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# A Review on Short Term effects of Radiotherapyon Memory in Patients with Tumor

**Sangeetha Joji[1] | Khansa Fathima[2]**

[1]Department of cognitive Neuroscience and Psychology, JSS Academy of Higher Education and Research, Mysore, India.
[2]Department of Medical Physics, JSS Academy of Higher Education and Research, Mysore, India.

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## ABSTRACT

The objective of the review is to evaluate the short-term effects of radiotherapy on memory performance in patients with tumors. This article presents a neuropsychological account of the memory ability after radiation therapy. By drawing attention to memory loss of cancer patients after radiation, we hope to illustrate and emphasize the importance of neuropsychological sequelae when evaluating the short-term outcome of radiotherapy for cancer patients

**KEYWORDS:** Radiation, Memory, Tumor, Neuropsychology, Cancer

## INTRODUCTION

Every year many hundreds of thousands of patients worldwide undergo radiotherapy for primary brain tumors and for brain metastases originating from extracranial tumors. Radiation is an indispensable treatment mainstay for the majority of these brain tumors. Brain radiotherapy is subdivided into whole brain radiotherapy (WBRT) in which the entire brain and brainstem are irradiated, and partial brain radiotherapy (PBRT) which includes treatment of the tumor or tumor bed and surrounding margin, and some healthy brain tissue subject to incidental irradiation.[1]

Although several parameters (e.g., cancer site, type and stage) determine choice of the most appropriate therapeutic approach, radiation therapy, beside surgery, remains a main treatment modality for tumors of the CNS and for brain metastases [2]. The main objective of radiotherapy is to destroy tumor cells while inflicting the least possible injury to neighboring normal tissues; however, this is often not achievable or feasible. irradiation]. Neurocognitive defects are clearly linked with radiation therapy, particularly in children where they represent a major detrimental side effect of life-saving procedures [3]. Cognitive decline may become manifest numerous months to years after irradiation and get progressively worse.

The effects of radiotherapy on the central nervous system can be divided into three categories:[4] first, acute reactions that occur within the first hours or days after treatment and are associated with increased intracranial pressure; second, delayed reactions that are considered short-term effects that occur between a few weeks to a few months after the completion of treatment; and, third, long-term, delayed effects that occur from months to years after the completion of treatment. It has been found that most long-term survivors of high-grade glioma have shown significant cognitive difficulties that, nonetheless, probably were

due to multiple factors, including irradiation, the disease itself, and the effects of surgery.[5] More specifically, in a study of five patients with brain tumors and six individuals in a control group, it was found that patients suffered from impairment of memory functions 1.5 months after the completion of radiotherapy.[6] Similarly, in another study, slowness in reaction time (RT) was found as late as 6 months after the completion of radiotherapy.[7] Furthermore, after longer follow-up in the same study, RTs were at baseline level, and no other changes in the cognitive functioning of the patients were detected. However, because of the lack of a healthy control group in that study, it was difficult to say whether there were changes in the patients' cognitive functioning already at baseline.

Thus, these results suggest that, in particular, short-term effects may be harmful in relation to cognitive performance. However, the short-term effects of radiotherapy on cognitive functioning, and especially attention, have not been investigated systematically. Attentional and memory functions that are known to be associated widely with cerebral networksmay be susceptible to disturbance in patients with brain tumors.[8]

Memory is one of the most important cognitive functions and is closely related to the quality of life of cancer survivors. McDougall et al, found that most cancer survivors exhibited varying degrees of memory impairment, which affected their return to the society.[9] In cognitive neuropsychology, prospective memory (PM) is defined as the future plans or intentions of memory [10] and is a memory component that is most closely related to daily activities. McDaniel et al, classified PM into event- based prospective memory (EBPM) and time- based prospective memory (TBPM), which are required to perform a purposeful behavior in the presence of specific target events and goals.[11] Whether you have memory or concentration problems (sometimes described as a mental fog or chemo brain) depends on the type of treatment you receive, your age, and other health-related factors. Cancer treatments such as chemotherapy may cause difficulty with thinking, concentrating, or remembering things. So can some types of radiation therapy to the brain and immunotherapy. These cognitive problems may start during or after cancer treatment. Some people notice very small changes, such as a bit more difficulty remembering things, whereas others have much greater memory or concentration problems.

## 2.NEUROPSYCHOLOGY OF MEMORY

To understand how the brain accomplishes learning and memory, one must also obtain information at the brain systems or neuropsychological level. The hippocampus is very important for memory function and is particularly susceptible to radiation. The hippocampus is one of the 2 active sites of neurogenesis in the mammalian brain. The proliferation of neuronal precursors in the sub granular zone of the dentate gyrus generates cells that migrate further to the granule cell layer and differentiate into mature neuronal and glial phenotypes.[12] Recent studies have proven that radiation effects are age-, brain region-, and sex-specific[13,14] Among the brain regions, the prefrontal cortex (PFC) and the hippocampus are the most sensitive to irradiation[15]. The PFC is a key regulatory region that collects inputs from all other cortical regions and then plans and directs an array of motor, cognitive, and social behaviour's.[16] Some hippocampal cells are highly proliferative, and studies have shown that the loss of these cells after radiotherapy can lead to cognitive impairment [17]. The medial temporal region became associated with memory functionsprimarily because of the noted patient H.M[18]. In 1953 in an effortto relieve severe epilepsy, this individual sustained bilateral removal of hippocampal gyrus, amygdala, and the anterior two thirds of the hippocampus. Although it has traditionally been held that the hippocampal removal was the critical aspect of the neurosurgery that caused amnesia, recent work with monkeys has raised the possibility that the amygdala may play an important role as well[19].

In a clinical investigation done by Kuan-Yin Hsiao, M.D.etal oncognitive function before and after radiation therapy in patients with nasopharyngeal carcinoma the cognitive functioning scores had significantly declined in the domains of short-term memory, language abilities, and list-generating fluency. The results of the study indicated that RT could have deleterious effects on cognitive function in patients with NPC. Efforts should be made to reduce the radiation dose and irradiated volume of temporal lobes without compromising the coverage of target volume.

The decreases in cognitive functioning scores were also analyzed by age, gender, education, chemotherapy, hypertension, diabetes, and smoking history respectively. There were no associations between cognitive functioning decline and any of the analyzed baseline variables. Compared with healthy siblings, children with leukemia who were treated with cranial RT were found to have significantly lower intelligent quotients[20]and reading age assessment[21]. The problem of cognitive impairment associated with cranial irradiation is well recognized in adults as well. The present results indicated a general lowering of the cognitive functioning scores after RT. In addition, they noted that the radiation dose to the temporal lobes was positively correlated with the grade ofcognitive decline. The impairment of neurocognitive performance was associated with the high dose–volume percentage of the temporal lobes as well.

In another study by Linda C. W. Lam, M.R.C.Psych. S. F. Leung, F.R.C.R. Y. L. Chan, F.R.C.R. on Progress of Memory Function After Radiation Therapy in Patients With Nasopharyngeal Carcinoma, effects of cranial irradiation have attracted much concern. Follow- up studies of patients who received cranial RT and survived childhood tumors have revealed a high incidence of significant intellectual deficit[23-26]. Children treated for medulloblastoma with cranial RT were found to have lower intelligent quotients (IQs) and specific cognitive deficits involving reading, arithmetic, and visuospatial functions[27]. Similarly, children who had received cranial RT for acute lymphoblastic leukaemia suffered impaired performance in IQ tests, reading, arithmetic, attentional ability, and psychosocial functioning[28,29]. Gender, age at the time of administration of RT, use of chemotherapy, and radiation dose have been suggested as determinants for neurotoxicity.

## 3.NEUROCOGNITIVE ASSESSMENT

Neurocognitive assessment comprised a mental status examination and a battery of neuropsychological tests. A checklist of psychiatric symptoms guided the mental status examination.[30] The neuropsychological evaluation included the Chinese version of the Wechsler Adult Intelligence Scale–Revised (WAIS-R) verbal subtests, digit and visual spans,[31]and Rey auditory and visual learning tests[32]. Subjective memory problems and related complaints were recorded by using an interview with standard questions; subjects were asked about the presence of subjective memory problems, their duration, their nature (recent or remote memory), and their impact on daily life (missed appointments, need of written reminder). Although conventional objective criteria for radiation- induced brain injury usually rely on imaging, the role of neurocognitive assessment should not be undervalued. A comprehensive multidimensional assessment including neuropsychological assessment, imaging investigation, and memory questionnaires is important for the early detection of radiation-induced brain injury.

## 4.MEMORY INTERVENTIONS

There are no standard therapeutic interventions for treatment-related cognitive deficits:

Exercise is a key factor in improving both memory and mood after whole-brain radiation treatments. Radiation knocks out the ability of the brain to produce new nerve cells, called neurons. Exercise might help by increasing blood flow to the hippocampus area of the brain, which is an important structure for learning, memory, and spatial navigation Do things that exercise the brain. These can include doing puzzles, word games, painting, playing an instrument or learning a new hobby.

Behavioral Physical activity has been hypothesized to help with cognitive dysfunction due to aging [40], following stroke [41], or in Alzheimer's disease [42]. Radiation-related cognitive dysfunction has similarities with all these types of dementia and it was hypothesized that exercise may help improve symptoms in a similar manner. In a prospective mouse model of radiation-induced cognitive injury, half the mice that had undergone whole brain irradiation were offered access to a running wheel one month after their treatment [43]. They found mice that voluntarily ran on the treadmill daily had better spatial memory retention, as well as partial restoration of new born neurons in the dentate gyrus of the hippocampus. Although the effects of physical activity have not been prospectively evaluated in humans, these results suggest exercise as a potential therapeutic intervention in patients hoping to maintain higher quality of life after brain radiation.

Mindful meditation has also been proposed to be helpful in both subjective and objective measures of cognitive function in patients having undergone

treatment for cancer [44]. There have been several studies suggesting that meditation engages and modulates neural circuits involved in higher order cognitive processes that are often impaired in cancer-related cognitive deficits; however, randomized evidence is still required to help define the roll of mindful meditation in helping to abrogate cognitive effects of treatment [45,46]. It is thought that perhaps meditation practice provides mental training within the domains of attention, memory and executive function. This is proposed to work through regulation of emotional responses and sense of self [47], regulation of the immune system [48], stress reduction and improved sleep quality.

**Pharmacologic Interventions**

The permanent cognitive decline that is often associated to brain radiotherapy is likelymultifactorial in its origins; thus, improved understanding of the mechanisms of IR-induced cognitive decline will be needed in order to select candidate therapeutics.

## 5.CONCLUSION

When radiation therapy is used in the treatment of nasopharyngeal carcinoma (NPC), the temporal lobes are at risk because they lie directly in the path of the radiation beams. Damage to the temporal lobes, particularly the medial aspects, is incontrovertibly associated with memory. It follows therefore that radiation therapy for NPC has the attendant risk of memory loss as an enduring side-effect.[49]

T.J.'sneuropsychologicalassessment demonstrates the degree of cognitive impairment that can arise following radiotherapy for NPC and stresses the importance of neuropsychological sequelae when evaluating the long-term outcome of this form of treatment. T. J.'s principal deficit is a permanently disabling memory disorder reflected in both anterograde and retrograde amnesia (although see Bederson, Harsh, Walker & Wilson, 1990, for a case of temporal lobe necrosis in which an initial memory impairment ameliorated after fenestration and internal shunting). In addition, there was some evidence of subclinical intellectual deficits.

One view is that radiation primarily injures the vascular system and that neural necrosis is secondary to that. A second proposal is that radiation damages glial cells with consequent white-matter damage. A third possibility is that damage to glial cells leads to the release of antigens which in turn causes an allergic response resulting in necrosis.

It Highlights the nature and severity of late-onset neuropsychological deficits that can arise following radiation therapy for NPC and, by implication, other courses of radiotherapy which necessitate radiation of the temporal lobes (e.g. pituitary tumours).

## REFERENCES


[1] Rooney, Jessica W; Laack, Nadia N (2013). Pharmacological interventions to treat or prevent neurocognitive decline after brain radiation. CNS Oncology, 2(6), 531–541. doi:10.2217/cns.13.60

[2] Delaney, G.; Jacob, S.; Featherstone, C.; Barton, M. The role of radiotherapy in cancer treatment: Estimating optimal utilization from a review of evidence-based clinical guidelines. Cancer 2005, 104, 1129–1137.

[3] Askins, M.A.; Moore, B.D., 3rd. Preventing neurocognitive late e_ects in childhood cancer survivors. J. Child Neurol. 2008, 23, 1160–1171.

[4] Müller RP. Radiation-induced injury of the central nervous system. In: J Dunst, R Sauer, editors. Late sequelae in oncology. Berlin:Springler Verlag, 1995: 23– 7.Crossref Google Scholar

[5] Archibald YM, Lunn D, Ruttan LA, Macdonald DR, Del Maestro RF, Barr HWK, et al. Cognitive functioning in long-term survivors of high-grade glioma. J Neurosurg 1994; 80: 247– 53.Crossref CAS PubMed Web of Science®Google Scholar

[6] Armstrong C, Mollman J, Corn BW, Alavi J, Grossman M. Effects of radiation therapy on adult brain behavior: evidence for a rebound phenomenon in a Phase 1 trial. Neurology 1993; 43: 1961– 5.Crossref CAS PubMed Web of Science®Google Scholar

[7] Vigliani MC, Sichez N, Poisson M, Delattre JY. A prospective study of cognitive functions following conventional radiotherapy for supratentorial gliomas in young adults: 4-year results. Int J Radiat Oncol Biol Phys 1996; 35: 527– 33. Crossref CAS PubMed Web of Science®Google Scholar

[8] Posner MI, Dehaene S. Attentional networks. Trends Neurosci 1994; 17: 75– 9. Crossref PubMed Web of Science®Google Scholar

[9] McDougall GJ Jr, Oliver JS, Scogin F. Memory and cancer: a review of the literature. Arch Psychiatr Nurs. 2014;28(3): 180-186.

[10] Arnold NR, Bayen UJ, Bohm MF. Is prospective memory related to depression and anxiety? A hierarchical MPT modelling ap-proach. Memory. 2015;23(8):1215-1228.

[11] McDaniel MA, Einstein GO. The neuropsychology of pro-spective memory in normal aging: a componential approach. Neuropsychologia. 2011;49(8):2147-2155

[12] Palmer TD, Takahashi J, Gage FH. The adult rat hippocampus contains primordial neural stem cells. Mol Cell Neurosci 1997; 8:389-404; PMID:9143557; https://doi.org/10.1006/mcne.1996.0595

[13] Koturbash I, Zemp F, Kolb B, Kovalchuk O. Sex-specificradiation-induced microRNAome responses in the hippocampus, cerebellum and frontal cortex in a mouse model. Mutat Res 2011; 722:114-8; PMID:20478395; https://doi.org/10.1016/j.mrgentox.2010.05.007 [PubMed] [CrossRef] [Google Scholar]

[14] Hudson D, Kovalchuk I, Koturbash I, Kolb B, Martin OA, Kovalchuk O. Induction and persistence of radiation-induced DNA damage is more pronounced in young animals than in old animals. Aging (Albany NY) 2011; 3:609-20; PMID:21685513; https://doi.org/10.18632/aging.100340 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[15] Andres-Mach M, Rola R, Fike JR. Radiation effects on neural precursor cells in the dentate gyrus. Cell Tissue Res 2008; 331:251-62; PMID:17786480; https://doi.org/10.1007/s00441-007-0480-9 [PubMed] [CrossRef] [Google Scholar]

[16] Kolb B, Mychasiuk R, Muhammad A, Li Y, Frost DO, Gibb R. Experience and the developing prefrontal cortex. Proc Natl Acad Sci U S A 2012; 109 Suppl 2:17186-93; PMID:23045653; https://doi.org/10.1073/pnas.1121251109.

[17] Georg Kuhn H, Blomgren K. Developmental dysregulation of adult neurogenesis. Eur J Neurosci. 2011;33(6):1115–22.

[18] Scoville, W.B., and Milner, B. 1957. Loss of recent memory after bilateral hippocampal lesions. J. Neurol. Neurosurg. Psychiat. 80: 11-21.

[19] Mishkin, M. 1978. Memory in monkeys severely impaired by combined but not by separate removal of amygdala and hippocampus. Nature 273: 297-298.

[20] Moss AH, Nannis ED, Poplack DG. The effects of prophylactic treatment of the central nervous system on the intellectual functioning of children with acute lymphocytic leukemia. Am J Med 1981;71:47–52.

[21] Eiser C. Intellectual abilities among survivors of childhood leukaemia as a function of CNS irradiation. Arch Dis Child 1978;53:391–395.

[22] Williams JM, Davis KS: Central nervous system prophylactic treatment for childhood leukemia: neuropsychological outcome studies. Cancer Treat Rev 1986; 13:113–127.

[23] Cousens P, Waters B, Said J, et al: Cognitive effects of cranial irradiation in leukemia: a survey and meta-analysis. J Child Psychol Psychiatry 1988; 29:839–852

[24] Roman D, Sperduto P: Neuropsychological effects of cranial radiation: current knowledge and future directions. Int J Radiat Oncol Biol Phys 1995; 31:983–998

[25] Fossen A, Abrahamsen TG, Storm-Mathisen I: Psychological outcome in children treated for brain tumor. Pediatr Hematol Oncol 1998; 15:479–488

[26] Copeland DR, de Moor C, Moore BD 3rd, et al: Neurocognitive development of children after a cerebellar tumor in infancy: a longitudinal study. J Clin Oncol 1999; 17:3476–3486

[27] Mulhern RK, Reddick WE, Palmer SL, et al: Neurocognitive deficits in medulloblastoma survivors and white matter loss. Ann Neurol 1999; 46:834–841

[28] Smibert E, Anderson V, Godber T, et al: Risk factors for intellectual and educational sequelae of cranial irradiation in childhood acute lymphoblastic leukaemia. Br J Cancer 1996; 73:825–830.

[29] Hill JM, Kornblith AB, Jones D, et al: A comparative study of the long-term psychosocial functioning of childhood acute lymphoblastic leukemia survivors treated by intrathecal methotrexate with or without cranial radiation. Cancer 1998; 82:208–218.

[30] Janca A, Hiller W: ICD-10 checklists: a tool for clinicians' use of the ICD-10 classification of mental and behavioral disorders. Compr Psychiatry 1996; 37:180–187

[31] Janca A, Hiller W: ICD-10 checklists: a tool for clinicians' use of the ICD-10 classification of mental and behavioral disorders. Compr Psychiatry 1996; 37:180–187

[32] Lezak MD: Memory I: tests, in Neuropsychological Assessment, 3rd edition. New York, Oxford University Press, 1995, pp 486–487

[33] Van Praag H, Shubert T, Zhao C et al. Exercise enhances learning and hippocampal neurogenesis in aged mice. J. Neurosci. 25, 8680–8685 (2005).

[34] Luo CX, Jiang J, Zhou QG et al. Voluntary exercise-induced neurogenesis in the postischemic dentate gyrus is associated with spatial memory recovery from stroke. J. Neurosci. Res. 85, 1637–1646 (2007).

[35] Adlard PA, Perreau VM, Pop V et al. Voluntary exercise decreases amyloid load in a transgenic model of Alzheimer's disease. J. Neurosci. 25, 4217–4221 (2005).

[36] Wong-Goodrich SJ, Pfau ML, Flores CT et al. Voluntary running prevents progressive memory decline and increases adult hippocampal neurogenesis and growth factor expression after whole-brain irradiation. Cancer Res. 70, 9329–9338 (2010).

[37] Biegler KA, Chaoul MA, Cohen L. Cancer, cognitive impairment, and meditation. Acta Oncol. 48, 18–26 (2009). 45 Mackenzie MJ, Carlson LE, Speca M. Mindfulness-based stress reduction in oncology. Evid. Based Integr. Med. 2, 139–145 (2005).

[38] Matchim Y, Armer JM. Measuring the psycological impact of mindfulness meditation on health among patients with cancer: a literature review. Oncol. Nurs. Forum 34, 1059–1066 (2007).

[39] Davidson RJ. Affective style, psychopathology, and resilience: brain mechanisms and plasticity. Am. Psychol. 55, 1196–1214 (2000).

[40] Van Praag H, Shubert T, Zhao C et al. Exercise enhances learning and hippocampal neurogenesis in aged mice. J. Neurosci. 25, 8680–8685 (2005).

[41] Luo CX, Jiang J, Zhou QG et al. Voluntary exercise-induced neurogenesis in the postischemic dentate gyrus is associated with spatial memory recovery from stroke. J. Neurosci. Res. 85, 1637–1646 (2007).

[42] Adlard PA, Perreau VM, Pop V et al. Voluntary exercise decreases amyloid load in a transgenic model of Alzheimer's disease. J. Neurosci. 25, 4217–4221 (2005).

[43] Biegler KA, Chaoul MA, Cohen L. Cancer, cognitive impairment, and meditation. Acta Oncol. 48, 18–26 (2009). 45 Mackenzie MJ, Carlson LE, Speca M. Mindfulness-based stress reduction in oncology. Evid. Based Integr. Med. 2, 139–145 (2005).

[44] Matchim Y, Armer JM. Measuring the psycological impact of mindfulness meditation on health among patients with cancer: a literature review. Oncol. Nurs. Forum 34, 1059–1066 (2007).

[45] Davidson RJ. Affective style, psychopathology, and resilience: brain mechanisms and plasticity. Am. Psychol. 55, 1196–1214 (2000).

[46] Davidson RJ, Kabat-Zinn J, Schumacher J et al. Alterations in brain and immune function produced by mindfulness meditation. Psychosom. Med. 65, 564–570 (2003).

[47] Carlson LE, Garland SN. Impact of mindfulness-based stress reduction (MBSR) on sleep, mood, stress and fatigue symptoms in cancer outpatients. Int. J. Behav. Med. 12, 278–285 (2005).

[48] Kliewer SA, Umesono K, Noonan DJ et al. Convergence of 9-cis retinoic acid and peroxisome proliferator signalling pathways through heterodimer formation of their receptors. Nature 358, 771–774 (1992)

[49] Alan J. Parkin* and Nicola M. Hunkin Lboratory of Experimenfal PsyrhoIogy, University of Sussex, Brighton, East Sussex BN I 9QC, UK. British Journal of Clinical Psychology (1991). 30, 349-357