Addiction Biology

REVIEW

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Implications from addiction research towards the understanding and treatment of obesity

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ABSTRACT

Recent research indicates similarities between obesity and addictive disorders on both the phenomenological and neurobiological level. In particular, neuroendocrine and imaging studies suggest a close link between the homeostatic regulation of appetite on the on hand, and motivation and reward expectancy on the other. In addition, findings from neuropsychological studies additionally demonstrate alterations of cognitive function in both obesity and addictive disorders that possibly contribute to a lack of control in resisting consumption. In this review, recent findings on overlapping neurobiological and phenomenological pathways are summarized and the impact with regard to new treatment approaches for obesity is discussed.

Keywords Addiction, dependence, imaging, neurobiology, neuroendocrinology, obesity.

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INTRODUCTION

Recent findings on motivational processes in appetite regulation call into question the long-accepted assumption that body weight is exclusively regulated by the endogenous balancing of food supply and a metabolically controlled feedback on appetite. Thus, ingestion is not only initiated by an intrinsic sensation of hunger to ensure energy homeostasis, but is also via neuronal processes influenced by rewarding, i.e. positively reinforcing features of food. This exostatic system modulates the motivation for ingestion using information on the hedonic properties of food based on earlier experiences and expectations within the context, in which it is presented.

Adaptive processes within the motivational system, especially those associated with sensitisation and conditioning, are central elements in the pathophysiology of addictive disorders. As a consequence of these adaptive processes, subjects show an attentional and cognitive bias towards rewarding stimuli on the one hand, and a neglect of alternative, often vital actions, on the other hand (Loeber *et al*. 2009; von der Goltz & Kiefer 2009). If reactions of obese patients to food-associated stimuli (e.g. smell of food) are compared with reactions of addictive patients confronted with cues associated with their preferred substance, phenomenological similarities are obvious and recent neurobiological findings, especially from the fields of neuroendocrinology and imaging, support the idea of a close link between obesity and addictive disorders. Thus, in order to explain the ethiopathogenesis of obesity, models developed to describe the bases of addictive disorders might be helpful. For this purpose an integrative approach should be applied, including also models of homeostatic (dys-) regulation, which explain the maintenance of a positive energy balance for example by glucose dysallocation and set-point shift [Selfish-Brain Theory (Peters *et al*. 2007)].

The following article refers to recent findings demonstrating similarities between obesity and addictive disorders on a phenomenological and neurobiological level in order to allow an integrative reflection on these disorders.

EVOLUTIONARY AND PHENOMENOLOGICAL ASPECTS

The endogenous and exostatic system developed in an environment that can be characterized by an uncertain food supply and the necessity of food searching behaviour in order to ensure intake and conservation of appropriate amounts of energy. While homeostatic and exostatic systems only played a supplementary role during this

time, today, in a situation of increased food supply, exostatic factors are of high significance for the regulation of food intake and the development of overweight (Berthoud & Morrison 2008).

Similarities concerning the intake behaviour of obese and addicted patients are well known for quite a long time; they show a similar course of disease and patients often do not change their behaviour despite of negative health consequences. Both disorders usually become chronic and episodes of excessive consumption as well as phases of restriction or abstinence are observed, often ending up in relapses to old patterns of behaviour (Wadden 1993). Obese and addicted patients often show an impulsive intake behaviour associated with loss of control (Colles, Dixon & O'Brian 2008). Food, especially high-carbohydrate and high-fat food, seems to act as reinforcer similar to addictive drugs; consequently, behaviour 'rewarded' by carbohydrates or addictive drugs is performed more often (Epstein *et al.* 2007a)

In contrast to addictive drugs, the extent of the rewarding effect of food seems to be modulated by the current state of hunger, which in turn is influenced by homeostatic mechanisms. While the intake of the substance in addicted patients is usually only limited by aversive consequences (e.g. negative physical, psychological or social consequences), food intake is limited by saturation. Thus, for food intake two functions seem to be important: one that is controlling food intake by energy homeostasis and a second one controlling food intake by its reinforcing properties. In contrast, drugs have a reinforcing, rather dose-dependent, effect separated from energy homeostasis.

NEUROBIOLOGICAL ASPECTS

The development of addictive disorders is based on processes that are similar to physiological learning and contribute to their persistence (Hyman, Malenka & Nestler 2006; von der Goltz & Kiefer 2009). For the pathogenesis of addictive disorders reward-associated learning plays a major role. Substances of abuse have an activating effect on the dopaminergic mesolimbic reinforcement system ('reward system') and thereby stimulate learning processes leading to an attentional bias to possibly rewarding stimuli. The mesolimbic pathway comprises the ventral tegmental area (VTA) of the midbrain and connects to the limbic system via the nucleus accumbens (NAC), the amygdala and the hippocampus as well as the medial PFC. The release of dopamine to the NAC has been suggested to be responsible for the hedonic feeling of incentives, natural as well as artificial (Wise & Bozarth 1987) Already 10 years ago it was demonstrated that food, like addictive substances, activates the mesolimbic reward system and causes a short-term increase of dopamine in the NAC (Bassareo & Di Chiara 1999). Following restricted access to sucrose a decrease in D2 receptor binding in the NAC of rats was shown (Bello, Lucas & Hajnal 2002); moreover, rats with intermittent sugar and food access also showed reduction in D2 receptor mRNA in NAC compared with *ad libitum* food controls (Spangler *et al.* 2004). Mu-opioid receptor binding in NAC, cingulate, hippocampus and coeruleus was enhanced following three weeks of intermittent carbohydrate diet (Colantuoni *et al.* 2001).

Appetite-regulating peptides, especially leptin, ghrelin and orexin, possibly link the appetite and energy homeostatic regulating system, controlled by the lateral hypothalamus (LH), and the mesolimbic reward system. Recent studies (Figlewicz *et al.* 2003; Choi *et al.* 2010) show, that these hormones modulate via receptors in the ventral tegmentum of the midbrain (VTA) the activity of dopaminergic neurons that project to the NAC as part of the ventral striatum and to the PFC. These neural projections are elements of the mesolimbic reward system (Fig. 1).

Leptin is generated in the white adipocellular; high concentrations lead to a reduction of appetite via negative feedback mainly via the hypothalamus (Elmquist, Elias & Saper 1999). Recent data now suggest a direct effect of leptin on the transmission rate within dopaminergic synapses in the NAC. Leptin receptors are expressed in dopaminergic neurons of the ventral tegmentum of the midbrain (Figlewicz *et al.* 2003); intracranial leptin infusion reduces extracellular dopamine in the NAC about 35% (Krügel *et al.* 2003). In pre-clinical trials administration of leptin was associated with increased intracranial self-stimulation (Fulton, Woodside & Shizgai 2000) and alcohol self-administration (Kiefer *et al.* 2001b). Clinical trials demonstrate that leptin plasma levels are positively correlated with alcohol consumption and craving of alcohol-dependent patients (Kiefer *et al.* 2001a, 2005; Hillemacher *et al.* 2007). It is assumed that the leptin-mediated reduction of the basal dopaminergic activity in the mesolimbic system at least partly increases the rewarding effect of addictive substances (Kiefer & Wiedemann 2004).

Ghrelin is preferably produced as a peptide hormone in the gastric fundus and in the pancreas cells (Inui *et al.* 2004); a synthesis was also observed in the hypothalamus (Mondal *et al.* 2005). In contrast to leptin, ghrelin stimulates appetite, food intake and weight gain (Toshinai *et al.* 2003). Ghrelin receptors are located in dopaminergic neurons within the ventral tegmentum of the midbrain and stimulate the firing rate of neurons projecting to the NAC (Abizaid *et al.* 2006). There is a growing body of evidence that ghrelin increases feeding by acting on the mesolimbic dopaminergic pathways and not only via homeostatic energy centres. Pre-clinical studies show, that local administration of ghrelin into the VTA of mice

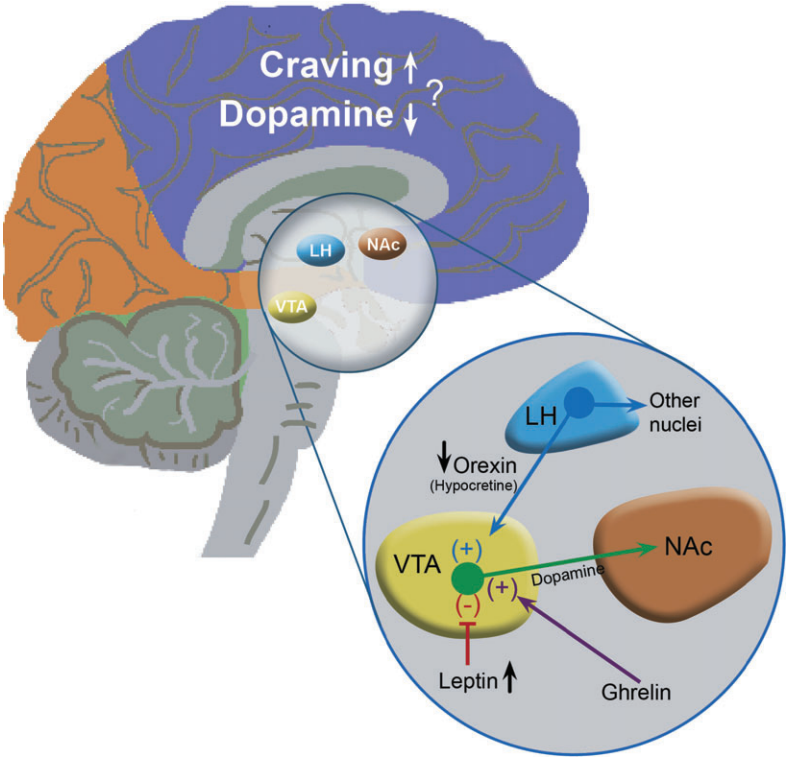

Figure 1 Appetite-regulating peptides such as leptin, ghrelin and orexin link energy homeostasis-regulating systems [lateral hypothalamus (LH)] with the mesolimbic system, where dopaminergic neurons project from the ventral tegmentum (VTA) to the nucleus accumbens (NAC). Recent findings indicate that an inhibition of the dopaminergic activity (high leptin, low ghrelin and orexin) correlates with an increase in craving for addictive substances

induced an increase of locomotor activity and an increase of dopamine in the NAC (Jerlhag *et al.* 2007) and that this activation is attenuated by VTA administration of a N-methyl-D-aspartartic acid (NMDA) antagonist (Jerlhag *et al.* 2010, 2011). As food intake has been shown to induce release of acetylcholine in the VTA (Rada *et al.* 2000), the observation that the unselective nicotinic antagonist mecamylamine significantly antagonized the stimulatory effect of local administration of ghrelin into third ventricle on locomotor activity and dopamine overflow in NAC indicates that these effects of ghrelin are also mediated by nicotinic acetylcholince receptors (nAChRs) (Jerlhag *et al.* 2006). In mice, both ghrelin receptor dysfunction and antagonism were shown to suppress the intake of rewarding food (Egecioglu *et al.* 2010). Ghrelin receptor antagonism was shown to decrease alcohol consumption in mice (Kaur & Ryabinin 2010); correspondingly, in alcohol dependence patients increased ghrelin plasma levels were shown (Kraus *et al.* 2005).

A third peptide connecting hypothalamic and mesolimbic regulation is *orexin* (hypocretin). Orexin is a peptide hormone that was originally associated with the regulation of ingestion (Sakurai *et al.* 1998) and the circadian rhythm (Chemelli *et al.* 1999). Orexin-producing neurons are located in the LH und project beside other brain regions to the ventral tegmentum of the midbrain. They are activated directly by hypoglycaemia as well as by other appetite-associated neuropeptides such as ghrelin and increase the urge for food intake. In contrast, hyperglycaemia and leptin inhibit the secretion of orexin (Kohno, Suyama & Yada 2008). Comparable with ghrelin, receptors for orexin were found in dopaminergic neurons. The injection of orexin in the ventral tegmentum of the midbrain stimulates dopamine release in the NAC (Narita *et al.* 2006), injecting in other brain regions (perifornical hypothalamus, LH) an increased ingestion (Sweet *et al.* 1999). A pre-clinical trial on alcohol-preferring rats further demonstrated that the pre-treatment with an orexin receptor antagonist prevents the resumption of alcohol consumption after exposure to olfactory alcohol stimuli (Lawrence *et al.* 2006). In addition, Choi *et al.* (2010) demonstrated in rats that blockade of orexin signalling attenuates reward-based feeding. Recently, a positive correlation of orexin plasma levels and nicotine craving among smokers as well as an inverse correlation with leptin plasma levels could be verified (Von der Goltz *et al.* 2010).

Studies to all three peptides support the hypothesis of a close link between homeostatic and motivational systems. In phases of a negative energy balance (hunger) the motivational system could direct the attention and orientation to caloric reinforcers and food-signalizing stimuli.

FINDINGS FROM IMAGING AND NEUROPSYCHOLOGICAL STUDIES

During the last decade findings from studies using functional magnetic resonance imaging (f-MRI) allowed

the examination of food effects on the dopaminergic mesolimbic system in humans. For example, Small, Zatorre & Dagher (2001) demonstrated that the consumption of chocolate activates the striatum with the NAC as receiver for dopaminergic projections. With regard to addictive disorders it is well known that drugs but also drug-associated stimuli activate the mesolimbic system (Goldstein & Volkow 2002; Heinz *et al.* 2004), thereby contributing to succumbing to craving and relapse (Grüsser *et al.* 2004). However, only recently, Rothermund *et al.* (2007) were able to demonstrate that not only food but also visual stimuli of high caloric food induce striatal activation in obese patients. Thus, the dynamic activation patterns in the mesolimbic system after presentation of food-associated stimuli are comparable with the ones found with regard to addictive behaviour and support the hypothesise of mechanisms of addictive behaviour in obesity. Furthermore, we found in an own investigation a significant positive correlation of stimuli-induced brain activation (left ventral striatum) in response to food stimuli and the BMI in individuals with normal- ($N = 6$, BMI 18,5–24) and overweight ($n = 9$, BMI > 30) suggesting a linear relationship between the activation of the mesolimbic system by food cues, food intake and the body mass (Grosshans *et al.* 2009).

In line with this, there are several studies using neuropsychological measures that demonstrated a close link between abnormal patterns of eating and addictive behaviour. Results from a visual probe task revealed for obese patients an enhanced automatic orientation towards food-associated stimuli. Such biases in the attentional processing of disorder-specific stimuli are well known for addictive disorders (for reviews see Franken 2003; Robbins & Ehrman 2004; Field & Cox 2008) and have also been demonstrated for other eating disorders (for a review see Faunce 2002; Dobson & Dozois 2004; or Shafran *et al.* 2007 and Smeets *et al.* 2008 for more recent experimental studies). In an own study (Loeber *et al.* 2009) we used a visual dot probe task and were able to demonstrate that alcohol-dependent patients are faster in reacting to a dot probe that was presented in the position of an alcohol-associated picture compared with a dot probe presented in the position of a neutral picture thus indicating attentional bias to alcohol-associated stimuli. For eating disorders an attentional bias to weight/body shape-associated cues as well as food cues has been demonstrated, but only recently, there are studies demonstrating an attentional bias to food cues also for obese individuals (Castellanos *et al.* 2009; Nijs *et al.* 2010). Thus, Castellanos *et al.* (2009) found that while obese and normal-weight individuals did not differ in attentional orienting towards food-associated stimuli during fasting, only obese individuals maintained the increased attention to food images after feeding and decreased self-report of hunger. In line with this, Nijs *et al.* (2010) report that overweight/obese individuals appear to automatically direct their attention to food-related stimuli, to a greater extent than normal-weight individuals, particularly when food-deprived. Using a bogus taste task they also demonstrated an increased food intake of obese patients compared with normal-weight controls in a laboratory setting.

In line with this, models of incentive sensitization of eating (Berridge 2007) and addictive behaviour (Robinson & Berridge 2000, 2008) these findings demonstrate a common mechanism of sensitization to disorder-specific stimuli and a close link of obesity and addictive disorders. Dysregulation of the dopaminergic mesolimbic brain reward system seems to play a key role for the development and maintenance of addictive behaviour as well as of obesity. Thus, findings could repeatedly be replicated, showing a reduced dopamine-D2-receptor availability in the closer region of the NAC (ventral striatum) in addicted patients [cocaine: (Volkow *et al.* 1993); amphetamines: (Volkow *et al.* 2001); alcohol: (Heinz *et al.* 2004)]. Comparable findings were also reported for obesity. In a raclopride PET study obese patients compared with normal-weight controls showed a reduced dopamine-D2-receptor availability (Wang *et al.* 2001). In this context it is especially important that the striatal D2-receptor availability was significantly negatively correlated with the body mass index (BMI); the more pronounced the obesity the lesser the dopamine-D2 availability (Wang *et al.* 2001).

Polymorphisms of dopamine receptor and transporter genes also have an impact on the degree of rewarding effects individually perceived during ingestion. Thus, a higher risk for the development of substance dependence and obesity could be verified for a polymorphism within the coding sequence of the D2 receptor (TaQ1 Al allele) associated with a reduction in the D2-receptor availability (Blum *et al.* 1996). Findings with regard to the reinforcing effects of ingestion in connection with the Taq 1-A1-allele in obese patients and patients with normal weight demonstrated that reinforcing effects and ingestion were significantly increased in obese patients with the Taq1-A1-allele (Epstein *et al.* 2007b). Recent f-MRT data examining the impact on food-associated pictures on the dopaminergic activity in the striatum underline the significance of this finding for obese patients: In patients with the Taq1 A1-allele more pronounced mesolimbic activation was found after presentation of food-associated stimuli (Stice *et al.* 2008). Following these results the authors conclude that excessive ingestion compensates for reduced striatal functionality and that the resulting positive energy balance leads to obesity. Nevertheless, it has been unclear whether such reward hyposensitivity in obese individuals is manifested before the development of obesity and related solely to genetic

factors (reward deficiency syndrome) or whether overeating can cause disruption in reward processing. Recent pre-clinical data with rats suggest that the access to high-caloric food causes a following significant down-regulation of d2-receptors and the development of addiction-like reward deficits and the onset of compulsive-like food seeking (Johnson & Kenny 2010).

Recent data allow the assumption that reduced dopamine-D2 receptor availability in patients with obesity is associated with a lower activity in the prefrontal region, the medial orbitofrontal cortex and the anterior gyrus cinguli (Volkow *et al.* 2008). Corresponding findings of an association of reduced D2 receptor availability and reduced prefrontal activity were reported for patients with metamphetamine and cocaine dependence (Volkow *et al.* 1993; Volkow *et al.* 2001). These findings support the hypothesises that in addition to the incentive salience of disorder-specific stimuli impairment of cognitive control processes (e.g. response inhibition) plays a crucial role for the maintenance of addictive behaviour as well as of obesity. The neurotoxic effects of chronic alcohol consumption and withdrawal from alcohol especially on the PFC (Kril *et al.* 1997; De Witte *et al.* 2003) and an association of frontal lobe function and impairment of executive function (Noel *et al.* 2001; Chanraud *et al.* 2007) are well described (see Moselhy, Georgiou & Kahn 2001 for a review). In line with this, Goldstein & Volkow (2002) put forward the idea of drug addiction as a syndrome of impaired response inhibition and salience attribution. The authors postulate that while stimuli that are regularly associated with the drug become especially salient, impairment of inhibitory control for conditioned drug-associated responses contributes to a loss of self-directed behaviour. Interestingly, there are also some studies demonstrating a link between obesity and an impairment of cognitive function supporting the idea that, like in addiction, incentive salience and impairments of cognitive control might be two central aspects of obesity. Obesity has recently been linked to Alzheimer disease, dementia and cognitive impairment (Jagust *et al.* 2005). Imaging studies demonstrated alterations in brain structure. For example, Taki *et al.* (2008) reported in men a significant negative correlation of the regional grey matter volume of the bilateral medial temporal lobes, anterior lobe of the cerebellum, occipital lobe, frontal lobe, precuneus and midbrain with the BMI. There are several factors that might mediate these associations including diabetes, hypertension and vascular disease. For example, leptin is highly correlated with components of the metabolic syndrome, and Holden *et al.* (2006) demonstrated that low serum leptin is associated with poorer cognitive functioning, independent of BMI. However, up to now, most studies investigating cognitive impairment of obese individuals are concentrating on cognitive impairment related to Alzheimer disease and degeneration of hippocampus volume. While Mobbs *et al.* (2008) used an affective go/no-go shifting task with food-related and object words and found that bulimics have inhibition problems and act impulsive, especially with food-related stimuli, to our best knowledge, there are no studies available investigating an impairment of inhibitory control processes in obese individuals. However, such studies are warranted as an impairment of cognitive control processes like inhibitory control might contribute to a loss of control in the presence of disorder-specific stimuli as assumed for addictive behaviour (Goldstein & Volkow 2002). Interestingly, comparing activation patterns to food-associated stimuli of weigth-loss maintainers and obese individuals, McCaffery *et al.* (2009) found greater activation to food cues of weight-loss maintainers in the left superior frontal region and right middle temporal region. This finding supports the assumption that impairment of prefrontal function might contribute to difficulties of obese individuals to resist external eating cues.

CONSEQUENCES FOR TREATMENT

Obesity is a major and cost-intensive health problem. For decades the prevalence of obesity has been increasing continuously on a worldwide scale, primarily in the United States (Ogden *et al.* 2006) as well as in Europe (Hyde 2008). Obesity is associated with a cluster of partly severe and cost-intensive somatic and psychiatric concomitant diseases, such as cardiac-vascular diseases, diabetes mellitus type II, orthopaedic long-term effects, cancer and depressive disorders. In addition, with increasing duration and grade of obesity, treatment is getting even more complicated and cost intensive (Weintraub *et al.* 1992). Further, even after significant weight loss, negative health consequences are often not reversible (Pi-Sunyer 1993).

As obesity is a disorder with an increasing prevalence for decades, effective prevention and therapy models are investigated including also modulation of environmental risk factors such as socioeconomic status as well as media consumption (Hebebrand & Hinney 2009). Previous prevention and therapy approaches in adults (Hoffmeister *et al.* 1996; Luepker *et al.* 1996) and children (Dorsey *et al.* 2005), targeting at a healthy lifestyle, weight loss and control of cardiovascular risk factors, only led to minimal effects concerning a long-term reduction of body weight or proved completely ineffective (Swinburn, Gill & Kumanyika 2005).

The fact that similarities exist between certain aspects of obesity and addictive disorders on a phenomenological and neurobiological level introduces new treatment possibilities that result from a closer reflection of obesity comparing certain aspects of addictive behaviour. During the

past decades the development of evidence-based psychotherapy for addictive disorders achieved a significant progress. At present, psychotherapeutic treatment is characterized by the combination of different evidence-based interventions to enhance abstinence motivation and to help the patient to develop coping strategies to successfully handle high-risk relapse situations. Motivational interviewing techniques (Miller & Rollnick 1999) and cognitive behavioural interventions are among the interventions with highest efficacy. For example, the review provided by Miller, Wilbourne & Hettema (2003) provides a ranking of evidence based interventions and lists the following cognitive-behavioural interventions within the first ten ranks: community reinforcement approach, self-change, self-control training, behaviour contracts, social competence training, communication and marital therapy. Similar results are provided by other reviews and meta-analysis and provide also evidence for the efficacy of cue exposure treatment (e.g. Chambless and Ollendick 2001; Berglund *et al*. 2003; Slattery *et al*. 2003). All these interventions aim at reducing the cognitive focusing on supposed rewarding stimuli mediate by the mesolimbic reward system or at minimizing this cognitive focusing by introducing alternative reinforcers (Kiefer & Mann 2007). For example, cue exposure treatment aims at an extinction of cue-associated conditioned responses by withholding the reinforcer, i.e. drug consumption. Community-based reinforcement approaches strengthen activities, which are incompatible with further substance consumption, for example by rewarding abstinence with vouchers. In contrast, motivational enhancement approaches try to help the patient to reflect on positive and negative consequences of his or her behaviour and to build up motivation for abstinence. Cognitive-behavioural coping training supports the patients in developing coping strategies for high risk relapse situations and thereby strengthens self-efficacy (Bandura 1977).

In contrast, motivational enhancement approaches try to help the patient to reflect on positive and negative consequences of his or her behaviour and to build up motivation for abstinence.

In Project Match, one of the largest treatment trials, three different behavioural interventions (motivation enhancement therapy, cognitive-behavioural therapy, 12-step facilitation therapy), were tested with the aim to enhance treatment efficacy by matching treatment interventions with a priori defined patients' characteristics (e.g. motivation to change, self-efficacy perception, personality characteristics). While the results demonstrated that all three interventions were effective with regard to the reduction of drinking behaviour, only limited evidence was found for an enhancement of treatment efficacy by matching (Project MATCH Research Group 1998). Similar results were reported in the United Kingdom Alcohol Treatment Trial (UKATT Research Team 2008) and suggest that apart from self-reported or behavioural criteria neurobiological aspects or genetic variants might be more effective to define subgroups with different treatment responses (Mann *et al*. 2009). Consequently, in Project Combine (e.g. Pettinati, Anton & Willenbring 2006) as well as Predict (Mann *et al*. 2009), the efficacy of a combined behavioural (integrating motivational interviewing, cognitive behavioural interventions and community reinforcement) and pharmacological treatment is tested and genetic and further objective measures are assessed to predict treatment success. The results suggest that behavioural as well as pharmacological treatment with Naltrexone is effective (Donovan *et al*. 2008) and support the idea that genetic variants can predict treatment response (Anton *et al*. 2008).

Based on the findings with regard to similarities between obesity and addictive behaviour reviewed above, it seems promising to adapt treatment approaches developed for addictive behaviour for the treatment of obesity. At present, the treatment of obesity is still focusing very much on adaption of a healthier lifestyle and nutrition schemas whereas cognitive-behavioural treatment interventions and the use of motivational interviewing techniques are not implemented systematically. However, psychotherapeutic treatment of obesity can be an important aspect of the treatment, especially with regard to long-term effects of maintaining weight loss (Garaulet & Pérez de Heredia 2009). At present, psychotherapeutic treatment interventions concentrate on self-control strategies with regard to eating, drinking and exercising, stimulus control techniques, contingence management and social support. Thus, in contrast to therapeutic interventions for addictive behaviour, strategies to address implicit attention and decision processes as well as techniques like cue exposure training to change cue-associated responses are less used. Basic aspects of the psychotherapeutic treatment of obesity could also include strategies to strengthen the patients' motivation to lose weight and to adhere to a healthy nutrition scheme, information about automatic responses to food-associated cues and the development of coping strategies to resist externally triggered urges to eat. For example, Harris, Bargh & Brownell (2009) demonstrated in several experimental studies that television food advertising primes automatic eating behaviours. In line with this, Boggiano *et al*. (2008) found in an animal study that context cues previously associated with overeating may trigger overeating relapses. Thus, patients should be aware of individual automatic cue-associated responses that might sabotage attempts to adhere to healthy reduced calorie regimens and therapists should support their patients in developing strategies to inhibit cue-associated responses and to resist overeating.

With regard to pharmacotherapy there is evidence for quite some time that substances developed for relapse prevention of addictive patients are effective for obesity as well—and vice versa. This can not only be regarded as further evidence for neurobiological pathways involved in both disorders, but also opens up new perspectives for a faster transfer and testing of pharmaceuticals successfully tested in addiction research. Exemplary substances for a cross efficacy in both disorders are substances such as cannabinoid antagonists (rimonabant, meanwhile withdrawn from sale (Volkow *et al.* 1993; Sweet *et al.* 1999), certain anticonvulsants (topiramate (Pi-Sunyer 1993; Johnson *et al.* 2007) and opiate antagonists [naltrexone (Mondal *et al.* 2005; Peters *et al.* 2007)]. All these substances have a modulatory effect on the dopaminergic mesolimbic system. Thus, new pharmaceuticals with a similar pharmacodynamic, which proved already efficacious for the treatment of addictive disorders (e.g. dopamine D3 antagonists or the corticotrophin-releasing hormone antagonists (Stice *et al.* 2008), should be tested for the treatment of obesity.

SUMMARY

Studies on phenomenological, neurobiological and neuropsychological similarities of obesity and addictive disorders underline the importance of a closer consideration of eating behaviour of obese individuals with regard to addictive mechanisms. Taking into account the increased incidence of obesity and adjunct concomitant disorders as well as a multiplication of the associated treatment costs, findings with regard to basic mechanisms of addictive behaviour and evidence-based treatment interventions should be applied, at least hypothetically, to this disorder, formerly mainly considered and treated by specialists for internal medicine. The examination of psychotherapeutic interventions primarily influencing motivational processes can be a first step in this direction. While both addiction and obesity have been considered as independent entities, the relevance of overlapping findings with regard to genetic vulnerability, neurobiological feedback mechanisms and effectiveness of psychopharmacological treatment approaches for the field of psychiatry is reflected at present in the discussion to include obesity as a disorder in the psychiatric chapter of the 5th revision of the Diagnostic and Statistical Manual of Mental Disorders (Devlin 2007; Volkow & O'Brien 2007). This contribution is supposed to encourage the discussion on this subject.

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Authors Contribution

All authors have critically reviewed content and approved final version submitted for publication.

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