



# Organization and dissemination of evidence based research in neurodevelopmental disorders

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# Overview

- The UCI Child Development Center
  - School and Clinic
  - Training and Dissemination
- Information gathered at CDC
- Factors of neurodevelopmental disorders
- Effects of maternal smoking during pregnancy
- Brain hemodynamics during cigarette smoking, a Near Infrared Spectroscopy study
- Studying the beneficial effects of exercise in the context of the Laboratory-School Protocol



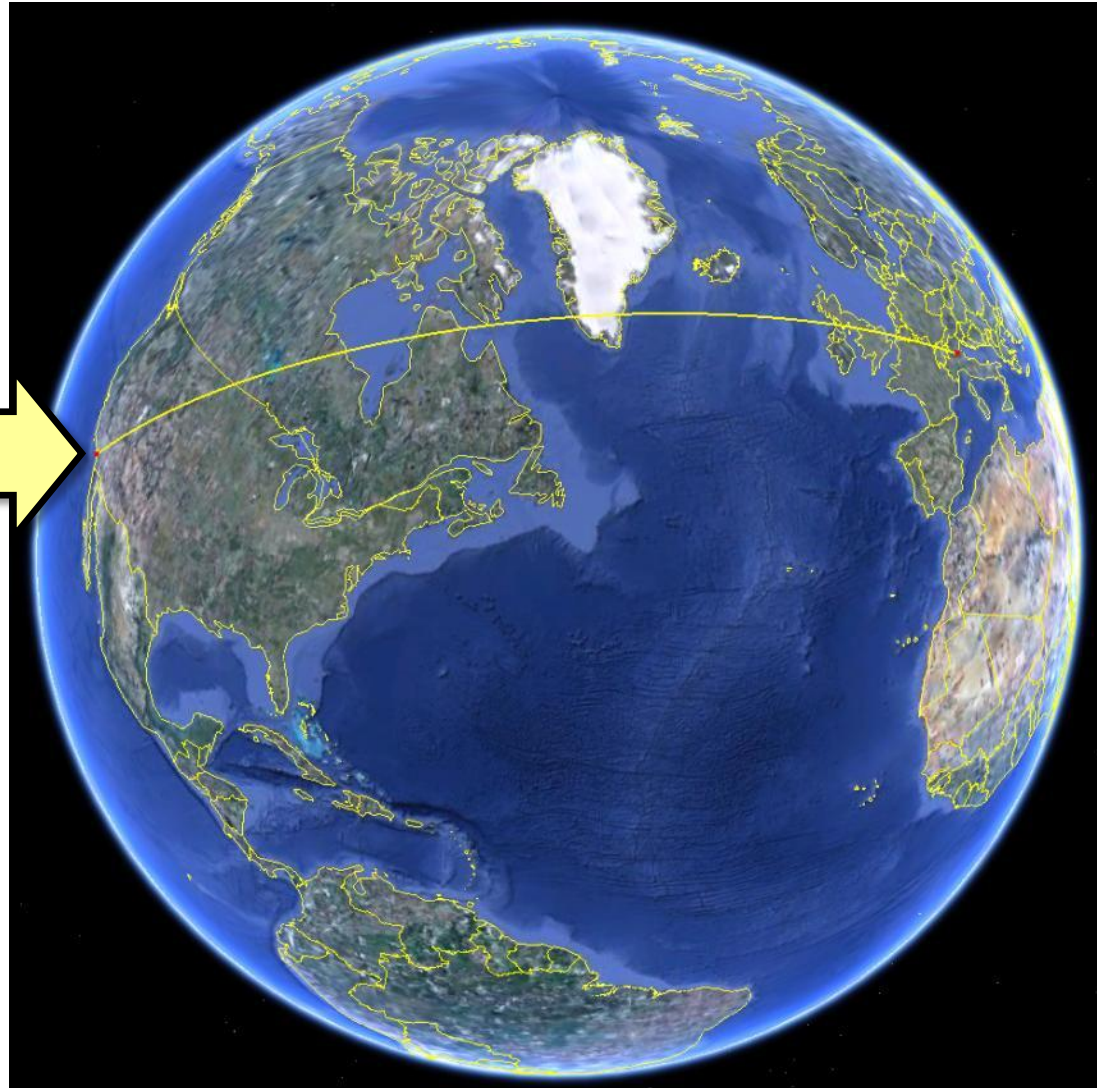
# UCI Child Development Center (CDC)

Irvine  
California  
USA



50 km south  
of Los Angeles

9840 km west  
of Verona





# CDC School and Clinic

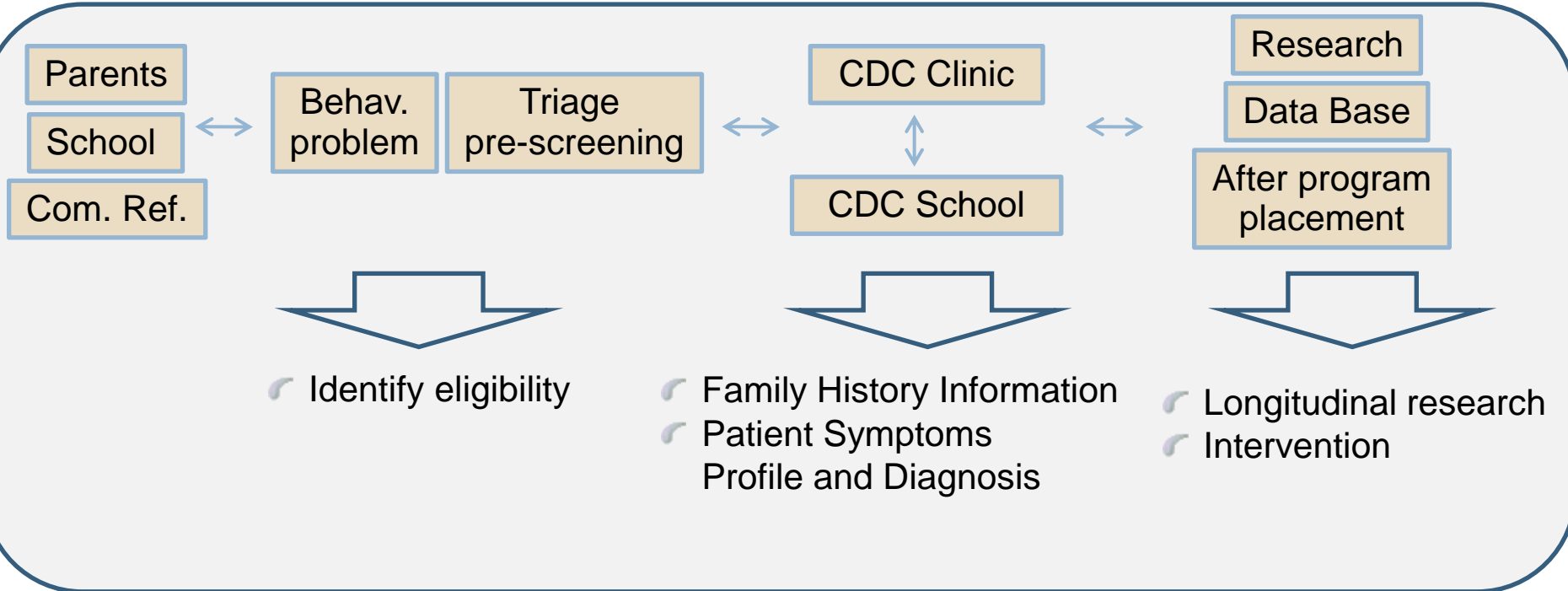


## Mission

- **improve child mental health** by expanding scientific knowledge of child and adolescent psychiatric disorders
- deliver **evidence-based clinical care**
- **translate and disseminate** new scientifically sound information to mental health professionals, pediatricians, educators, parents, and policy makers around the world



# The Child Development Center



- ☛ Training and Dissemination
- ☛ Encourage creating and testing of hypothesis



# Training and Dissemination

- Training
  - Undergraduate students
  - Graduate students
  - Visiting scientists
- Publications
  - Articles, book chapters, proceedings, and abstracts
- Website
  - <http://www.cdc.uci.edu>
- Events organized by CDC
  - Classes:  
Psychology 145 and 199
  - Continuing education symposium
- Events with CDC participation
  - American Academy of Child and Adolescent Psychiatry (AACAP)
  - Undergraduate research opportunities (UROP)
  - Excellence in Research





# Website

# <http://www.cdc.uci.edu>

- Neuropsychological and/or psychoeducational evaluations
- Cognitive behavioral interventions
- Educational therapy
- Research studies
- Professional assessment of neurodevelopmental and behavioral problems
- Professional counseling services
- Adolescent social skills coaching services
- School program





# Evidence-Based Practice in Psychology

## Definition

- EBPP is the **integration of the best available research with clinical expertise in the context of patient characteristics, culture, and preferences.** Institute of Medicine (2001, p. 147).

## Purpose

- **to promote effective psychological practice and enhance public health by applying empirically supported principles of psychological assessment, case, formulation, therapeutic relationship, and intervention.**—Adopted by APA Council of Representatives, August 17, 2005

## Relevance

- The prevalence of children's behavioral disorders reaches 10-20% of youth in the United States (about 15 million children). (National Advisory Mental Health Council Workgroup on Child and Adolescent Mental Health Intervention Development and Deployment, 2001; President's New Freedom Commission on Mental Health, 2003; U.S. Public Health Service, 2000)





# Information gathered at the CDC

## Family History Questionnaire

Academic history ▪ childhood medical history ▪ family history ▪ medication history ▪ neurodevelopmental disorders ▪ pregnancy and neonatal history

## Neuropsychological Evaluation

Beck Youth Inventory ▪ Bender Gestalt Test ▪ Continuous Performance Test ▪ Conners ▪ Crinella Neuromotor AB ▪ Crinella Sleep Scale ▪ CTMT ▪ EVT2 ▪ FIQ ▪ K-BIT ▪ K-SNAP ▪ MASC ▪ Nelson-Denny Reading Test ▪ POMS ▪ PPVT-IV ▪ QUEST ▪ **Raven Progressive Matrices** ▪ RBC ▪ RT ▪ SNAP-IV ▪ SPQ ▪ SWAN ▪ Tower of London ▪ TOWRE ▪ TVPS-III ▪ VINELAND-II ▪ WAIS-III ▪ WASI ▪ WCST CV ▪ WIAT-II ▪ WIAT-III ▪ WISC-IV ▪ WJ-III ▪ WMS-III ▪ WPPSI-III ▪ WRAML2 ▪ Youth S R 11-18

## Target Behaviors

Presence of : Compliance skills ▪ Relationship skills ▪ Productivity skills Evaluation: CGI-I ▪ CGI-S ▪ CDI-Parent ▪ PGA



# Methods of identifying neurodevelopmental disorders

- Psychiatric interview and biosocial history of the patient
- Apply standardized rating techniques:
  - Checklist to meet minimum criteria (e.g. DSM-IV)
  - Rating scales cut-off scores
- Psychological testing
  - Psychometric standards
  - Neuropsychological testing
- Brain Imaging
- Heritability (Genetics)



# Diagnosis of neurodevelopmental disorders

- Psychiatric interview for neuropsychiatric disorders
- Biosocial history is ~95% of diagnosis (Adolf Meyer)
- Getting adequate history is an extraordinary complex process
- Focus on history includes current problems
- Diagnoses of psychiatric disorders are controversial because:
  - they are based on clinical assessment of behavioral symptoms
  - there are no laboratory test that can determine the presence of a disorder
  - there are time sensitive symptoms and behaviors



# Factors of neurodevelopmental disorders

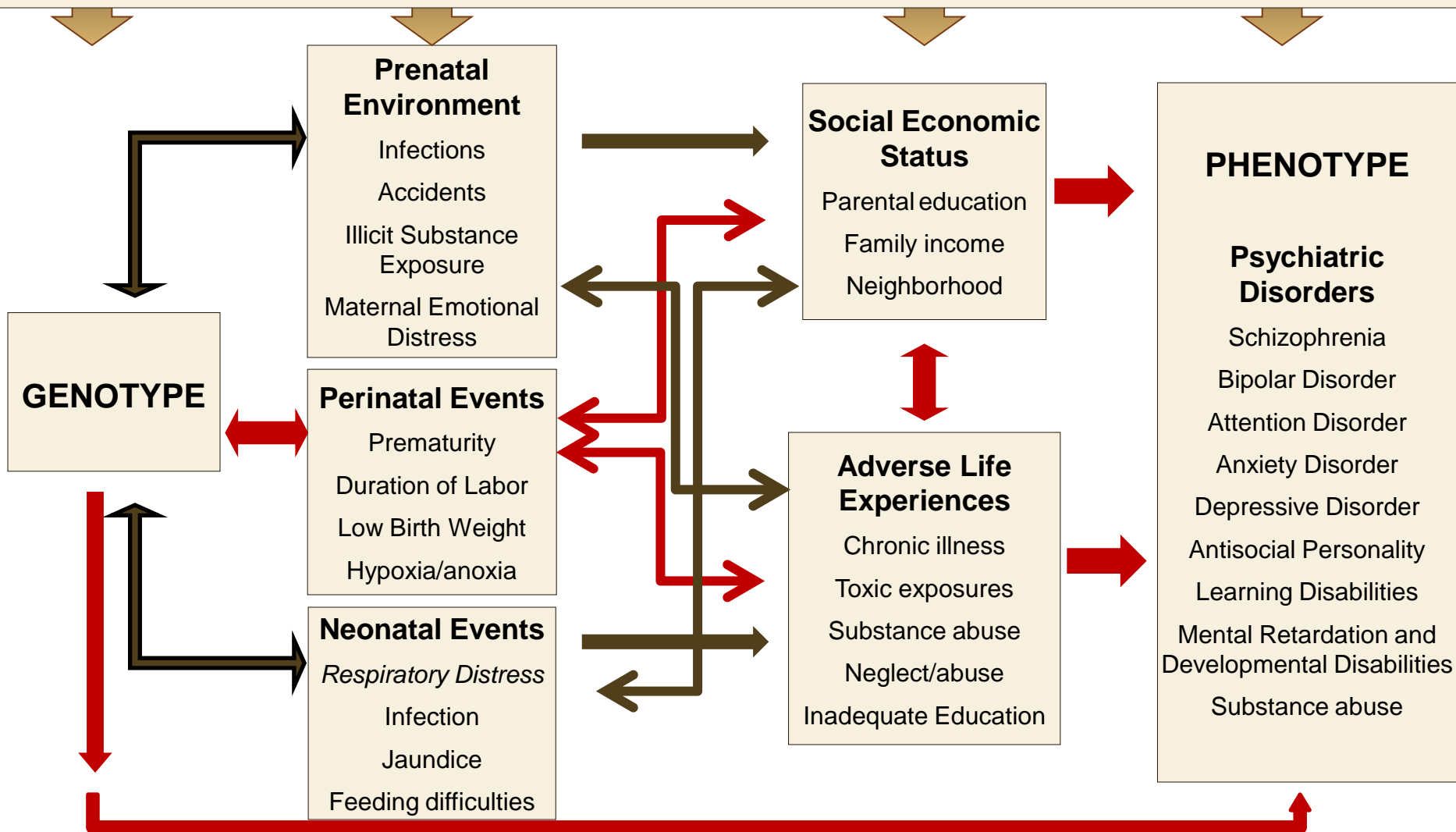
Dr. Frank Crinella

Genetic Risk

Accidents of Nature

Modifiers & Potentiators

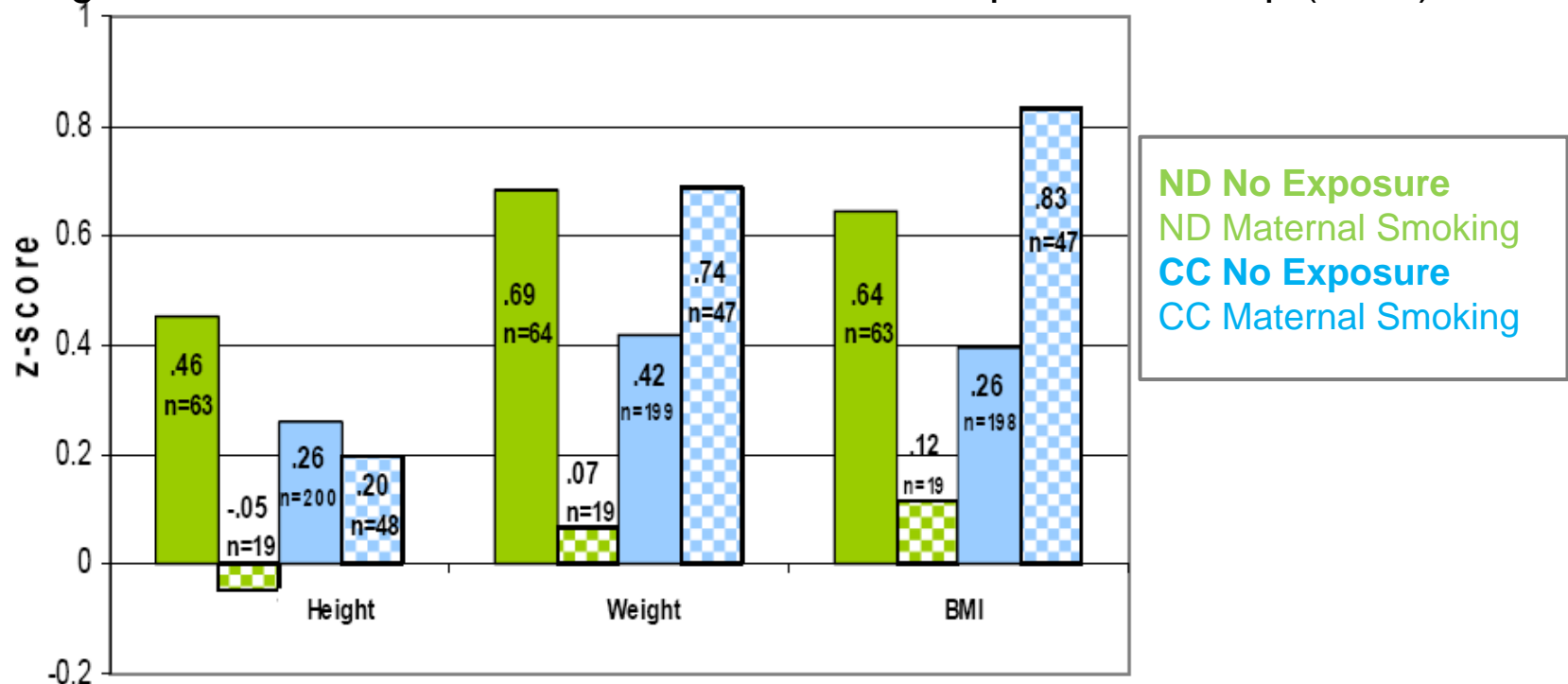
Environmental Outcomes





# Maternal gestational smoking and growth characteristics of children with neurodevelopmental (ND) problems and classmate controls (CC) (age 9-11)

T. L. Wigal, J. M. Swanson, F. Crinella et al. MTA Cooperative Group (2009) *DOHAD*.



The final size estimates of height, weight and BMI in adulthood revealed a different pattern of effects of maternal smoking during pregnancy on adult size in children with attention problems and in control peers. In the first group maternal smoking was associated to reduced height and weight but no difference in BMI. In the control peers, there was no difference in adult height, but a large increase in adult weight was observed, which produced a corresponding increase in BMI. (*The Developmental Origins of Health and Disease (DOHaD) approach*)



# Effects of maternal smoking during pregnancy: summary

- Consequences of maternal smoking on the newborn
  - abnormal physical size and growth of offspring
  - low birth weight followed by weight rebound and increased risk for obesity
  - increased risk for a psychiatric diagnosis
- Hypothesis: adaptive response associated with hypoxia in utero may elicit a “brain sparing” response
- Typical pattern of growth associated with maternal smoking:
  - Asymmetric growth due to shunting of nutrients from the body to the brain
  - The resulting “thrifty phenotype”
  - Adaptive advantage in the fetal environment
  - Risk in later environments due to permanent abnormal conditions

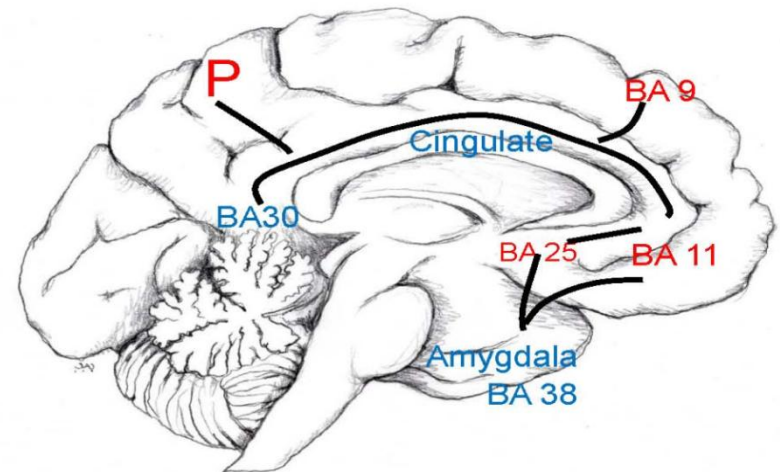
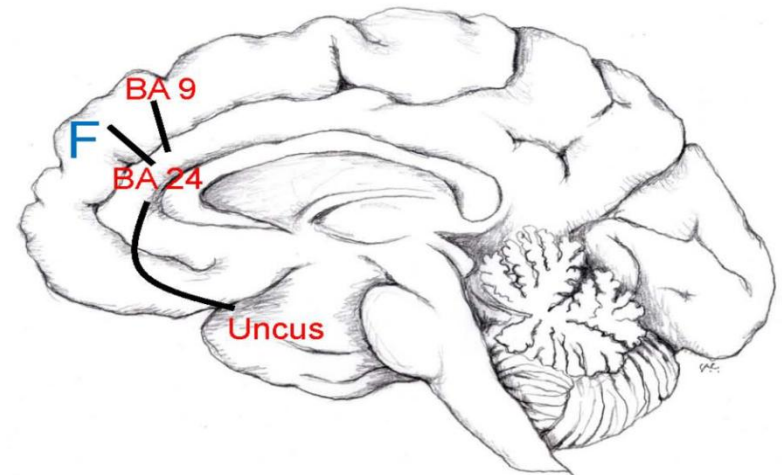




# What neural networks correlate with observed behaviors?

- Neural networks are centers of neuronal activity interconnected to process information
- Nicotine-induced reductions in length of retaliation were predicted by brain metabolism in response to nicotine in non-smokers. (From J. G. Gehricke et al. 2009)

Length Retaliation





# Brain hemodynamics during cigarette smoking

- Smoking is the leading cause of preventable disease in the U.S.
- Nicotine, the major psychoactive ingredient in cigarettes, has substantial effects on cerebral activity and cognitive performance
- Effects of smoking in cerebral oxygenation may alter cognitive performance.
- Little is know of the cerebrovascular reactivity during smoking



**Dr. Jean G. Gehricke**  
Behavior and Brain  
Imaging Laboratory



**Dr. Tim Wigal**  
Child Development Center



**Dr. Enrico Gratton**  
Laboratory for  
Fluorescence Dynamics



# Brain hemodynamics in young smokers with attention problems

## Pilot Study

- Aim: characterize cigarette smoking effects on brain hemodynamics using Near Infrared Spectroscopy (NIRS)
- Sample size **N = 5**
- Participants were selected from a larger study (the imaging-genetics study)
- Participants were screened for drug and substance abuse

Characteristics	Statistics
Age (years)	22.6 $\pm$ 1.1
Sex (percent male)	100%
Ethnicity (percent Caucasian)	60%
Body mass index	32.3 $\pm$ 3.5
Employed	60%
Number of cigarettes/day	8.4 $\pm$ 5.0
Age started smoking regularly (years)	17.2 $\pm$ 0.8
Number of quit attempts	2.2 $\pm$ 1.3
Expired carbon monoxide (ppm)	7.0 $\pm$ 3.3



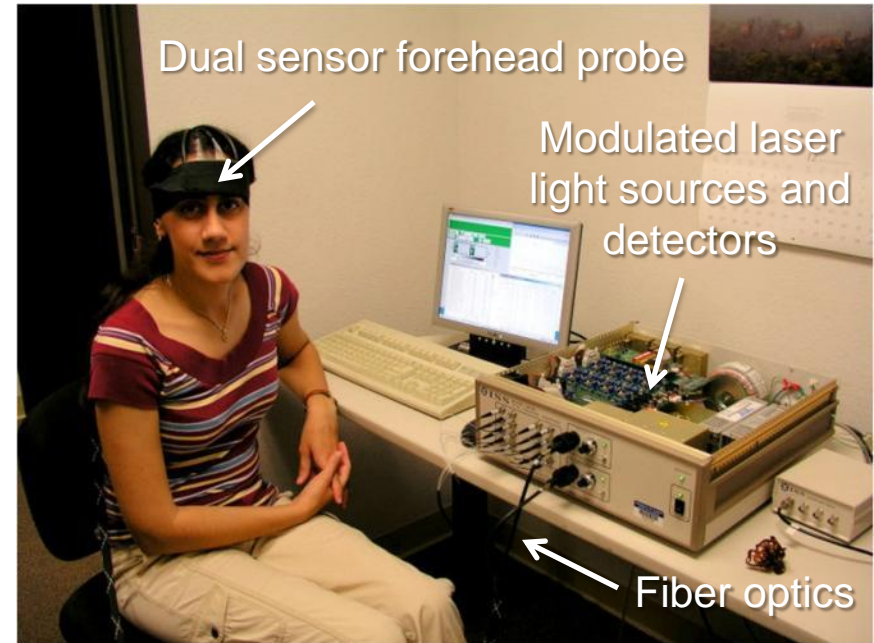
# Measuring hemodynamics in the brain with Near Infrared Spectroscopy (NIRS)

## Characteristics

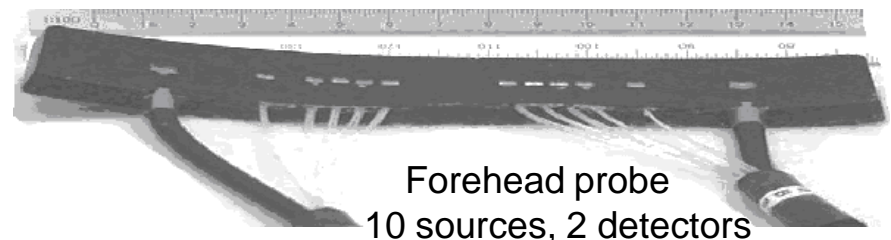
- Low energy levels ( $\sim 800$  nm)
- Non invasive ( $\sim 2$  cm in tissue)
- Real-time resolved (ms)
- Motion insensitive
- Portable instrument
- Cost-effective

## Hemodynamic parameters

- Oxygenated hemoglobin [O<sub>2</sub>Hb]
- Deoxygenated hemoglobin [HHb]
- Total hemoglobin [tHb]
- Oxidized cytochrome AA3 [ctO<sub>2</sub>]
- Tissue oxygenation StO<sub>2</sub>



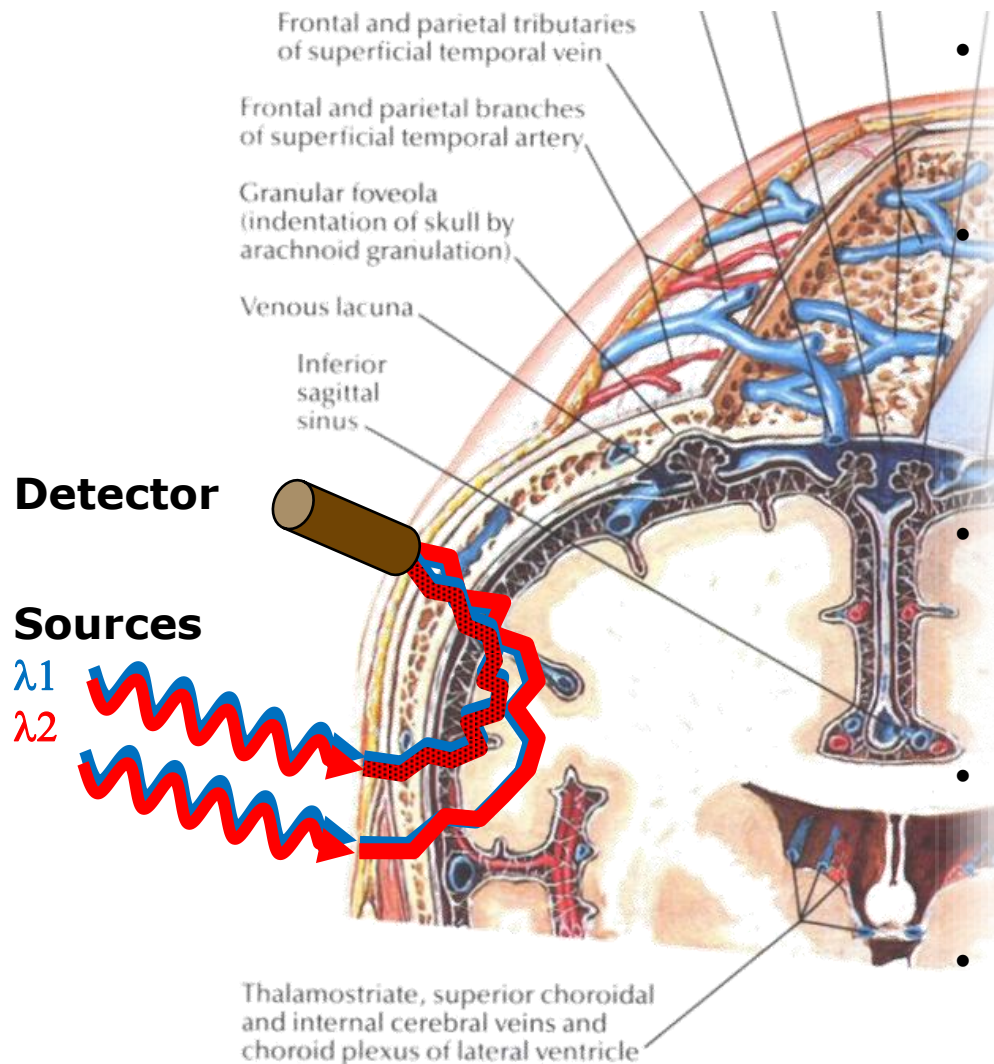
The NIRS setup at the CDC using an OxiplexTS instrument (ISS Inc., Urbana-Champaign, IL)







# Measuring the brain with NIRS



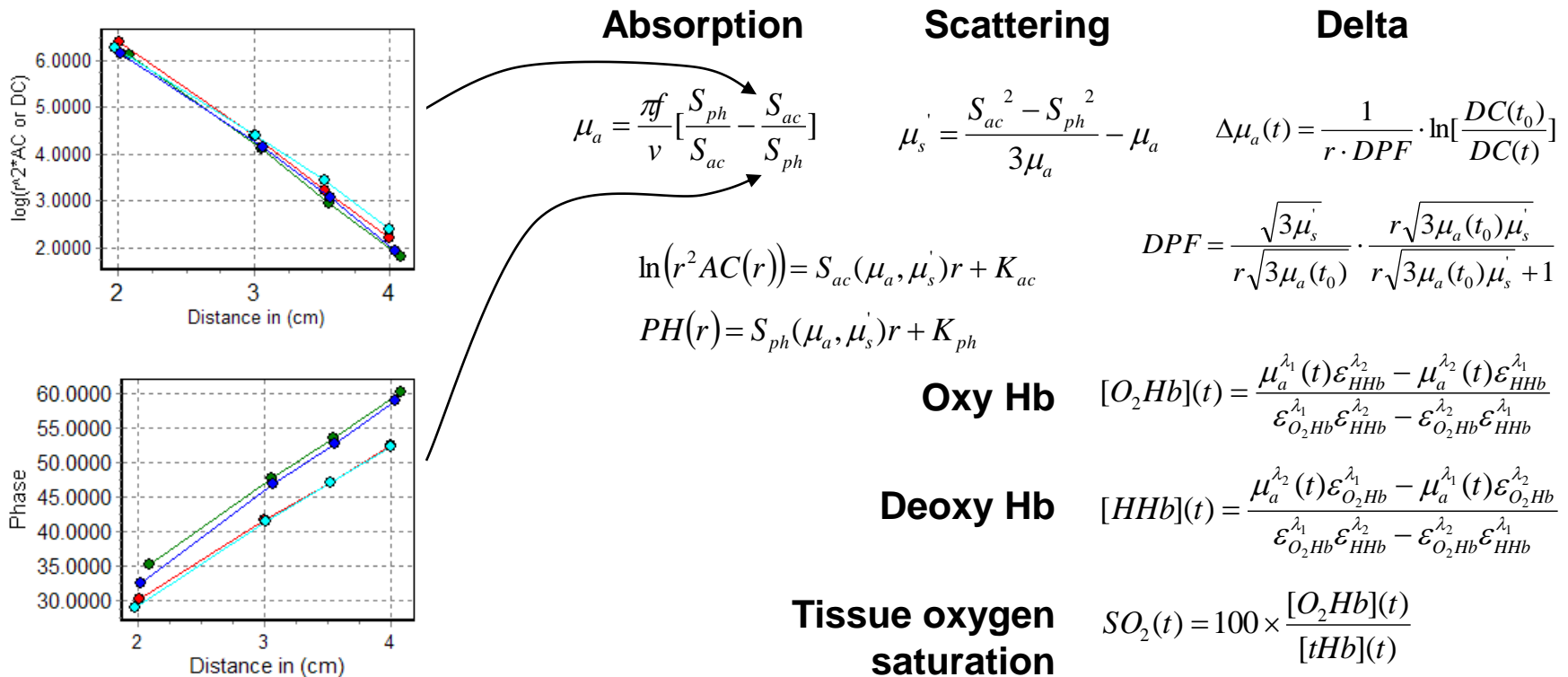
F. Netter, Table 94

- **Near Infrared light** (690-900nm) penetrates deep (~2 cm) into tissue due to *low absorbance*.
- **Frequency-domain approach:** High-frequency modulated laser light (110 MHz) is *phase-shifted* and *demodulated* in the tissue due to *scattering* and *absorption*.
- **Multiple source-detector distances** allow to calculate *scattering* and *absorption coefficients* and concentrations.
- **Multiple wavelengths** (690 and 830 nm) allow to *separate oxy- from deoxy-hemoglobin*.
- **Multiple channel probes** allow to simultaneously examine different areas (e.g. left & right frontal lobes).



# Calculating spectroscopic parameters from multi-distance measurements

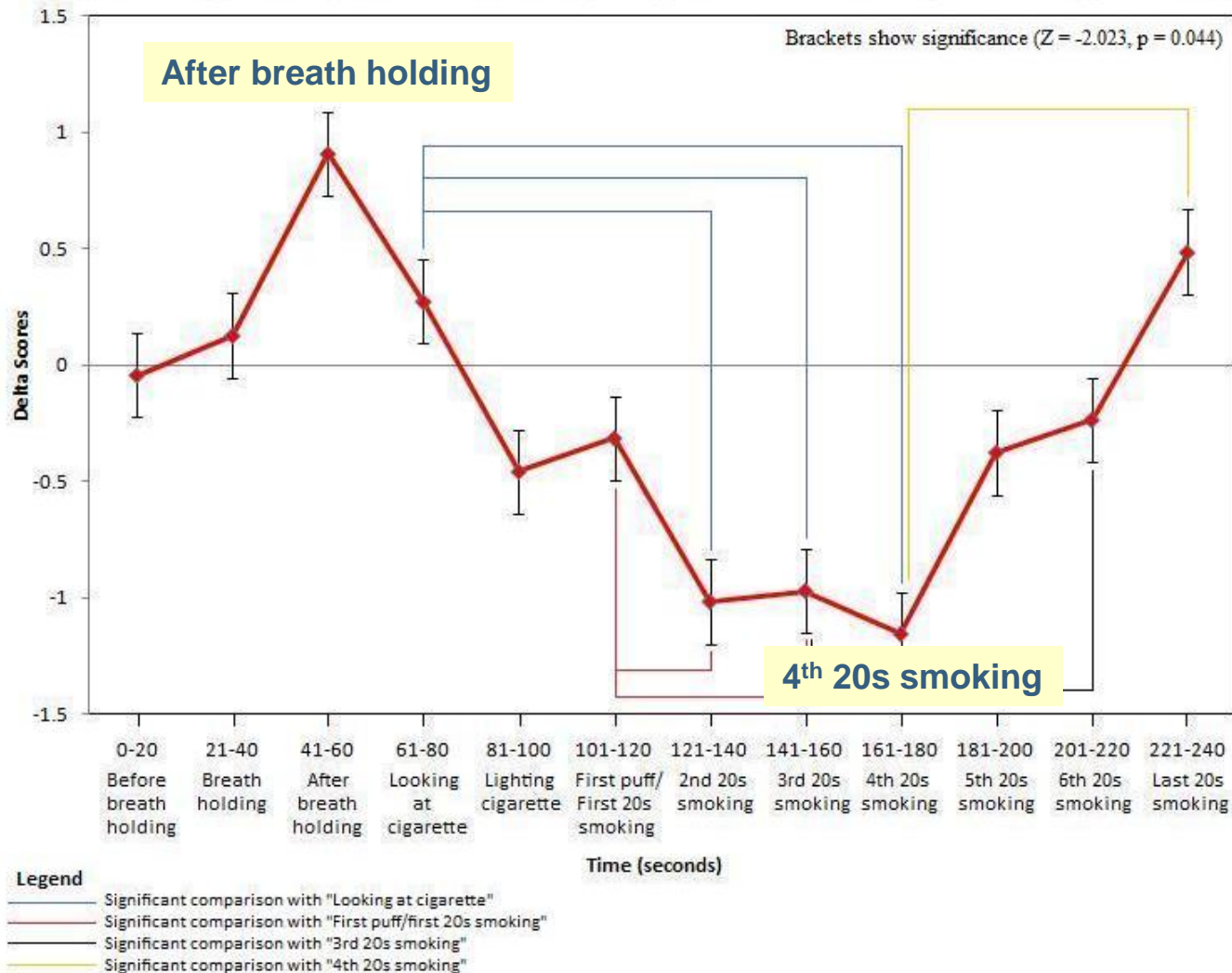
Using the multi-distance approach, absorption and scattering coefficients of homogeneous samples can be determined from the slopes of AC, DC and Phase vs. source-detector distance.





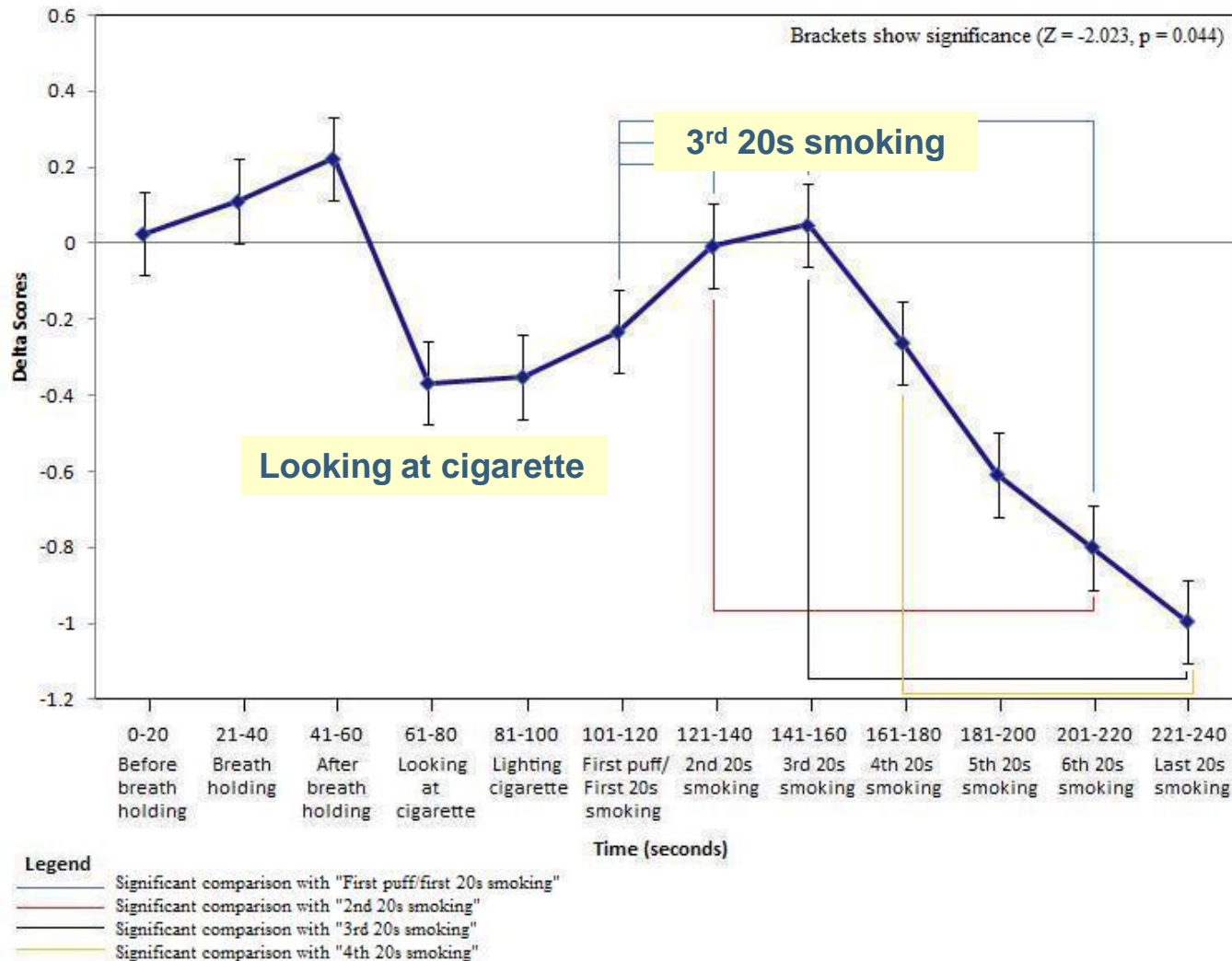


# Changes in average oxyhemoglobin concentration during breath holding and smoking





# Changes in average **deoxyhemoglobin concentration** during breath holding and smoking



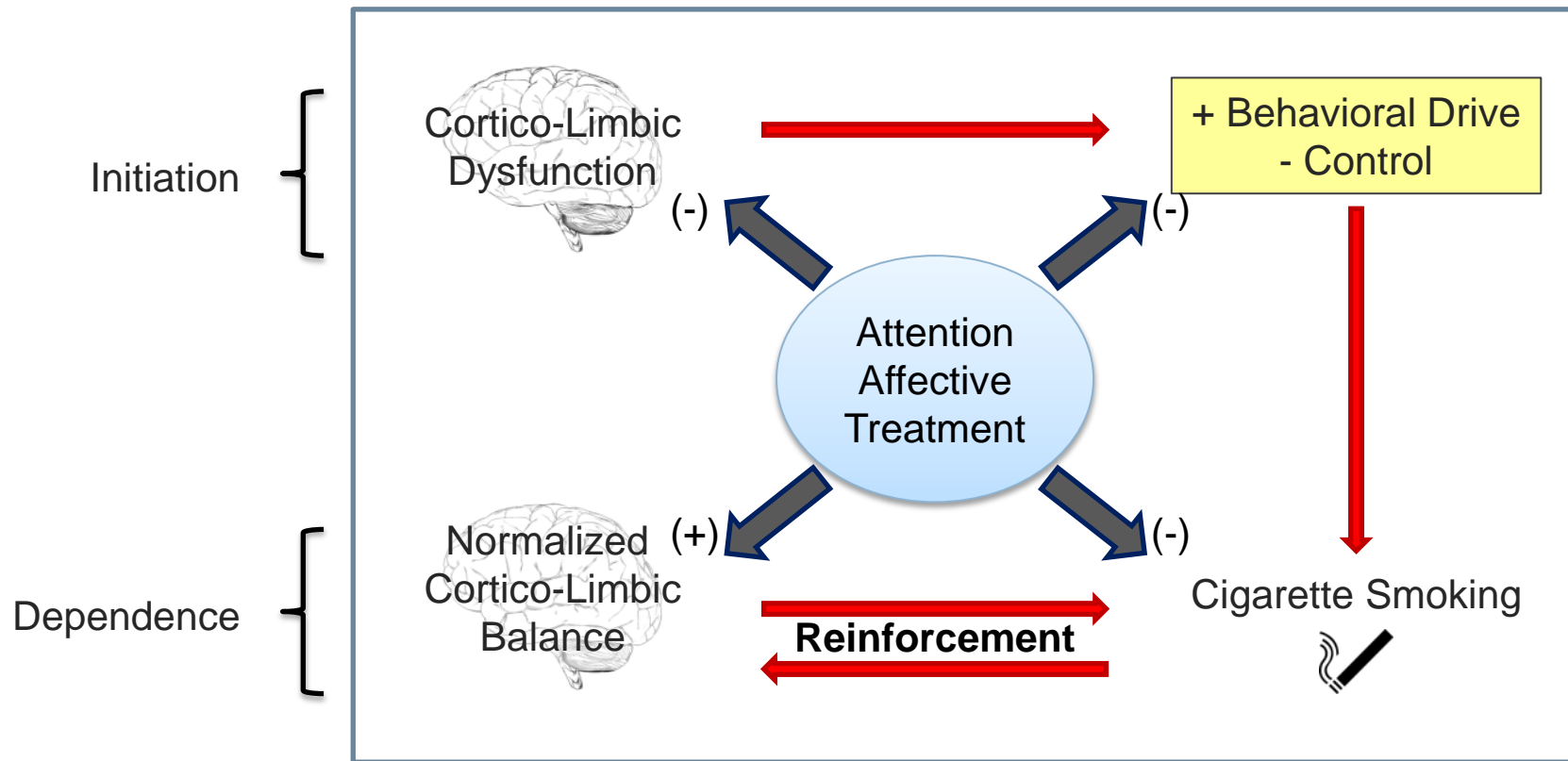


# Preliminary conclusions and future directions

- We observed a **significant change in the brain hemodynamics**, time sensitive to nicotine exposure after withdrawal.
- **Initial reduction in oxyhemoglobin concentrations** may be explained by vasoconstriction of cerebral arteries due to nicotine (Terborg et al., 2002).
- **Increase in oxyhemoglobin concentration later** in the smoking period might be a counter to nicotine due to liver metabolism (Benowitz, 1996) or incomplete arterial vasodilation by cotinine (Terborg et al., 2002).
- Does the oxygenation return to the baseline after smoking?
- Is the baseline of smokers different from non-smokers?



# Bio-developmental model of smoking for people with attentional and emotional difficulties





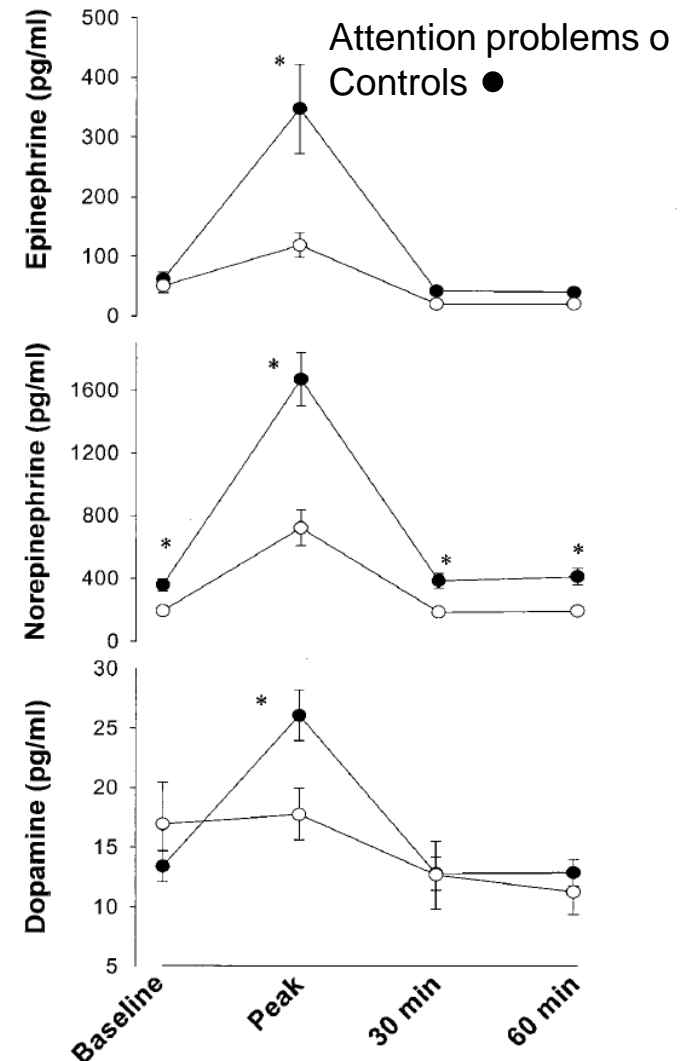
# Studying the beneficial effects of exercise in the context of the Laboratory-School Protocol

- The **laboratory school protocol** (LSP) provides a rigorously controlled environment in a school-like setting to examine dynamic aspects of responses to intervention and treatment. Tight control of the timing and context of measurements is exercised by establishing a cycle of activities repeated across each study day.
- We test intervention programs that integrate exercise in the routine life of children with problems of irritability, inattention, anxiety and learning.



# Effects of exercise on catecholamine CA levels in children with attention problems

- Exercise and other stresses share a common pathway that leads to increased CA output
- CA response to exercise is also stimulated by reduced oxygen availability to the working tissue
- The increase in circulating CA in response to exercise in healthy children was absent in children with attention problems.



Wigal S. et al., 2003, *Pediatric Research*





# Future direction: monitoring effects of exercise on mental performance

Hours	Time	Activity	Responsibilities
	8:00	Subject arrival, Temperature, Vitals, Height, Weight, HR equipment & activity monitor prep, Breakfast	Subjects have height, weight, temperature and vitals measured. Polar HR & Activity monitors are applied. Subjects eat breakfast.
-0.5	9:00	Class#1, PERMP#1, SKAMP#1	<i>2 counselors on task duty.</i>
0	9:30	Non-exercise or Exercise Intervention	After class, subjects are led various indoor recreational activities during the non-exercise intervention week or to a bout of exercise using the SPARK curriculum during the three exercise-intervention weeks.
	10:15	Class#2, PERMP#2, SKAMP#2	Subjects go directly to the classroom. <i>2 counselors on task duty.</i>
	10:45	Indoor Recess Activities	Subjects choose activity (e.g., arts & crafts, video viewing, card game).
.75	11:00	Class#3, PERMP#3, SKAMP#3	Subjects line up to go directly to class. <i>2 counselors on task duty.</i>
	11:30	Snack, Indoor Recess Activities	Subjects eat snack and choose activity (e.g., arts & crafts, video viewing, card game).
1.50	11:45	Class#4, PERMP#4, SKAMP#4	Subjects line up to go directly to class. <i>2 counselors on task duty.</i>
	12:15	Indoor Recess Activities, Lunch	Subjects eat lunch and choose activity (e.g., arts & crafts, video viewing).
3.00	1:15	Class#5, PERMP#5, SKAMP#5	Subjects line up to go directly to class. <i>2 counselors on task duty.</i>
	1:45	Dismissal, Prizes	Subjects have vitals measured. Subjects choose prize. Investigator reviews assessment reports with parents.



# Conclusions and Discussion

- Information gathered at the CDC school and clinic is the foundation for novel intervention in children and young adults with problems in attention and emotion regulation.
- Management of a large amount of variables, observational sessions and clinical visits is necessary to achieve the methodological rigor necessary for longitudinal studies.
- We presented a pilot study of brain neurovascular changes during smoking.
- We showed an example of the laboratory school protocol.



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