

An Overview of the Neurological Consequences of Obesity and Diabetes

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Citation: Chrysanthus Chukwuma SR (2020) An Overview of the Neurological Consequences of Obesity and Diabetes. J Neurosci Neuropsych 3: 106

Abstract

Obesity and type 2 diabetes are both inextricably-linked conditions which have been indicted in neurological aberrations. However, rigorous research modalities have not been upto date, even though, the scourge has reached pandemic proportions. Neuroamine and neuroendocrine systems are involved in mediating impairment of the hippocampus in obese and diabetic patients in areas associated with memory and are expansively susceptible to neurological perturbation. In such instances, encompassing care must involve inter alia blood sugar restoration and sustenance, weight reduction and control of several cardiovascular disease risk factors because comorbid obesity and diabetes enmesh with coagulopathy and endothelial dysfunction. Accelerating incidence of the comorbidity poses an enormous burden on healthcare, thus requiring medical intervention of life-long stringent control and treatment for complications arising due to neuropathy and cognitive dysfunction.

Keywords: Comorbid; Brain Atrophy/Shrinkage; Age; Therapy; Sedentary Lifestyle

Introduction

Globally, the presence of obesity is accelerating in leaps and bounds with its encompassing effect on diverse organs and systems of the body culminating in debilitating conditions. Due to the invariable impacts of obesity with resultant dysfunctional presentations in disparate regions of the human body including the neurological aspects, there is every probability of heterogeneity at the population level [1]. Thus, necessitating an ecological analysis of obesity at the population level.

One of the main issues of obesity is the coexistence with one or more of certain disorders, such as cancer, cardiovascular disease or elevated cardiovascular risk, hypertension and diabetes [2,3].

Diabetes prevalence and comorbid brain dysfunctions are accelerating globally, especially in LMICs with encumbrance in substantial pecuniary dimensions. Diverse comorbidities for diabetes include CNS perturbations which are molecular alterations in the CNS from chronic hyperglycemia. These are ostensibly a etiologic comorbidities in psychiatric disorders and in the metabolic syndrome when protein and carbohydrate diets impact plasma concentrations of numerous transmitters associated with brain functionality [4].

Cognitive Abberation

Expansive epidemiologic studies undergird the association between diabetes and cognitive dysfunction [5]. Patients presenting comorbid obesity and diabetes have elevated rates of cognitive dysfunctionality as they grow older. Studies indicate that obesity is an excess risk factor in the development of cerebral dysfunction as exhibited in cognitive aberrations and psychopathological presentations. However, certain advantages have been observed in the elderly overweight persons as the "Obesity paradox", where psychological well-being is maintained [6].

Shrinkage of Brain Size

Obesity can cause a distinct and perspicuous shrinkage in brain size without the contribution of any other noxious factor. The brain regions which are predominantly susceptible to obesity-linked atrophy are the cingulate gyrus, frontal lobes and the hippocampus [7]. However, it is suggested that type 2 diabetes markedly shrinks the volume of the hippocampal and other brain structural entities [8,9]. A vast majority of associated structural metamorphoses occur in the hippocampus. The brain atrophy detected in diabetic subjects may be attributable to stroke.

Also, hyperinsulinaemia contributes to brain atrophy via vasoactive impacts on cerebral arteries and neurotoxicity due to compromised amyloid clearance from the brain, and enhancing the formation of neurofibrillary tangles. In addition, elevated HbA1c and age have been indicted in brain atrophy [9,10].

Insulin resistance and type 2 diabetes are characteristically the metabolic alterations depicted in obesity [11], with resultant insulin resistance; there is every chance for progression to insulin deficiency/diabetes. This is accompanied by enhanced permeability of minute molecules through the blood brain barrier (BBB). Thus, diet-induced insulin resistance enhances the permeability causing larger molecules to permeate the BBB [12,13]. The resultant diabetes induces the shrinkage of the normally tight junctions between endothelial cells and creating lacunae in those cells. Therefore, obesity can cause the breakdown of the protective BBB leading to adverse impairments in learning and memory.

Furthermore, type 2 diabetes and obesity are two inextricably-linked conditions which are associated with brain atrophy [9]. The veritable mechanisms by which obesity results in brain atrophy and cognitive disruption are intricately complex, and ostensibly connected to diabetes, gene-environment interaction, vulnerability or susceptibility, cytokines and brain metabolites [14].

Homeostasis

The major factor underlying the increase of obesity and type 2 diabetes is food with concomitant dysregulated lipid metabolism. There has always been the rigorous and expansive attempt for the human body to develop, promote and sustain a nuanced and intricate system for energy homeostasis. Homeostasis is the sustenance of basic physiologic functionalities irrespective of the alterations in the internal or external milieu. Contemporary diet predilections and lifestyle choices have invariably disrupted the homeostasis to a certain extent, thus resulting in epidemic levels of metabolic perturbations in type 2 diabetes, obesity and cardiovascular disease [3]. The functionality of the CNS in the regulation of postprandial glucose concentrations is perspicuously established with the CNS as a receptor and integrator of information emanating from the afferent neurons, circulating hormones, and postprandial generator of nutrients with subsequent driving of changes in glucose output by the hepatic organ and uptake of glucose by peripheral tissues [15]. Extensive ecological analyses are needed to elucidate the interactive mechanisms of these factors.

Vascular Perturbations

Type 1 diabetes expresses additional impairment via intensive and expansive glycation of major brain structural proteins. Formation of advanced glycosylation end-products (AGEs) [16] promotes atherosclerotic development in type 2 diabetes because of elevated oxidative stress. AGE interactions with the complimentary or corresponding promote formidable vascular cell alterations in vascular tone control. The resultant expansive damage on the vasculature of diabetic patients ostensibly culminates in stroke.

Kinetic or Motion Dysfunction

Furthermore, chronic tic disorder and Tourette syndrome are connected with a remarkable risk of circulatory system abnormalities, obesity and type 2 diabetes which calls for optimal monitoring of cardiometabolic health in these motion or kinetic disorders, especially in comorbid attention -deficit/hyperactivity disorder (ADHD) patients [17].

Neuropathy

Diabetic neuropathy is nerve deterioration emanating from diabetes, and impinges on diverse bodily functions. An excess of one-third of diabetic subjects present with impairment of the autonomic nervous system. About half of diabetic patients exhibit peripheral neuropathy, while one-quarter of diabetic individuals have focal neuropathy, for instance, carpal tunnel syndrome [18]. Also, within 25 years of diagnosis, half of diabetic subjects develop neuropathy. These sorts of nerve derangements are irreversible; but there is the possibility of prediabetes reversal by means of lifestyle metamorphosis, such as diet and exercise, and resultant decrease in the risk of sequelae, such as diabetic neuropathy. Within the ambit of the peripheral nervous system, obesity-induced changes in the autonomic nervous system trigger dysfunctional alterations in sympathetic-parasympathetic functionalities, whereas changes in the sensory-somatic nervous system are associated with peripheral neuropathy [19], a ubiquitous sequela of diabetic neuropathy.

Treatment and Control

Since the neurological resultant impact of obesity and dyslipidaemia are extremely morbid, the beneficial disease-modifying therapeutic agent is the targeting of obesity, per se. Lifestyle choices and interventions involving combined dietary manipulations, caloric restriction and exercise make for easy access and frugal modality to harness or curb obesity and revert to neurological functionality [20]. Although, diet and exercise interventions are optimal therapeutic modalities, compliance remains a constraint and a challenge promoting the pertinence for both bariatric surgery and pharmacotherapy in the control and treatment of obesity-mediated neurological impairment; and provision for optimized systemic metabolic profile.

Pharmacotherapy and bariatric surgeries may be important adjuvants in morbid obesity treatment which may later dissipate long-term effectivity and efficacy. Deep brain stimulation (DBS) requires delivery of electrical impulse to defined brain targets for the modulation of a specific perturbed neuronal network, and positioning as an efficacious intervention for kinetic degenerative disorders [21]. These significantly correlate with properly enhanced cognitive and nerve functionalities. Ecological physiological advantages, proper cellular metabolism, restoration of glucose and insulin energy homeostasis, impacts of reduced metabolic inflammation, enhanced lipid profiles and eradication of disruptive regulatory dyslipidaemia [20] constitute the benefits for such measures. The role of the CNS in homeostatically regulating postprandial glucose levels is evidenced. Thus, contemporary peripheral therapies function to retard type 2 diabetes progressions with a combinatorial type 2 diabetes and obesity therapeutic regimen targeted at the CNS, the primary locale of derangement for the two disorders. They have a resultant debilitating effect on the progression of both obesity and type 2 diabetes [15].

Inasmuch as there are extensive extant data undergirding obesity as a stringent mediator of PNS and CNS damage, there is no optimum intervention currently available to curb cognitive deterioration, polyneuropathy and autonomic polyneuropathy. In essence, there are no extant specific pharmacotherapeutic regimens available for CNS comorbidity linked with diabetes; although, certain herbal medicines, prebiotics and probiotics have become of significance in the control and treatment of these CNS sequelae [4].

Certain drugs, such as adiponectin are beneficial in the treatment of obesity and coexisting cardiovascular disease and diabetes [22]. Apelin is the ultimate protection antecedent to the presence of obesity-associated metabolic impairments, such as cardiovascular disease, insulin resistance and type 2 Diabetes [23]. Non-obese diabetic patients feature mostly compromised insulin secretion; but in non-obese patients having type 2 diabetes, metformin targeting insulin resistance is recommendable as compared to the preandrial insulin secretagogue, repaglinide that controls HbA1c. Metformin has been observed to reduce postprandial concentrations of glycaemia, triglycerides and FFA with equitable potency in comparison to repaglinide. Also, metformin decreased fasting and postprandial cholesterolaemia and insulinaemia compared to repaglinide [24]. These suggest that metformin is preferable in non-obese type 2 diabetic patients with fasting and postprandial glucose and lipid metabolism as targets. Diabetes progression in obesity complicated with defective glucose tolerance is preventable by weight reduction and effective physical activity [25]. In type 2 diabetes, deliberate weight dissipation creates improved metabolic control and a frugal or limited requirement for antidiabetic therapy. In obese patients presenting with varied cardiometabolic risk factors, rimonabant is recommended as a beneficial intervention agent. Other agents, such as incretin-promoting oral DPP-4 inhibitors [26] and the mimetics, incretin are representative for therapy; and therefore, reliable for type 2 diabetes and obesity [25]. Most of these drugs are associated with untoward weight gain but not metformin that enhances modest weight dissipation.

Discussion

Fundamentally, obesity is due to inappropriate dietary predilections and pronounced physical inactivity. It connotes a dilemma of grave and global pandemic with burden that encompasses socioeconomic and medical issues, challenges and opportunities. Obesity with its never-ending accomplice, type 2 diabetes, elevates cardiovascular disease risk and certain oncological conditions, and it is a prominent protagonist of varied facets of the metabolic syndrome which include hypertension, hyperglycemia, insulin resistance of prediabetes and type 2 diabetes as well as dyslipidaemia [20].

Diabetes, obesity and diet-induced metabolic impairment constitute risk factors to develop expansive presentations of neurologic dysfunction in both the CNS and PNS. Obesity and diabetes are linked [26,27] with benign cognitive aberration in the morphology of the hippocampus with correlates in Alzheimer-type dementia [28]. The PNS is impacted by both obesity and diabetes. Thus the inextricable linkage between obesity and polyneuropathy constitutes a complication usually encountered in prediabetic and diabetic subjects, secondary to aggregated obesity-induced dyslipidaemia [20].

Conclusion

Ecological analyses at the population level are pertinent to elucidate the adverse impact of these aberrations on the neurological system including parameters of neurotoxicity, lipotoxicity and metabolic inflammatory mechanisms as protagonists in the neurological consequences of diabetes and obesity. Also of importance is the presenting outcome of pharmacotherapy, lifestyle predilections and surgical interventions in comorbid diabetes and obesity-propelled neurological consequences.

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