Insights into the developing brain using the sleep EEG

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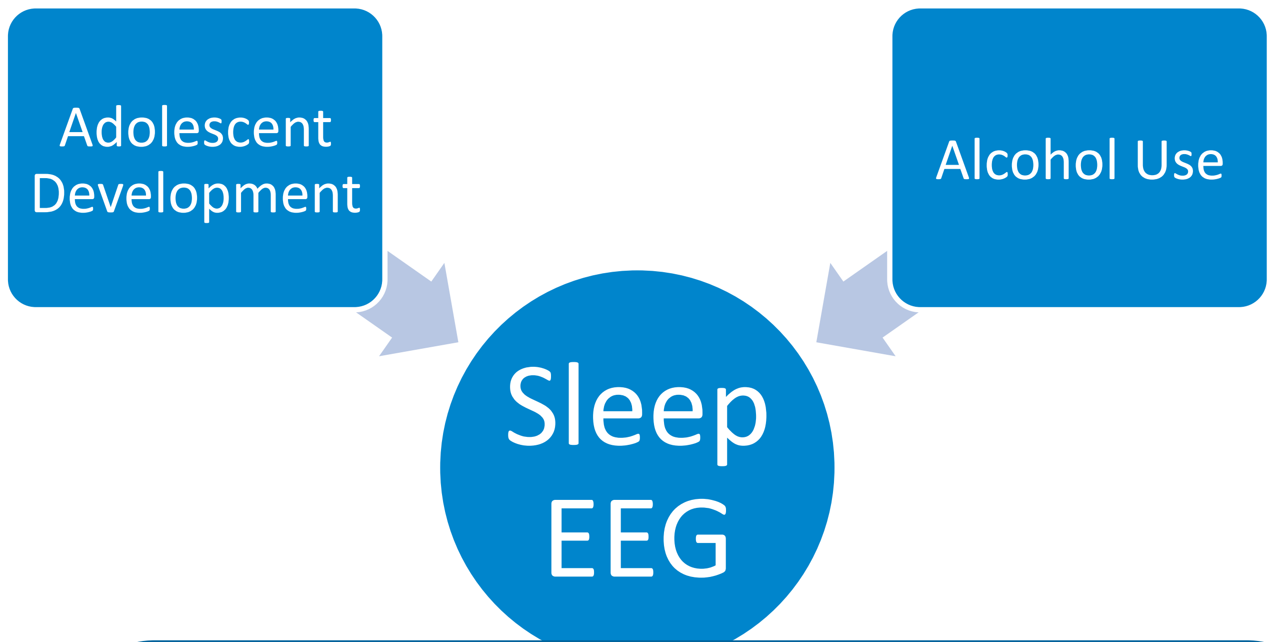
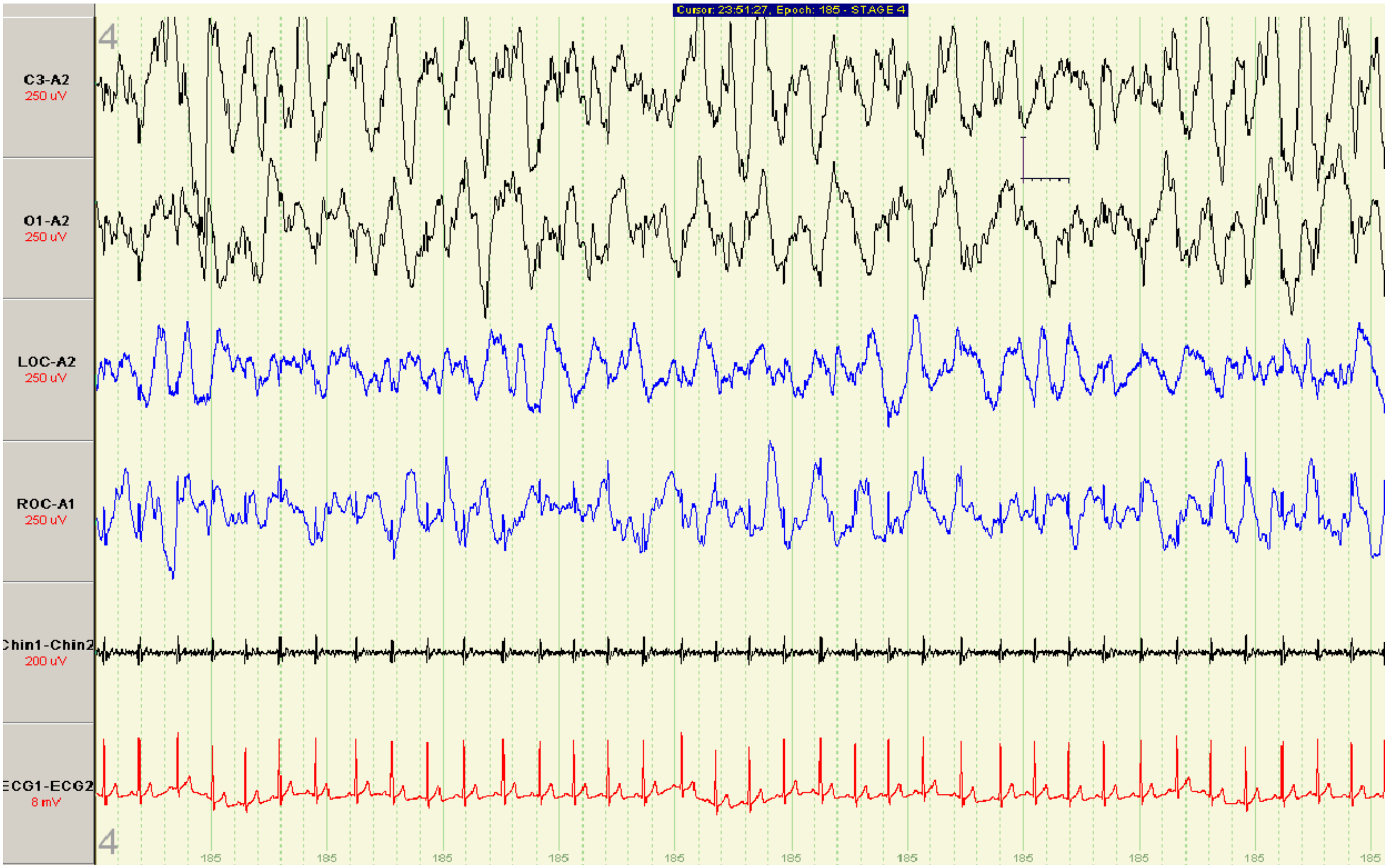


- Sensitive marker of cortical functioning.
- Sensitive to impact of chronic alcohol use.
- Sleep state is undisturbed by active behavior and less impacted by external stimuli compared to wake.
- Allows investigation of regional differences in EEG activity reflective of differences in the underlying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

Slow wave sleep (25 % of the night) and slow wave activity



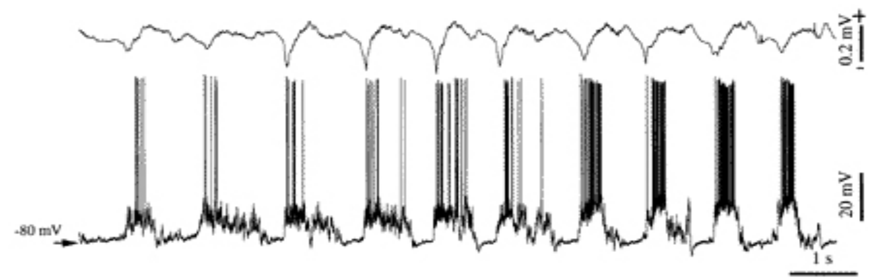
What is needed for the production of high amplitude slow delta waves?

- Ca^{++} mediated burst firing of neuronal membranes in cortical tissue.

Steriade & Amzica
Sleep Research Online
1(1): 1-10, 1998

Surface EEG

Extra-cellular recording
from layer V

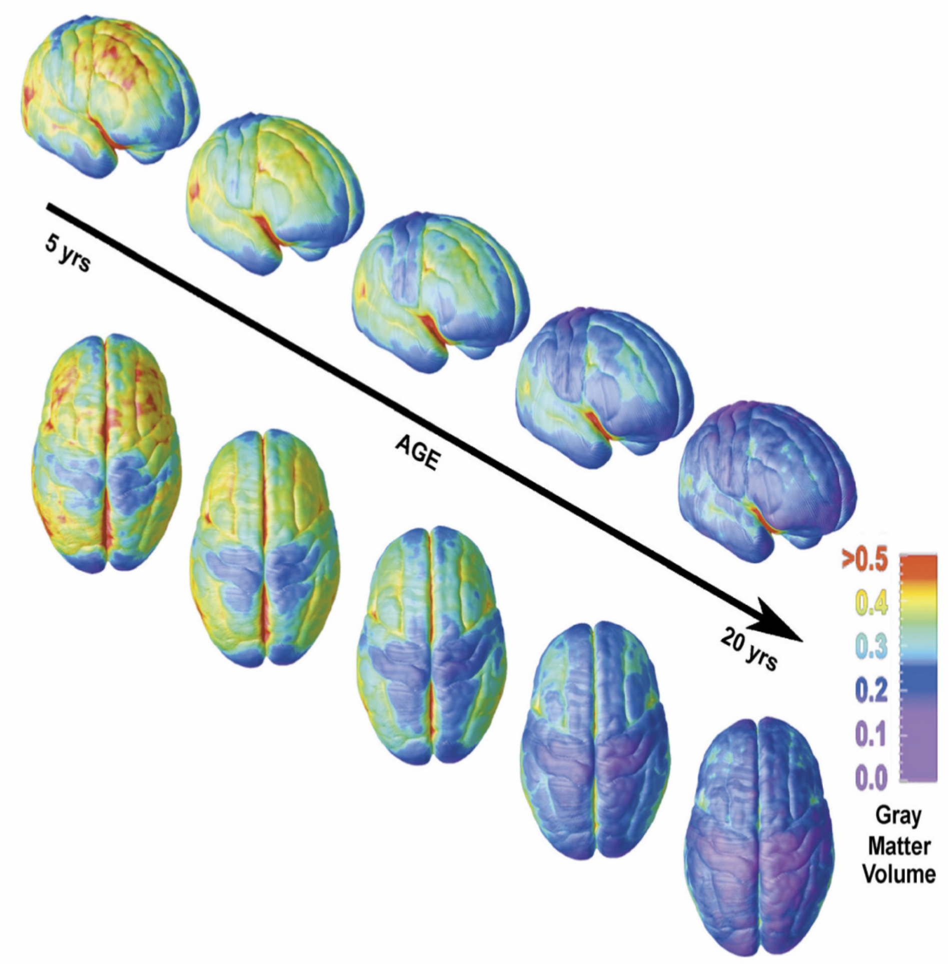


- Large numbers of healthy neurons
- Good synchronization over large cortical distances (high bandwidth white matter pathways)

Changes in brain structure across adolescence

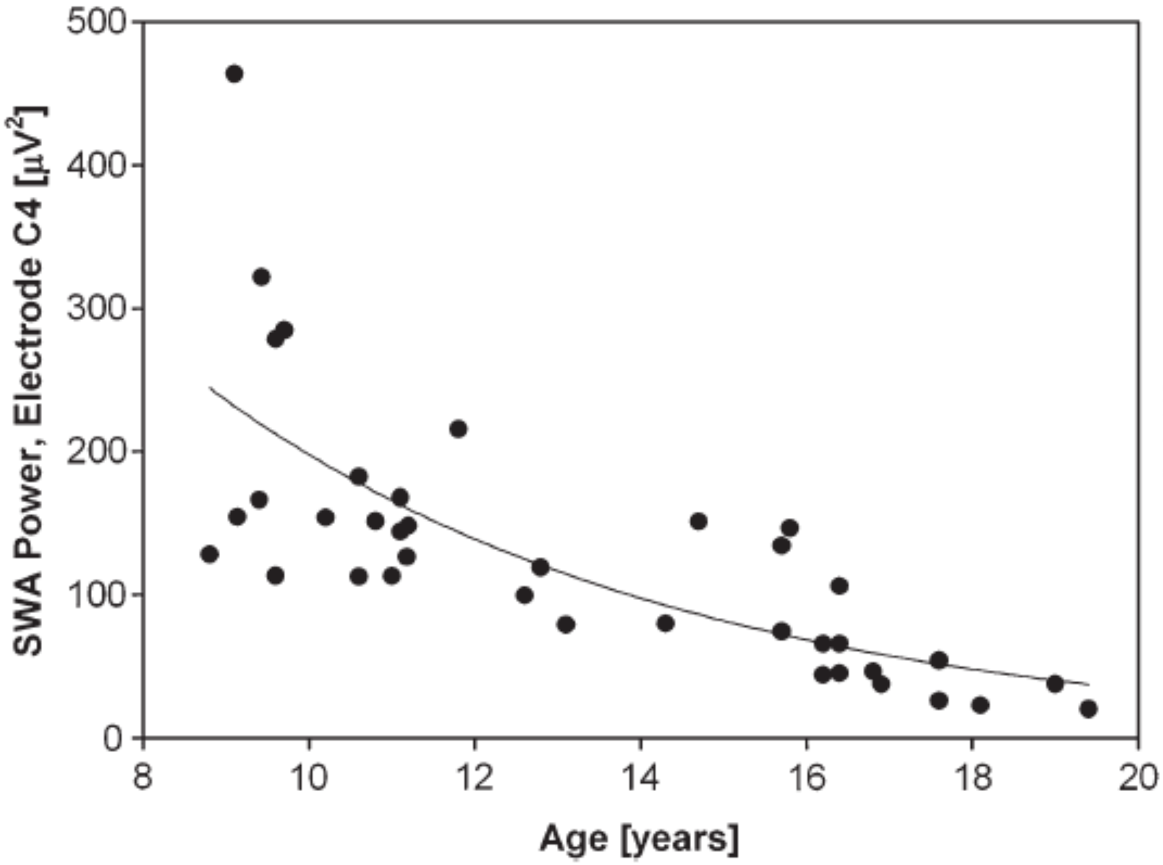
White matter volume increases and gray matter decreases in several brain regions during adolescence (Sowell et al., 1999; Giedd et al., 1999; Paus, 2010).

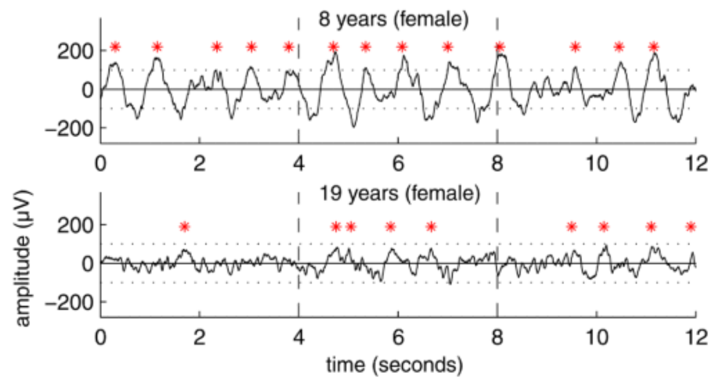
Growth in cortical regions is earlier in posterior than anterior regions (Shaw et al., 2008).



Giedd et al., J Am Acad Child Adolesc Psychiatry 2009

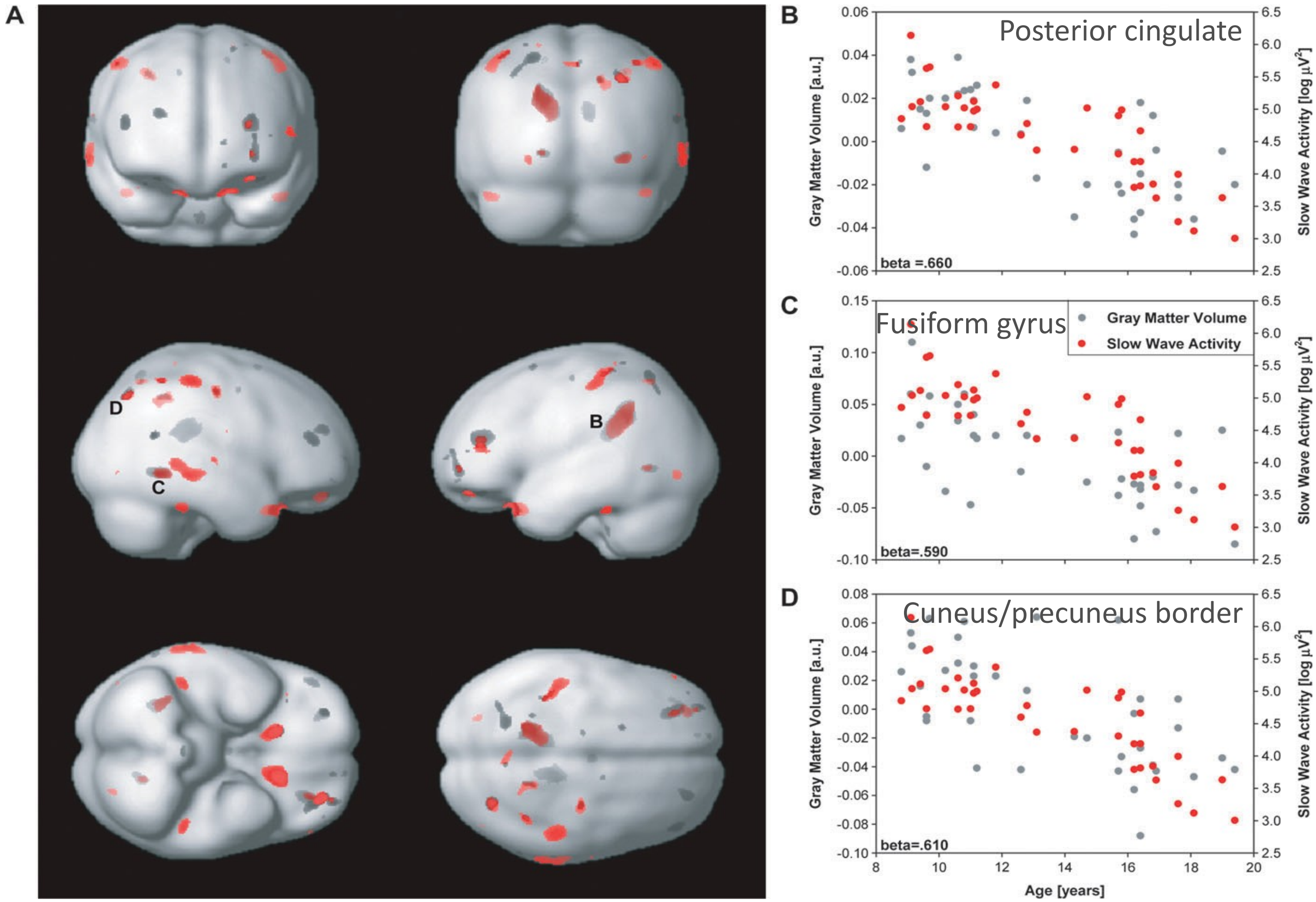
Cross-sectional data: Exponential decline in slow wave activity (1-4.4 Hz) during sleep across adolescence





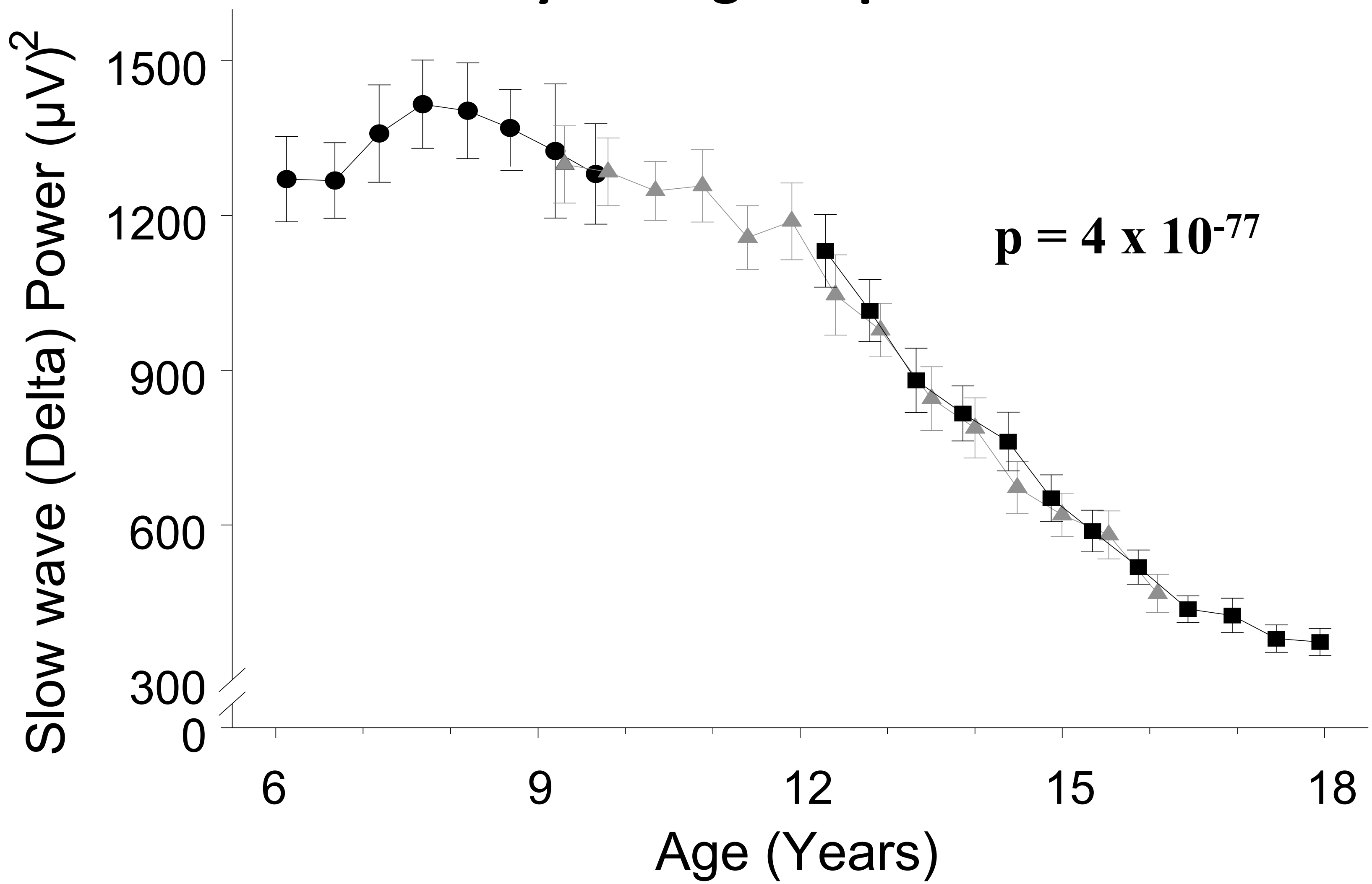
Buchmann et al., Cerebral Cortex, 2011

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

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).

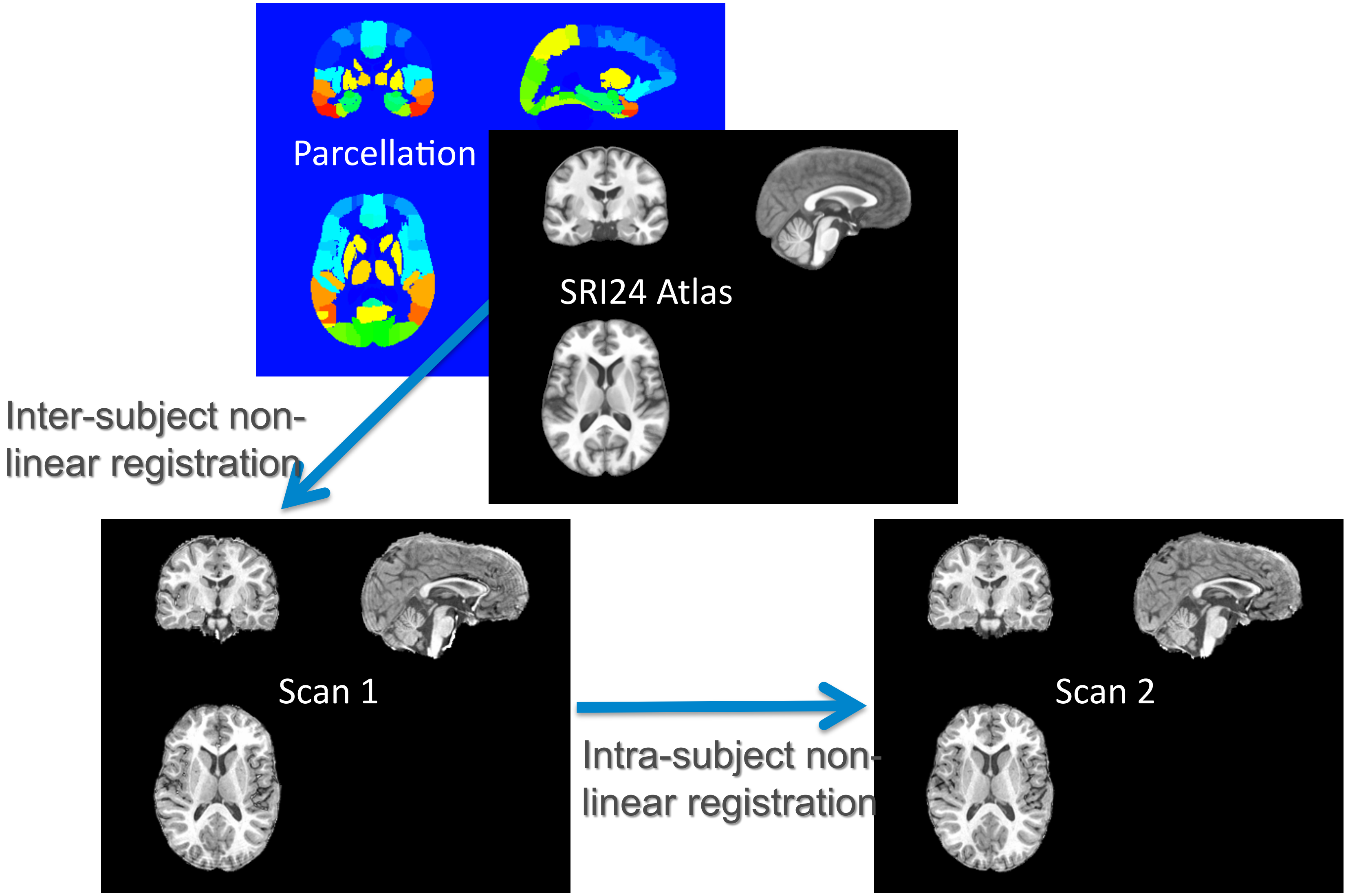
Sullivan et al., Neuroimage 2011; Baker et al., J Sleep Res 2012

Characteristics of participants at the start of the study

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

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

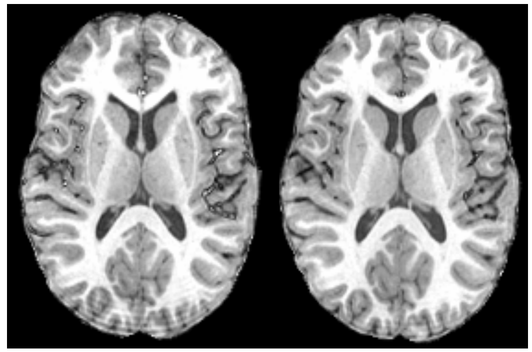
Sequential method of registration



Sullivan et al., Neuroimage 2011; Rohlfing et al., Hum Brain Map 2010

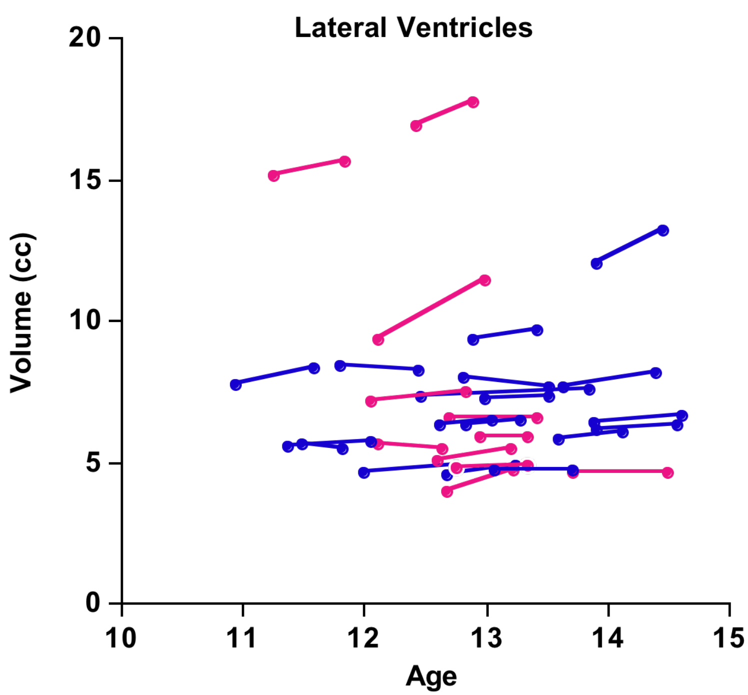
Developmental changes in regional brain structure over 7 months in early adolescence

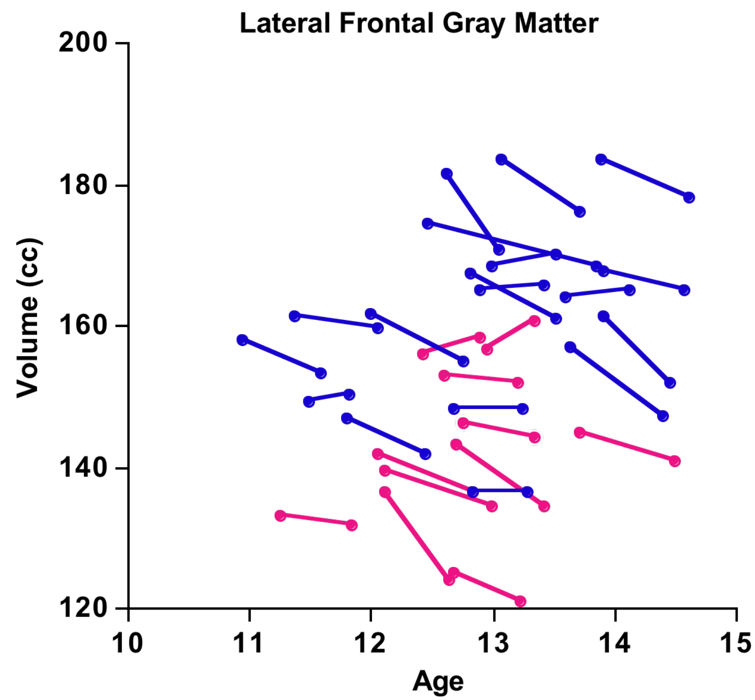
initial 6-mo later



Lateral ventricles
Temporal horn
Cortical sulci
Sylvan fissures

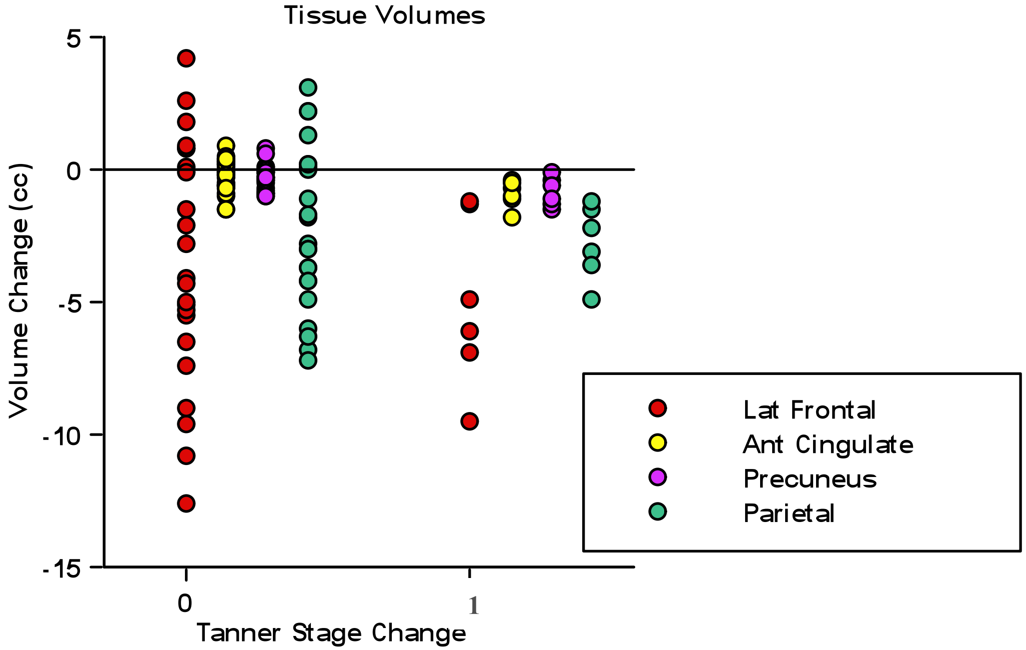
Lateral frontal
Medial frontal
Anterior cingulate
Precuneus
Parietal

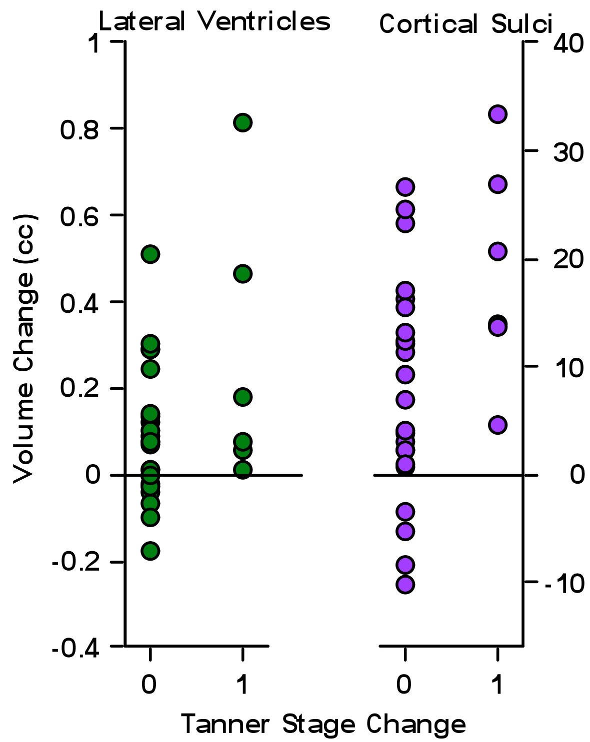




Sullivan et al., Neuroimage 2011

An advancement in pubertal stage heralds a decrease in brain volume





Sullivan et al., Neuroimage 2011

Summary

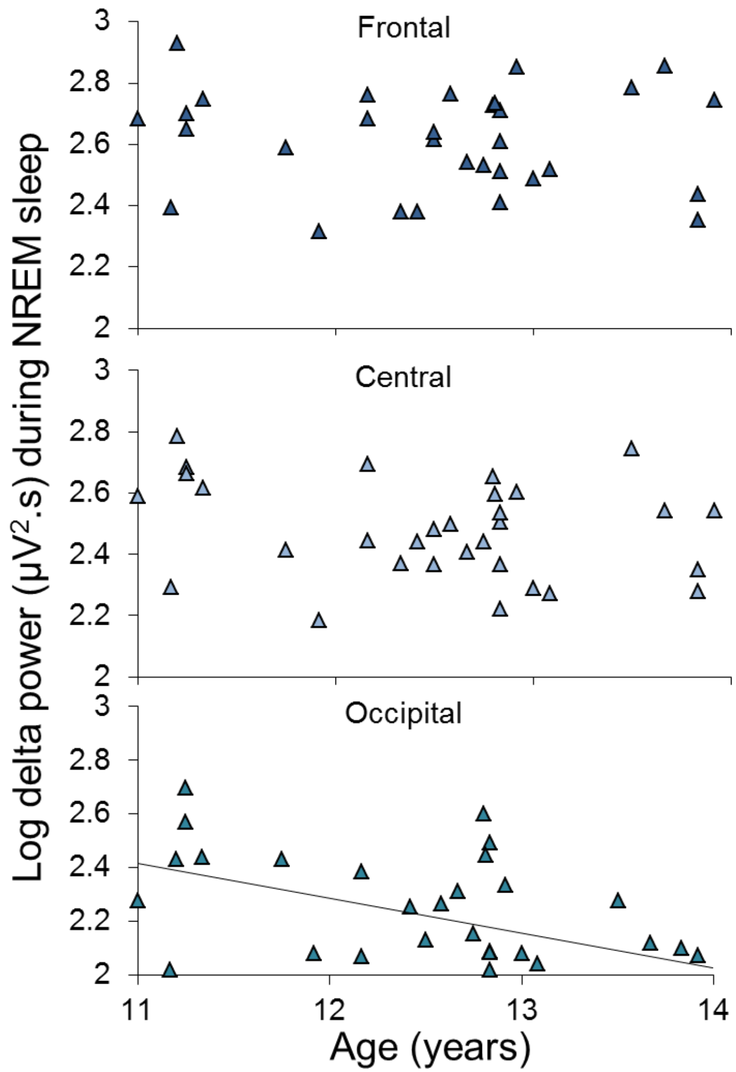
- Longitudinal MRI assessment using a sequential method of registration reveals significant regional gray matter volume changes over 7 months in young, healthy adolescents.
- An advancement in pubertal stage was significantly associated with declines in regionally-specific gray matter volume and expansion of lateral ventricles, supporting a role of pubertal development in brain maturation.

Longitudinal analysis of sleep architecture in young adolescents (n = 30)

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

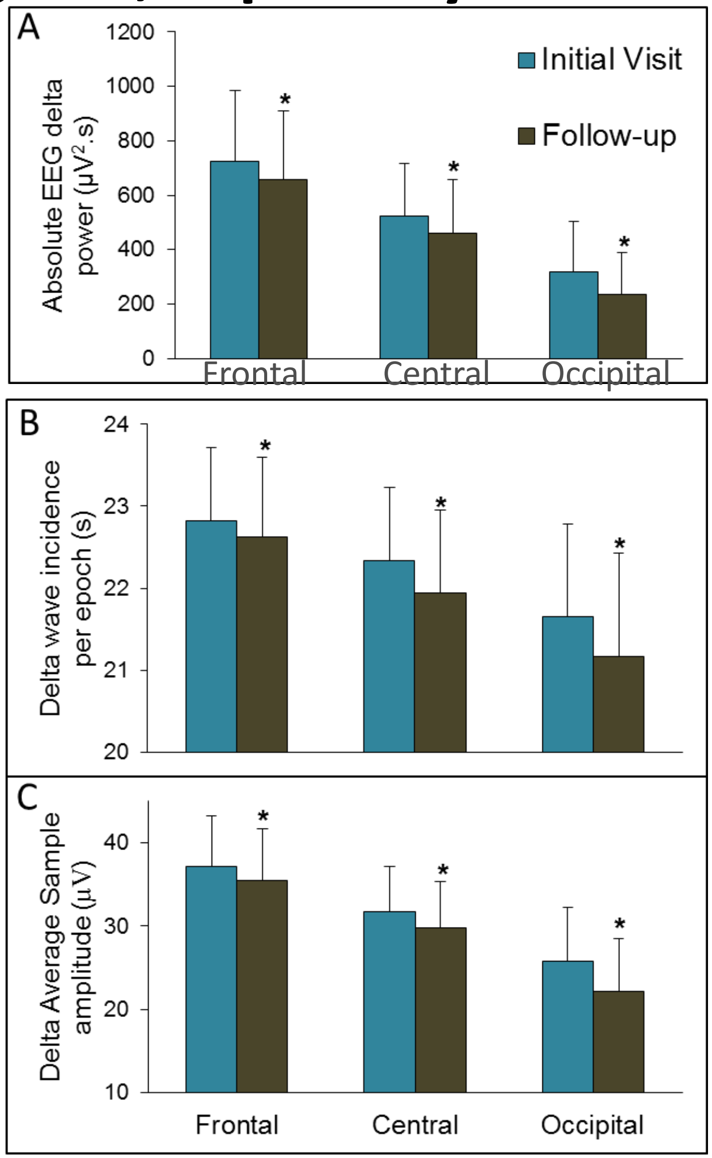
* Significantly different from baseline

Cross sectional results: Advancing age predicted a significant decline in slow wave activity in the occipital region



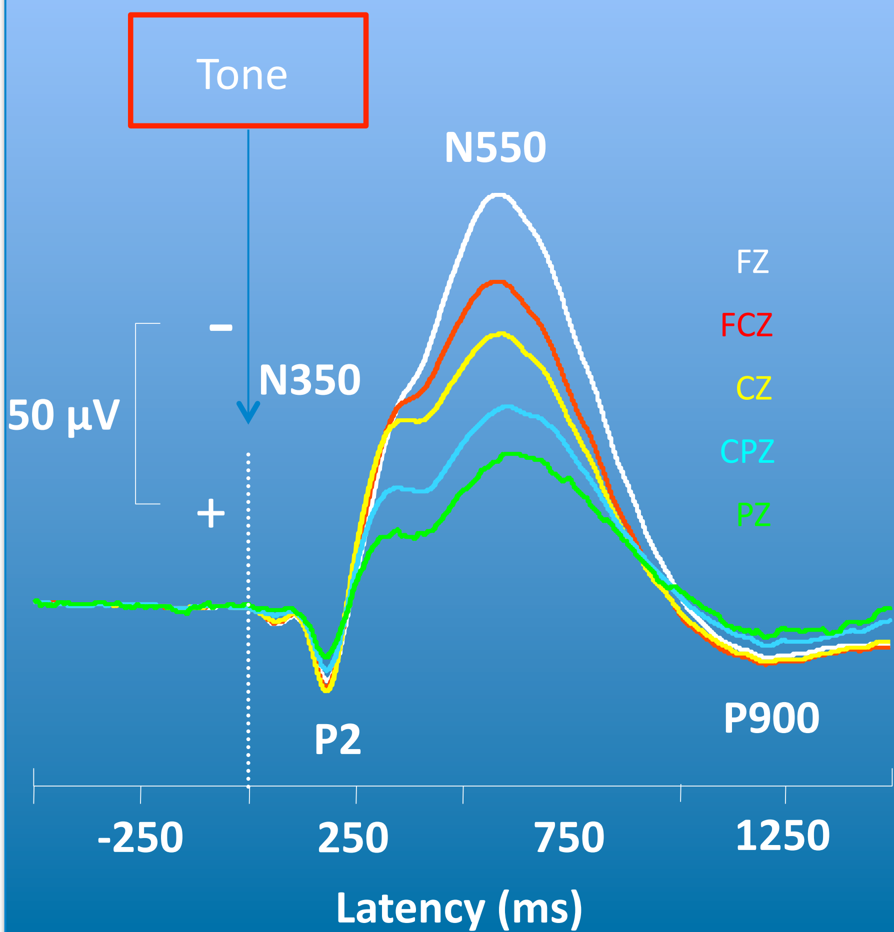
Baker et al., J Sleep Res 2012

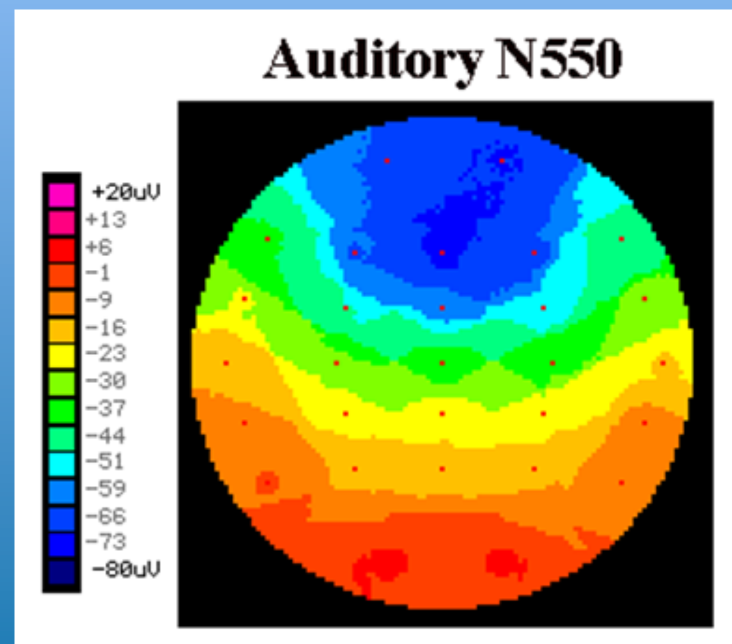
Longitudinal data: Slow wave activity is significantly lower in all regions, especially the occipital region



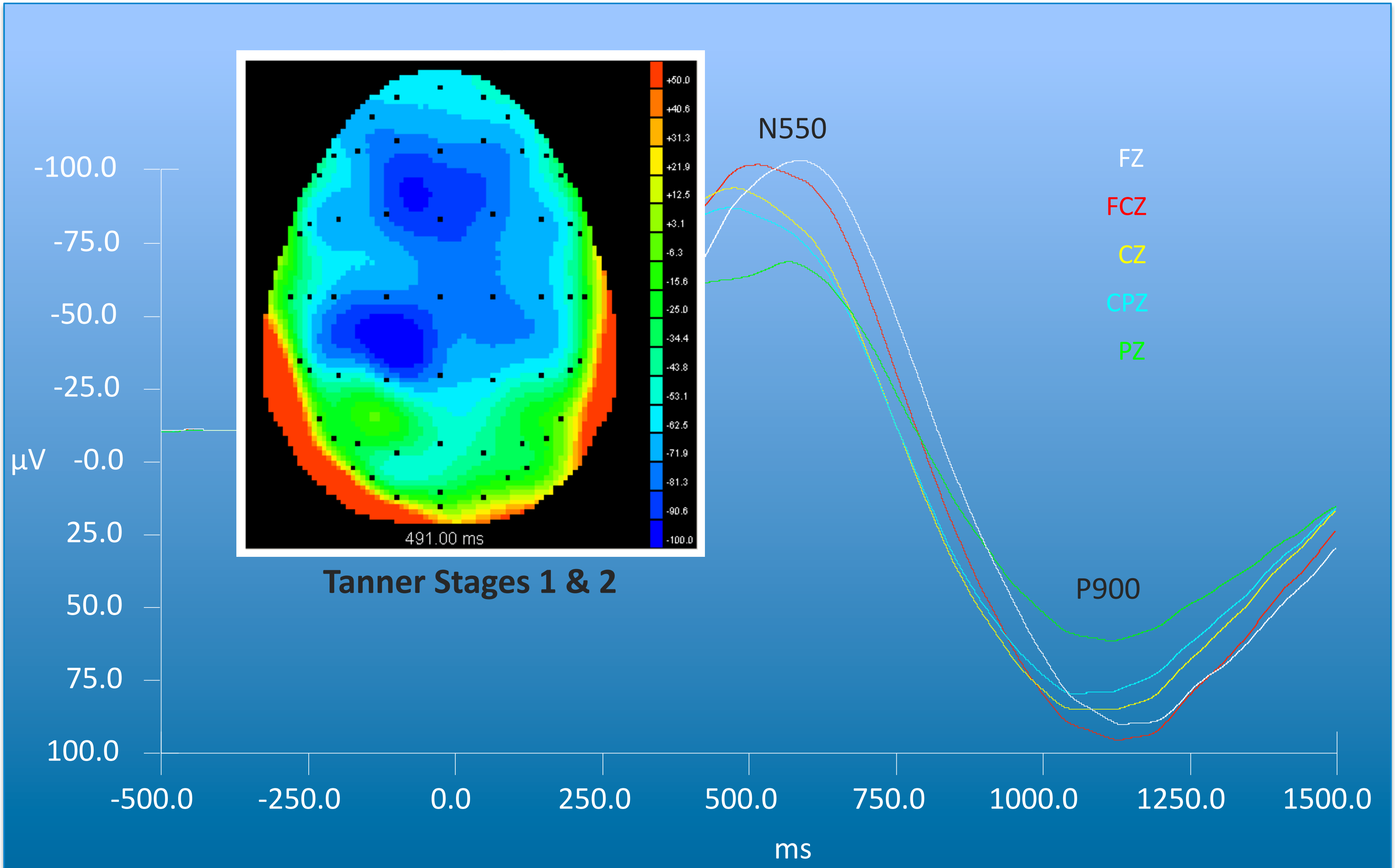
Baker et al., J Sleep Res 2012

Experimentally evoked slow wave K-complexes

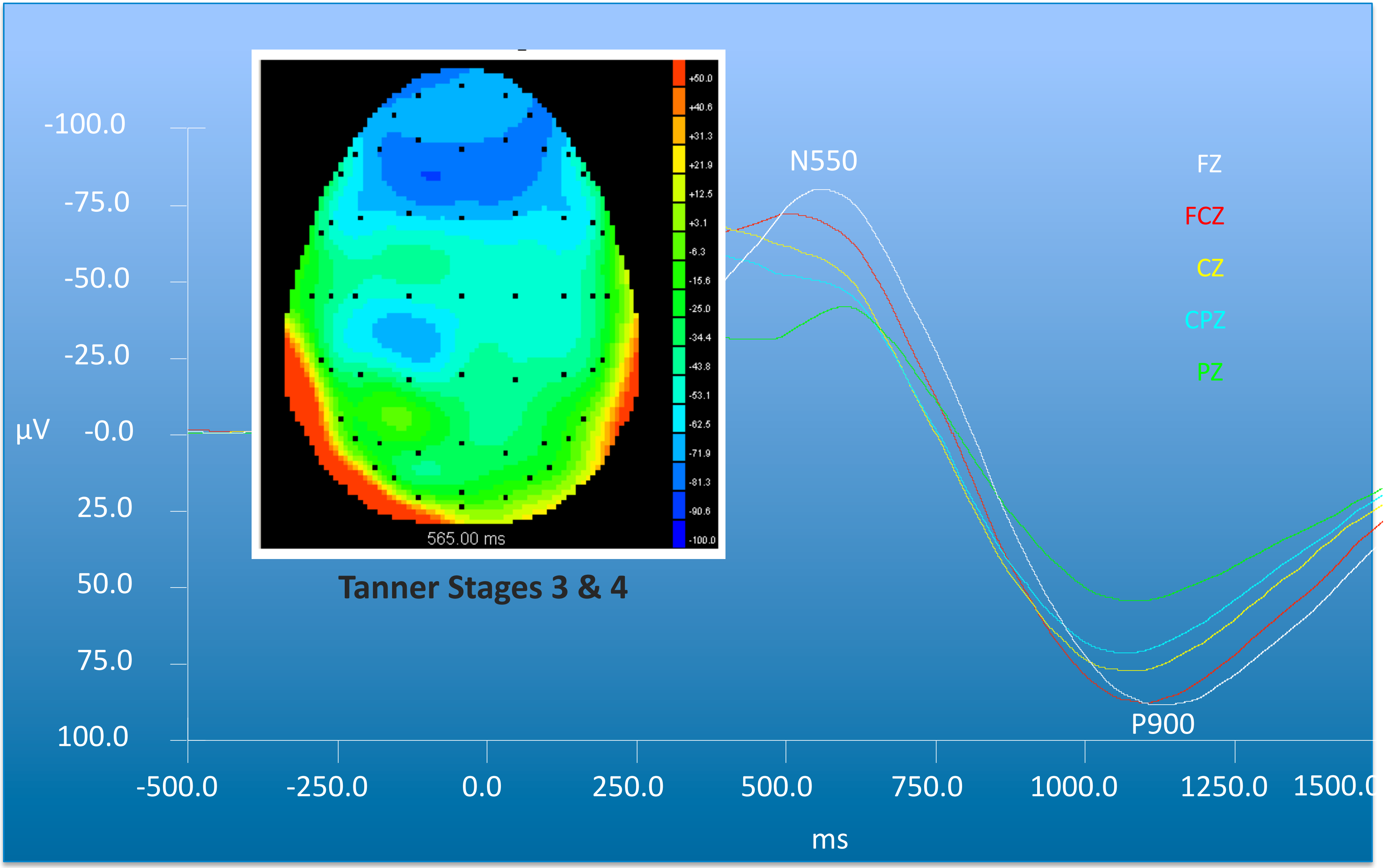




Averaged Stage 2 Auditory Evoked K-complex: Broad activation across the scalp in early puberty



Averaged Stage 2 Auditory Evoked K-complex: Frontal focused activation in advanced pubertal stages



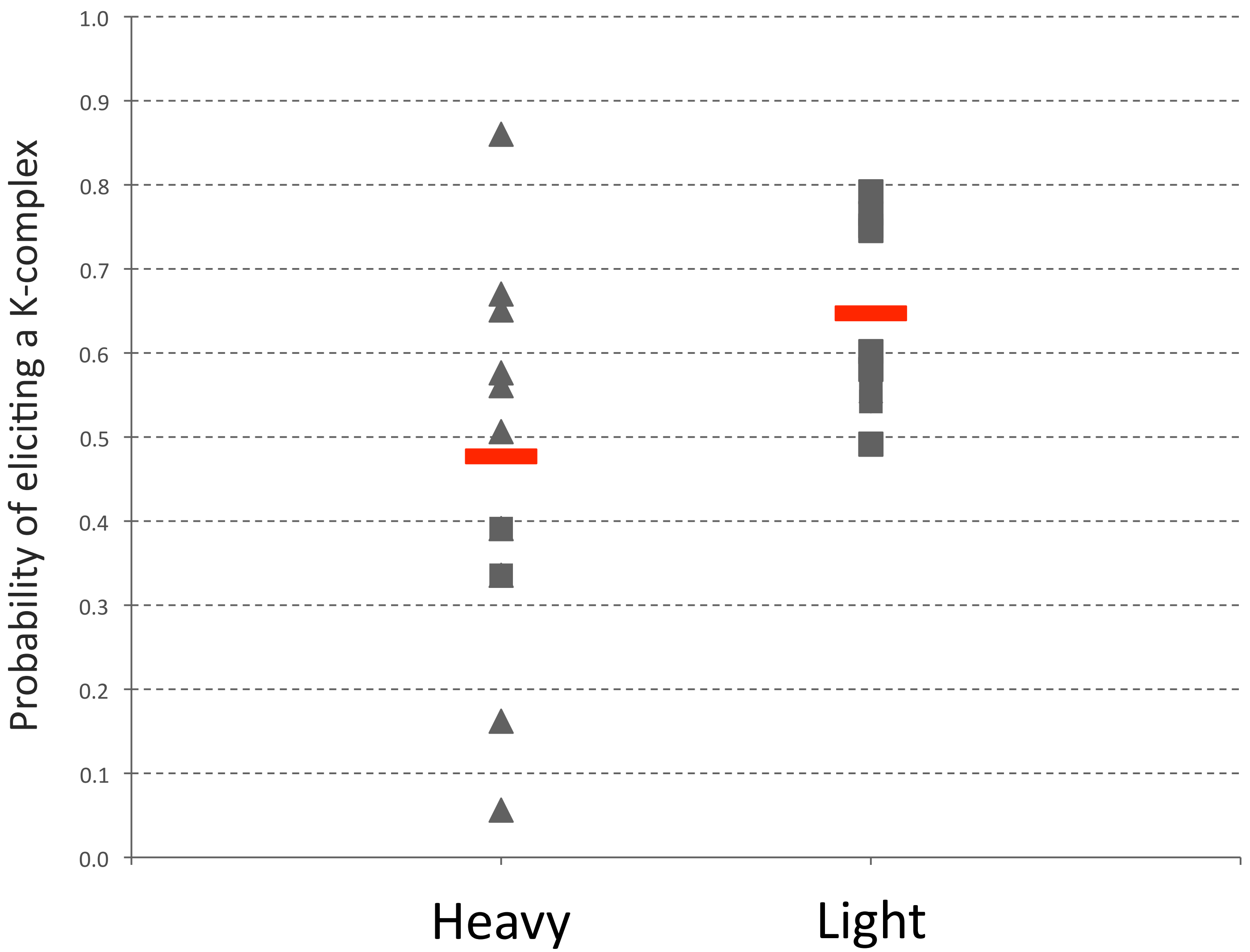
Summary

- 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

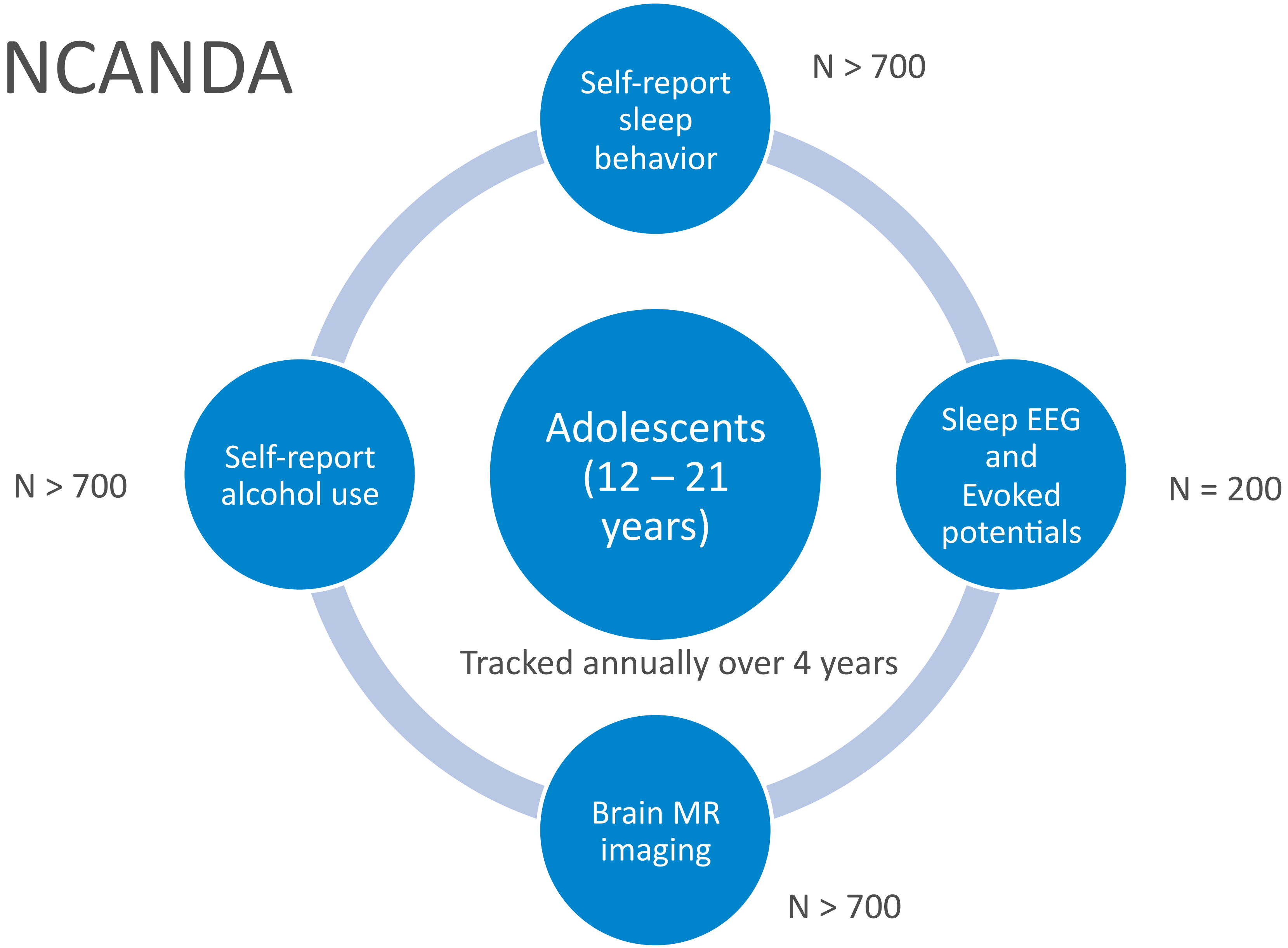
Consequences of poor sleep in adolescents

- 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.

Shibley et al., J Psychiat Prac 2008; Wong et al., Alcohol Clin Exp Res 2004; Roberts et al., J Adolesc Health 2008; Hasler and Clark, Alcohol Clin Exp Res 2013

NCANDA


Self-report
sleep
behavior
N > 700
Self-report
alcohol use
N > 700
Adolescents
(12 – 21
years)
Sleep EEG
and
Evoked
potentials
N = 200
Tracked annually over 4 years
Brain MR
imaging
N > 700

NCANDA: SRI International Data Collection Site

Data Collection:

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National Consortium on Alcohol and NeuroDevelopment in Adolescence
N-CANDA
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