Developmental considerations of the affective/emotional brain

Dr. Caitlin Hudac
University of South Carolina
PY 888 – Affective (Cognitive) Neuroscience
Spring 2023

C14 Mon 4/24: Student presentations

"What I learned in class this semester…"

Oral presentation: (10%, 100 points): Students will describe how one specific developmental, clinical, or cultural factor may influence affective neuroscience.

You will be assessed on:

- Succinct description and level of familiarity with your topic
- Critical analysis of the existing literature
- Presentation style and/or slides
- Response to questions (at least 2 minutes)

Oral presentation rubric

Proposal papers – structure

Final written paper (30%, 300 points): Proposals should be 7-9 double-spaced pages in length (including title page but excluding references) and written in APA style.

This paper will reflect your knowledge and synthesis of affective neuroscience theories, concepts, and methodologies. It must include theoretical support, utilization, or extension of course materials, and critical analysis of your topic. This project requires some creative thinking, but you are encouraged to brainstorm with Dr. Hudac and your peers.

Theoretical paper proposal

- The paper should review a **specific** topic in affective neuroscience. It is required that the topic have a focus on affect/emotion and the brain. You must demonstrate **knowledge and expertise of at least one methodology**.
  - Title page (1 page)
  - **Moderate** introduction (~3-5 pages): Describe the current scientific need to **review** the proposal topic, provide adequate and compelling background materials.
  - **Detailed description of a primary source** (1 page): In a dedicated 1-2 paragraphs, summarize the objective, methodology, specific hypotheses, and results of one critical paper that addresses your proposal topic.
  - **Limitations in the literature** (~2 pages): An extended discussion should review the outstanding questions in the field and propose what kinds of studies are needed to address these limitations.
  - You may consider ending the proposal with 2-5 sentences describing the broader impact of this potential work.

Empirical paper proposal

- The paper should be centered on a **novel** topic in affective neuroscience (i.e., somehow investigating links between affect/emotion and the brain) and should include all the elements found in a brief report journal article:
  - Title page (1 page)
  - **Brief** introduction (~2-4 pages): Describe the current scientific need to **address** the proposal topic, provide adequate and compelling background materials.
  - **Current study objective** (1 page): In a dedicated 1-2 paragraphs, summarize the objective, overview the method that will be utilized, and generate specific hypotheses.
  - **Methods** (~3 pages): Briefly describe inclusion/exclusion criteria for your study participants. Fully describe the stimuli and experimental design. Describe equipment to be used, including appropriate settings. Outline planned data processing needs and how you will extract the outcome variables.
  - Discussion is not required, but you may consider ending the proposal with 2-5 sentences describing the broader impact of this potential work.

Final paper details

- **You are required to consult with Dr. Hudac (worth 25 points)**. You will have an opportunity to consult with Dr. Hudac on the last day of class (10-minute slots). However, you may also opt to schedule your consultation earlier in the semester (and as often as you'd like!). This may be helpful in planning your final paper.
- **Optional draft**: You will have the opportunity to turn in a draft to Dr. Hudac for preliminary grading if sent to Dr. Hudac before **4/10/23 @ 11:59 pm**. She will return the draft with brief comments ASAP in the order received. You will not be penalized if you choose not to submit a draft.
- **Late papers**: For every 24 hours the paper is late, Dr. Hudac will deduct 25 points from your final grade.

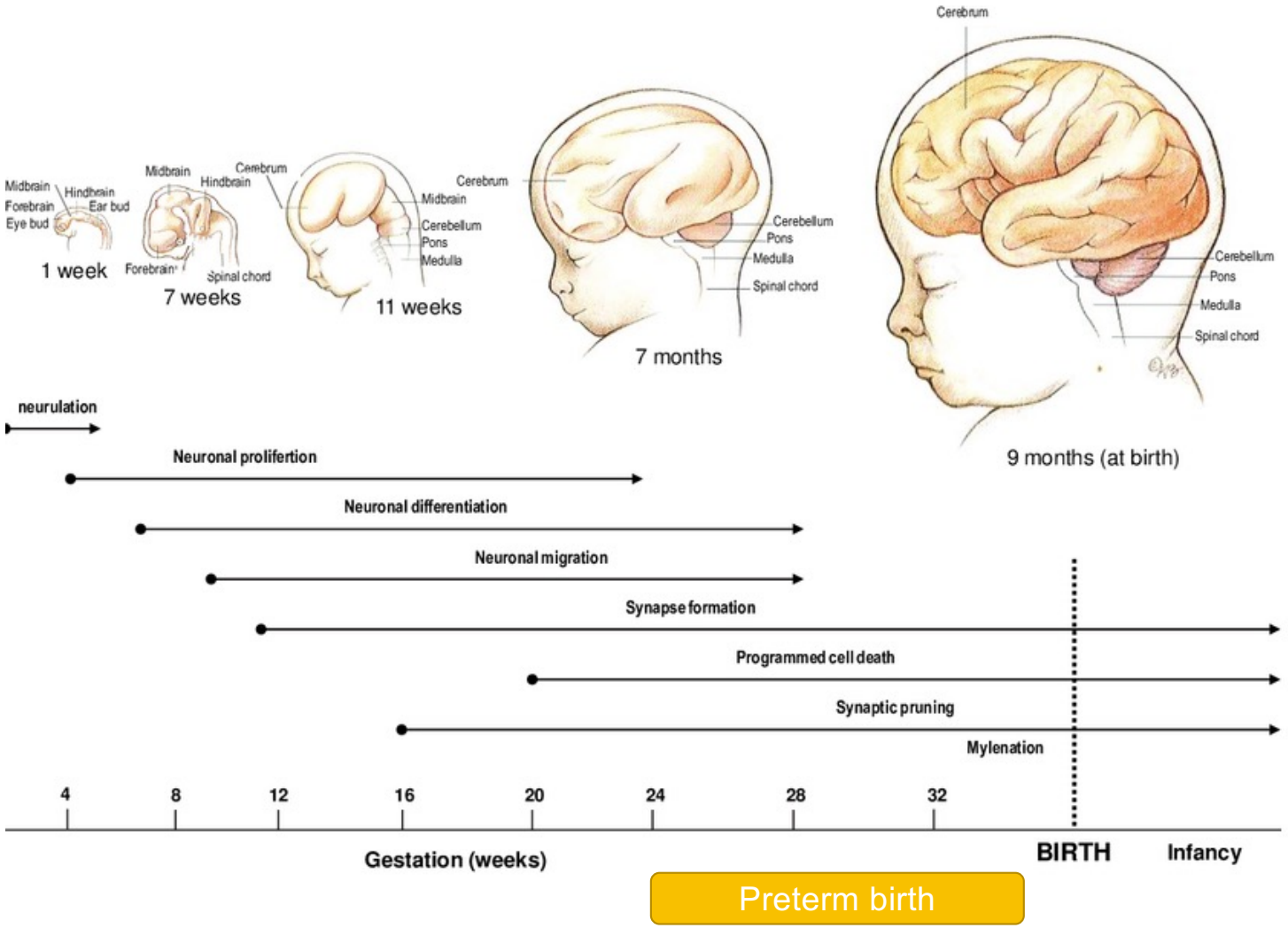
Paper rubric

Developmental considerations of the affective/emotional brain

- Anticipated changes from different methods
  - Maturation → Function / capacity
- Need for large, longitudinal datasets

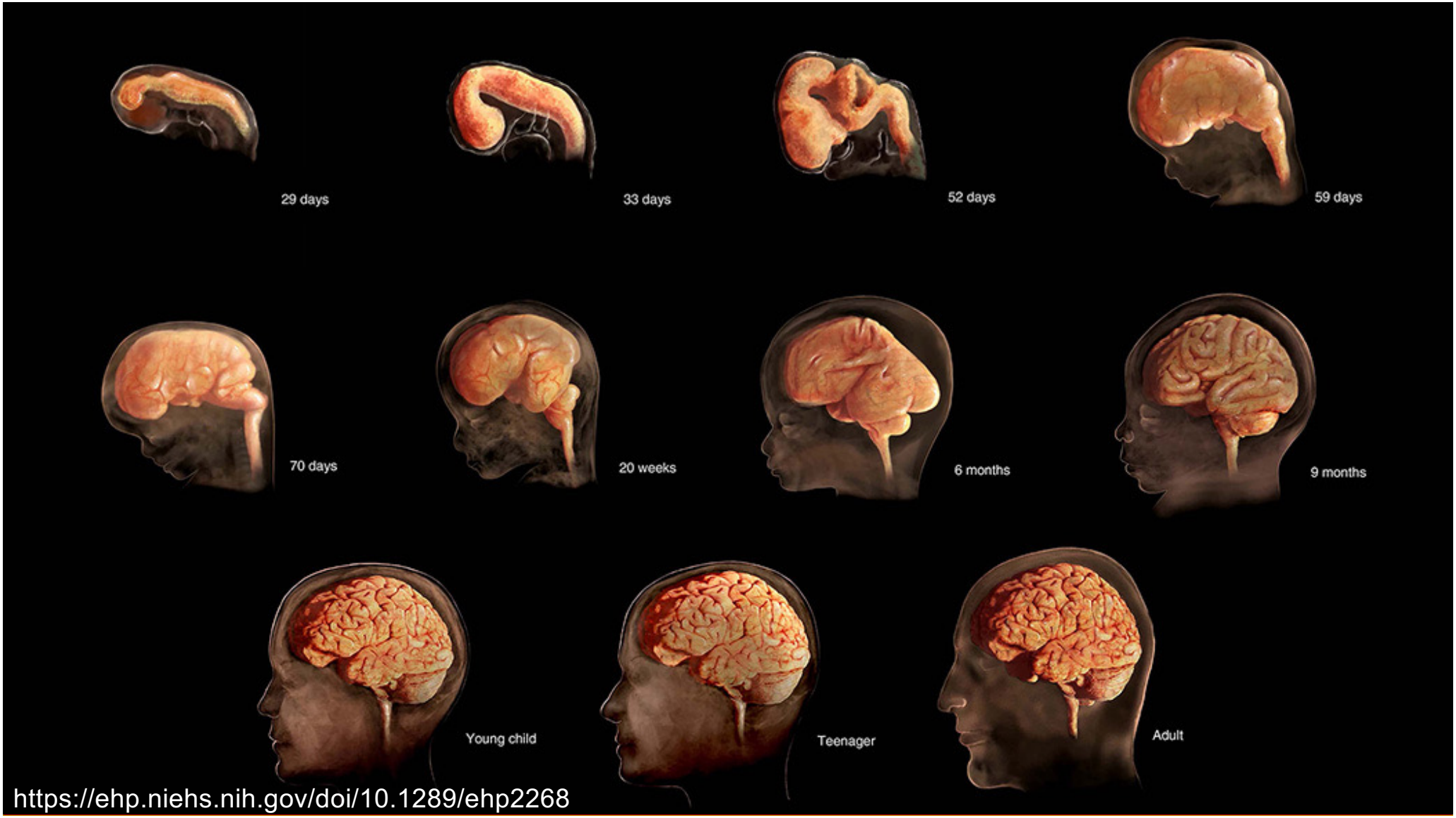
Anticipated changes: fMRI / sMRI

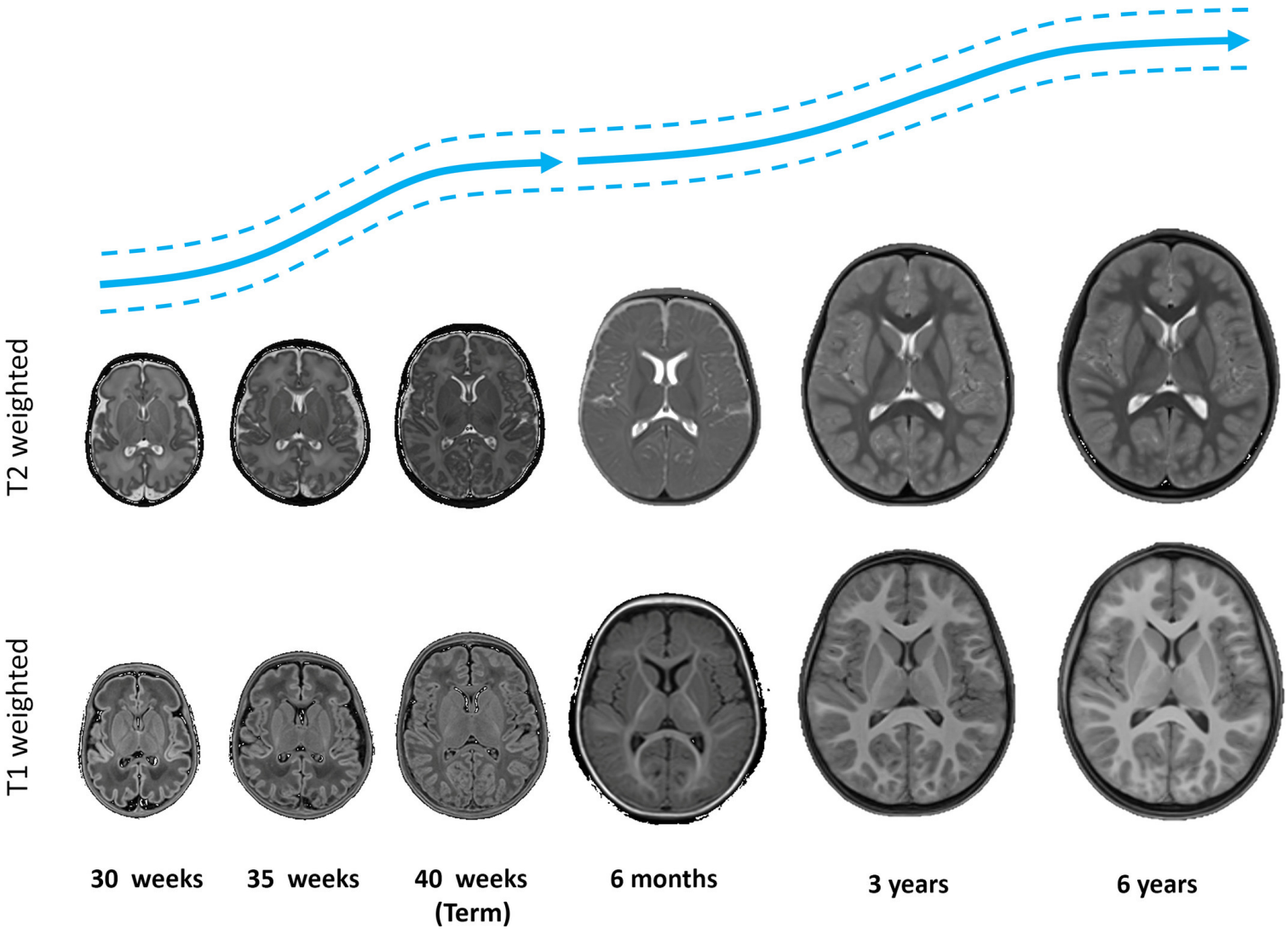
- Developmental changes related to:
  - # synapses / synaptic growth → Impacts connectivity
  - Synaptic pruning → Impacts efficiency
  - Density/volume → Impacts capacity
- Often need to consider combinatory effects



Preterm birth

Silburn, S. R., Nutton, G., Arney, F., & Moss, B. (2011)


29 days
33 days
52 days
59 days
70 days
20 weeks
6 months
9 months
Young child
Teenager
Adult
https://ehp.niehs.nih.gov/doi/10.1289/ehp2268



Batalle, D., Edwards, A. D., & O'Muircheartaigh, J. (2018).

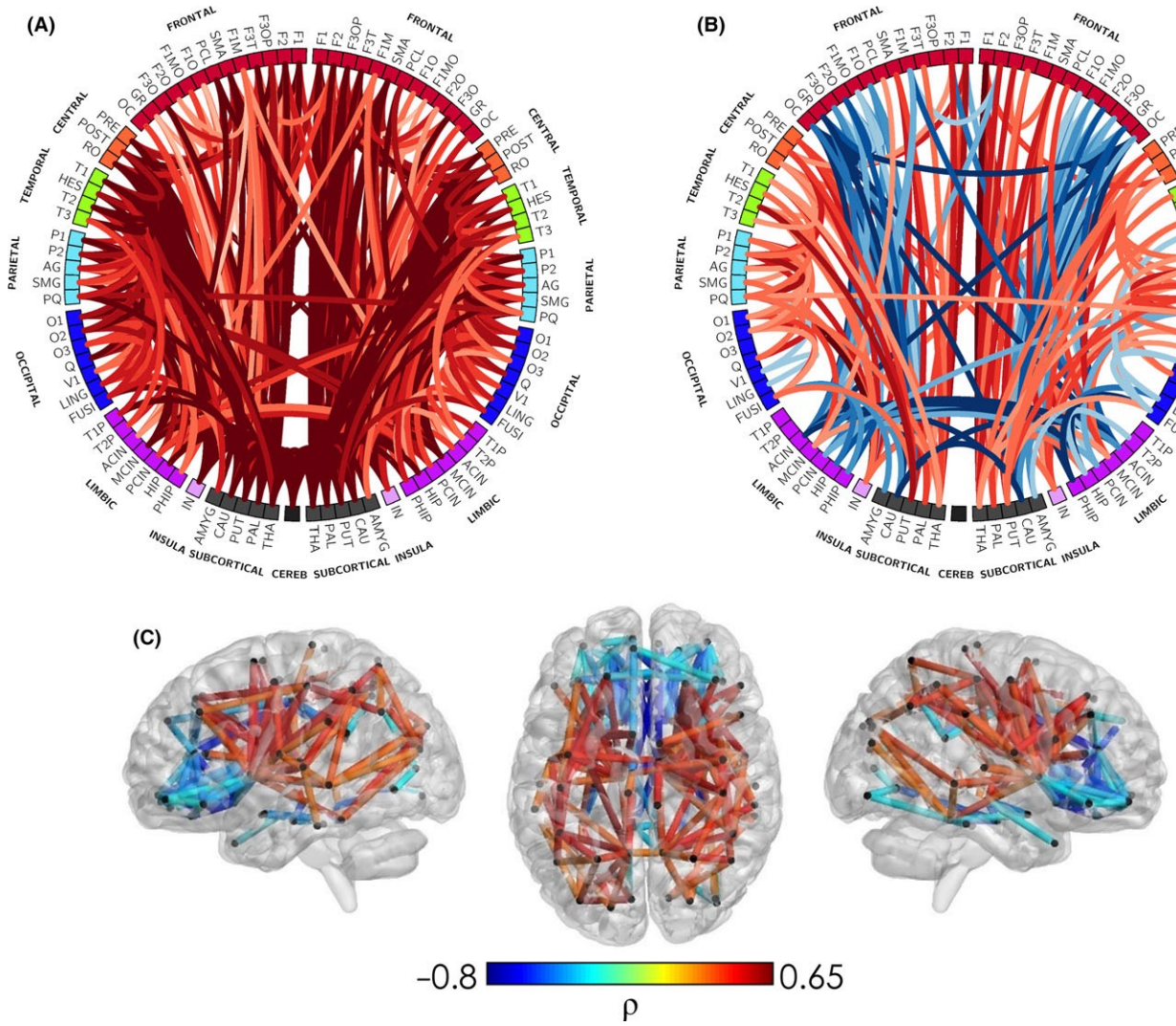
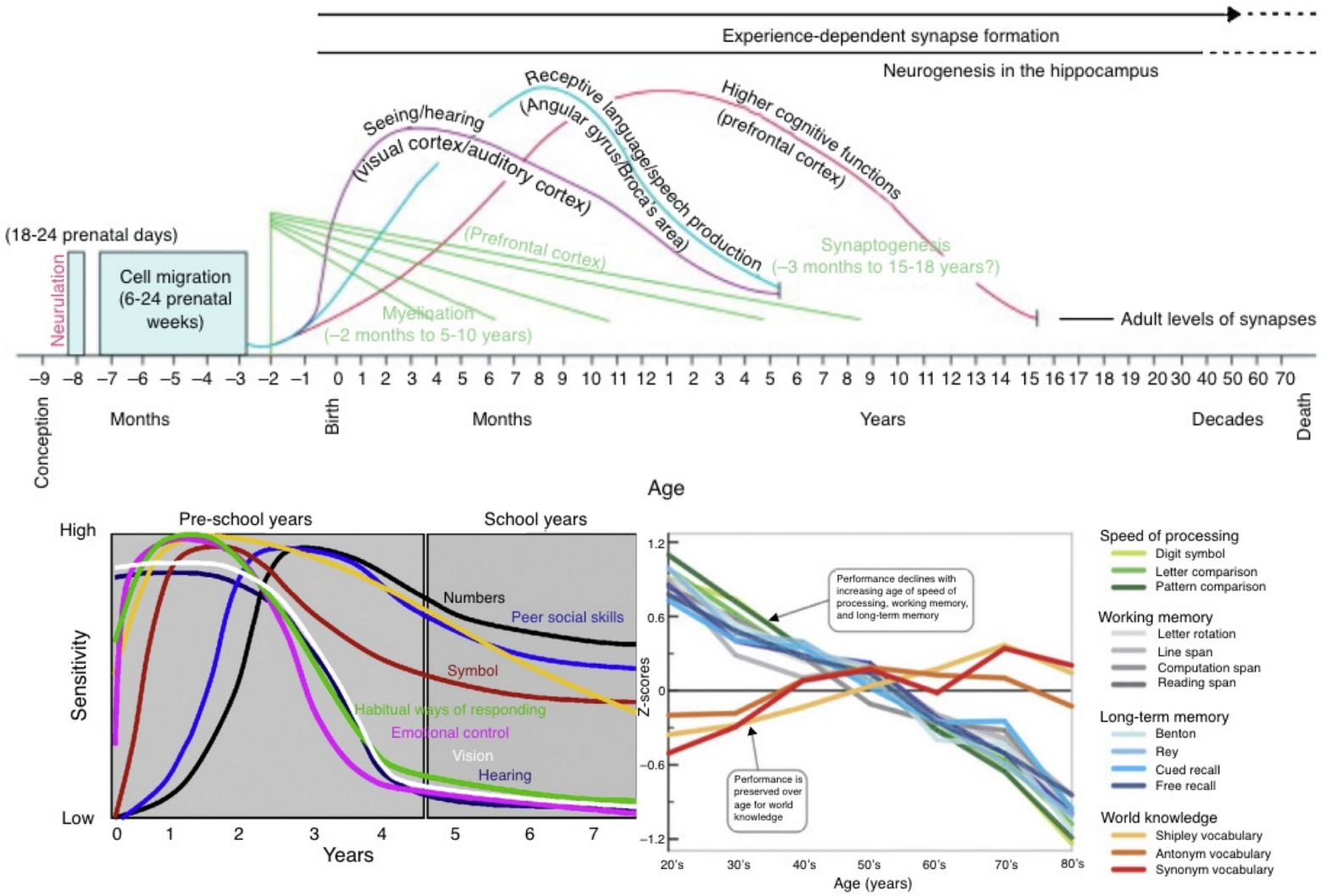


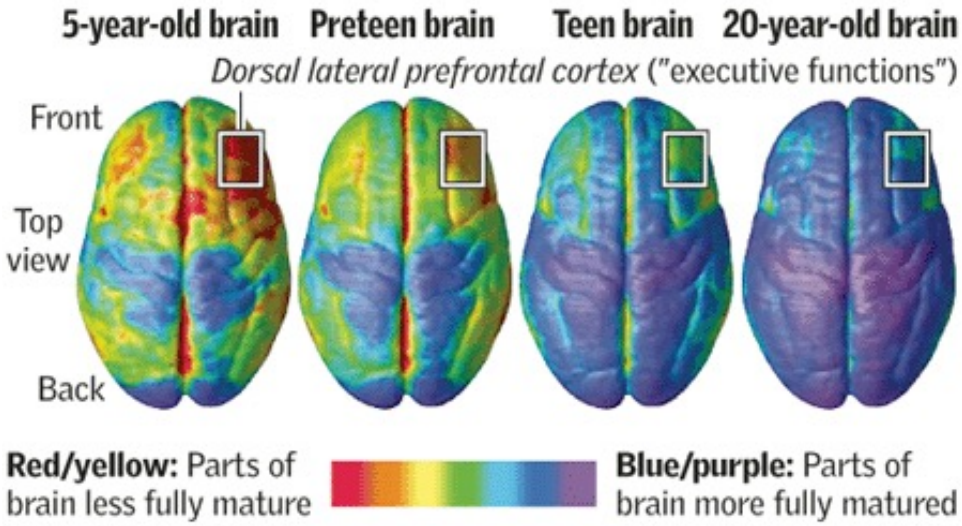
Figure 3 Network representation of developing microstructure. **The correlation of corrected age at MRI with structural connections weighted by NODDI intracellular volume fraction index** (or neurite density index, NDI), in a population of 65 infants scanned between 25 and 45 weeks of postmenstrual age (PMA). In panel (A) NDI parameters increase with age for most white matter connections, as would be expected. However, when assessed in relative terms (%) of the total connectivity in each subject (panel B and C), it is possible to separate which connections are developing at a relative faster or slower pace. This clarifies the expected heterochronicity in the early development of brain connectivity, with **a general trend of connections between somatosensory, central, subcortical and temporal areas to show faster development (red) than frontolimbic and interhemispheric connections (blue).** Adapted from Batalle et al. (2017) [

Batalle, D., Edwards, A. D., & O'Muircheartaigh, J. (2018).

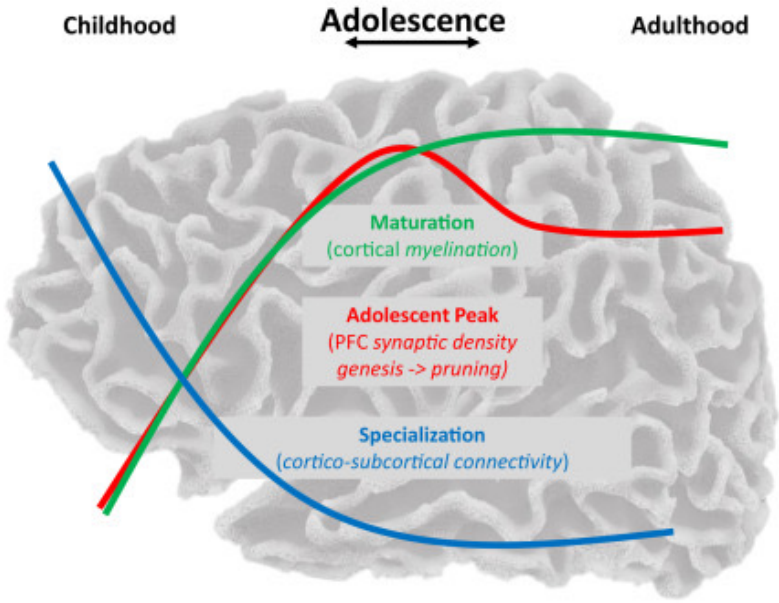


Leisman et al., 2015

Adolescent brain: Puberty



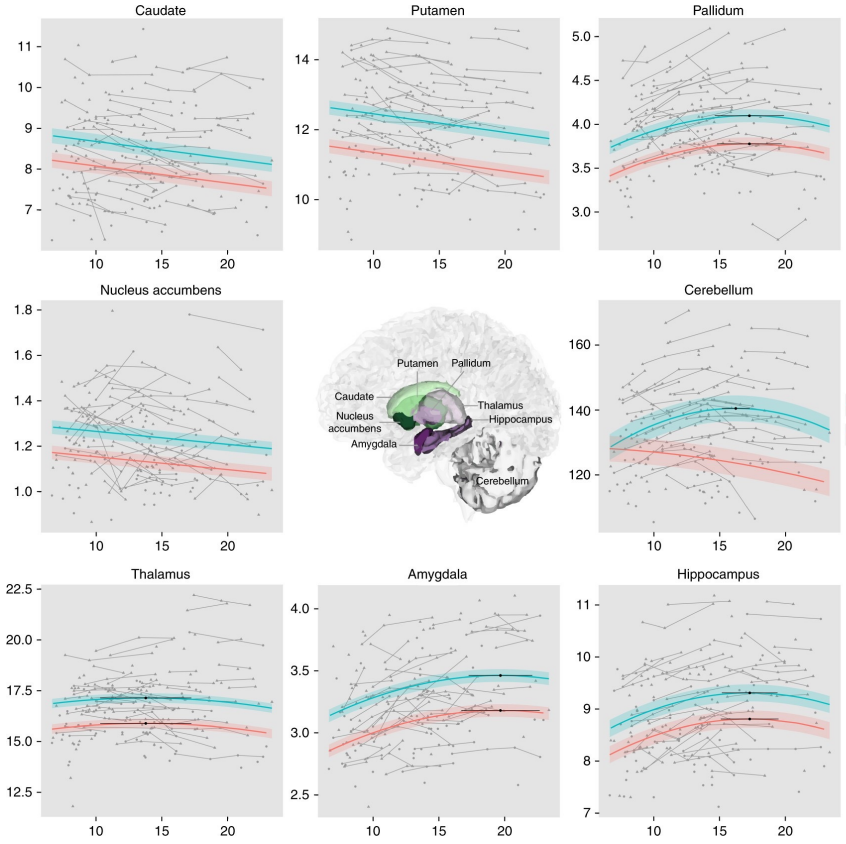
Summary of work by Nitin Gogtay & Jay Giedd, 2004

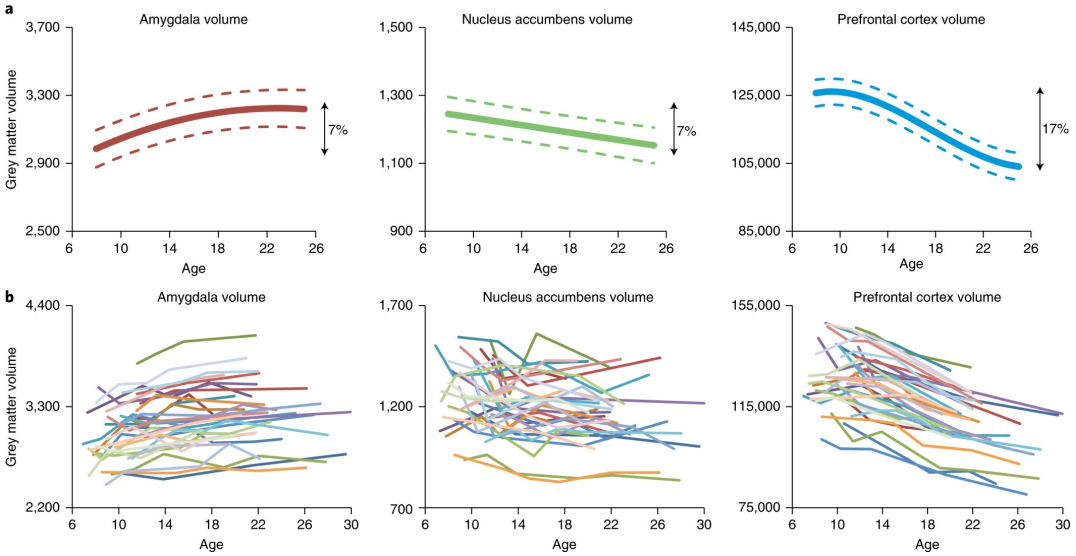


Luna, Tervo-Clemmens, & Calabrao, 2021

https://www.youtube.com/watch?v=Gnm8f76zx0g

Adolescent brain: Puberty





Foulkes & Blakemore, 2018

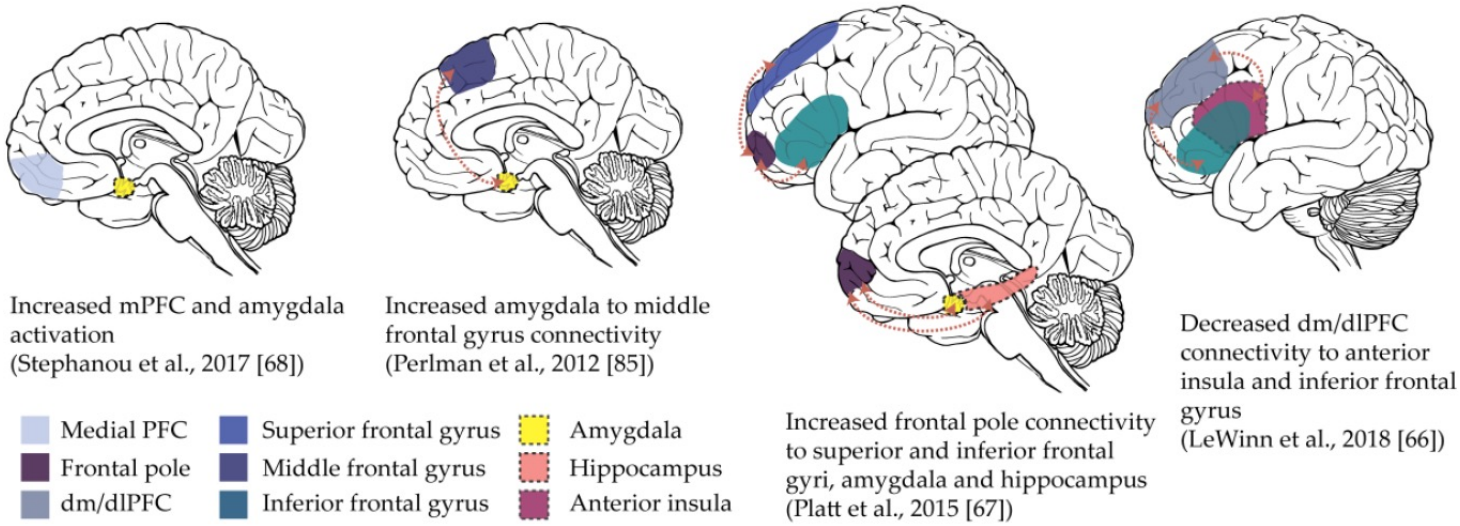


Figure 1. Patterns of altered neural activation and connectivity during emotion regulation in adolescents with depression. Overall, studies to date have demonstrated altered activation and connectivity in the amygdala and across regions of prefrontal cortex. The directionality of effects (greater or lesser in depressed compared to non-depressed participants), and the specific set of regions involved however varies across studies. (PFC: prefrontal cortex, dm/dlPFC: dorsomedial/dorsolateral PFC).

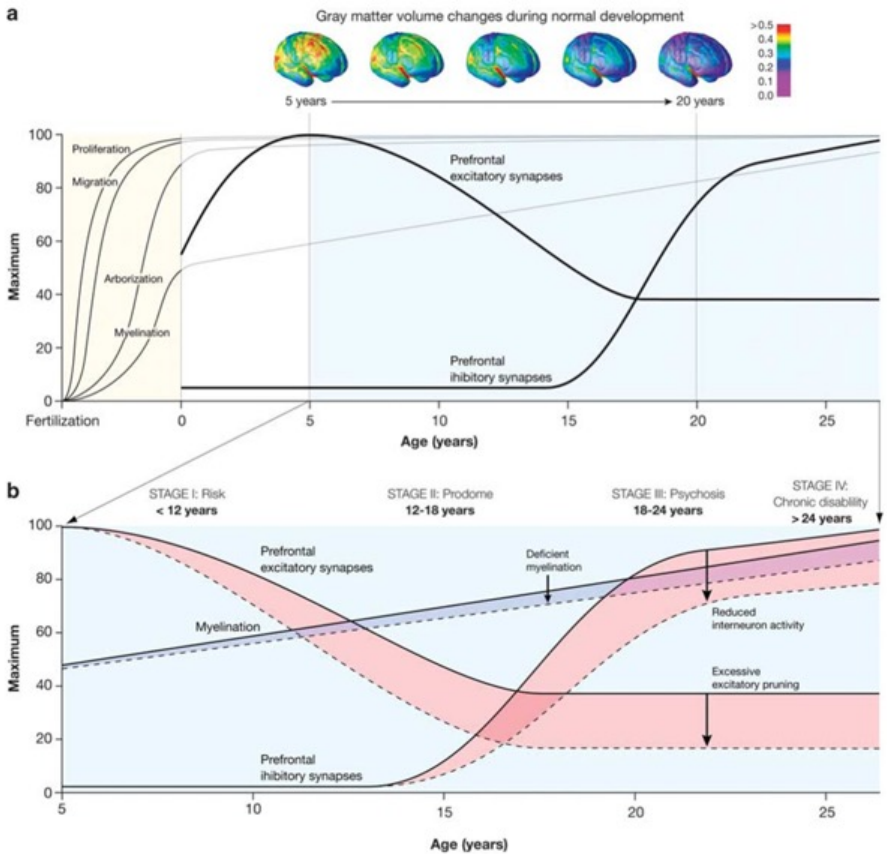
Young et al, 2019

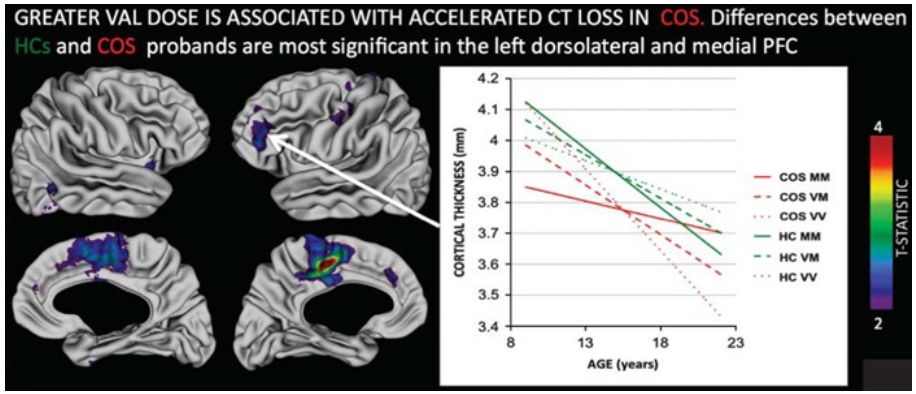
Table 1. Reviewed evidence investigating links between emotion regulation and anxiety and depression in adolescence. Findings are organized according to negative and positive emotion regulation, and by methodology. (dlPFC: dorsolateral prefrontal cortex; dmPFC: dorsomedial prefrontal cortex; IFG: inferior frontal gyrus; IFL: inferior frontal lobule; MFG: middle frontal gyrus; PFC: prefrontal cortex; RSA: respiratory sinus arrhythmia; SFG: superior frontal gyrus; vlPFC: ventrolateral PFC).

Self-Report	Behavioral	Psychophysiological	Neural (fMRI)
Normative Age-Related Changes			
Increased use of 'adaptive' strategies, less use of 'maladaptive' strategies with age [5,12].	Reappraisal, but not distraction, improves linearly with age (ability does not always correlate with self-reported everyday use [26–28]).	Some evidence of age-related changes in RSA across adolescence [29].	Reduced amygdala reactivity with age [30–33], greater inverse PFC-amygdala connectivity, indicating better 'top-down' regulation [34,35].
Negative Emotion Regulation			
Associations with symptoms of anxiety			
More use of 'maladaptive' and less use of 'adaptive' strategies in anxiety disorders [36,37]. Social anxiety linked to reduced 'emotional clarity', reduced acceptance [38], and increased rumination [39].	Impaired reappraisal generation in anxiety disorders [40,41]. No differences in 'amplifying' or 'suppressing' expressive behaviors [42].	Greater number of visual fixations during negative images [43] and greater pupil dilation when 'upregulating' response to negative images [44] in adolescents with anxiety disorders.	Positive amygdala–vlPFC connectivity during affect labeling predicted future anxiety symptoms [45].
Associations with symptoms of depression			
More use of 'maladaptive', less use of 'adaptive' strategies in depression [36]. Specifically, less use of reappraisal [46], reduced acceptance [47] and higher suppression [48].	Mixed findings for reappraisal efficacy [49–51] in adolescents with depression.	Changes in RSA with age, linked to better 'acceptance', 'impulse control' and 'ability to use emotion regulation strategies' [52] in individuals with depression and conduct problems. RSA predicts more maladaptive emotion regulation in previously depressed adolescents [53]. Limited evidence of direct relationship between RSA and depression [54,55].	Evidence of disrupted activation and connectivity across emotion regulation neural circuitry (e.g., amygdala, PFC) in depression, but specific patterns of effects vary across studies ([49–51,56], see Figure 1).
Impacts link between stress and psychopathology			
Self-blame, catastrophizing, and rumination mediates the association between stress and depression [57]; rumination and impulsive responding links stress and internalizing symptoms [58].	Cognitive reappraisal mediates link between depressive symptoms and 'emotional recovery' from an experimental stressor [59].	RSA mediates the association between stress and anxiety [55]	Amygdala–vlPFC connectivity during incidental emotion regulation mediates the relationship between rumination and depressive symptoms [60]
Positive Emotion Regulation			
Associations with symptoms of anxiety			
Not investigated	Not investigated	Greater number of visual fixations during positive images in adolescents with anxiety disorders [43].	Not investigated
Associations with symptoms of depression			
Lower levels and shorter duration of positive affect [61,62], parental and self 'dampening' of positive emotions [63], lack of parental 'enhancing' [64] associated with depressive symptoms.	Reduced persistence of positive affect in conflict situation [65], low maternal positivity [66], and increased maternal dampening [67] associated with depressive symptoms.	Not investigated	Reduced activation of ventral striatum and PFC in response to reward (Forbes, 2011 #123 [68]), regulation not investigated
Impacts link between stress and psychopathology			
Not investigated	Not investigated	Not investigated	Not investigated

Young et al, 2019

Developmental model of schizophrenia

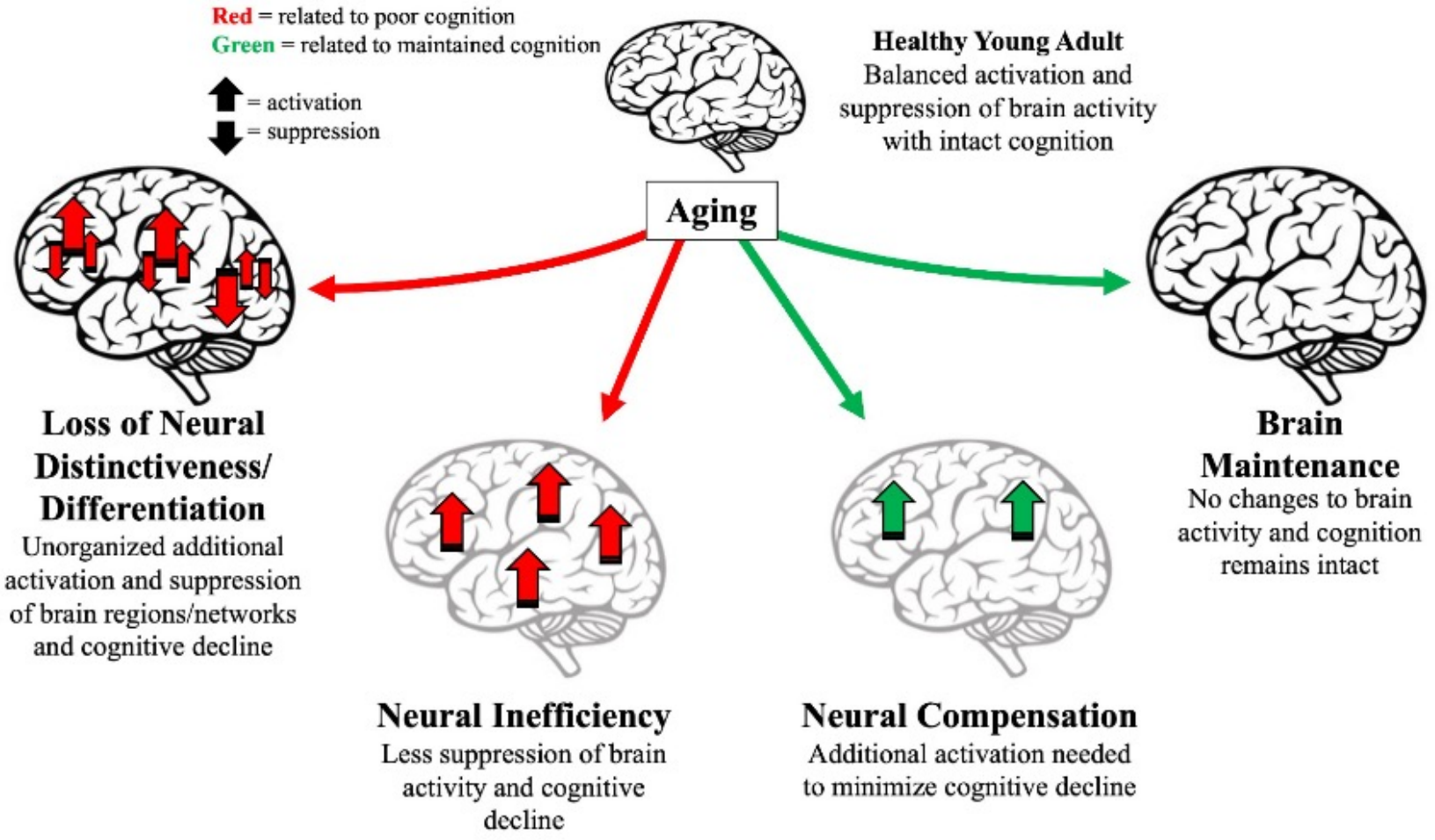




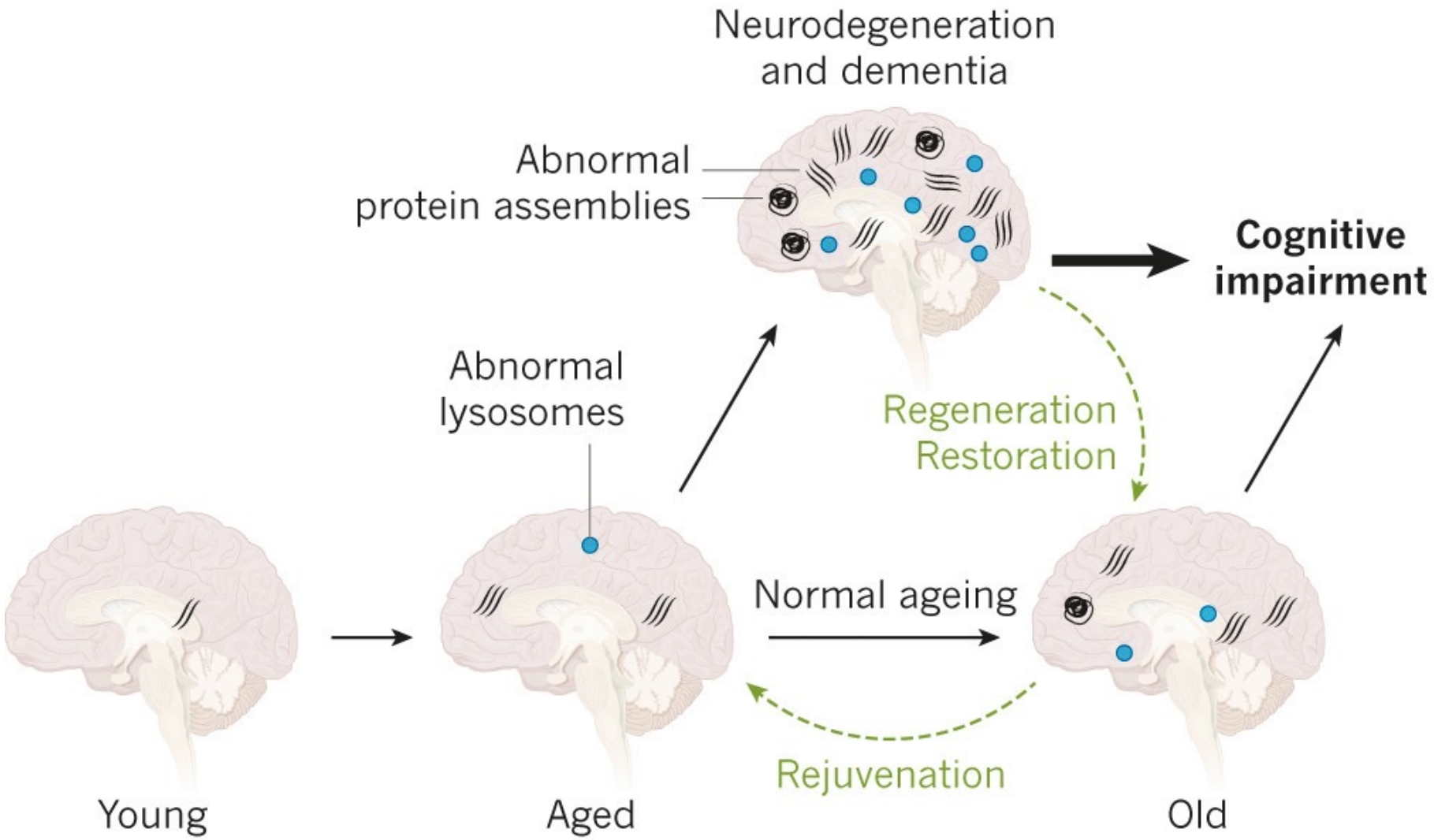
Regions where the relationship between COMT Val158Met Val allele dose and cortical thickness change is significantly different in healthy controls (HCs) as compared to probands with childhood-onset schizophrenia (COS). The inset plot illustrates this interaction for the left dorsolateral prefrontal region, where increased Val dose attenuates cortical thinning on HCs, but accelerates it in probands with COS. Note that by adulthood, COS Val homozygotes have persistent cortical thickness deficits compared with HCs, whereas Met homozygotes do not. All colored regions shown survive false discovery rate correction for multiple comparisons at $q < 0.05$.85

Rapoport et al., 2012

Patterns of Brain Aging



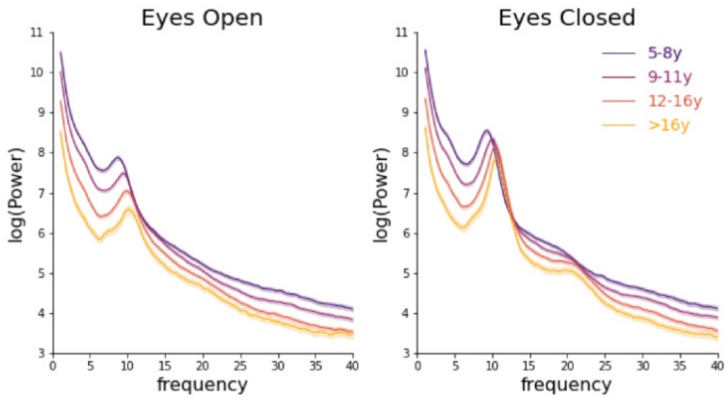
McDonough, Nolin, & Visscher, 2022



Wyss-Coray, 2016

Anticipated changes: EEG spectra

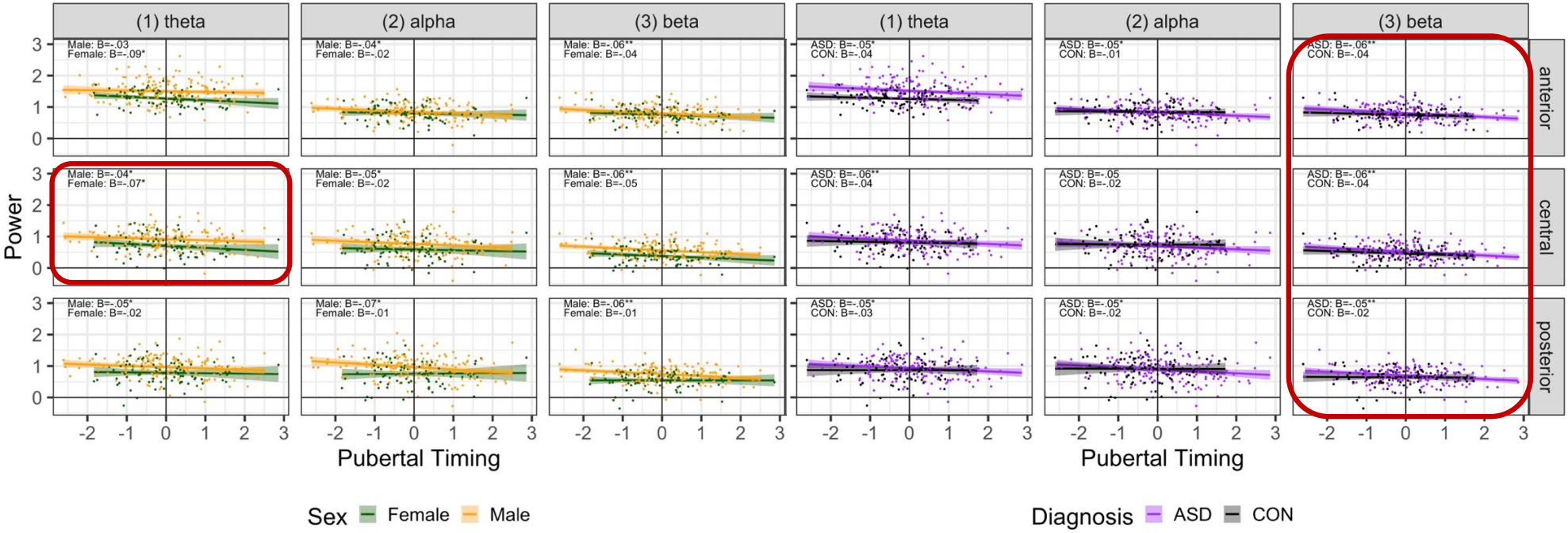
- Spectra power decreases over age
  - More specifically, new evidence suggesting that it reduces with pubertal development/maturation



Caffarra et al., 2022

Anticipated changes: EEG spectra

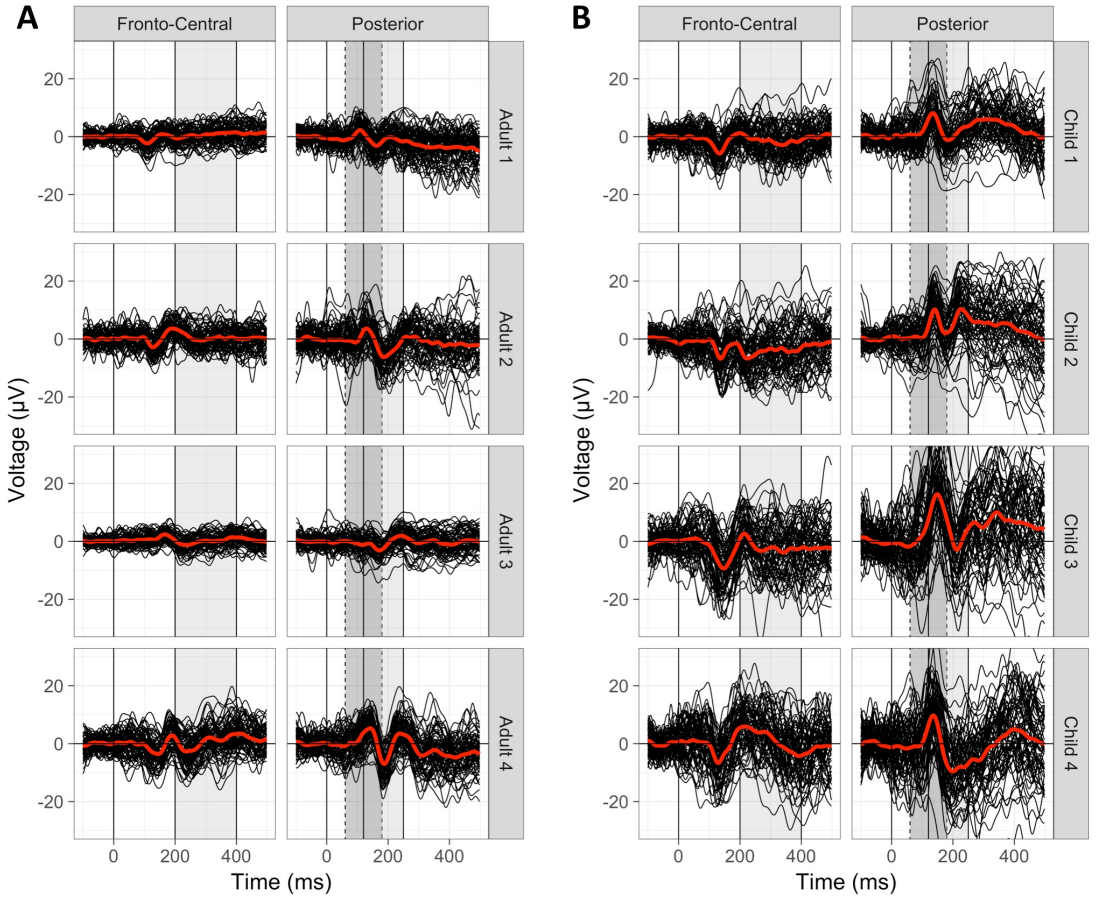
With relatively early pubertal maturity, spectral power reduces;
Particularly notable in ASD and males



Rea et al., in revision

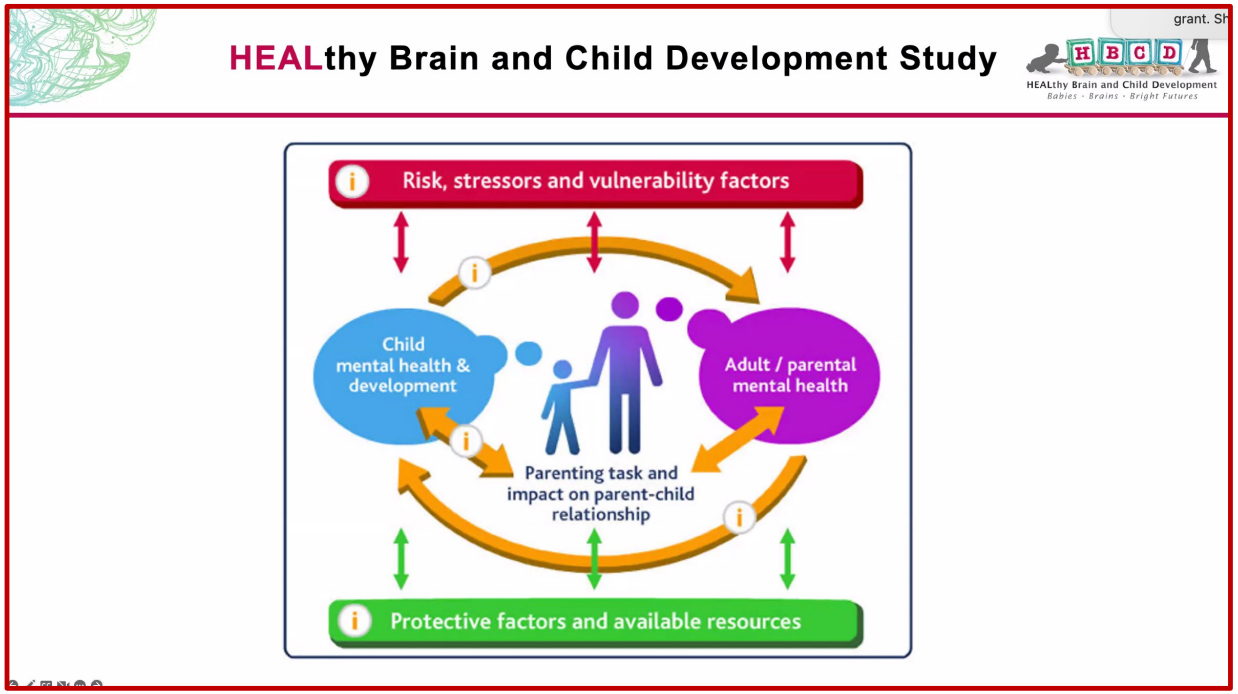
Anticipated changes: ERP

- Brain waves become faster
  - Latency reduces (i.e., peaks closer to stimulus onset)
- With synaptic pruning and increased cortical volume:
  - Amplitude decreases



Hudac et al., 2021

Example from HBCD



~7,200 infants
300 / site

– Funded Institutions and Locations

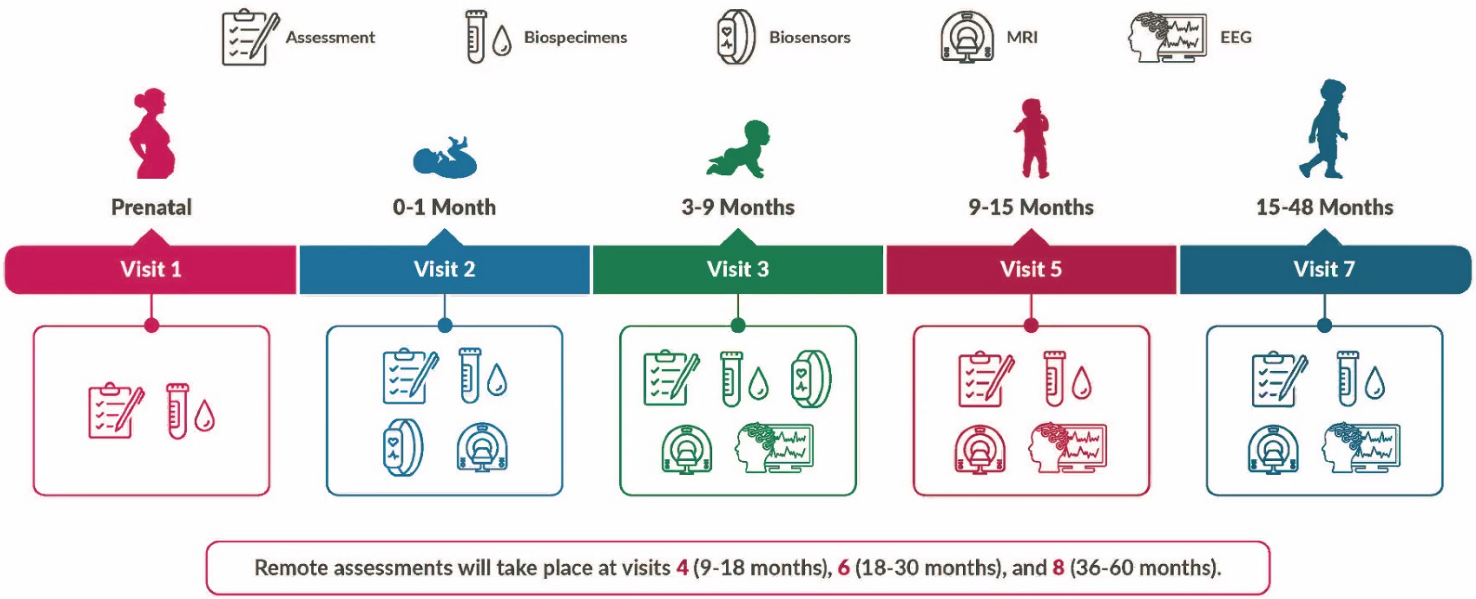
Phase II

- **Arkansas Children's Hospital Research Institute** – Arkansas
- **Boston Children's Hospital** – Massachusetts
- **Cedars-Sinai Medical Center** – California
- **Children's Hospital of Los Angeles** – California
- **Children's Hospital of Philadelphia** – Pennsylvania
- **Cincinnati Children's Hospital Medical Center** – Ohio
- **Emory University** – Georgia
- **Johns Hopkins University/ Kennedy Krieger Institute** – Maryland
- **New York University School of Medicine** – New York
- **Northwestern University** – Illinois
- **Oklahoma State University Center for Health Sciences** – Oklahoma
- **Oregon Health and Science University** – Oregon
- **Pennsylvania State University** – Pennsylvania
- **University of Alabama at Birmingham** – Alabama
- **University of California, San Diego** – California
- **University of Florida** – Florida
- **University of Maryland** – Maryland
- **University of Minnesota** – Minnesota
- **University of New Mexico Health Sciences Center** – New Mexico
- **University of North Carolina Chapel Hill** – North Carolina
- **University of Vermont** – Vermont
- **University of Wisconsin-Madison** – Wisconsin
- **Vanderbilt University** – Tennessee
- **Virginia Tech** - Virginia
- **Washington University** – Missouri

HEALthy Brain and Child Development Study

HEALthy Brain and Child Development
Babies · Brains · Bright Futures

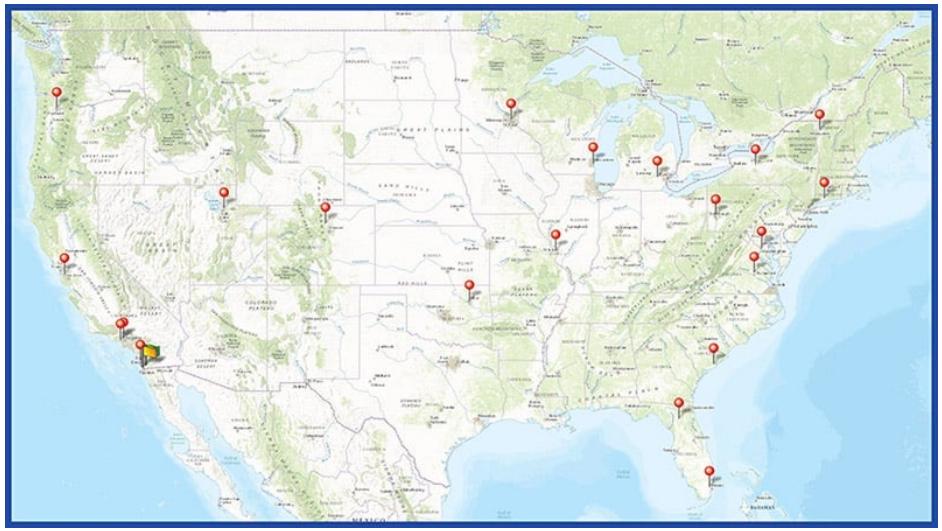
Timeline of Events



Remote assessments will take place at visits **4** (9-18 months), **6** (18-30 months), and **8** (36-60 months).

Will connect to Adolescent Brain Cognitive Development (ABCD) Study

- 11,880 children enrolled at ages 9-10 across the US
- Goal is to retain 10,000 into early adulthood



Adolescent Brain Cognitive Development®

Teen Brains. Today's Science. Brighter Future.

ABCD Study

TIMELINE OF EVENTS

	9-10		10-11		11-12
STUDENT TIME	6–7 hours	15 minutes	2 hours	15 minutes	6–7 hours
STUDENT ACTIVITY		every 3–6 months		every 3–6 months	
PARENT TIME	3 hours	5 minutes	1 hour	5 minutes	3 hours
PARENT ACTIVITY					

REPEAT ... *until age 19-20*

LEGEND: In-Person Visit · Phone Call · Paper and Pencil Tests · iPad Tasks · Brain Scan · Biosamples · Interview

ABCD Youth Protocol Summary: Baseline

Physical Health

PhenX Anthropometrics (height/ weight/waist measurements)

Snellen Vision Screener

Edinburgh Handedness Inventory

Youth Risk Behavior Survey - Exercise

Pubertal Development Scale and Menstrual Cycle Survey

Screen Time Survey

Brain Imaging

Structural MRI

- 3D T1 - Weighted
- 3D T2 - Weighted
- Diffusion Tensor Imaging

Functional MRI (fMRI)

- Resting State
- Monetary Incentive Delay Task
- Stop Signal Task
- Emotional N-Back Task

Biospecimens

Subset of participants:
Breathalyzer (alcohol screen)
Oral fluids (drug screen)
Blood (DNA)

Oral Fluids (DNA, pubertal hormones)

Hair (substance use metabolites)

Baby Teeth (substance and environmental toxin exposure)

Mental Health

Kiddie Schedule for Affective Disorders and Schizophrenia

- Background Items Survey
- Diagnostic Interview for DSM-5 (Mood, Social Anxiety, Generalized Anxiety Disorder, Suicide, and Sleep modules)

UPPS-P for Children - Short Form (ABCD version)

PhenX Behavioral Inhibition/ Behavioral Approach System (BIS/BAS) Scales

Prodromal Psychosis Scale

Youth Resilience Scale

Neurocognition

NIH Toolbox Tasks:

- Picture Vocabulary
- Flanker Inhibitory Control & Attention
- List Sorting Working Memory
- Dimensional Change Card Sort
- Pattern Comparison Processing Speed
- Picture Sequence Memory
- Oral Reading Recognition

Rey Auditory Verbal Learning Task

Cash Choice Task

Little Man Task

Matrix Reasoning Task

RAVLT Delayed Recall

Substance Use

For most participants*:

Participant Last Use Survey (PLUS) for substance use within the last 24 hrs

PhenX Peer Group Deviance Survey

PATH Intention to Use Tobacco Survey

Timeline Follow-Back Survey

Caffeine Intake Survey

Culture & Environment

Prosocial Behavior Survey

PhenX Acculturation Survey

Parental Monitoring Survey

Acceptance Subscale from Children's Report of Parental Behavior Inventory - Short

PhenX Family Environment Scale - Family Conflict

PhenX Neighborhood Safety/Crime Survey

PhenX School Risk & Protective Factors Survey

Adolescent Brain Cognitive Development®

Teen Brains. Today's Science. Brighter Future.

ABCDStudy.org

*For participants with differing levels of substance use, follow-up items include: 1) Low level (ever had sip or puff): iSay II Q2 Sipping Items, Tobacco Low-Level Use Measure, Marijuana Low-Level Use Measure; 2) Moderate level (ever had a full drink or more than a puff): PhenX Acute Subjective Response to Alcohol, Tobacco, or Marijuana; 3) Heavy level (used substance two or more days in the past 12 months): Hangover Symptom Scale, Rutgers Alcohol Problem Index (RAPI), Nicotine Dependence (PATH), Marijuana Problem Index (MAPI), Drug Problem Index (DAPI).

TABLE 1
Existing Pdiatric Neuroimaging Data Collection and Sharing Initiatives

	Data Sets Currently Available	*Age Range (Years)*	*Variables Collected*	*Strengths*	*Limitations*
Philadelphia Neurodevelopmental Cohort	TD: 1,445	8–21	Neuroimaging: sMRI, DWI, ASL, tfMRI, rsfMRI Other: Kiddie–SADS; Penn CNB	All data acquired on same scanner platform. Genotype available.	rsfMRI collected with relatively long TR (3,000 ms).
Adolescent Brain Cognitive Development	TD: 4,010 (inaugural data release)	9–10	Neuroimaging: sMRI, DWI, tfMRI, rsfMRI Other: Kiddie–SADS and other clinical measures, NIH toolbox, physical, cultural, biological measures	Uses harmonized HCP protocol. Genotype, longitudinal, and sleep data will be available.	Data collection ongoing. Data collection on different scanner platforms.
HCP Lifespan Development	TD: 1,350	5–21	Neuroimaging: sMRI, multishell DWI, tfMRI, rsfMRI Other: extensive battery of social, behavioral, and neurocognitive measures	Uses harmonized HCP protocol. rsfMRI collected with short TR (720 ms). Genotype, sleep data, and pubertal status will be available. Longitudinal data available for subset.	Data collection ongoing.
IMAGEN	TD: > 2,000	14, follow up at 16, 19, 22	Neuroimaging: sMRI, DWI, tfMRI, rsfMRI Other: extensive battery of social, behavioral, and neurocognitive measures	Longitudinal data collected at multiple timepoints will be available. Genotype and pubertal status available. Collaboration with ENIGMA.	Data collection on different scanner platforms. Recruitment emphasized ethnic homogeneity.
ABIDE I and II	ABIDE I ASD: 539, TD: 573 ABIDE II ASD: 521, TD: 593	5–64	Neuroimaging: sMRI, rsfMRI Other: some clinical assessments	Wide age ranges available. Preprocessed neuroimaging data available.	Data collection on different scanner platforms. Limited phenotypic information.
ADHD-200	ADHD: 285 TD: 491	7–21	Neuroimaging: sMRI, rsfMRI Other: some clinical assessments	Wide age ranges available.	Data collection on different scanner platforms. Limited phenotypic information.
SchizConnect	Schizophrenia: 384 TD: 632	0–67	Neuroimaging: sMRI, tfMRI, rsfMRI Other: some clinical assessments	Wide age ranges available.	Data collection on different scanner platforms. Phenotypic information varies by dataset.
Nathan Kline Institute–Rockland	TD: > 1,000	6–85	Neuroimaging: sMRI, DWI, tfMRI, rsfMRI Other: extensive battery of social, behavioral, and neurocognitive measures	rsfMRI data collected at to different TRs (645 and 1,400 ms) available. All data acquired on same scanner platform.	Limited task fMRI data available.
Pediatric Imaging, Neurocognition, and Genetics	TD: > 1,000	3–20	Neuroimaging: sMRI, DWI, rsfMRI Other: extensive battery of social, behavioral, and neurocognitive measures	Genotype available.	Data collection on different scanner platforms.

Uddin & Karlsgodt, 2018

Outstanding questions / needs

- **Access to research**
  - Participants access (undue burden?); diversity (Dotson & Duarte, 2020)
  - Sharing data across sites → Need for LARGE datasets
- **Acquisition of data**
  - Are methods and accommodations comparable for populations? Effort/fatigue?
- **Analysis**
  - Addressing neurodiversity: is it appropriate to find "atypical" processing (e.g., lack of clinical/env group activations)
  - Prediction models, statistical decisions (Poldrack, Huckins, & Varaoquox, 2020)
- **Dissemination:** Where are those null findings?

Monday discussion

- **Readings targeting development**
  - Lloyd-Fox, S., Papademetriou, M., Darboe, M. K., Everdell, N. L., Wegmuller, R., Prentice, A. M., ... & Elwell, C. E. (2014). Functional near infrared spectroscopy (fNIRS) to assess cognitive function in infants in rural Africa. Scientific reports, 4(1), 1-8.
  - Reider, L. B., Bierstedt, L., Burris, J. L., Vallorani, A., Gunther, K. E., Buss, K. A., ... & LoBue, V. (2022). Developmental patterns of affective attention across the first 2 years of life. Child development, 93(6), e607-e621.
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Goals of breakout rooms

1. **5 minutes**: Identify specific needs of your populations in order to assess affective or emotional brain processes
   - *Clinical / Dev / environmental factors*
2. **5 minutes**: What solutions may be used to address the needs of your population?
3. **5 minutes:** What needs are difficult to address or have outstanding problems?

	Needs	Solution?	Outstanding issue
1			
2			
3			
4			
5			
6			
7			
8			
…			
n			

#1	Pop	Needs	Solution?
1			
2			
3			
4			
5			
6			