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GASTROINTESTINAL CANCER AND THERAPEUTICS

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CANCER SCIENCE AND TARGETED THERAPIES

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ACS-HOMS: The aberrancy in CNS signals and other factors related to altered homeostasis, obesity and metabolic syndrome

Introduction: ‘The obese-obese world’: The obesity and metabolic syndrome (MetS) are a global epidemic of such magnitude that the today’s health scenario can be summed up as the ‘Obese-obese World’. Obesity and MetS deteriorate the quality of life and alter course of various chronic diseases, and on their own, are risk factors for diabetes, hypertension, cardiovascular disease and stroke, neurological degenerative diseases and cancers. Modern day lifestyle drives for excess calorie intake, comparatively reduced energy expenditure and storage of surplus energy in adipose tissue, an accentuated evolutionary need to fill body nutrients stores, leading to obesity, appended by pathophysiological alterations termed MetS.

The regulation of energy intake: Specialised neurons in hypothalamus and brainstem primarily regulate energy homeostasis, food intake, and body weight, and integrate multiple peripheral metabolic inputs, such as nutrients, gut-derived hormones, and adiposity-related signals. There are several neuropeptides involved, including melanin-concentrating hormone (MCH) and the orexins. An abnormal alteration in ghrelin and leptin levels can lead to weight gain and obesity. Increase in adipose tissue leads to overproduction of leptin and hypothalamus resistant to leptin action. The reward circuitry involves interactions between several systems including opioids, endocannabinoids, serotonin, and dopamine. The obese individuals appear to have abnormalities in dopaminergic activity, and an imbalance in the brain circuits promoting reward seeking and those governing cognitive control leads to an overriding stimulus to feeding, even in the absence of an energy deficit. Dorsal striatum is hyperactive in obese and may contribute aberrancy of satiety signals. The genetics involving various mutations contribute up to 70% towards a person’s vulnerability to obesity.

The regulation of energy expenditure: Energy is consumed in processes of physical activity, basal metabolism, and adaptive thermogenesis, which are modulated by the brain, especially the hypothalamic melanocortin system. Brown adipose tissue (BAT) plays a major role in thermogenesis. Central regulation of BAT thermogenesis is dependent on sympathetic outflow to BAT. Norepinephrine released from sympathetic nerve terminals binds to β 3-adrenergic receptors on adipocytes in BAT to promote enhanced thermogenesis. In addition, many hormonal and nutrient signals, such as glucose, insulin, leptin, and GLP-1, also influence sympathetic outflow to BAT.

Conclusion: Fallouts of surplus energy storage: The obese subjects with BMI >30 show atrophy in the frontal lobes, anterior cingulate gyrus, hippocampus, and thalamus. MetS affects various cognitive domains including executive functioning, processing speed, and overall intellectual functioning. There is impaired vascular reactivity, endothelial dysfunction, neuroinflammation, oxidative stress and altered brain metabolism.

Biography

Vinod Nikhra is a consultant and faculty at NDMC Medical College and Hindu Rao Hospital, a multispecialty, thousand bedded, public hospital, New Delhi. He is an MD in Internal Medicine and qualified and trained in nephrology, endocrinology, and cardiology, and hospital management, and Fellow of International Medical Sciences Academy and Royal Society of Medicine, London. He has been Editor of “Madhya: the midage”, the official Journal of Association for Health in Middle-Aged, on Editorial Board of Open Access Journal of Gerontology and Geriatric Medicine, on Reviewer panel of, among others, the Family Practice, an Oxford University medical journal and International Journal of Obesity. He is Author of four books, which include his widely acclaimed books, ‘Aging slowly, Living longer’ and ‘The Anti-obesity Guide’, and over 60 papers in international, national and other journals, some of which are available on www.researchgate.net. He has travelled widely and participated and spoken over in various international Conferences. Some of his talks are available on YouTube.

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