

NCANDA: Baseline Findings Discussion

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Sandra Brown

Discussion Intro

- **Thank PIs** for excellent presentations providing a strong introduction to baseline findings and **NIAAA** for opportunity to conduct this important study
- I will first briefly **summarize the findings** reported today with **comments on the individual components** and then make **broader comments on the success and needs** in efforts moving forward for this and developmental neuroimaging focused adolescent alcohol research

Sample- Tapert presentation comments

- Reviewed the design, methods and Sample of NCANDA
- **Fully successful ascertainment-** full targeted sample of 830, which despite careful screening, is sufficiently heterogeneous to investigate individual differences of interest-equal gender rep, representative of each site and collectively of racial/ethnic composition of US, Half 1 or more critical risk characteristics
- **Comprehensive clinical battery-** developmentally tailored, primarily automated (90%), categorical (DSM IV & V dx) and dimensional measures-sensitive to changes in use and functioning as well as environment
- **Rigorous methods-** training, monitoring, ongoing supervision assure fidelity and reliability across sites and over time
- Baseline findings **consistent with extant literature and risk & age related predictions** of NCANDA
- **Early evidence of high follow-up (>95%)** which is core value of this program of study

Sample- Tapert -Issues in Future

- **Follow- up most critical** and preliminary info is promising
- **Need for flexibility to adapt to cultural and use changes** (eg already including E-cigarettes, detailed MJ, designer drugs) and NP measures to target newly identified functions as study progresses
- **Behavioral assessments need to have sensitivity** comparable to neuroimaging and neurocognitive assessments for maximal value to research community
- Will come back to this last point with recommendations.

Neuropsych/Sleep- Sullivan

- Described **comprehensive battery- 8 domains and speed & accuracy** measures for each. Demonstrated sufficient sensitivity to identify age, gender, puberty and use related differences.
- Some measures particularly target a priori risk/phenotype (behavioral undercontrol)– **delayed discounting**- most useful as we investigate trajectory of regional and microstructure (neural network) developmental differences in subpopulations.
- Noteworthy- emerging distinctions in relations to **age versus puberty (accuracy versus speed)**
- Long term asset in **distinguishing precursors from consequences** of use among **high risk subtypes** and mapping onto neurologically based phenotypes

Neuropsych/Sleep- Baker

- Given important **links between neurocognition and sleep**, and sleep and development more generally, the detailed sleep data is important. 2 sites- SRI and Pitt- also have detailed physiological measures from overnight study
- Baseline findings **confirm expected age patterns**- shorter sleep duration, shift in sleep wake cycle, and social “Jet Lag” phenomenon as well as **gender chronotype** differences and use related differences.
- PARTICULARLY encourage this group to use **new technologies** to provide day time, natural environment measurement via cell phones and wearable health devces- measure activity, sleep time and duration, physiological measures such as Heart rate and heart rate variability- among others.

Neuroimaging-Phefferbaum

- **Rigorous methods: Neuroinformatics pipeline** (really Torsten and Killian), use of multiple **cross site phantoms**, detailed neuroradiological **reviews of clinical value** (11% anomalies, 3% clinically significant);
- **Multiple scanners-** demonstrated data harmonization with sufficient sensitivity for structural analyses
- Initial findings—**age related differences** in cortical vol and thickness, independently **confirmed with the national PING data set** (national study led by Terry Jernigan) serves as critical foundation going forward
- **Use related differences-** regional vol and thickness (frontal, temporal, and cingulate)-non users versus users; **Distinctive frontal and parietal cortex differences with nonusers and BINGE drinkers**
- Age findings are strong foundation for longitudinal evals underway

Microstructure- Pohl

- Important approach to **diffusion weighted imaging within white matter**; Tract Based Spatial Statistics-**articulated developmental differences across this heterogeneous sample in regions of Interest** and of potential importance to the emergence of addictive behavior
- **Maturity of fiber organization** of commissural and projection systems- earlier than limbic system- could this be foundation for **neuroanatomical phenotype ???**
- This approach (neuroimaging based/behaviorally confirmed) is opportunity to **fundamentally transform the understanding of addictive behavior and interventions**- way to produce “precision medicine” for addictive disorders.
- Need for **detailed linkage with the neurocognitive and behavioral and affective measures** of the study

General Recommendations/Insights (1)

- NCANDA generated a **nationally representative sample of adequate heterogeneity** to serve as strong foundation for the longitudinal evaluations, model comparisons, and of value to other scientists in the future.
- **Model for large scale integration of sciences- Automated assessment battery, sophisticated neuroinformatics pipeline---model for “Big Data” approach in the addictions—data base serve as national resource.**
- **Rigor in methods** is exquisitely valuable as is the specification of the **algorithms for metrics** for all components (neuroimaging, neurocognitive, clinical and environmental) –
- Sets a high standard with standardized, developmentally tailored core plus **flexibility of rapid hypothesis testing with built in replication.**

General Recommendations/Insights (2)

- **Imaging methods- demonstrated harmonization across sites and across scanner types- NCANDA is model for methods and analytics to produce confidence in accuracy and sensitivity of measurement which is most valuable to multisite projects of the future and adds value to the scientific community to be able to do this- can include more scientists in studies going forward.**
- **Findings under scientific evaluation- 5 papers published or under review.**
- **Utilize a model of continuous improvement-components not yet analyzed- stress/trauma, genetic, hormones; Build in new technologies for measurement in the natural environment (activity, sleep, affect, physiological measures, use of alcohol and other drugs)**
- **Close collaboration with animal studies to test findings and intervention studies to test mechanisms and models of change.**