Effects of proton therapy on cognition in adults with brain tumors: a systematic review

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Purpose

Proton therapy (pt) is increasingly employed in treating of intracranial neoplasms due to its ability to spare surrounding healthy tissue. However, its effects on cognitive function in adult patients remain unclear, despite rising clinical adoption. This review systematically evaluates evidence on neurocognitive outcomes in adults treated with pt for primary intracranial tumors, and assess its impact across multiple cognitive domains.

Methods

This review followed PRISMA guidelines and was registered on PROSPERO (ID: CRD42024591714). Eligible studies included adults (> 18 years) with primary brain tumors treated with PT and assessed using standardized neuropsychological tests. Pediatric populations, metastases, self-report-only assessments, and other radiotherapy techniques were excluded. Literature was searched across PubMed, Embase, and Scopus. Methodological quality was appraised using the Mixed Methods Appraisal Tool.

Results

Eight studies comprising 310 patients (247 receiving PT) were included. Tumor types varied and included gliomas, meningiomas, craniopharyngiomas, and others. Overall, PT was associated with stable or improved outcomes in global cognition, memory, language, executive function, attention, working memory, and visuospatial abilities. No study reported progressive cognitive decline. Improvements were often observed over long-term follow-up, particularly in patients without treatment-induced toxicity. Subgroup analyses revealed better recovery in left-sided lesions and worse outcomes in patients with radiation-induced brain lesions or toxicities.

Conclusion

PT appears to be a cognitively sparing modality for treating intracranial neoplasms in adults. While most cognitive domains are preserved or improve over time, patients experiencing treatment-related toxicities may be at higher risk of impairment. Future large-scale, multicenter trials with longer follow-ups and domain-specific assessments are warranted to confirm these findings and optimize treatment protocols.

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Contributions

All authors contributed to the study conception and design. The idea for the article was proposed by Pravettoni Gabriella. The literature search and material preparation, data collection and analysis were performed by Scagliotti Elena, Capetti Benedetta and Conti Lorenzo. The first draft of the manuscript was written by Scagliotti Elena, Capetti Benedetta, Conti Lorenzo and all authors commented on previous versions of the manuscript. All authors reviewed and commented on previous versions of the manuscript. All authors read and approved the final manuscript. The work was supervised by Locatelli Marco and Pravettoni Gabriella.

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Ethics declarations

Declarations

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript. The authors have no relevant financial or non-financial interests to disclose.

Competing interests

The authors declare no competing interests.

Additional information

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