



International Journal of Medical Research & Health Sciences

www.ijmrhs.com Volume 2 Issue 1 Jan-Mar 2013 Coden: IJMRHS Copyright ©2013 ISSN: 2319-5886

Received: 9th Dec 2012

Revised: 25th Dec 2012

Accepted: 31st Dec 2012

Original research article

DEHYDROEPIANDROSTERONE LEVELS AND COGNITIVE FUNCTION IN AGING

*Rathna Kumari U¹, Padma K²

¹PG Resident, ² Director, Institute of Physiology and experimental medicine, Madras Medical College, Chennai-03

* corresponding author email: uratna_1986@yahoo.co.in

ABSTRACT

Background: Dehydroepiandrosterone (DHEA) is a steroid hormone secreted by the adrenal cortex. Recent research reports show that DHEA has various beneficial effects including neuro protective effects and that the decline in its production with aging may contribute to neuronal dysfunction and degeneration, and thus cognitive decline. **Aim:** To assess the cognitive functions and estimate the levels of DHEA in subjects of the same age group. **Materials and Methods:** A cross sectional comparative study of sixty healthy male participants between 60 to 70 years of age was done. They did not have other medical disorders likely to affect cognitive function. Their performance in the principal domains of cognition, i.e. memory, attention and concentration, verbal fluency, language and visuospatial functioning was observed. Serum levels of DHEA were estimated for all the participants by ELISA method. **Results:** A significant positive correlation was observed between DHEA level and three domains of cognition viz., visuospatial skills ($r = 0.95$), verbal fluency ($r = 0.49$) and short term memory ($r = 0.28$). No association was found with other domains of cognition. **Conclusion:** Subjects with low levels of serum DHEA among the same age group showed a significant decline in visuospatial skills, short term memory and verbal fluency.

Keywords: Dehydroepiandrosterone sulphate, Cognitive function.

INTRODUCTION

Dehydroepiandrosterone (DHEA) is a steroid, mainly of adrenal origin, that is found in relatively high concentrations in human plasma. It serves as a precursor of both androgenic and estrogenic steroid hormones. In the circulation, DHEA exists both free and bound to sulphate (DHEA-S). Thus, DHEA-S serves as the principal storage form of DHEA. DHEAS – has many intrinsic effects like antiaging, antiobesity, antidiabetic, anti atherogenic and neuroprotective effects¹. A

progressive decrease in circulating levels of DHEA with age has long been recognized, with peak levels occurring between the third and fourth decades of life and decreasing progressively thereafter by about 90% over the age of 85. Though DHEAS levels peak at around 25 years of age and starts declining with increase in age, it is subject to wide inter-individual variations. Its levels are also affected by factors like gender, physical activity etc. Recent research reports show

that decline in DHEA production with aging may contribute to neuronal dysfunction and degeneration, and thus cognitive decline. Animal experiments showed that DHEAS can enhance neuronal and glial survival and differentiation in culture^{2, 3}. Administration of DHEA has been reported to have striking beneficial effects on memory. Their cognitive performances were directly related to increases in plasma levels of DHEA and DHEA-S⁴. The present study thus was performed to investigate possible associations between DHEA levels and cognitive performance in healthy elderly men.

MATERIALS AND METHODS

After the institutional ethical approval the present study was conducted in the Institute of Physiology and Experimental medicine, Madras Medical College, Chennai. After obtaining informed consent, sixty healthy male subjects (who had completed at least 10 years of basic school education) aged between 60 and 70 years were selected randomly from the urban population of

Chennai city. They did not have other medical disorders likely to affect cognitive function. We explained the scope and details of the study to the subjects. The subjects underwent routine clinical examination and biochemical tests to satisfy the selection criteria. Fasting blood samples of the subjects were obtained for estimation of DHEA-S. Fasting blood samples were obtained under strict aseptic precautions, by venepuncture of the antecubital vein. The serum was separated and stored in the deep freezer at -20⁰ C. The serum levels of DHEA-S was measured using ELISA kits viz. serum Dehydroepiandrosterone sulphate estimation supplied by Cal biotech Inc (California). The Addenbrooke's Cognitive Examination- Revised (ACE-R)¹⁶ was applied to all the participants. It is a brief and simple cognitive screening tool. It is established as a sensitive screening test for Mild Cognitive Impairment, dementia and Alzheimer's disease. It takes about 15 minutes to administer this test for each participant.

Table: 1. ACE-R five major domains of cognition and normal values.

	Normal Values	Below normal/poor
Attention	16 and above	<16
Memory	17 and above	<17
Verbal fluency	9 and above	<9
Language	22 and above	<22
Visuospatial functioning	14 and above	<14

RESULTS

In our study the mean DHEA level ($\mu\text{g/dl}$) of the subjects was (142.9 ± 36). We observed a significant positive correlation between DHEA level and three domains of cognition viz.,

visuospatial skills ($r = 0.95$), verbal fluency ($r = 0.49$) and short term memory ($r = 0.28$). No significant association was found with other domains of cognition

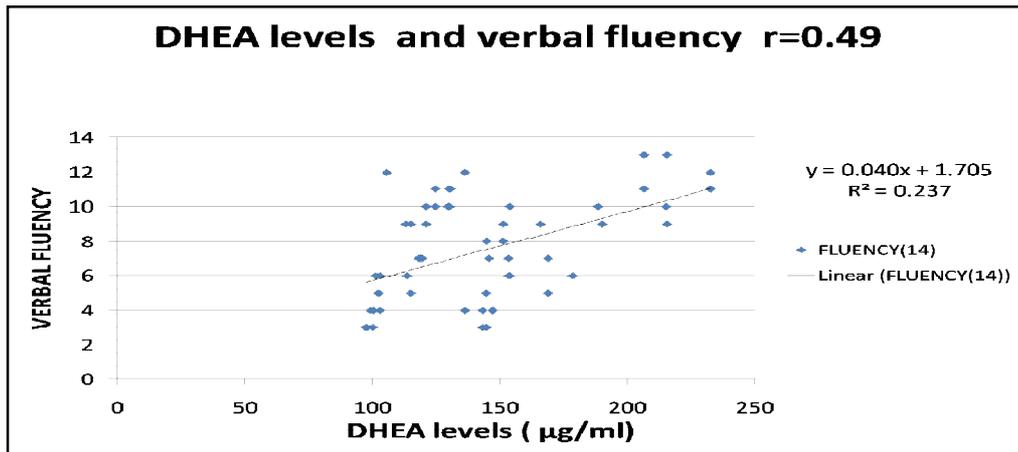


Fig:1. Correlation between DHEA (µg/dl) and verbal fluency.

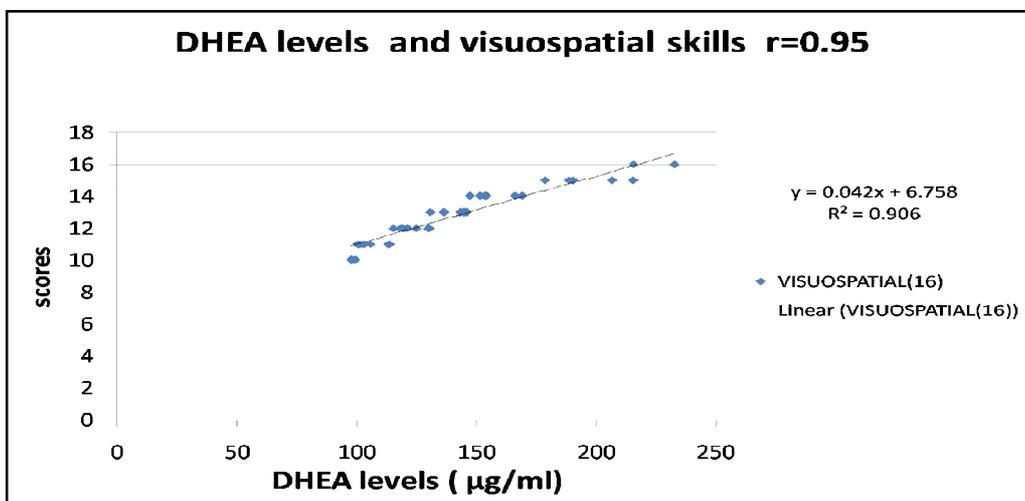


Fig:2. Correlation between DHEA (µg/dl) and visuospatial skills.

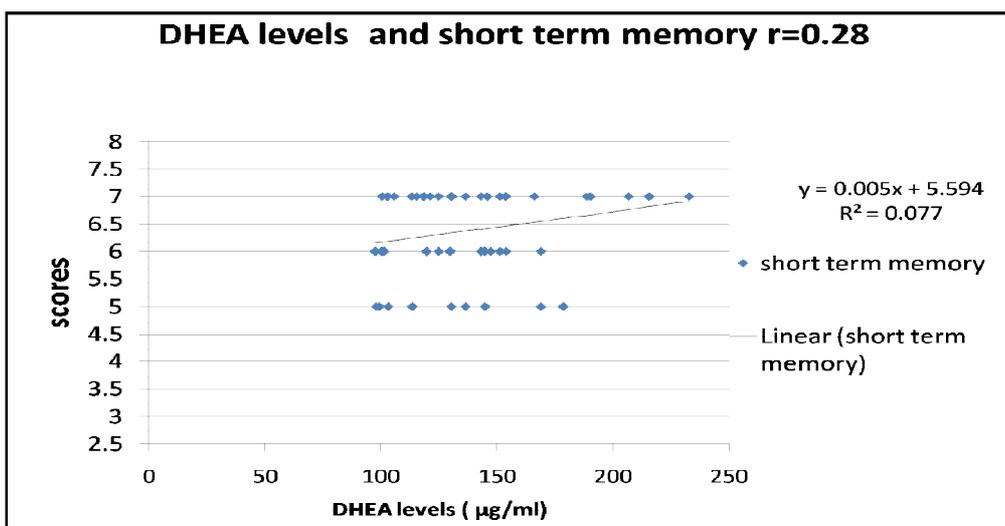


Fig:3. Correlation between DHEA (µg/dl) and short term memory.

Table 2. Correlation between DHEA and Visuospatial skills

		DHEA	VISUOSPA
Pearson Correlation	DHEA	1.000	.952**
	VISUOSPA	.952**	1.000
Sig. (2-tailed)	DHEA	.	.000
	VISUOSPA	.000	.
N	DHEA	60	60
	VISUOSPA	60	60

** . Correlation is significant at the 0.01 level

Table 3. Correlation between DHEA and Short Term Memory.

		DHEA	STM
Pearson Correlation	DHEA	1.000	.279*
	STM	.279*	1.000
Sig. (2-tailed)	DHEA	.	.031
	STM	.031	.
N	DHEA	60	60
	STM	60	60

*. Correlation is significant at the 0.05 level

Table 4. Correlation between DHEA and Verbal Fluency

		DHEA	FLUEN
Pearson Correlation	DHEA	1.000	.487**
	FLUEN	.487**	1.000
Sig. (2-tailed)	DHEA	.	.000
	FLUEN	.000	.
N	DHEA	60	60
	FLUEN	60	60

** . Correlation is significant at the 0.01 level

Table 5: Correlation between DHEA and Long Term Memory.

		DHEA	LTM
Pearson Correlation	DHEA	1.000	.059
	LTM	.059	1.000
Sig. (2-tailed)	DHEA	.	.655
	LTM	.655	.
N	DHEA	60	60
	LTM	60	60

No significant correlation

Table 6: Correlation between DHEA and Language skills.

		DHEA	LANG
Pearson Correlation	DHEA	1.000	.068
	LANG	.068	1.000
Sig. (2-tailed)	DHEA	.	.604
	LANG	.604	.
N	DHEA	60	60
	LANG	60	60

No significant correlation

DISCUSSION

Debonnel et al in the year 1996 showed that DHEA acts on the central nervous system to increase the effects of the excitatory neurotransmitter, glutamate, and decrease the effects of the inhibitory neurotransmitter, GABA⁵. DHEA and its sulfated form are considered neuroactive because they affect the GABA-A receptor complex and NMDA-mediated glutamate transmission via sigma receptors¹². Studies have also shown that DHEA increases neuronal excitability, enhances neuronal plasticity and acts as a neuroprotective agent⁶.

Blauer et al in 1991 observed that both the immunological and neural effects of DHEA/S may be related to their powerful antiglucocorticoid action⁷. It has been proved that very high levels of cortisol can cause damage to neurons, particularly in the hippocampus⁸. The adverse effects of cortisol which might be seen during stress or trauma may be counteracted by the high levels of DHEA. Lower levels of DHEA in older adults may make them more vulnerable to the damaging effects of cortisol⁹. In vitro studies have proved that DHEA can increase the proliferation of human neural stem cells and the number of neurons.

Some research studies showed lower levels of DHEA in the serum of patients diagnosed with dementia¹⁰. DHEA and DHEA sulfate are proved to be neurosteroids that modulates learning and memory¹¹.

Wolf et al in 1997 found significant improvement following DHEA administration compared with placebo in both immediate recall and delayed recall memory test¹³. Higher endogenous DHEAS levels were independently and favorably associated with better executive function, concentration, and working memory¹⁵. Cross-sectional studies have reported a relationship between the prevalence of Alzheimer's disease and low dehydroepiandrosterone sulphate (DHEA-S) plasma levels¹⁴.

CONCLUSION

In an aim to find an association between DHEA levels and cognitive functions in healthy ageing, we found that higher levels of DHEA was linked to better visuospatial skills, verbal fluency and short term memory. Recently, there has been a resurgence of interest in DHEA, because it has been suggested that it might have anti-ageing effects. It has also been suggested that serum DHEA may be represented as a biomarker of healthy aging and physiological methods of improving its levels by physical activity, diet etc., are topics of recent research. Hence, age related cognitive decline, Alzheimer's disease and its associated complications which are considered as an expanded spectrum of accelerated ageing can attribute a part of its pathogenesis to lowering DHEA levels. Further research on this topic can derive clues to pathogenesis of ageing.

REFERENCES

1. Adams JB. Control of secretion and function of C19-delta 5-steroids of the human adrenal gland. *Mol Cell Endocrinol* 1985; 41:1-17.
2. Roberts E, Bologna L, Flood JF, Smith GE. Effects of dehydroepiandrosterone and its sulfate on brain tissue in culture and on memory in mice. *Brain Res.* 1978; 406:357-62.
3. Bologna L, Sharma J, Roberts E. 1987 Dehydroepiandrosterone, and its sulfated derivative reduce neuronal death and enhance astrocytic differentiation in brain cell cultures. *J Neurosci Res.* 1987; 17:225-34
4. Wolkowitz, Owen M., et al. Dehydroepiandrosterone (DHEA) treatment of depression. *Biological Psychiatry.* 1997; 41(3): 311-18.
5. Debonnel G, Bergeron R, and de Montigny C. Potentiation by dehydroepiandrosterone of the neuronal response to N-methyl-D-aspartate in the CA3 region of the rat dorsal hippocampus:

- an effect mediated via sigma receptors. *Journal of Endocrinology* 1996;150:S33-42.
6. Kimonides VG, Khatibi NH, Svendsen CN, Sofroniew MV, Herbert J. Dehydroepiandrosterone (DHEA) and DHEA-sulfate (DHEAS) protect hippocampal neurons against excitatory amino acid-induced neurotoxicity. *Proceedings of the National Academy of Sciences USA* 1998; 95:1852-57.
 7. Blauer KL, Poth M, Rogers WM, Bernton EW. Dehydroepiandrosterone antagonises the suppressive effects of dexamethasone on lymphocyte proliferation. *Endocrinology* 1991; 129:3174-79.
 8. Lupien SJ, de Leon M, de Santi S, Convit A, Tarshish C, Nair NPV. Cortisol levels during human aging predict hippocampal atrophy and memory deficits. *Nature Neuroscience* 1998; 1(1):69-73.
 9. Herbert J. Stress, the brain, and mental illness. *BMJ* 1997; 315:530-35.
 10. Hillen T, Lun A, Reischies FM, Borchelt M, Steinhagen TE, Schaub RT. DHEA-S plasma levels and incidence of Alzheimer's disease. *Biological Psychiatry* 2000; 47(2):161-163.
 11. Baulieu EE, Robel P. Dehydroepiandrosterone and dehydroepiandrosterone Sulfate as neuroactive neurosteroids. *J Endocrinol* 1996; 150:S221-39
 12. Bergeron R, Montigny CD, Debonnel G. Potentiation of neuronal NMDA response induced by dehydroepiandrosterone and its suppression by progesterone: effects mediated by sigma receptors. *J Neurosci* 1996; 16(3):1193-202.
 13. Wolf OT, Neumann O, Hellhammer DH, Geiben AC, Strasburger CJ, Dressendorfer RA, et al. Effects of a 2-week physiological dehydroepiandrosterone substitution on cognitive performance and well-being in healthy elderly women and men. *J Clin Endocrinol Metab* 1997; 82(7):2363-67.
 14. Hillen, Thomas, et al. DHEA-S plasma levels and incidence of Alzheimer's disease. *Biological psychiatry*.2000; 47(2): 161-63.
 15. Davis SR, Shah S, McKenzie D, Kulkarni J, Davison S, Bell R. Dehydroepiandrosterone Sulfate Levels Are Associated with More Favorable Cognitive Function in Women. *Clinical Endocrinology and Metabolism* 2008; 93(3):801-08.
 16. Mioshi, Eneida, et al. The Addenbrooke's Cognitive Examination Revised (ACE-R): a brief cognitive test battery for dementia screening. *International journal of geriatric psychiatry*. 2006; 21(11): 1078-85.