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Editorial: Nutrition Research Reviews

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Editorial

Cognitive performance in children and whether this can be improved by nutritional means is an area of investigation fraught with experimental challenges, making it difficult to draw useful conclusions. Hoyland *et al.*⁽¹⁾ have here provided a much-needed systematic review of the evidence on the specific question of the effects of breakfast on children's cognitive performance and, unsurprisingly, have concluded that the effects are generally positive, most clearly shown for memory and attention tasks and most easily demonstrated in nutritionally vulnerable children. However, the benefits of food before schoolwork are not necessarily purely, or even mostly, physiological; they could be due to some other factors associated with the meal provision, such as improved motivation to learn due to the reduction of hunger, or better attendance when the breakfast is provided at school. Given the poor quality of much of the research to date, the review concludes with a series of suggestions for future studies, including their design, power, the type and amount of food provided and its potential mechanisms of action, the timing and breadth of cognitive tasks tested and, finally, the need to investigate the effect of breakfast in adolescents. In the meantime, it is surely worthwhile, though not necessarily easy in the case of the last age group mentioned, to encourage the consumption of breakfast by schoolchildren, many of whom (even the relatively affluent) currently skip it. Breakfast skippers are also likely to have a higher BMI and be overweight than breakfast eaters; however, the question as to whether eating habits affect the development of visceral adipose tissue in children and adolescents has not been much addressed, according to Suliga⁽²⁾ in her review. This author argues strongly that more work is needed in these age groups in order to inform us as to how best to prevent the development of visceral fat and its potential health consequences (type 2 diabetes and CVD). The evidence shows that, perhaps surprisingly, visceral adipose tissue deposition seems to be somewhat independent of general fatness in children and adolescents, but is influenced by genetic factors, ethnicity, growth and maturation (including the levels of sex hormones). Some interventions that might be beneficial in preventing visceral fatness among children and adolescents include the promotion of physical activity and the prevention of smoking and alcohol consumption, though much more research into lifestyle factors, including dietary ones, is needed in order to clarify which are most important, and how they could best be improved.

Prevention of CVD is the theme of the review by Sirtori *et al.*⁽³⁾, who consider the possible protective role of functional foods against dyslipidaemia and CVD. A welcome addition to the list of potential ingredients (soluble fibre, phytosterols and stanols, soya protein, legumes including lupins, and *n*-3 fatty acids) is dark chocolate, which has been shown to prevent dyslipidaemia and hypertension. Other recent candidates (with a seasonal flavour!) include

nuts, cinnamon and a resin from the myrrh tree superbly named 'guggul gum' or 'guggulipid', though more work is needed on these. However, the results from trials investigating tea and coffee are controversial, and vitamin E's effects are at best confusing (due to its multiple forms), and at worst actually disadvantageous with respect to CVD prevention. Alcohol and nicotine abuse are potential hazards to be negotiated at this time of year; their effects on the brain at the molecular level are here discussed by Flatscher-Bader & Wilce⁽⁴⁾, who describe the pathways leading to addiction, understanding of which may eventually lead to the ability to identify individuals predisposed to alcohol and/or tobacco abuse (they tend to go together) and hopefully the development of effective treatments.

Seasonal lack of sunlight in northern latitudes is a known route to vitamin D deficiency, now increasingly recognised as a problem even in 'sunny' countries, particularly among those with dark skin. However, as pointed out by Wang⁽⁵⁾, in a critical review of the analytical techniques used to evaluate vitamin D status, there is a lack of standardisation among the assays (liquid chromatography–MS and various immunoassays) used to measure serum 25-hydroxyvitamin D, making it difficult to compare data from different studies. Nonetheless, there is strong epidemiological evidence linking vitamin D status with bone health, muscle strength and several other diseases, notably CVD, type 2 diabetes, autoimmune diseases and several cancers. These associations are further explored by Borrodale & Kimlin⁽⁶⁾, who note that the epidemiological evidence is inconsistent and fraught with confounding factors (such as obesity), and that therefore large intervention trials are still needed to confirm causal linkages. The discovery of vitamin D receptors in many tissues has generated much research interest into possible mechanisms by which the vitamin (actually a steroid hormone) might exert its protective effects, which have so far been shown to include immunomodulatory and even antimicrobial roles. Somewhat ironically, therefore, the vitamin created by the action on skin of UV light, a known carcinogen, may prove to have a key role in cancer prevention. Dietary Ca has also been shown to protect against certain cancers, independently from the effects of vitamin D, though of course the two are intimately connected physiologically; the possible molecular mechanisms involved are here examined by Centeno *et al.*⁽⁷⁾ in the context of low-Ca diets. It seems that these might cause dysregulation of proliferative and apoptotic pathways that lead to the development and progression of cancer of the colon, breast, prostate and ovaries. These authors also argue that, in the case of breast cancer, dysregulation of the vitamin D endocrine system could also be involved via a reduced response of breast cells to calcitriol and promotion of oncogenic transformation. The paradoxical hypertensive effect of low-Ca diets could also be explained via vitamin D, i.e. low Ca causing raised circulating levels

of 1,25-dihydroxyvitamin D₃, which would stimulate Ca influx into vascular smooth muscle, increasing vascular tone and hence raising blood pressure; conversely, high-Ca diets suppress vitamin D₃ production and thus reduce blood pressure. Ca also affects lipid metabolism and lipogenic genes in adipocytes, as well as cortisol production, perhaps contributing to visceral fat deposition among those with low dietary Ca intakes.

Visceral adipose tissue is known to release pro-inflammatory cytokines, which in turn damage endothelial cells (leading to CVD) and adversely affect glucose metabolism (leading to insulin resistance, type 2 diabetes and CVD). Thus anti-inflammatory drugs or supplements could be beneficial in prevention of these diseases. van der Spuy & Pretorius⁽⁸⁾ examine the case for the use of resveratrol, an increasingly popular, naturally occurring (in grapes) phenolic substance, which has been shown in animal models to be anti-inflammatory, vasoprotective and insulin-sensitising. It also has anti-cancer effects (*in vitro*) and can apparently act as an anti- or pro-oxidant depending on the dose and context. However, these authors highlight some areas of concern in the prolonged use of resveratrol supplements for treatment of obesity and other ailments, especially among children, since there is some evidence (in mice) that it causes kidney toxicity at relatively low doses (pro-oxidant effect). The safety in the long term of this supplement therefore needs to be tested in both adult and young animals before it should be recommended.

The most important endogenous cellular antioxidant is the tripeptide glutathione, the synthesis of which requires cysteine (rate-limiting). This amino acid can itself be generated from homocysteine by the trans-sulfuration pathway (in the liver, kidney, intestine, pancreas and adrenals), an alternative pathway for homocysteine metabolism to its folate- and B₁₂-dependent methylation to methionine (i.e. the methionine cycle) occurring in most cells. As well as this role, cysteine, along with the other sulfur amino acids (and their derivatives, notably S-adenosylmethionine; SAM), is involved in numerous other biological functions (as well as protein synthesis), as described by Bauchart-Thevret *et al.*⁽⁹⁾. These authors focus on the intestine as an important player in sulfur amino acid metabolism, and its functional and nutritional importance in health and disease. Dietary cysteine and methionine metabolised in the intestine are important for normal intestinal mucosal growth. Further, these authors argue that SAM could play a key role in epigenetic regulation (via methylation of DNA) of gene expression in intestinal epithelial cells, and hence affect intestinal cell survival and proliferation, while the redox role of glutathione could be influential in the prevention of bowel cancer and also, possibly, inflammatory bowel diseases.

Gut metabolism in ruminants is the theme of the review by Patra & Saxena⁽¹⁰⁾, who address the economically and ecologically important question of the role of saponins in

modifying the microbial population and fermentation in the rumen, and ruminant production. Saponins are naturally occurring phytochemicals which, when added to the feed, modify the composition of the microbial population in the rumen in a rather specific manner that can be manipulated by the type and concentration of saponin used. Improved efficiency of microbial protein synthesis (and hence improved protein flow to the duodenum) is an effect which would have commercial implications (due to improved feed efficiency), while the inhibition of the production of the greenhouse gas methane would ameliorate the effect of ruminant production on global warming. More research is needed in this area in order to achieve consistent beneficial effects, but clearly the achievement of ruminant production strategies that are 'greener' than at present is a goal well worth striving for.

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