir Sie der richtigen Versuchsgruppe zuordnen können. Dazu möchte ich gerne einige Fragen stellen. Insgesamt würde unser Gespräch etwa 5min dauern. Haben Sie dafür jetzt Zeit oder darf ich zu einem späteren Zeitpunkt noch einmal anrufen?

Bevor wir mit der Beantwortung der Fragen fortfahren, möchte ich Sie noch darauf hinweisen, dass selbstverständlich alle Informationen, die Sie uns geben, streng vertraulich behandelt werden. Sind Sie damit einverstanden?

Sind Sie derzeit Raucher oder Nichtraucher? **wenn nein**: früher?	Raucher ☐ Nichtraucher ☐ Ja Wann aufgehört? Nein __________________
Machen Sie derzeit eine Diät?	Ja ☐ Nein ☐
Wie groß sind Sie?	
Wie viel wiegen Sie derzeit?	
BMI (kg/m²)	*Später errechnen, nicht fragen* *Varianz in beiden Gruppen ähnlich halten*
Waren Sie schon jemals in psycholog., psychotherap. oder psychiatrischer Behandlung?	Ja ☐ Nein ☐
Sind bei Ihnen neurolog. Erkrankungen aufgetreten? *Schlaganfall, Schädel-Hirn-Trauma, Sonstige*	Ja ☐ Nein ☐

Leiden Sie an Allergien?	Ja ☐ Nein ☐ *Zunächst alle Allergien ausschließen.*
Sind sie derzeit stark erkältet oder ist ihr Geschmackssinn anderweitig eingeschränkt?	Ja ☐ Nein ☐
Nehmen Sie regelmäßig Medikamente ein?	Ja ☐ Nein ☐ Wenn ja, welche?: ______________________________ ______________________________ *Nicht erlaubt sind:* *Psychopharmaka, Allergiemedikamente, Medik. mit Einfluss auf das autonome Nervensystem* *Okay sind: Kontrazeptiva*
Bei Frauen: Haben Sie regelmäßige monatliche Regelblutungen?	Ja ☐ Nein ☐ **Wenn ja:** Wann hat ihre letzte Regel angefangen? ____________________
Wenn Ausschluss: Frau/ Herr…, da wir in unserer Studie sehr strenge Einschlusskriterien haben, muss ich Ihnen leider mitteilen, dass Sie dieser Studie nicht teilnehmen können. Wenn wir aber Probanden für andere Studien suchen, würden wir sehr gern wieder auf Sie zurückkommen. Vielen Dank noch einmal für Ihr Interesse und Ihre Zeit.	

So, wir sind am Ende angekommen. Vielen Dank für Ihre Unterstützung Herr/Frau…

Soweit ich das anhand der Fragen beurteilen kann, sind Sie sehr gut für unsere Studie geeignet und ich würde Sie gern zu einem Termin einladen.

Ich möchte Sie bitten ab etwa 1 Stunde vor dem Termin nichts mehr zu essen.

Ich werde Ihnen noch eine Bestätigungsemail mit unserer Anschrift und genauem Datum und Uhrzeit zuschicken. Falls sie den Termin kurzfristig doch absagen oder verschieben möchten, rufen Sie bitte bei Frau Meemken (0341 9940-2431) oder bei Frau Menger (0341 9940-2214) an.

Email:________________________

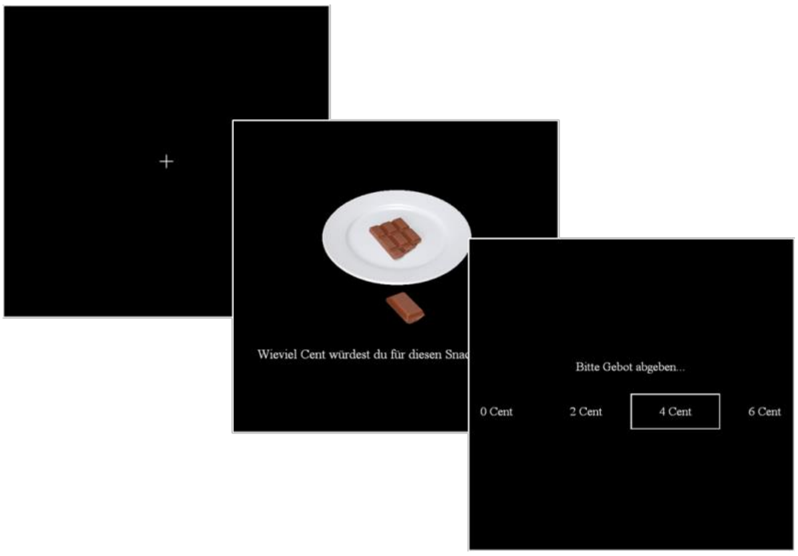
Termin:_______________________

Participant Instructions

Instruktion – Teil 1

In diesem Teil geht es darum, einen Snack auszuwählen, um den Sie im nachfolgenden Experiment spielen.

In jedem Durchgang wird Ihnen ein einzelner Snack präsentiert. Für jeden Durchgang haben Sie 6 Cent zur Verfügung. Ihre Aufgabe ist es, den Preis zu bieten (0, 2, 4 oder 6 Cent), den Ihnen ein einzelner Snack Wert ist, z.B. ein Stück Schokolade. Pro Snack haben Sie 4 Sekunden Zeit, um ein Gebot abzugeben.



Das Ganze läuft wie eine Auktion ab, bei der nach einer bestimmten Regel die Snacks versteigert werden. Nach jedem Durchgang wird ein zufälliger Preis zwischen 2 und 6 Cent aus einer Urne gezogen und mit dem Preis verglichen, den Sie geboten haben. Wenn Ihr Gebot höher oder gleich dem aus der Urne gezogenen Preis ist, haben Sie den Snack erfolgreich ersteigert und zahlen dafür den gezogenen Preis. Ist Ihr Gebot niedriger als der gezogene Preis, erhalten Sie den Snack nicht und bezahlen auch nichts dafür. Als Feedback sehen Sie einen…

…lachenden Smiley, wenn Sie einen Snack ersteigert haben

oder

…einen traurigen Smiley, wenn Sie keinen Snack ersteigert haben.

Am Ende des Experiments wird aus all den Durchgängen, in denen Sie erfolgreich waren, ein **zufälliger Durchgang** ausgewählt und Sie erhalten den **Snack** für den **gezogenen Preis.** Das **Restgeld** mal 100 (max. 4 €) dürfen Sie **behalten.**

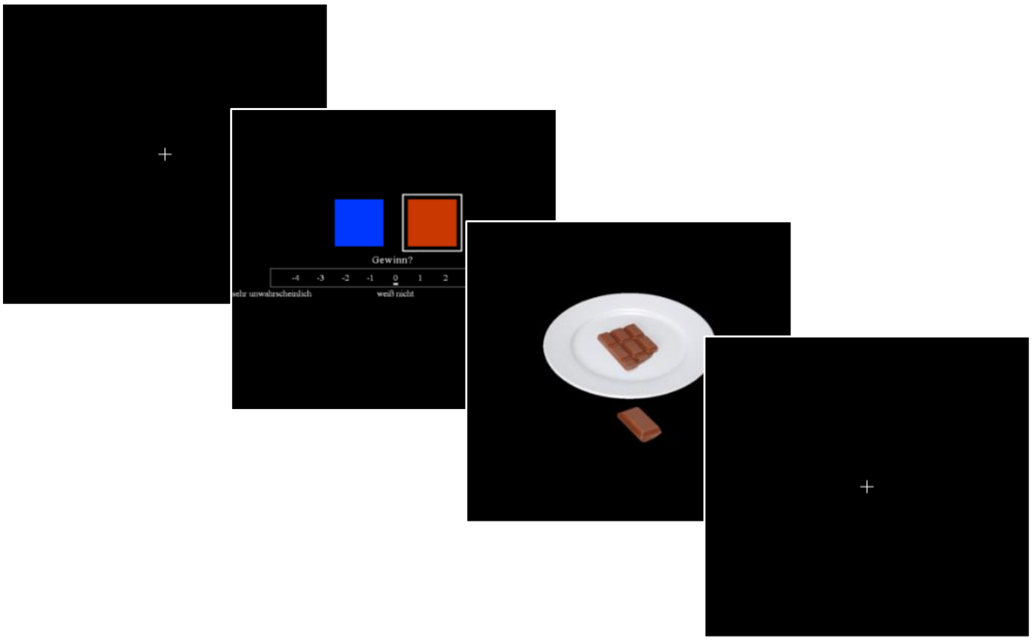
Die beste Strategie ist, möglichst immer den Preis zu bieten, den Ihnen der Snack Wert ist. Da der Preis, den Sie im Endeffekt zahlen, vom Ziehen aus der Urne abhängt, können Sie den Preis nicht durch Ihre Gebote beeinflussen. Würden Sie weniger bieten als der Snack Ihnen Wert ist, wäre es unwahrscheinlich, einen Snack zu ersteigern. Würden Sie mehr bieten als Ihnen der Snack Wert ist, besteht die Möglichkeit, am Ende zu viel für einen Snack zu bezahlen.
Haben Sie noch Fragen?

Teil 2 – Passiv – Instruktion
In diesem Experiment geht es darum, den Zusammenhang zwischen einer Farbe und einem Gewinn herauszufinden. Dieser Zusammenhang soll erlernt werden, um eine richtige **Vorhersage** treffen zu können. Es handelt sich dabei um einen **Lernprozess.**

In jedem Durchgang sehen Sie zwei Farben. **Eine der Farben** resultiert ab und zu in einem **Gewinn** – Die andere nicht.

Ein weißer Rahmen markiert die Farbe, um die es im jeweiligen Durchgang geht. Ihre Aufgabe ist es, mittels einer Skala eine Vorhersage zu treffen, wie wahrscheinlich ein nachfolgender Gewinn ist. Mit Hilfe der Antworttasten können Sie den Cursor auf einer Skala zwischen -4 (nicht wahrscheinlich) über 0 (weiß nicht) bis +4 (sehr wahrscheinlich) bewegen.

Ob ein Gewinn angezeigt wird, hängt davon ab, ob die weiß umrandete Farbe mit dem Gewinn zusammenhängt oder nicht (**nicht** von Ihrer Antwort). Ihre Aufgabe ist es, diesen Zusammenhang vorherzusagen. An Ihren Antworten sehen wir, ob Ihre Vorhersage richtig war.

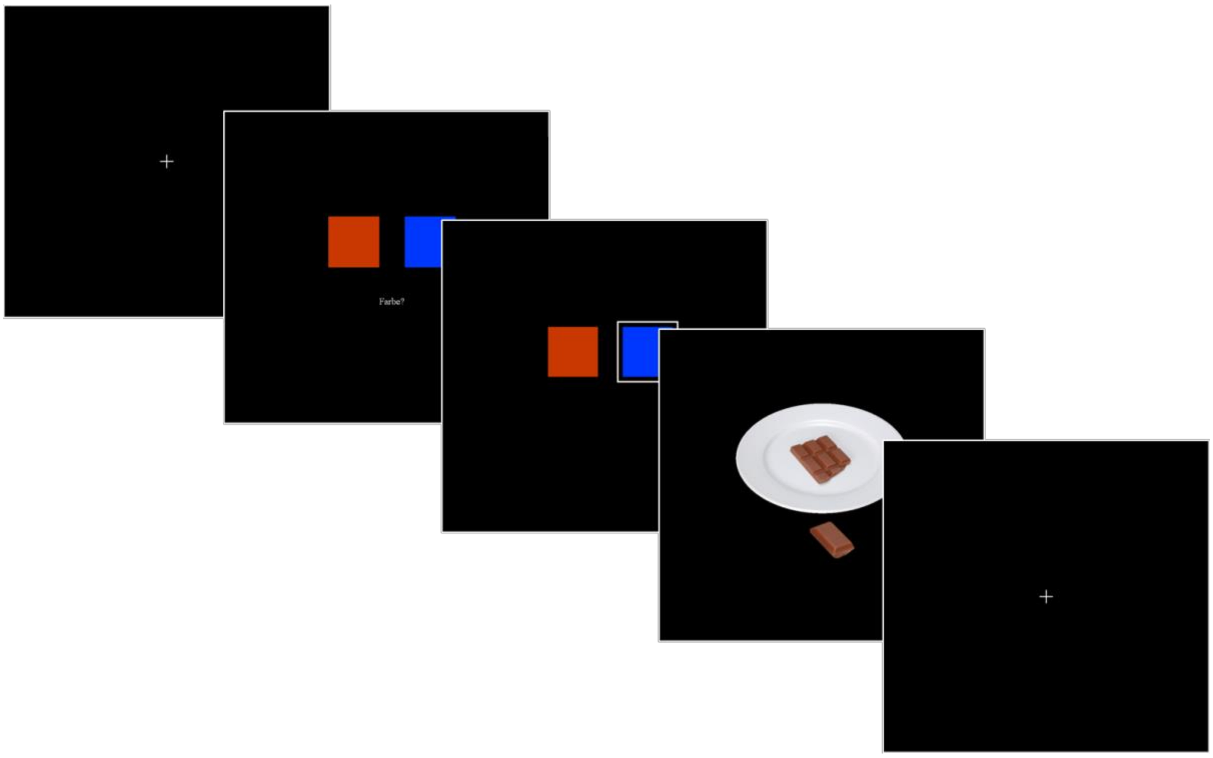


Je besser Ihre Vorhersagen sind, desto wahrscheinlicher ist es, einen zusätzlichen Bonus in Form eines Snacks oder in Form von Geld zu gewinnen. Dieser Bonus wird Ihnen im Anschluss an das Experiment ausgehändigt.
Der **Zusammenhang** zwischen einer Farbe und dem Gewinn kann sich nach einiger Zeit **verändern.**
Die Position der Farben spielt keine Rolle!
Haben Sie noch Fragen?

Teil 2 – Aktiv – Instruktion

In diesem Experiment geht es darum, den Zusammenhang zwischen einer Farbe und einer Belohnung zu beobachten. Dieser Zusammenhang soll erlernt werden, um eine richtige **Entscheidung** treffen zu können. Es handelt sich dabei um einen **Lernprozess.**

In jedem Durchgang sehen Sie zwei Farben. Bei **einer der Farben** können Sie ab und zu eine **Belohnung** erhalten. Die andere Farbe wird nicht belohnt. Ihre Aufgabe ist es, mit Hilfe der Antworttasten eine Farbe auszuwählen, die Ihrer Meinung nach zu einer Belohnung führt. Ein weißer Rahmen markiert die Farbe, die Sie gewählt haben.



Je besser Ihre Entscheidungen sind, desto wahrscheinlicher ist es, einen zusätzlichen Bonus in Form eines Snacks oder in Form von Geld zu gewinnen. Dieser Bonus wird Ihnen im Anschluss an das Experiment ausgehändigt.

Der **Zusammenhang** zwischen einer Farbe und einer Belohnung kann sich nach einiger Zeit **verändern.**

Die Position der Farben spielt keine Rolle!

Haben Sie noch Fragen?

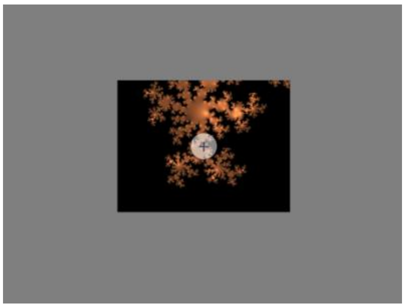
Instruktionen

Die folgende Aufgabe besteht aus zwei Teilen. Insgesamt dauert die Bearbeitung der Aufgabe 15 Minuten. Als Teil der Aufgabe werden Geschmacksstoffe über ein sogenanntes Gustometer ausgegeben. Es ist wichtig, dass diese Stoffe auf die Mitte der Zunge geleitet werden. Ihr Blick sollte sich auf das Zentrum des Bildschirms konzentrieren, um die Aufmerksamkeit auf die bearbeitete Aufgabe zu richten. Dazu gibt es als Stütze dort ein kleines Fixationskreuz.

Heute werden lediglich zwei Aufgabenteile bearbeitet. Die Aufgabe wird beim zweiten Termin sehr ähnlich ablaufen.

Im ersten der drei Teile soll nach freier Wahl eine von zwei möglichen Tasten gedrückt werden. Die Tasten bewirken die Ausschüttung eines Geschmacksstoffes. Wiederholter Tastendruck erhöht die Wahrscheinlichkeit und Menge dieser Ausschüttung. Es wird also nicht jeder Tastendruck belohnt. Ihre Aufgabe ist es, den Zusammenhang zwischen Taste und Geschmack zu lernen. Es werden 30 Aufgaben bearbeitet.

Im zweiten Teil der Aufgabe werden verschiedene Bilder gezeigt. Die Bilder sind mit Geschmacksstoffen assoziiert und es werden mit einer gewissen Wahrscheinlichkeit kleinere Mengen des Geschmacksstoffes ausgeschüttet, wenn das dazugehörige Bild gezeigt wird. Es erfolgt nicht auf jedes Bild eine Belohnung. Ihre Aufgabe ist es, den Zusammenhang zwischen Bild und Geschmack zu lernen. Es werden 67 Aufgaben bearbeitet.



Nach jedem Aufgabenteil gibt es eine einminütige Pause, während derer Sie Ihre Augen schließen oder einen Schluck Wasser zu sich nehmen können. Bitte stehen Sie jedoch nicht vom Computer auf, um zu sichern, dass Sie zum Beginn der nächsten Aufgabe und zum Lesen einer kurzen Instruktion teilnahmefähig sind.

Falls weitere Fragen bestehen, können Sie diese gerne dem Versuchsleiter stellen.

Authorship Declarations

[signatures not included in online publication of this document]

Authors' Contributions – Study 1

Title: Keeping track of promised rewards: Obesity predicts enhanced flexibility when learning from observation

Journal: Appetite (2018)

Authors: Marie T. Meemken*, Jana Kube*, Carolin Wickner, Annette Horstmann

* shared first co-authors

	MT Meemken	J Kube	C Wickner	A Horstmann
Study Design	x	x	x	x
Data Collection	x	x		
Data Analysis	x	x		x
Manuscript Draft	x	x		
Manuscript Revision	x	x		x

Dipl. psych. Jana Kube

Prof. Dr. rer. nat. Annette Horstmann

Authors' Contributions – Study 2

Title: Appetitive Pavlovian-to-Instrumental Transfer in Participants with Normal-Weight and Obesity

Journal: Nutrients (2019)

Authors: Marie T. Meemken, Annette Horstmann

	MT Meemken	A Horstmann
Study Design	x	x
Data Collection	x	
Data Analysis	x	x
Manuscript Draft	x	
Manuscript Revision	x	x

Prof. Dr. rer. nat. Annette Horstmann

Curriculum Vitae

[not included in online publication of this document]

Scientific Publications and Talks

Scientific Papers

Meemken, M.-T., Horstmann, A. (2019) Appetitive Pavlovian-to-Instrumental Transfer in Participants with Normal-Weight and Obesity. Nutrients 11(5), 1037, doi:10.3390/nu11051037.

Meemken, M.-T. & Kube, J., Wickner, C., Horstmann, A. (2018) Keeping track of promised rewards: Obesity predicts enhanced flexibility when learning from observation. Appetite, 131, doi:10.1016/j.appet.2018.08.029.

Lavallee, C. F., **Meemken, M.-T.**, Herrmann, C. S., & Huster, R. J. (2014). When holding your horses meets the deer in the headlights: Time-frequency characteristics of global and selective stopping under conditions of proactive and reactive control. Frontiers in Human Neuroscience, 8: 994. doi:10.3389/fnhum.2014.00994.

Poster Presentations

Meemken, M.-T. & Horstmann, A. (2017). Appetitive Pavlovian-to-Instrumental Transfer with taste stimulation in humans with and without obesity. Talk presented at 25th Annual Meeting of the Society for the Study of Ingestive Behavior (SSIB). Montréal, QC, Canada. 2017/07/18 – 2017/07/22.

Meemken, M.-T., Lavallee, C.F., Herrmann, C.S. & Huster, R.J. (2014) Dissociating Reactive and Proactive Control Mechanisms During Global and Selective Motor Inhibition. Poster session presented at the Annual Meeting of the Organization for Human Brain Mapping in Hamburg, Germany, 2014/06/08 – 2014/06/12.

Lavallee, C.F., **Meemken, M.-T.**, Huster, R.J. & Herrmann, C.S. (2013) Time-Frequency Characteristics of Reactive and Proactive Control Mechanisms during Global and Selective Response Inhibition. Poster session presented at the 53rd Annual Meeting of the Society for Psychophysiological Research in Florence, Italy, 2013/10/02 – 2013/10/06.

Lectures

Meemken, M.-T. (2015). Maladaptive plasticity in behavioral disorders and addiction. Lecture. Berlin School of Mind and Brain, Humboldt University Berlin, Germany, 2015/10/06 – 2015/10/08.

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