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Western-style diet impairs stimulus control by food deprivation state cues: Implications for obesogenic environments ☆

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ABSTRACT

In western and westernized societies, large portions of the population live in what are considered to be "obesogenic" environments. Among other things, obesogenic environments are characterized by a high prevalence of external cues that are associated with highly palatable, energy-dense foods. One prominent hypothesis suggests that these external cues become such powerful conditioned elicitors of appetitive and eating behavior that they overwhelm the internal, physiological mechanisms that serve to maintain energy balance. The present research investigated a learning mechanism that may underlie this loss of internal relative to external control. In Experiment 1, rats were provided with both auditory cues (external stimuli) and varying levels of food deprivation (internal stimuli) that they could use to solve a simple discrimination task. Despite having access to clearly discriminable external cues, we found that the deprivation cues gained substantial discriminative control over conditioned responding. Experiment 2 found that, compared to standard chow, maintenance on a "western-style" diet high in saturated fat and sugar weakened discriminative control by food deprivation cues, but did not impair learning when external cues were also trained as relevant discriminative signals for sucrose. Thus, eating a western-style diet contributed to a loss of internal control over appetitive behavior relative to external cues. We discuss how this relative loss of control by food deprivation signals may result from interference with hippocampal-dependent learning and memory processes, forming the basis of a vicious-cycle of excessive intake, body weight gain, and progressive cognitive decline that may begin very early in life.

Introduction

The control of energy intake and body weight involves the interplay between food-related environmental cues and physiological signals arising from the internal milieu. For example, environmental food cues are often thought to evoke learned appetitive and eating behaviors whereas internal satiety signals suppress the evocation of those responses (Woods, 2004). Within this framework, excess energy intake and body weight gain result when the power of environmental cues to evoke feeding behavior exceeds the ability of internal signals to inhibit feeding.

This shift toward external relative to internal control of intake has been described as a consequence of living in what has been termed an "obesogenic" environment (e.g., Swinburn et al., 2011). Obesogenic environments are characterized by an abundance of low cost, energy-dense, highly palatable foods and beverages. It is thought that external cues associated with these foods and beverages can become strong elicitors of eating. Furthermore, sophisticated marketing and advertising practices maximize exposure to these cues and heighten their salience. It has been hypothesized that these external factors combine to overwhelm the capacity of internal physiological control mechanisms to prevent positive energy balance and avoid body weight gain (e.g., Corsica & Hood, 2011; King, 2013; Zheng, Lenard, Shin, & Berthoud, 2009). The result has been high and/or growing rates of obesity, especially in western or westernized societies where obesogenic environments are most prevalent (e.g., Malik, Willett, & Hu, 2013; Sturm & Hattori, 2013).

Of particular relevance to this Special Issue of Appetite, obesogenic environments have also been linked to excessive weight gain in children and adolescents (Osei-Assibey et al., 2012; Saelens et al., 2012). For example, rates of childhood obesity are elevated in neighborhoods with higher compared to lower numbers of fast food outlets (Carroll-Scott et al., 2013). Obesity rates are also higher for children that attend schools in neighborhoods with relatively

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high numbers of convenience stores and fast food restaurants (Wasserman et al., 2014; but see Williams et al., 2014). In addition, the results of some studies show that exposure to TV advertising for energy-dense foods (Andreyeva, Kelly, & Harris, 2011; Boyland et al., 2011) and receptivity to this type of advertising are positively correlated with childhood BMI (McClure et al., 2013).

Similar to the population at large, the incidence of obesity has doubled in children ages 6–11 and tripled in adolescents ages 12–19 since 1980 (Ogden, Carroll, Kit, & Flegal, 2012). In addition, like their adult counterparts, children that are overweight or obese exhibit increased risk factors for Type II diabetes, hypertension, and other comorbidities (Daniels et al., 2005). Obese children are also likely to become obese adults – at which time the severity and range of threats to health and quality of life are magnified (Freedman et al., 2005; Guo & Chumlea, 1999).

One of the most pernicious of these threats is cognitive decline. Previous research has identified obesity and increased body adiposity in mid-life with the development of late-life cognitive dementias such as Alzheimer's disease (Gustafson, 2008; Whitmer, 2007). As several reports in the current issue confirm (e.g., Convit et al., Verdejo-Garcia et al., Nederkoorn et al., Kahn et al., Bruce et al.), evidence is also accumulating that obesity is associated with impaired cognitive functioning in children and adolescents (Kamijo et al., 2012; Liang, Matheson, Kaye, & Boutelle, 2014; Schwartz et al., 2013). These links raise concerns that excessive weight gain and obesity in childhood increase the risk for more serious cognitive disorders that are usually diagnosed much later in life (Elias, Goodell, & Waldstein, 2012; Smith, Hay, Campbell, & Trollor, 2011).

We think that an important first step toward addressing these concerns is to consider why so many people of all ages have such difficulty resisting the temptations of the obesogenic environment. To say that the physiological controls of intake are overwhelmed by an onslaught of environmental cues that goad us to eat provides only a partial answer. A more complete account must identify and explain the mechanisms that initiate and maintain this hypothetical change in the relationship between the physiological and environmental controls of intake.

Previously, we proposed a model that describes how both internal cues corresponding to hunger and satiety and external cues associated with foods and the postingestive consequences of eating participate in the *learned* control of energy intake and body weight (e.g., Davidson, Sample, & Swithers, 2014; Davidson, Tracy, Schier, & Swithers, 2014). One purpose of the current research is to assess the extent to which these internal cues are able to compete with external cues for the control of conditioned appetitive behavior when both types of cues are valid signals of food reward. A second goal is to examine the hypothesis that dietary factors common to obesogenic environments can weaken the internal relative to external controls of intake. Based on the findings of the present experiments and the results of earlier work, we will also consider how the mechanisms that underlie such a diet-induced shift from internal toward external control of intake may be related to deficits in certain types of cognitive functions.

The rationale for our present studies is based largely on three sets of previous findings. First, research in our laboratory has shown that rats can use the interoceptive stimulus consequences of different levels of food deprivation as discriminative cues for the delivery of either mild shock (e.g., Davidson, 1987) or sucrose pellets (e.g., Davidson et al., 2005). Evidence for this learning has been obtained after as few as three reinforced trials (Davidson, Flynn, & Jarrard, 1992), and discriminative control generalizes from cues produced by food deprivation and satiation to hormonal manipulations that are known to promote or suppress feeding behavior (e.g., exogenous administration of ghrelin (Davidson et al., 2005) or CCK and leptin (Kanoski, Walls, & Davidson, 2007), respectively). These latter findings confirm that interoceptive cues arising from hunger and satiety, rather than exteroceptive stimuli produced by features of the deprivation regimen, were the basis of discriminative responding.

Second, other studies have shown that the ability of rats and humans to use their interoceptive energy or hydrational state cues as discriminative stimuli depends on the functional integrity of the hippocampus (e.g., Francis & Stevenson, 2011; Hebben, Corkin, Eichenbaum, & Shedlack, 1985; Hirsh, Leber, & Gillman, 1978). For example, hippocampal lesions have been shown to impair discriminative responding when cues produced either by different levels of food deprivation or by food versus water deprivation serve as discriminative stimuli (Davidson & Jarrard, 1993; Davidson et al., 2010; Kennedy & Dimitropoulos, 2014; Kennedy & Shapiro, 2009). In contrast, simple discrimination performance based on conventional auditory and visual cues is largely unaffected by hippocampal damage (e.g., Jarrard & Davidson, 1991).

Third, studies have shown that rats maintained on a western-style diet high in both saturated fat and sugar exhibit impairments on a variety of learning and memory problems that are known to depend on the hippocampus. These same rats are not impaired in learning simple discriminations and other learning and memory problems that are hippocampal-independent (Davidson et al., 2012; Hargrave et al., in this issue; Kanoski, Zhang, Zheng, & Davidson, 2010; Molteni, Barnard, Ying, Roberts, & Gomez-Pinilla, 2002). Rats maintained on these diets also exhibit signs of brain pathologies such as increased blood–brain barrier permeability, elevated markers of hippocampal inflammation, and reduced levels of brain neurotrophic factors (Grayson et al., 2013; Hsu & Kanoski, 2014; Kanoski et al., 2007; Miller & Spencer, 2014; Molteni et al., 2002; Sobesky et al., 2014). Moreover, pathological symptoms have been observed most prominently in rats that also showed both heightened sensitivity to the obesity-promoting effects of these diets and impaired hippocampal-dependent learning and memory performance (Davidson et al., 2012, 2013). These findings establish a link between the ability of these diets to promote weight gain and their ability to disrupt hippocampal-dependent learning and memory functions.

Considered together, these three sets of findings indicate that (a) interoceptive stimuli arising from different levels of food deprivation can gain associative control over behavior; (b) the hippocampus is a neural substrate for this type of associative control, but for not simple associative learning about external stimuli; and (c) consuming a high-saturated fat, high-sugar diet characteristic of obesogenic environments is associated not only with obesity but also with the development of hippocampal pathologies and impairments in hippocampal-dependent learning and memory processes. Against this backdrop, this paper evaluates the possibility that diets high in saturated fat and sugar interfere with hippocampal functioning and thereby reduce the control of energy intake by internal relative to external cues.

Experiment 1

Our theoretical framework suggests that appetitive behavior is normally under the joint control of external food-related cues and interoceptive cues related to hunger and satiety. Experiment 1 assessed this hypothesis by training rats with both food deprivation cues and external cues as compound discriminative cues for sucrose pellets. After asymptotic discrimination performance was achieved, the external cues were removed to assess discriminative control by deprivation cues alone. Then, following retraining with the deprivation cue/external cue compound, rats were tested with the discriminative contingencies reversed for the external cues, while the deprivation cue contingency remained the same. Thus, the training contingencies of the deprivation cues were now in opposition to the training contingencies of the external cues (i.e., the