Progress in Neurobiology xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Progress in Neurobiology

journal homepage: www.elsevier.com/locate/pneurobio

Obesity – A neuropsychological disease? Systematic review and neuropsychological model

Kamila Jauch-Chara *, Kerstin M. Oltmanns

Department of Psychiatry and Psychotherapy, University of Luebeck, Ratzeburger Allee 160, 23538 Luebeck, Germany

ARTICLE INFO

Article history:
Received 10 December 2012
Received in revised form 26 November 2013
Accepted 8 December 2013
Available online xxx

Keywords:
Body weight regulation
Psychosocial stress
Depression
Addiction
Reward centers

ABSTRACT

Obesity is a global epidemic associated with a series of secondary complications and comorbid diseases such as diabetes mellitus, cardiovascular disease, sleep-breathing disorders, and certain forms of cancer. On the surface, it seems that obesity is simply the phenotypic manifestation of deliberately flawed food intake behavior with the consequence of dysbalanced energy uptake and expenditure and can easily be reversed by caloric restriction and exercise. Notwithstanding this assumption, the disappointing outcomes of long-term clinical studies based on this assumption show that the problem is much more complex. Obviously, recent studies render that specific neurocircuits involved in appetite regulation are etiologically integrated in the pathomechanism, suggesting obesity should be regarded as a neurobiological disease rather than the consequence of detrimental food intake habits. Moreover, apart from the physical manifestation of overeating, a growing body of evidence suggests a close relationship with psychological components comprising mood disturbances, altered reward perception and motivation, or addictive behavior. Given that current dietary and pharmacological strategies to overcome the burgeoning threat of the obesity problem are of limited efficacy, bear the risk of adverse side-effects, and in most cases are not curative, new concepts integratively focusing on the fundamental neurobiological and psychological mechanisms underlying overeating are urgently required. This new approach to develop preventive and therapeutic strategies would justify assigning obesity to the spectrum of neuropsychological diseases. Our objective is to give an overview on the current literature that argues for this view and, on the basis of this knowledge, to deduce an integrative model for the development of obesity originating from disturbed neuropsychological functioning.

Contents

Abbreviations: ACC, anterior cingulate cortex; ACTH, adrenocorticotropin; ATP, adenosinetriphophate; BMI, body mass index; BT, behavioral therapy; cAMP, cycliccadenosine monophospate; CBT, cognitive behavioral therapy; CREB, cyclic AMP response element binding; CRF, corticotrophin-releasing factor; CRH, corticotropin-releasing hormone; DLPFC, dorsolateral prefrontal cortex; DSM, Diagnostic and Statistical Manual of Mental Disorders; FTO, obesity-associated gene; GLUT, glucose transporter; HPA axis, hypothalamus–pituitary–adrenal axis; LH, lateral hypothalamus; LTD, long-term depression; LTP, long-term potentiation; NA, nucleus accumbens; NHANES, National Health and Nutrition Examination Survey; NPY, neuropeptide Y; PCr, phosphocreatine; PFC, prefrontal cortex; tDCS, direct current stimulation; TMS, transcranial magnetic stimulation; VMH, ventromedial nucleus of hypothalamus; VTA, ventral tegmental area; WHO, World Health Organization.

* Corresponding author. Tel.: +49 0451 500 6342; fax: +49 0451 500 3480.
E-mail address: kamila.jauchchara@uk-sh.de (K. Jauch-Chara).

0301-0082/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.pneurobio.2013.12.001

1. Introduction

In recent years, the prevalence of obesity has reached epidemic proportions. While in the 1980s the National Health and Nutrition Examination Survey (NHANES) estimated that 32.1% of people in the United States were overweight (body mass index [BMI] between 25 and 30 kg/m^2) and 15.0% were obese (BMI $\geq$ 30.0 kg/m^2), data from 2007 to 2008 indicate that 68.0% of US adults had a BMI $>$ 25, of whom 33.8% met the definition of obesity (Flegal et al., 2010). Currently, the World Health Organization (WHO) estimates that over 1 billion people around the globe are overweight and 300 million are obese (Waxman and Norum, 2004; Ford and Mokdad, 2008). It is predicted that by the year 2020 almost half of all American adults will meet the WHO criteria for obesity (Stewart et al., 2009) and that by 2030 almost 90% will display a BMI $>$ 25.0 (Wang et al., 2008). In the United States, the proportion of the population meeting the clinical definition of obese has tripled in the last 20 years (Bessesen, 2008), while in Europe the prevalence of obesity has also increased over the past decades. In the 1980s, 15% of males and 22% of females had a BMI $\geq$ 30 (The WHO MONICA Project, 1988) whereas in the 2000s up to 28.3% of men and 36.5% women were considered obese (Berghofer et al., 2008).

Obesity, however, does not limit itself to a metabolically regulated matter of visual appearance but, much more importantly, has a number of severe consequences on the individual's overall health status. Data suggest an association between obesity and poorer health-related quality of life due to chronic disorders, smoking, and alcohol abuse (Sturm and Wells, 2001). A BMI $\geq$ 30 is considered a major risk factor for cardiovascular diseases (Ogden et al., 2007; Manson et al., 1995) and type 2 diabetes mellitus (Field et al., 2001; Oguma et al., 2005). Apart from this health hazard, excess weight gain also represents an enormous economic burden and results in one of the most extensive cash disbursements in national health care budgets (Wolf and Colditz, 1998). In the United States, for example, the overall direct costs of obesity treatment in 1995 were 2.7 times higher than those for arterial hypertension therapy (Finkelstein et al., 2003). By 1998, however, obesity related medical expenses were estimated to be as high as $78.5 billion, while they accounted for an estimated 10% of total annual US medical expenses, i.e. $147 billion, in 2008 (Finkelstein et al., 2009).

To date, treatment of obesity has been fraught with disappointment for attending physicians as well as concerned subjects. Available therapeutic interventions for obesity such as diet, exercise, and pharmacological therapy are only promising for the duration of the actual treatment interval, while body weight reduction frequently regresses after a return to previous nutritional habits. Initially, diets (Sacks et al., 2009), exercise (Miller et al., 1997), and drug therapy (Rucker et al., 2007) indeed result in weight loss but, unfortunately, weight regain after discontinuation of the treatment as well as the lack of distinction between achievement and maintenance of weight loss (Mark, 2006; Wing et al., 2008) limit their efficacy in the long run. One must thus recognize that the factual causes of the obesity epidemic as well as the underlying mechanisms that control food intake behavior are still incompletely understood. In fact, there is a dichotomous conception of pathomechanisms, varying from a simple imbalance between energy intake and energy expenditure, to thrifty or 'saver' genes and the unhealthy modern lifestyle, up to metabolic or neuroendocrine alterations. This conceptual inhomogeneity reflects general disorientation in the attempt to solve the problem and illustrates the urgent need for a new and more efficient approach. In the following review we discuss traditional views, explain why current treatment strategies do not meet their expectations at this point, provide a synthesis of current findings indicating a close relationship between obesity and neurobiological as well as psychological aspects of overeating, and describe a model in which obesity development and the functional systems of stress and reward perception are integrated.

2. Conventional models of obesity genesis

2.1. Excessive food intake and lack of physical activity

At first glance, obesity is a consequence of excessive food intake accompanied by a lack of physical activity in everyday life (Webber, 2003). It is currently considered that the type of food consumed, i.e. trans-fats and refined white flour carbohydrates in conjunction with low fiber content, may play an important role in the development of obesity. Indeed, data indicate that the high density, high palatability and widespread availability of food, high frequency of meals, boosted energy density of nutrients, and the preference for snacks over full meals all promote energy overconsumption, whereas concomitantly technical progress as well as sedentary occupational and leisure-time activities reduce the level of physical activity (French et al., 2001). Moreover, advertisements that declare high carbohydrate and energy dense foods as 'low fat products' falsely imply that these foodstuffs are of

Please cite this article in press as: Jauch-Chara, K., Oltmanns, K.M., Obesity – A neuropsychological disease? Systematic review and neuropsychological model. Prog. Neurobiol. (2014), http://dx.doi.org/10.1016/j.pneurobio.2013.12.001