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Title: C-SMART for Patients with Primary Brain Tumors: A Feasibility and Acceptability Pilot of a Novel Neuropsychological Rehabilitation Intervention and Neurobiological Research Procedures

Cognitive decline in patients with brain tumors is incredibly common, affecting up to 90% of our patients, and, understandably, negatively impacting their daily functioning, employment status, relationships, and independence. Research on the prevalence and characterization of these cognitive changes in primary brain tumors abound. Significantly less work has developed and tested interventions to reduce cognitive changes or protect from further decline in brain tumor, e.g., cognitive rehabilitation in neuro-oncology. The existing work developing and testing cognitive rehabilitation for our patients with brain tumor have all focused on either group based or computerized programs that are not tailored to the individual patient's areas of strengths and vulnerability. Using an expert and patient advisory board, we recently developed a tailored cognitive rehabilitation intervention with integrated mindfulness meditation training for patients with primary brain tumors: C-SMART (Cognitive Strategies, Mindfulness, and Rehabilitation Therapy). In C-SMART, mindfulness meditation focuses on training present-moment attention with nonjudgmental awareness and compassion. The integration of mindfulness with cognitive rehabilitation, which trains specific strategies to achieve daily living goals, is novel in neuro-oncology and may impart overarching benefits compared to either in isolation. We are currently funded to trial the CSMART intervention in a small one-arm pilot study to gather initial feasibility and acceptability data. With the ACS-IRG, we will increase our sample size to comprehensively evaluate feasibility and acceptability for three main primary brain tumor types – glioblastoma, IDH-mutant glioma (e.g., low-grade gliomas), and meningioma. We have compelling reason to believe that the cognitive rehabilitation needs of each tumor type may be different given distinct effects on cognition as well as diverse disease processes. Our current limited understanding of cognitive rehabilitation in neuro-oncology does not provide these much needed data for adequate adaptation by tumor type. Furthermore, specialty brain images that provide data on functional connectivity, or the ability for different brain regions to communicate with one another, has the potential to serve as a biomarker of neurocognitive wellness, or neuroplasticity, in the setting of C-SMART. To-date, no work has been done to investigate functional connectivity as an outcome of cognitive rehabilitation in patients with brain tumors, despite many studies demonstrating the relationship between neurocognition and functional connectivity. The proposed ACS-IRG Pilot Grant will test the feasibility and acceptability of C-SMART for each primary brain tumor subtype (glioblastoma n=10, IDHmutant glioma n =10, and meningioma n=10) and initiate the study of functional connectivity as an outcome of C-SMART by trialing longitudinal functional brain scans in one participant from each tumor type (n=3) at pre- and post-C-SMART. Importantly, these data are necessary to secure larger grants that will grow this line of inquiry to positively impact our patients with brain tumors and cognitive decline, as well as advance the fields of neuropsychology and neuro-oncology in developing evidence-based cognitive rehabilitation for our patients.