J Physiol 590.12 (2012) p 2831

TRANSLATIONAL PERSPECTIVES

Sugar highs and lows: the impact of diet on cognitive function

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In Western society, the prevalence of a hypercaloric diet consisting of a high sugar intake and highly processed foods coincided with an exponential rise in diabetes and metabolic syndrome as well as cardiovascular diseases and cancer. Evidence emphasizing the unfavourable effects of 'irresponsible eating' is emerging in regards to the big three Western diseases . . . cardiovascular disease, diabetes and cancer. Recent evidence has emerged supporting the connection between dietary intake and cognitive health, particularly in regards to the ageing population. A healthier diet during middle age years (B-vitamins, antioxidants, polyunsaturated fatty acids, etc.) was associated with better cognitive function later in life (Kesse-Guyot *et al.* 2012). In addition, higher polyphenol intake in the elderly was associated with better cognitive performance (Valls-Pedret *et al.* 2012). However, data on the effects of diet on learning, memory and cognition are scarce. Bowman *et al.* demonstrate a positive association between nutrient biomarker intake, cognitive function and brain volume (Bowman *et al.* 2012). Instead of providing additional data on a healthier diet and cognitive outcomes, the study by Agrawal and Gomez-Pinilla in a recent issue of *The Journal of Physiology* is one of the first to describe the negative consequence of a diet on learning and cognition (Agrawal & Gomez-Pinilla, 2012). The authors elegantly investigate the metabolic consequences of a high sugar intake coupled with a deficiency of omega-3 fatty acids on cognitive abilities and the potential association with insulin action and signalling mediators. As one might expect, the unhealthy diet (high fructose intake, low omega-3 fatty acids) was associated with lower cognitive scores and insulin resistance.

In the vasculature, insulin is a vasodilator and increases blood flow to promote glucose delivery to the muscle and other tissue beds. This vasodilator function is blunted in insulin resistant individuals and suggests that an impairment of insulin action is coupled to a decreased perfusion of the tissues (Barrett *et al.* 2009). Obviously, chronic hypoperfusion to any tissue bed induces a multitude of problems (atrophy, etc.) and may further reduce insulin sensitivity. The same insulin/blood flow coupling mechanism may also be present in the cerebral circulation. Agrawal & Gomez-Pinilla demonstrate that animals with the highest insulin resistance index also have the longest latency time on a learning and memory challenge. Accordingly, we might expect that the animals with the highest insulin resistance may demonstrate a lower cerebral blood flow, and therefore less brain plasticity. In other words, insulin resistance and impairment of the insulin receptor signalling cascade in the hippocampus may be accompanied by decreasing regional blood flow and reduced memory.

In humans, cerebral hypoperfusion is associated with lower cognitive function scores, and with dementia and lower brain volume (Rabbitt *et al.* 2006). Preventing or delaying the cognitive decline is of paramount importance with the expanding ageing population. The study by Agrawal & Gomez-Pinilla suggests that consuming omega-3 fatty acids and preventing insulin resistance may protect learning and memory ability with ageing. We might also suggest that maintaining optimum cerebral perfusion is also an important mechanism to preserve cognitive function. Along these lines, dietary interventions thought to improve peripheral perfusion or vascular function may also be operative in the brain. For example, the vasoprotective effects of a high nitrate diet shown in the periphery (Webb *et al.* 2008) and similar favourable changes in cerebral blood flow were recently reported after a high nitrate whole-food based dietary intervention (Presley *et al.* 2011). A similar case could be made for exercise interventions, which have parallel benefits on vascular function in the periphery and cerebral circulation, and are also associated with higher cognitive function scores. In summary, the study by Agrawal & Gomez-Pinilla provides mechanistic evidence linking poor dietary health and cognitive impairment. This observation is consistent with the idea that many important risk factors for cognitive decline with ageing have major effects on the vasculature. These risk factors include: diabetes, hypertension, hyperlipidaemia, sleep apnoea and physical inactivity. How these risk factors might interact with other pathophysiological mechanisms that contribute to cognitive decline is poorly understood, but the good news is that they are modifiable and that lifestyle-related public health guidelines are almost certainly protective against age-related cognitive decline.

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DOI: 10.1113/jphysiol.2012.234328