AGE BASED VARIATION IN SHORT TERM MEMORY IN FEMALE SUBJECTS.

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Abstract : Background & Objectives: Memory is our ability to process, retain and subsequently recall information of the past learned experiences. Memory is divided into sensory memory, short term and long term memory depending on its processing status. Sensory memory by verbal mode undergoes encoding to form short term memory. This study has been planned with the aim to study the effect of age on memory in females which will reflect the effect of female sex hormones on memory. **Method:** The study was carried out on 120 female subjects after seeking their consent and sorting out inclusive and exclusion criteria, using California Verbal Learning Test II. For comparing age-wise memory status, following groups were formed of 30 subjects each: Group A :21-30 years; Group B : 31-40 years; Group C :41-50 years; Group D: 51-60 years. **Results:** Intergroup comparison showed best memory score for group A for immediate free recall for all 5 trials, short delay recall, long delay recall and recognition memory. Memory score decreased gradually within other groups with progression of age. **Interpretation & Conclusion:** The present study, therefore showed that recall of memory decreases as age advances, perhaps due to decreased hormone levels.

Keywords: Age, Short term memory, Learning, Recall Memory, Female Sex Hormones.

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Introduction: Since time is immemorial, humans have tried to understand the concept of memory. It is an important part of what makes us truly human, and yet it is one of the most elusive and misunderstood part of human attributes.

Memory is the ability to process, store/retain and subsequently recall information of the past learned experiences. It is the sum total of knowledge we remember, gives us the capability to learn and adapt from previous experiences as well as to build normal way of living life. In simple terms of Physiology, memory forms by a set of processed neural connections in the brain[1]. Memory is divided into sensory memory, short term/ working memory and long term memory depending upon its time span. Sensory memory is an ultra short term memory which is formed through the sensory stimuli received through the five senses (sight, smell, hearing, touch and taste). It is the ability to retain impressions of sensory information after the original stimuli have ended[2].

Short term memory which interests a person, undergoes encoding to form short term memory. It is the ability to remember and process information at the same time. It holds a small amount of information in a readily available form for a short period of time, from 10 to 15 seconds upto 1 minute. It is also known as working memory. Long term memory is intended for storage of information over a long period of time, as it is very resistant to decay. It can store a seemingly unlimited amount of information for an indefinite period. It has a further subdivision into explicit (declarative) and implicit (procedural) memory. Explicit is further subdivided into episodic and semantic memory, and implicit is subdivided into motor skills and emotional memory[3].

Memory (sights, sounds, words, emotions) is encoded in the same part of the brain that originally created that fragment (visual cortex, motor cortex, language area, amygdala, etc). After that it undergoes consolidation process in hippocampus and related structures. Recall of a memory, effectively reactivates the similar neural patterns generated during the original encoding. This kind of distributed memory ensure that even if part of the brain is damaged, some parts of an experience of any event may still remain[3].Verbal information is better retained when it is self-generated rather received passively. Specifically, self-generation involves an individual's production of verbal information

based on a cue or set of cues, (semantic, phonological, or visual), as opposed to hearing or reading the full phonological or orthographic form. In the clinical setting, the application of self-generation procedures has been found to improve memory in both non demented elderly individuals and patients with Alzheimer's disease, frontal lobe dementia, and in a number of other conditions. Overall , the clinical studies support that active participation during verbal encoding engages memory mechanisms that supplement those during passive observation, leading to improvements in memory performance[4].

Dementia is a degeneration of the brain and therefore of many cognitive processes, including memory. Memory deficits are often evident before any other signs of dementia are obvious. Monitoring memory function can therefore be useful for early diagnosis of dementia, which in turn can help with the management of the disorder, potentially therapeutically slowing down the progression. For example, it has been shown that early deficits in episodic memory abilities can be indicative of the likelihood of a person developing Alzheimer's disease later on in life[5].

Mild cognitive impairment (MCI) is widely considered a prodromal phase of dementia because many individuals diagnosed with MCI convert to Alzheimer's disease. Understanding cognitive complaint in MCI is important because it is essential part of the MCI diagnostic criteria, and cognitive complaint may be an early and predictive marker of unhealthy brain aging. Cross- sectional studies suggest that subjective cognitive complaint in MCI is related to poorer verbal episodic memory performances[6]**.** In respect of the earlier studies, the present study aims to study the effect of age and female sex hormones on memory.

Material and method: The present study was carried on 120 female subjects in the department of Physiology of Shri Guru Ram Rai Institute of Medical and Health Sciences, Patel Nagar, Dehradun. For comparing age-wise memory status, following groups were formed of 30 subjects each: Group A - 21-30 years, Group B - 31-40 years, Group C - 41-50 years, Group D - 51-60 years. All the chosen subjects were physically and mentally fit, non smoker, non alcoholic and of same socio-economic and educational status. All were free from any auditory and verbal diseases. Subjects were also screened and excluded for medical conditions known to have impact on cognitive and memory functions, e.g. neurological or psychiatric disorders, head injury, cardiovascular disease, hypertension and diabetes mellitus. Approval from college's ethical committee was taken. All the subjects were made familiar with the method prior application on them and Informed consent was taken from all subjects.

Materials: The test adopted for the above study was California Verbal Learning Test-II (CVLT-II); (Delis et al 1987)[7]. It is a standard technique and has been adopted for various neurological studies based on memory. This test consisted of word lists of absolutely familiar 16 words from four different categories. In List A, there were four animals, four vegetables, four ways of travelling, and four pieces of furniture. In List B, there were four animals, four vegetables, four instruments, and four parts of house (Distractors). List C consisted of 8 novel distractors (categories same as list A). List D consists of 8 novel distractors (categories unrelated to any category A or B). Two of the four categories (animals and vegetables) were common to both lists. **Procedure of Test:** California Verbal Learning Test-II (CVLT-II) was administered to subjects. The evaluator read a list of words (List A), and participants were asked to recall as many of the words as they could, in any order **(Immediate free recall (IR): List A)**. This procedure was repeated four times (trials 2-5), so that there were five trials total. Following the list-learning procedure in Trials 2 to 5, participant heard a second list of words (List B) and subsequently tried to name as many of these words as possible **(Immediate Free Recall of Distractors (IRD): List B).** Then, the participant was asked to name as many words as possible from the first list again **(Short-Delay Free Recall (SDFR): List A).** Following this free recall task, participants are given a cued recall task, in which they are

asked to name all the words from the first list that belonged to each of the four categories **(Short-Delay Cued Recall (SDCR)).** Following a delay of approximately 20 to 30 min, she was asked to recall words from the first list that was read to them **(Long-Delay Free Recall (LDFR)).** Participants were not expecting this free recall condition, as they were not told that there would be further tests with the word lists. The categories were then provided as cues **(Long-Delay Cued Recall (LDCR)).** Following this, a yes/no recognition task was given, in which participants had to respond yes or no as to whether a word had been on the List A with the help of List C and List D **(Long-Delay Yes/No Recognition (LDY/NR)).** After another delay of approximately 15 minutes, they were given a two choice, forced choice recognition task **(Long Delay Forced Choice Recognition (LDFCR)).** Data collected was subjected to ANOVA and post hoc (bonferroni's) tests using SPSS software version 23.

Observations & results:

Table 1 : Memory status in different age groups

	Group A	Group B	Group C	Group D
IR	15.46 ± 0.43	15.25 ± 0.53	14.84 ± 0.79	14.0 ± 1.50
IRD	13.40 ± 1.47	13.06 ± 1.43	12.93 ± 1.65	10.6 ± 2.85
SDFR	15.53 ± 0.50	15.36 ± 0.66	15.20 ± 1.39	14.56 ± 0.72
SDCR	16.00 ± 0.00	16.00 ± 0.00	16.00 ± 0.00	16.00 ± 0.00
LDFR	16.00 ± 0.00	16.00 ± 0.00	15.93 ± 0.25	15.86 ± 0.34
LDCR	16.00 ± 0.00	16.0 ± 0.00	16.00 ± 0.00	16.00 ± 0.00
LDY/NR	48.00 ± 0.00	48.00± 0.00	47.00 ± 2.44	46.80 ± 2.60
LDFCR	16.00 ± 0.00	16.00 ± 0.00	15.80 ± 0.61	15.80 ± 0.53

(Mean ± s.d)

By **ANOVA** : IR $_{596\ (df)}$ F $_{(14.706)}$ = 0.000***, IRD $_{116\ (df)}$ F $_{12.990}$ = 0.000 ***, SDFR $_{116\ (df)}$ F $_{6.709}$ = 0.000***, LDFR $_{116\ (df)}$ F $_{2.658}$= 0.006***, LDY/NR $_{116\ (df)}$ F $_{3.672}$ =0.014**, RFC $_{116(df)}$ F $_{2.090}$=).105.

P value: <0.05-significant, <0.001-Highly significant

Table 2 : Multiple intergroup comparison (post hoc bonferroni's test)

Subtests	Group interaction significance (p<0.05)											
	A			B			C			D		
	B	C	D	A	C	D	A	B	D	A	B	C
IR	1.00	0.05	0.000	1.000	0.52	0.000	0.05	0.52	0.003	0.000	0.000	0.003
IRD	1.00	1.00	0.000	1.000	1.00	0.000	1.00	1.00	0.000	0.000	0.000	0.000
SDFR	1.00	0.90	0.000	1.000	1.00	0.004	0.90	1.00	0.042	0.000	0.004	0.042
LDFR	1.00	1.00	0.106	1.000	1.00	0.106	1.00	1.00	1.000	0.106	0.106	1.000
LDY/NR	1.00	0.27	0.05	1.000	0.27	0.05	0.27	0.27	1.000	0.05	0.05	1.000
LDFCR	1.00	0.34	0.679	1.000	0.34	0.679	0.34	0.34	1.000	0.679	0.679	1.000

By above analysis and results, it was inferred that both Free Recall as well as Recognition

memory had progressive declining trend from younger (reproductive) groups towards elderly (menopausal) groups.

Discussion: Ageing has its effects on the molecules, cells, vasculature, gross morphology, and cognition. The effects of ageing on the brain and cognition are widespread and have multiple etiologies[8]. Present study found statistically significant decline of short term memory as depicted by decline in memory score especially for immediate free recall, free recall of distractors , short delay & long delay free recall as well as recognition memory with progression of age in female subjects as in Figure 1.

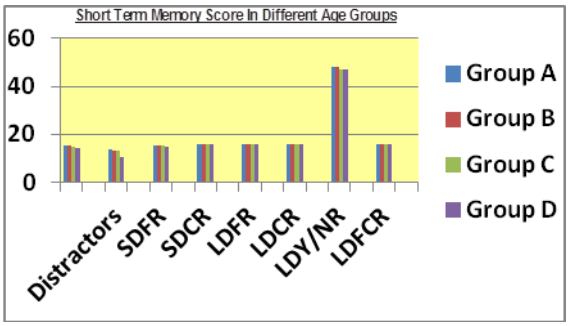

FIG: 1

Findings of the present study is concordant with the study done by Hara et al which suggest that human and non human primates are vulnerable to age and menopause- related decline in working memory, which depend on the energy-demanding excitation of pre-frontal cortex (PFC) neurons. Their findings suggested that hormone replacement therapy benefits cognitive aging, in part, by promoting mitochondrial and synaptic health in the PFC[10].

Vannest et al found that , as in other studies of verbal memory and aging, there were widespread age – related decreases in connectivity in many regions of the verbal encoding network engaged during self generation of words, as well as changes in task- negative ("read > generate") and default mode networks more active during the baseline reading task. These changes occurred independently of a small, but significant, decrease in memory performance for generated words with age[4].

The present study is also supported by the results of the study done by Mazurek et al that the subjects who experienced the memory retrieval as 'knowing' (which we interpret as semantic strategy), older participants performed worse than younger participants, and indeed than other older participants who 'remembered' the information. Older participants were not more likely to use a semantic strategy than younger people, suggesting there is no age deficit in the ability to use an episodic strategy. In a recent meta-analysis of recognition memory tests, aging was found to affect 'knowing' less than 'remembering', which is the opposite of the present study has shown here. However, people with diagnosed Alzheimer's suffered equally on 'remembering' and on 'knowing'. This again suggested that may be some of menopausal females of the present study might have had undiagnosed mental pathologies and therefore showed a larger deficit when using a semantic strategy[5].

Episodic memory depends on the integrity of the hippocampus and adjacent medial temporal lobe structures, and studies in rodents document robust effects of estrogen on hippocampal synaptic plasticity, hippocampal long- term potentiation, and hippocampal-mediated cognitive behaviours[9] . Verbal memory is the sensory memory with aural stimuli, also known as echoic memory. Estrogen is thought to have a facilitating effect on tasks of verbal memory in which women typically excel, such as articulation, speed and coordination. Role of estrogen can further be supported by studies conducted during mid luteal phase of menstrual cycle as women perform better at a higher level of the hormone on these tasks[12,13]. In younger women, verbal episodic memory is reported to be sensitive to estrogen effects, although progesterone concentrations were significantly positively associated with verbal memory and global cognition in early age group women has also been reported[14,11]. Menopause signals the end of spontaneous ovarian function and a woman's reproductive life. Endocrine changes accompanying the menopause include a gradual albeit erratic decline in estrogen levels over several years,

which drop to a low level in the postmenopause. These changes in estrogen levels have been speculated to account for the increased memory complaints during this period. Estrogen has neuroprotective and neurotrophic effects and, after the menopause which could be of faster rate in brain atrophy than in men[15]. Variations in the hormonal milieu after menopause may influence neural processes concerned with cognition, cognitive aging, and mood, where cognitive outcomes were standardized composite measures of verbal episodic memory, executive functions, and global cognition[14]. Estradiol induces gene transcription and rapid membrane signaling mediated by estrogen receptor alpha (ER∝), estrogen receptor–beta (ERß), and a recently characterized G-protein coupled estrogen receptor, each with distinct distributions and ability to influence estradiol-dependent signaling. Estrogens signal through a multitude of mechanisms in inducing axonal sprouting, regeneration, synaptic transmission, and the prevention of cell death. Estrogen receptors (ER) can activate production of brain derived neurotrophic factor (BDNF), which has shown to protect against ischaemic injury and retain cognitive function. In vitro studies have shown protective effects of estrogens from excitotoxicity by increasing the apoptosis regulator Bcl-2. Estrogens have been shown to protect against oxidative stress induced by amyloid-ß fibrils alone or in a complex with acetylcholinesterase, making estrogens a target for AD therapeutics[11]. Better deep engraved memory and other cognitive functions like visuospatial skills, language, memory, attention, in females as compared to males further supports the association of estrogen with cognition[13,16]. Endogenous sex steroid levels were unassociated with cognitive composites, but sex hormone binding globulin (SHBG) was positively associated with verbal memory[14,17]. Gifford et al provides new information about the cognitive and neuro anatomical correlates of memory complaint by suggesting that a memory complaint in mild cognitive impairment is related to worse immediate and delayed recall performances. Their findings enhance the prior literature by investigating detailed verbal episodic learning and memory performances (i.e. total learning, learning slope, immediate recall, delayed recall, recognition), rather than a global composite measure in older adults with MCI[6].

Mind body medicine provided a conceptual framework to bridge the gap between the frequency of memory complaints in post-menopausal women and the development of a more holistic treatment approach. It is likely that cognitive deficits might not be solely caused by declines in estrogen production, but may also likely to stem from reductions in sleep quality, increased depression levels, and the onset of hot flashes. They also suggested that mind body interventions may hold promise for treating cognitive declines associated with the menopausal transition, and had discussed how these therapies may be used alone or in combination with HT depending on the preferences of the patient and her medical provider[18].

Summary & Conclusion: As the age advances there is gradual decline in recollection of memories in females. The reason could be gradual cognitive impairment associated with decline in hormone levels especially estrogen hormone with advancing age. Menopause signals the end of ovarian function and women's reproductive life so hormonal estimation along with assessment of memory status is suggested for further research to give better correlation with age and also to rule out other causes for decline in memory with age in healthy individuals. As memory declines with age so timely mind body intervention may be helpful in improving memory of menopausal women.

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