the local connectome associated with metabolites of interest, controlling for age and sex, and correcting for multiple comparisons (FDR < .050 with 4000 permutations). A profile approach was used to interpret diffusion metrics, contrasting quantitative anisotropy (QA) with fractional anisotropy (FA). Local connectome tracks were then clustered to identify the larger white matter tract.
Results: Glx (p = .008) and tCr (p = .032) were significantly associated with history of TBI with LoC. Increased Glx was associated with increased QA in 11,001 tracks, accounting for 1.4% of the total white matter tracks in the brain. 90% of tracks were identified in bilateral cingulum (33%), bilateral thalamic (13%), bilateral corticospinal (13%), corpus callosum (12%), left arcuate fasciculus (9%), left fronto-parietal aslant tracts (6%), and bilateral inferior fronto-occipital fasciculus (4%) tracts. In contrast, FA was not associated with Glx. The same pattern emerged for tCr, with 10,542 tracks identified predominantly in bilateral cingulum (29%), corpus callosum (21%), bilateral corticospinal (15%), bilateral corticostriatal (7%), bilateral medial lemniscus (7%), left cortico-pontine (3%), left thalamic (2%), and bilateral superior longitudinal fasciculus (2%) tracts. Post-hoc exploratory analyses of mean QA across regions of cingulum found that increased QA was associated with self-report measures of headache intensity, fatigue, and perceived change in executive functioning.
Conclusions: Results provided evidence that multimodal imaging can identify subtle markers of initial TBI severity years after injury. Neurometabolite concentrations were associated with diffuse changes in the local connectome; the pattern of discrepancy between FA and QA was suggestive of reduced potential for neuroplasticity. Exploratory analyses further indicated that variability in white matter density in the cingulum, an important connection for limbic regions, was associated with a range of problems commonly reported in clinical settings, which may be informative for diagnosis and treatment planning.

Categories: Acquired Brain Injury (TBI/Cerebrovascular Injury & Disease - Adult)
Keyword 1: brain injury
Keyword 2: magnetic resonance spectroscopy
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22 The Effect of Ibogaine on Cognitive Functioning

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Objective: To determine the effects of the non-classic psychedelic, ibogaine, on cognitive functioning. Ibogaine is an indole alkaloid derived from the Tabernanthe Iboga plant family, indigenous to Africa, and traditionally used in spiritual and healing ceremonies. Ibogaine has primarily been studied with respect to its clinical efficacy in reducing substance addiction. There are, however, indications that it also may enhance recovery from traumatic experiences. Ibogaine is a Schedule 1 substance in the USA.
Participants and Methods: Participants were U.S. Special Operations Veterans who had independently and voluntarily referred themselves for an ibogaine retreat at a specialized clinic outside the USA prior to learning about this observational study. After meeting rigorous screening requirements, 30 participants were enrolled, all endorsing histories of combat and repeated blast exposure, as well as traumatic brain injury. Participants were seen in person pre-treatment, post-treatment, and one-month post-treatment for neuropsychological testing, neuroimaging, and collection of clinical outcome measures. All 30 participants were seen pre- and post-treatment, of whom 27 were also able to return one-month post-treatment.
The neuropsychological battery included the the Hopkins Verbal Learning Test (HVLT), the Brief Visuospatial Memory Test - Revised (BVMT-R), the Wechsler Adult Intelligence Scale - Fourth Edition (WAIS-IV) Working Memory Index (Digit Span and Arithmetic) and Processing Speed Index (Symbol Search and Coding), and the Delis-Kaplan Executive Function System (D-KEFS) tests of Verbal Fluency (VF), Trail Making (TMT), Color Word (CW), and Tower Test (TT). For repeated measures, alternate forms were used whenever possible.
Results: Repeated-measures ANOVA revealed significant effects of time, with post-treatment improvements across multiple measures including processing speed (WAIS-IV PSI;

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F(2,25) = 26.957, p < .001), executive functions (CW Conditions 3 and 4: F(1.445,25) = 11.383, p < .001 and F(1.381,25) = 7.687, p = .004, respectively), verbal fluency (VF Condition 3 correct and accuracy: F(2,25) = 6.419, p = .003 and F(2,25) = 153.076, p < .001, respectively), and verbal learning (HVLT Total Recall (alternate forms used at each time point): F(1.563,23) = 6.958, p = .004). Score progression graphs are presented. Performance on all other cognitive measures did not significantly change following treatment.
Conclusions: To our knowledge, this is the first prospective study examining neuropsychological test performance following ibogaine use at post-treatment and one-month post-treatment time points. Our results indicated that several cognitive domains improved either post-treatment or one-month post-ibogaine treatment, suggesting ibogaine's therapeutic potential for cognition in the context of traumatic brain injury and mood disorders. Potential explanations include neuroplastic changes, reduction of PTSD and mood-related effects on cognitive functioning, and practice effects. While we found no evidence of negative cognitive consequences for up to one-month post-single-ibogaine treatment, further study of this substance is necessary to clarify its clinical utility and safety parameters.

Categories: Acquired Brain Injury (TBI/Cerebrovascular Injury & Disease - Adult)
Keyword 1: cognitive functioning
Keyword 2: traumatic brain injury
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23 Developmental Outcomes and Educational Service Utilization for Pediatric Brain Tumor Survivors Treated with Proton Radiotherapy Prior to Four Years of Age

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Objective: Pediatric brain tumor survivors treated with proton radiation therapy (PRT) prior to 4 years of age are at high risk for poor cognitive and developmental outcomes. This cross-sectional study examined developmental outcomes and educational service utilization at follow-up in a cohort of pediatric survivors treated with PRT before the age of 4 years.
Participants and Methods: A total of 46 patients (58.7% female, 93.5% White) were assessed using age-appropriate measures for executive, behavioral, and adaptive functioning. Mean age at PRT was 2.4 years (SD=0.9, range 1.0-3.9 years); mean age at follow-up was 7.0 years (SD=4.8, range 2.0-18.6 years). Mean follow-up interval was 4.57 years (SD=4.52, range 0.9-16.2 years). Diagnoses included ependymoma (n=26, 54.2%), medulloblastoma (n=7, 14.6%), craniopharyngioma (n=4, 8.3%), and a few other tumor types. Infratentorial tumors were most common (69.6%). Treatment included prior surgical resection (93.5%) and chemotherapy (60.9%). Posterior fossa syndrome was present in 10.9% (n=5). PRT field consisted of focal (n=41, 89.1%) or craniospinal irradiation (CSI) (n=5, 10.9%). The impact of demographic, diagnostic, and treatment-related factors was examined, including age at PRT, gender, time interval since PRT, radiation field, and tumor location, on intelligence quotient (IQ), adaptive skills, and executive functioning. Rates of impairment (T-scores >65) were calculated. The utilization of educational services was determined.
Results: Mean IQ (SS = 97.6, SD=16.3), as well as mean global executive functioning (Mean T=53.4, SD=11.1) and adaptive skills (Mean SS = 92.5, SD=21.4), as assessed by parent rating scales (BRIEF; SIB), were in the average range. Despite mean scores being within the average range, a large proportion of patients demonstrated difficulties with social withdrawal (28.3%) and activities of daily living (28.3%) (BASC), and global executive dysfunction (17.4%) (BRIEF). Younger age at PRT was associated with lower global adaptive skills at follow-up (r=.39, p=.005), better activities of daily living (r=.53, p<.001), lower social skills (r=.43, p=.002), and more hyperactivity (r=-.37, p=.008), but not aggression, anxiety, depression, somatization, atypical behaviors, withdrawal, or attention problems. Longer follow-up interval was correlated with better activities of daily living (r=.46, p<.001), but more anxiety (r=.39, p=.006). Gender, SES, radiation field, history of hydrocephalus, and location of tumor were not significantly related to primary outcome variables. Posterior fossa syndrome was

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