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Review article

Cognition, Brain Function and Plasticity in the Overweight and Obese - A Review

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Abstract

Obesity has been a growing health concern globally. As the prevalence of obesity is increasing rapidly worldwide, studying the mechanisms, manifestations and prevention of obesity is very important. This review aims to look at brain function and cognition in those who are obese or overweight. Obesity has been a risk factor for dementia, cognitive decline and also Alzheimer's disease. There is evidence that neurological consequences can occur with obesity. The normal human energy system for obesity can become impaired, which can result in cognitive impairment. Studies have demonstrated that cognitive impairment could happen due to factors associated with obesity like diabetes, hypertension, high cholesterol and metabolic syndrome. Obesity is related with reduced brain plasticity, motor control and cognition however, the research looking at how cognitive function is influenced by obesity is limited. However, overweight and obesity, as well as their related non-communicable diseases, are largely preventable. Evidence has shown that obesity effects on cognitive function are not immediately understood as obesity may affect cognitive function of various people in different ways, especially with different age groups. More research should be carried out for understanding how structure and function of the brain may facilitate associations of age and obesity with cognition.

Keywords: Obesity; Cognition; Brain function; Brain plasticity; Alzheimer's disease

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Introduction

Obesity has been a commonly known public health problem resulting in reduced life expectancy and increased mortality [1]. As stated by the World Health Organisation (WHO), obesity cases have almost tripled globally after 1975 [2]. The WHO has defined overweight and obesity as excessive or abnormal accumulation of fat which has an adverse effect on health. People who have Body Mass Index's (BMIs) between 25kg/m^2 and 29.9kg/m^2 are considered overweight where as those who have BMIs of ≥30kg/m^2 are considered to be obese [3]. Childhood obesity is also common. In 2016, over 340 million adolescents and children between 5 and 19 years of age were obese or overweight [2]. Studies have found that obesity has neurological consequences. Obesity has been shown to cause decreased motor control and cognition along with changed brain plasticity [4]. As obesity has been a public health concern resulting in Type 2 Diabetes (T2D), Cardiovascular Diseases (CVDs), hypertension and dyslipidaemia, limited research is available that examines the reason for it influencing cognitive function. In this review, brain function and cognition of obese and overweight people and changes related to obesity in brain plasticity are the main focal points. The review will also cover deficit effects in relation with obesity in cognition and motor control. Finally, the implications and future research directions will be discussed.

Obesity and Cognition

In obesity, the normal human energy system physiology can become impaired and result in cognitive impairment. Obesity can affect cognition and the Central Nervous System (CNS), which includes decision making, attention, verbal learning and executive function [4]. Cognitive function is the ability of a person for gaining knowledge and information by constantly applying language skills, memory and attention [5]. Obesity can affect cognitive function due to changes in structure and brain function [6-8]. Obese females had a poor performance for executive functioning tests compared to normal weight females [8]. A reduction in executive functioning was involved with the grey matter volume reducing in the left orbito frontal region [8]. Midlife obesity can cause more dementia development for older people [9]. A systematic review compared the CVD risk factor impacts, such as obesity, T2D, dyslipidaemia and hypertension, on cognition and reported a reduction in all cognitive domains [10]. Studies have shown a negative link between brains functioning and increased body fat for old women [8].

Childhood obesity is also becoming more prevalent. Childhood obesity was found to involve deficits in cognition regarding attention and shifting abilities [11]. A cross-sectional study of overweight children established that fatness was associated with worse scores, especially of mathematics, reading and executive function, while fitness with better cognition, achievement and behaviour [12]. Overweight children have spatial cognitive task problems and results have shown differences for both mental rotation accuracy and motor ability [13]. Children who were overweight had more errors when rotation tasks were difficult in comparison with children of normal weight [13]. For adolescents and children, obesity can cause poorer cognitive performances, especially for executive functions [14,15]. Studies

have found that cognitive functions, including executive and attention functions were reduced in obese adolescents [16,17]. A pilot study demonstrated that obese adolescents contained insufficient cognitive domains, including impairment in executive functions and attention [16]. The cross-sectional association between cognitive performance and Visceral Fat (VF) showed larger volumes of VF in adolescents (12-18 year olds) was involved with lower performance for the six executive function measures (p=0.0001 to 0.02) [17].

A population based study showed associations specific to gender between impairment and obesity for the developmental functioning's specific aspects [18]. High subcutaneous and paediatric overweight fat both resulted in delayed motor development for infants [19]. Overweight children were shown to have significantly lower perceived and actual physical competence [20]. Children who were overweight contained various difficulties with fundamental movement skills [21]. Lower perceived and actual physical competence may be significant contributing factors for obesity in children [20]. In obese or overweight children, fine and gross motor control were found to be poorer along with a delay in motor development [18,22-24]. Obese children displayed lower gross motor skill levels in comparison with healthy weight peers [22]. The largest differences were seen in balance and loco motor skills [22]. Overweight children had reduced performance for manual dexterity, intelligence and gross motor skills (coordination and fitness) in comparison with healthy weight children [23] and weight related differences were found in gross along with fine motor skill in children who were obese [24].

A Chinese study in patients of both genders confirmed that overweight causes decreased cognitive impairment risk in older Chinese people between 60 and 98 years of age [25]. When adjusted for hypercholesterolemia, drinking, hypertension, smoking, education level, diabetes, gender and age, overweight was largely involved with lower cognitive impairment risks [Odds Ratio (OR) = 0.458; 95% CI 0.298, 0.703; p<0.001] [25]. This study confirmed that although obesity can be a factor involved with cognitive impairment, it affects cognitive function differently for various age groups [25]. In contrast, obesity had not affected cognitive task accuracies on related to planning executive function, attention or memory in premenopausal women who were healthy [26]. Morbid obesity however had been involved with larger latencies for correct responses for lower lengths of memory span and tasks specific to memory [26]. However, obesity was not related to cognitive performance in association with planning and attention executive function for women who are otherwise healthy and premenopausal [26].

Cognition and Body Mass Index

A previous systematic review showed that high BMI can be associated with poor cognitive performances, especially for processing memory and speed along with executive function domains [10]. BMI was found to be inversely associated with strength, balance, agility, running speed and fine motor precision [27]. A lower prevalence of fundamental motor skills, including running, hopping, kicking or sliding has also been observed [28]. Higher waist-to-hip ratios or BMIs for middle-aged adults had been involved with faster declines of cognition for memory and learning abilities [29,30], along with executive functioning [30]. A significant negative correlation had been located between metabolic activity and BMI for the cingulated gyrus and prefrontal cortex [7]. With increase in BMI, white matter volumes for both posterior and anterior regions appeared to be significantly larger [8].

A study in older females reported that higher BMI caused reduced grey matter volumes for the right precentral gyri, right inferior frontal and left orbito frontal including the para-hippocampal, right cerebellar regions, lingual and fusiform gyri, and increased white matter volumes in the parietal, temporal and frontal lobes [8]. A cross-sectional study which was based from population [Neurological Disorders of Central Spain (*NEDICES*)], looked at cognitive function for a large sample that was population-based for obese and overweight old participants in comparison with controls having a BMI of <25kg/m^2 [31]. During this study, obese and overweight participants performed poorer in formal neuropsychological tests compared with controls, suggesting that high BMI impairs cognition in older people [31]. In contrast, some studies have found that higher fat-free mass and higher adiposity for old people resulted in improved cognitive performances [32]. Higher fat-free mass and a lower BMI was found to cause slow decline of cognitive function [32], however the findings were not explained by confounding of pre-existing conditions.

Type 2 Diabetes (T2D), Fasting Plasma Insulin (FPI) levels and BMI had been hugely associated with atrophy in temporal, sub cortical and frontal brain regions [33]. BMI had been correlated negatively with brain atrophy [33]. Obese individuals with BMI more than 30kg/m^2, had atrophy for the anterior cingulated gyrus, hippocampus, thalamus and frontal lobes in comparison with normal BMI people [33]. Overweight individuals contained atrophy in the corona radiate and basal ganglia of the White Matter (WM) [33]. An increased deterioration in executive functions was involved with reductions for total brain volume related to midlife obesity in individuals from the prospective Framingham Offspring Cohort Study [34]. These were related to abnormalities in myelin and neurons [35].

Increased BMI for midlife is related to myelin or neuronal abnormalities, especially for the frontal lobe [35]. Since white matter for the frontal lobes is affected by aging compared to other lobes, these results demonstrate increased aging for people with high adiposity levels [35]. As a result, higher BMI levels could increase chances of developing diseases related to age such as AD [35]. BMI and age of middle and older adults contributed independently to decreased brain volume [36]. People who had higher midlife BMI had reduced cognition [36] and older people had larger reduced cognition if they were obese or overweight in middle age [37,38]. Higher midlife BMI scores occur before sharper cognitive decline and lower general cognitive abilities for both males and females while associations were not mediated by increased dementia risks [37].

A Systematic review showed evidence that midlife obesity was related to cognitive aging, while on the other hand, this association was weaker in the elderly [38]. Midlife obesity (95% CI 3.98, 1.47, Relative Risk ratios (RR) 2.42), increased cognitive impairment risks while overweight people with more than 10% weight had increased cognitive impairment risks (95% CI 11.2, 1.62, RR 4.27) [39]. Apart from BMI, other adiposity measures can be related with brain changes and cognitive performance. Visceral adiposity had been correlated inversely with verbal attention and memory while high visceral adiposity was related to larger ventricular and smaller hippocampus volume [40]. Visceral Adipose Tissue (VAT) had negative associations for verbal attention (r=0.18, p=0.01) and memory (r=0.21, p=0.005) [39]. Higher VAT had associations with larger ventricular volume (F=6.07, p=0.02) along with lower hippocampal volume (F=5.39, p=0.02) [40].

Atrophy of the temporal lobe was associated with higher BMI for older females [41]. However, in comparison with BMI, there was a stronger association for central adiposity with cognitive impairment dementia and development risks in women [42]. Therefore, studies which use BMI as obesity's only indicator could not be sensitive enough for capturing cognitive dysfunctions induced by obesity. A negative correlation had been determined between hippocampal volume and waist-to-hip ratio, while a positive correlation between waist-to-hip ratios and white matter hyper-intensities [43]. Smaller hippocampal volumes had been related to larger waist–to-hip ratios for older adults of both genders [43]. Maternal obesity causes hippocampal functional changes, resulting in cognitive function shortfalls, including memory and learning for offspring [44]. Neuroimaging studies have demonstrated anterior cingulate gyrus, frontal lobe atrophy, thalamus and hippocampus in obese and older people [32]. Higher BMI caused lower brain volumes for obese and overweight older participants [32]. Increases of BMI are related to deficient white matter integrity, smaller grey matter volume for various brain regions (such as the prefrontal cortex) and lower metabolic activities in the cingulate gyrus and prefrontal cortex in the uncinated fasciculus, which is a structure that connects the frontal and temporal lobes [6-8,45,46]. Smaller grey matter volumes within left orbitofrontal regions can be related to poorer executive performance for women who are obese [8].

Obesity and Brain Plasticity

Brain plasticity is also termed neuroplasticity, which is the ability of the brain to carry out adaptable changes and re-establish connections. Obesity can be related with reduced brain plasticity, cognition and motor control however, research which examines how it can influence cognitive function is limited. Obesity effects on motor behaviours and cognition may be assessed by a number of factors which are involved in deteriorating motor and cognitive functions. Different mechanisms such as the metabolic syndrome, including hypertension, diabetes and dyslipidaemia, are involved in obesity pathophysiology. Dysregulation of leptin and insulin, brain structure, Blood-Brain Barrier (BBB), inflammation, oxidative stress and cerebrovascular function can be affected by obesity [47-50]. Changes of structure for the hippocampus, cerebellum and medial orbitofrontal cortex that are related to memory, motor learning and control, and reward-based learning [51-53], could be linked with deficits in motor and cognitive domains.

Cognition can be affected due to obesity mainly because of changes in brain structure and function [6,32,45]. However, some studies suggest that metabolism changes related with obesity impair brain functions while interacting with age [54]. In obese people, the cortical thickness for the right medial orbitofrontal and left superior frontal cortex of the brain and the volumes of ventral brainstem and diencephalon become lower [55]. Various studies have suggested that obesity possibly causes the brain's structural changes which may result in cognitive changes. Studies have shown that increased body weight was related to lower whole brain volume for middle-aged adults [36,45]. Negative relationships between neuronal injury and grey matter density were present for hippocampus and cerebellum [56]. However, processes showing obesity's effects on the structure of the brain remain unclear.

Diet influences gut microbiota which in return affects behaviours and the brain through immune, hormonal, metabolic and neural pathways [57,58]. Obesity caused by diet encourages the brain's reactive oxygen species similar to adiposity and body weight [59,60]. High fat diets increase inflammatory signalling and oxidative stress in the brain [61]. Inflammatory signalling and oxidative stress may increase inside the brain during obesity because of diets with high fat [61]. Consumption of western diet may damage the hippocampus and lead to dementia by degrading the BBB [62]. Saturated fatty acid intake for children can impair both relational and item memories [63]. High fat diets impaired long-term spatial memory in adolescents however they did not affect short-term memory. This suggests selective consolidation impairment in the hippocampus, caused because of pro-inflammatory cytokine expressions increasing [64].

In animal studies, triglycerides lowered Insulin-like Growth Factor (IGF) passages towards brain tissue through the cerebrospinal fluid, weakened hippocampal potentiation for the longer term and inhibited leptin transportation throughout BBBs [65-67]. Insulin resistance was observed inside the cerebral cortex tissues for mice consuming high fat diets that developed degenerated synaptic integrity and reduced spatial memory [68]. Gut microbiota transplantation for mice, obese from diets, for lean mice appear to be enough for encouraging neurobehavioral changes through disrupting cerebrovascular homeostasis and increasing neuro-inflammation [69,70]. Gut microbiota modulate various neurotrophins, including synaptophysin and Brain-Derived Neurotrophic Factor (BDNF), for affecting neural plasticity [71,72]. As a result, diet can change gut microbiota, influencing neurotrophins and neurophysiology and eventually impacting behaviours and cognition.

The satiety hormone Leptin helps in controlling appetite and energy expenditure [73]. Leptin is a cytokine which is related with axonal growth, synaptogenesis or even neurogenesis additionally with hypothalamic functions [74-76]. Leptin resistance may occur in obese people [77] causing changes in energy expenditure and an increased food intake [78]. In comparison with the ones containing low leptin levels, older people with higher leptin levelshad less decline of cognitive function throughout aging [79]. People who have small waist circumference with high leptin level scan be related with less cognitive decline throughout ten years [80]. Leptin presence could reduce amyloid production and increase beta-amyloid removal [81]. Old people who have higher leptin levels have lower risks of developing dementia [82]. *GABAergic neurons* are neurons that produce Gamma-Amino Butyric Acid (GABA)**.** The effects of leptin take place when it connects with presynaptic GABAergic neurons by crossing the BBB [78,83]. Obese mice with impaired leptin signalling were found to have increased basal hippocampal inflammation [84,85] and deficits of hippocampal-dependent memory [86].

Adiponectin helps to regulate fatty acid breakdown and glucose levels. It brings its effects on the brain similar to leptin for encouraging weight reduction [87]. The level of adiponectin can be associated negatively with adiposity and protects hippocampal cells [88]. Aging animals can contain reduced hippocampal adiponectin that are independent of the high fat diet intakes [89]. As a result, adiponectin is quite useful in preventing neurodegeneration. Neurotrophins, including BDNF and Insulin-like Growth Factor *1* (*IGF-1*), encourages obesity effects for behaviours and cognition. The liver produces IGF-1 which is then bound to the insulin receptors or IGF-1 in order for cell proliferation and growth to be stimulated and brain beta-amyloid clearance to be encouraged [90]. People who are obese normally have IGF-1 resistance, which damages their capabilities of preventing beta-amyloid neurodegeneration and deposition [91,92]. BDNF binds with many receptors, including Low-affinity Nerve Growth Factor (LNGF) and Tyrosine

Kinase *Receptor* B (*TrkB*) receptors, for stimulating synaptogenesis, neurogenesis and supporting neuronal survival [93-95]. Low BDNF is usually present in cardio metabolic diseases [96]. Obesity caused by diet can reduce presynaptic synaptophysin and hippocampal BDNF expressions, similar to spatial learning impairments with in mice [97]. High fat diets lower BDNF levels inside the hippocampus [98] while impaired hippocampal synaptic cognition and plasticity happen due to the effects of BDNFs on dendritic spines [86].

Cognitive Impairment & Dementia

In obesity, the normal human energy system could become impaired and can result in cognitive impairment. Dementia and cognitive impairment are common diseases related to age among people and are a huge challenge to health resources and social care [25]. Dementia is when severe cognitive decline takes place for compromising a person's daily functions [99]. Dementia has affected 47 million people around the world and could rise towards 150 million during 2050 [100]. Epidemiological data has shown that dementia can affect 5% to 10% of people who are either 65 years of age or older in countries of higher-income [101]. The yearly age-specific dementia incidence ranges from 0.1% between 60 and 64 year old people to 8.6% for 95 year old people [101]. The prevalence usually becomes double approximately every five years, when people are 65 years old or above [25]. Associations between dementia and BMI was investigated in a meta-analysis which established that obesity and overweight during midlife increases dementia risk [102]. In older adults, higher dementia risks were related to midlife overweight or obesity, especially with metabolic abnormalities [39,49,103-106]. The 10-year declines for the global cognitive scores were faster for obese people (-0.49; 95% CI -0.55, -0.42) compared with people of normal weight (-0.42; 95% CI -0.50, -0.34), (p = 0.03) [105]. Being obese and under 65 years of age contained positive associations on incident dementia with Risk Ratios (RR) of 1.41 (95% CI 1.66, 1.20), however it was opposite for those of 65 years of age or more, with a Risk Ratio (RR) of 0.83 (95% CI 0.94, 0.74) [107]. Prevention as a result is important and research has shown preventing dementia risk factors may result in a 35% risk ratio reduction [108].

Obesity, Cognition and Alzheimer's Disease

There are risks of developing dementia with Obesity, which includes AD, along with cognitive decline [32]. The AD prevalence during 2000 in the United States was around 4.5 million people and it was predicted that this number could increase to 14 million during 2050 [109]. Studies have demonstrated possible mechanisms for links between increased AD prevalence and obesity [8]. Cognition disorders and AD usually causes dementia for older adults most frequently compared with other conditions [99]. Studies have shown that obesity makes neurodegenerative disease risks higher including AD along with dementia in later life [3]. Hippocampal damage and temporal lobe atrophy are both AD hallmarks [110,111]. A longitudinal study demonstrated that for individuals without dementia, entorhinal cortex atrophy was related to AD risks [110].

There may be a transitional stage in people from normal aging to clinically probable AD [99]. Memory impairments related to no or minimal decline of functions usually occurs with this mild cognitive impairment phase [99]. A few meta-analyses have demonstrated huge links for AD and obesity along with different types of dementia [102,107]. Other studies have also indicated that obesity can increase AD risks [102], while middle age obesity could increase dementia risks in older age [112]. In a meta-analysis, the pooled Relative Risks (RRs) in AD along with other dementia types for the BMIs of overweight people in midlife along with normal BMIs had been 1.35 (95% CI 1.54, 1.19) and 1.26 (95% CI 1.44, 1.10) [102]. The pooled AD relative risks and other dementia types for the BMIs of obese people in midlife in relation with normal BMIs were 2.04 (95% CI 2.62, 1.59) and 1.64 (95% CI 2.00, 1.34) [102]. However BMI which was continuous for old age had no association with dementia [102].

Another meta-analysis investigated cognitive impairment before AD diagnosis took place, indicating deficits which were preclinical in executive functioning, perceptual speed, episodic memory and global functioning indicated AD development [113]. Based on 47 studies, this meta-analysis demonstrated marked preclinical deficits for executive functioning and perceptual speed, episodic memory, global cognitive ability, and smaller deficits in attention, visuospatial skill and verbal ability [113]. Multiple cognitive domain deficits took place before clinical AD developments [99].

Inflammation and Cognition

Obesity may cause excess fat to be stored inside the visceral tissue which can cause changes in the inflammatory system and release of free fatty acids, which can adversely affect the nervous system [102,107]. Animals which had diets with high fat for inducing obesity had hippocampal and structure function modifications and also memory and executive function deficits [114,115]. Western blot analysis for the hippocampus demonstrated higher T231 and p-Tau S202/T205 levels for older High Fat or High Cholesterol (HFHC) rats, which showed abnormal Tau protein phosphorylation which follows the HFHC diet exposure [116]. For different animals, inflammation of the hypothalamus disrupted hypothalamic integrations for autonomic or neuroendocrine signals with nutritional status or satiety, metabolic control of energy expenditure or food intake along with causing damage to BBBs for median eminences which can suggest a weakness towards circulating Free Fatty Acids (FFAs) [117].

Satiety caused by leptins is lower in obese animals while higher hypothalamic inflammatory signalling results in reduced appetite control and activity along with leptin resistance. Mice which had metabolic syndrome caused due to diets with higher fat had endoplasmic reticulum resistance within the hippocampus, resulting in calcium homeostasis and insulin signalling both becoming impaired [117]. Endoplasmic reticulum resistance results in increased folded proteins and decreased protein synthesis, which may be a physiological link between cognitive impairments and metabolic syndrome [117].

Role of Insulin resistance and Obesity on Cognition

Obesity related pathophysiological changes are present regarding reduced body fitness especially cardiovascular health, vascular changes, inflammation and insulin resistance [118,119]. Studies have shown that the metabolic syndrome can be a risk factor for increased cognitive aging, in particular for older people and those with increased inflammation levels [119]. Several mechanisms can reveal associations between the cognitive decline and metabolic syndrome, which includes macro-vascular and micro-vascular disease, insulin resistance, inflammation and adiposity [119]. Therefore, early identification and treatment are necessary.

Due to insulin resistance, cells can fail in metabolizing glucose, triggering increases of insulin. Insulin signalling can be similar with tau phosphorylation, which leads towards AD [120,121]. Insulin

dysregulation in obese people could have larger risks of dementia. Insulin action disruptions in the brain cause neuronal function and synaptogenesis impairments. Additionally, insulin signalling controls tau protein phosphorylation, which is an early component for AD development [120,121]. Insulin deficiency and insulin resistance have key roles in causing neurodegeneration and cognitive impairment, especially AD [122].

Hormones such as leptin and insulin play important roles for modulating synaptic structure and function inside the CNS [123]. Insulin helps to modulate hippocampal synaptic plasticity [123]. Insulin resistance is caused by obesity or larger consumption of fat [124,125]. Insulin concentrations are variable for adiposity while negative relationships between insulin sensitivity and VF amounts are present [126]. Adipokines (leptin and adiponectin), were significantly correlated to insulin sensitivity [126]. Circulating insulin levels and signalling pathways become different throughout obesity; these interact with inflammatory processes for controlling behaviours and cognition [127]. Obesity is associated with increased neuro-inflammation which results in brain region dysfunction related to mood regulation, memory and learning, including the hippocampus [127]. Insulin receptors in cortical and hippocampal brain structures are widespread and insulin signalling contributes to declarative memory formation [128]. Dysfunctional insulin signalling causes inflammation and encourages tau pathology and beta-amyloid which contributes towards neurodegeneration [129,130]. Insulin resistance causes neurodegeneration and impairment of cognition as IGFs and insulin control brain plasticity, metabolism and neuronal survival [115,116,122,131]. IGF-I's peripheral levels are related to regulation of glucose [131]. As observed in diabetes, obesity and aging, a reduced sensitivity to IGF-I or insulin in the brain decreases *Amyloid*-β (*Aβ*) clearance, which can make amyloid toxicity higher [131]. IGF-I and insulin could control insulin degrading enzyme levels in the brain, also causing accumulation of Aβ [131].

Obesity, Cognition and Type 2 Diabetes

Insulin disturbances can take place in people who are obese [122,132]. Insulin resistance also has huge roles for both cognitive impairments and obesity [133]. Youth obesity increases T2D risks, causing neurocognitive deficits later on. BDNFs are proteins that help to modulate fat oxidation, neuroplasticity, appetite regulation and glucose regulation for adults. Associations between BDNF level changes and diabetes risk factor changes after exercise training lasting 6 months for obese adolescents. Concentrations of BDNF are related to retention motor skill performances once learning takes place [134]. Deficits in memory and spatial learning along with short-term memory for male offspring from obese mothers had been related to neurogenesis derived from the brain and BDNF level reductions alongside increases of apoptosis within the hippocampal dentate gyrus [44]. IGFs and insulin regulate plasticity, energy metabolism and neuronal survival, required for memory and learning [122].

Discussion

Obesity is a multifaceted condition with effect on many organ systems including the brain. It causes associated impairment of glucose metabolism and T2D which have an adverse effect on brain function. Obesity has a negative effect on the brain at all age groups. It is found to have adverse effect on the developing brain and brain plasticity as well as cognitive function in the older age group which may lead to disorders such as dementia and AD. Such conditions pose a significant health implication to those affected and challenge the health economy. Significant negative associations were found between BMI and baseline prefrontal metabolic activities which possibly had contributed to cognitive performance impairments in overweight and obese people [7]. With aging, there are higher cognitive impairment risks along with gradual decline in cognitive function [135]. Therefore, strategies are needed to reduce disease-related cognitive impairment and slow declines related with old age.

In children, obesity has been found to have an association with attention, reading, executive function, mathematics and mental rotation [11-13]. Obesity impacts adversely on fine and gross motor development in young children as well as their cognitive ability to do complex tasks and intelligence scores. A delay in motor development and poor fine and gross motor control has been observed in overweight or obese children [19-21]. Along with its importance in weight maintenance and health risk reduction throughout an epidemic of childhood obesity, physical activity could be a significant and simple process of improving mental functioning for children which is central towards cognitive development [12]. Various studies looked at relationships between cognitive impairment and obesity however study findings can differ mostly due to study populations being varied [25].

As per this review, a few studies have suggested that a high BMI may have detrimental effects in older people, especially impaired cognition. However, some studies of cognition and high BMI for older people showed differing findings. One reason could be because of the small study numbers contained in the pooled analyses [102] that may have reduced the general inability of findings. Obesity together with its effects on the BBB and pro-inflammatory cytokines may affect cognition and brain plasticity as per experimental animal studies. Insulin disturbances can take place in people who are obese [122,132]. Insulin resistance has huge roles for both cognitive impairment and obesity [133]. Studies have suggested changed brain activation and structure due to obesity may influence cognition [6,8,32,45]. Obesity can influence musculoskeletal systems into degrading motor performance [136]. As motor performances may depend on cognitive abilities [137], obesity could contribute indirectly towards motor deficits while cognitive decline takes place. Studies have shown that obesity affects both motor behaviour and cognition through various processes however the validity of these mechanisms needs to be investigated further.

Studies have shown associations between higher dementia risk and increased BMI [138], however others have shown non-linear associations [32], no associations [139] or inverse associations [140,141]. While a few studies showed harmful effects of high BMI for cognitive function, others showed improvements for cognition. Studies examining older age adiposity also have results that are conflicting. Studies comparing adiposity with older age cognition have conflicting results such as neutral effect or even neuroprotective effect however they could be explained with the choice of adiposity measures [32]. Evidence about preventing cognitive impairment related with age in older people who have interventions to their lifestyle are important, however it is still unknown if it can prevent underlying neurodegeneration [100]. There currently is limited success regarding medical treatments for dementia and cognitive impairment despite therapeutic advances. Therefore non-medical approaches such as weight reduction and exercise need to be explored in more detail.

Implications and Future Prospects

Obesity is gradually increasing, which causes a reduced quality of life, aversive motor behaviours and cognitive effects [2]. A recent study has reported that people who are severely overweight may not be able to find new neural pathways and reconnect their brains, which may have significant implications, especially for those who have had a stroke or brain injury [142]. However, overweight and obesity, as well as their related Non-Communicable Diseases (NCDs), are largely preventable. Overweight or obesity differs between later life and mid-life because they are both risk factors in the development of incident dementia. A meta-analysis and systematic review suggested a positive association for obesity in later dementia and mid-life but the opposite in later life [107]. Therefore, there needs to be more investigations regarding whether mid-life weight reductions reduced dementia risks. While more research is required, exercise interventions which improve brain health by using neuroprotective mechanisms are promising in order to preserve cognitive performance.

Conclusion

To conclude, obesity is a large social and health issue. Other than problems related to health, obesity additionally impairs motor performance and cognition. Evidence is present that obesity has neurological consequences and affects brain structure, BBB's, cerebrovascular function, leptin/insulin dysregulation, oxidative stress and inflammation, which are involved in deteriorating motor and cognitive functions. Obesity affects cognition and motor behaviours mainly due to changes in brain functions and musculoskeletal system. Previous studies have demonstrated that brain plasticity alteration related with obesity are problems causing permanent harm, especially for younger people. As a result, combating obesity throughout childhood would be a solution. Therefore, introducing physical activity for children and adults can prevent functional decline related to old age and reduce obesity.

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