Physiology & Behavior 103 (2011) 59–68

Contents lists available at ScienceDirect

Physiology & Behavior

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

Western diet consumption and cognitive impairment: Links to hippocampal dysfunction and obesity

Scott E. Kanoski [a], Terry L. Davidson [b,*]

[a] University of Pennsylvania, Department of Psychology, Philadelphia, PA, United States
[b] Purdue University, Department of Psychological Sciences, West Lafayette, IN, United States

ARTICLE INFO

Article history:
Received 24 September 2010
Received in revised form 5 November 2010
Accepted 4 December 2010

Keywords:
Ingestive behavior
Pavlovian
Dementia
Alzheimer's Disease
Hippocampus

ABSTRACT

Intake of saturated fats and simple carbohydrates, two of the primary components of a modern Western diet, is linked with the development of obesity and Alzheimer's Disease. The present paper summarizes research showing that Western diet intake is associated with cognitive impairment, with a specific emphasis on learning and memory functions that are dependent on the integrity of the hippocampus. The paper then considers evidence that saturated fat and simple carbohydrate intake is correlated with neurobiological changes in the hippocampus that may be related to the ability of these dietary components to impair cognitive function. Finally, a model is described proposing that Western diet consumption contributes to the development of excessive food intake and obesity, in part, by interfering with a type of hippocampal-dependent memory inhibition that is critical in the ability of animals to refrain from responding to environmental cues associated with food, and ultimately from consuming energy intake in excess of that driven solely by caloric need.

1. Introduction

Obesity and Alzheimer's Disease (AD) are two of the most serious and costly health challenges facing Western cultures. Since 1980, the prevalence of obesity in the United States has increased by 75%, with fully one third of men and women now classified as obese [1]. Obesity is a main component of what is termed the "metabolic syndrome," which also includes glucose intolerance, insulin resistance, high triglyceride levels, low levels of high density lipoprotein (HDL) density, and hypertension as primary characteristics [2]. There is currently little agreement about the causes of the continuing rise in obesity, and treatments that can stem or reverse this trend have not yet been developed. Similarly, the incidence of AD in the global population is projected to increase four-fold over the next 40 years [3], afflicting as many as 14 million people in the United States alone by 2050 [4]. AD is characterized by a severe, age-related decline in memory and cognitive functioning. At present, there is no cure for AD and its root causes remain elusive. In addition to the high cost in terms of quality of life, the estimated annual U.S. healthcare costs for the victims of obesity and AD presently exceeds $140 billion [5] and $170 billion [6], respectively. Thus, identifying risk factors and strategies for preventing or delaying the onset and progression of both of these disorders is of paramount importance.

Traditionally, investigators have viewed the problems of obesity and related metabolic disorders on one hand (e.g., Type II Diabetes Mellitus, hypertension) and AD and cognitive dementias on the other, as involving distinct etiologies, which target different underlying behavioral and biological functions that rely on largely separate brain structures and circuits. For example, it is abundantly clear that manipulations of the hypothalamus (e.g., surgical, genetic, hormonal) can have profound effects on eating and body weight gain for experimental animals and that increases in energy intake and body weight regulation in humans are accompanied by marked changes in hypothalamic neurohormonal signaling pathways [7]. In contrast, the hippocampus is the site of structural abnormalities associated with early stages of AD and other cognitive dementias [8,9]. In fact, the hippocampus is preferentially susceptible compared to other brain regions to a variety of insults (e.g., environmental toxicants, cardiovascular and metabolic perturbations) that have cognitive dysfunction as their signature symptoms [10]. In addition, findings that selective removal of the hippocampus is accompanied by specific types of learning and memory impairment have also focused much research attention on the hippocampus as a substrate for amnesias and other forms of cognitive decline [11].

In spite of these differences, evidence is beginning to accumulate for important commonalities in the etiologies of both energy dysregulation and cognitive impairment. Specifically, saturated fats and refined carbohydrates are the principal components of a "Western diet" that are believed to promote excess energy intake and body weight gain [12]. Several recent studies have also linked elevated intake of saturated fat and simple sugars to increased incidence of AD

* Corresponding author.
E-mail address: davidson@psych.purdue.edu (T.L. Davidson).

0031-9384/$ – see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.physbeh.2010.12.003

[13–15] and milder forms of cognitive dysfunction (e.g., [16–19]). In addition, several recent reports indicate that selective hippocampal damage in rodents and pathologies that are largely confined to the hippocampus in humans are associated with increased energy intake [20,21] and meal frequency (e.g., [22]). Thus, there is evidence suggesting that dietary factors are associated with the emergence of hippocampal pathology and that hippocampal pathology is associated with the emergence of increased food intake and body weight gain.

This paper has two main objectives: our primary aim is to review evidence that Western diets impair cognitive functioning, with special emphasis on the functions of the hippocampus. To achieve this objective, we will consider findings from studies that link consumption of saturated fats and simple carbohydrates to the development of cognitive dementias, including AD and mild cognitive impairment (MCI), a diagnosis given to individuals that exhibit deficits in memory, language, or other mental functions that exceed what is expected as part of normal aging, but that do not interfere significantly with their daily activities [23]. We will also assess the nature of learning and memory processes that may be altered by these diets and we will consider the possibility that such alterations are based on interference with the function of the hippocampus. Our second goal is to consider the hypothesis that the disruptive effects of Western diets on learning and memory function also contribute to the ability of these diets to promote excess food intake and body weight gain. Although diets high in saturated fats and sugars tend to be energy dense, this fact in itself does not explain why animals overeat them. That is, given that energy regulation depends on matching energy intake with energy expenditure, intake of Western diets in excess of energy needs reflects a failure of energy regulation. We will consider the possibility that this failure is based, in part, on disruption of hippocampal-dependent learning and memory processes that underlie control of appetitive behavior.

2. Components of Western diets associated with cognitive dysfunction

Although Western diets contain various combinations and concentrations of different sources of macro- and micronutrients, research has focused primarily on cognitive impairment produced by consumption of two of the primary components of that diet, namely saturated fats and simple sugars.

2.1. Saturated fats

Fatty acids are categorized into saturated fatty acids (SFA) and unsaturated fatty acids, including mono (MUFA) and polyunsaturated (PUFA) fatty acids. While intake of PUFAs, particularly Omega-3 fatty acids, is considered to be protective against cognitive decline (see [24] for review), intake of SFA appears to have the opposite effect. For example, data from cross-sectional (e.g., [25]) and longitudinal population-based studies (e.g., [26]) have shown that intake of SFA is correlated with impaired cognitive function. Morris and colleagues have evaluated the relationship between intake of dietary fats and the development of cognitive decline and dementia in humans in a series of population-based prospective studies that focused on age-related cognitive change. They reported that, for subjects aged 65 years and older, high intakes of SFA, but not total fat, over four- and six-year periods led to a greater risk for the development of AD and MCI [27,28]. In a more recent longitudinal prospective study, Eskelinen et al. [17] examined the relationship between SFA intake by humans and the development of clinical MCI 21 years later. The authors found that abundant dietary SFA was associated with an increased risk of developing MCI. However, cognitive impairment was not global, but tended to be more pronounced in specific types of learning and memory tasks. More specifically, SFA was associated with impaired performance in a test of prospective memory, which involves memory based on performing an intended action at some future time [29]. On the other hand, performance in other mnemonic domains, such as immediate verbal memory and semantic memory, was not linked with SFA intake.

One limitation in the studies described above is that differences in body mass index (BMI) or adiposity were not accounted for, thus making it difficult to dissociate the effects of SFAs on cognitive function from their effects on the development of body weight gain and obesity. However, relationships between SFA intake and cognitive decline have been found after adjusting for measures of hypertension (blood pressure, etc.) and the presence of adult-onset (i.e., Type II) diabetes [17,19], both of which are strongly correlated with BMI in humans [30].

Evidence from studies employing rodent models is also consistent with the hypothesis that SFA intake can lead to cognitive impairment. Greenwood and Winocur have shown that consumption of a high SFA diet with a complex carbohydrate source can impair learning and memory performance in rats (e.g.,[31,32]). One study [33] evaluated the effects of 3 months exposure to a diets high in either SFA, polyunsaturated fatty acids (PUFAs), or monounsaturated fatty acids (MUFAs) on the ability of rats to learn an appetitive operant conditioning task. They found that the rats receiving the SFA diet were impaired in learning the task, whereas intake of PUFAs or MUFAs had little impact on performance relative to a low fat control diet. Thus, diets high in SFA appear to have a larger disruptive effect on cognitive function in rodents relative to diets high in unsaturated fats or low in total fat.

2.2. Simple carbohydrates

Simple carbohydrates (mono and disaccharides, e.g., glucose, sucrose) are considered a major part of Western diets [34]. They can be differentiated from complex carbohydrates (polysaccharides, starch) based on a higher glycemic index, which is a measure of the effect that ingested substances have on postprandial blood glucose levels. Evidence shows that consumption of a meal containing simple carbohydrates can impair postprandial memory function relative to intake of complex carbohydrates. For instance, the effects of consuming a meal with a high or a low glycemic index on postprandial memory performance was examined in adult subjects with well controlled Type II Diabetes Mellitus (T2DM) [35]. It was found that the high glycemic meal led to poorer performance in memory tests that were given between 1 and 2 h after eating. Similarly, other studies have found that a higher relative to a lower glycemic load for a meal (i.e., higher glycemic index) can lead to poorer memory performance in nondiabetic subjects, including children [16] and normal weight undergraduate female subjects ([36], but see [37]). These studies suggest that consumption of simple relative to complex carbohydrates can impair postprandial memory performance in humans. Epidemiological and experimental research is needed to examine the possibility that *longer-term* intake of simple carbohydrates can also have a detrimental impact on cognitive function in human populations.

Perhaps more compelling evidence for a role of simple carbohydrate intake in cognitive impairment comes from a recent study that examined the effects of sucrose intake on performance in a novel object recognition task in rats [38]. This task is based on the tendency of rats to prefer the exploration of novel compared to familiar objects. Rats are familiarized with an object in a first phase, and are then presented with the familiar and a novel object in a second phase. Failure to explore the novel object more than the familiar object in the second phase can be interpreted as a memory deficit [18,38]. Rats given chronic daily access to a sucrose solution (32% sucrose solution) in addition to standard chow were impaired in learning and memory performance compared to rats that only received chow access, whereas performance was not affected in rats given chow