Transdisciplinary Research on Adolescent Brain Development: Identifying Unique Opportunities for Prevention & Policy

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Adolescence: A Perfect Storm

of *interacting* levels of change...

- rapid physical growth; onset of reproductive capacity,
- the activation of new drives and motivations;
- emergence of sex differences in facial structure, voice, and body characteristics;
- changes in sleep and circadian regulation; metabolic changes;
- a wide array of cognitive and emotional changes;
- profound changes in social context and social roles...

Biological/ Behavioral/ Neurobehavioral/ Peer/ Family/ School/ Culture/ Media....

Negative Spirals:
A Perfect Storm of Opportunities

Learning/Exploration/Acquiring Skills/Habits/Intrinsic Motivations/Attitudes/ Setting Goals & Priorities

Compelling need for transdisciplinary research to advance understanding of how to tip the balance toward:

Positive Developmental Spirals
TODAY: Four (Interwoven) Stories

- Transdisciplinary Developmental Science
  (Integrating knowledge across levels: interdisciplinary teams)

- Why focus on Adolescence? Important developmental inflection point

- Sleep/Arousal as example of one regulatory system illustrating the model

- Social-affective Learning as second example of particularly promising target
Transdisciplinary Developmental Science

Explosion of new knowledge: Neuroscience, genetics, epigenetics, gene/environment/development

from neurons to neighborhoods...
from cells to communities & cultures...
from molecules to meaning & metaphor...

To inform high-impact issues: clinical, public health, education, policy, justice...
Transdisciplinary Developmental Science

• **Enormous complexity....spanning several levels of understanding....**
  – from molecular and cellular, to neural networks, neural systems, brain-behavior interactions, individuals, parents, families, schools, peers, communities, SES, culture, ...

• **Developmental Processes...**
  – from neural migration, synapse formation, circuitry, to specific cognitive abilities, skills; social and emotional capacities; sense of self, meaning, purpose...
Slicing Into the Complexities? Building Integrative Understanding?

- Requires innovative integrative *teams* of researchers....
- Posing questions that slice deeply *and* extend to broader relevance
- Utilizing teams to (iteratively):
  - develop tractable & leverage-able questions
  - develop and refine heuristic models
  - test key features of the model with innovative and rigorous science...
Targeting issues of impact (behavior, learning, decision-making, risk-taking clinical, educational, and social policy)

• To prioritize innovative targeted approaches
  – Developmental inflection points and/or developmental processes that create vulnerabilities and opportunities...
  – Using interventions (e.g. behavioral or training) as experiments....
  – Advancing mechanistic understanding that can be leveraged across levels
Mechanistic Understanding ➔ Effective Prevention (*and* identification of high-risk groups)

Medical Example: Role of Bad Sunburn During Childhood and Risk for Skin Cancer as an Adult

GEDI
Gene x Environment x Development Interactions . . . .

UV light mechanism; preventative interventions
Mechanistic Understanding of Developmental Trajectories: CAVEATS

UNDERSTANDING OF BIOLOGIC MECHANISMS:

≠ Determinism
≠ BIOLOGIC TREATMENT

Can inform:
• Optimal developmental timing for behavioral interventions…
• Identify targets for learning, training, skill development…
• Leverage points for education, social, or health policy interventions…
Outline: Four (Interwoven) Stories

Transdisciplinary Developmental Science (Integrating knowledge across levels: interdisciplinary teams)

Why focus on Adolescence? Important developmental inflection point...

Sleep/Arousal as example of one regulatory system illustrating

Social-affective Learning (motivation) as example of promising extension
The Dark Side: The Health Paradox of Adolescence

- Adolescence is (physically) the healthiest period of the lifespan: prior to adult declines; beyond the frailties of infancy and childhood:
  - Improvements in strength, speed, reaction time, reasoning abilities, immune function …
  - Increased resistance to cold, heat, hunger, dehydration, and most types of injury …

- Yet: overall morbidity and mortality rates *increase* > 200% from childhood to late adolescence
Morbidity & Mortality in Adolescence:

• Primary sources of death/disability are related to problems with *control of behavior and emotion*

• Increasing rates of accidents, suicide, homicide, depression, alcohol & substance use, violence, reckless behaviors, eating disorders, STDs, health problems related to risky sexual behaviors... obesity

• Behaviors with long-term health (lifetime) consequences
Figure 1: Mortality During Childhood and Adolescence

2003 Number of Deaths

- All causes
- Injuries
- Homicide
- Suicide

5-14 year-olds:
- All causes: 6,954
- Injuries: 2,618
- Homicide: 324
- Suicide: 250

15-24 year-olds:
- All causes: 33,568
- Injuries: 15,272
- Homicide: 5,368
- Suicide: 3,988

Age Group and Causes of Mortality
Adolescence: an inflection-point in life course trajectory

Probability of Smoking Initiation

Age

Female

Male
Example 2: Alcohol Use by Age

Source: SAMHSA National Survey on Drug Use and Health 2003
Why the Health Paradox of Adolescence?

Why is the physically healthiest time of the life span a period of such high morbidity and mortality?

The United States spends about a BILLION dollars a year on programs to counsel adolescents on violence, gangs, suicide, sex, substance use and other potential pitfalls. Few of these work.

-- D. Dobbs (October 2011)
Why the Health Paradox of Adolescence?

Role of social-affective changes at puberty (biasing some behavioral, motivational, and decision-making)...

*interacting with*

Risk-promoting social contexts...

*Understanding adolescence as a period of social–affective engagement and goal flexibility*

**Crone and Dahl** *Nature Reviews Neuroscience* 13, 636-650; 2012

Meta-analysis of fMRI and a heuristic model....

Relevance to education, social development, economic....
What is Adolescence?
What is Adolescence?

• That awkward period between the onset of puberty and attaining adult status/roles
Some Aspects of Puberty Have Been Occurring Earlier
7.2 Age at menarche, 1860–1970.
Herman-Giddens et al 1997: 17,000 Girls in US Pediatric Practices: % with Tanner 2 Breast/Pubic Hair Development
Physiology of Puberty: Males

Prenatal Testes Release Hormones

- GnRH Pulse Generator Active
- GnRH Inhibited
- GnRH brake Lifted

Secondary Sex Characteristics

- Neurokinin B (tachykinin peptide)
- Kisspeptin (G protein-coupled receptor)
The past 150 years have witnessed a quiet revolution in human development that still sweeps across the globe today: children nearly everywhere are growing faster, reaching reproductive and physical maturity at earlier ages, and achieving larger adult sizes than perhaps ever in human history.

--Carol M Worthman, Ph.D.
Adolescence is NOT an invention of industrialized societies...

An anthropological study of adolescence in 187 different societies, Schlegel and Barry.
Schlegel: Across 187 pre-industrial societies

Interval between attaining puberty and taking on adult roles in virtually every society

Interval between childhood and ‘adult’ was typically 2-4 years in the majority of traditional societies studied...
Puberty & Adult Roles in Contemporary Society

• Average age of menarche is now age 12;
• Average age of taking on adult social roles—starting careers, marriage, owning a home, choosing to become parents…?

• ADOLESCENCE HAS EXPANDED from a 2-4 year interval in traditional societies to an 8-15 year interval in contemporary society.
Adolescence: A Perfect Storm of interacting levels of change...

rapid physical growth; sexually dimorphic alterations in facial structure, voice, and body characteristics; metabolic changes; the activation of new drives and motivations; changes in sleep and circadian regulation; a wide array of cognitive and emotional changes; profound changes in social context and social roles...

Biological/ Behavioral/ Neurobehavioral/ Peer/ Family/ School/ Culture/ Media....

Negative Spirals:
Puberty as a bio-behavioral activation of socio-affective changes

• A natural inclination toward novelty and exploration
  • Cross species data & evolutionary perspective
  • Individual differences & social context effects

• *Increased sensation-seeking*

• *Increased motivational salience of social status*

• Effects of specific hormones? (*Testosterone*  
  Estradiol  Oxytocin)?
  • Mechanistic questions at the level of dopamine,  
    reward-prediction error, reinforcement learning,  
    motivational learning....?
Human Puberty: *Igniting Passions* in the Developing Brain

- Profound changes in romantic interest, motivation, emotional intensity
- Increase in sensation-seeking
- Intensification of specific types of goal-directed behavior (particularly goals related to social-status)

A period of natural motivational learning?  
*Social sculpting of intrinsic motivations?*

The affective (feeling-based) aspect of wanting, liking, desiring particular kinds of goals and priorities....
Adolescent Brain Development

Frontal-Cortical Engagement (variable)

Social brain network
- mPFC
- TPJ
- ACC
- insula

Cognitive control system
- DLPFC
- Parietal cortex

Motivational/Goal Flexibility

Onset of puberty

Limbic Engagement:
- Affective salience of social cues & context

Subcortical structures
- Ventral striatum
- Amygdala

Social / Affective Influences

Positive growth trajectories: e.g., adaptive exploration, mature long-term goals, social competence

Negative growth trajectories: e.g., excessive risk-taking, substance use, depression, social withdrawal

Time/Development
Adolescent Risk Taking: Sensation-seeking and Status-seeking?
Empirical Evidence for Puberty-Specific Neurobehavioral Changes?

- Pubertal increase in fear reactivity (Quevedo et al 2009)
- Complex changes in reward processing (Forbes et al 2009, 2010; Forbes & Dahl 2010; Op de Macks et al 2011)
- Complex (and sexually dimorphic) structural (MTL and gray matter maturation) Bramen et al 2010; and white matter DTI changes (Ladouceur et al 2011)
- Pubertal changes in face processing (Scherf et al 2011)
- Pubertal changes in sleep regulation & sleep interactions with reward and motivation) (Sadeh et al 2010; Holm et al 2009; Hasler et al 2012)
- Testosterone and OFC-amygdala coupling; VS-amygdala...fear as excitement...
Tipping Points in Development?

Examples focusing on:

Risk-taking
Sleep
Motivational learning
Outline:

Transdisciplinary Developmental Science
(Integrating knowledge across levels:
interdisciplinary teams)

Adolescence as an important developmental
inflection point: a) puberty/onset
b) transition to adulthood

Sleep/Arousal as example of one regulatory
system illustrating model

Social-affective Learning as one example of
promising extension
Introduction:
Why Sleep?

- Growing evidence for sleep role in learning, memory, and brain development
- Intertwined with several aspects of physical and emotional health, as well as metabolic balance (obesity)
- Critical implications for intervention and policy for youth
Sleep and Brain Development?
Maps of slow wave activity (SWA) during non rapid eye movement (NREM) sleep. Topographical distribution of SWA (EEG power between 1 and 4.5 Hz) for three age groups (5-8 years, n=6; 11-14 years, n=9; 17-20 years, n=5). Maps are based on 109 electrodes (indicated by coloured crosses) from the first 60 min of NREM sleep stages 2 and 3. Maps were normalized for each individual and then averaged for each age group. Values are colour coded (maxima in red, minima in blue) and plotted on the planar projection of the hemispheric scalp model. Each map was proportionally scaled, and values between the electrodes were interpolated (courtesy of Reto Huber, Ph.D., data adapted from {Kurth, 2010 #380}).
(A) SWA distribution for age groups: Top 25% of SWA values are mapped. (B). Regions of interest (ROIs) based on anatomical electrode localization using specific Brodmann areas. (C). SWA topography maturation reflected by the ROI with maximal SWA (SWA maxima located in vision in n = 5 subjects, visuomotor n = 3, simple motor n = 3, complex motor n = 12, language n = 6, cognitive control n = 34). The age of subjects with maximal SWA in the same ROI was averaged (thin vertical lines) and variability is presented as mean ± 2 * SE. (with permission from {Kurth, 2012 #398}).
Implications:

• Neural systems that are undergoing the most active learning, adaptation, plasticity during awake show parallel changes in depth of sleep
  – Instantiate the learning
  – Need to retune/re-calibrate ‘off-line’

• What are the consequences of sleep deficits?
The sleeping child outplays the adult’s capacity to convert implicit into explicit knowledge
Wilhelm et al 2013 Nature Neuroscience

When sleep followed implicit training on motor sequence, children > gains in explicit learning (compared to adults).

Greater explicit learning was linked to higher SWS in children and stronger hippocampal activation at explicit knowledge retrieval...

Superiority of children in extracting invariant features from complex environments (SWS memory reprocessing...
Sleep, Learning, Affect & Brain Development

Developmental Trajectory
Brain/Behavior/Social Context
INTERACTIONS

Cognitive Processes, Learning & Brain Plasticity

SLEEP

emotion
motivation

flexibility, skills, regulation

arousal

continuity and patterning
(amount/structure)

type
(REM/NREM)
depth/disruption
(initiate/maintain)

circadian
(timing/variability)

Clinical and Policy: Early intervention and Prevention
Sleep: Pubertal Changes in Sleep Regulation?

- Some developmental changes in sleep regulation appear to be linked to puberty:
  - Increased Sleepiness
  - Circadian/sleep changes
Sleep: Pubertal Changes in Sleep Regulation?

- Increased Sleepiness
- Circadian shift in preference toward later sleep and wake times

• Consider these two sets of biological change in sleep tendencies, in earlier periods of human history...
Social factors in contemporary society contribute to LATE bedtimes/sleep onset times:

- Peers and social activities
- Greater freedom to self-select bedtimes
- Access to light and social cues
- Access to arousing/stimulating activities
- Stress/anxiety or excitement → difficulty falling asleep
- Major circadian shift on weekends/vacation
- Work, Sports, Homework, Projects, meds...
The School-Sleep Squeeze

• Despite *average* school night bedtimes of 11:30 pm in high school seniors, the average wake-up time on school days is 6:15 am.

• Greater than 10% of US high school students must get up before 5:30 am to catch buses

• More than 15% of high school students report averaging 6 or less hours in bed on school days (need 8 or more)
Contributing Factors/Vicious Cycle

- “Catch-up” sleep on week-ends pushes circadian system to further delay
- Use of stimulants (caffeine and nicotine) can contribute to Difficulty Falling Asleep
- Blue spectra light (TV, computer, personal device screens) > red-orange light
- Stress and conflict contribute to emotional arousal and further Difficulty Falling Asleep
Sleep Timing In Contemporary Societies: Social Jet-lag in Adolescence

- Shift in time of mid-sleep on “free” days
- Delay begins at puberty and is marked across the 2nd decade
- Is the inflection a “biological marker for the end of adolescence?”

Roenneberg et al., Current Biol., 2004
In sum:

Teen World

Late Bedtime
Weekend Sleep-in
Tired During School Week
Less Sleep
What are the consequences?

• If 30-40% of U.S. adolescents are typically getting less than optimal sleep *and* jet-lag like circadian shifts what are the costs?
Sleep, Stress, and Emotion Regulation: Progress, Clinical and Policy Relevance

• Mechanistic understanding of how sleep/arousal regulation is intertwined with affect regulation
• Focus on Puberty/Adolescence
• Early-intervention/prevention for anxiety and depression
• “Social Jet Lag”
• Policy: School start times
• Driving policies and falling asleep vehicle deaths...
• Sleep and wake interactions fundamental to learning and brain plasticity?
Several Studies Examining Changing School Start Times

• Improved: attendance, grades, mood...

Carrell, Maghakian, and West

A’s from Zzzz’s? The Causal Effect of School Start Time on the Academic Achievement of Adolescents

– examined the causal effect of school start time on academic achievement with the randomized placement of students to courses and instructors

– starting the school day 50 minutes later: significant positive effect on student achievement, roughly equivalent to raising teacher quality 1 SD
Consequences of Insufficient Sleep in Adolescents

- Sleepiness (lapses)
- Tiredness, motivation
- Difficulties with focused attention
- Irritability, reactive aggression
- Decreased mood, depression?
- Negative synergy with alcohol effects
- Direct effects on learning, memory consolidation
- Increase use of caffeine, stimulants
- Increase in obesity, metabolic syndrome
- INTERACTIONS ACROSS DOMAINS?
A Small Biological Change at Puberty Can Lead to a Spiral of Negative Effects

• Late night/erratic schedules ⇒ Sleep Deprivation
  ⇒ erodes mood and motivation
  ⇒ greater stress and affective problems
  ⇒ interferes further w sleep/arousal regulation
  ⇒ greater difficulty falling asleep

• Social context that amplifies the biologic change ⇒ a torrential spiral?
Adolescent Brain Development

Learning, Adaption, Adjustments to Social Contexts

Cognitive & Affective Functioning

Pubertal Changes in sleep

Onset of puberty

SCN: Responsivity to light and social cues

Sleep/Arousal Regulation

Positive growth trajectories:
e.g. adaptive exploration, mature long-term goals, social competence

Negative growth trajectories:
e.g. excessive risk-taking, substance use, depression, social withdrawal

Time/Development
Outline: Four (Interwoven) Stories

1. Trans-disciplinary Developmental Science (Integrating knowledge across levels: interdisciplinary teams)
2. Adolescence as one (very important) developmental inflection point (model of pubertal changes in key neural systems)
3. Sleep as example of one regulatory system that fits the model
4. Social-affective Learning as one extension of the model
The Feeling of Motivation in the Developing Brain: The Social Sculpting of Intrinsic Motivations
...acquired ‘natural’ or intrinsic motivations...
the feelings that underpin particular goals and priorities...
Overview

*Developmental Affective Neuroscience*: Moving beyond traditional focus on emotion (and emotion regulation) to examine *the development of neural systems that underpin motivational feelings*...

- Considering the (learning) processes that underpin *acquired motivational feelings* (including key developmental windows of opportunity)
- Adolescence as a key developmental window for affective motivational learning
- Specific role of social experiences in sculpting new ‘intrinsic’ or appetitive motivations
Broadening affective neuroscience (some conceptual issues)

• Emotions as neural signals (feelings) of automatic ‘valuing’
• Emotions as part of a system to send and receive social signals (in the realm of feelings)
• Emotions as neural signals (feelings) that create automatic ‘action-tendencies’
“Motivation” is complex (conceptually and semantically)

• Cognitive dimensions of working toward goals (in ways that require effort, executive functions, cognitive control, DLPFC)

• Natural, intrinsic, appetitive motivations

• *Acquired versions of natural, intrinsic, appetitive motivations*....

Consider the differences between John (hates running) and occasionally forces himself to run and Jill (loves running/addicted) who would have to use effort to keep from running every day (other examples...or Kate reads literature to get honors in English, Kelly hides under her covers with a flashlight *loving* to read...)
Targeting the Adolescent Transition: A Period of Multiple Vulnerabilities for Negative Spirals
Motivational Learning and Positive Spirals?

• Increase/alterations in 
  
  *Natural (intrinsic) motivations*

  *Through procedural learning processes...*

  *Implicit learning*

  *Relevance to ‘self’ and identity formation...*
Adolescence: Intense Emotions and Motivational Learning at Puberty as A Period of Opportunity

• Igniting Passions:
  – Sports
  – Literature/Arts/Music
  – Science
  – Politics
  – Caring for others
  – Inspired Goals
  – Idealism & Larger Purpose
  – Changing the world in positive ways
Summary: Adolescence

• A developmental window of social-affective learning—a time of igniting passions in ways that create vulnerability for developing destructive versions of negative spirals—addictions, reckless & risky behavior, and emotional disorders.

• Also opportunities for motivational learning that can lead toward healthy ‘passions’...

• Getting traction into understanding unique changes at the onset of adolescence...to impact the spiraling interactions continue across all of adolescence...

• Crucial need for trans-disciplinary teams...
Thank you