Parsing Relationships Between Neural Variability and Cognitive Flexibility Throughout Development

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- Defining cognitive flexibility and neural variability
- Developmental changes in cognitive flexibility and neural variability
- Studies linking flexible behavior to neural variability across the lifespan
- Piecing it together (aka, conjecture)
- What is the role of adolescent reversal learning and exploration? (aka, open discussion)

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Defining Cognitive Flexibility

Adaptively responding to changing environmental demands, contexts, or goals: switching tasks, switching strategies to solve a problem, thinking differently about a situation

Task Shifting: Shifting between tasks

Set Shifting: Shifting between relevant features of stimuli within a task; attention shifting

Reversal Learning: Updating learned reward-related contingencies

Defining Neural Variability

Variance-based: SD of neural activity over time; mean successive square differences

Neuron

CellPress

Volume 109, Issue 5, 3 March 2021, Pages 751-766

Perspective

Behavior needs neural variability

Leonhard Waschke[1,2,6], Niels A. Kloosterman[1,2], Jonas Obleser[3,4,5], Douglas D. Garrett[1,2,5]

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Defining Neural Variability

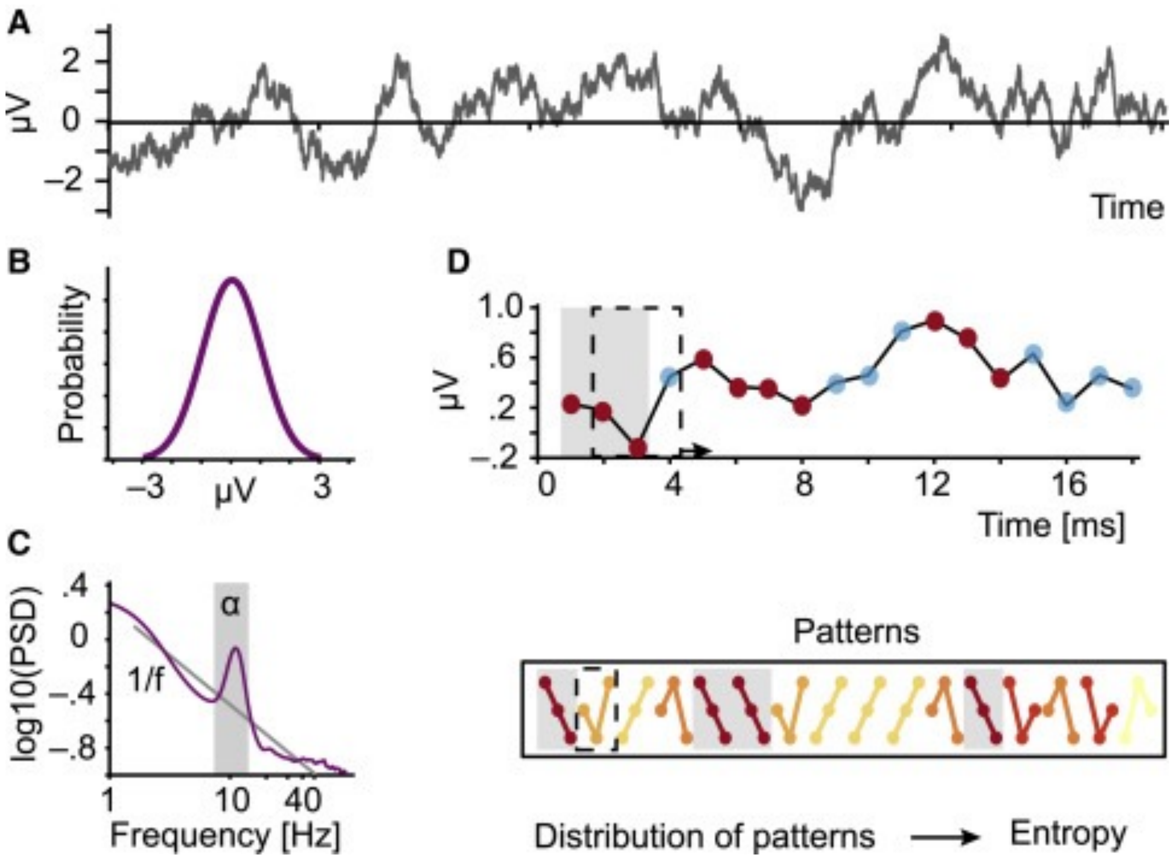
Variance-based: SD of neural activity over time; mean successive square differences

Frequency-based: oscillatory power (frequency-specific variation); 1/f

Information theory based: entropy-based measures (irregularity of time series, i.e, the distribution of temporal patterns in the data); measures of dimensionality (PCA)

- Multiscale entropy (entropy at different timescales)
- Weighted permutation entropy (re-weights entropy by distributional width of signal to control for variance differences)

Defining Neural Variability



Defining Neural Variability

Variance-based: SD of neural activity over time; mean successive square differences

Frequency-based: oscillatory power (frequency-specific variation); 1/f

Information theory based: entropy-based measures; dimensionality measures

Brain state variability: shifting between dominant patterns of whole-brain activity or relative expression (amplitude) of a given brain state

Table 1. Overview of common measures to quantify neural variability

Measure family	Example measure	Neural signal	Overview	Resources
Variance-based measures	time series variance	all types	variance (or SD) of neural activity across time (Cohen and Maunsell, 2009; Garrett et al., 2013a)	VarTbX (https://github.com/LNDG/vartbx); in-built functions of most programming and analyses platforms (R, Python, MATLAB)
	Fano factor	spiking	variance divided by the mean (or "mean-matched") across conditions before variance estimation (Churchland et al., 2010)	In-built functions of most programming and analysis platforms
Frequency-based measures	spectral power	LFP, MEG/EEG, BOLD	(time-resolved) estimates of oscillatory power, more commonly in low frequencies (e.g., 2–10 Hz), computed using Fourier-based methods (Pachitariu et al., 2015)	Fieldtrip (Oostenveld et al., 2011): https://www.fieldtriptoolbox.org/; Python MNE (Gramfort et al., 2013): https://mne.tools/stable/index.html; BrainStorm (Tadel et al., 2011): https://neuroimage.usc.edu/brainstorm/
	1/f exponent	LFP, MEG/EEG	separation of oscillatory and aperiodic activity by analyzing peaks and steepness of power spectra; typically not time resolved, but estimated from data sections (e.g., single trials)	FOOOF (Donoghue et al., 2020): https://github.com/fooof-tools/fooof; eBOSC (Kosciessa et al., 2020a): https://github.com/jkosciessa/eBOSC; IRASA (Wen and Liu, 2016): https://github.com/raphaelvallat/yasa/
Information-theoretic measures	MSE	LFP, MEG/EEG, BOLD	irregularity of time series at different temporal scales; based on recurring patterns (Costa et al., 2002; Kosciessa et al., 2020b); also, time resolved and for sparse data (Grandy et al., 2016)	mMSE (Kloosterman et al., 2020; Kosciessa et al., 2020b): modification of original MSE, controlling power-related, scale-specific biases in estimation (https://github.com/LNDG/mMSE; https://www.fieldtriptoolbox.org/example/entropy_analysis/)
	WPE	LFP, MEG/EEG	time-resolved irregularity of time series using symbolic patterns; amplitude information re-introduced by weighting with variance (Bandt and Pompe, 2002; Fadlallah et al., 2013)	see code within Waschke et al., 2019
"Shared" variability	noise correlations	spiking	correlation of post-stimulus spike distributions (across trial) between pairs of neurons (Cohen and Kohn, 2011)	spike sorting: KiloSort (Pachitariu et al., 2016); Spyke (Swindale and Spacek, 2014); SpyKING Circus (Yger et al., 2018)
	dFC	MEG/EEG, BOLD	time-resolved functional connectivity estimates based on correlations between time series of different brain regions (Hutchison et al., 2013)	GIFT: https://trendscenter.org/software/gift/; DynaConn (Sakoğlu et al., 2010); CONN (Whitfield-Gabrieli and Nieto-Castanon, 2012)

It is also important to note that different variability measures do not necessarily trace back to the same generating neural mechanism.

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Developmental Changes in Cognitive Flexibility

Task and set shifting improve from childhood to adolescence (most rapid improvements ~7-9 years old) and improve at a slower rate from adolescence to adulthood

Reversal learning peaks in adolescence, due to less perseverate "win-stay" behavior and faster remapping of stimulus responses

How do developmental changes in cognitive flexibility relate to neural variability?
Does adolescent reversal learning and/or adolescent-to-adult shifts in neural variability *enable* subsequent flexibility?

Developmental Changes in Neural Variability

Variance-based: declines with age in resting BOLD (increases in task??)

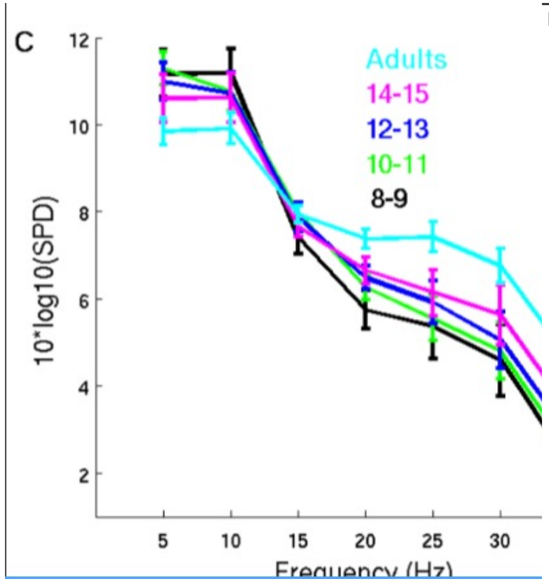
Frequency-based: oscillatory power declines, 1/f flattens (in EEG)

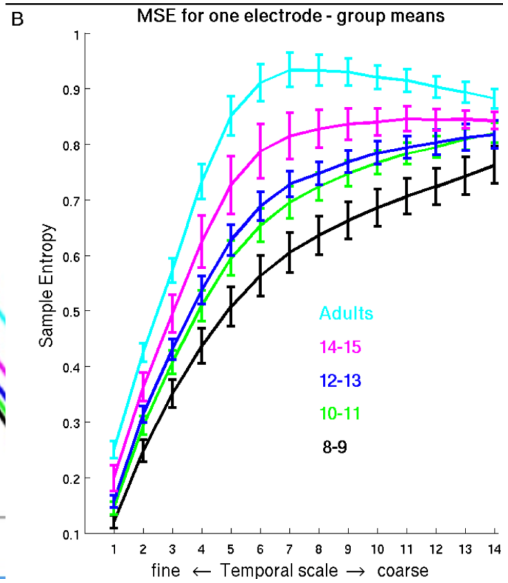
Information-theory based: multi-scale entropy increases (in EEG and maybe BOLD)

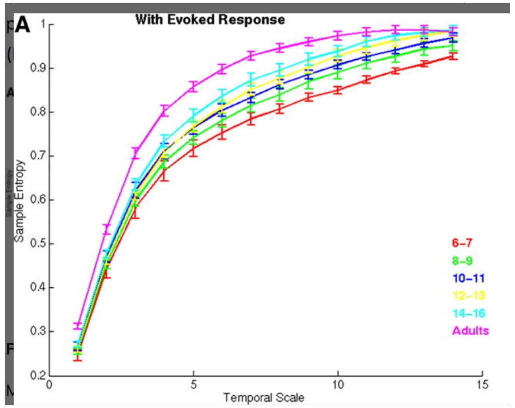
Brain state variability: Montez paper, increased time spent in modular states and dominant brain states, state flexibility ?

Developmental Changes in Neural Variability

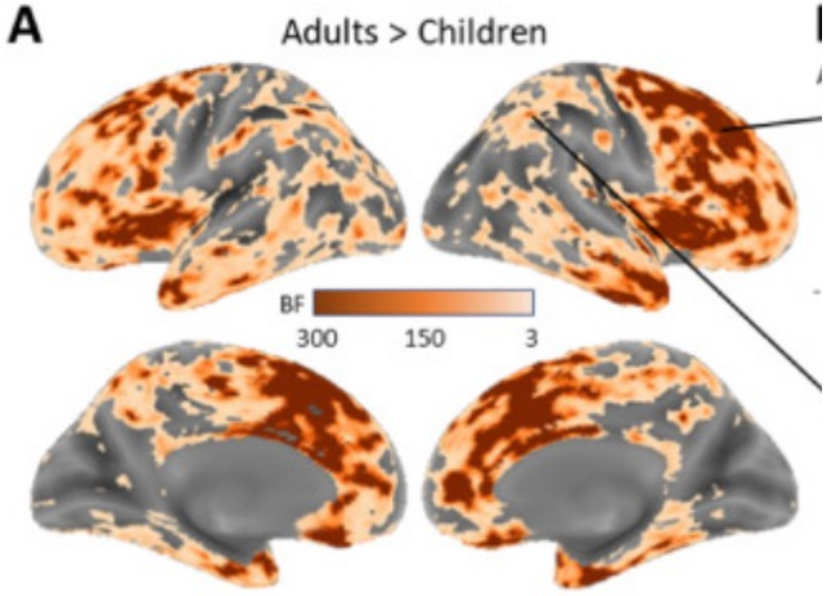
EEG 1/f and MSE over development, N = 55







BOLD entropy, 18 children, 14 adults

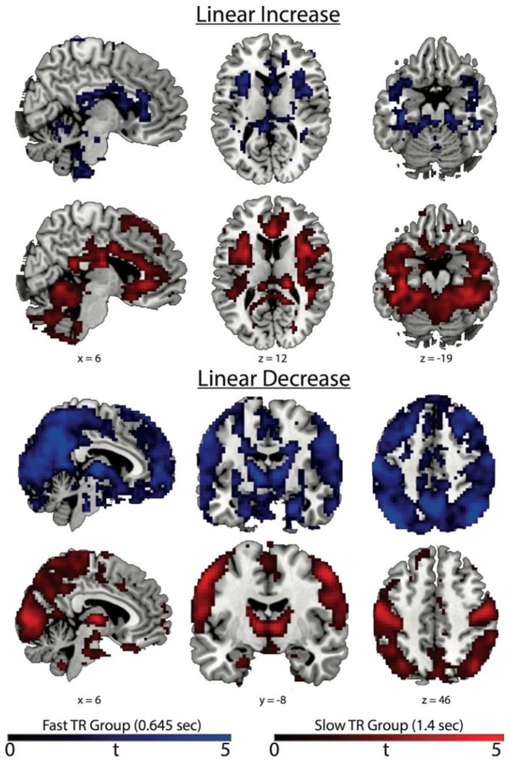


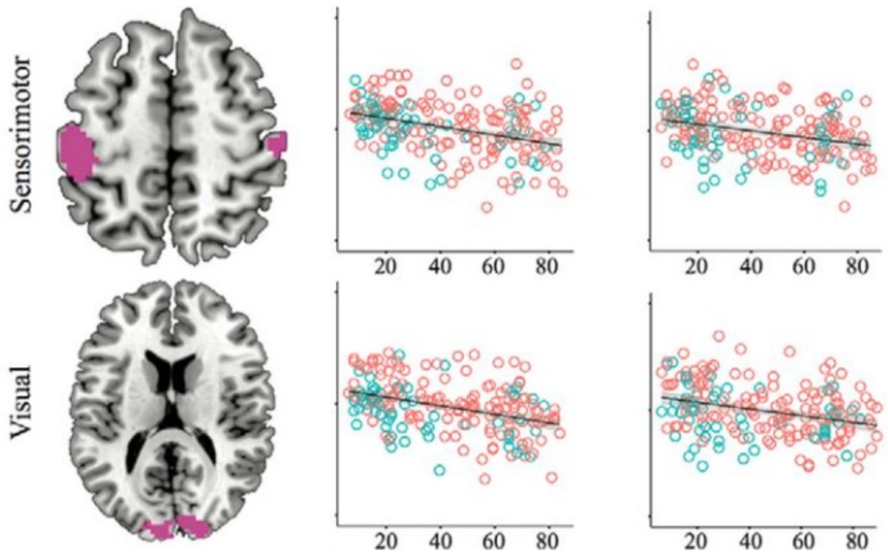
McIntosh et al., 2008, Plos Comp Bio

Amalric et al., 2023, Cortex

Developmental Changes in Neural Variability

Resting-state BOLD MSSD age 6-80





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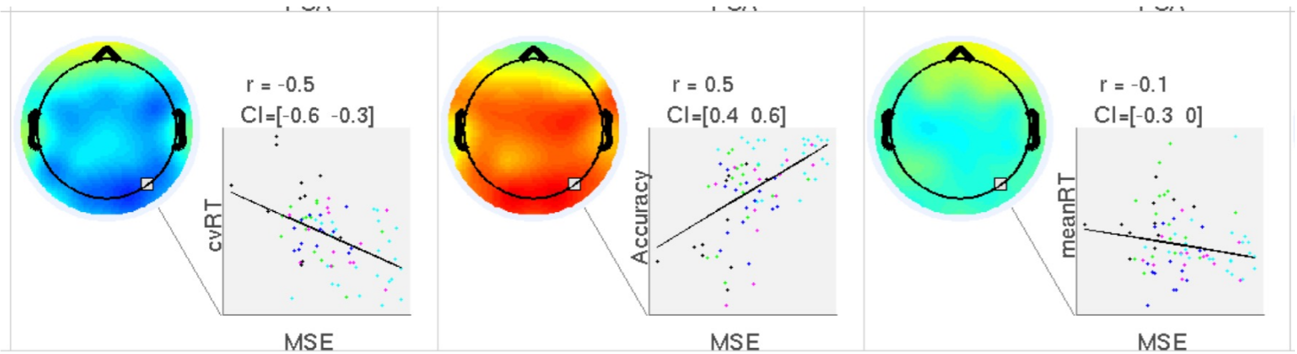
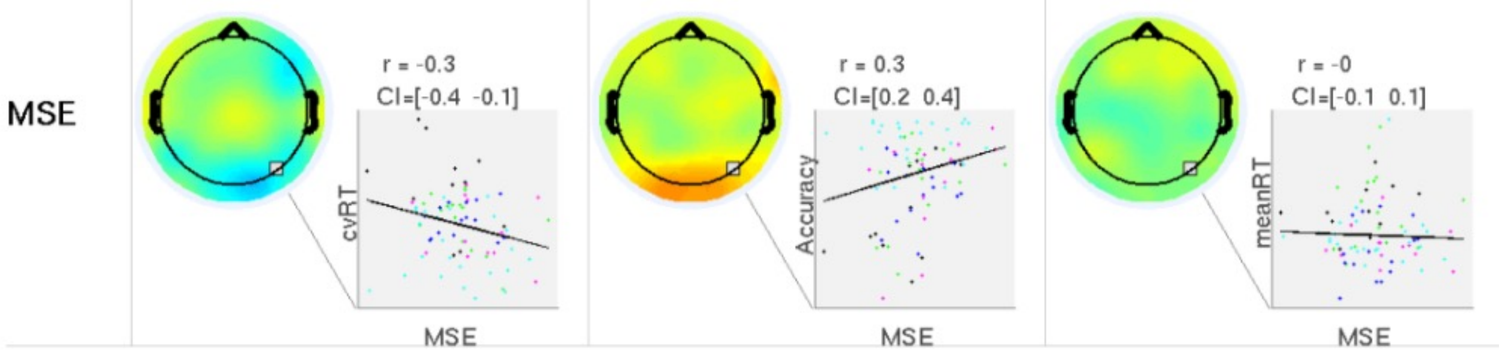
Relationships Between EEG Entropy and RT/Accuracy Development

N, Age: 55 children (8-15 years), 24 adults (20-33 years)
Cognitive flexibility: N/A, face recognition task
Neural variability: MSE in EEG

Higher MSE = lower variability in RT and higher accuracy

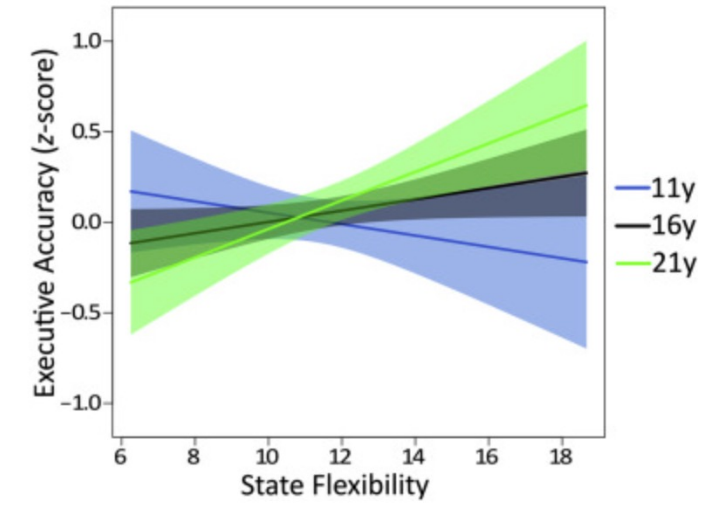


The above associations weaken when controlling for age



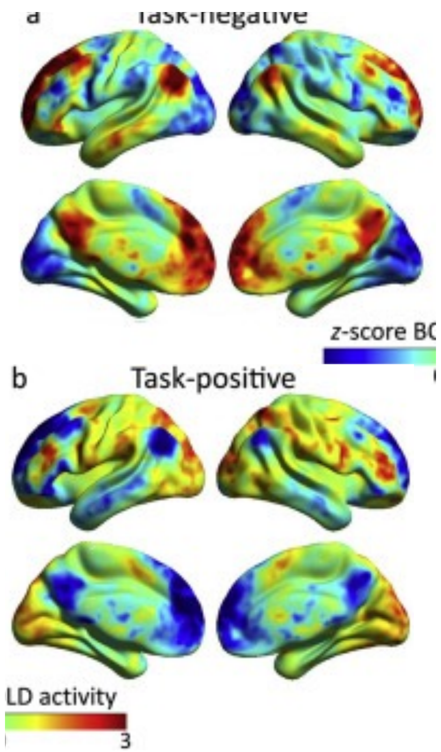
Medaglia et al., 2018, NeuroImage

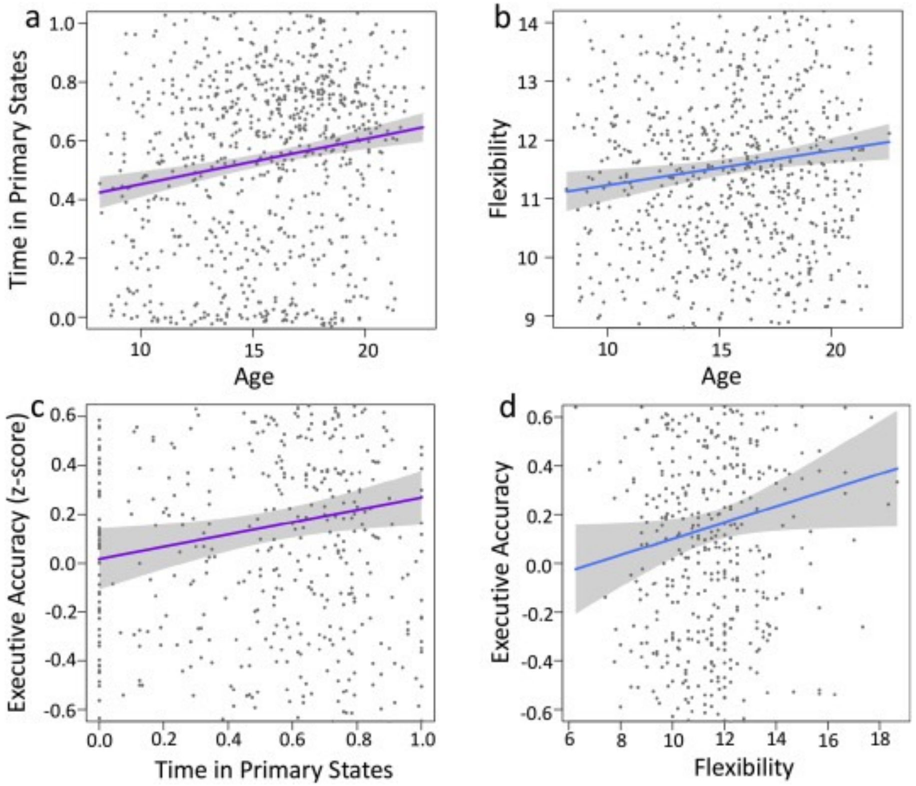
Relationships Between fMRI Brain States and Flexibility Development



N, Age: 780, ages 8-22
Cognitive flexibility: EF battery
Neural variability: Time in dominant states and state flexibility

Time spent in the two dominant brain states increases with age and EF

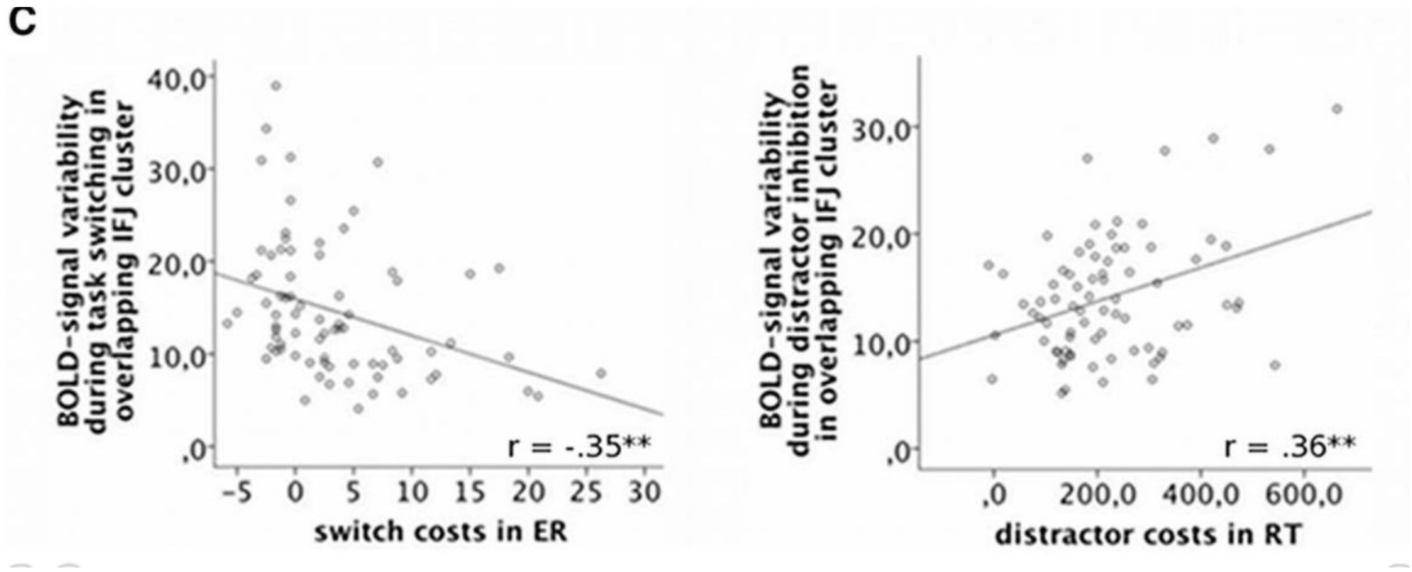




Relationships Between BOLD Variability, Flexibility, and Stability: Middle Age

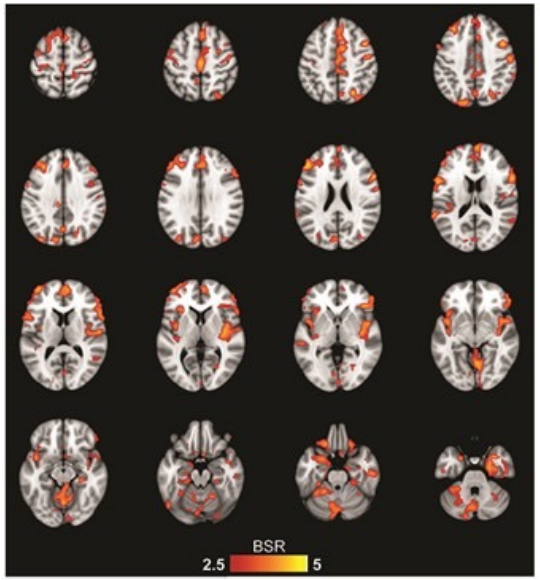
N: 76
Age: 20-51 years
Cognitive flexibility: task switching
Cognitive stability: distractor inhibition
Neural variability: difference of residuals

Higher trial-to-trial BOLD signal variability in the **IFJ** is associated with lower task switch error rate costs (better flexibility) but higher distractor costs (worse stability)

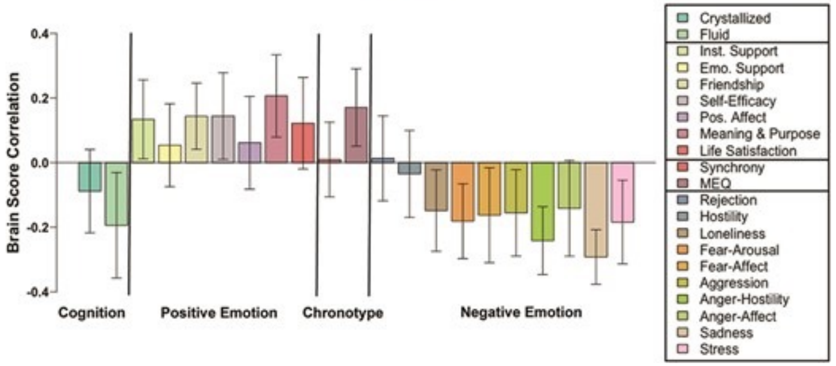


Relationships Between Resting BOLD SD and Fluid Cognition: Lifespan

N, Age: 157 ages 20-86
Cognitive flexibility: fluid cognition (NIH toolbox)
Neural variability: BOLD SD



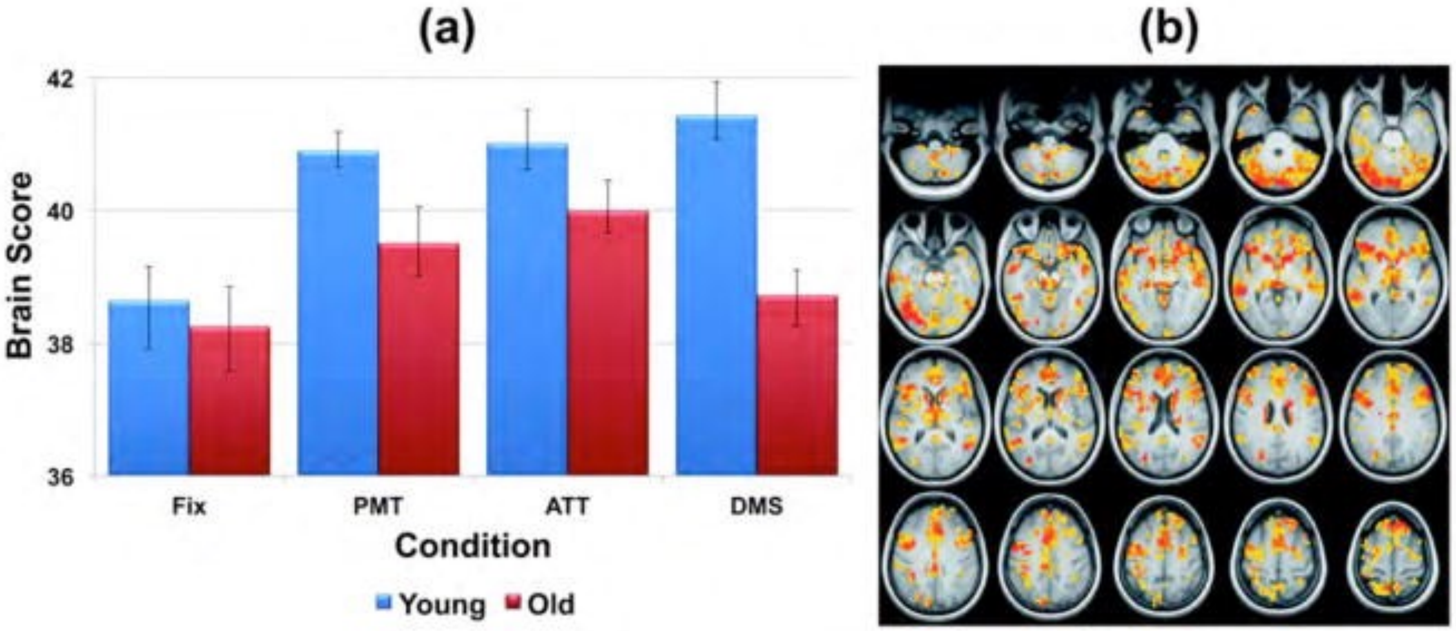
Lower resting BOLD SD in the highlighted brain regions is associated with better fluid cognition, controlling for age



Relationships Between Task BOLD SD and Fluid Cognitive: Aging

N, Age: 18 young adults (20-3), 27 older adults (56-85)
Cognitive flexibility: fluid cognition (NIH toolbox)
Neural variability: BOLD SD

Young adults show bigger increase in BOLD SD from fix to the three tasks in the brain regions highlighted



Summary

Greater cognitive flexibility generally linked to:

Lower BOLD variability during rest
Higher BOLD variability during task, bigger increase in BOLD variability from rest-task

Higher EEG entropy

More time in dominant brain states but also more flexible switching (in young adults)

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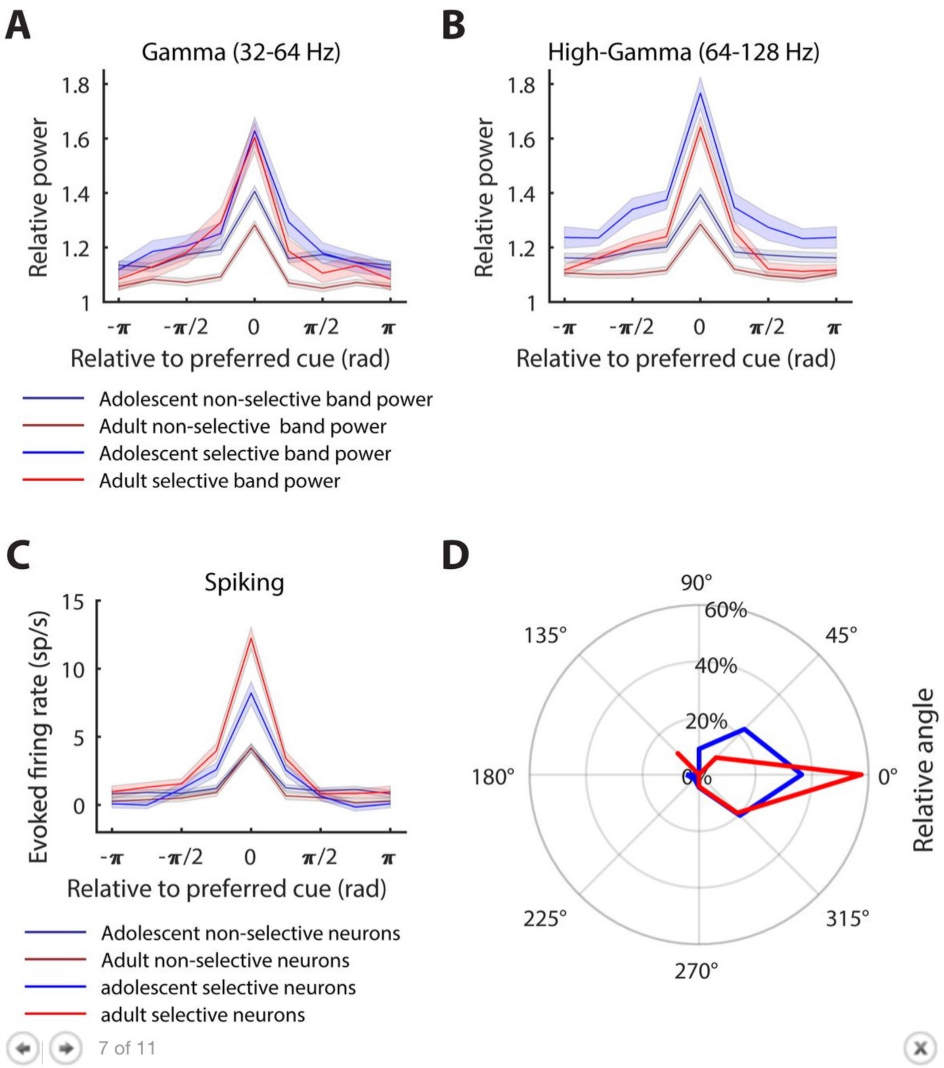
BOLD variability down with age during rest
Oscillatory power down with age; 1/f flatter with age
Multiscale entropy up with age

- Balancing of E/I (increase in inhibitory strength, pruning of interconnected excitatory synapses) + growth of cortical myelination leads to reduced prevalence and synchrony of low-frequency *spontaneous* neural activity → BOLD amplitude decrease, EEG power decrease, 1/f flattening
- Lower synchronized spontaneous activity allows for stimulus-induced or task-relevant neural activity to be more easily detected → higher circuit signal-to-noise

Strong Gamma Frequency Oscillations in the Adolescent Prefrontal Cortex

Zhengyang Wang, Balbir Singh, Xin Zhou, and Christos Constantinidis

Journal of Neuroscience 6 April 2022, 42 (14) 2917-2929; DOI: https://doi.org/10.1523/JNEUROSCI.1604-21.2022



Stimulus onset quenches neural variability: a widespread cortical phenomenon

Abstract

Neural responses are typically characterized by computing the mean firing rate, but response variability can exist across trials. Many studies have examined the effect of a stimulus on the mean response, but few have examined the effect on response variability. We measured neural variability in 13 extracellularly recorded datasets and one intracellularly recorded dataset from seven areas spanning the four cortical lobes in monkeys and cats. In every case, stimulus onset caused a decline in neural variability. This occurred even when the stimulus produced little change in mean firing rate. The variability decline was observed in membrane potential recordings, in the spiking of individual neurons and in correlated spiking variability measured with implanted 96-electrode arrays. The variability decline was observed for all stimuli tested, regardless of whether the animal was awake, behaving or anaesthetized. This widespread variability decline suggests a rather general property of cortex, that its state is stabilized by an input.

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Oscillatory power down with age; 1/f flatter with age
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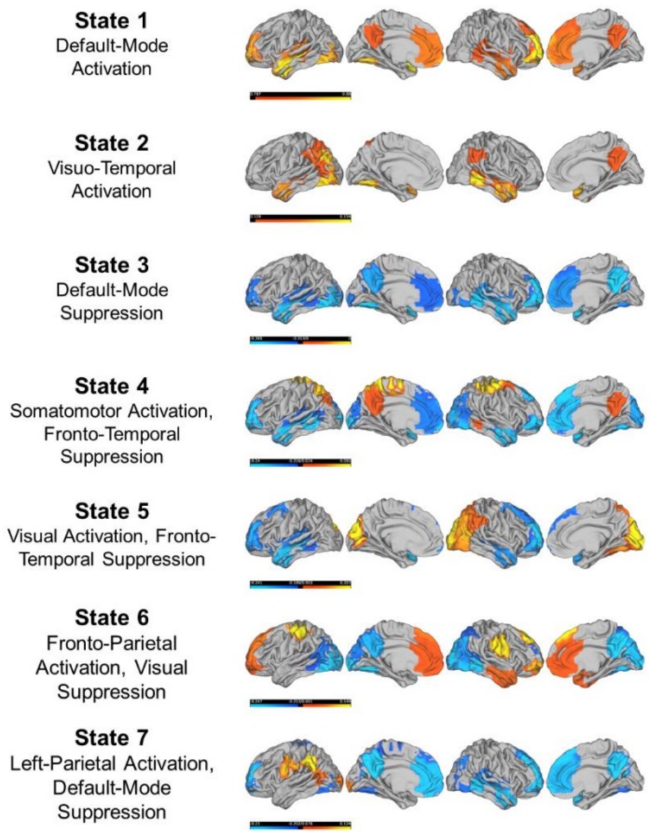
- Balancing of E/I (increase in inhibitory strength, pruning of interconnected excitatory synapses) + growth of cortical myelination leads to reduced prevalence and synchrony of low-frequency *spontaneous* neural activity → BOLD amplitude decrease, EEG power decrease, 1/f flattening
- Lower synchronized spontaneous activity allows for stimulus-induced or task-relevant neural activity to be more easily detected → higher circuit signal-to-noise

- The reduction in strength and power of spontaneous activity (desynchronization) → results in an increase in signal entropy
- Greater entropy allows for more possible dynamical states to be reached → criticality

"cognitive flexibility emerges when a neural system avoids locking into a stereotypical, rhythmic pattern of activity, while instead continuously exploring its full dynamic range"

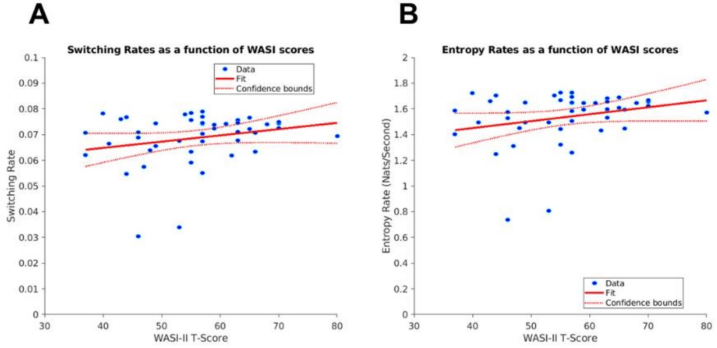
Relationships Between MEG switching, entropy, and cognition

N, Age: 46 children, 8-13 years old
Cognitive flexibility: NA, WASI-I, SDQ
Neural variability: MEG activity patterns in temporally-discrete states: *state switching and entropy rate*



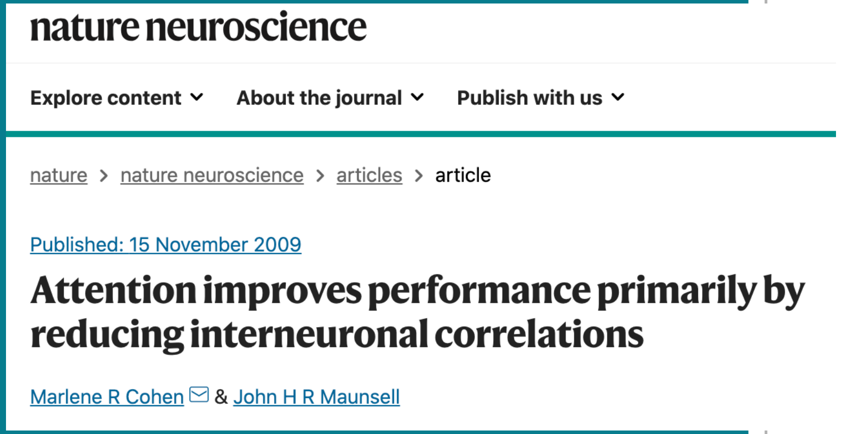
Individual variation in state entropy was highly correlated (.99) with state switching rates

Significant relationships between cognitive ability and brain switching rates & entropy



McIntosh et al., 2008, Plos Comp Bio

Neuromodulatory Mechanisms


nature neuroscience

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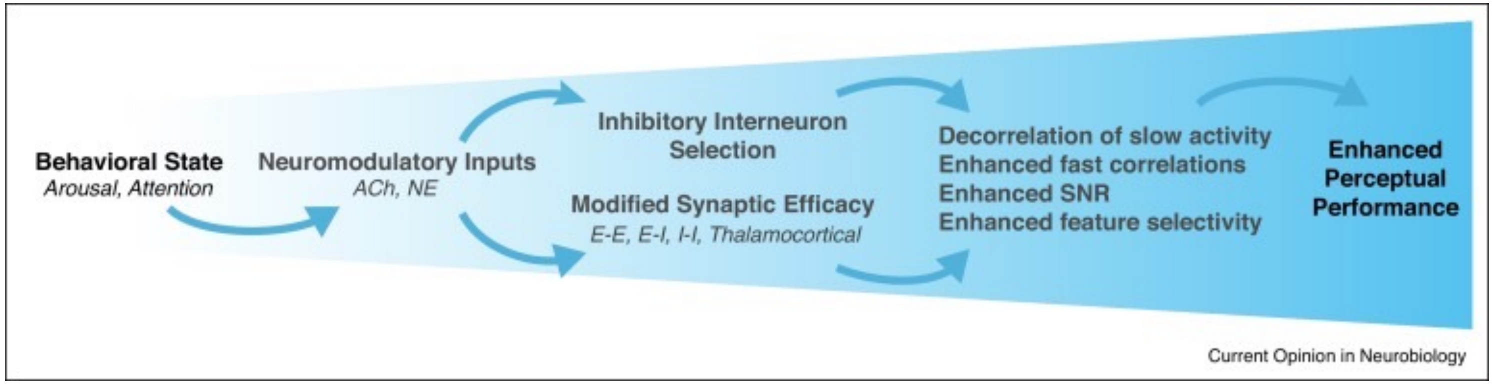
Published: 15 November 2009

Attention improves performance primarily by reducing interneuronal correlations

Marlene R Cohen & John H R Maunsell

Arousal (measured by time-resolved pupil dilation) is tightly linked to reductions in low-frequency power, both in non-human animals (McGinley et al., 2015a, 2015b; Neske et al., 2019; Reimer et al., 2014) and humans (Dahl et al., 2020; Meindertsma et al., 2017; Waschke et al., 2019). In addition to LC NE activity and its cortical projections (the LC-NE system), cholinergic activity from the basal forebrain also affects arousal and is linked to pupil size (Reimer et al., 2016). Both NE and cholinergic activity affect neural excitability and suppress the generation of synchronous activity in lower frequencies (McCormick, 1992; McGinley et al., 2015a), leading to a reduction in low frequency power, a phenomenon often called “desynchronization” (Fries et al., 2001; Harris and Thiele, 2011; Mitchell et al., 2009).

We found that attention adaptively decreased correlated variability in a population of neurons



Cardin, 2019, Current Opinion in Neurobio

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Developmental Changes in Cognitive Flexibility

What is the role of adolescent reversal learning?

Variability-Stability-Flexibility Behavioral Development

Review of General Psychology
Volume 21, Issue 2, June 2017, Pages 123-131

https://doi-org.pitt.idm.oclc.org/10.1037/gpr0000110

SAGE journals

Article

The Variability-Stability-Flexibility Pattern: A Possible Key to Understanding the Flexibility of the Human Mind

Thea Ionescu

Abstract
Flexibility is a defining characteristic of our species. The current literature presents cognitive flexibility as having several meanings; this lack of a single definition may hinder work on understanding the concept. In this article, I begin with describing the variability–stability–flexibility pattern in the development of various abilities and then argue that as part of this chain, flexibility can be considered a property of the cognitive system and not in itself an ability. The implications of and challenges to this view are discussed. This view can foster progress in the understanding of cognitive flexibility: It can serve as a unifying framework in which to study the dynamic flow of stability and flexibility in the functioning of the cognitive system.

Card sorting
Object use
Language
Categorization