

(neighborhood-specific variables and academic support) in survivors of childhood ALL.

Participants and Methods: Forty-four participants (38.6% female, 72.7% non-Hispanic White, ages 6-17) previously diagnosed with low-risk or standard-risk pre-B cell ALL and treated with chemotherapy-only were included. Participants were evaluated on performance-based measures of EF (cognitive flexibility, verbal fluency, working memory, and processing speed) and academic achievement (word reading and math calculation), and parent-ratings of EF and adaptive functioning. All measures were expressed as T-scores with lower scores indicating better performance. Neighborhood-specific variables were based on participants' zip codes and census block group, and included area deprivation index (ADI) and child opportunity index (COI). Lower ADI and COI indicate lesser deprivation and greater opportunity. Individualized education plan (IEP) status was used as a proxy of academic support, coded dichotomously as with or without IEP. Percentages of participants showing impairments in functional outcomes were calculated using a cutoff of ≥ 1 SD above the normative mean. Partial correlations were conducted while controlling for age at evaluation, age at diagnosis, sex, and verbal IQ, to examine whether participants with poorer performance-based and parent-rated EF would show reduced functional outcomes. Multiple regression analyses were conducted to evaluate whether neighborhood-specific variables and IEP status would predict functional outcomes while controlling for covariates.

Results: Compared to population norms, survivors of childhood ALL showed worse functional outcomes. Within adaptive functioning, 45.5% of participants showed impairment in activities of daily living and leadership. Adaptive functioning was significantly positively correlated with parent-rated, but not performance-based, EF ($r=0.694$, $p<0.001$). Compared to female survivors, male survivors were at increased risk for adaptive functioning difficulties ($r=-0.401$, $p<0.05$). Impairments for word reading and math calculation were 25% and 41.7%, respectively. Greater math calculation was associated with better verbal fluency ($r=0.378$, $p<0.05$) and processing speed ($r=0.439$, $p<0.05$). Older participants at evaluation ($\beta=-0.580$, $p<0.001$) and those without IEP support ($\beta=0.465$, $p<0.05$) showed better word reading. Lower ADI predicted better verbal fluency ($\beta=0.282$,

$p=0.041$), however, neighborhood-specific variables were not associated with functional outcomes.

Conclusions: Prior findings indicate that performance-based measures and parent-ratings assess different constructs of EF. Thus, adaptive functioning may relate more to the behavioral construct of EF than its cognitive construct. Current findings also suggest that male survivors are at increased risk for reduced adaptive functioning, consistent with recent reports that male survivors of ALL are at greater risk for specific neurocognitive outcomes. Overall, functional outcomes may be more strongly related to EF than neighborhood-specific variables. Long-term goals include early screening of adaptive and academic difficulties, targeted intervention, and neuropsychological monitoring to support pediatric survivors' neurocognitive and psychosocial development.

Categories: Cancer

Keyword 1: cancer

Keyword 2: adaptive functioning

Keyword 3: academic achievement

Correspondence: Victoria C. Seghatol-Eslami, University of Alabama at Birmingham (UAB), vs129@uab.edu

25 High-resolution MRI Reveals Selective Patterns of Hippocampal Subfield Atrophy in Focal Epilepsy

Adam Schadler¹, Erik Kaestner¹, Alena Stasenko¹, Christine N. Smith¹, Catherine Tallman¹, Nigel P. Pedersen², Shahin Hakimian², Michelle S. Kim³, Daniel J. Peterson^{3,4}, Thomas J. Grabowski³, Daniel L. Drane², Carrie R. McDonald¹

¹University of California, San Diego, La Jolla, CA, USA. ²Emory University, Atlanta, GA, USA.

³Washington University, Seattle, WA, USA.

⁴Octave Bioscience, Menlo Park, CA, USA

Objective: Hippocampal pathology is a consistent feature in persons with temporal lobe epilepsy (TLE) and a strong biomarker of memory impairment. Histopathological studies have identified selective patterns of cell loss across hippocampal subfields in TLE, the most common being cellular loss in the cornu ammonis 1 (CA1) and dentate gyrus (DG).

Structural neuroimaging provides a non-invasive method to understand hippocampal pathology, but traditionally only at a whole-hippocampal level. However, recent methodological advances have enabled the non-invasive quantification of subfield pathology in patients, enabling potential integration into clinical workflow. In this study, we characterize patterns of hippocampal subfield atrophy in patients with TLE and examine the associations between subfield atrophy and clinical characteristics.

Participants and Methods: High-resolution T2 and T1-weighted MRI were collected from 31 participants (14 left TLE; 6 right TLE; 11 healthy controls [HC], aged 18-61 years).

Reconstructions of hippocampal subfields and estimates of their volumes were derived using the Automated Segmentation of Hippocampal Subfields (ASHS) pipeline. Total hippocampal volume was calculated by combining estimates of the subfields CA1-3, DG, and subiculum. To control for variations in head size, all volume estimates were divided by estimates of total brain volume. To assess disease effects on hippocampal atrophy, hippocampi were recoded as either ipsilateral or contralateral to the side of seizure focus. Two sample t-tests at a whole-hippocampus level were used to test for ipsilateral and contralateral volume loss in patients relative to HC. To assess whether we replicated the selective histopathological patterns of subfield atrophy, we carried out mixed-effects ANOVA, coding for an interaction between diagnostic group and hippocampal subfield. Finally, to assess effects of disease load, non-parametric correlations were performed between subfield volume and age of first seizure and duration of illness.

Results: Patients had significantly smaller total ipsilateral hippocampal volume compared with HC ($d=1.23$, $p<.005$). Contralateral hippocampus did not significantly differ between TLE and HC. Examining individual subfields for the ipsilateral hemisphere revealed significant main-effects for group ($F(1, 29)=8.2$, $p<0.01$), subfields ($F(4, 115)=550.5$, $p<0.005$), and their interaction ($F(4, 115)=8.1$, $p<0.001$). Post-hoc tests revealed that TLE had significantly smaller volume in the ipsilateral CA1 ($d=-2.0$, $p<0.001$) and DG ($d = -1.4$, $p<0.005$). Longer duration of illness was associated with smaller volume of ipsilateral CA2 ($\rho=-0.492$, $p<0.05$) and larger volume of contralateral whole-hippocampus ($\rho=0.689$, $p<0.001$), CA1 ($\rho=0.614$, $p < 0.005$), and DG ($\rho=0.450$, $p<0.05$).

Conclusions: Histopathological characterization after surgery has revealed important associations between hippocampal subfield cell loss and memory impairments in patients with TLE. Here we demonstrate that non-invasive neuroimaging can detect a pattern of subfield atrophy in TLE (i.e., CA1/DG) that matches the most common form of histopathologically-observed hippocampal sclerosis in TLE (HS Type 1) and has been linked directly to both verbal and visuospatial memory impairment. Finally, we found evidence that longer disease duration is associated with larger contralateral hippocampal volume, driven by increases in CA1 and DG. This may reflect subfield-specific functional reorganization to the unaffected brain tissue, a compensatory effect which may have important implications for patient function and successful treatment outcomes.

Categories: Epilepsy/Seizures

Keyword 1: epilepsy / seizure disorders

Keyword 2: hippocampus

Correspondence: Adam Schadler University of California, San Diego
 aschadler@health.ucsd.edu

26 The Importance of Executive Functioning for Academic Achievement Among a National Sample of Children with Epilepsy

Brandon Almy¹, David Marshall¹, Brittany L. Nordhaus¹, Erin Fedak Romanowski¹, Nancy McNamara¹, Elise Hodges¹, Madison M. Berl², Alyssa Ailion³, Donald J. Bearden⁴, Katrina Boyer³, Crystal M. Cooper⁵, Amanda M. Decrow⁶, Priscilla H. Duong⁷, Patricia Espe-Pfeifer⁸, Marsha Gabriel⁵, Jennifer I. Koop⁹, Kelly A. McNally¹⁰, Andrew Molnar¹¹, Emily Olsen¹², Kim E. Ono⁴, Kristina E. Patrick¹³, Brianna Paul¹⁴, Jonathan Romain¹⁵, Leigh N. Sepeta², Rebecca L.H. Stimp¹⁶, Greta N. Wilkening¹⁷, Mike Zaccariello¹⁸, Frank Zelko⁷
¹University of Michigan, Ann Arbor, MI, USA. ²Children's National Hospital, Washington, DC, USA. ³Boston Children's Hospital, Boston, MA, USA. ⁴Children's Hospital of Atlanta, Atlanta, GA, USA. ⁵Cook Children's Medical Center, Fort Worth, TX, USA. ⁶Atrium Health/Levine Children's Hospital, Charlotte, NC, USA. ⁷Ann and Robert H. Lurie Children's Hospital of