Insights into the developing brain using the sleep EEG

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Sleep EEG

- Sensitive marker of cortical functioning.
- Sensitive to impact of chronic alcohol use.
- Sleep state is undisturbed by active behavior and less impacted by external stimuli compared to wake.
- Allows investigation of regional differences in EEG activity reflective of differences in the underlying cortex.

Adolescent Development

Alcohol Use
Slow wave sleep (25 % of the night) and slow wave activity
What is needed for the production of high amplitude slow delta waves?

- Ca\(^{++}\) mediated burst firing of neuronal membranes in cortical tissue.
- Large numbers of healthy neurons
- Good synchronization over large cortical distances (high bandwidth white matter pathways)

Steriade & Amzica
Sleep Research Online
Changes in brain structure across adolescence

White matter volume increases and gray matter decreases in several brain regions during adolescence (Sowell et al., 1999; Giedd et al., 1999; Paus, 2010).

Growth in cortical regions is earlier in posterior than anterior regions (Shaw et al., 2008).
Cross-sectional data: Exponential decline in slow wave activity (1-4.4 Hz) during sleep across adolescence

Buchmann et al., Cerebral Cortex, 2011
Correlation between decline in gray matter volume and slow wave activity across adolescence

Buchmann et al., Cerebral Cortex, 2011
Longitudinal data reveals a clear picture of the decline in slow wave activity during sleep across adolescence.

- **Feinberg and Campbell, Am J Physiol Reg Integ Comp Physiol, 2013**

- **p = 4 x 10^{-77}**

- **Graph showing age (years) vs. slow wave (Delta) power (µV)^2**

  - Ages: 6, 9, 12, 15, 18
  - Power levels: 0, 300, 600, 900, 1200, 1500
Aims: Phase 1 R21 Feasibility Study

- Determine whether brain structural changes are detected with conventional MRI over a 7-month interval in young, healthy adolescents.
- Validate a sequential method of registration as a sensitive method of detecting longitudinal changes in cortical tissue volumes in adolescents.
- To investigate changes in sleep EEG over a 7-month interval in young, healthy adolescents.
- To investigate whether changes in the sleep EEG across adolescence vary according to topography and sleep stage (NREM or REM sleep).

Sullivan et al., Neuroimage 2011; Baker et al., J Sleep Res 2012
## Characteristics of participants at the start of the study

<table>
<thead>
<tr>
<th></th>
<th>Boys</th>
<th>Girls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample Size</td>
<td>18 [16]</td>
<td>15 [12]</td>
</tr>
<tr>
<td>Age (years, mean (SD))</td>
<td>12.7 (0.9)</td>
<td>12.4 (0.7)</td>
</tr>
<tr>
<td>Age range (years)</td>
<td>11 – 14</td>
<td>11 – 14</td>
</tr>
<tr>
<td>Tanner stage (median)</td>
<td>2*</td>
<td>3</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.61 (0.1)</td>
<td>1.58 (0.07)</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>50.8 (10.7)</td>
<td>47.8 (8.4)</td>
</tr>
<tr>
<td>Follow-up interval</td>
<td></td>
<td>6 – 8 months</td>
</tr>
</tbody>
</table>

*Significantly different from girls ($\chi^2 = 51.4$, $P < 0.01$, $n = 14$ girls).
Sequential method of registration

Inter-subject non-linear registration

Intra-subject non-linear registration

Sullivan et al., Neuroimage 2011; Rohlfing et al., Hum Brain Map 2010
Developmental changes in regional brain structure over 7 months in early adolescence

Lateral ventricles
Temporal horn
Cortical sulci
Sylvan fissures

Lateral frontal
Medial frontal
Anterior cingulate
Precuneus
Parietal

Sullivan et al., Neuroimage 2011
An advancement in pubertal stage heralds a decrease in brain volume

Sullivan et al., Neuroimage 2011
Summary

• Longitudinal MRI assessment using a sequential method of registration reveals significant regional gray matter volume changes over 7 months in young, healthy adolescents.

• An advancement in pubertal stage was significantly associated with declines in regionally-specific gray matter volume and expansion of lateral ventricles, supporting a role of pubertal development in brain maturation.
Longitudinal analysis of sleep architecture in young adolescents (n = 30)

<table>
<thead>
<tr>
<th></th>
<th>Initial</th>
<th>Follow-up 6-8 months later</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sleep time (min)</td>
<td>488.2 (49.6)</td>
<td>484.2 (49.1)</td>
</tr>
<tr>
<td>Sleep onset latency (min)</td>
<td>21.3 (12.5)</td>
<td>19.9 (19.2)</td>
</tr>
<tr>
<td>SWS (%)</td>
<td>25.6 (6.4)</td>
<td>24.5 (5.3)</td>
</tr>
<tr>
<td>REM (%)</td>
<td>19.3 (4.9)</td>
<td>21.7 (3.5)*</td>
</tr>
<tr>
<td>Stage 2 (%)</td>
<td>51.8 (5.8)</td>
<td>51.4 (4.3)</td>
</tr>
</tbody>
</table>

* Significantly different from baseline
Cross sectional results: Advancing age predicted a significant decline in slow wave activity in the occipital region.
Longitudinal data: Slow wave activity is significantly lower in all regions, especially the occipital region.
Experimentally evoked slow wave K-complexes
Averaged Stage 2 Auditory Evoked K-complex: Broad activation across the scalp in early puberty
Averaged Stage 2 Auditory Evoked K-complex: Frontal focused activation in advanced pubertal stages.
Summary

• Delta power declined most prominently in the occipital region with advancing age across adolescence.
• Declines in delta power were not sleep stage specific, being evident in NREM and REM sleep.
• Delta power declined to the same extent in boys and girls.
• The topographical pattern of evoked slow wave K-complexes matures across puberty towards the adult pattern of a frontal dominance.
Looking forward to NCANDA

• Longitudinally track normal developmental changes in brain structure, sleep EEG, and evoked K-complexes across a broad age range in adolescents (12 – 21 years).
• Do changes in the sleep EEG and evoked K-complexes in frontal, central, parietal, and occipital regions correspond to regional changes in gray and white matter across adolescence?
• Are the developmental changes in sleep and brain structure in adolescence impacted by alcohol exposure?
K-Complex Elicitation in Light and Heavy Drinking Adolescents (Age 18 - 21 years)
Sleep is more than just a functional measure of brain changes: sleep behavior impacts risk taking in youth

Adolescence is associated with:

• A shift to later bedtimes
• A shift in chronotype towards eveningness, with a preference for evening activities
• Early wake up times constrained by school schedule
• A reduction in sleep duration on school nights of 14 min per year
• An increase in daytime sleepiness
• Increased prevalence of insomnia

Colrain and Baker, Neuropsych Rev 2011
Consequences of poor sleep in adolescents

- Adolescents with sleep problems report more mood disturbances, inattention and memory problems, conduct disorders, and increased drug and alcohol use.
- Poor sleep quality and chronic insomnia predict alcohol use in adolescents.
- A tendency towards eveningness is associated with greater alcohol and other substance use.
- A larger weekday–weekend sleep difference is linked to increased risk-taking behaviors, substance use, and depressed mood.

With a longitudinal design, NCANDA will be able to evaluate the impact of sleep behavior on subsequent alcohol use in adolescents.

Adolescents (12 – 21 years)

NCANDA

Self-report sleep behavior
N > 700

Self-report alcohol use
N > 700

Sleep EEG and Evoked potentials
N = 200

Brain MR imaging
N > 700

Tracked annually over 4 years
NCANDA: SRI International Data Collection Site

Data Collection:

*SRI International*

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