

Age & Sex Differences in Cognitive, Motor, & Sleep Indices: Initial Findings of the National Consortium on Alcohol & NeuroDevelopment in Adolescence

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NCANDA FUNDING: NIAAA • NIMH • NICHD • NIDA





Age & Sex Differences in Cognitive, Motor, & Sleep Indices: Initial Findings of the National Consortium on Alcohol & NeuroDevelopment in Adolescence

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Susan Tapert, Edith Sullivan

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Disclosures

Financial and Academic Interests



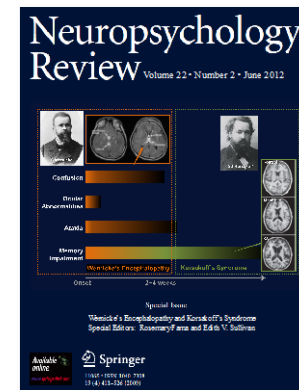
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Professor

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Stanford University School of Medicine**



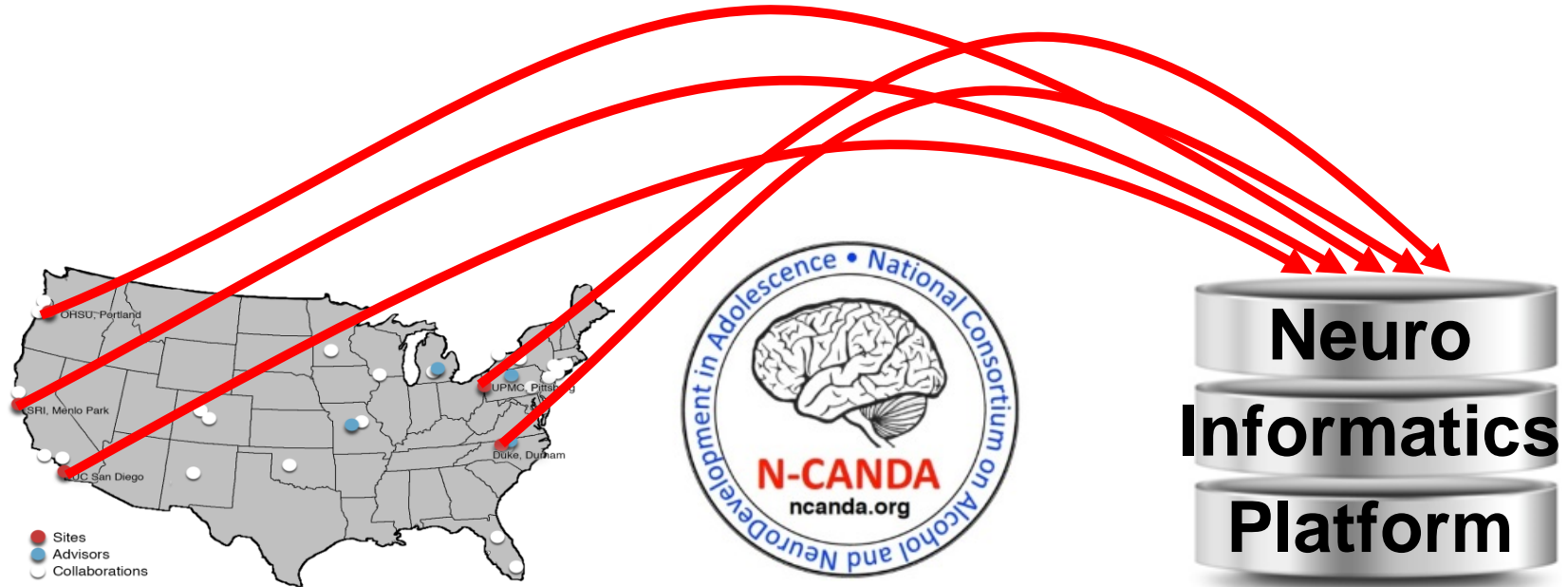
Editor-in-Chief



Salary and research support

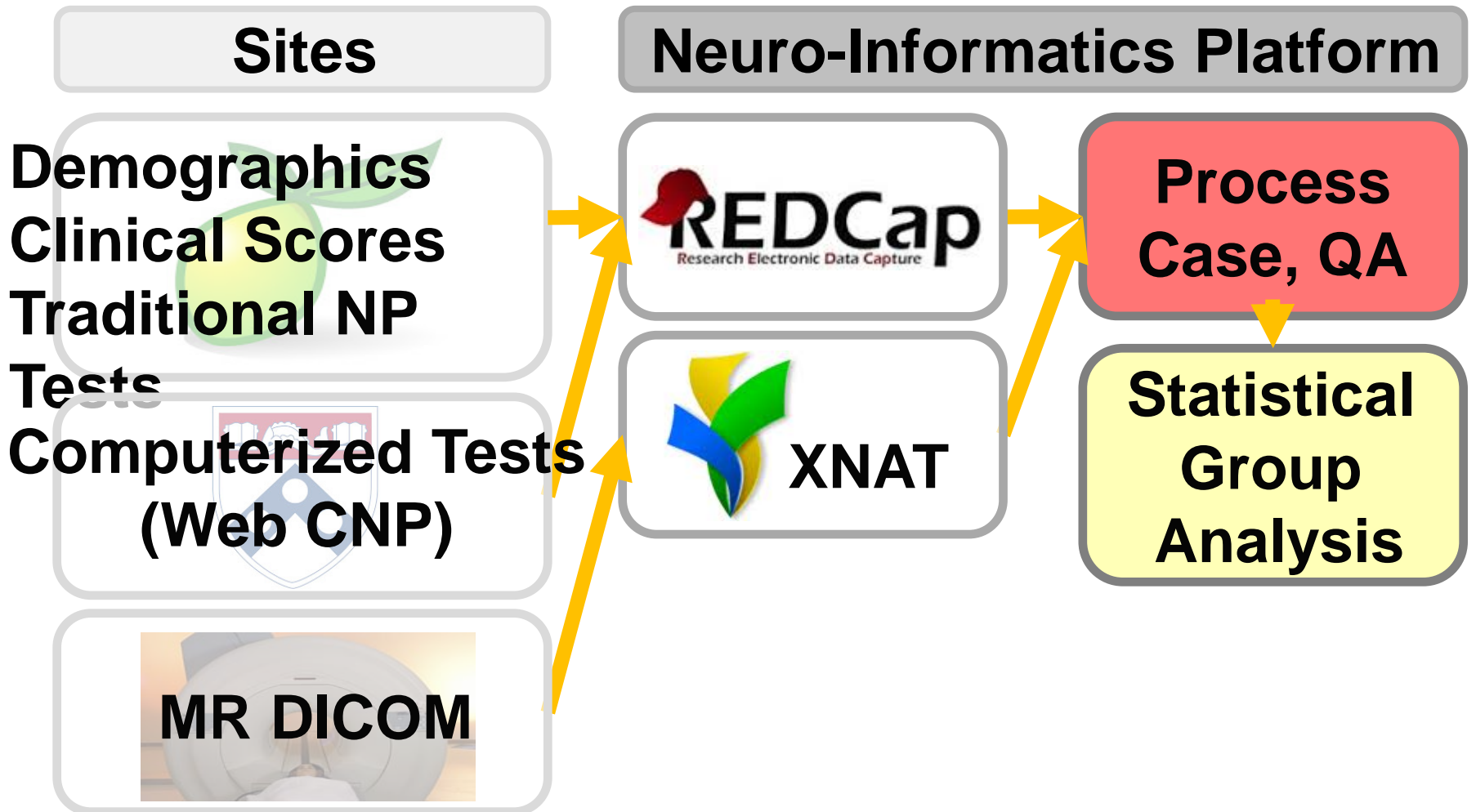


NCANDA - Data Analysis



- Monitoring brain development of 831 adolescents over a 5 year period and recruited from 5 U.S. sites to**
- **determine the effects of early, heavy alcohol use on brain structure and function**
 - **identify factors that predict Alcohol Use Disorder**

NCANDA – Data Flow



**Fusing data across
time, sites, and modalities**

NCANDA – Data Flow

Sites

Neuro-Informatics Platform

Demographics
Clinical Scores
Traditional NP
Tests

Computerized Tests
(Web CNP)

MR DICOM

 **REDCap**
Research Electronic Data Capture

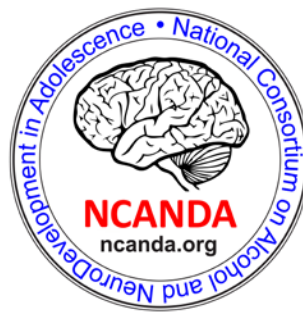
 **XNAT**

**Process
Case**

**Statistical
Group
Analysis**

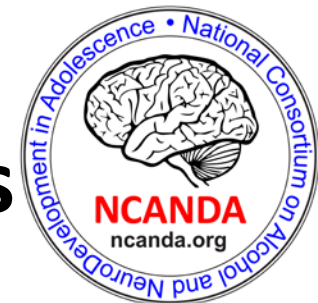
Report

**Provide comprehensive report of
measurements to scientists**



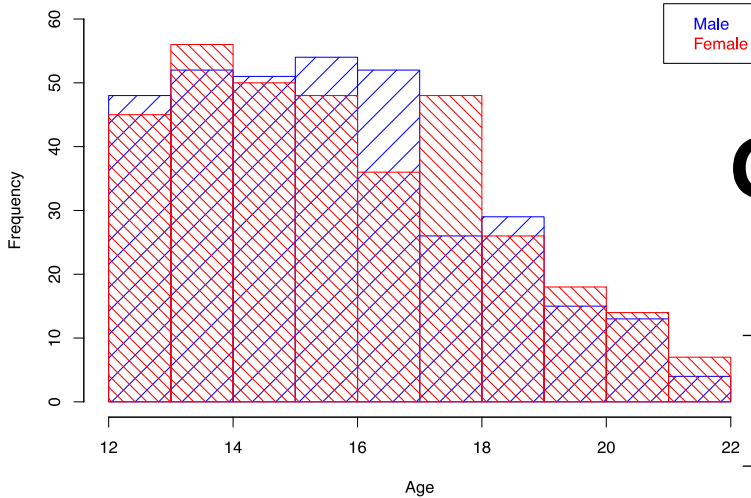
Neuropsychology Testing Procedures

- **Combination of traditional pencil & paper tests and computerized tests (UPenn Computerized NP Battery-WebCNP)**
- **Examiners at each site were initially trained and continue to undergo annual calibration with two team leaders**
 - **Devin Prouty, Ph.D.** from SRI and **Lindsay Squeglia, Ph.D.** now at MUSC oversee test administration, data scoring, data entry, and data uploading to Redcap
 - **Kevin Cummins, M.A.** at UCSD installs programs and upgrades on all test computers at each site
 - **Weiwei Chu, M.A.** at SRI curates all Redcap data by conducting range and ID checking, identifying misclassified data, and finding missing data. She reports errors to sites for correction.



Group Characteristics

age = 12-21 years



No/Low Drinker
(N=692)

		Male	Female
Age (years)	mean	15.6	15.8
	N	344	348
Pubertal Development Scale	median	3.0	3.6
	N	339	345
Socioeconomic status	mean	17.0	16.6
	N	326	326
Handedness	L/R/A	33/261/49	23/290/35
Self-declared Ethnicity			
Caucasian	N	251	235
African-American		34	53
Asian		27	25
Pacific Islander		1	3
American Indian		3	0
Mixed		28	32

Neuropsychology Protocol

8 RFA-required functional domains; valid across wide age range



Executive Function & Attention

Penn Continuous Performance Task
LeJuez Distress Tolerance: PASAT
SRI Stroop Match-to-Sample
Penn Conditional Exclusion Task
Penn Fractal N-back Task

Emotion Processing/Regulation

Penn Emotion Recognition Task
Penn Emotion Differentiation Test

Handedness & Dexterity

Edinburgh Handedness Inventory
Grooved Pegboard
Penn Motor Praxis Task

Intelligence

Penn Logical Reasoning test
Penn Matrix Analysis Test
WRAT-4 Vocabulary

Memory: Immediate-Delayed

Penn Visual Object Learning
Penn Word Memory
Penn Facial Memory

Reward Seeking & Learning

Stanger Delay Discounting Task

Visual Discrimination

Landolt C - Acuity
Ishihara – Color

Achievement

Penn Vocabulary Test
WRAT-4 Arithmetic

Traditional Tests

Rey-Osterrieth Complex Figure
Ataxia – Walk-a-Line
Digit Symbol Substitution

Neuropsychology Test Battery

25 tests → ~250 primary variables from ~1000 measures



Test				
Ishihara Test	May be completed during clinical assessment.	20 min.	}	
Landolt C				
Edinburgh Handedness Questionnaire				
WRAT- 4 Reading		5 min.	→	
Penn WebCNP				
Motor Praxis Test	Administered on the MacBook Air. Must be completed in one session.	WebCNP	}	
Penn Facial Memory Test				
Penn Word Memory Test				
Penn Continuous Performance Test-Number Letter Version				
Short Fractal N- Back Test - 2 Back Version				
Penn Matrix Analysis Test				
Penn Facial Memory Test - Delayed				
Penn Word Memory Test - Delayed				
Break				
Penn Short Visual Object Learning Test	Administered on the MacBook Air. Must be completed in one session.	60 min.	}	
Emotion Recognition Test				
Penn Conditional Exclusion Task				
Measured Emotion Differentiation				
Penn Vocabulary Test				
Penn Logical Reasoning				
Short Visual Object Learning Test - Delayed				
Stroop Match to Sample	Administered on the Dell laptop.	60 min.	}	
Stanger Delay Discounting Task				
PASAT-C Lejuez Distress Tolerance				
Rey-O Copy	Must be completed in one session.	60 min.	}	
Rey-O Immediate				
WRAT- 4 Arithmetic				Must be completed in ~30 minutes.
Ataxia				
Grooved Pegboard				
Rey-O Delayed				
WAIS-IV Coding [Symbols can be distractors to the Rey-O]				

Baseline NP battery = 180 min.
Follow-up = 150 min.

Neuropsychological Tests in Domain Composites



Executive Function & Attention

Penn Continuous Performance Task
LeJuez Distress Tolerance: PASAT
SRI Stroop Match-to-Sample
Penn Conditional Exclusion Task
Penn Fractal N-back Task

Emotion Processing/Regulation

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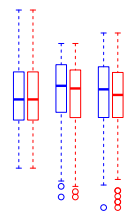
Creation of Neuropsychological Test Composite Scores

- **Data reduction**
 - Computerized tests yield accuracy and speed measures
 - Create composite scores reflecting 8 target functional domains
- **Test composite construction → 3-step process**
 - Standardize each measure on scores achieved by all no/low drinking male and female adolescents and express them as a Z-score, with a mean = $0 \pm SD$
 - Transform all scores (including reaction time) so that higher score reflect better performance
 - Calculate the mean Z-score of all measures that comprised a composite

Accuracy Composites

General Ability

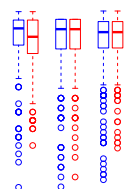
Adjusted Z-score



CNP Vocabulary
WRAT4 Arithmetic
WRAT4 Reading

Attention

Adjusted Z-score

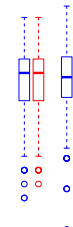


CNP CPT Letters
CNP CPT Numbers
CNP CPT Total



Emotion

Adjusted Z-score

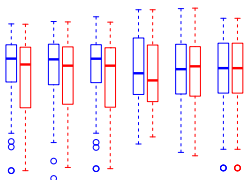


CNP Identification
CNP Discrimination

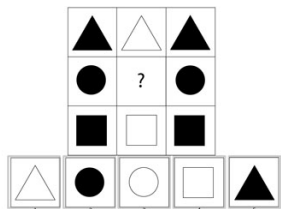


Abstraction

Adjusted Z-score

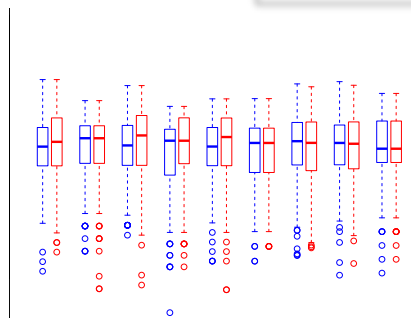


CNP Conditional Exclusion
CNP Matrix Reasoning
CNP Logical Reasoning



Episodic Memory

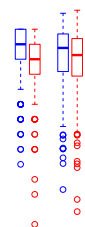
Adjusted Z-score



CNP Face Memory
CNP Word Memory
CNP Visual Object Learning

Working Memory

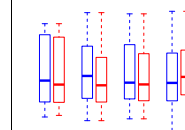
Adjusted Z-score



CNP Fractal 2-back
CNP Fractal 1 - 2 back

Balance

Adjusted Z-score



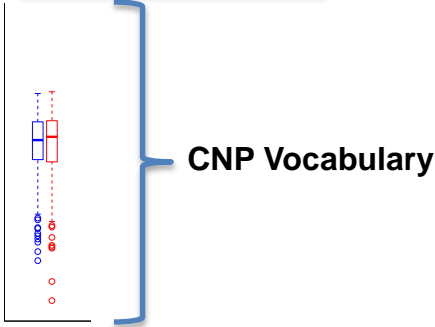
Stand Heel-to-Toe
Stand on One Leg
Walk Heel-to-Toe



Speed Composites

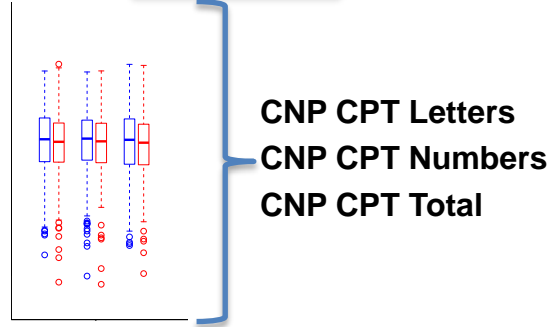
General Ability

Adjusted Z-score



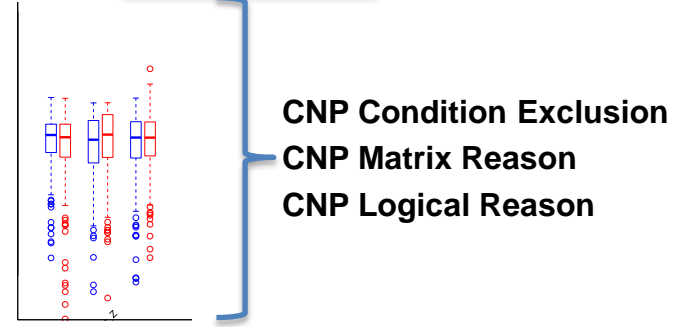
Attention

Adjusted Z-score



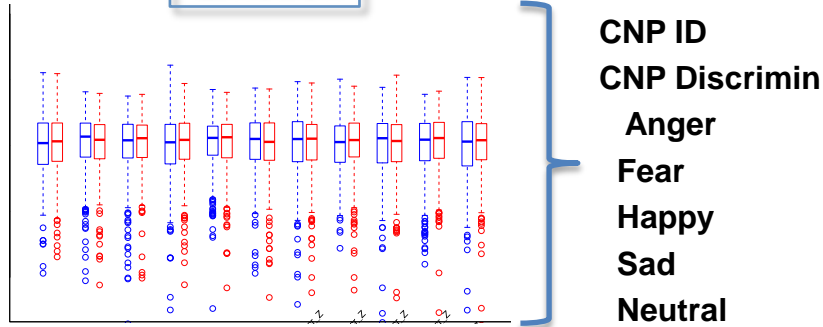
Abstraction

Adjusted Z-score



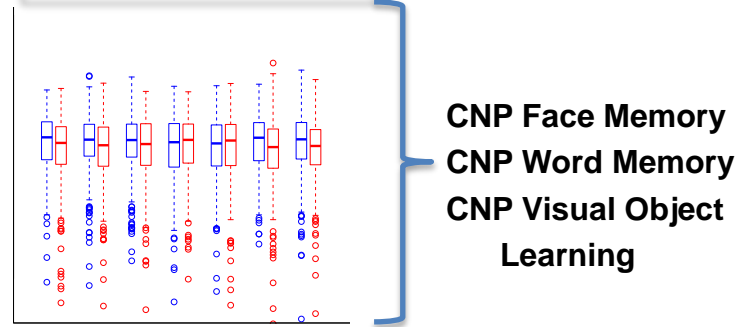
Emotion

Adjusted Z-score



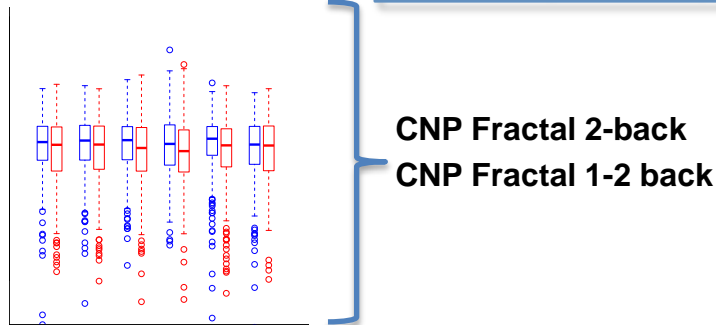
Episodic Memory

Adjusted Z-score



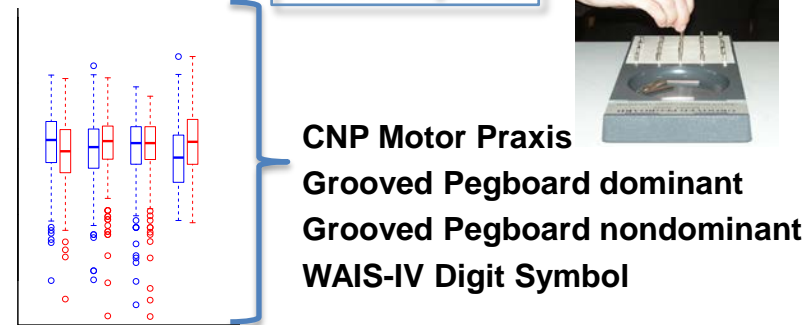
Working Memory

Adjusted Z-score



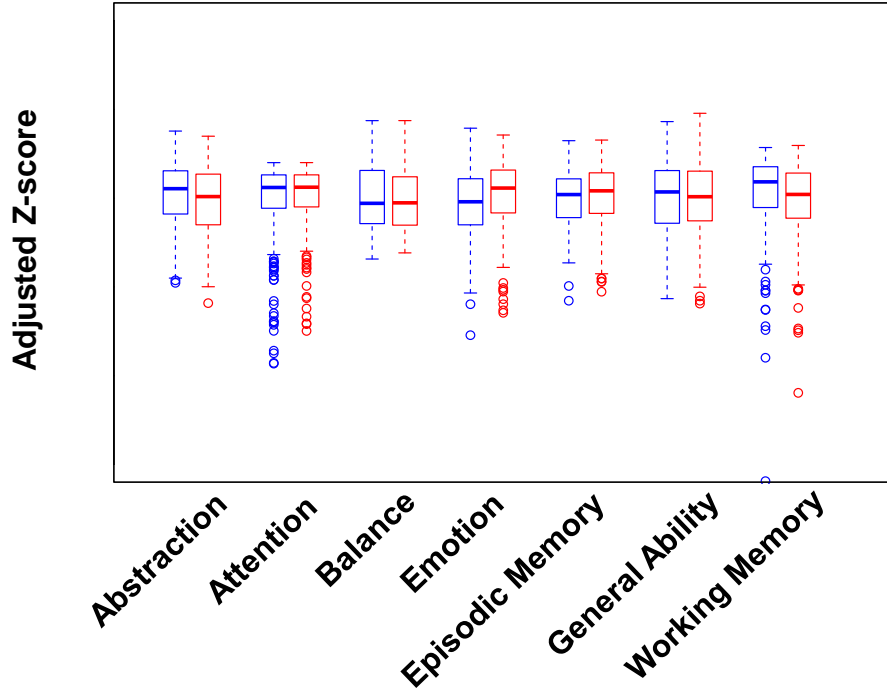
Motor Speed

Adjusted Z-score

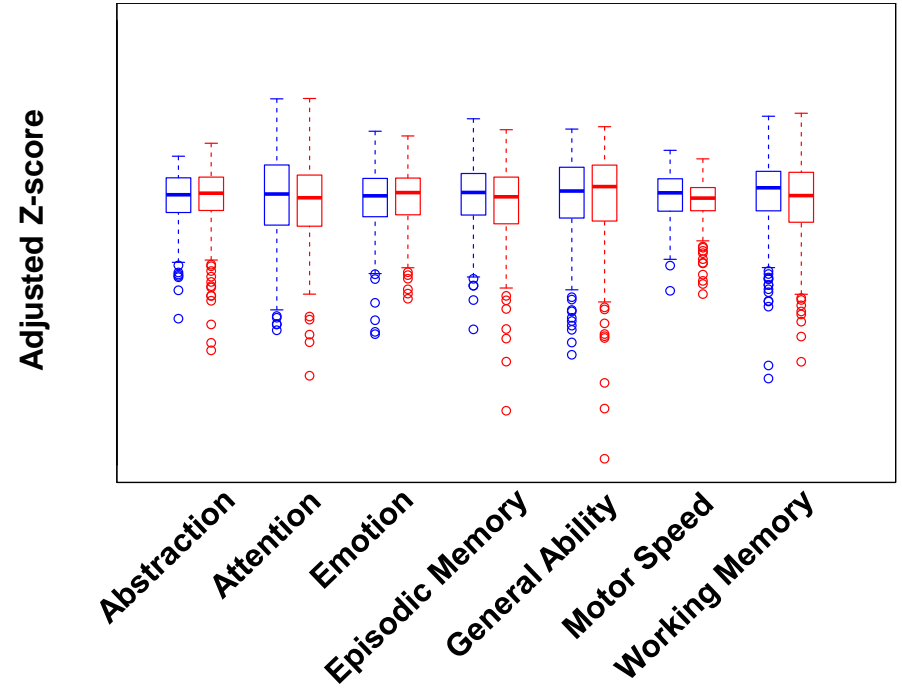


Individual and Total Composite Scores

Total Accuracy

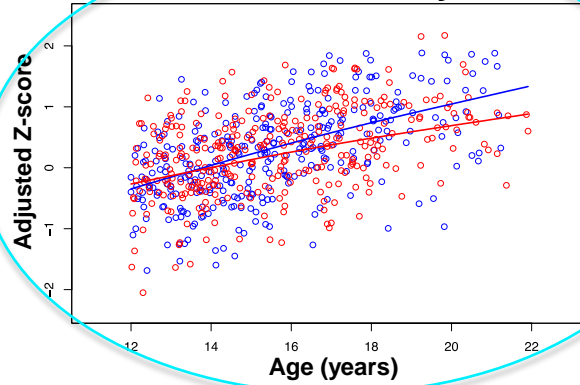


Total Speed

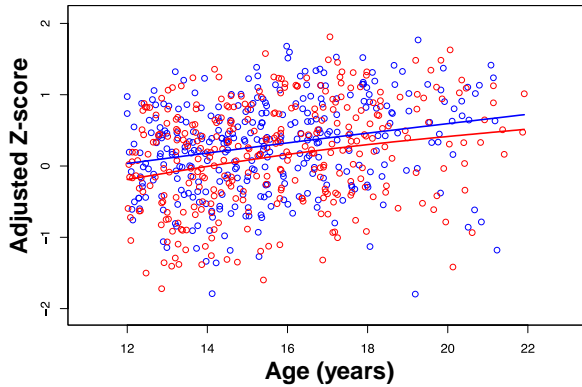


Accuracy Composites

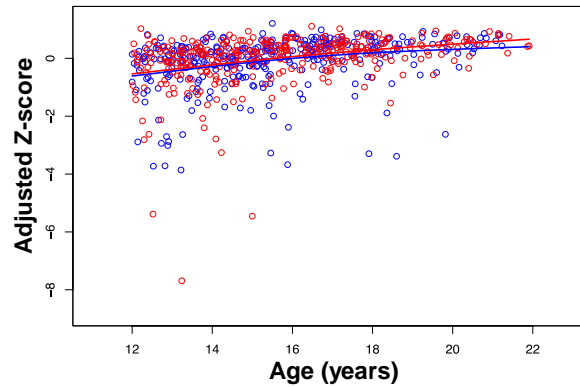
General Ability



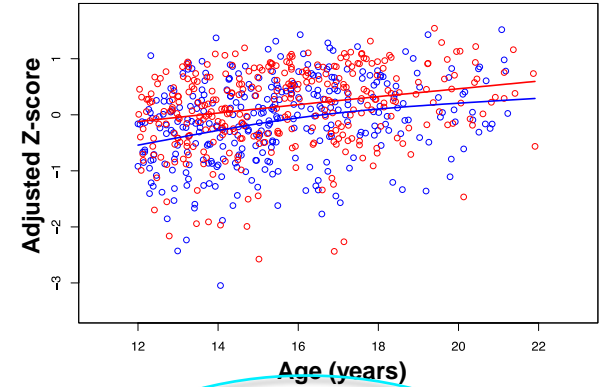
Abstraction



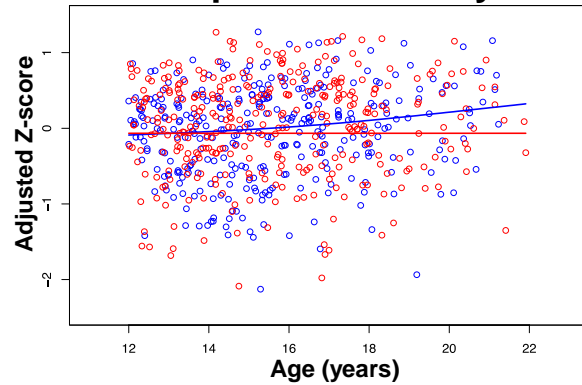
Attention



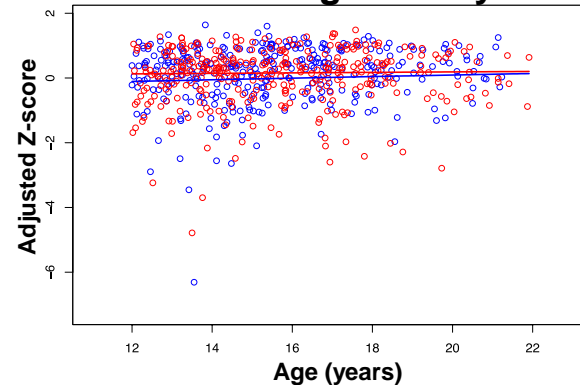
Emotion



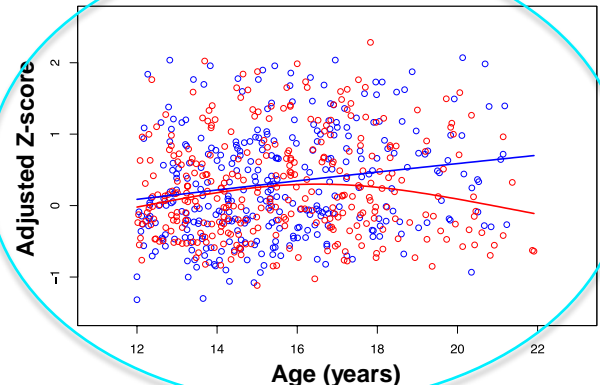
Episodic Memory



Working Memory

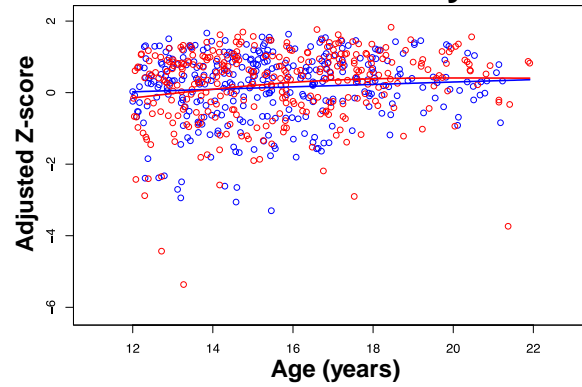


Balance

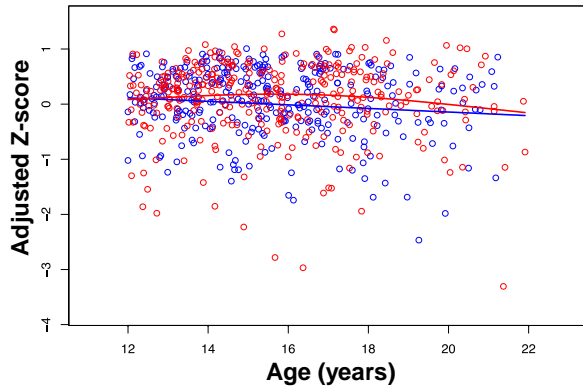


Speed Composites

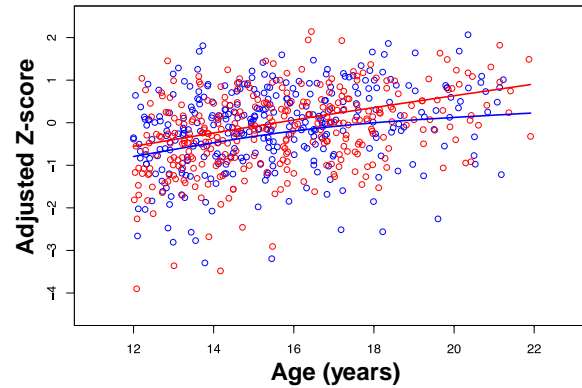
General Ability



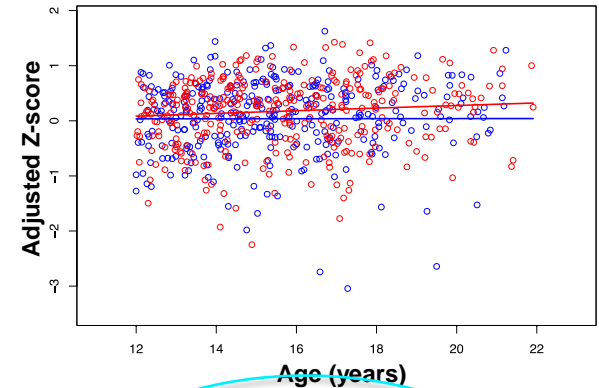
Abstraction



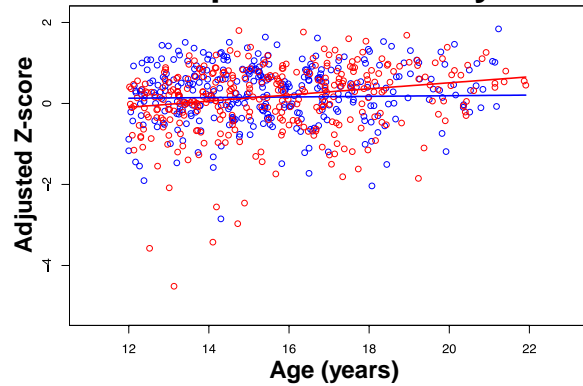
Attention



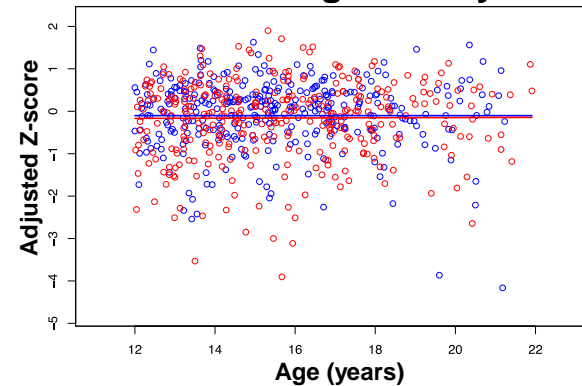
Emotion



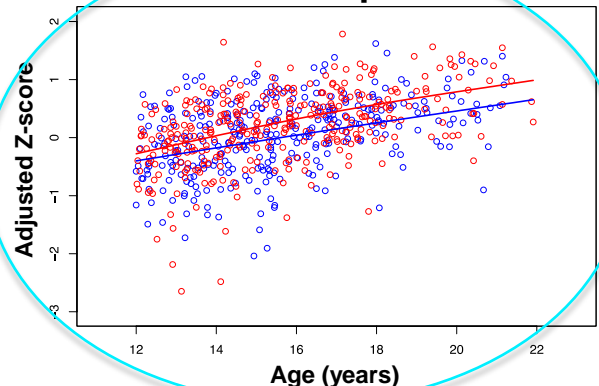
Episodic Memory



Working Memory

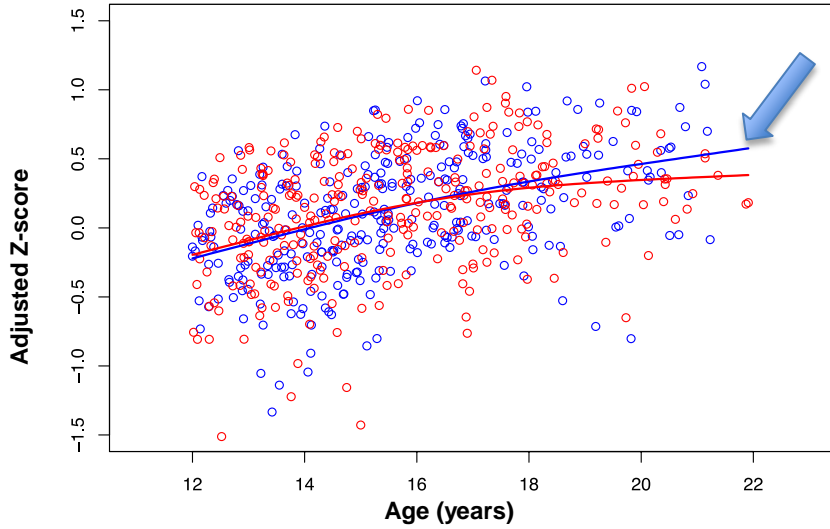


Motor Speed

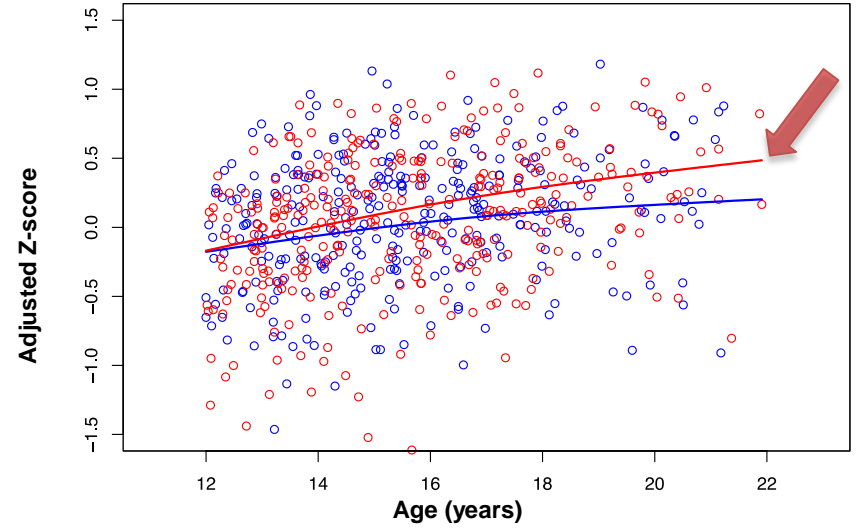


Total Composites

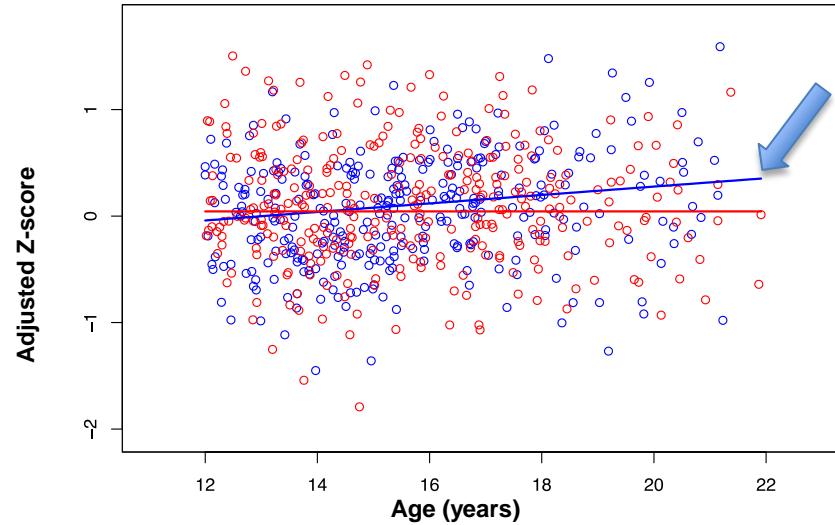
Accuracy



Speed

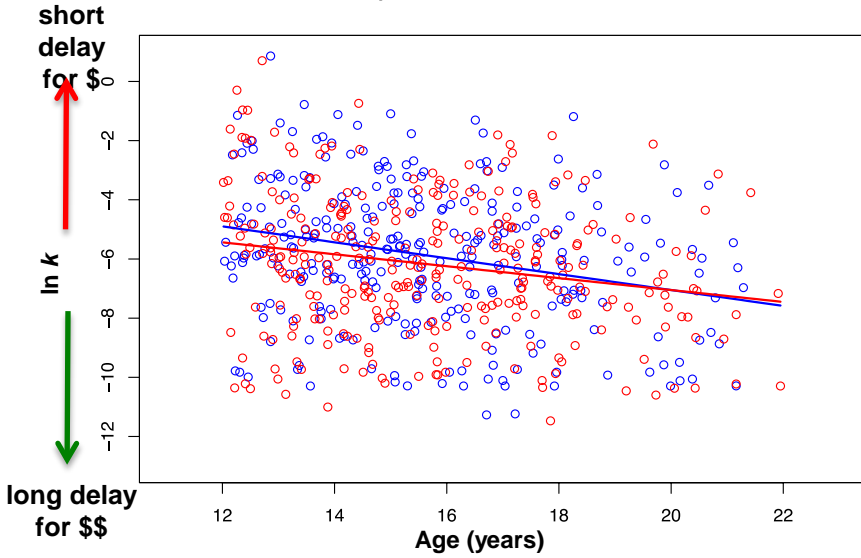


Accuracy - Speed

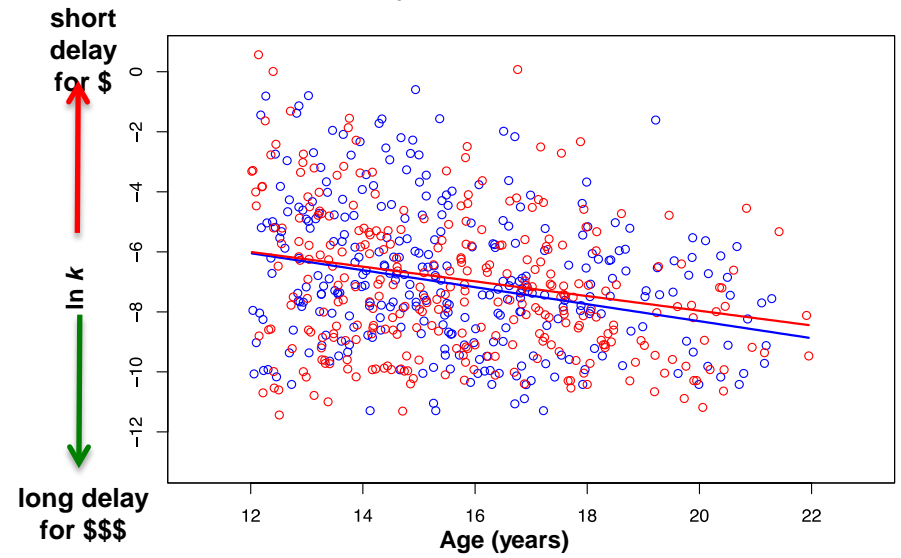


Delay Discounting Task

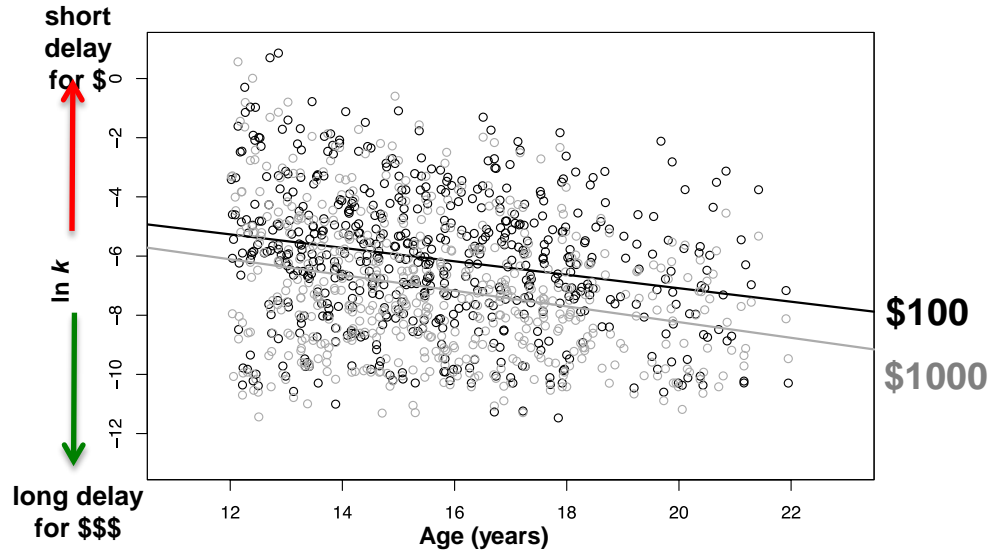
\$100 Condition



\$1000 Condition

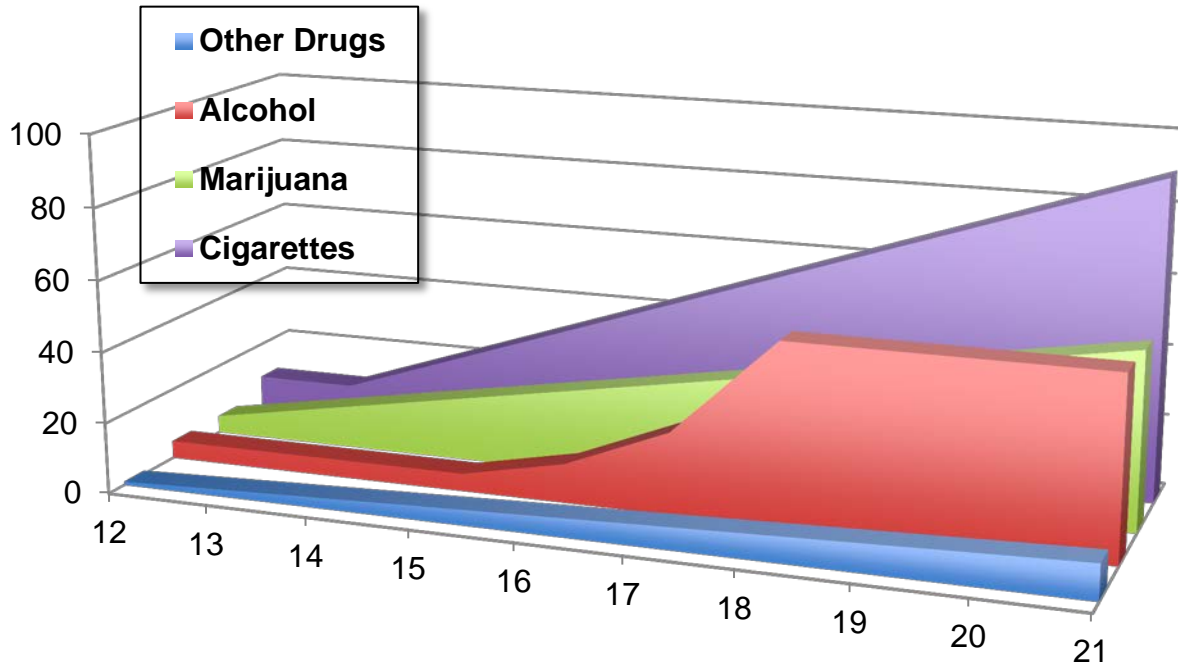


\$100 - \$1000 Difference

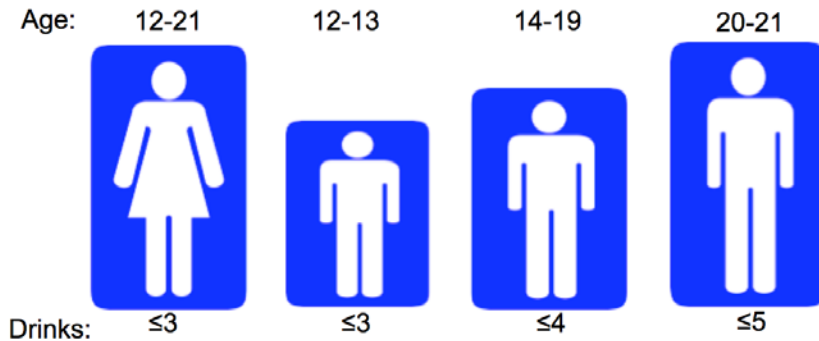


Alcohol and Drug Use Criteria

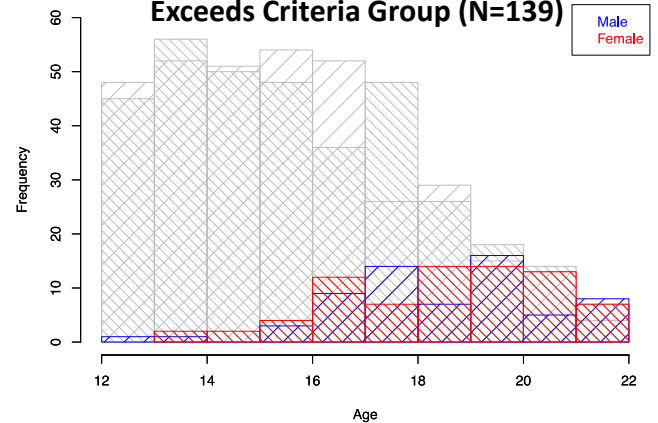
No/low vs. Exceeds



Max Drinks on One Day by Age and Sex

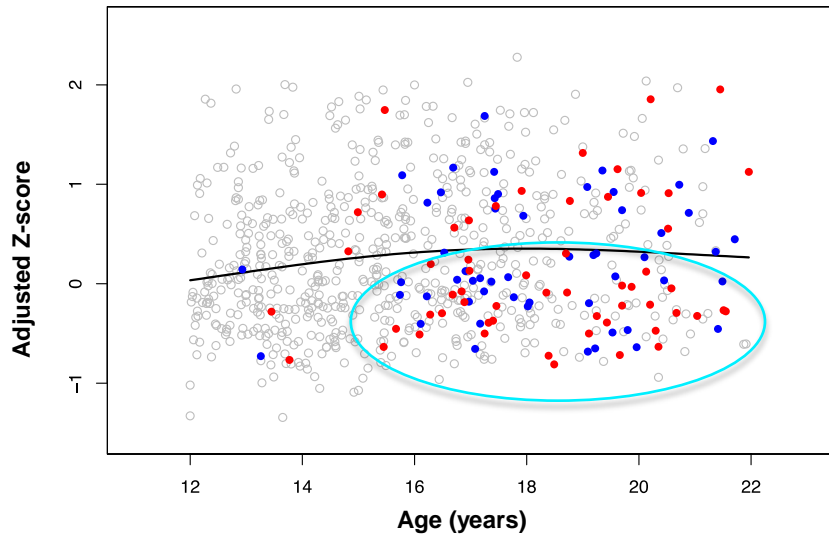


Exceeds Criteria Group (N=139)

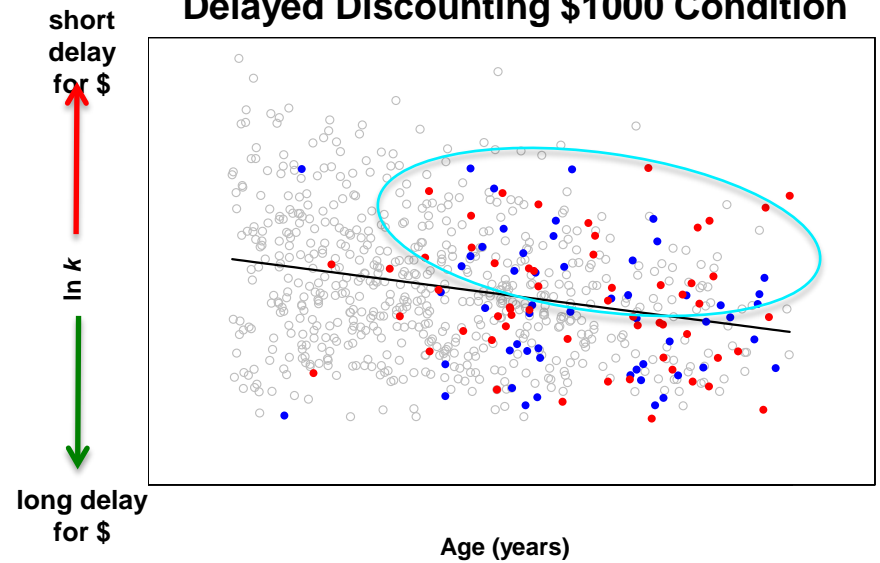


Accuracy: No/Low > Exceeds Drinkers

Balance Accuracy

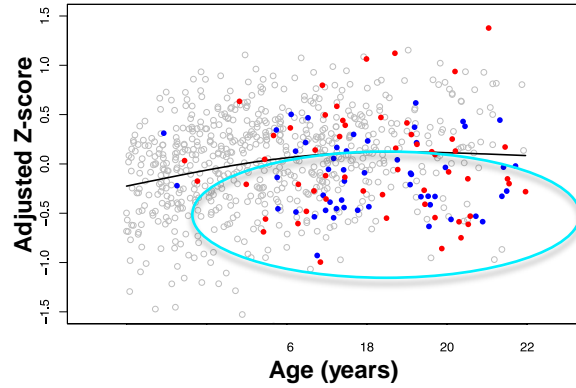


Delayed Discounting \$1000 Condition

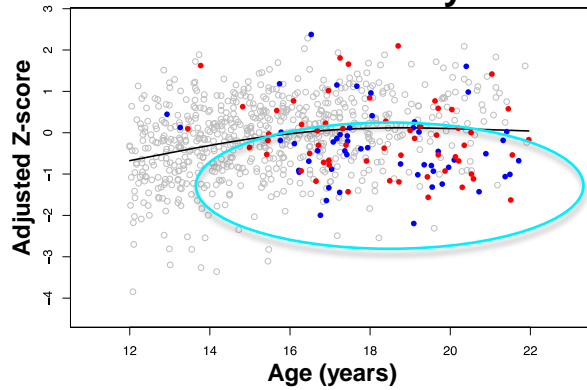


Speed Composites: No/Low > Exceeds Drinkers

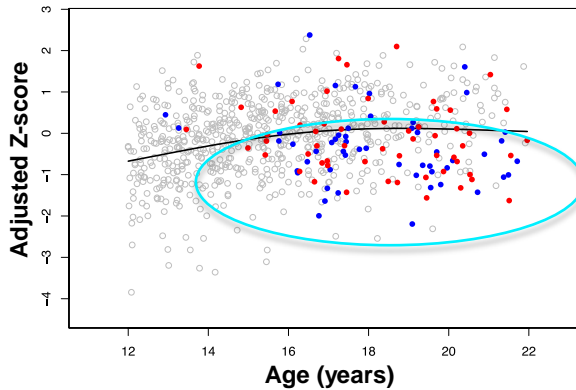
Total Speed



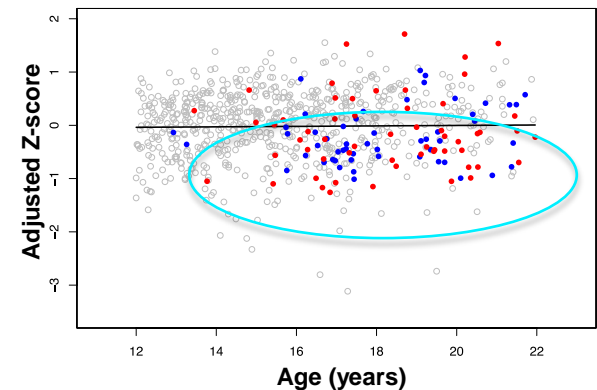
General Ability



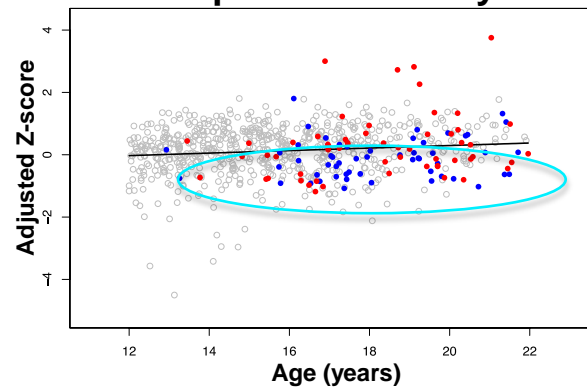
Attention



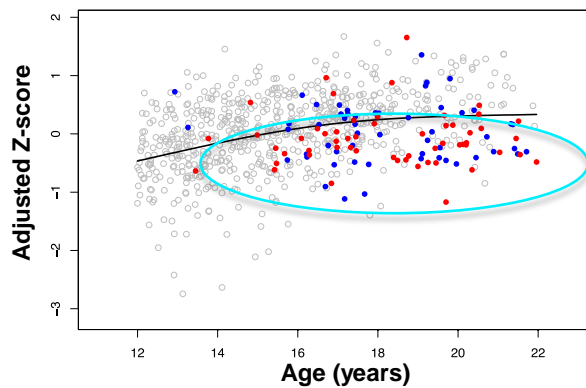
Emotion



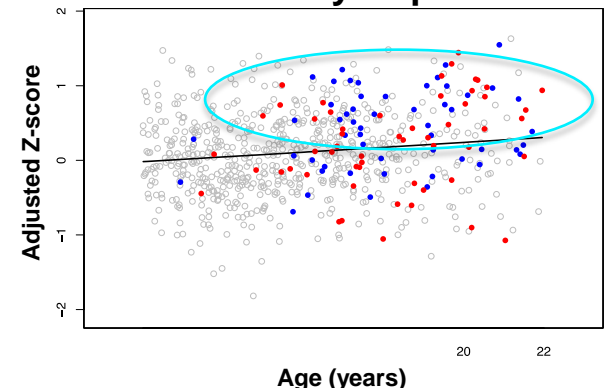
Episodic Memory



Motor



Accuracy - Speed



Neuropsychological Test Summary

- **No/low drinking group**

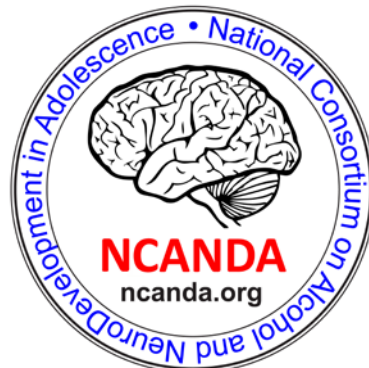
- Age differences were greater in Accuracy composite scores (General Ability, Abstraction, Attention, Emotion, and Balance) than Speed scores.
- Delay Discounting performance in younger boys and girls was consistent with poor impulse control

- **Exceeded-threshold group**

- After accounting for age, sex, and other demographic factors, the exceeded-threshold group performed significantly below the no/low-drinking group:
 - Balance and response time (General Ability, Attention, Episodic Memory, Emotion, and Motor)
- Speed-accuracy trade-off → Faster speed at the expense of accuracy
- Delay Discounting performance was consistent with poor impulse control in exceed group regardless of age
- Even where statistically significant, identified differences were modest.

Neuropsychological Test Summary

- Whether the performance differences between no/low-drinking adolescents and those who exceeded drinking thresholds are attributable to drinking or to other modulating factors requires the ongoing, **longitudinal study** of this NCANDA cohort.



Disclosures

Financial and Academic Interests



Fiona C. Baker, Ph.D.

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Center for Health Sciences, SRI International**

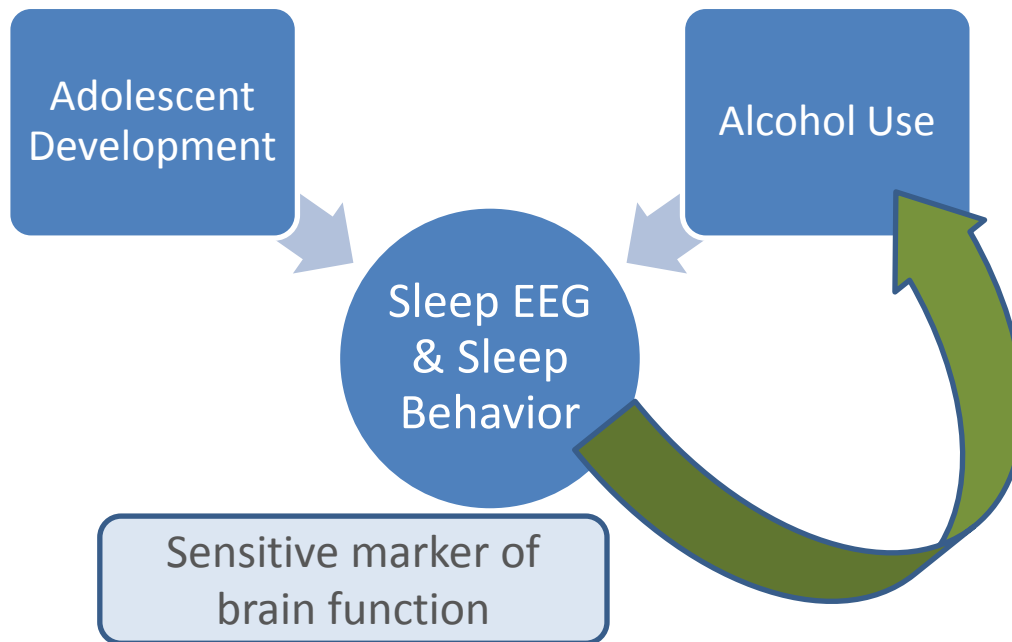
and

**Brain Function Research Group, University of the
Witwatersrand, South Africa**

Salary and research support: NIAAA, NHLBI

Why Consider Sleep?

1. Examine the developmental trajectory of functional sleep measures and how they are impacted by alcohol exposure.
2. Examine sleep behavior as a predictor of hazardous alcohol drinking in adolescents.



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.
- Shorter sleep duration predict alcohol-related problems.
- 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.

NCANDA Sleep Behavior Metrics



Sleep Quality

- Pittsburgh Sleep Quality Index (Buysse et al., 1989)
- During the past month, how would you rate your sleep quality overall? (Very good – Very bad)

Daytime sleepiness

- Cleveland Adolescent Sleepiness Questionnaire (Spilsbury et al., 2007)
- In the morning when I am in school, I fall asleep (Never – Always)

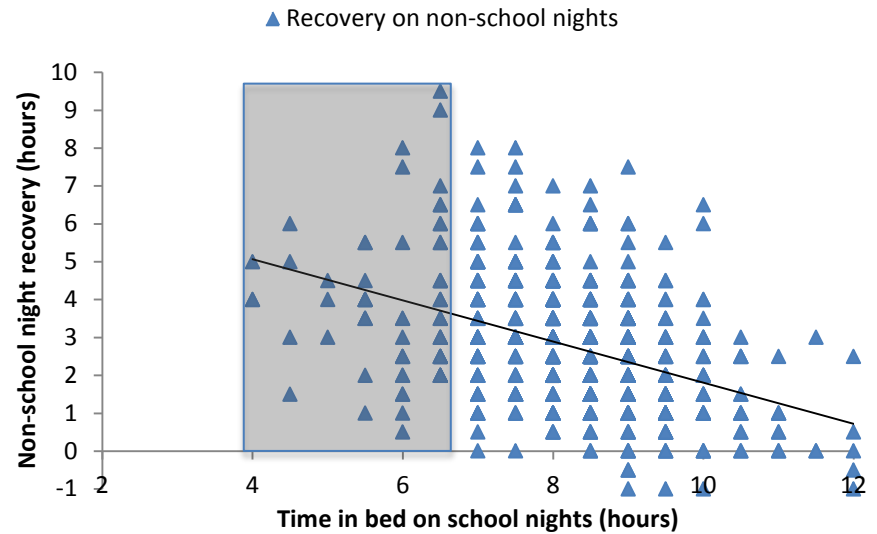
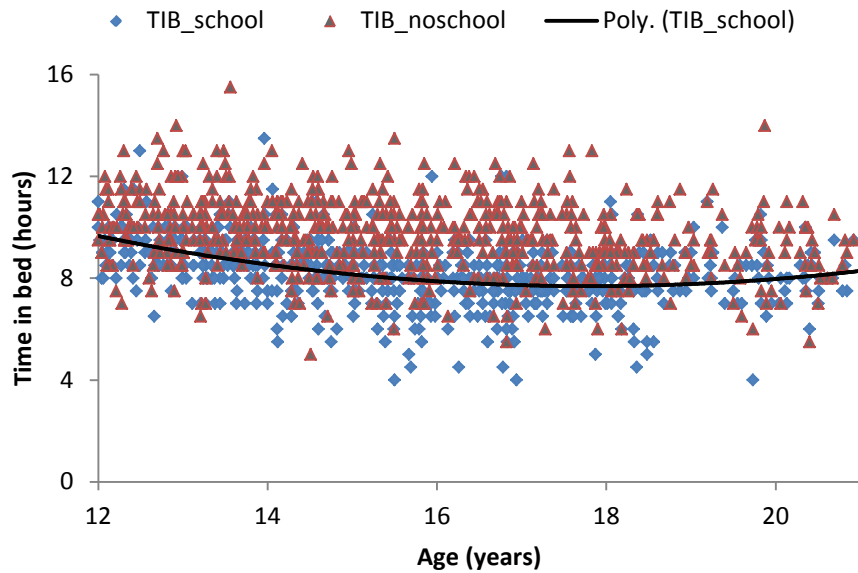
Chronotype

- Composite Scale of Morningness (Smith et al., 1989)
- One hears about “morning” and “evening” types of people. Which ONE of these types do you consider yourself to be? (Extreme evening – Extreme morning)

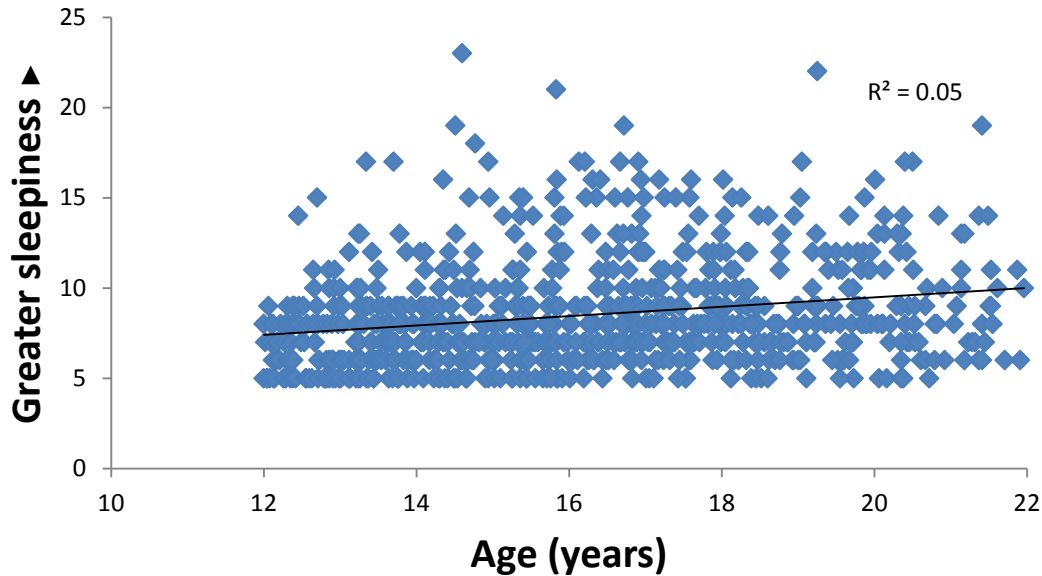
Sleep Behavior

- Bedtimes and Wakeup times
- Weekdays and weekends

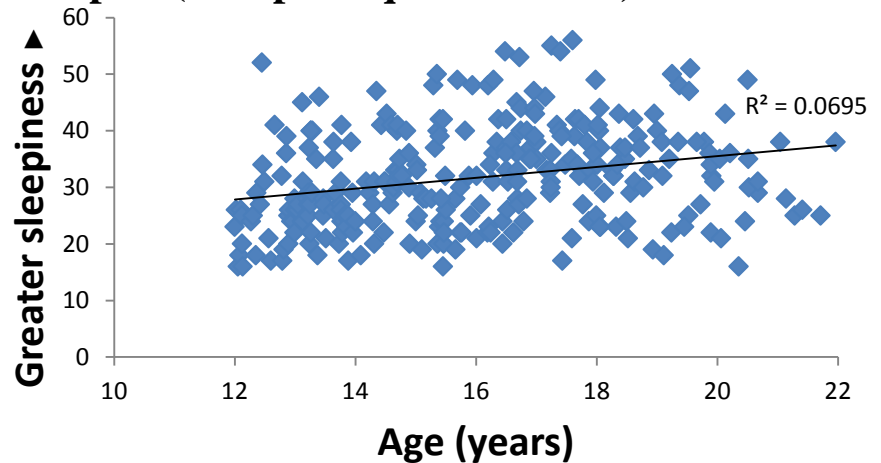
NCANDA Baseline Sleep Data: Time in Bed



Daytime Sleepiness



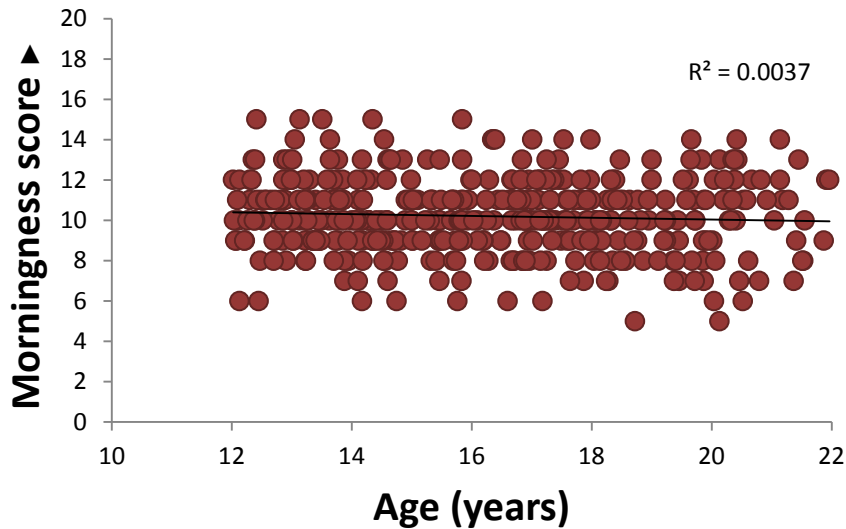
University of Pittsburgh and SRI International samples (Complete questionnaire)



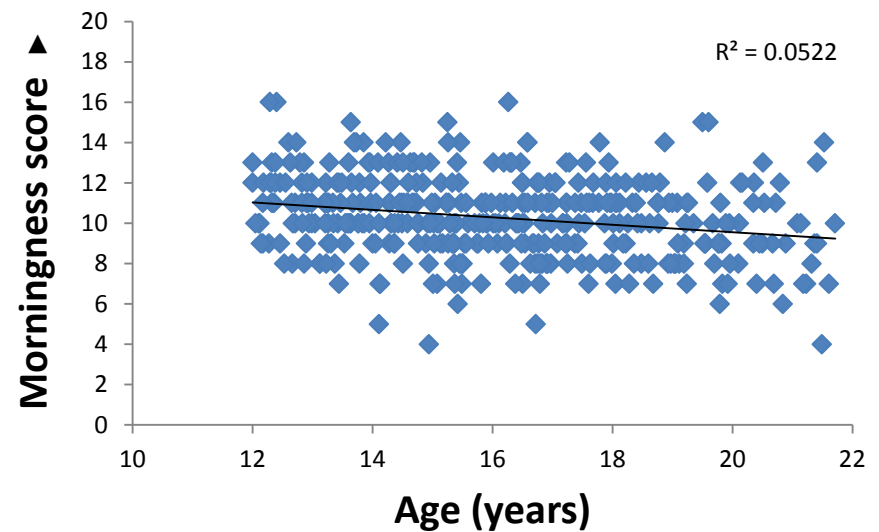
Chronotype



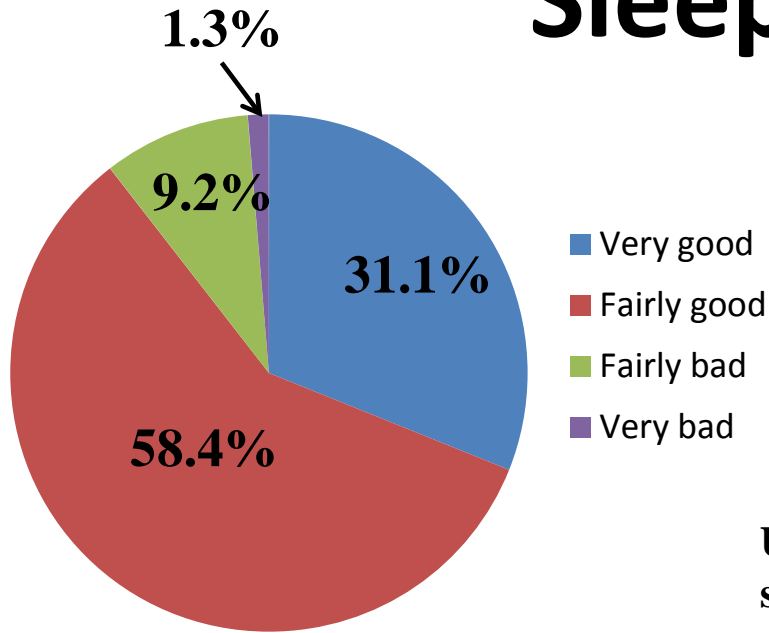
Morningness Eveningness: Girls



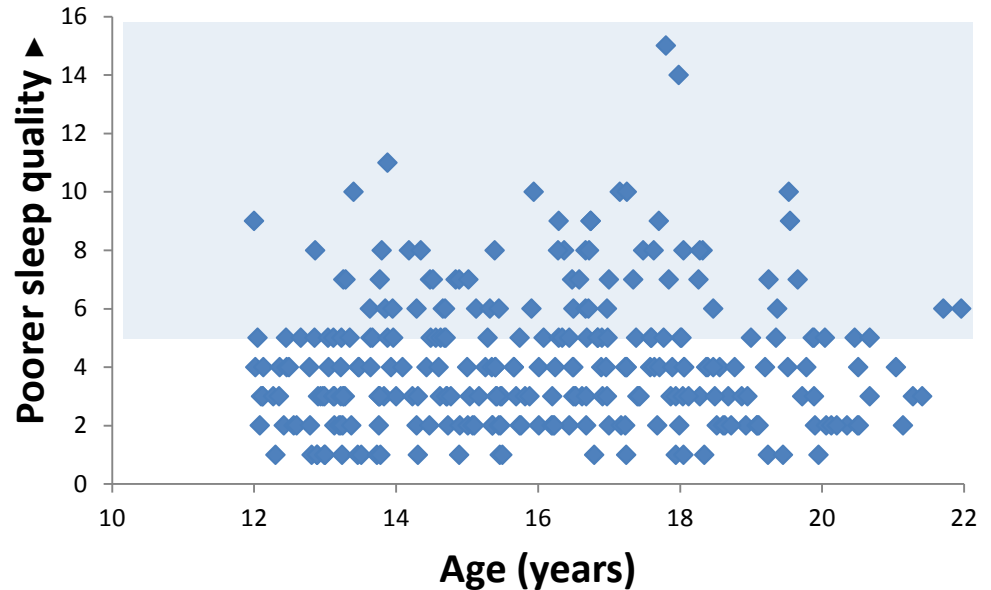
Morningness Eveningness: Boys



Sleep Quality

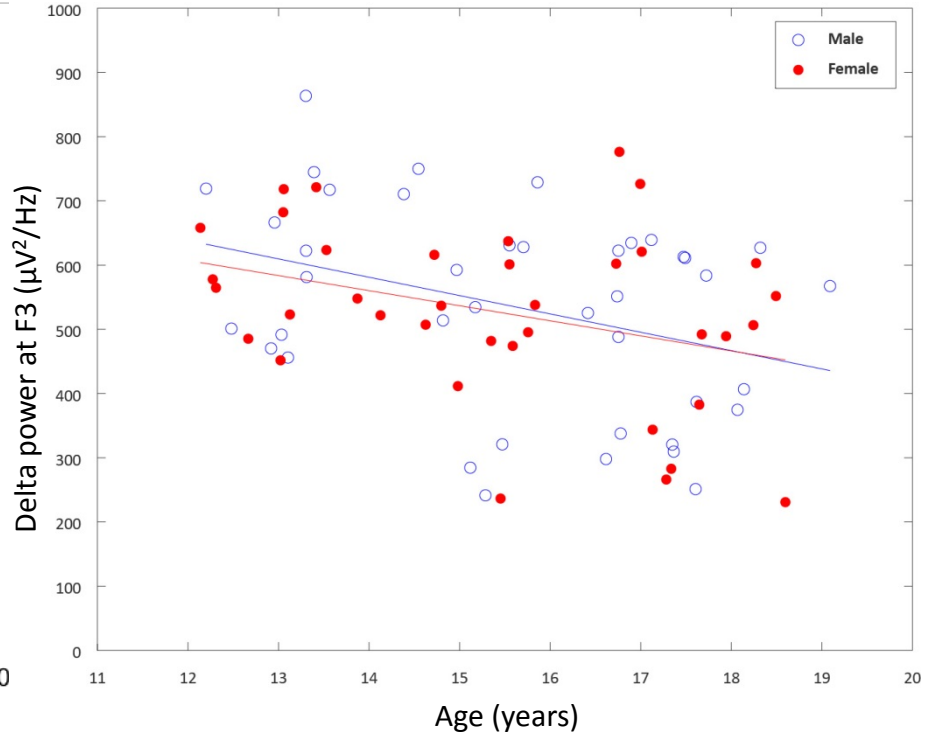
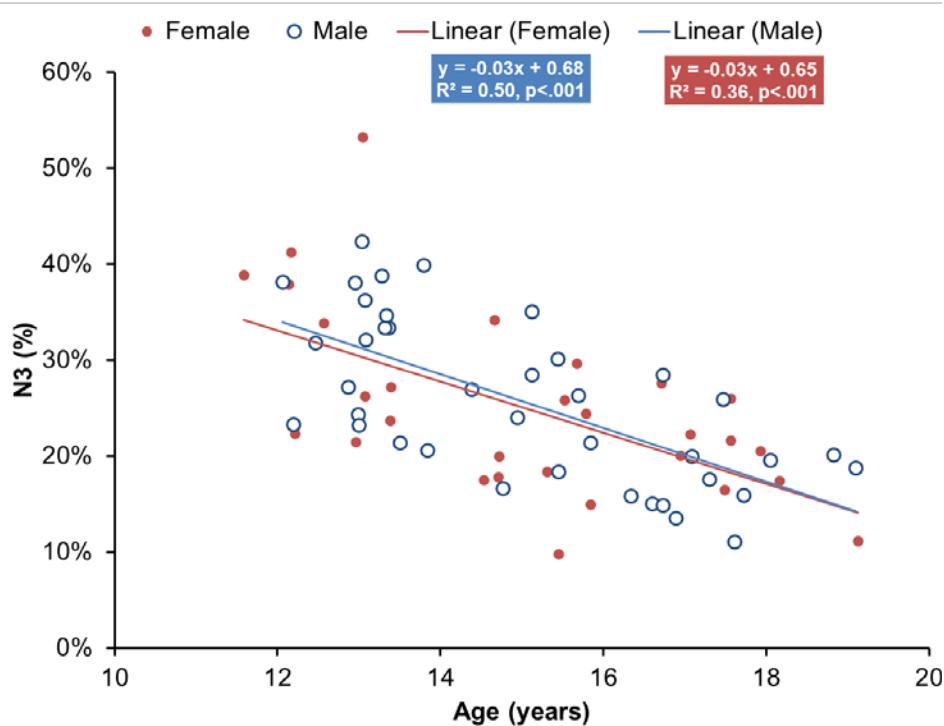


University of Pittsburgh and SRI International samples (Complete questionnaire)

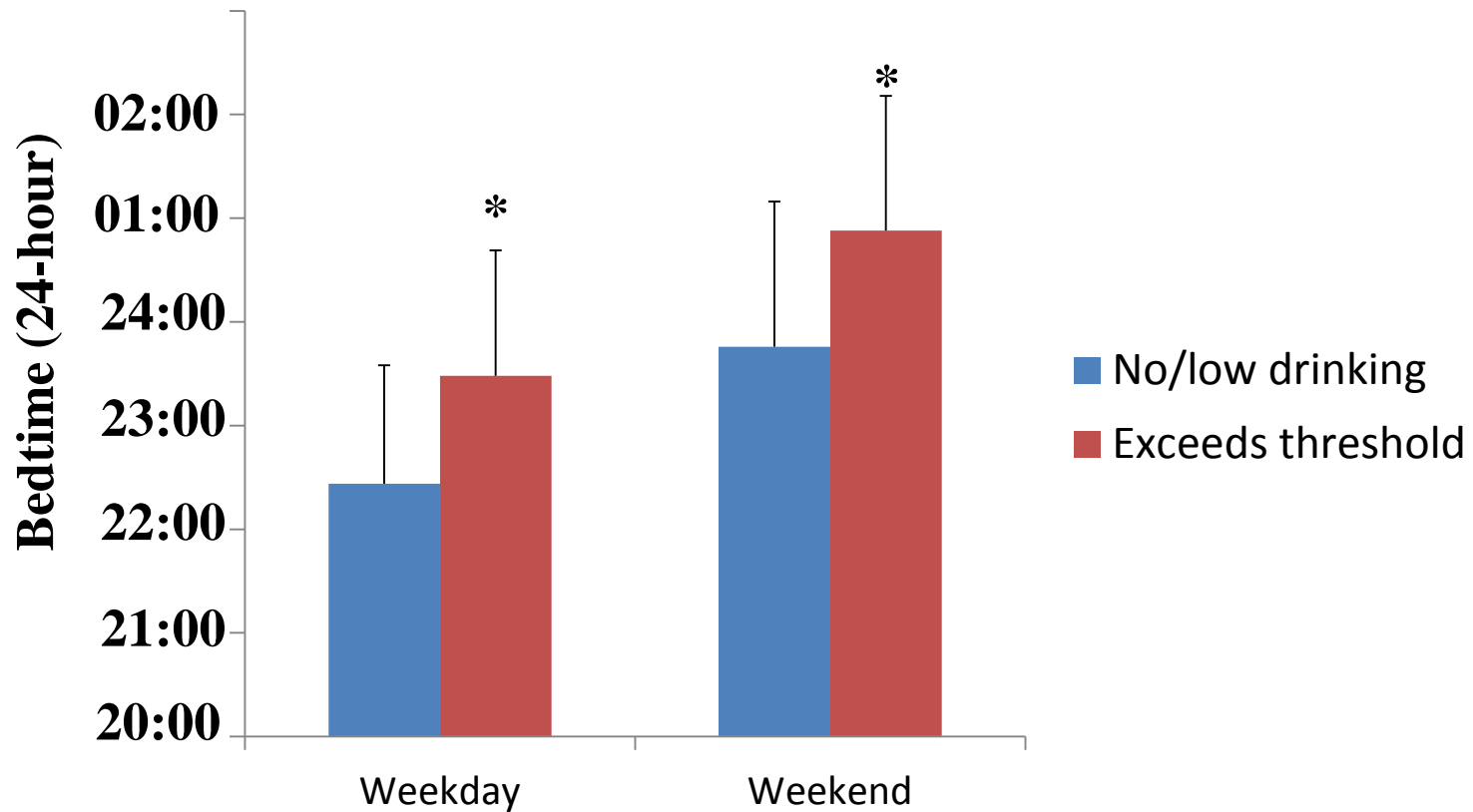


NCANDA Baseline Sleep EEG

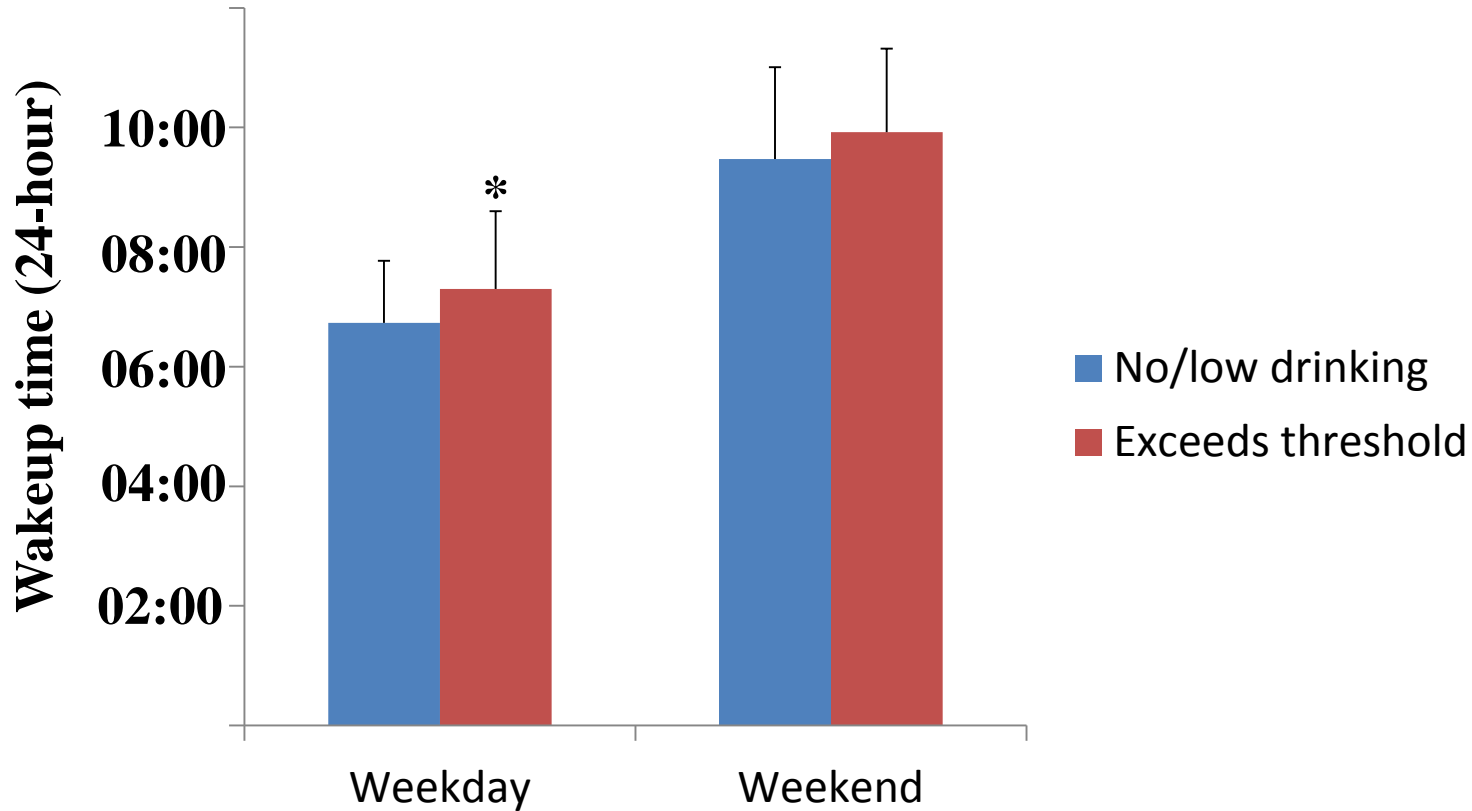
Age-related differences in slow wave sleep (N3) and frontal EEG delta power



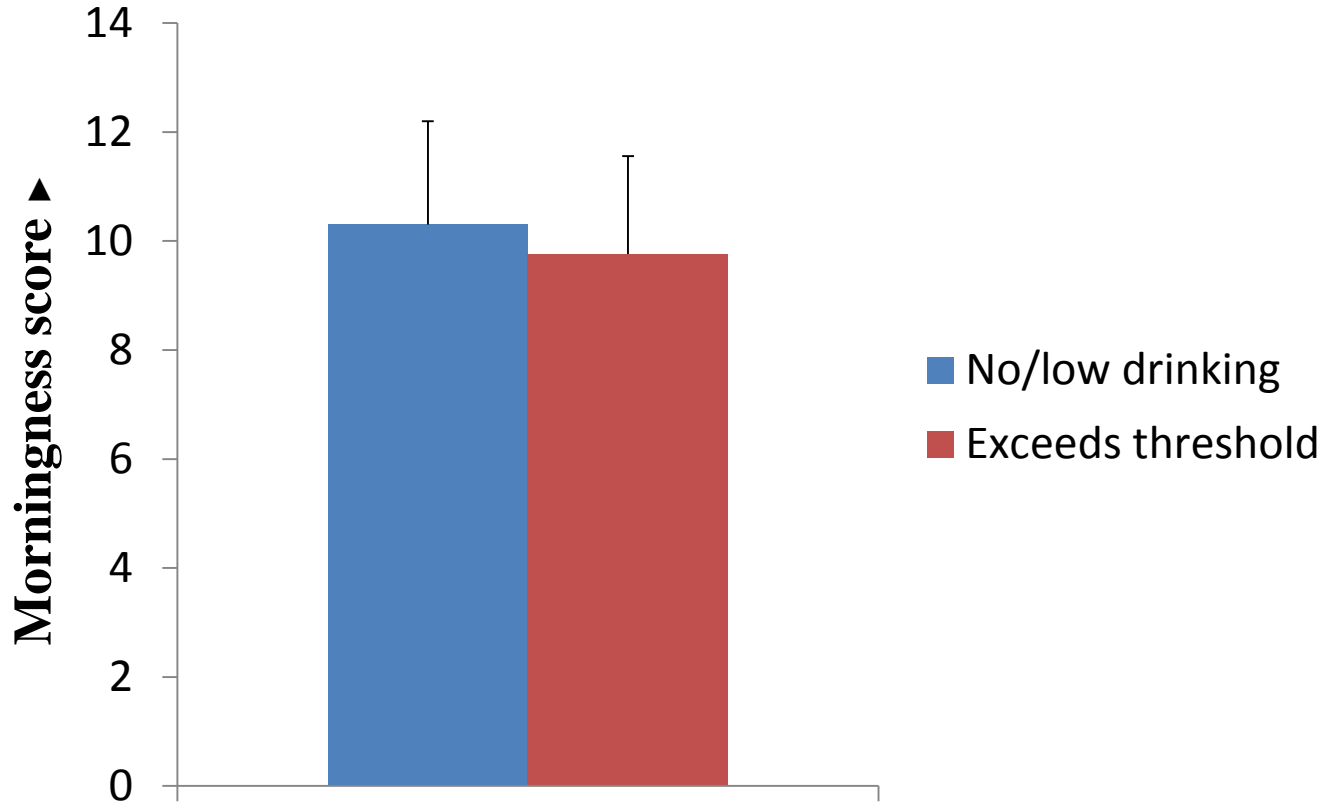
No/low Drinking vs Exceeded Threshold: Bedtime



No/low Drinking vs Exceeded Threshold: Wake-up time



No/low Drinking vs Exceeded Threshold: Chronotype



Summary of baseline sleep behavior



- Cross-sectional results confirm findings of others showing that older adolescents have shorter time in bed and later bedtimes.
- Older adolescents are more likely to be evening-types, particularly evident in boys.
- Adolescents show high weekday-weekend variability in time in bed.

Summary continued...



- Adolescents who exceed drinking thresholds have later bedtimes on both weekdays and weekends, and later wake-up times on weekdays than others.
- Adolescents who exceed drinking thresholds tend to have greater eveningness tendency and a poorer sleep quality.

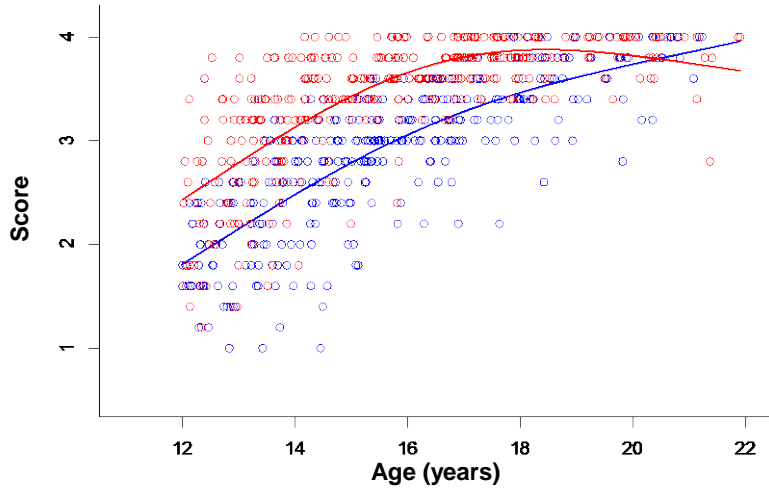
With a longitudinal design, NCANDA will be able to evaluate the impact of sleep behavior on subsequent alcohol use in adolescents and how the transition to alcohol use impacts sleep behavior.

NCANDA will also longitudinally explore associations between neuropsychological performance, sleep behavior, and alcohol use in maturing adolescents.

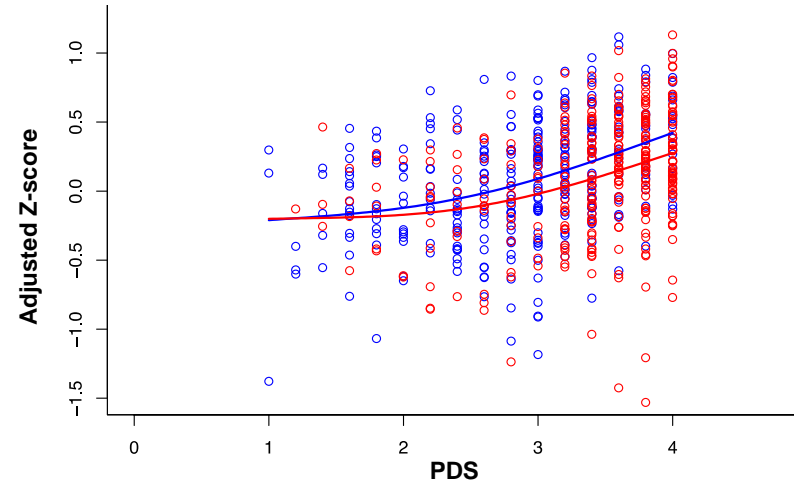


Composites with Greatest PDS Sex Effects

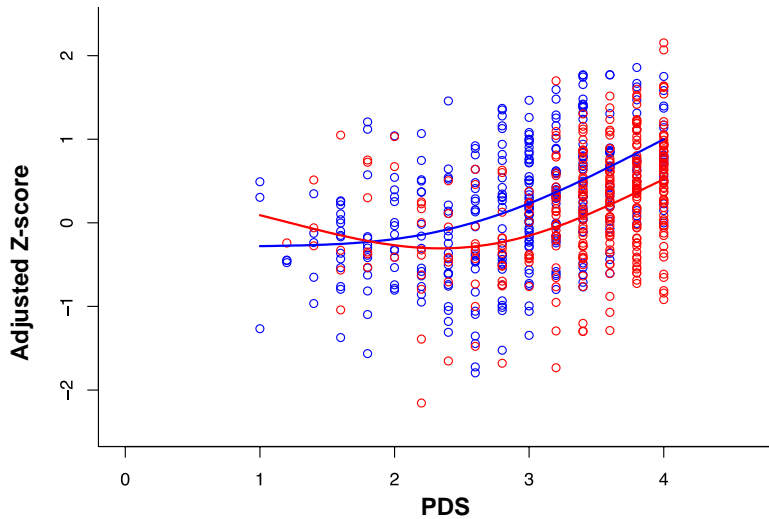
Pubertal Development Scale (PDS)



Total Accuracy



General Ability Accuracy



Abstraction Accuracy

