Review

Neuroscience

A Comprehensive Review on the Role of Obesity in Functional Cognition (Part I)

Epidemiology and Alternations in Brain Structure

Ronnie Callaghan*

University of Central Oklahoma, 100 N University Dr, Edmond, OK 73034, USA

*: All correspondence should be sent to: Dr. Ronnie Callaghan.

Author's Contact: Ronnie Callaghan, Ph.D., E-mail: roncallaghan@yahoo.com

DOI: https://doi.org/10.15354/si.23.re692

Funding: No funding source declared.

COI: The author declares no competing interest.

The condition of obesity, which is defined by an excessive amount of adipose tissue, is being increasingly acknowledged as having significant consequences for the structure and functioning of the brain. Numerous studies have demonstrated that obesity is linked to significant modifications in the structure of the brain, encompassing variations in the volume of gray matter, the integrity of white matter, and modifications in particular brain regions responsible for regulating appetite and cognitive control. For example, research employing neuroimaging methodologies such as magnetic resonance imaging has consistently indicated that individuals with obesity frequently display diminished gray matter volume in areas such as the prefrontal cortex, which is known to play a critical role in processes such as decision-making and impulse control. Furthermore, there have been observations of white matter abnormalities that impact the interconnection among brain regions responsible for hunger regulation and reward processing. These abnormalities may potentially play a role in the development of overeating tendencies and compromised self-control. The aforementioned alterations in structure are not solely connected to obesity, but are also correlated with cognitive deficits, namely in domains pertaining to memory, attention, and executive functioning. Gaining a comprehensive understanding of the complex correlation between obesity and brain structure is of utmost importance, as it provides valuable insights into the neurological foundations of cognitive impairments in individuals affected by obesity. Moreover, this knowledge serves as a basis for the creation of specific interventions aimed at alleviating the cognitive repercussions associated with this widespread public health issue.

Keywords: Obesity; Cognition; Epidemiology; Brain Structure; Outcomes

Science Insights, 2023 September 30; Vol. 43, No. 3, pp.1039-1047.

OBESITY is a complex and multifaceted medical condition characterized by the excessive accumulation of adipose tissue, primarily in the form of body fat, leading to an individual's body weight being significantly above what is considered healthy or within a normal range for their age, sex, and height. It is commonly quantified using body mass index (BMI), a widely accepted anthropometric measure that relates an individual's weight to their height. Typically, a BMI of 30 or higher is indicative of obesity (1). However, obesity extends beyond the realm of mere body composition and is recognized as a chronic disease with systemic implications. Beyond its evident physical manifestations, obesity is associated with a range of comorbidities, including metabolic disturbances, cardiovascular diseases, insulin resistance, and an increased risk of various cancers (2). Furthermore, it is increasingly acknowledged that obesity exerts a profound influence on mental health and cognitive function (3), making it a matter of significant concern in both the fields of medicine and psychology. Understanding the nuanced aspects of obesity is essential for comprehending its intricate relationship with cognitive function and its broader impact on an individual's health and well-being.

Cognitive function refers to the diverse set of mental processes and abilities that collectively enable individuals to acquire, process, store, and apply information from their environment. It encompasses a wide range of mental processes, including perception, attention, memory, language, problem-solving, decision-making, and executive functions. Cognitive abilities are crucial for daily life activities, social interactions, learning, and adapting to novel situations (4). Cognitive processes are highly interconnected and interdependent, allowing individuals to perform complex tasks, make informed choices, and navigate the challenges of their surroundings.

One fundamental aspect of cognitive function is memory, which involves the encoding, storage, and retrieval of information (5). Memory can be further divided into various subtypes, such as working memory, episodic memory, and semantic memory. Working memory enables temporary storage and manipulation of information, critical for tasks like mental arithmetic or following complex instructions. Episodic memory relates to the ability to recall specific events or experiences from the past, while semantic memory involves general knowledge about the world, including facts and concepts. Attention is another pivotal cognitive function, determining what information receives priority and processing resources. Selective attention allows individuals to focus on relevant stimuli while ignoring distractions, while sustained attention is essential for maintaining focus over extended periods. Cognitive deficits in attention can impact an individual's ability to concentrate, filter information, and engage effectively in various tasks, from studying to driving. Executive functions are a set of high-level cognitive processes responsible for planning, organizing, initiating, and regulating goal-directed behaviors. These functions encompass tasks such as decision-making, problem-solving, inhibitory control, and cognitive flexibility. Effective executive functioning is essential for managing complex tasks, adapting to changing circumstances, and achieving long-term goals. In sum, cognitive function represents a complex and multifaceted set of mental processes and abilities that underpin human cognition and behavior. Understanding these processes is essential when investigating the impact of factors like obesity on cognitive function, as it provides the foundational knowledge necessary to explore the intricate relationship between the two domains.

The exploration of the relationship between obesity and cognitive function is of paramount importance due to the rising prevalence of obesity worldwide. Obesity is a global health crisis, with its incidence steadily increasing in both developed and developing nations (6). This epidemic is not limited to adults but extends to children and adolescents, raising concerns about the long-term health consequences for individuals and society as a whole. Given the well-established link between obesity and a range of physical health issues, such as cardiovascular diseases, diabetes, and certain cancers, it is imperative to investigate its impact on cognitive function. Understanding how obesity affects cognitive processes is not only relevant from a public health perspective but also sheds light on potential interventions to mitigate its detrimental consequences. Furthermore, the brain is a highly metabolically active organ, and it is susceptible to the systemic changes that occur in obesity. Research has demonstrated that obesity is associated with alterations in brain structure and function, including changes in brain volume, white matter integrity, and neuroinflammation (7). These structural and functional changes are thought to underline the cognitive deficits observed in obese individuals. Therefore, studying the relationship between obesity and cognition can provide valuable insights into the mechanisms through which obesity affects the brain, potentially leading to novel therapeutic strategies to address both cognitive impairment and the underlying metabolic disturbances. Additionally, as cognitive function is a critical determinant of an individual's quality of life, understanding how obesity influences cognitive processes has broader implications. Impaired cognition can impact an individual's educational attainment, employment opportunities, and social functioning (8). It may also contribute to mental health issues such as depression and anxiety. Therefore, investigating the interplay between obesity and cognition is essential not only for mitigating the physical health consequences of obesity but also for addressing the holistic well-being and socio-economic implications associated with cognitive impairment in obese individuals.

Therefore, the study of the relationship between obesity and cognition is motivated by the urgent need to address the global obesity epidemic, unravel the mechanisms linking obesity to cognitive deficits, and improve the overall health and well-being of affected individuals. It has the potential to inform preventive strategies, therapeutic interventions, and public health policies aimed at reducing the burden of obesity-related cognitive impairment and its associated societal challenges.

The Prevalence and Trends of Obesity

The prevalence and trends of obesity have garnered significant attention in recent decades, reflecting the profound impact of this global health issue (8). Obesity is characterized by an excessive accumulation of adipose tissue and is assessed primarily through the BMI, which is calculated as an individual's weight in kilograms divided by the square of their height in meters. The prevalence of obesity has risen dramatically worldwide, reaching epidemic proportions (9). This increase in obesity rates is not confined to a specific age group, gender, or socio-economic class, making it a public health challenge that affects populations across the lifespan. Furthermore, the prevalence of childhood and adolescent obesity has surged, raising concerns about the early onset of obesity-related health complications. Understanding the prevalence and trends of obesity is pivotal for health policymakers, researchers, and healthcare providers, as it informs the allocation of resources and the development of targeted interventions to address this burgeoning global health crisis. Furthermore, examining the socio-economic and demographic factors contributing to obesity prevalence allows for a more nuanced understanding of the disparities in its distribution, facilitating the implementation of equitable strategies to combat this multifaceted health issue (10).

Global Obesity Epidemic

Obesity has become a major public health concern in recent decades. The complex interplay of genetic, environmental, behavioral, and socio-economic factors has contributed to the rapid rise in obesity rates across the globe. Understanding the epidemiology of obesity is vital for developing targeted interventions, informing public health policies, and addressing the multifaceted challenges posed by this global health issue.

Epidemiological studies have documented a disturbing increase in obesity prevalence worldwide. According to data from the World Health Organization (WHO), the global prevalence of obesity nearly tripled between 1975 and 2016, with an estimated 13.4% of the global population being obese in 2016 (11). The prevalence of obesity varies substantially across regions and countries, with higher rates often observed in high-income nations. These variations are influenced by cultural norms, dietary habits, physical activity levels, and socio-economic conditions. Tracking trends in global obesity prevalence is essential for assessing the scale of the problem and guiding public health efforts to combat this epidemic.

Global obesity epidemiology highlights significant socio-economic disparities in obesity rates. Obesity tends to be more prevalent among individuals from lower socio-economic backgrounds, particularly in high-income countries (12). This paradoxical relationship between socio-economic status and obesity can be attributed to various factors, including limited access to healthy foods, lower levels of physical activity, and higher exposure to obesogenic environments in disadvantaged communities. Understanding these disparities is crucial for designing targeted interventions that address the root causes of obesity and reduce health inequalities on a global scale.

The epidemiology of global obesity underscores the multifactorial nature of this condition. Several risk factors and determinants contribute to the development of obesity, including genetic predisposition, dietary patterns, physical activity levels, and environmental influences (13). The obesogenic environment, characterized by the abundance of calorie-dense foods and sedentary lifestyles, plays a significant role in driving the obesity epidemic. Genetic factors can interact with these environmental influences, making some individuals more susceptible to obesity than others (14). A comprehensive understanding of these determinants is essential for developing effective public health strategies to prevent and manage obesity on a global scale.

The global obesity epidemiology has profound implications for public health. Obesity is associated with a wide range of health complications, including diabetes, cardiovascular diseases, certain cancers, and mental health disorders. These health consequences not only reduce the quality of life for individuals but also strain healthcare systems and increase healthcare costs. Consequently, public health interventions are crucial to mitigate the obesity epidemic (15). Strategies may include promoting healthier diets, increasing physical activity opportunities, implementing policy changes, and fostering a supportive built environment that encourages active living. By addressing the root causes of obesity and adopting a multi-pronged approach, public health initiatives can play a pivotal role in curbing the global obesity epidemic and improving the health and well-being of populations worldwide.

Obesity in Different Age Groups

Obesity is a pervasive public health issue that affects individuals across various age groups, from early childhood to late adulthood. The prevalence of obesity has risen globally, leading to significant health and socioeconomic implications.

Childhood and adolescent obesity represent a critical public health concern due to their potential long-term consequences. In recent decades, the prevalence of obesity among children and adolescents has increased substantially (16). This age group faces unique challenges, including exposure to obesogenic environments, limited autonomy in dietary choices, and susceptibility to peer and societal influences. Obesity during childhood and adolescence is associated with an elevated risk of adult obesity, as well as immediate health consequences such as type 2 diabetes, cardiovascular diseases, and psychosocial problems (17). Early intervention through family-based approaches, improved school nutrition, and increased physical activity opportunities is crucial for mitigating the long-term health impact of obesity in this age group.

Young adulthood is a transitional phase characterized by numerous life changes, including higher education, employment, and independent living. These changes can influence dietary choices and physical activity patterns, making young adults susceptible to weight gain and obesity (18). Obesity during this stage of life is associated with increased risks of chronic diseases, such as hypertension and metabolic syndrome, and can have lasting effects on future health. Public health initiatives targeting this age group should focus on promoting healthy behaviors, fostering access to nutritious food options, and addressing the unique challenges young adults face as they transition to adulthood.

Middle-aged adults often experience a gradual increase in body weight due to various factors, including metabolic changes and lifestyle habits. Obesity in middle-aged individuals is strongly linked to an elevated risk of chronic diseases, such as type 2 diabetes and cardiovascular diseases (19). The challenges of managing obesity at this stage may include juggling work and family responsibilities, which can limit time for physical activity and healthy meal preparation. Effective interventions should emphasize lifestyle modifications, regular health check-ups, and tailored support to manage obesity-related health conditions in this age group.

Obesity in older adults presents unique considerations, as it can intersect with age-related health concerns. While obesity can be associated with an increased risk of certain health conditions, such as osteoarthritis and functional limitations, it may also provide some protection against frailty and osteoporosis (20). Weight management in older adults should prioritize preserving muscle mass, promoting mobility, and addressing specific nutritional needs associated with aging (21). Healthcare providers and public health programs should offer personalized approaches to obesity management in older age, recognizing the potential benefits and risks associated with weight status in this population.

Obesity is a multifaceted issue that affects individuals of all age groups, each facing distinct challenges and health outcomes. Tailored interventions that consider the developmental stage and unique circumstances of different age groups are essential for effectively addressing the obesity epidemic and improving the overall health and well-being of populations across the lifespan.

Socioeconomic and Demographic Factors Contributing to Obesity

Obesity is a complex and multifaceted health issue influenced by a range of factors, including socioeconomic and demographic variables. Understanding how these factors contribute to obesity is critical for addressing this global public health concern effectively. Socioeconomic and demographic disparities in obesity prevalence persist worldwide, highlighting the need to explore the intricate relationships between income, education, race, ethnicity, and obesity.

Socioeconomic status, commonly measured by factors such as income, education, and occupation, plays a significant role in shaping obesity prevalence. Extensive research has consistently shown an inverse relationship between SES and obesity, with lower SES individuals at a higher risk of developing obesity (22). Limited access to healthier foods, reduced opportunities for physical activity, and increased exposure to obesogenic environments in low-income neighborhoods contribute to this association. Furthermore, the stressors associated with lower SES may lead to unhealthy coping mechanisms, including overeating. Addressing socioeconomic disparities in obesity requires efforts to reduce income inequality, improve access to nutritious foods, and enhance opportunities for physical activity in disadvantaged communities.

Educational attainment is closely linked to obesity, as individuals with higher levels of education tend to have lower obesity rates. Education influences health literacy, dietary knowledge, and the ability to make informed choices regarding nutrition and physical activity. Higher educational attainment often correlates with access to better job opportunities and higher income, which can support a healthier lifestyle (23). Conversely, limited educational opportunities can restrict access to information and resources necessary for obesity prevention and management. Public health initiatives should emphasize educational interventions that empower individuals with the knowledge and skills to make healthier choices, regardless of their educational background.

Race and ethnicity are important demographic factors contributing to obesity disparities. In many countries, minority populations, particularly Black and Hispanic communities, have higher obesity rates compared to white populations (24). These disparities are influenced by a combination of social, cultural, and environmental factors. Minority populations often face greater barriers to accessing fresh, affordable foods and safe places for physical activity (25). Additionally, the stressors associated with racial discrimination can contribute to weight gain. To address racial and ethnic disparities in obesity, culturally tailored interventions and policies that address structural inequities are essential. Promoting community-based programs and improving healthcare access can help mitigate these disparities.

Socioeconomic and demographic factors are integral components of the complex obesity puzzle. The relationships between income, education, race, ethnicity, and obesity are multifaceted and interconnected (26). As such, comprehensive strategies to combat obesity must take into account these factors to ensure equitable outcomes. Addressing disparities in obesity requires a multifaceted approach that combines policy changes, educational initiatives, and community-based interventions. By acknowledging and actively addressing the socioeconomic and demographic factors contributing to obesity, public health efforts can become more effective in reducing obesity rates and improving the overall health and well-being of diverse populations.

Obesity and Brain Structure

The relationship between obesity and brain structure is a subject of increasing interest within the field of neuroscience and public health. Recent research has demonstrated a connection between excess body fat and alterations in brain morphology, particularly in regions related to cognitive control, reward processing, and appetite regulation (7). Structural neuroimaging studies have revealed that obesity is associated with reductions in gray matter volume in areas such as the prefrontal cortex and the hippocampus, potentially contributing to deficits in executive functions and memory (27, 28). These findings suggest that obesity is not solely a result of poor dietary and lifestyle choices but may also involve complex neurobiological mechanisms. Understanding the impact of obesity on brain structure is essential for elucidating the neural underpinnings of obesity-related behaviors and developing targeted interventions to address this global health concern.

Impact of Obesity on Brain Volume

The impact of obesity on brain volume is a topic of growing significance in both neuroscientific and public health research. Beyond its well-established association with various physical health problems, recent investigations have highlighted its detrimental effects on brain structure. Understanding how obesity influences brain volume is crucial for comprehending the cognitive and neurological consequences associated with this condition. This essay explores the multifaceted relationship between obesity and changes in brain volume, shedding light on the underlying mechanisms and implications for public health.

Research utilizing neuroimaging techniques, such as functional MRI, has identified specific brain regions susceptible to volume alterations in the context of obesity (29). Notably, the prefrontal cortex, responsible for executive functions like decision-making and impulse control, is one of the areas affected. Additionally, the hippocampus, vital for memory and learning, can experience structural changes associated with obesity. These findings suggest that obesity may impact cognitive processes and behavior by modifying the morphology of brain regions crucial for higher-order functions.

Several mechanisms have been proposed to explain the link between obesity and alterations in brain volume. Chronic inflammation may contribute to neuronal damage and structural changes in the brain (30). Additionally, insulin resistance and metabolic dysfunction associated with obesity may negatively affect neuroplasticity and neuronal health (31). Furthermore, obesity-related vascular changes, including hypertension and atherosclerosis, can impair blood flow to the brain, potentially leading to tissue damage and volume reductions (32, 33). Understanding these underlying mechanisms is essential for delineating the intricate relationship between obesity and brain structure.

The impact of obesity-related brain volume changes extends beyond structural alterations to cognitive and behavioral consequences. Research suggests that individuals with reduced brain volume in areas like the prefrontal cortex may exhibit deficits in impulse control, emotional regulation, and decision-making (34). Moreover, alterations in the hippocampus can contribute to memory and learning difficulties. These cognitive impairments can further exacerbate the challenges individuals with obesity face in managing their condition and adopting healthier lifestyles.

Recognizing the implications of obesity-related brain volume changes is vital for public health initiatives. It underscores the importance of obesity prevention and management from a neurological perspective, emphasizing the need for early intervention to mitigate brain structure alterations. Public health campaigns should promote not only physical health but also brain health, fostering awareness of the cognitive and neurological risks associated with obesity. Additionally, tailored interventions that address the underlying mechanisms of brain volume changes may offer new avenues for obesity treatment and prevention, ultimately improving the well-being of individuals affected by this condition.

Changes in White Matter Integrity

White matter, composed of myelinated nerve fibers that facilitate communication between different regions of the brain, plays a crucial role in cognitive functioning and information processing. Recent neuroimaging studies have provided compelling evidence suggesting that obesity is associated with alterations in white matter structure, which may have significant implications for cognitive and neurological health (35). Understanding the impact of obesity on white matter integrity is essential for gaining insights into the neurobiological consequences of this global health concern.

Research employing advanced neuroimaging techniques, such as diffusion tensor imaging (DTI), has revealed structural changes in white matter associated with obesity (36). These changes often manifest as reductions in white matter integrity, characterized by decreased fractional anisotropy (FA) and increased mean diffusivity (MD), reflecting compromised structural organization and increased diffusion of water molecules within white matter tracts (37). Such alterations can disrupt the efficient transmission of neural signals and affect various cognitive functions.

Several mechanisms have been proposed to explain the impact of obesity on white matter integrity (38). Chronic inflammation may contribute to oxidative stress and damage to myelin sheaths, leading to white matter alterations. Dysregulation of insulin signaling, often observed in obesity, can also have deleterious effects on white matter structure by impairing glucose metabolism, which is crucial for the maintenance of myelin. Furthermore, obesity-related vascular risk factors, such as hypertension and atherosclerosis, can lead to vascular damage, reducing blood flow to white matter regions and contributing to structural changes.

The consequences of obesity-related changes in white matter integrity extend to cognitive and functional impairments. Reduced white matter integrity has been associated with cognitive deficits in various domains, including memory, attention, and executive functions (39). These cognitive impairments can manifest as difficulties in decision-making, problem-solving, and emotional regulation, potentially affecting an individual's quality of life and daily functioning. Moreover, altered white matter integrity may also contribute to a higher risk of neurological conditions, such as dementia, in individuals with obesity.

It underscores the need for comprehensive healthcare approaches that consider both physical and neurological consequences of obesity. Public health campaigns should promote awareness of the cognitive risks associated with obesity and emphasize the importance of obesity prevention and management. Moreover, clinicians should consider assessing cognitive function and white matter integrity in individuals with obesity, as early intervention and lifestyle modifications may help mitigate the negative effects on brain structure and function. Overall, recognizing the relationship between obesity and white matter alterations offers new insights into the neurological aspects of obesity and highlights the importance of addressing this multifaceted issue comprehensively.

Neuroinflammation and Obesity

Obesity has been associated with a state of heightened immune activation within the central nervous system. This neuroinflammation, driven by various factors including the secretion of proinflammatory cytokines, microglial activation, and astrocytic response, has raised important questions about its role in the pathogenesis of obesity-related complications, including insulin resistance and cognitive dysfunction.

The mechanisms underlying neuroinflammation in obesity are multifaceted and involve a complex network of signaling pathways. One key contributor is the systemic release of proinflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), from adipose tissue (40). These cytokines can cross the blood-brain barrier and activate resident immune cells, including microglia and astrocytes, within the brain. This activation results in the production of additional proinflammatory mediators, including IL-1β and cyclooxygenase-2 (COX-2), which further fuel the inflammatory response. Additionally, the disruption of gut microbiota composition, a common feature of obesity, may contribute to neuroinflammation through the release of bacterial-derived toxins into circulation, which can impact the central nervous system.

Neuroinflammation in the context of obesity has far-reaching consequences for both metabolic and cognitive health. In terms of metabolic health, neuroinflammation is thought to contribute to the development of insulin resistance. Proinflammatory cytokines released within the brain can interfere with insulin signaling pathways, impair glucose uptake, and promote insulin resistance in peripheral tissues. Furthermore, neuroinflammation has been linked to disrupted appetite regulation, potentially contributing to overeating and further weight gain. In the realm of cognitive health, mounting evidence suggests that chronic neuroinflammation may underlie cognitive deficits observed in individuals with obesity, including impaired memory, attention, and executive functions.

Understanding the link between neuroinflammation and obesity opens avenues for potential therapeutic interventions. Targeting neuroinflammatory pathways may represent a novel approach to managing obesity-related complications. Anti-inflammatory agents, such as nonsteroidal anti-inflammatory drugs (NSAIDs) or specific cytokine inhibitors, have been investigated for their potential to mitigate neuroinflammation in preclinical studies (41). Lifestyle modifications, including weight loss and increased physical activity, have also shown promise in reducing systemic inflammation and may have beneficial effects on neuroinflammation. Moreover, strategies that modulate gut microbiota composition, such as probiotics and dietary interventions, may indirectly influence neuroinflammation by restoring a balanced microbial ecosystem.

The intricate relationship between neuroinflammation and obesity underscores the complexity of this multifaceted health issue. Neuroinflammation contributes to the metabolic and cognitive impairments associated with obesity and represents a potential therapeutic target for addressing these complications. Further research is needed to elucidate the specific mechanisms driving neuroinflammation in obesity and to develop effective interventions that can mitigate its effects. Recognizing the role of neuroinflammation in obesity-related health concerns highlights the importance of comprehensive approaches that address both the peripheral and central aspects of this global public health challenge.

Role of Insulin Resistance in Brain Alterations

While insulin is primarily recognized for its role in glucose homeostasis, it also plays a crucial role in brain function, including synaptic plasticity, neurotransmitter regulation, and cognitive processes. Emerging research has highlighted the adverse effects of insulin resistance on the brain, linking it to structural and functional alterations in neural circuits, as well as cognitive deficits (42). This essay explores the intricate relationship between insulin resistance and brain alterations, elucidating the mechanisms involved, potential consequences, and therapeutic implications.

Insulin resistance in the brain shares commonalities with peripheral insulin resistance, characterized by impaired cellular responses to insulin signaling. In the brain, this resistance may arise from the downregulation of insulin receptors or post-receptor signaling disruptions (43). Chronic hyperinsulinemia can lead to oxidative stress, inflammation, and dysfunction in brain regions critical for cognitive function. Additionally, alterations in insulin transport across the blood-brain barrier may further contribute to brain insulin resistance, affecting insulin's availability to neuronal cells.

Insulin resistance in the brain has been associated with structural and functional alterations in key regions, particularly the hippocampus and prefrontal cortex (44). Structural changes may include reduced gray matter volume, alterations in dendritic spine density, and disrupted synaptic plasticity. These alterations can negatively impact memory, learning, and executive functions. Functionally, insulin resistance may impair neurotransmitter regulation, synaptic transmission, and glucose metabolism in the brain, further contributing to cognitive deficits.

Cognitive consequences of brain alterations due to insulin resistance are wide-ranging and can manifest as difficulties in memory consolidation, attention, and executive function. Individuals with insulin resistance are at an increased risk of developing mild cognitive impairment and have a higher likelihood of progressing to more severe conditions, such as Alzheimer's disease (45). The effects of insulin resistance on cognitive function highlight the importance of understanding the link between metabolic health and brain health.

Recognizing the impact of insulin resistance on brain alterations offers potential therapeutic avenues for mitigating cognitive decline (46). Lifestyle modifications, including regular physical activity and a balanced diet, can improve insulin sensitivity and reduce systemic inflammation, potentially benefiting both metabolic and brain health. Medications targeting insulin resistance, such as insulin-sensitizing agents, may also hold promise in preserving cognitive function. Additionally, interventions that focus on optimizing vascular health and reducing oxidative stress could help counteract the adverse effects of insulin resistance on the brain.

The relationship between insulin resistance and brain alterations underscores the intricate interplay between metabolic and cognitive health. Insulin resistance in the brain can lead to structural and functional changes that contribute to cognitive deficits and increase the risk of neurodegenerative conditions. Understanding the mechanisms involved and exploring therapeutic strategies aimed at improving insulin sensitivity in the brain holds great potential for enhancing cognitive well-being and addressing the growing concern of cognitive decline in the context of metabolic dysfunction.

Conclusion

Obesity is a complex and persistent health disease characterized by the excessive buildup of adipose tissue in the body. In addition to its widely recognized correlation with numerous physical health complications, recent studies have thrown light on a strong relationship between obesity and changes in the structure of the brain. The utilization of neuroimaging methods, such as magnetic resonance imaging (MRI), has provided insights into notable alterations in the brain structures of persons affected by obesity. One of the most robust observations in the literature is the decrease in gray matter volume, namely in brain regions associated with cognitive control and decision-making, such as the prefrontal cortex. The aforementioned decrease has significant importance as it perhaps serves as the underlying cause for the cognitive impairments identified in individuals who are fat, such as deficiencies in executive function, attention, and memory.

Furthermore, there is a documented correlation between obesity and changes in the structural integrity of white matter, which in turn impacts the interconnectivity across various regions of the brain. Disruptions in the integrity of white matter tracts have been detected in regions that are important in the regulation of appetite, processing of reward, and control of impulsive behavior. The aforementioned alterations in structure could potentially exacerbate the difficulties that individuals with obesity encounter in managing their eating habits and selecting nutritious nutritional options.

The intricate mechanisms that underlie the correlation between obesity and brain anatomy are intricate and multifaceted. There is a prevailing belief that the presence of chronic inflammation, insulin resistance, and hormone dysregulation, which are frequently observed in cases of obesity, might have a role in causing changes to the structure of the brain. Furthermore, it is important to consider lifestyle factors, including dietary choices, levels of physical activity, and sleep patterns, since these have the potential to impact brain health and potentially serve as mediators in the association between obesity and brain structure.

The comprehension of the influence of obesity on brain structure is of utmost importance, as it carries significant implications for both clinical treatment and public health policies. Obesity is linked to cognitive deficits that can impede a person's capacity to participate in health-promoting activities, make well-informed decisions regarding their nutrition, and adhere to treatments aimed at managing their weight. Therefore, therapies targeted at mitigating cognitive impairments associated with obesity have the potential to enhance the efficacy of obesity treatment programs. In addition, it is imperative for public health initiatives to consider the cognitive implications of obesity while formulating methods to address the widespread obesity crisis on a global scale. In summary, the examination of the impact of obesity on brain structure emphasizes the complex relationship between physical well-being and cognitive abilities, emphasizing the necessity of a holistic strategy to tackle the diverse obstacles presented by obesity.■

References

1. Jeong SM, Lee DH, Rezende LFM, Giovannucci EL. Different correlation of body mass index with body fatness and obesity-related biomarker according to age, sex and race-ethnicity. Sci Rep 2023; 13(1):3472. DOI: https://doi.org/10.1038/s41598-023-30527-w
2. Jin X, Qiu T, Li L, Yu R, Chen X, Li C, Proud CG, Jiang T. Pathophysiology of obesity and its associated diseases. Acta Pharm Sin B 2023; 13(6):2403-2424. DOI: https://doi.org/10.1016/j.apsb.2023.01.012
3. Wang C, Chan JS, Ren L, Yan JH. Obesity reduces cognitive and motor functions across the lifespan. Neural Plast 2016; 2016:2473081. DOI: https://doi.org/10.1155/2016/2473081
4. Hu Y, Lei X, Smith JP, et al. Effects of Social Activities on Cognitive Functions: Evidence from CHARLS. In: National Research Council (US) Panel on Policy Research and Data Needs to Meet the Challenge of Aging in Asia; Smith JP, Majmundar M, editors. Aging in Asia: Findings from New and Emerging Data Initiatives. Washington (DC): National Academies Press (US); 2012. 12. Available at: https://www.ncbi.nlm.nih.gov/books/NBK109224/
5. Linday LA. Preserving cognitive function. Complement Ther Med 2022; 70:102859. DOI: https://doi.org/10.1016/j.ctim.2022.102859
6. Purnell JQ. Definitions, Classification, and Epidemiology of Obesity. 2023 May 4. In: Feingold KR, Anawalt B, Blackman MR, Boyce A, Chrousos G, Corpas E, de Herder WW, Dhatariya K, Dungan K, Hofland J, Kalra S, Kaltsas G, Kapoor N, Koch C, Kopp P, Korbonits M, Kovacs CS, Kuohung W, Laferrère B, Levy M, McGee EA, McLachlan R, New M, Purnell J, Sahay R, Shah AS, Singer F, Sperling MA, Stratakis CA, Trence DL, Wilson DP, editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000.
7. Gómez-Apo E, Mondragón-Maya A, Ferrari-Díaz M, Silva-Pereyra J. Structural brain changes associated with overweight and obesity. J Obes 2021; 2021:6613385. DOI: https://doi.org/10.1155/2021/6613385
8. Conway DS, Bermel RA, Planchon SM. The relationship between cognition, education, and employment in multiple sclerosis patients. Mult Scler J Exp Transl Clin 2022; 8(3):20552173221118309. DOI: https://doi.org/10.1177/20552173221118309
9. Hruby A, Hu FB. The epidemiology of obesity: A big picture. Pharmacoeconomics 2015; 33(7):673-689. DOI: https://doi.org/10.1007/s40273-014-0243-x
10. Lincoln KD, Abdou CM, Lloyd D. Race and socioeconomic differences in obesity and depression among Black and non-Hispanic White Americans. J Health Care Poor Underserved 2014; 25(1):257-275. DOI: https://doi.org/10.1353/hpu.2014.0038
11. World Health Organization (WHO). Obesity and overweight. Last access: September 11, 2023. Available at: https://www.who.int/news-room/fact-sheets/detail/obe

sity-and-overweight#:~:text=Worldwide%20obesity%20has%20nearly%20tripled,%2C%20and%2013%25%20were%20obese

12. Dinsa GD, Goryakin Y, Fumagalli E, Suhrcke M. Obesity and socioeconomic status in developing countries: A systematic review. Obes Rev 2012; 13(11):1067-1079. DOI: https://doi.org/10.1111/j.1467-789X.2012.01017.x
13. Lee A, Cardel M, Donahoo WT. Social and Environmental Factors Influencing Obesity. [Updated 2019 Oct 12]. In: Feingold KR, Anawalt B, Blackman MR, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000. Available at: https://www.ncbi.nlm.nih.gov/books/NBK278977/
14. Faith MS, Kral TVE. Social Environmental and Genetic Influences on Obesity and Obesity-Promoting Behaviors: Fostering Research Integration. In: Institute of Medicine (US) Committee on Assessing Interactions Among Social, Behavioral, and Genetic Factors in Health; Hernandez LM, Blazer DG, editors. Genes, Behavior, and the Social Environment: Moving Beyond the Nature/Nurture Debate. Washington (DC): National Academies Press (US); 2006. C. Available at: https://www.ncbi.nlm.nih.gov/books/NBK19935/
15. Tiwari A, Balasundaram P. Public Health Considerations Regarding Obesity. [Updated 2023 Jun 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan. Available at: https://www.ncbi.nlm.nih.gov/books/NBK572122/
16. Sanyaolu A, Okorie C, Qi X, Locke J, Rehman S. Childhood and adolescent obesity in the United States: A public health concern. Glob Pediatr Health 2019; 6:2333794X19891305. DOI: https://doi.org/10.1177/2333794X19891305
17. Kansra AR, Lakkunarajah S, Jay MS. Childhood and adolescent obesity: A review. Front Pediatr 2021; 8:581461. DOI: https://doi.org/10.3389/fped.2020.581461
18. Poobalan AS, Aucott LS, Clarke A, Smith WC. Diet behaviour among young people in transition to adulthood (18-25 year olds): A mixed method study. Health Psychol Behav Med 2014; 2(1):909-928. DOI: https://doi.org/10.1080/21642850.2014.931232
19. Park JH, Moon JH, Kim HJ, Kong MH, Oh YH. Sedentary lifestyle: Overview of updated evidence of potential health risks. Korean J Fam Med 2020; 41(6):365-373. DOI: https://doi.org/10.4082/kjfm.20.0165
20. Samper-Ternent R, Al Snih S. Obesity in older adults: Epidemiology and implications for disability and disease. Rev Clin Gerontol 2012; 22(1):10-34. DOI: https://doi.org/10.1017/s0959259811000190
21. Batsis JA, Zagaria AB. Addressing obesity in aging patients. Med Clin North Am 2018; 102(1):65-85. DOI: https://doi.org/10.1016/j.mcna.2017.08.007
22. Anekwe CV, Jarrell AR, Townsend MJ, Gaudier GI, Hiserodt JM, Stanford FC. Socioeconomics of obesity. Curr Obes Rep 2020; 9(3):272-279. DOI: https://doi.org/10.1007/s13679-020-00398-7
23. Zajacova A, Lawrence EM. The relationship between education and health: Reducing disparities through a contextual approach. Annu Rev Public Health 2018; 39:273-289. DOI: https://doi.org/10.1146/annurev-publhealth-031816-044628
24. Kirby JB, Liang L, Chen HJ, Wang Y. Race, place, and obesity: The complex relationships among community racial/ethnic composition, individual race/ethnicity, and obesity in the United States. Am J Public Health 2012; 102(8):1572-1578. DOI: https://doi.org/10.2105/AJPH.2011.300452
25. Hilmers A, Hilmers DC, Dave J. Neighborhood disparities in access to healthy foods and their effects on environmental justice. Am J Public Health 2012; 102(9):1644-1654. DOI: https://doi.org/10.2105/AJPH.2012.300865
26. Krueger PM, Reither EN. Mind the gap: Race/ethnic and socioeconomic disparities in obesity. Curr Diab Rep 2015; 15(11):95. DOI: https://doi.org/10.1007/s11892-015-0666-6
27. Stillman CM, Weinstein AM, Marsland AL, Gianaros PJ, Erickson KI. Body-brain connections: The effects of obesity and behavioral interventions on neurocognitive aging. Front Aging Neurosci 2017; 9:115. DOI: https://doi.org/10.3389/fnagi.2017.00115
28. Li G, Hu Y, Zhang W, Wang J, Ji W, Manza P, Volkow ND, Zhang Y, Wang GJ. Brain functional and structural magnetic resonance imaging of obesity and weight loss interventions. Mol Psychiatry 2023; 28(4):1466-1479. DOI: https://doi.org/10.1038/s41380-023-02025-y
29. Drelich-Zbroja A, Matuszek M, Kaczor M, Kuczyńska M. Functional magnetic resonance imaging and obesity-novel ways to seen the unseen. J Clin Med 2022; 11(12):3561. DOI: https://doi.org/10.3390/jcm11123561
30. Sankowski R, Mader S, Valdés-Ferrer SI. Systemic inflammation and the brain: novel roles of genetic, molecular, and environmental cues as drivers of neurodegeneration. Front Cell Neurosci 2015; 9:28. DOI: https://doi.org/10.3389/fncel.2015.00028
31. Sripetchwandee J, Chattipakorn N, Chattipakorn SC. Links between obesity-induced brain insulin resistance, brain mitochondrial dysfunction, and dementia. Front Endocrinol (Lausanne) 2018; 9:496. DOI: https://doi.org/10.3389/fendo.2018.00496
32. Henning RJ. Obesity and obesity-induced inflammatory disease contribute to atherosclerosis: A review of the pathophysiology and treatment of obesity. Am J Cardiovasc Dis 2021; 11(4):504-529.
33. Dorrance AM, Matin N, Pires PW. The effects of obesity on the cerebral vasculature. Curr Vasc Pharmacol 2014; 12(3):462-472. DOI: https://doi.org/10.2174/1570161112666140423222411
34. Herzberg MP, Hodel AS, Cowell RA, Hunt RH, Gunnar MR, Thomas KM. Risk taking, decision-making, and brain volume in youth adopted internationally from institutional care. Neuropsychologia 2018; 119:262-270. DOI: https://doi.org/10.1016/j.neuropsychologia.2018.08.022
35. Ronan L, Alexander-Bloch AF, Wagstyl K, Farooqi S,

Brayne C, Tyler LK; Cam-CAN; Fletcher PC. Obesity associated with increased brain age from midlife. Neurobiol Aging 2016; 47:63-70. DOI: https://doi.org/10.1016/j.neurobiolaging.2016.07.010

36. Kullmann S, Callaghan MF, Heni M, Weiskopf N, Scheffler K, Häring HU, Fritsche A, Veit R, Preissl H. Specific white matter tissue microstructure changes associated with obesity. Neuroimage 2016; 125:36-44. DOI: https://doi.org/10.1016/j.neuroimage.2015.10.006
37. Carbine KA, Duraccio KM, Hedges-Muncy A, Barnett KA, Kirwan CB, Jensen CD. White matter integrity disparities between normal-weight and overweight/obese adolescents: An automated fiber quantification tractography study. Brain Imaging Behav 2020; 14(1):308-319. DOI: https://doi.org/10.1007/s11682-019-00036-4
38. Lampe L, Zhang R, Beyer F, Huhn S, Kharabian Masouleh S, Preusser S, Bazin PL, Schroeter ML, Villringer A, Witte AV. Visceral obesity relates to deep white matter hyperintensities via inflammation. Ann Neurol 2019; 85(2):194-203. DOI: https://doi.org/10.1002/ana.25396
39. Peng X, Zhang R, Yan W, Zhou M, Lu S, Xie S. Reduced white matter integrity associated with cognitive deficits in patients with drug-naive first-episode schizophrenia revealed by diffusion tensor imaging. Am J Transl Res 2020; 12(8):4410-4421.
40. Popko K, Gorska E, Stelmaszczyk-Emmel A, Plywaczewski R, Stoklosa A, Gorecka D, Pyrzak B, Demkow U. Proinflammatory cytokines Il-6 and TNF-α and the development of inflammation in obese subjects. Eur J Med Res 2010; 15 Suppl 2(Suppl 2):120-122. DOI: https://doi.org/10.1186/2047-783x-15-s2-120
41. Kaduševičius E. Novel applications of NSAIDs: Insight and future perspectives in cardiovascular, neurodegenerative, diabetes and cancer disease therapy. Int J Mol Sci 2021; 22(12):6637. DOI: https://doi.org/10.3390/ijms22126637
42. Spinelli M, Fusco S, Grassi C. Brain insulin resistance and hippocampal plasticity: Mechanisms and biomarkers of cognitive decline. Front Neurosci 2019; 13:788. DOI: https://doi.org/10.3389/fnins.2019.00788
43. Rhea EM, Banks WA, Raber J. Insulin resistance in peripheral tissues and the brain: A tale of two sites. Biomedicines 2022; 10(7):1582. DOI: https://doi.org/10.3390/biomedicines10071582
44. Cui Y, Tang TY, Lu CQ, Ju S. Insulin resistance and cognitive impairment: Evidence from neuroimaging. J Magn Reson Imaging 2022; 56(6):1621-1649. DOI: https://doi.org/10.1002/jmri.28358
45. Benedict C, Grillo CA. Insulin resistance as a therapeutic target in the treatment of Alzheimer's disease: A state-of-the-art review. Front Neurosci 2018; 12:215. DOI: https://doi.org/10.3389/fnins.2018.00215
46. Rhea EM, Leclerc M, Yassine HN, Capuano AW, Tong H, Petyuk VA, Macauley SL, Fioramonti X, Carmichael O, Calon F, Arvanitakis Z. State of the science on brain insulin resistance and cognitive decline due to Alzheimer's disease. Aging Dis 2023. In press. DOI: https://doi.org/10.14336/AD.2023.0814

Received: June 10, 2023 | Revised: August 12, 2023 | Accepted: August 15, 2023