**Hippocampal Volume and Sleep Problems in School-Aged Children at High and Low Familial Likelihood of Autism**

Pari Mungalpara, B.S., Jeff Munson, Ph.D., Stephen Dager, M.D., Tanya St. John, Ph.D., Joseph Piven, M.D., Heather Hazlett, Ph.D., Robert Schultz, Ph.D., Natasha Marrus, M.D., Ph.D., Lonnie Zwaigenbaum, M.D., Alan Evans, Ph.D., Martin Styner, Ph.D., Kelly Botteron, M.D., Sun Hyung Kim. Ph.D., Robert McKinstry, M.D., Ph.D., D. Louis Collins, Ph.D., Juhi Pandey, Ph.D., Mark Shen, Ph.D., and Annette Estes, Ph.D. for the IBIS Network

**Background**

Healthy sleep during childhood is vital to health, cognition, and brain development. Some of the same subcortical regions associated with altered brain development in autistic children are also associated with sleep problems. The Infant Brain Imaging Study (IBIS) has previously reported that sleep problems are associated with enlarged hippocampal volumes in infant siblings later diagnosed with autism. However, the persistence of this relationship between sleep problems and hippocampal alterations in autistic school-age children is not well understood, even though clinically significant sleep problems affect over 80% of this population.

**Objectives**

To examine the relationship between hippocampal volume and sleep characteristics in school-aged children (7.0-11.11 years) at higher familial likelihood of Autism Spectrum Disorder (ASD) with an autism diagnosis (HL-ASD), no diagnosis (HL-noASD), and lower familial likelihood of autism (LL).

**Methods**

Hippocampal volumes were measured from awake MRI T1 and T2 images (Siemens 3 Tesla Prisma) across 4 sites (University of North Carolina, Washington University, Children’s Hospital of Philadelphia, University of Washington) utilizing all available data that has passed QC to date. Left and Right Hippocampal volumes were highly correlated so total volume is reported here. Sleep was measured with actimetry in the home for 10 days (Phillips Actiwatch and sleep diaries). Children with actimetry within 6 months of MRI were included (HL-ASD n=11; HL-noASD n=37; LL n=35). Sleep variables included average sleep duration (minutes), sleep duration variability (intra-individual standard deviation of sleep duration), average sleep efficiency (proportion; total time spent sleeping/total time spent in bed), and sleep efficiency variability (intra-individual standard deviation of sleep efficiency).

**Results**

Our findings revealed a significant relationship between enlarged hippocampi and sleep duration variability in both HL-ASD and HL-noASD, correcting for total brain tissue volume (see Table 1). No significant association between hippocampal volume and average sleep time, average sleep efficiency, or sleep efficiency variability was observed. Future analyses will evaluate other subcortical structures to determine whether this relationship is specific to the hippocampus and will include additional children as scans that pass QC become available.

**Conclusions**

Greater sleep duration variability is associated with larger bilateral hippocampal volume, controlling for total brain tissue volume, in children with higher familial likelihood of autism. Variability in sleep patterns can be an index of insomnia, found in high rates in autism. Investigating brain-sleep relationships has the potential to reveal developmental impacts of sleep problems in this vulnerable population.

**Table 1**

**Total Hippocampal Volume and Sleep Duration Variability (SDV) by Group**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Total Hippocampal Volume | | |
| *Predictors* | *Estimates* | *CI* | *p* |
| (Intercept) | 1938.07 | 350.70 – 3525.44 | **0.017** |
| total tissue vol 1k | 3.52 | 2.33 – 4.71 | **<0.001** |
| SDV | -3.15 | -12.76 – 6.45 | 0.515 |
| grp [HL-] | -838.96 | -1478.67 – -199.25 | **0.011** |
| grp [HL+] | -1159.94 | -2074.97 – -244.92 | **0.014** |
| SDV × grp [HL-] | 13.28 | 1.08 – 25.47 | **0.033** |
| SDV × grp [HL+] | 20.09 | 3.64 – 36.54 | **0.017** |
| Observations | 82 | | |
| R2 / R2 adjusted | 0.381 / 0.331 | | |

*Note.* The LL- control group is labeled as the intercept.