

Role of Cortisol in Cognitive Impairment (Alzheimer's Disease)

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Abstract:- As people grow older, their chances of facing cognitive impairment tend to rise, and this probability fluctuates in relation to their age. Research has pointed out that 21.04% of individuals between 60 to 69 years old encounter cognitive issues, a percentage that escalates to 23.91% for those aged 70 to 79, and peaks at 32.65% in the elderly population over eighty. This condition primarily stems from factors like high stress levels and hypertension, conditions often associated with the hormone 'cortisol.' Prevent cognitive decline, individuals can take initiative-taking steps such as supporting a balanced diet, emphasizing physical well-being, controlling blood pressure, and incorporating other beneficial practices that collectively reduce the risk. Despite the straightforward prevention methods, the complexities of contemporary lifestyles often lead people to overlook these crucial aspects. In this study, our focus aims to delve into the impact of the 'cortisol' hormone on mental health conditions (AD), how it functions and is secreted within the body, and suggest strategies to prevent such challenges in a rapidly evolving societal landscape.

Keywords: Cortisol, Cognitive Impairment, AD, Hippocampal Damage.

I. INTRODUCTION

The proper functioning of the human body heavily relies on the presence of adrenal hormones, essential for regulating many physiological processes. These crucial hormones, synthesized by the adrenal glands situated on top of each kidney as part of the intricate endocrine system, function as vital messengers in keeping overall health and well-being. By releasing a combination of hormones such as adrenaline, DHEA, aldosterone, and cortisol, the adrenal glands actively modulate various bodily functions, including metabolic activities and stress responses. Amongst these hormones, cortisol here plays a key role, especially about its impact on cognitive function, earning it the title of a stress hormone due to its significant role in the body's response to stressors.

Research shows that cortisol is a powerful steroid hormone secreted from adrenal cortex and followed up by activating the hypothalamic-pituitary-adrenocortical (HPA) axis, it is crucial in shaping an individual's response to life's

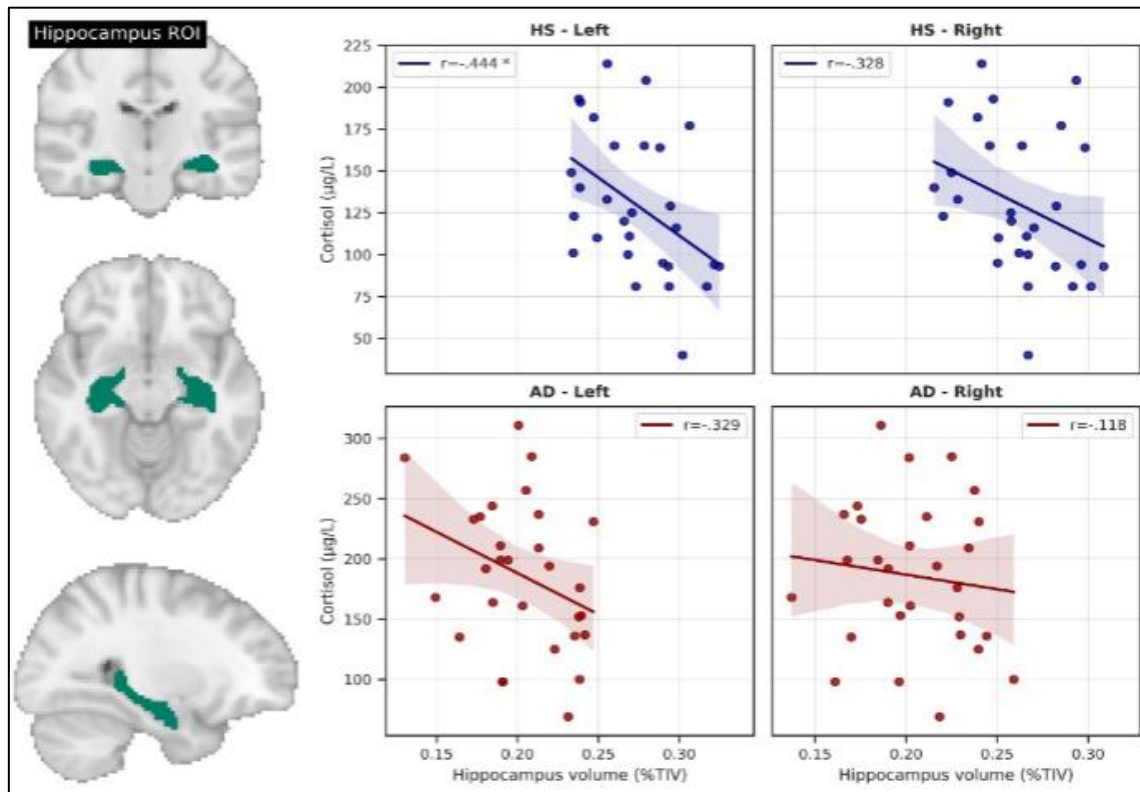
stressors. Serving as a vital element in the body's adaptive mechanism, the HPA axis dynamically adjusts its functioning following changing situations and external influences, (McEwen, 2003). Under conditions of stress and disruption, the HPA response can significantly impact an individual's health, potentially contributing to the onset of conditions such as cardiovascular diseases, diabetes, cognitive decline during aging, as well as various psychiatric disorders like depression and post-traumatic stress disorder (PTSD), (Charmandari, Tsigos, & Chrousos, 2005).

Research writes down that stress has a diverse impact on cognitive functioning (McEwen and Sapolsky, 1995; McEwen and Gianaros, 2011; McEwen, 2012). The timing and amount of cortisol released play a crucial role in figuring out the severity of cognitive impairment (Kirschbaum et al., 1996; Domes et al., 2005; Schilling et al., 2013; Yehuda et al., 2007). The effects of cortisol-related impairment can manifest both acutely and chronically (Lupien et al., 1994; Vedhara et al., 2000; Buchanan and Lovallo, 2001; Mizoguchi et al., 2004). In stressful situations, older adults experience a decline in verbal memory performance. Additionally, the presence of glucocorticoids during the aging process is associated with later cognitive decline (Lupien S, de Leon M, de Santi S, Convit A, Tarshish C, Nair NP, Thakur M, McEwen BS, Hauger RL, Meaney MJ, 1998).

II. CORTISOL IN ALZHEIMER'S DISEASE

Alzheimer's disease is a sinister disorder which hampers the brain, damaging its memory, brain power, assiduousness while suffering from it. According to research AD lies into neurodegenerative disorder.

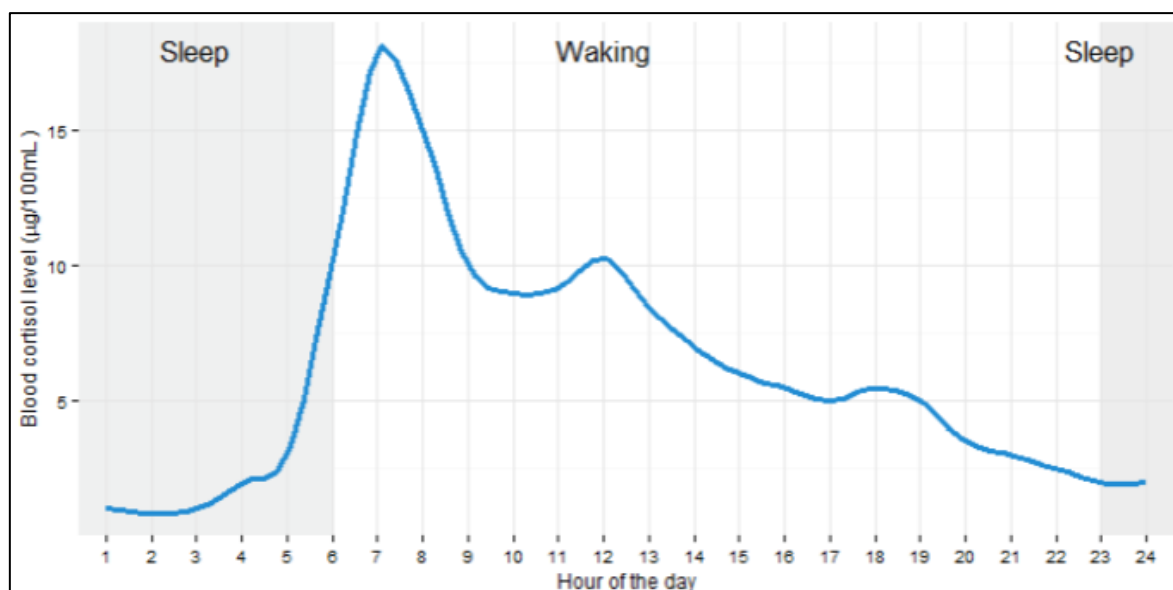
Findings has shown that 'glucocorticoid cascade hypothesis' (Sapolsky et al., 1986), which shows prominent level of glucocorticoids that can damage the hippocampus, ensuing deficiency of inhibitory control over HPA axis, resulting in even higher glucocorticoid level and more hippocampus damage (Fig:1). This suggests that high cortisol level in Alzheimer's disease can damage the hippocampus, reduce brain metabolism, and worsen dementia, more than 30 years ago higher cortisol level and more hippocampal damage was found in AD patients.



(Fig:1) Hippocampus Volume and Cortisol Levels. Scatterplots depict total intracranial volume (TIV)-corrected hippocampus volumes from AAL atlas region of interest (ROI) and unadjusted relationships with serum cortisol level. * = significant correlation, corrected for age and education. HS, healthy seniors, AD, Alzheimer's patients.

A study shows that β -amyloid deposition, tauhyperphosphorylation; alongside synaptic deficits are a key link to AD disease (Green et al., 2006; Lante et al., 2015; Toledo et al., 2012; Wang et al., 2018). This discovery gives rise to the 'glucocorticoid-cascade' theory, which posits that the excessive secretion of glucocorticoids resulting from prolonged stress may significantly contribute to cognitive impairment and the development of Alzheimer's disease (Sapolsky et al., 1986). Hormones plummet at their vertex 30-40 minutes after waking up in the morning

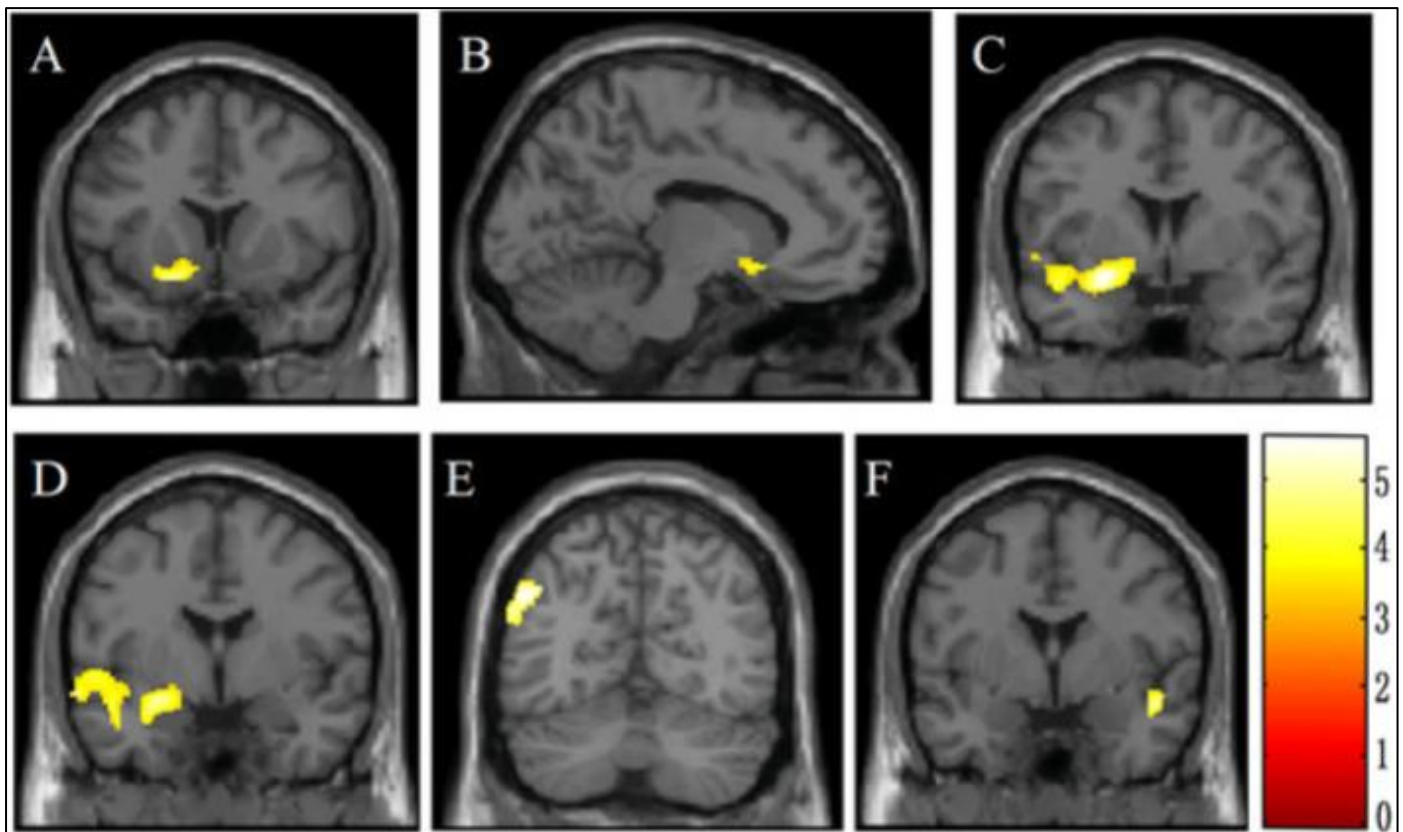
(cortisol awakening response; CAR (Stalder et al., 2016)) (Fig:2), and then drops all day long (Russell and Lightman, 2019). High cortisol level in the morning is most often seen in AD-related HPA axis agitated activity (Gil-Bea et al., 2010; Giubilei et al., 2001; Laske et al., 2009; Notarianni, 2013). A meta-analysis writes down that cortisol levels are highest in the morning among patients with Alzheimer's disease when compared to cognitively normal individual (blood test).



(Fig:2) Blood Cortisol Level Over the Day (Data Source from Lovallo and Thomas, 2000)

Cortisol levels ratio in saliva, urine, blood plasma or cerebrospinal fluid (CSF) are augmented in patients with AD and mild cognitive impairment (MCI) (Martignoni, et al., 1990, Popp, et al., 2015). Lower Gray matter volume is also related to higher concentration in cortisol level as evaluated by magnetic resonance imaging (MRI) (Fig:3). This negative effect is seen in both, people with dementia as well as people without it (Geerlings, et al., 2015, Toledo, et al., 2013). Such brain variation can lead the threat to cognitive decline (Csernansky, et al., 2006, Huang, et al.,

2009). Women has ominously greater cortisol response than men (Peskind et al 1996). A study conducted by de Leon et al. (1988) determined a positive correlation between the severity of dementia and the human cortisol response to an IV glucose load in nine cases of Alzheimer's disease (AD) and one case of vascular dementia (VaD) characterized by hippocampal atrophy. In contrast, Lawlor et al. (1994) reported no association between elevated cortisol levels and overall brain atrophy.



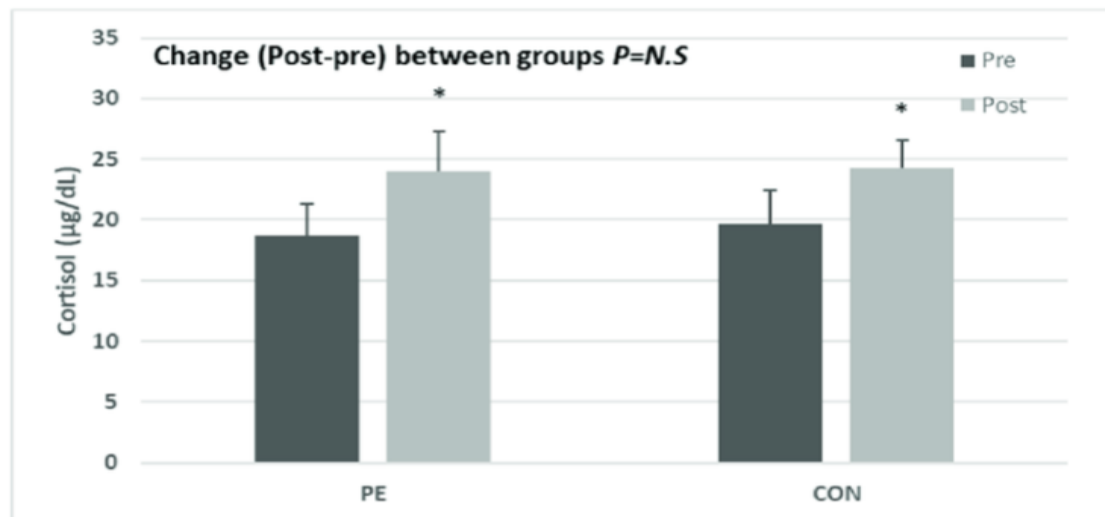
(Fig:3) Lower Gray Matter in MRI

III. PREVENTION TECHNIQUES

➤ Physical Exercise

Participating in physical activity can lead to lower stress levels (heart rate, blood pressure; Forcier et al., 2006; Hamer et al., 2006; Wipfli & Ramirez, 2013). One proposed mechanism by which exercise aids in the management of stress more effectively pertains to the regulation of the HPA-axis by the body. (Chen et al., 2017). Rendering to research, individuals with higher levels of physical activity exhibit a specific daily pattern of cortisol levels. In comparison to their less active counterparts, these individuals often experience lower cortisol levels upon waking, with peaks occurring at contrasting times

throughout the day. This difference highlights the critical role of consistent physical activity in maintaining proper cortisol regulation. In cases where physical activity is inconsistent or reduced, the natural cortisol awakening response may be disrupted, potentially resulting in imbalances in cortisol production. On the other hand, those who participate in moderate to vigorous physical activity demonstrate a more stable regulation of the hypothalamic-pituitary-adrenal (HPA) axis, which supports appropriate cortisol secretion. A significant reduction in cortisol levels is observed in individuals who engross in physical activities five times a week, as well as in those who participate in such activities three times a week (Beserra et al., 2018).



(Fig:4) Effect of Pilates Exercise on Cortisol Hormone Level, Bars Representation

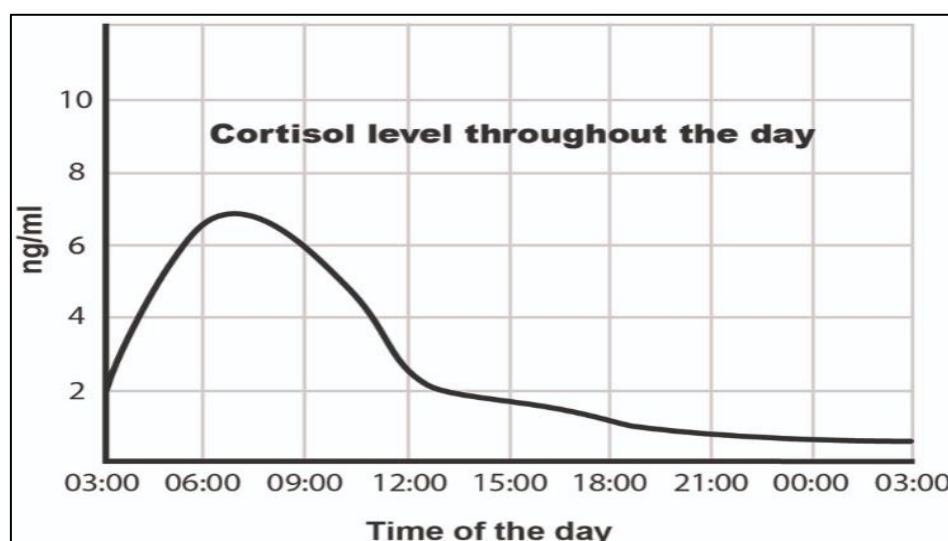
➤ *Balanced Diet*

One of the renowned effects of long-term stress is weight gain which is linked to cortisol hormone and the way it reacts to the body. Consumption of hyperpalatable food can increase the risk of high cortisol in the body (Fazzino et al., 2019; Yau & Potenza, 2013). Dietary differences show vulnerability in stress management. Certain nutrients influence cortisol levels, including phospholipids such as phosphatidylserine and phosphatidic acid. According to research published in European Food Research and Technology, a supplementation regimen providing a complex dose of 400 mg per day over a period of six weeks can significantly reduce cortisol levels. Egg yolk serves as a natural source of phosphatidylserine and is a protein-rich food that contributes to a balanced diet and hormone regulation, including cortisol (Siepka E, Bobak Ł, Gładkowski W., 2015). A meta-analysis by Long and Benton indicates that supplementation with vitamins and minerals can enhance stress management. Additionally, a survey of college students revealed that those who consume nutritious foods, such as salads, fruits, and vegetables, experience lower stress levels, whereas those who frequently

eat junk food tend to exhibit elevated cortisol levels (El Ansari et al). Maintaining a healthy diet may promote balanced cortisol levels and reduce the risk of cognitive impairment-related issues.

➤ *Sleep*

Humans sleeps on an average of 7-8 hours per day (Basner et al., 2007). Insufficient sleep can lead to noticeable changes in mood, decreased alertness, and impaired cognitive function, with the negative effects compounding over time (Veasey et al., 2002). Cold-pressor task on the people with bad sleep showed that they have aggravated cortisol response and strong reaction towards stress (Goodin et al., 2012). Animal studies have shown that sleeping less or not sleeping at all disturbs basal and stress-induced HPA responses. Sleep deprivation on both acute and chronic level has shown increased level of f basal corticosterone and adrenocorticotrophic hormone (Meerlo, Koehl, van der Borght, and Turek., 2002). A pilot study has indicated a direct correlation between poor sleep quality, reduced sleep duration, and increased cortisol levels.



(Fig: 5) Low Cortisol Level Due to Quality Sleep.

Sleep disturbances can be addressed through various conventional practices aimed at lowering cortisol levels and alleviating stress, with meditation being a prominent example. A foundational study in neuropsychobiology indicates that meditation can facilitate significant sleep improvement across all age groups. Typically, meditation is integrated with other techniques, such as Integrative Body-Mind Training (IMBT), which employs mental imagery and physical relaxation to manage stress and promote a sense of calm (Tang, 2011). Additionally, Mindfulness-Based Stress Reduction (MBSR) and Mindfulness-Based Cognitive Therapy (MBCT) combine meditation with psychoeducational elements (Fjorback et al., 2011). In summary, engaging in meditation can reduce the likelihood of cognitive decline and lower stress levels, which are directly associated with enhanced sleep quality, fewer sleep disruptions, and decreased cortisol production.

IV. CONCLUSION

With our current fast-paced, ever-booming nation's economy and the constant push on lifestyles, many are building stress levels much more easily than ever before that can rapidly enhance the level of the hormone cortisol. Everyone knows that high levels of stress enhance the need for elevated levels of cortisol, which is a factor for increasing the risk of cognitive decline-including with a relationship to disorders such as Alzheimer's Disease (AD). Although it has been found that a real scientific cause of AD is still not established, a direct correlation between the aging process in human beings and the incidence of age-related cognitive problems like dementia and AD has been proved. Thus, the number of cases of cognitive impairments rose in proportion directly correlated with the growing levels of stress in our society. This research paper explores in greater depth how high levels of cortisol contribute to cognitive decline, especially AD, and provides insight into preventive measures that would allow for proper regulation of cortisol and lower the prospects of cognitive impairment soon.

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