



HUMAN BRAIN; PHYSIOLOGICAL ALTERATIONS OCCURRING UNDERLYING PRO- CESS OF AGING

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ABSTRACT... Aging is an irreversible and universal phenomenon of every living organism's life. Many recent studies provide evidences that is strictly related to decline in cognitive function impairment but along with various causes behind these abnormal changes, change in brain function and structure is one of the most important factors are being widely used to study the hypothesis that 'the deficits in and temporal order memory are closely related. Increase in age causes reduction in memory processing tasks, which involve information storage and processing. In other explanation it is mentioned that frontal activity, differences underlying aging is associated with recruitment of brain areas and neural circuit efficiency reduction. In case of young subjects increase in activity mean shorter reaction time but in older subjects results are opposite.

Key words: Aging, Positron Emission Topographic studies, frontal functioning, primates.

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STATEMENT OF NOVELTY

Aging is accompanied by the decline in brain physiology, particularly decline in the response and adaptation. The current paper reviews the physiological alterations occurring in human brain during the process of aging.

INTRODUCTION

Aging is an irreversible and universal phenomenon of every living organism's life. With the advent of age abnormal and reversal changes occurs in our body most of them are deleterious in nature such as loss in hearing ability, taste, loss of teeth, and reduction in sensitivity to growth factors, loss of lean tissues, reduction in reaction time, whitening of hairs. Similar changes occur also in our brain such as reduction in reaction time, neurochemical alterations, synaptic degeneration, gray and white matter atrophy^{1,2}. Aging is strictly related to decline in cognitive function impairment but along with various causes behind these abnormal changes, change in brain function and structure is one of the most important factors.

BRAIN FUNCTION ALTERATIONS

Recent studies (Raz², 2000; Parkin and Java³, 2000;

Cabeza¹, 2001; Calautti⁴ et al., 2001) provided evidences that normal aging do not have very much damaging effect on brain activity. It may be due to the reason that there is no direct relationship between brain activity and brain structure. Brain imaging techniques are most authentic way to relate brain with behavioral changes. Instead of this fact that there is large amount of work carried out on change in brain structure, change in brain functioning is relatively a young field of research. Here are some reviews of the studies carried out to explain the relatedness of change in brain structure to the cognitive functioning.

NEUROIMAGING STUDIES OF BRAIN FUNCTIONING

These studies are carried out in both rest and cognitive tests performing situations in older adults. At rest, differential sensitivity to frontal lobes is found along with consistent decrease in metabolic rates and regional blood flow in cerebral areas. Which is similar to the findings in middle age adults?^{5,6} There is limited number of experiments carried out to explain age-related differences in the patterns of brain activation during attention⁷, visual perception.^{8,4}

TEMPORAL-ORDER AND ITEM MEMORY IN RELATION TO NEURAL ACTIVATION

(PET) positron Emission Topographic studies are being widely used to study the hypothesis that 'the deficits in frontal functioning and temporal order memory are closely related'. It is well known that change in frontal lobe structure and function is related to the memory problems.⁹ Structural MRI studies or volumetric changes in brain reveals that contraction in frontal lobe volume is most prominent.¹⁰ Content memory which is also called as 'Item Memory' depends on frontal cortex more than content memory (Temporal Order Memory).¹¹ As context memory is more closely associated with the brain parts that are greatly affected by aging so context memory is more sensitive to aging. It is now verified that the tests used to check frontal alterations no more reflects content memory. Due to this fact PET is used to directly link frontal alterations with item and temporal memory. In both old and young adults.¹² Higher memory performance was confirmed in young adults by behavioral results. Further investigation proves that during temporal order retrieval in young adults the right prefrontal cortex is more activated than item retrieval.¹³ This finding has no contradiction with the evidences provided by early studies in human and primates that prefrontal lesion has affects more on temporal memory than item memory.

CHANGE IN MEMORY TASKS AND BRAIN ACTIVITY WITH AGE

Increase in age causes reduction in memory processing tasks which involves information storage and processing.³ In young individuals while performing working memory tasks depending upon stimulus regions in posterior parietal cortex and in medial and lateral prefrontal are tend to be activated. Verbal tasks and spatial tasks are associated with left and right hemisphere activity respectively.¹⁴ But in case of aged subjects while performing spatial and verbal tasks left and right hemispheric activity occurs and frontal regions lateralization is less clear.^{14,15} In addition to these hemispheric differences in young adults, while considering task-dependent differences there are large differences in the activity of dorso and

ventrolateral PFC.^{16,17}

According to the two-stage model of working memory, dorso and ventrolateral PFC are mainly concerned with manipulation or stored item and maintaining information respectively during tasks of working memory^{18,19} but there is variable age related differences in both regions. As compared to temporal storage in working memory the elders are more inaccurate in tasks related to executive control and manipulation²⁰ in brain activity the greatest difference is found in dorsolateral region but task-related activity in ventrolateral and dorsolateral regions of PFC whereas during various working memory tasks the difference in activation is only located in dorsolateral.^{21,22,23}

Experimentally investigations were made by studying aging effects on retrieval, encoding, storage and various other stages of working memory. The only difference was found in retrieval stage, as minimum degree of activation is made in dorsolateral region of PFC.²³ However, age such age related differences are not verified by other studies.²⁴

In all latter reports differences were observed in ventrolateral region of PFC and MTL consistently. These are the areas with lesser or no activation at all in older subjects. At the end there is no valid evidence about the reduction in activity in particular region in PFC.

AGING AND HIGH DEMAND MEMORY TASKS

To describe increase or decrease in prefrontal regional activity in older subjects one explanation comes from 'prefrontal-effort hypothesis. The pattern that was found in younger adults during both working²⁵ and episodic memories²⁶ was the difference in activity of left prefrontal region by recruitment of additional resources during high demand tasks. More activation occurs in prefrontal region when tasks difficulty increases. It term PageJ3 term as compensation on neural level because older adults prevent from declining in their performance of prefrontal by recruiting extra regions.²⁷ The supportive arguments were made that there is similar reduction in prefrontal

activity by attention division and by aging. It supports that available attention resources claim equal effect by high cognitive processing and by age.

Another study was made in which performance during single and dual-tasks were compared and it was revealed that during dual-tasks left PFC is activated poor performers of both old and young subjects but not in good young subjects.²⁸ In addition to this an experiment was made among difficult or temporal order and simple or recognition tasks. The results shows that right PFC is more activated than left one in young subjects and in old subjects the results are totally opposite but in case of posterior regions there is no age related difference was found.¹ The final evidence is provided by the findings in which it was revealed that longer reaction time and poorer performance is accompanied by reduction in frontal activity.^{23,27,29}

In other explanation it is mentioned that frontal activity, differences underlying aging is associated with recruitment of brain areas and neural circuit efficiency reduction.^{22,29} Over posterior regions the inhibitory control of frontal region is attributed by neural efficiency reduction.^{22,27,30} During short term memory tasks in older subjects there is weaker inhibitory action as compared to the younger subjects.³¹ According to this concept usefulness of increase in activity are not always but sometimes in cognitive functioning it is detrimental. Between reaction time and brain activity the neural circuit with reduced efficiency may reflect as positive correlation by slowing down cognitive processes. The evidence to this concept is provided by a study in which association between occipital and medial temporal as well as parietal regions to the reaction time was studied. In case of young subjects increase in activity mean shorter reaction time but in older subjects results are opposite.³²

CONCLUSION

In conclusion, aging involves deleterious changes in our brain and our all body as well. Most evidently global decrease occurs in PFC while performing high demand cognitive tasks and during rest. But

the changes involving decrease are not universal sometimes it may involve increase such as in case of activation in task-related elderly subjects. There is no clear evidence about the relationship of posterior *region* brain activity and aging. Reduction in neural efficiency reflects decrease and to compensate high demanding tasks the recruitment of extra regions reflects high frontal activity.

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REFERENCES

1. CABEZA, R. **Functional neuroimaging of cognitive aging.** In Cabeza R and Kingstone A (Eds), Handbook of functional neuroimaging of cognition, pp. 331-377. Cambridge, MA: MIT Press 2009.
2. Raz, N. **Aging of the brain and its impact on cognitive performance: Integration of structural and functional findings.** In Hand-book of Aging and Cognition-II (F. I. M., Craik and T. A. Salt-house, Eds.). Erlbaum, Mahwah, NJ 2000.
3. PARKIN, A.J. and JAVA, R.I. **Determinants of age-related memory loss.** In Perfect T J and Maylor EA (Eds), Models of cognitive aging, pp. 188-203. Oxford: University Press 2000.
4. CALAUTTI, C .. SERRATI, C .. and BARON, J.C. **Effects of age on brain activation during auditory-cued thumb-to-index opposition: A positron emission tomography study.** Stroke, 2001;32: 139-1 46.
5. KUHL, D.E., METTER, E.J., RIEGE, W. H., and PHELPS, M.E. **Effects of human aging on patterns of local cerebral glucose utilization determined by the [18F] fluorodeoxyglucose method.** Journal of Cerebral Blood Flow and Metabolism, 1982;2: 163-1 71.
6. SCHULTZ, s K., O'LEARY. D.S., BOLES, P. L.L., WATKINS, G.L., HICHA, R.D., and ANDREASEN, N.C. **Age-related changes in regional cerebral blood flow among young to mid-life adults.** Neuroreport, 1999;10: 2493-2496.
7. JOHANNSEN, P, JAKOBSEN, J, BRUHN, P, HANSEN, SB., GEE, A .. STODKILDE, J. H , and GJEDDE, A. **Cortical sites of sustained and divided attention in normal elderly humans.** NeuroImage, 1997;6: 145-155.
8. GRADY, C. L., MAISOG, J. M., HORWITZ, B., UNGERLEIDER, L. G., MENTIS, M. J., SALERNO. J. A., PIETRINIP, *et al.* **Age-related changes in cortical blood flow activation during visual processing of faces and location.** Journal of Neuroscience, 1994;14:1450-1462.

9. WEST, R. L. **An application of prefrontal cortex function theory to cognitive aging.** Psychological Bulletin. 1996;120, 272- 292.
10. Raz, N., Gunning F. M., Head, D., Dupuis, J. H., McOuain, J., Briggs, S_ D., Loken, W. J., Thornton, A. E .. Acker, J. D. **Selective aging of the human cerebral cortex observed in vivo: Differential vulnerability or the prefrontal way matter.** Cerebral Cortex, 1997;7(3), 268-282.
11. Schacter, D.L. **Memory, amnesia and frontal lobe dysfunction.** Psychobiology, 15, 21-36.
12. Parkin, A. J .. Walter, B. M., Hunkin, M. **Relationships between normal aging, frontal lobe function, and memory for temporal and spatial information.** Neuropsychology, 1995;9, 304-312.
13. Cabeza, R., Anderson. N.D., Houle, S., Mangels, J. A., Nyberg, L. **Age-Related Differences in Neural Activity during Item and Temporal - Order Memory Retrieval: A Positron Emission Tomography Study.** Journal of Cognitive Neuroscience 2000;12:1, pp. 197-206.
14. REUTER, L. P.A., JONIDES, J., SMITH, E.E., HARTLEY, A., MILLER, A., MARSHUET, C., and KOEPPE, R.A. **Age differences in the frontal lateralization of verbal and spatial working memory revealed by PET.** Journal of Cognitive Neuroscience, 2000;12: 174-187.
15. Cabeza. R. **Functional neuroimaging of cognitive aging.** In **Handbook of Functional Neuroimaging of Cognition** (R. Cabeza and A. Kingstone, Eds.), 2001;pp. 331 - 377. MIT Press, Cambridge, MA.
16. BRAVER, T. S .. COHEN, J.D., NYSTROM, L.E .. JONIDES, J., SMITH, E. E., and NOLL, D.C. (1997). **A parametric study of prefrontal cortex involvement in human working memory.** NeuroImage. 5: 49-62
Butters, M. A., Kaszniak, A. W., Glisky, E. L., Eslinger, P. J., Schacter, D. I. (1994). **Recency discrimination deficits in frontal lobe patients.** Neuropsychology, 8, 343-353.
17. STERN, C. E., OWEN, A. M., TRACEY, I., LOOK, R. B., ROSEN, B. R .. and PETRIDES, M. **Activity in ventrolateral and mid-dorsolateral prefrontal cortex during nonspatial visual working memory processing: Evidence from functional magnetic resonance Imaging.** NeuroImage, 2000;11 : 392-399.
18. OWEN, A. M., EVANS, A. C., and PETRIDES, M. **Evidence for a two-stage model of spatial working memory processing within the lateral frontal cortex: A positron emission tomography study.** Cerebral Cortex, 1996;6: 31-38.
19. PETRIDES, M. **Functional organization of the human frontal cortex for mnemonic processing. Evidence from neuroimaging studies.** Ahnals of the New York Academy of Sciences, 1995;769: 85-96.
20. VERHAEGHEN. P., MARCOEN, A., and GOOSSENS, L. **Facts and fiction about memory aging: A quantitative integration of research findings.** Journal of Gerontology, 1993;48: Pt 57-171.
21. NAGAHAMA, Y, FUKUYAMA, H, YAMAUCHI, H., KATSUMI, Y., MAGAT A, Y., SHIBASAKI, H, and KIMURA, J. **Age-related changes in cerebral blood flow activation during a Card Sorting Test.** Experimental Brain Research, 1997;114: 571-577.
22. ESPOSITO, G., KIRKYB, B. S., VAN HORN, J. D., ELLORE, T. M., and BERMAN, K. F. **Context-dependent, neural system-specific neurophysiological concomitants of ageing: Mapping PET correlates during cognitive activation.** Brain, 1999;122: 963-979.
23. RYPMA, B. and D'ESPOSITO, M. **Isolating the neural mechanisms of age-related changes in human working memory.** Nature Neurosci2nco, 2000;3: 509-515.
24. MITCHELL, K. J, JOHNSON, M. K, RAYE, C. L., and D'ESPOSITO, M. (2000). **fMRI evidence of age-related hippocampal dysfunction in feature binding in working memory.** Cognitive Brain Research, 2000;10: 197-206.
25. RYPMA, B. and D'ESPOSITO, M. **The roles of prefrontal brain regions in components of working memory: Effects of memory load and individual differences.** Proceedings or the National Academy of Sciences of the USA, 1999;96: 6558-6563.
26. NOLDE, S. F., JOHNSON, M. K., and RAYE, CL **The role of prefrontal cortex during tests of episodic memory.** Trends in Cognitive Sciences, 1998;2: 399-406.
27. GRADY, C. L. and CRAIK, F.I. **Changes in memory processing with age.** Current Opinion in Neurobiology, 2000;10: 224-231.
28. SMITH, E. E., GEVA. A., JONIOES. J., MILLER, A., REUTER-LORENZ, P, and KOEPPE, R A. **The neural basis of task-switching in working memory: Effects of performance and aging.** Proceedings of the National Academy of Sciences of the USA, 2001;98: 2095-2100.
29. MADDEN D. J., TURKINGTON. T. G., PROVENZALE JM, D ENNY LL, HAWK TC, G OTTLOB LR, and COLEMANRE. **Adult age differences in the functional neuroanatomy of verbal recognition memory.** Human Brain Mapping, 1999;7: 115-135.
30. HASHER, L. and ZACKS, R. T. **Working memory,**

- comprehension and aging: A review and a new view.** Psychology of Learning and Motivation, 1988;22: 193-225.
31. DELLA-MAGGIORE, V., SEKULER, A. B, GRADY, C. L., BENNETT, P J., SEKULER, R ., and MCINTOSH, A. R. **Corticolimbic interactions associated with performance on a short-term memory task are modified by age.** Journal of Neuroscience, 2000;20: 8410-8416.
32. GRADY, C. L., MCINTOSH, A R., BOOKSTEIN, F., HORWITZ, B., RAPOPORT, S. I., and HAXBY, J. V. (1998a). **Age-related changes in regional cerebral blood flow during working memory for faces.** NeuroImage, 8:409-425.



“The weathers keep on changing;
the life carries on.
ENJOY it.”

Shuja Tahir

