METABOLIC SYNDROME : A DISEASE OF THE BRAIN.

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Introduction: Association between brain dysfunction and pathogenesis of metabolic syndrome leading to cardiovascular diseases, type 2 diabetes and insulin resistance are reviewed.
Methods: Medline search till Dec, 2009 and articles published in various national and international journals were reviewed. Experts working in the field were also consulted.
Results: Increased intake of refined carbohydrates, linoleic acid, saturated and total fat and low dietary n-3 fatty acids and other long chain polyunsarurated fatty acids(PUFA) in conjunction with sedentary behaviour and mental stress and various personality traits can predispose inflammation and central obesity. There may be increased sympathetic activity with increased secretion of catecholamine, cortisol and serotonin and proinflammatory cytokines that appear to be underlying mechanisms of metabolic syndrome. Excess secretion of these neurotransmitters in conjunction of underlying long chain PUFA deficiency, may damage the neurons via proinflammatory cytokines, in the ventromedial hypothalamus and insulin receptors in the brain, especially during fetal life, infancy and childhood, resulting into their dysfunction. Since 30-50% of the fatty acids in the brain are long chain PUFA, especially omega-3 fatty acids, which are incorporated in the cell membrane phospholipids, it is possible that their supplementation may be protective.Omega-3 fatty acids are also known to enhance parasympathetic activity and increase the secretion of anti-inflammatory cytokines IL-4 and IL-10, as well as acetylecholine in the hippocampus. It is possible that marginal deficiency of long chain PUFA, especially n-3 fatty acids, due to poor dietary intake during the critical period of brain growth and development in the fetus and infant, and also possibly in the child, adolescents and adults, may enhance the release of tumor necrosis factor-alpha, interleukin-1,2 and 6 and cause neuronal dysfunction. Experimental studies indicate that ventromedial hypothalamic lesion in rats induces hyperphagia, resulting into glucose intolerance and insulin resistance. Treatment with neuropeptide Y abolished the hyperphagia and ob mRNA(leptin mRNA) in these rats. Longterm infusion of norepinephrine and serotonin into the ventromedial hypothalamus, impaired pancreatic islet function in as much as, ventromedial hypothalamic norepinephrine and serotonin levels are elevated in hyperinsulinemic and insulin resistant animals. Treatment with insulin was associated with restoration of these hypothalamic neurotransmitter abnormalities indicating that a dysfunction of ventromedial hypothalamus can impair pancreatic beta cells resulting into metabolic abnormalities consistent with metabolic syndrome. Treatment with omega-3 fatty acids, meditation, beta blockers, ACE inhibitors, and oestrogen may have a beneficial influence on insulin receptors and ventromedial hypothalamic dysfunction. However, no definite and precise insight into the patho-physiological link between metabolic syndrome and brain and nutrition is available. Despite this weakness, epidemiological studies and intervention trials indicate that treatment with n-3 fatty acids may be applied to clinical practice and used to direct therapy for prevention of type 2 diabetes, hypertension, coronary artery disease, and atherosclerosis, indicating that metabolic syndrome may also respond to this treatment.

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