Editorial

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Do impaired memory and body weight regulation originate in childhood with diet-induced hippocampal dysfunction?[1–3]

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Previous research has identified obesity and increased body adiposity in midlife with late-life cognitive dementias such as Alzheimer disease (1). However, there is also evidence that cognitive deficits related to obesity may begin decades earlier (2). For example, recent reports have linked high BMI and body adiposity in children and adolescents to deficits in indexes of inhibition, cognitive flexibility, and decision making and with increases in impulsivity and perseverative errors (3)

There are reasons to suspect that intake of the Western diet, so-named because of its widespread popularity in Western and westernized societies, is an important contributor to both obesity and cognitive dysfunction. Rodents that are maintained on a diet with a composition similar to the Western diet (ie, high in saturated fat and sugar) exhibit increased blood-brain barrier (BBB) permeability and selective accumulation of exogenous substances in the hippocampus. Reducing the protection provided by the BBB appears to increase the vulnerability of the hippocampus to pathologies including elevated concentrations of proinflammatory cytokines, intrusion of microglia, reduced concentrations of brain-derived neurotrophic factor, and disruption of neurohormonal signaling (4). Moreover, these diet-induced effects have often been accompanied by impaired performance on hippocampal-dependent, but not on hippocampal-independent, learning and memory tasks (5).

In this issue of Journal, Baym et al (6) provide supporting evidence that consuming a Western diet is associated with hippocampal dysfunction in children aged 7–9 y. Specifically, they found a significant correlation between intake of saturated fat (self-reported by the children with the help of their parents) and performance on a hippocampal-dependent relational memory task. In contrast, the consumption of foods high in omega-3 fatty acids, which are not a major component of the Western diet, was positively and significantly correlated with relational memory performance. In their study, intakes of saturated fats and omega-3 fatty acids were not significantly correlated with IQ or with performance on the Flanker test of inhibitory executive function. These outcomes make it difficult to attribute the effects on memory of either dietary component to nonspecific (eg, sensory, attentional) factors or to a global impact on cognitive functioning. A somewhat surprising finding was that item memory performance, which has been described as hippocampal independent, was also negatively correlated with intake of saturated fats. This finding indicates that further study is needed to understand the brain structures and functions that are affected in children who consume a Western diet.

The relative roles of saturated fat and sugar in producing the adverse effects of the Western diet also merit additional investigation. Baym et al found that sugar consumption by the children in their study was not significantly correlated with relational or item memory performance. But as the authors noted, in other studies, intake of refined sugars has been associated with learning and memory impairments in both rodents and adult humans. On the other hand, consuming saturated fats is not always bad. Ketogenic diets, which are very high in saturated fats (~80% of energy) and very low in carbohydrate (~5% of energy), are reported to have beneficial effects on metabolic functioning (7), and a recent study from our laboratory found that rats maintained on a ketogenic diet exhibited no deficits relative to feed pellet–fed controls on either hippocampal-dependent or hippocampal-independent learning and memory problems (8). Thus, the combination of saturated fats and sugars may be what makes the Western diet harmful. The children studied by Baym et al also consumed sugar. Perhaps the amount of sugar they consumed exceeded the threshold level needed for the negative effects of dietary saturated fats to be manifested.

Also of interest, Baym et al reported that the BMI of the children in their study was not a strong predictor of memory performance. This outcome indicates that elevated body weight per se is not a good predictor of hippocampal dysfunction. However, it leaves open the converse possibility that hippocampal dysfunction is a reliable predictor of subsequent excess body weight gain. The memory of a recent meal has been shown to reduce subsequent intake (9). If the ability to retrieve the memory of recent meals is impaired by hippocampal dysfunction then overeating and weight gain could ensue (10). In addition, hippocampal damage impairs the ability of rats to use interoceptive cues arising from different levels of food deprivation as discriminative cues (11). If the intake of a Western diet also disrupts

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hippocampal function, this could promote weight gain by impairing the ability to use interoceptive hunger and satiety cues to control intake. Other findings have shown that, for rats fed a Western diet, impairments in a hippocampal-dependent spatial memory task occur before significant excess body weight gain (12). Another study showed that performance by rats on a hippocampal-dependent discrimination problem measured after 24 d with a Western-style diet was strongly and negatively correlated with body weight measured after 90 d of being fed the diet. In contrast, body weight at 24 d with the Western-style diet was not significantly correlated with discrimination performance after 90 d of being fed that diet. These results support the hypothesis that diet-induced hippocampal deficits precede weight gain (5). Considered together with the results of Baym et al, these findings suggest that it might be possible to use performance on relational memory or other hippocampal-dependent tasks to identify children who are most at risk of subsequent weight gain and obesity.

Determining causality from the relations found by Baym et al will require new intervention trials. Nonetheless, their findings suggest the possibility that the emergence of serious memory dysfunction later in life might be traced to the intake of Western diet in childhood (2, 3). If so, therapeutic interventions administered in childhood, when pathophysiologic and functional changes in the hippocampus are just beginning, could provide long-lasting protection from both cognitive deficits and obesity when those children become adults. The results of Baym et al also suggest that a shift away from saturated fats to omega-3 fatty acids may have this desired effect. However, given the widespread popularity and attractiveness of the current Western diet, this type of transition may be very difficult to accomplish.

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