Obesity and Its Role in Neurocognition

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Given the zeitgeist of our times, where adults live longer, and lead increasingly sedentary lives, we are treating more individuals within the geriatric age group and obesity is reaching pandemic proportions in the developing and developed world. The increasing geriatric population has also increased our interface with neurodegenerative diseases. As we care more for the elderly, we are likely to encounter more neurodegeneration and that will pose important questions regarding the factors that contribute to disease development and progression. In answering these questions, it will be important to focus our attention on the modifiable risk factors.

The role of inflammation in neurodegeneration has been extensively explored and established especially in diseases like Alzheimer's disease, Parkinson's disease and other dementias. In literature, the role of obesity in perpetuating inflammation as well as its association with neurodegeneration has been published extensively as well. However, it is important to ask if obesity is also an important etiological factor in emergent cases of neurodegeneration. To study the impact of obesity on neurodegeneration in the elderly is tricky[1]. Aging influences weight changes which in turn could influence or be influenced by hormonal changes. Therefore, inflammatory pathways are possibly both modified as well as modifiers of metabolic pathways that ultimately alter cognition.

In obese individuals, an adipokine, by the name of leptin is secreted by adipose tissue. Leptin has an impact in modifying cognition and is known to impact the hypothalamus and hippocampus[2]. Hypothalamus plays an important role in regulating the minutia of the endocrinological milieu and hippocampus is the seat of memory and cognitive flexibility. Therefore, endocrinological fine tuning pathways appear to be closely intertwined with cognitive pathways and their association appears obvious.

Another important temporal association that hints at a close association is the role of microglial regulation, which can contribute to dementia[3].

Brain aging is related to the diminishing function of microglial cells which are essentially the macrophages of the brain. With age, the ability of the hypothalamus to regulate metabolism is affected and this could in turn result in a dysfunction of microglia within the hypothalamus leading to obesity or potentially resulting from obesity, if the feedback loop between metabolic pathways and hypothalamus is disrupted.

In conducting experiments to validate and quantify these associations, it is important to have clear definitions and measurements, which is a challenge. The diagnostic and prognostic markers for disease progression in neurodegenerative disease are still being fine tuned and the definitions for obesity contain different thresholds and reference ranges for clinical use.

Standardization of existing reference ranges and disease markers will aid clear inferences in clinical settings which could provide clarity in concluding results. More collaboration between clinicians, researchers and clinical trialists in the two distinct fields could help include simple affordable lab tests to data collection efforts, and aid focused scientific exploration.

In the meantime, it is important to clinically be aware of the potential etiological roles of obesity in neurocognition and use that as an additional incentive to treat obesity aggressively.

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References

1. Sui SX, Pasco JA. Obesity and brain function: the brain-body crosstalk. Medicina (Kaunas). 2020;56(10):499.
2. Flores-Cordero JA, Pérez-Pérez A, Jiménez-Cortegana C, Alba G, Flores-Barragán A, Sánchez-Margalet V. Obesity as a risk factor for dementia and Alzheimer's disease: the role of leptin. Int J Mol Sci. 2022;23(9):5202.
3. Chowen JA, Garcia-Segura LM. Microglia, neurodegeneration and loss of neuroendocrine control. Prog Neurobiol. 2020;184:101720.

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