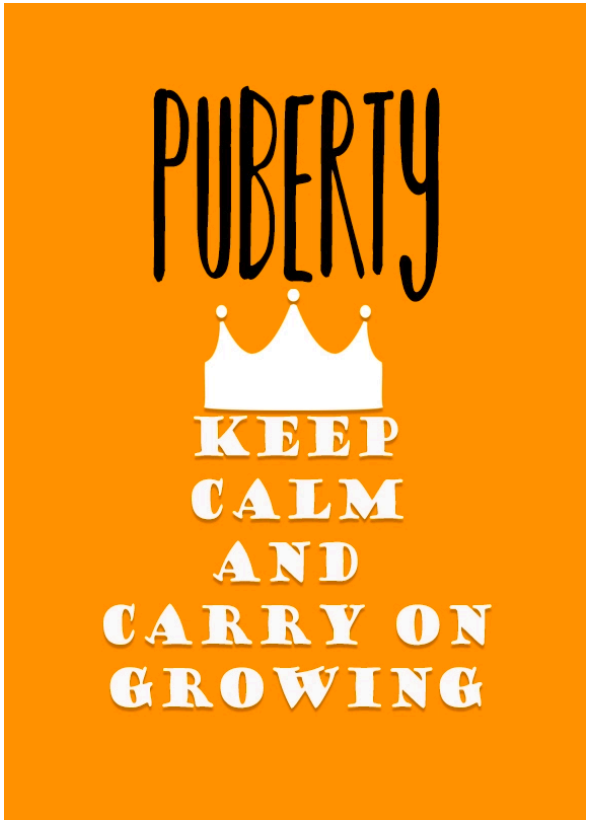
Puberty and Brain Development

Jennifer H. Pfeifer

University of Oregon

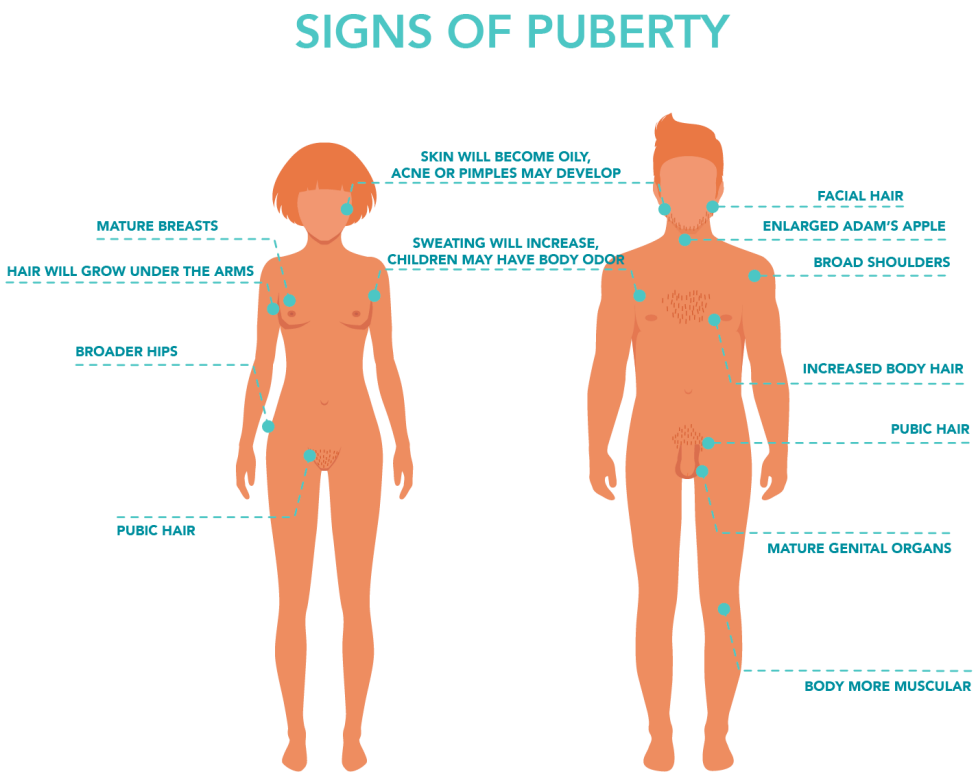


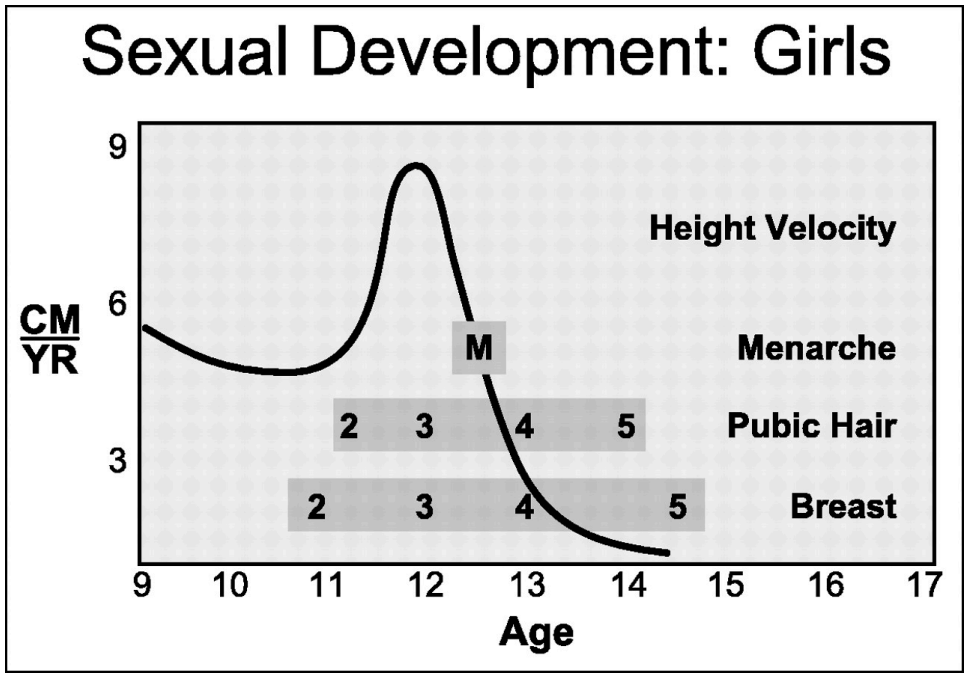
Adolescent Brain and Cognitive Development

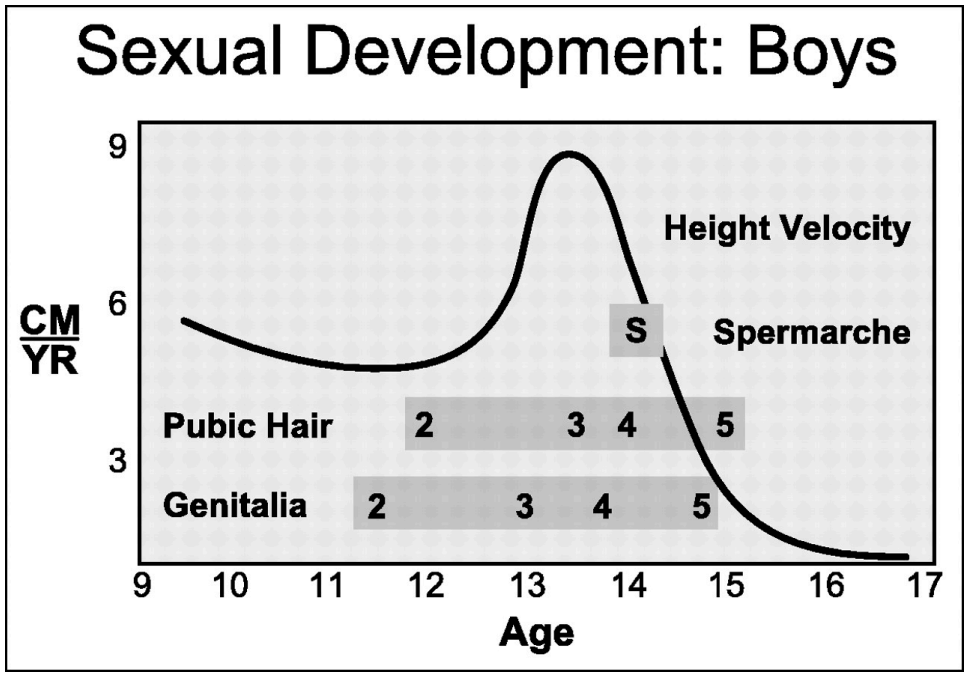
- Who is an adolescent?
- Common definition: Adolescence has a biological beginning in puberty – and a social ending with the assumption of adult rights, roles, and responsibilities.

A “Biological Beginning”

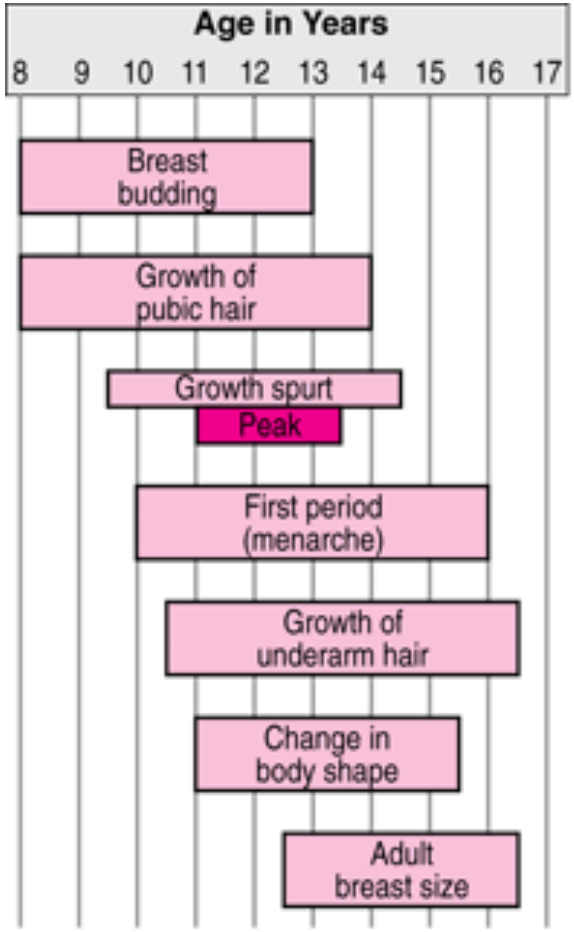
- Puberty
- Multiple phases:
  - Adrenarche
  - Growth spurt
  - Gonadarche



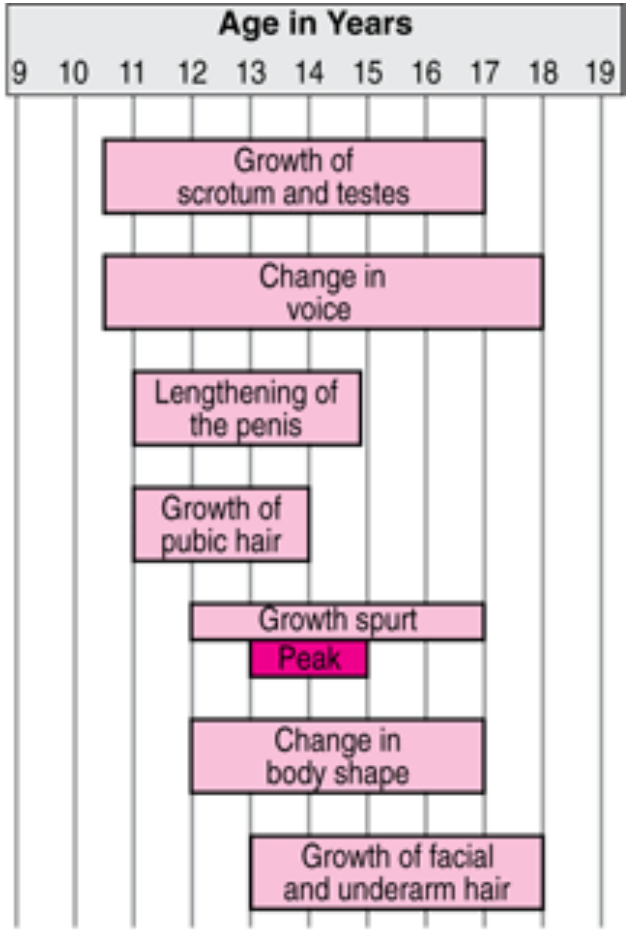

Sexual Development: Girls
CM
YR
9
6
3
Height Velocity
M
Menarche
2 3 4 5
Pubic Hair
2 3 4 5
Breast
9 10 11 12 13 14 15 16 17
Age


Sexual Development: Boys
CM
YR
9
6
3
Height Velocity
S
Spermarche
Pubic Hair
2 3 4 5
Genitalia
2 3 4 5
9 10 11 12 13 14 15 16 17
Age

Rosen (2004)


Age in Years
8 9 10 11 12 13 14 15 16 17
Breast budding
Growth of pubic hair
Growth spurt
Peak
First period (menarche)
Growth of underarm hair
Change in body shape
Adult breast size

Girls


Age in Years
9 10 11 12 13 14 15 16 17 18 19
Growth of scrotum and testes
Change in voice
Lengthening of the penis
Growth of pubic hair
Growth spurt
Peak
Change in body shape
Growth of facial and underarm hair

Boys

Puberty is a more nuanced measure of maturation than chronological age

- Puberty is arguably a better measure of maturation during early to mid adolescence
- Pubertal **stage** vs **timing** vs **tempo**
  - Stage: how 'mature' are you?
  - Timing: relative to same-age, same-sex peers (early, on-time, or late)?
  - Tempo: how fast (or not) are you moving through puberty?
- Note: after secondary sex characteristics finish maturing, hormone levels continue to increase until mid-twenties

Somerville (2016)

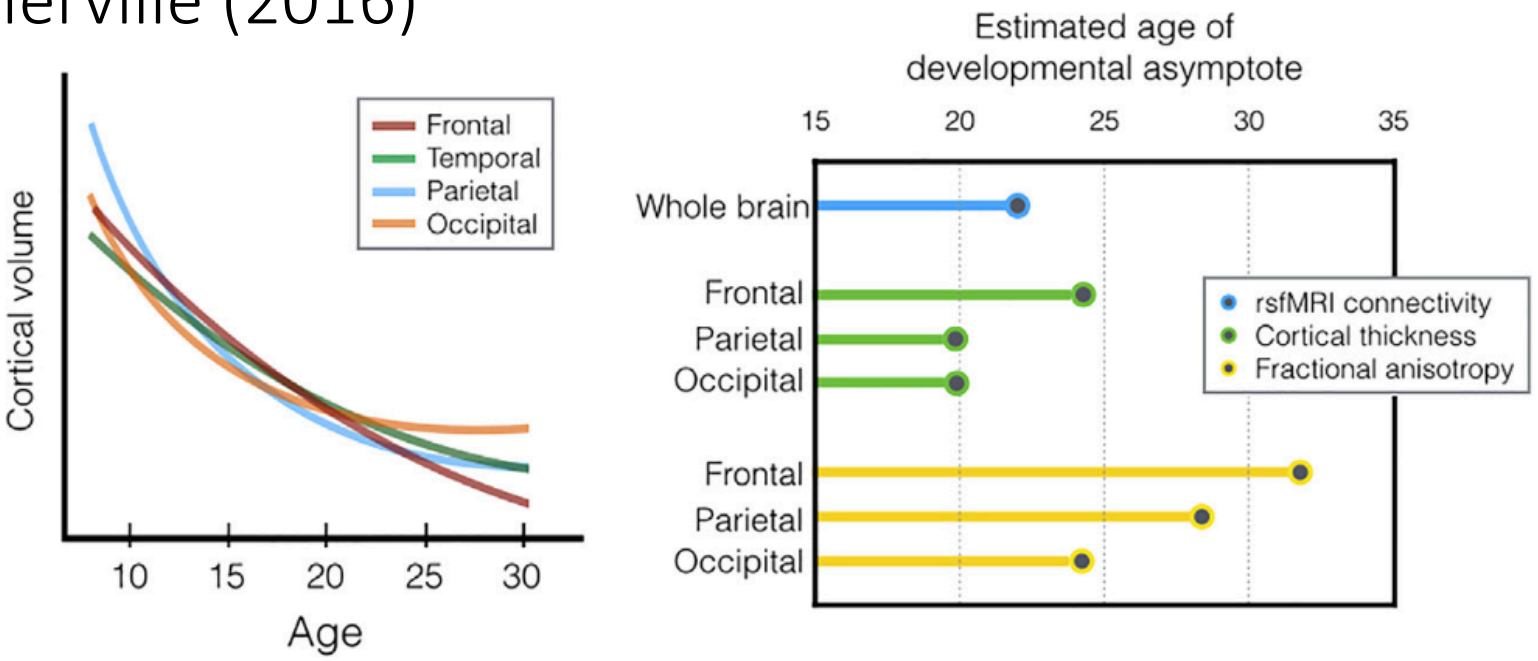


Figure 1. Regional and Methodological Variance in Neurodevelopmental Indices

(A) Trajectories of cortical gray matter volume adjusting for total brain volume. Trajectories are schematized from data reported in Ostby et al. (2009).

(B) Ages of developmental asymptote for connectivity and structural data. Resting-state functional connectivity (rsfMRI) data from Dosenbach et al. (2010) and the other measures reflect data reported in Tamnes et al. (2010). Note that the operationalization of "asymptote" varies by study.

A “Social Ending” (?)

adult·ing
(noun)

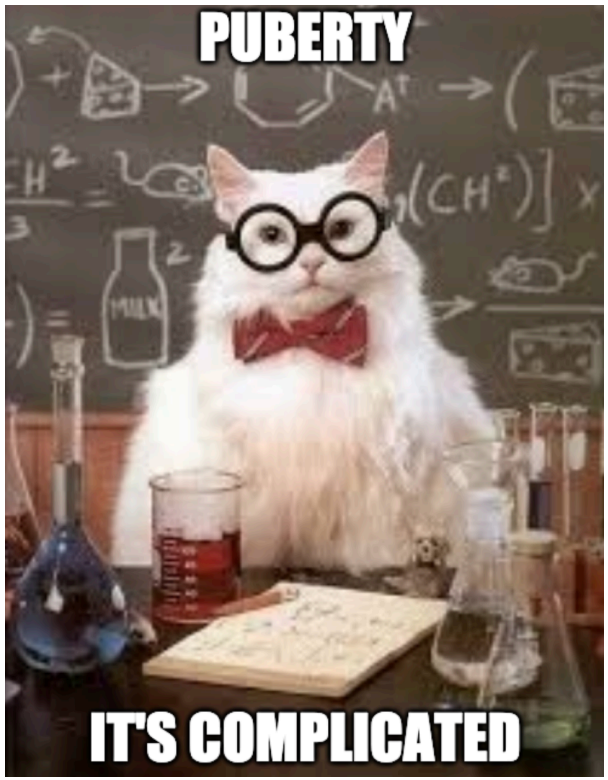
The practice of behaving in a way characteristic of a responsible adult, especially the accomplishment of mundane but necessary tasks.

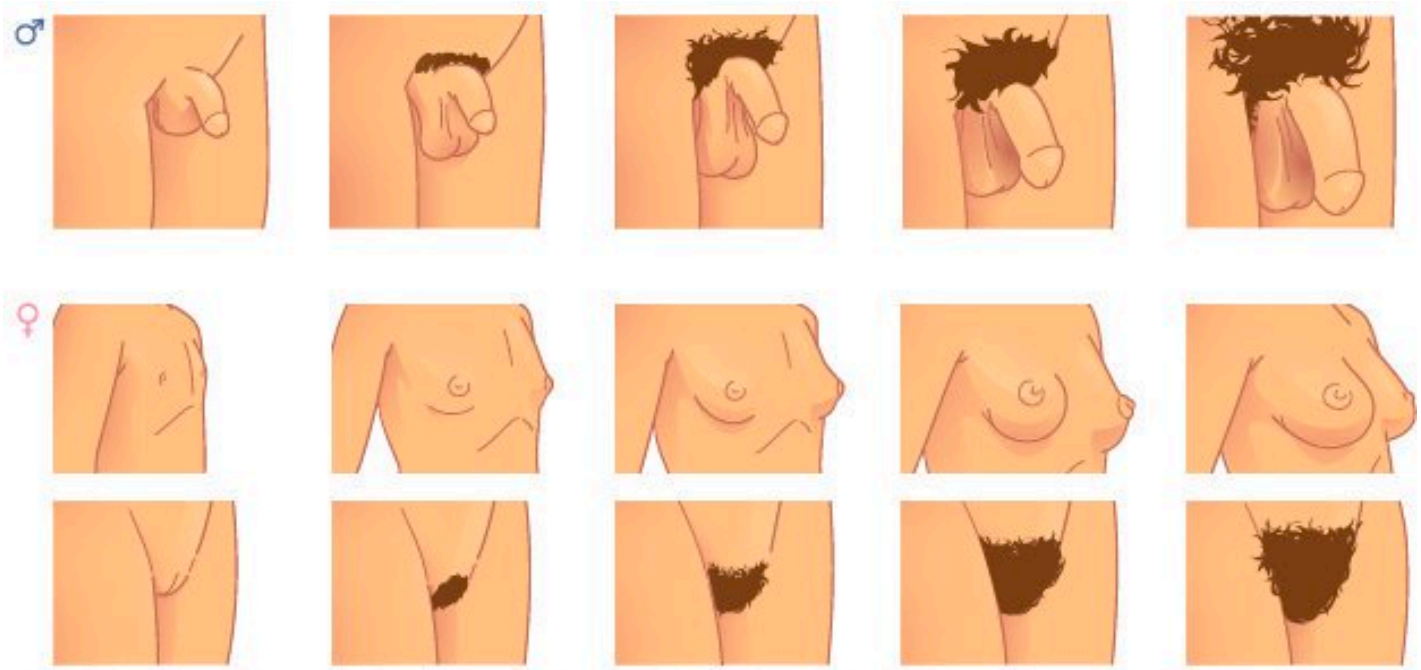
How does puberty impact brain development?: Perspectives from animal models

- Organization-Activation hypothesis about effects of steroid hormones (Sisk & Foster, 2004; Schulz et al., 2009):
  - **Organizational effects:** Hormones permanently change neural structure (during sensitive periods)
  - **Activational effects:** Hormones temporarily change activity of neural systems
  - See also Juraska & Willing, 2017
- Recent insight: organizational effects aren't limited to perinatal period – they happen in adolescence, too!

How can we study puberty's impact on *human* brain development?

- Ways to measure puberty
  - Secondary sexual characteristics
    - Physician/nurse practitioner exams
    - Self-report (text, line drawings, or photographs)
  - Hormones
    - Testosterone, DHEA(-S), Estradiol, Progesterone
    - How many samples? Saliva? What time of day? Hair?
- How does ABCD do it?
  - Parent/self report on Pubertal Development Scale (Petersen et al., 1988)
  - 1 saliva sample (DHEA, T; and E2 in girls)





Stage I

No sexual hair ♂ ♀
Flat-appearing chest with raised nipple ♀

Pre-pubertal

Stage II

Pubic hair appears ♂ ♀ (pubarche)
Testicular enlargement ♂
Breast bud forms ♀ (thelarche)

~ 8–11.5 years

Stage III

Coarsening of pubic hair ♂ ♀
Penis size/length ↑ ♂
Breast enlarges, mound forms ♀

~ 11.5–13 years

Stage IV

Coarse hair across pubis, sparing thigh ♂ ♀
Penis width/glans ↑ ♂
Breast enlarges, raised areola, mound on mound ♀

~ 13–15 years

Stage V

Coarse hair across pubis and medial thigh ♂ ♀
Penis and testis enlarge to adult size ♂
Adult breast contour, areola flattens ♀

Usually > 15 years

Handy reviews to bookmark

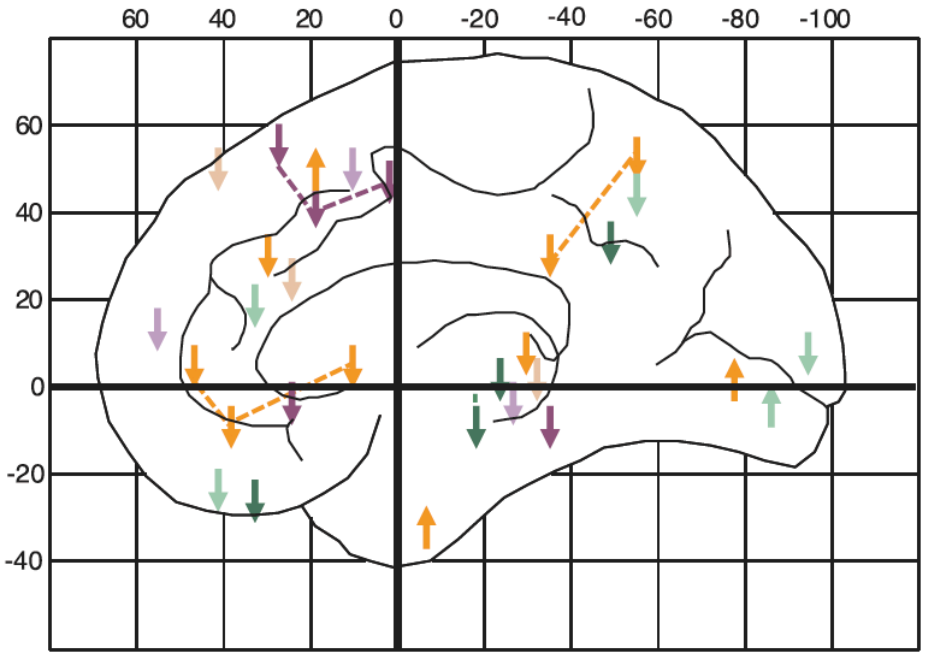
- Vijayakumar, Op de Macks, Shirtcliff, & Pfeifer (2018) – all neuroimaging modalities
- Byrne et al. (2017) – adrenarche
- Herting & Sowell (2017) – structure
- Goddings et al. (2019) – structure
- Dai & Sherf (2019) – fMRI/EEG
- Barendse & Pfeifer (forthcoming Handbook of Dev Cog Neuro)

Puberty and global cortical GM (cross-sectional)

	Without Age		With Age		Age	Sample size
	Female	Male	Female	Male		
Pubertal stage						
Peper et al., 2009b					9	214
Koolschijn et al., 2014					8-25	215
Bramen et al., 2011					10-14	80
Pfefferbaum et al., 2015					12-22	674
Testosterone						
Peper et al., 2009c					10-15	78
Koolschijn et al., 2014					8-25	215
Bramen et al., 2011					10-14	80
Paus et al., 2010					12-18	419
Estradiol						
Peper et al., 2009c					10-15	78
Koolschijn et al., 2014					8-25	215

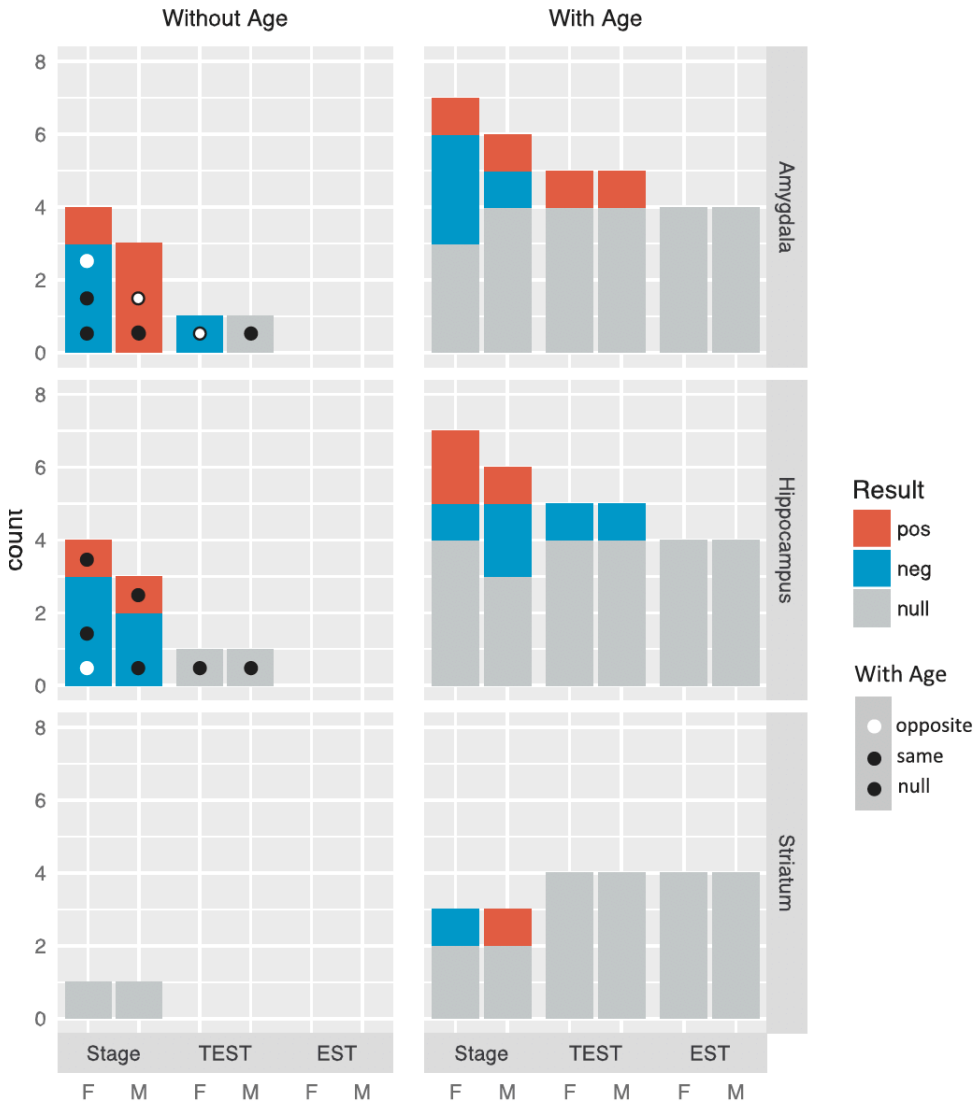
positive
negative
null

Puberty and regional cortical GM



- Consistent decreases in frontal, temporal GM with self-report and hormonal indices of puberty (timing)

Puberty and subcortical GM (amygdala, hippocampus, striatum)



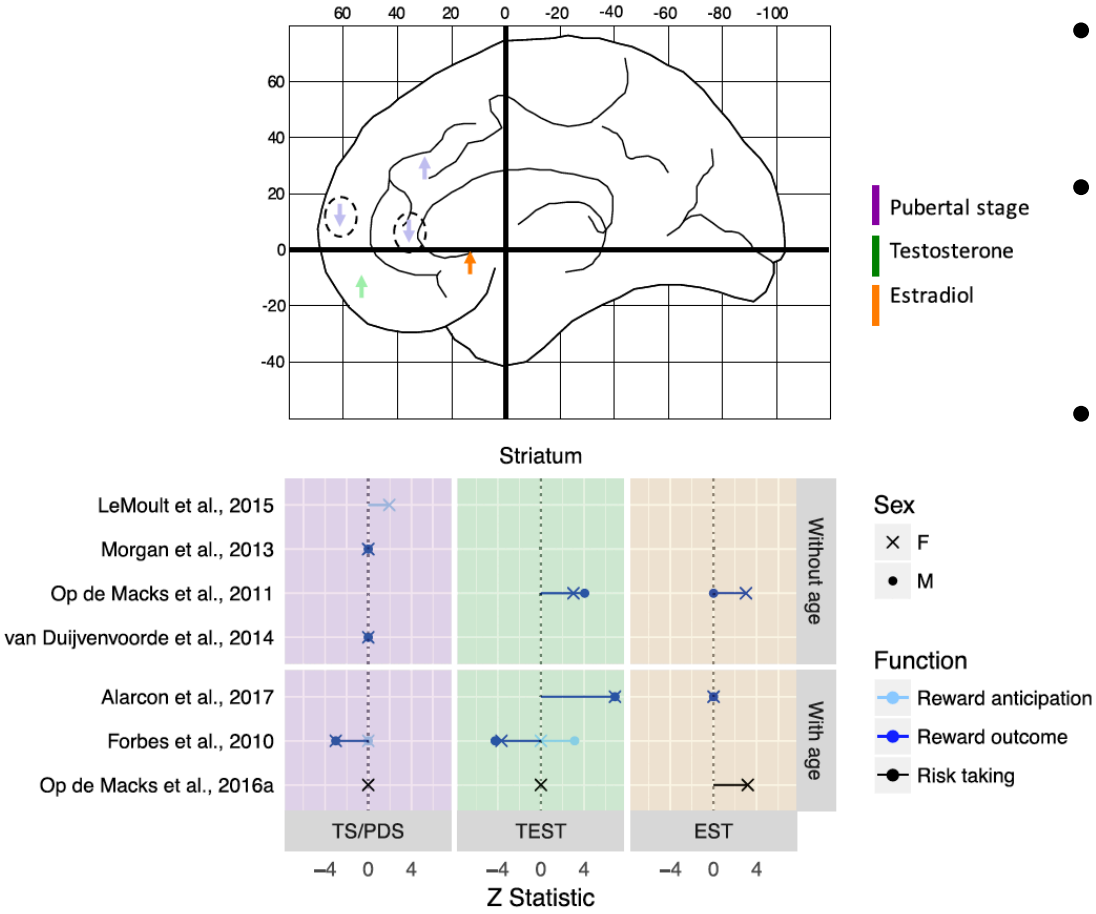
Puberty and WM volume/density, FA, & MD

A)	Volume/density	
	Without age	With age
Pubertal stage		
Chavarria et al., 2014	CC	
Pfefferbaum et al., 2015	global	
Perrin et al., 2009	all lobes	
Peper et al., 2009b		occipital
Pangelinan et al., 2016		CST
Testosterone		
Paus et al., 2010	global	
Herve et al., 2009	CST	CST
Perrin et al., 2008	global	
Peper et al., 2009c		global/regional
Pangelinan et al., 2016		CST
Estradiol		
Paus et al., 2010		global/regional

B)	FA		MD	
	Female	Male	Female	Male
Pubertal stage				
Bava et al., 2012	CST, SCR		ILF, forceps major	
Herting et al., 2012	insula			
	superior front	superior front		
Menzies et al., 2015		SLF, ILF, CLT, CST		SLF, ILF, CLT, CST
Testosterone				
Barendse et al., 2018				
Herting et al., 2012	precentral	superior temp, front, angular gyrus, thalamus, CC, IC		superior front
Peper et al., 2015			subcortico-temp	
Menzies et al., 2015 *				SLF, ILF, CLT, CST
Estradiol				
Herting et al., 2012	angular gyrus, IC, SLF	Cingulum, superior front, precuneus, thalamus		
Peper et al., 2015				
Menzies et al., 2015 *				SLF, ILF, CLT, CST

positive
negative
null

Reward Processes



- Mixed effects in a small number of studies
- Primarily increases, and primarily to reward outcomes
- Decreases observed in armPFC/pgACC, but did not control for age

Braams et al. (2015)

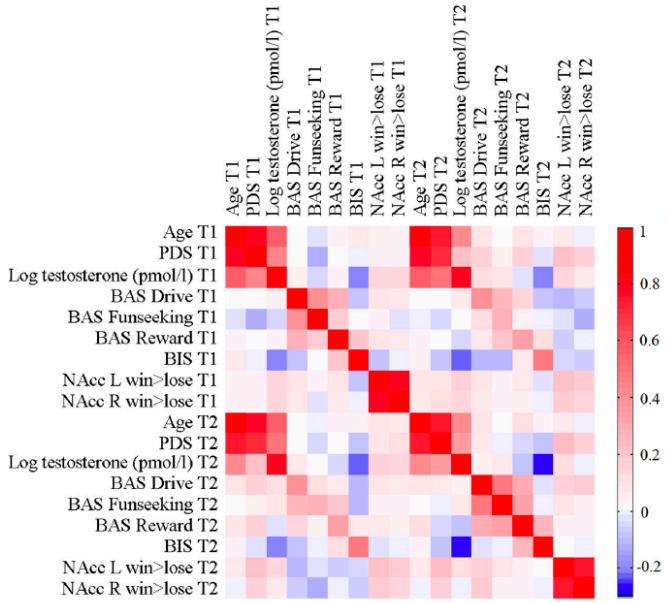
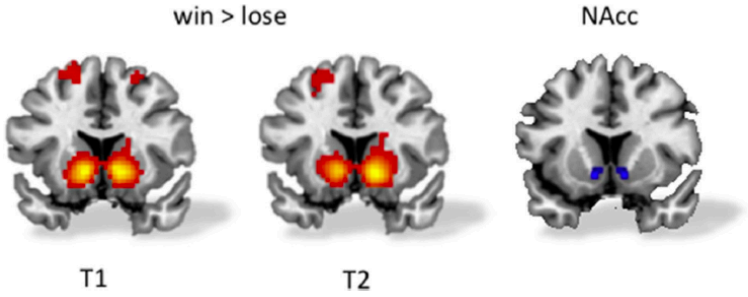
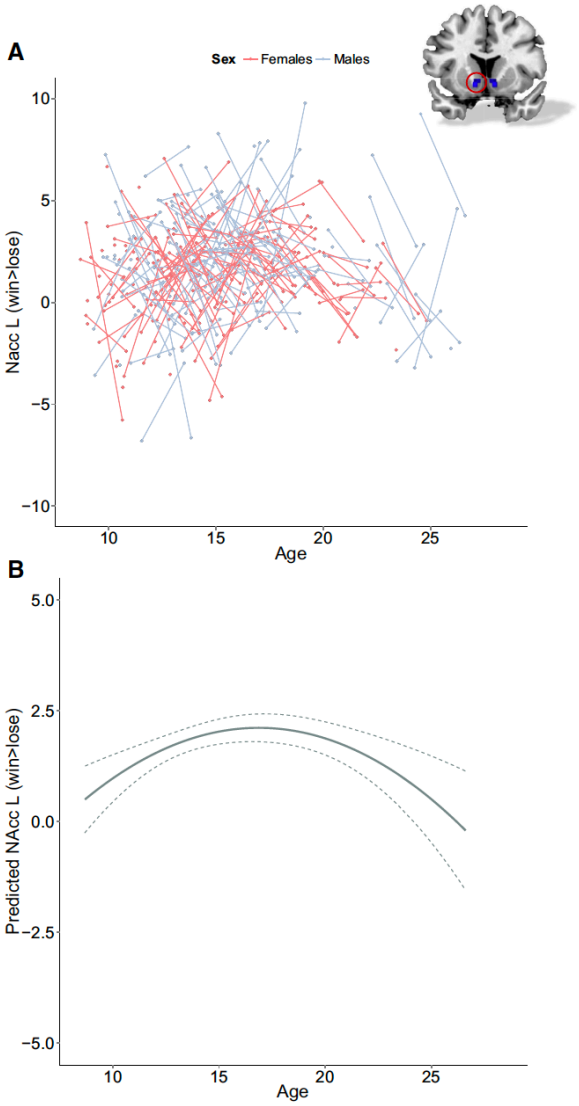
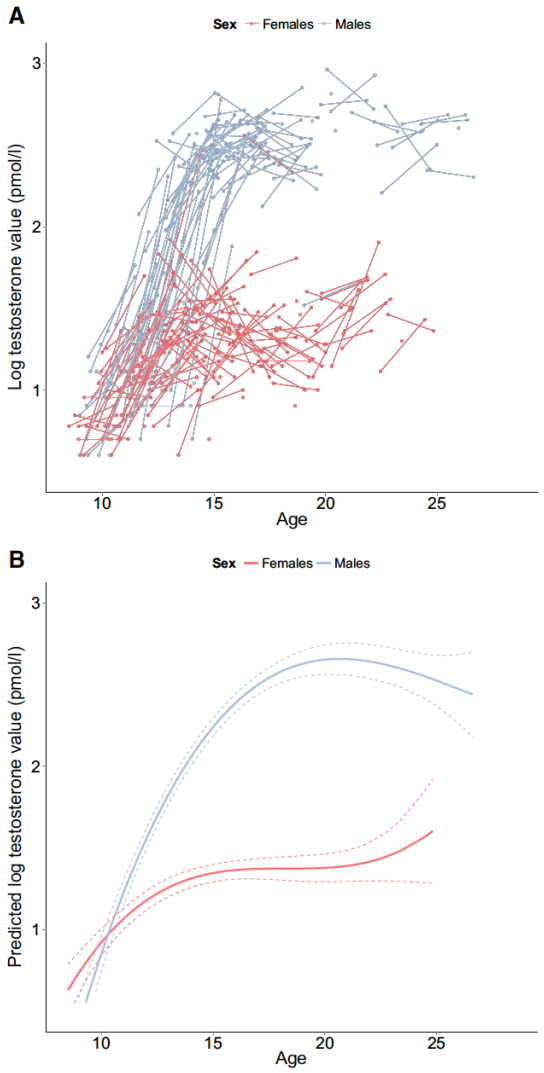


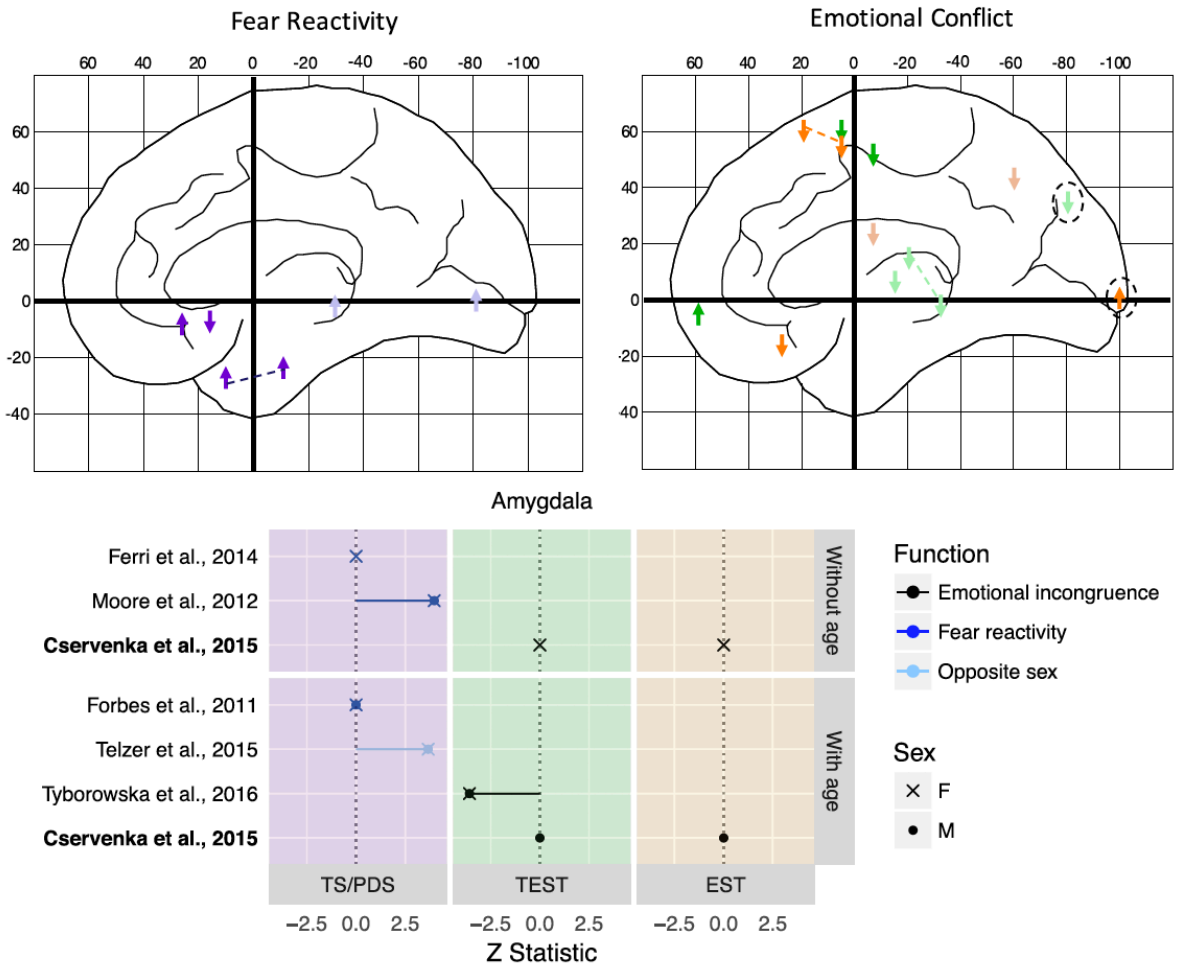
Figure 3. Correlation matrix of all variables on time points 1 and 2.







Affective Processes



- Very mixed effects in a small number of studies
- Some studies find decreases to threatening stimuli
- More whole-brain information

“Labeling” analysis (Dai & Scherf, 2019)

- No convergence in locus/direction of puberty-reward processing
- No convergence in locus/direction of cognitive processing
- Amygdala frequently implicated in puberty-facial emotion processing, but direction of effects is mixed
- Puberty-social information processing is positively related, but in widely varying regions
- Some potential concerns = lumps together PDS and hormones; equally weights early studies with small Ns; does not account for potential variability introduced by ROI vs whole-brain approaches

Summary of Vijayakumar et al. (2018)

- PFC is among the most consistently associated regions with pubertal maturation (superior/inferior frontal and anterior cingulate cortices)
- Amgydala and hippocampus structure are associated with pubertal stage (varies by sex); ventral striatum activation to reward receipt associated with pubertal stage and testosterone
- Functional activation patterns are still somewhat unclear
- Longitudinal pubertal and hormonal processes, rather than absolute stages/levels, more likely to be informative

Brain development mediates link between puberty and mental health: early evidence

- Larger pituitary volumes mediated relationships between:
  - Early pubertal timing and increased depressive symptoms (Whittle et al., 2012)
  - Greater DHEA levels and increased social anxiety symptoms (Murray et al., 2016)
- Larger hippocampal volume mediated link between greater T levels and increased depressive symptoms in girls (Ellis et al., 2019)
- Weaker activation in posterior insula elicited by happy emotional expressions mediated link between greater DHEA levels and increased externalizing symptoms (Whittle et al., 2015)
- Amygdala connectivity during emotion processing mediated link between early adrenarcheal timing and increased anxiety symptoms (Barendse et al., 2019)

Making a pitch for puberty

- Puberty is just as complicated as it felt when you were going through it – think carefully about how you index pubertal maturation
- Pubertal processes independent of age (e.g., earlier pubertal timing, more rapid pubertal tempo) are known to be associated with increased risk for mental health problems, substance use disorders, eating disorders, and antisocial behavior (Graber, 2013; Patton et al., 2004; Mendle et al., 2018)
- ABCD provides an *unprecedented* opportunity to understand how puberty impacts brain development, mental health, substance use
  - Annual assessments
  - Differences by sex, race/ethnicity, SES, adversity – except for sex, largely unaddressed in prior research