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RT and cognitive function

Radiation dose, driving performance, and cognitive function in patients with head and neck cancer

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Abstract

Seven head and neck cancer patients participated in a driving evaluation in a driving simulator. Radiation dose on the temporal lobes was moderately associated with time to complete a cognitive test and with driving performance. Results indicated that incidental irradiation may contribute to a decrease in cognition and in unsafe driving performance, which seems to be time-dependent.

Keywords: Adverse effects; Cognition disorders; Neuropsychological tests; Traffic accidents

Increasing evidence associates radiation therapy for the treatment of head and neck cancer (HNC) with neurotoxicity [1—4]. Incidental irradiation injury to nerve fibers and vasculature in the central nervous system including the temporal lobes during treatment for HNC has been documented [1—3]. This exposure creates a significant risk of cognitive deficits [1,5—7]. Whereas these cognitive deficits may be subtle, many domains of cognition — attention, memory, visuospatial functioning, information processing speed, executive functioning, and reaction time — can be affected [1,5,7]. Yuen and associates have attempted to link these cognitive deficits associated with cancer therapy (radiation or chemoradiation) for HNC with its effect on the important life activity of motor vehicle operation [8,9]. They found that patients who received cancer therapy for HNC had a poorer driving competence and greater risks of unsafe driving performance [8,9]. Specifically, HNC patients had slower brake reaction time and more steering variability when compared to normal controls [8]. In addition, when patients perceived impairments in their own cognitive function, they tended to self-restrict driving [9]. Despite this, their reported traffic violations and accidents after the completion of cancer therapy was higher compared to reported violations and accidents prior to HNC diagnosis [9]. To further understand the adverse effects of cancer therapy on driving performance, we investigated the associations among radiation dose, cognitive function, and driving performance in patients undergoing treatment for HNC.

Methods

Seven patients with HNC (6 male and 1 female) were recruited through the Head and Neck Tumor Program at Hollings Cancer Center, Medical University of South Carolina, Charleston, South Carolina, USA. All participants met the following entry criteria into the study: (1) 18 years-of-age or older; (2) composite IQ score greater than 80 as measured by the Shipley Institute of Living Test [10]; (3) a best corrected visual acuity of better than 20/30 based on a brief vision screening using a Snelling eye chart; (4) a valid state driver's license; (5) no self-reported deafness; (6) no history of neurological disorder or medical disorder affecting the central nervous system; and (7) no self-reported psychosis. After informed consent, each participated in an objective laboratory evaluation of driving performance in a state-of-the-art virtual reality driving simulator.

The evaluation procedure and the characteristics of the driving simulator have been reported in detail previously [8]. Briefly, a licensed clinical psychologist administered the intelligence and vision screening, and the Trail-Making Test, Part B (TMT-B) [11]. The TMT-B is a test of selective and divided attention, working memory, visuomotor processing speed, and executive function [11]. TMT-B has been validated as a sensitive measure for cognitive dysfunction [11,12] and is used to measure the cognitive domains that are affected by chemo and/or radiation therapy [13]. TMT-B is a timed task requiring the sequential connection of 12 alternate numbers (1—13) and letters (A—L) spaced randomly on the page [14]. The participant was required to perform this

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task, using pencil and paper, as quickly and accurately as he or she was able without lifting the pencil from the paper. Completion time in seconds constitutes the final score – higher score indicating poor performance. Prior studies have demonstrated a significant association between a higher score on TMT-B and a poorer driving performance [15–18]. The simulator driving scenarios require participants to respond to situations frequently encountered while driving in the real world obeying all traffic signs and signals along the simulated roadway. To minimize the effect that the novelty of the driving simulator might have on performance, participants practiced for 10–15 min on a training course (in a virtual environment slightly different from the testing environment). After this training session, the participants completed a 12-min evaluation course. The principle measures from the driving simulator were the average speed (in miles per hour), the steering variability (i.e., standard deviation of vehicle lateral offset from the center of driving lane in inches) recorded every second averaged across the course, the mean brake reaction time (in milliseconds), and the number of fatal collisions during the evaluation course. The estimated maximum radiation dose incidentally received by the temporal lobes during radiation therapy was extracted from the 3D CT scan.

Results

The mean age of the participants was 57.6 ± 8.8 years-of-age. Six participants were driving at the time of the study. Six were taking medication – primarily for controlling blood pressure and pain relief (e.g., low-potency narcotics). A review of each participant's medical chart revealed no adverse side-effects of peripheral neuropathy, hypothyroidism, retinopathy, or anemia from radiation or chemoradiation therapy. Table 1 shows the treatment-related medical information for the participants. For participants who received chemoradiation therapy, weekly cisplatin, alone or with paclitaxel, was typically administered. One participant received 5 cycles of rituximab. A typical radiation fractionation schedule for the participants was 1.8–2 Gy per day, five days a week, for 7 consecutive weeks (i.e., 35 fractions), resulting in a total dose of up to 70 Gy. The median maximum radiation dose incidentally delivered to the left temporal lobe was 3.9 Gy (mean = 12.9 Gy; range = 0.8–67.3 Gy), and the median maximum radiation dose to the right temporal lobe was 6.9 Gy (mean = 13.8 Gy; range = 0.6–64.3 Gy).

Four (57%) participants had impaired cognition based on the standard cut-off score of 91 s on the TMT-B [22,23]. Two participants were unable to complete the test and were assigned a null value of 500 s [24]. The median score of the TMT-B was 92 s (range from 44 to 500 s). The zero-order correlation coefficients (as indicated by Spearman's rho correlations) for the association between the TMT-B score and the average speed and mean brake reaction time were −0.63 and 0.71, respectively. There was a high negative association ($r_s = -0.72$) between the TMT-B score and the duration of post-radiation therapy.

The magnitude of the association (as indicated by Spearman's rho correlations) between the estimated maximum radiation dose to the temporal lobes and the TMT-B score as well as the correlation between the average speed, the mean brake reaction time, and the number of fatal collisions during the driving simulator evaluation was 0.4 or above (Table 2). Statistical significance was not achieved due to the small sample size. According to Franzblau et al. [25], a correlation coefficient about 0.40–0.60 is moderate in strength, and a correlation coefficient about 0.60–0.80 is regarded as high.

Conclusions

In this pilot study, we found a high prevalence (~60%) of measurable cognitive deficits in the radiation-treated HNC

Table 1
Treatment-related medical information of the HNC participants

Gender	Age (years)	Cancer stage	Cancer type	Tumor site	Surgery	Therapy	Rad therapy	TMT-B (s)
Male	54	TxN2bM0	SCCA of the neck	R neck	R neck dissection	Rad	Half-way completed	187
Male	66	T2N2c (tonsil); T1 (epiglottis)	SCCA tonsil and epiglottis	R tonsil, epiglottis	None	Chemorad	Completed 1.4 mths ago	500
Female	64	TxN2aM0	Poorly differential carcinoma	L neck	L neck dissection	Rad	One week left	500
Male	54	T1N2bM0	SCCA nasopharynx	Nasopharynx	None	Chemorad	Completed 4.9 mths ago	92
Male	41	T1N0M0	SCCA tongue	R tongue	R neck dissection and partial glossectomy	Rad	Completed 24.3 mths ago	49
Male	59	1A	Diffused large B-cell non-Hodgkin's lymphoma	L neck	None	Chemorad	Completed one week ago	72
Male	65	T2N1Mx	SCCA tonsil	R tonsil	None	Chemorad	Completed 32.3 mths ago	44

Note. SCCA = squamous cell carcinoma; rad = radiation; chemorad = chemoradiation; 500 s was assigned to those who were unable to complete the TMT-B.