Improving the validity of brain-behavior associations

Russ Poldrack
Stanford University

What does a brain-behavior association mean?

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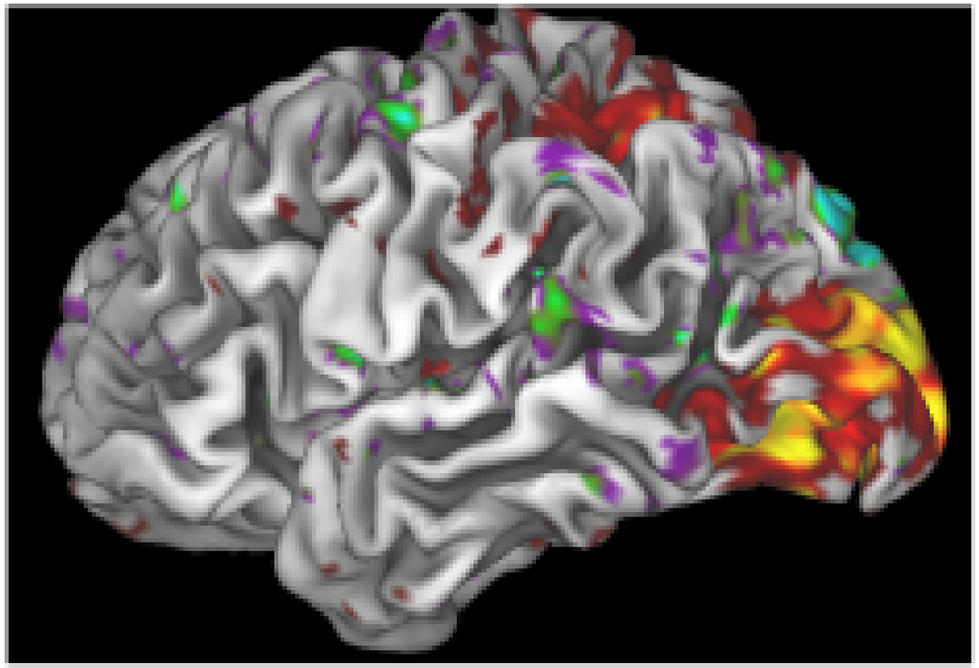

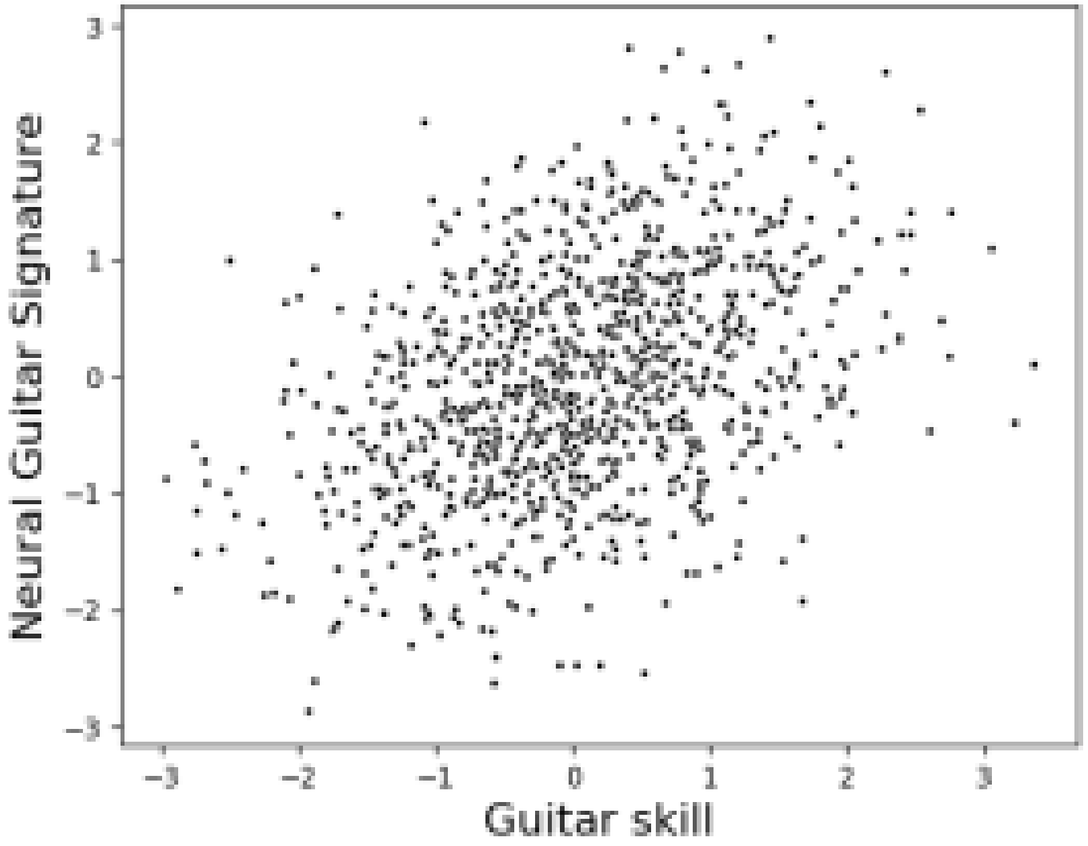

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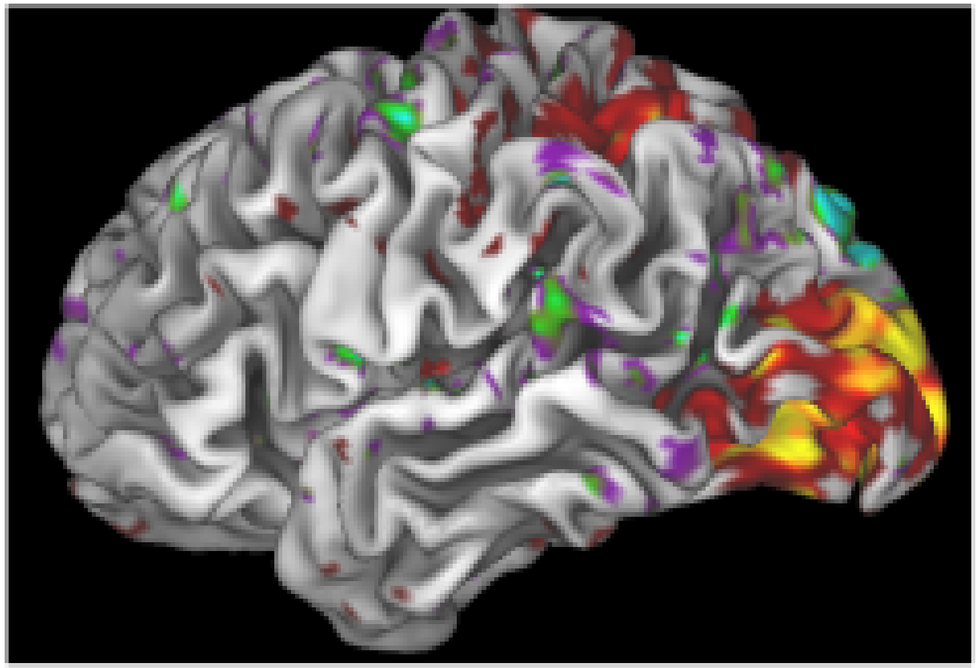

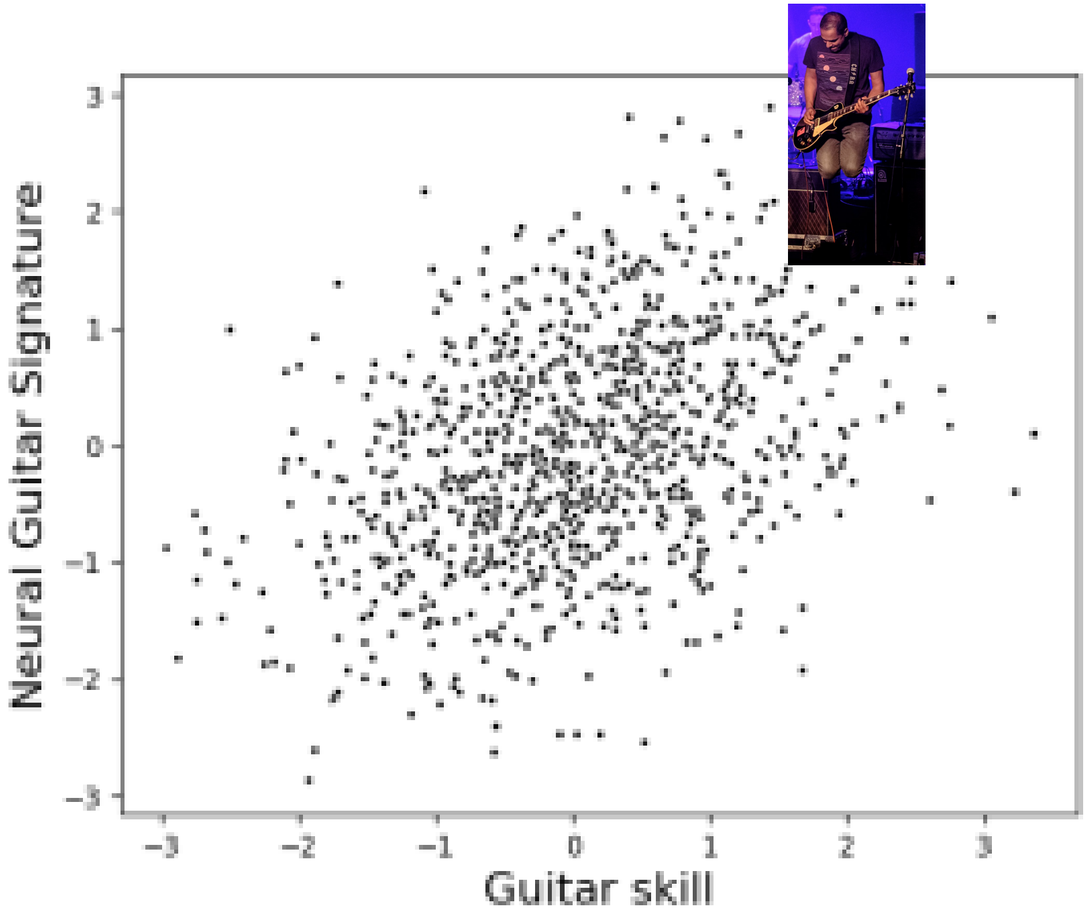

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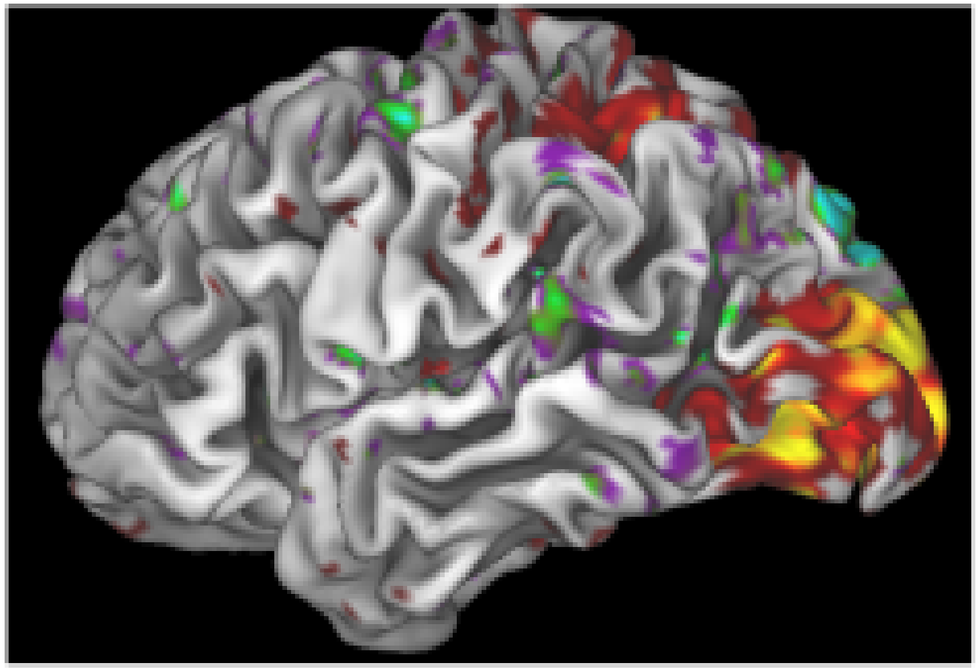

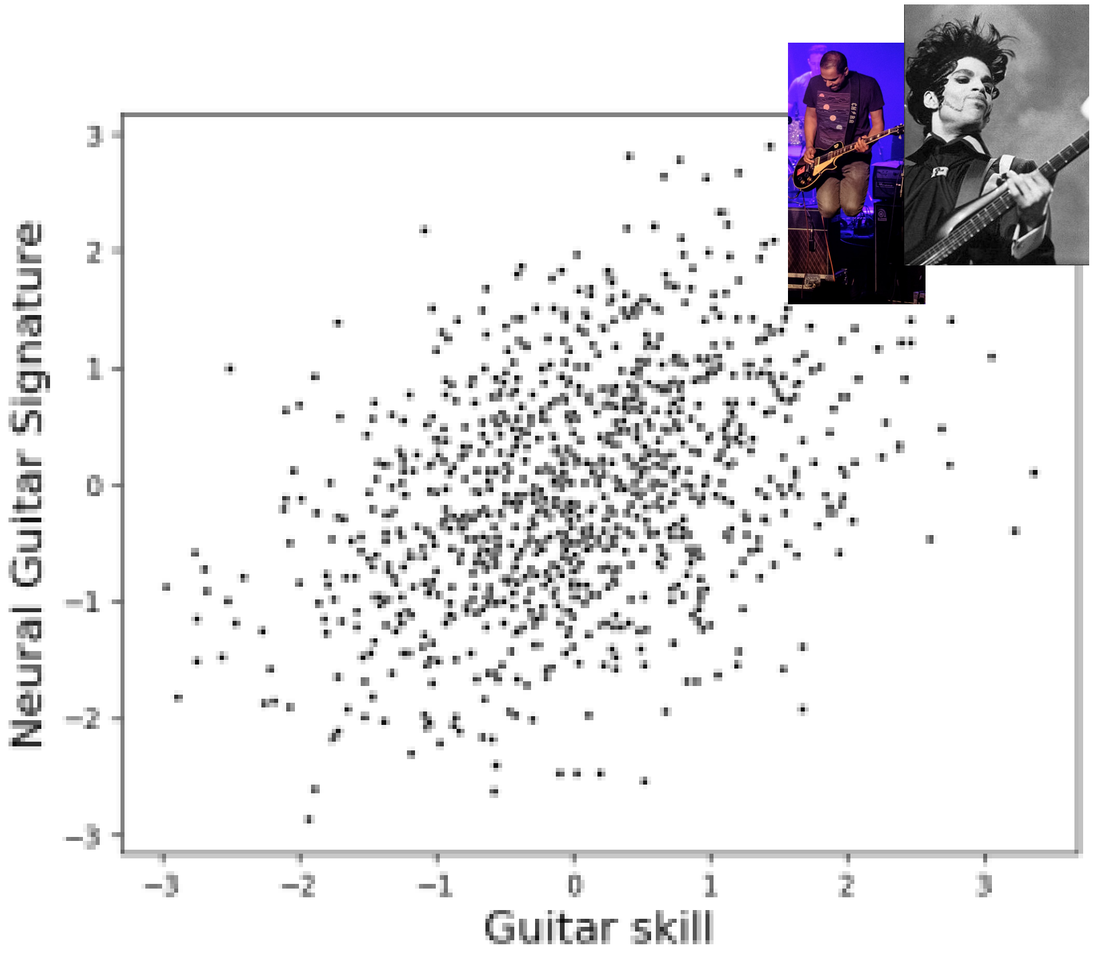

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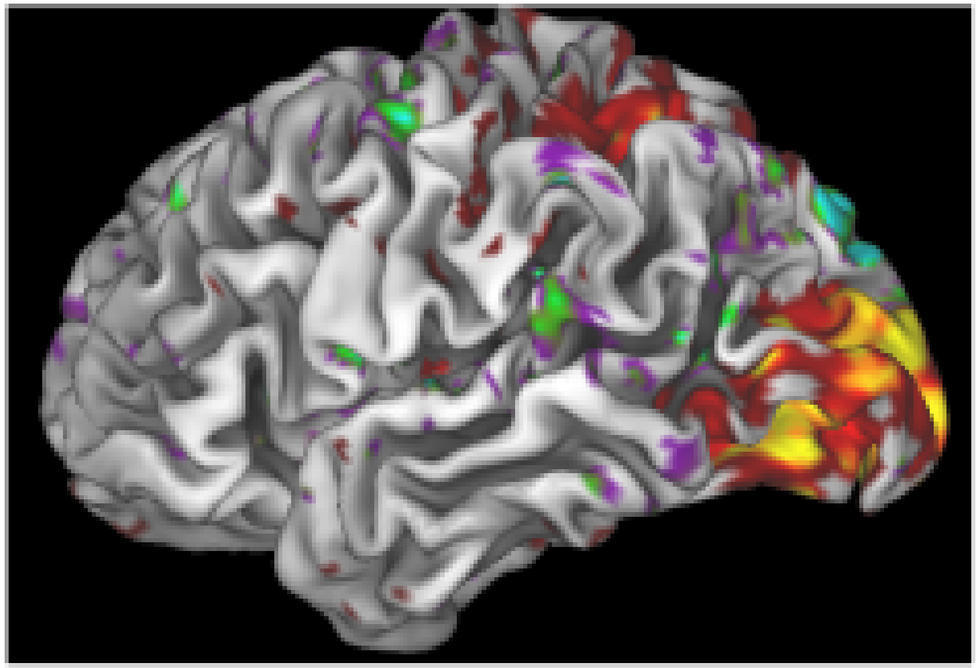
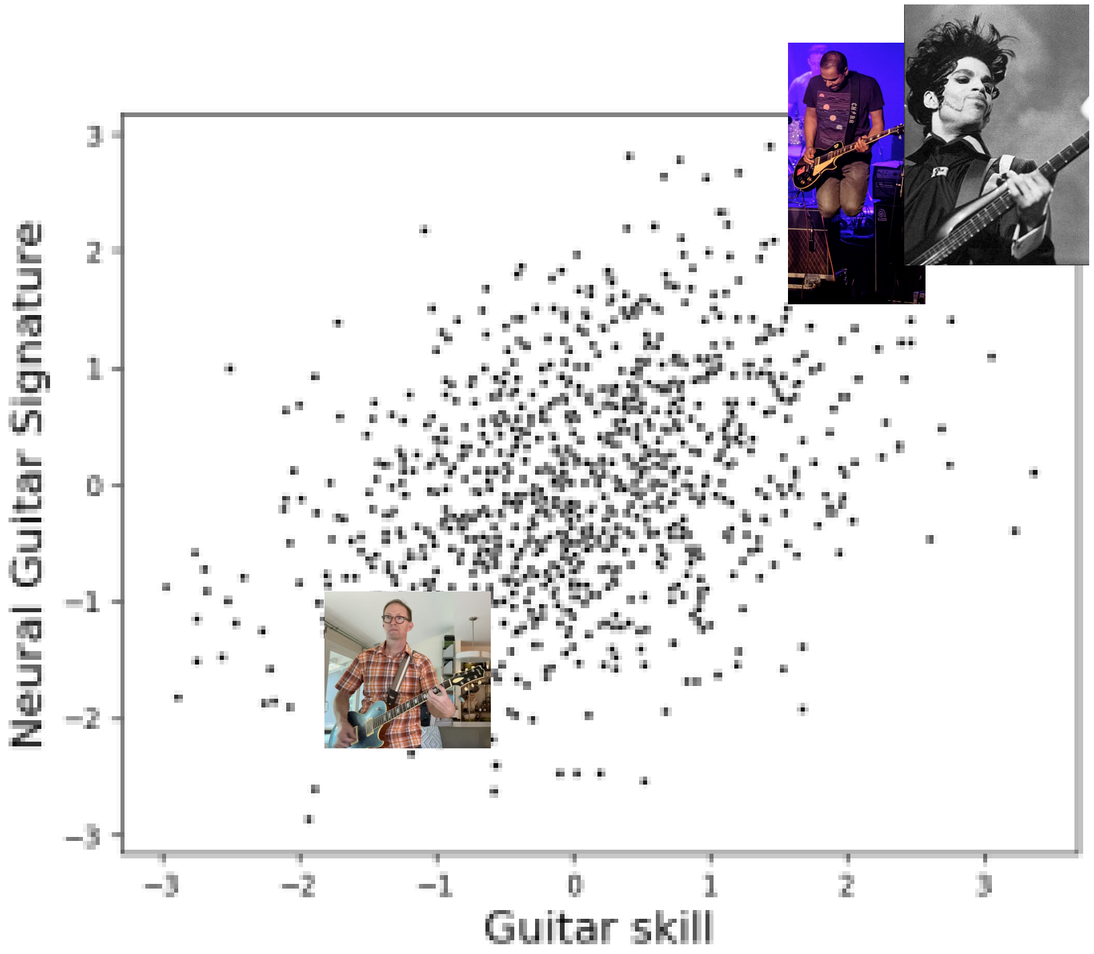
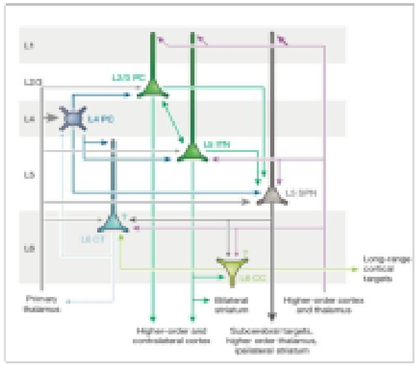
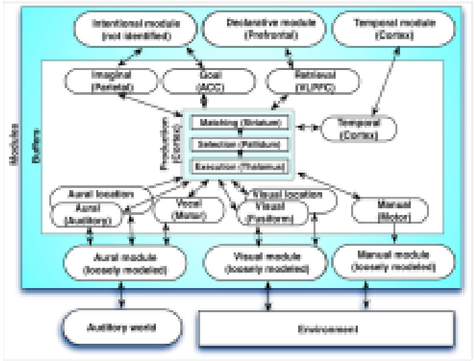








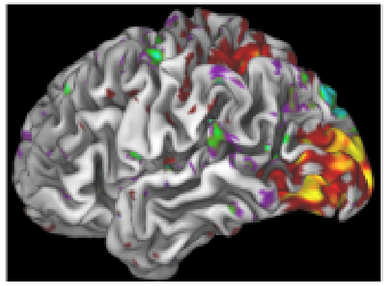
brain

cognition

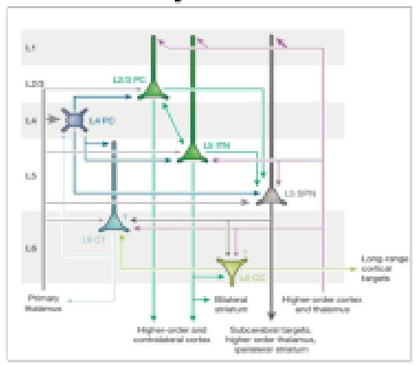
fMRI

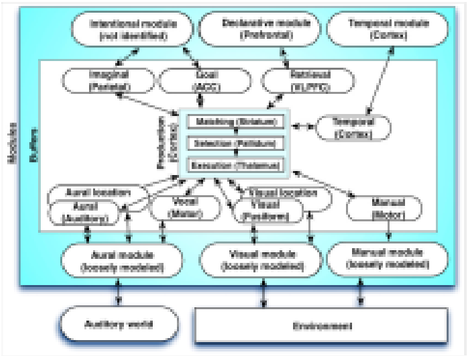
behavior

observed



latent





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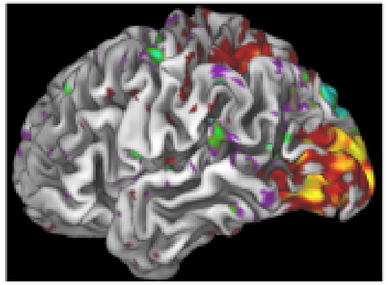

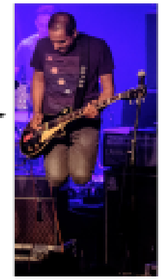

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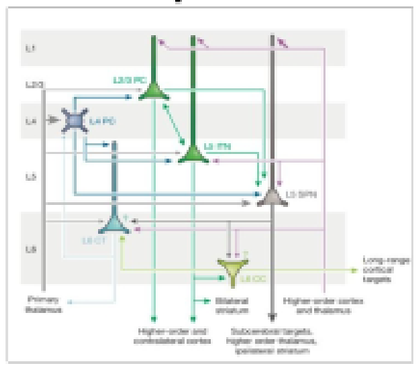

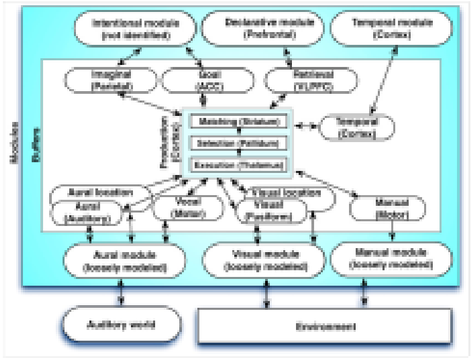

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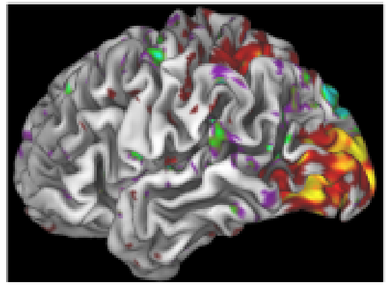

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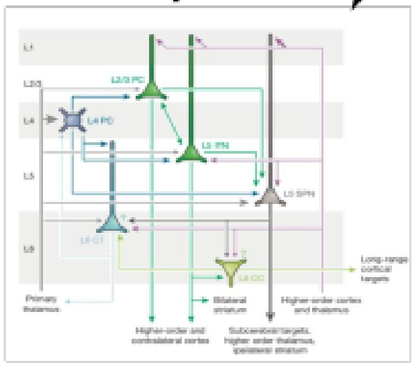

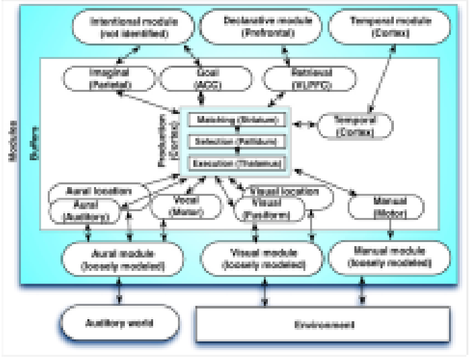

brain

cognition

Assuming this model is true, what kinds of neural differences could give rise to cognitive differences?

“Brain efficiency”

> “A series of investigations in normal subjects indicate an inverse relationship between brain glucose metabolic rate and psychometric measures of intelligence. . .These studies have been interpreted as evidence for a *brain efficiency model of intelligence*:
>
> Intelligence is not a function of how hard the brain works but rather how efficiently it works.” (Haier et al., 1992)

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Is this really an explanation?

Efficiency: A thought experiment

- A Prius and a Porsche both drive from San Francisco to Los Angeles via the same route at the same speed.
- The Prius uses half as much fuel as the Porsche. How do we explain this?

Efficiency: A thought experiment

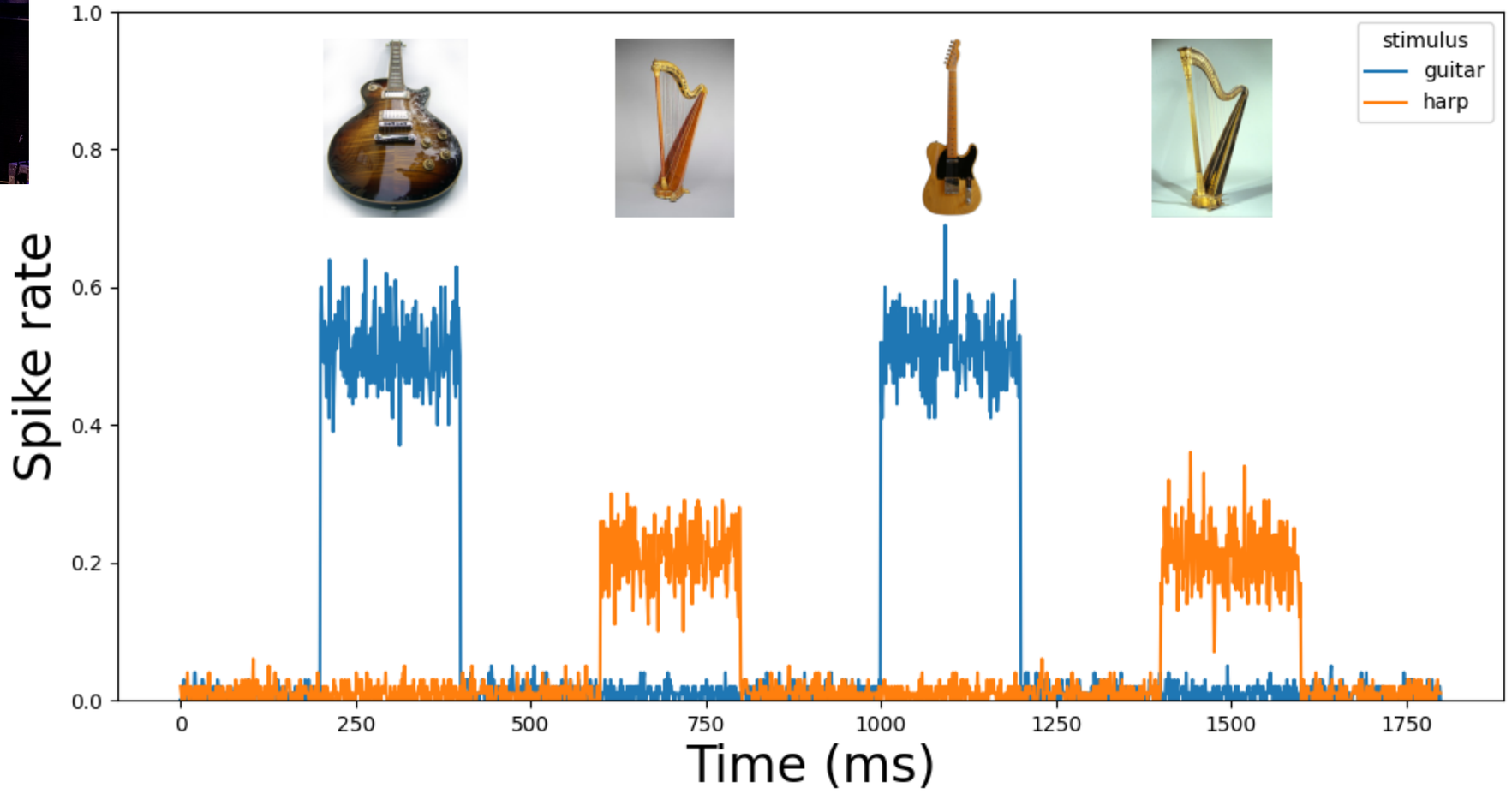
1. The Prius has a gas-electric hybrid engine (which uses surplus engine power to generate electricity which is then turned back into drive power) and regenerative braking (which captures energy that would otherwise be lost as heat).
2. The Prius is more efficient.

Poldrack, 2015

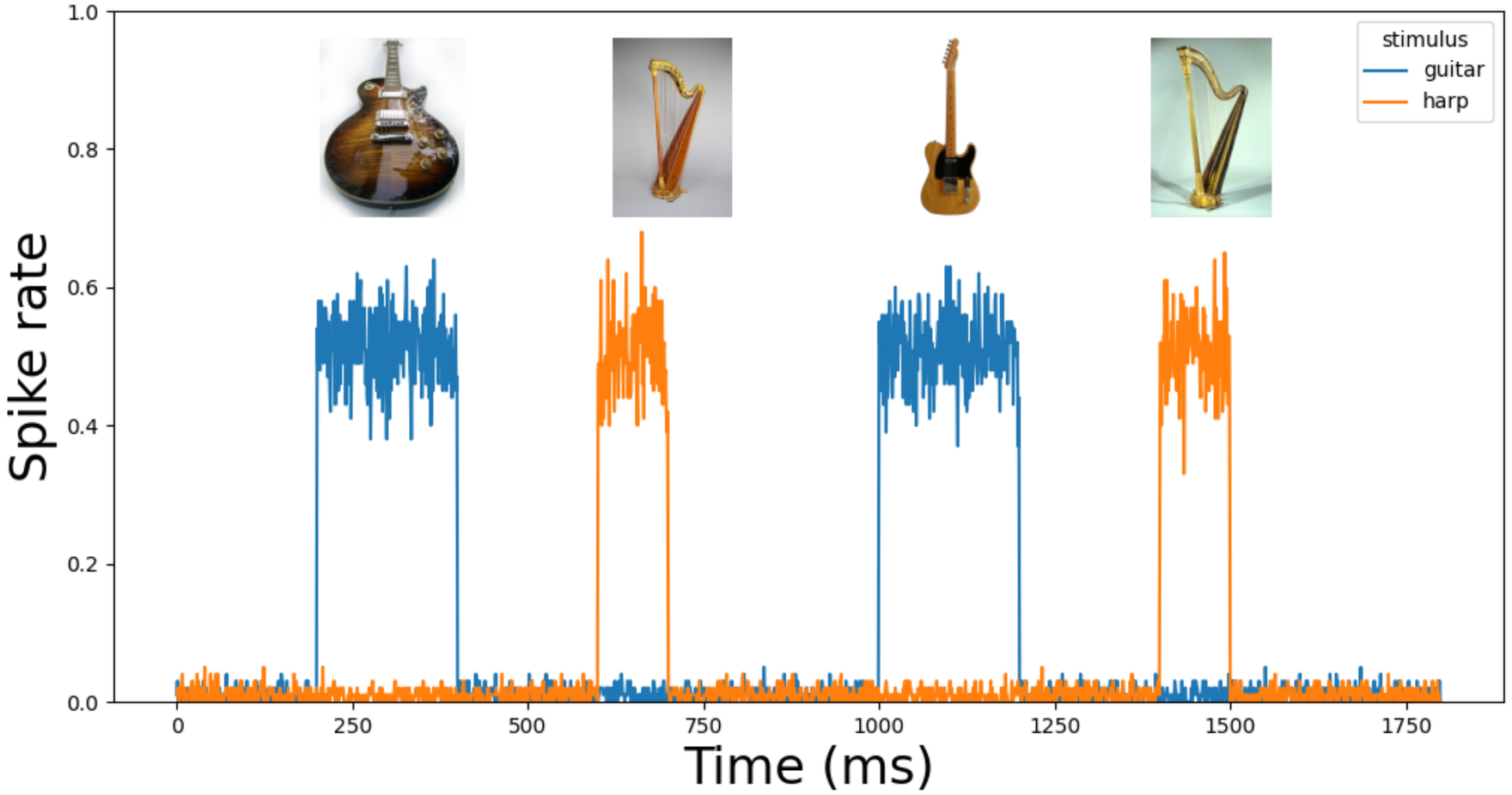
Explaining brain-behavior associations

- “Efficiency” is a non-explanation
  - It simply renames the phenomenon
- What kinds of neural differences might actually explain these associations?
  - Different intensity of neuronal activity
  - Different duration of neuronal activity

Difference in intensity of neural activity

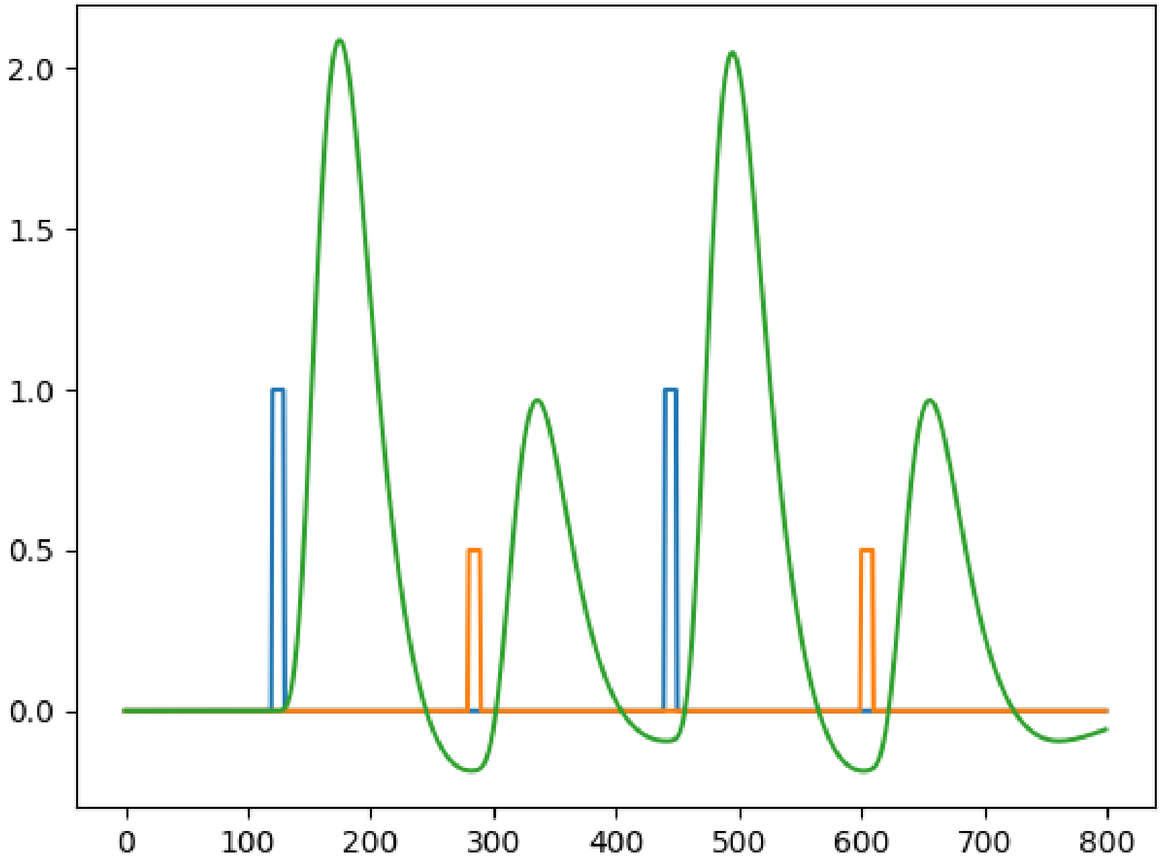


Difference in duration of neural activity

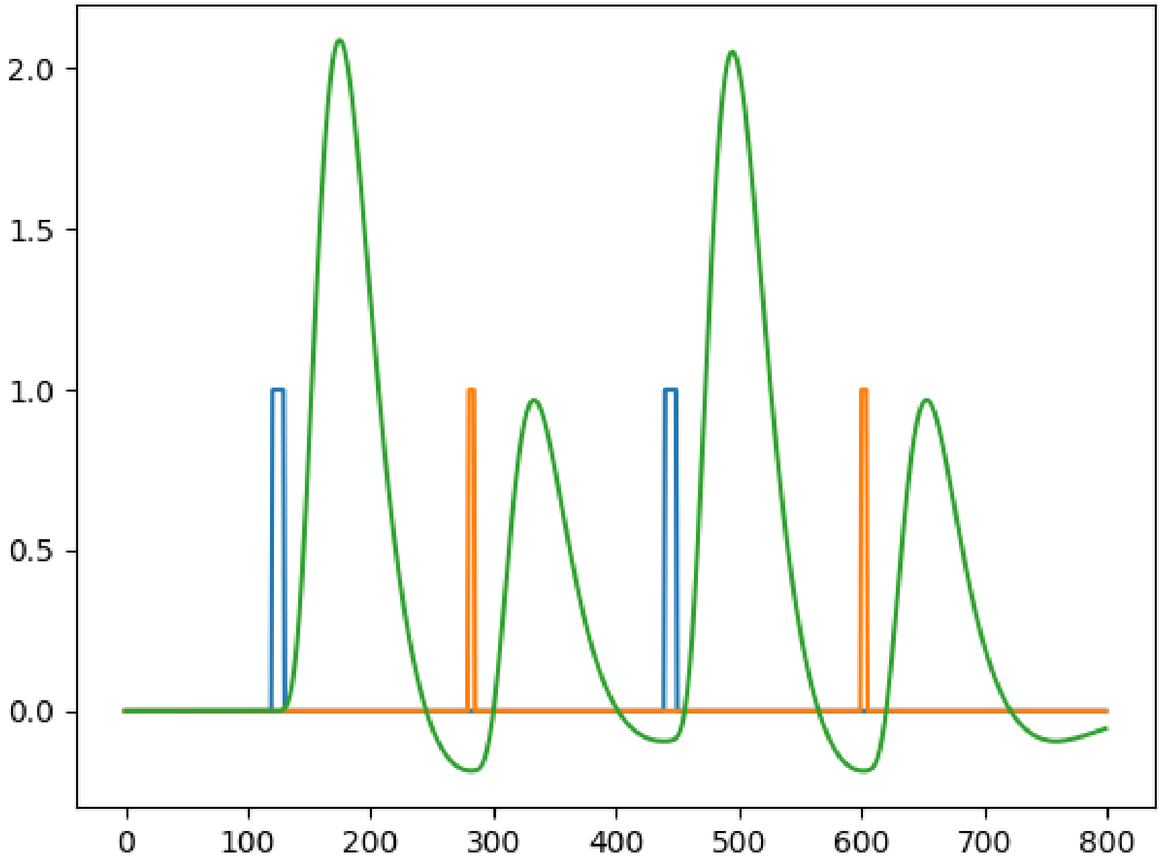


Changes in rate vs. duration of neural firing are indistinguishable in fMRI

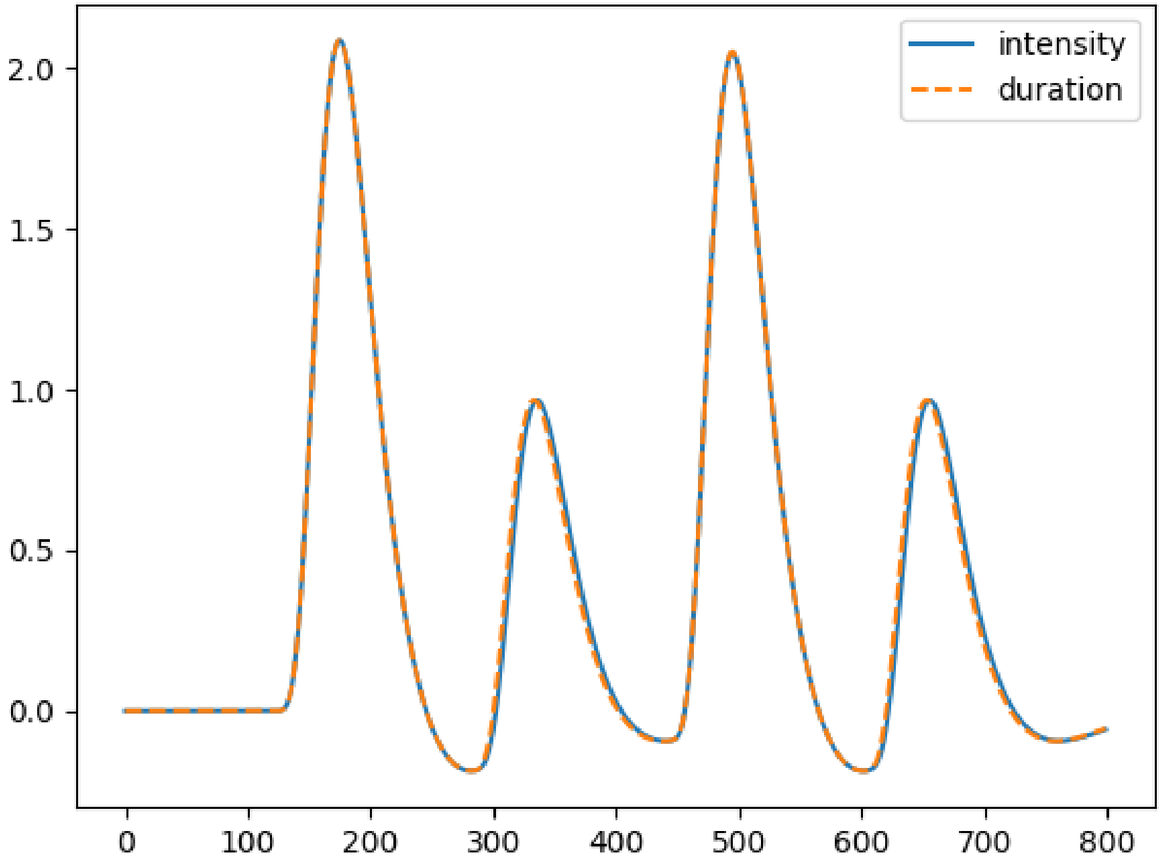
Same duration, different amplitude



Same amplitude, different duration



The effects of amplitude and duration are indistinguishable in the fMRI signal

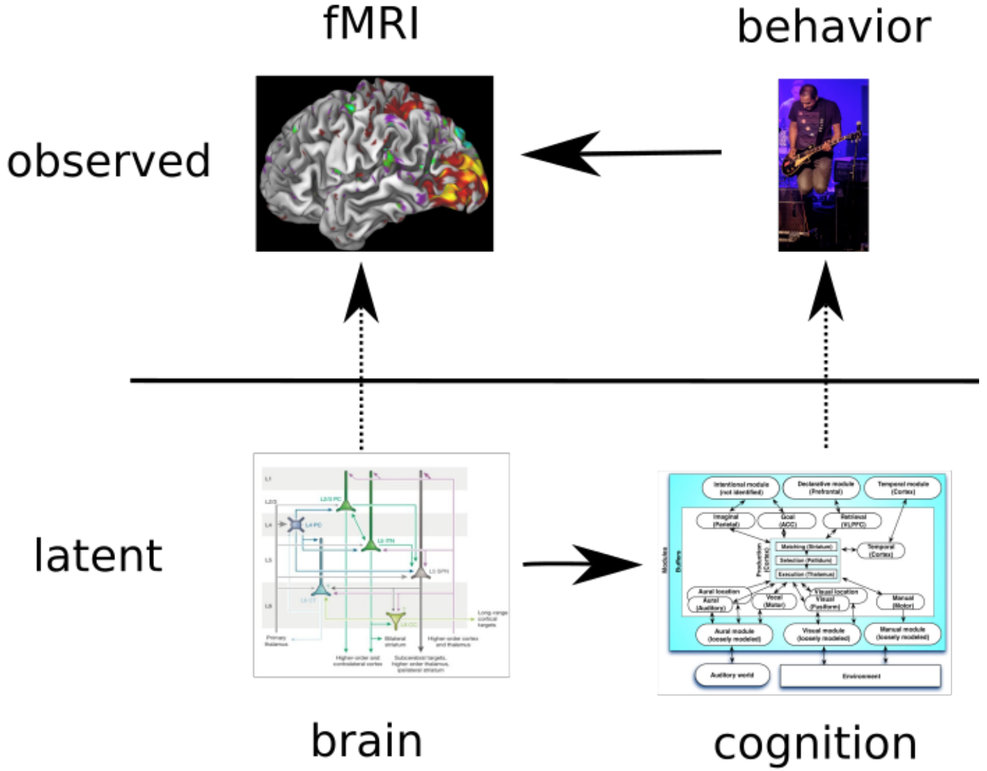


The response time paradox

- In cognitive psychology, differences in RT are the measure of interest
  - Thus, nearly all task comparisons will exhibit a difference in RT

Mumford et al. 2023

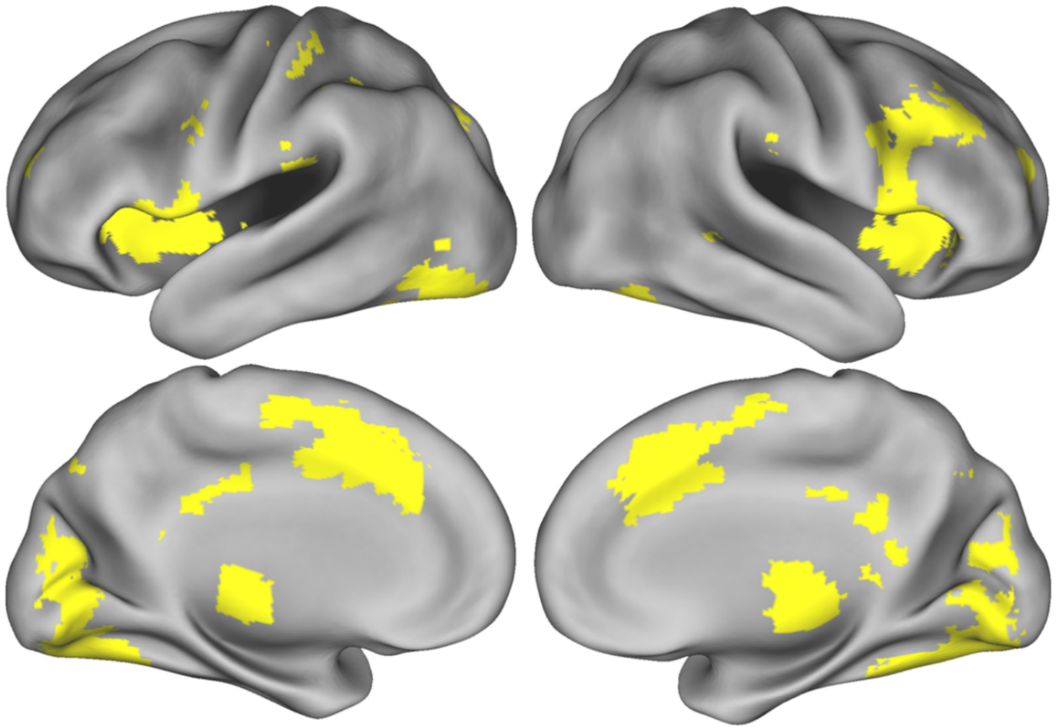
The response time paradox



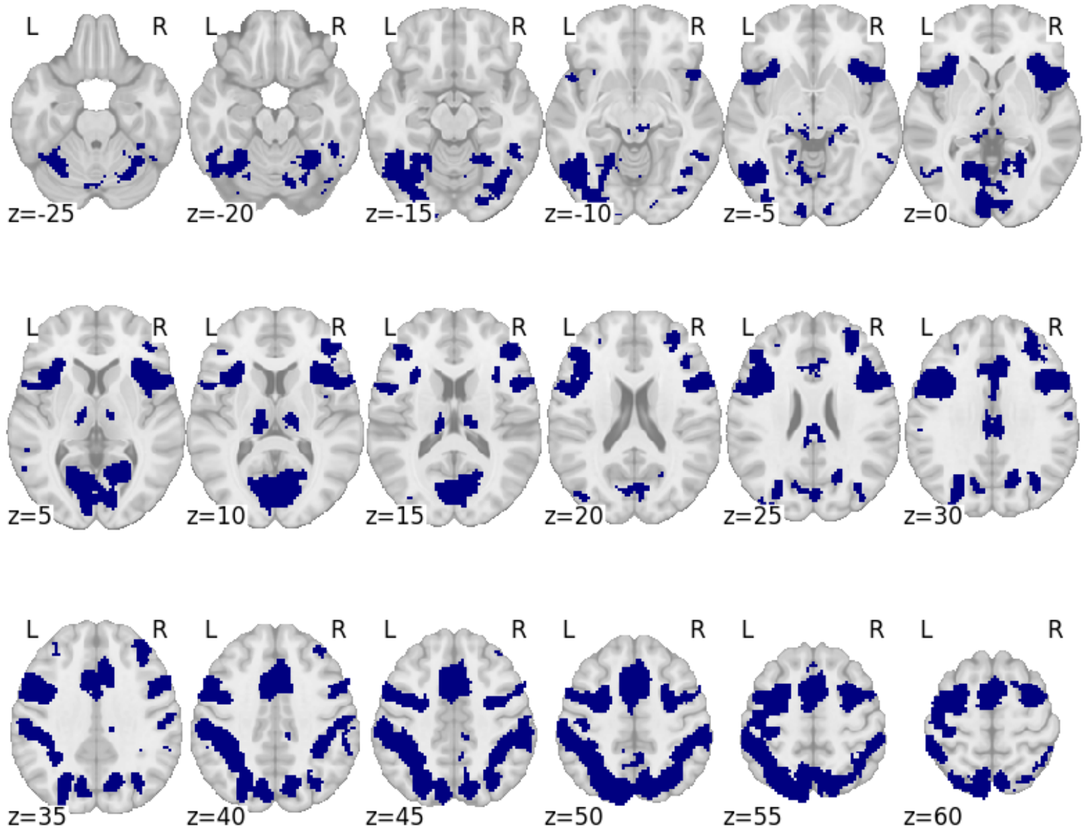
- From the standpoint of fMRI, these same RT differences reflect a potential confound
  - We can't tell whether the differences in activation are truly due to differences in neural computation, or simply

Mumford et al. 2023

Response time correlates in fMRI are very strong



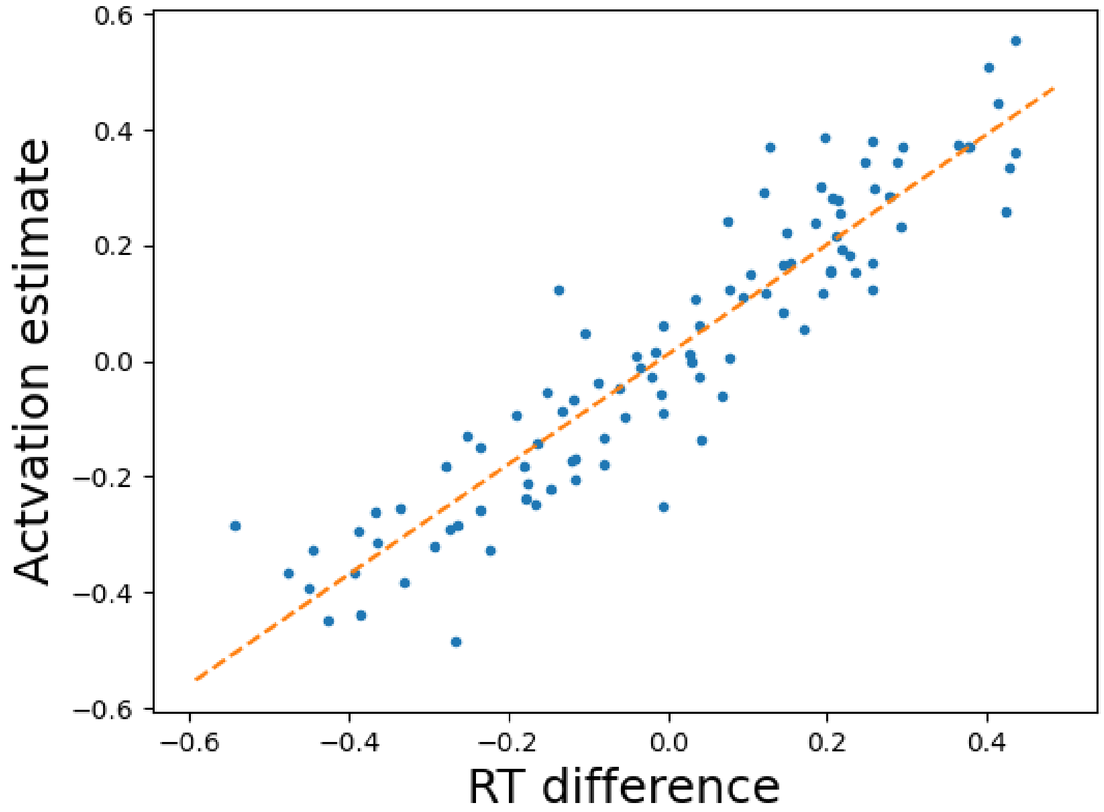
Yarkoni et al., 2009



Mumford et al, 2023

What about brain-behavior associations?

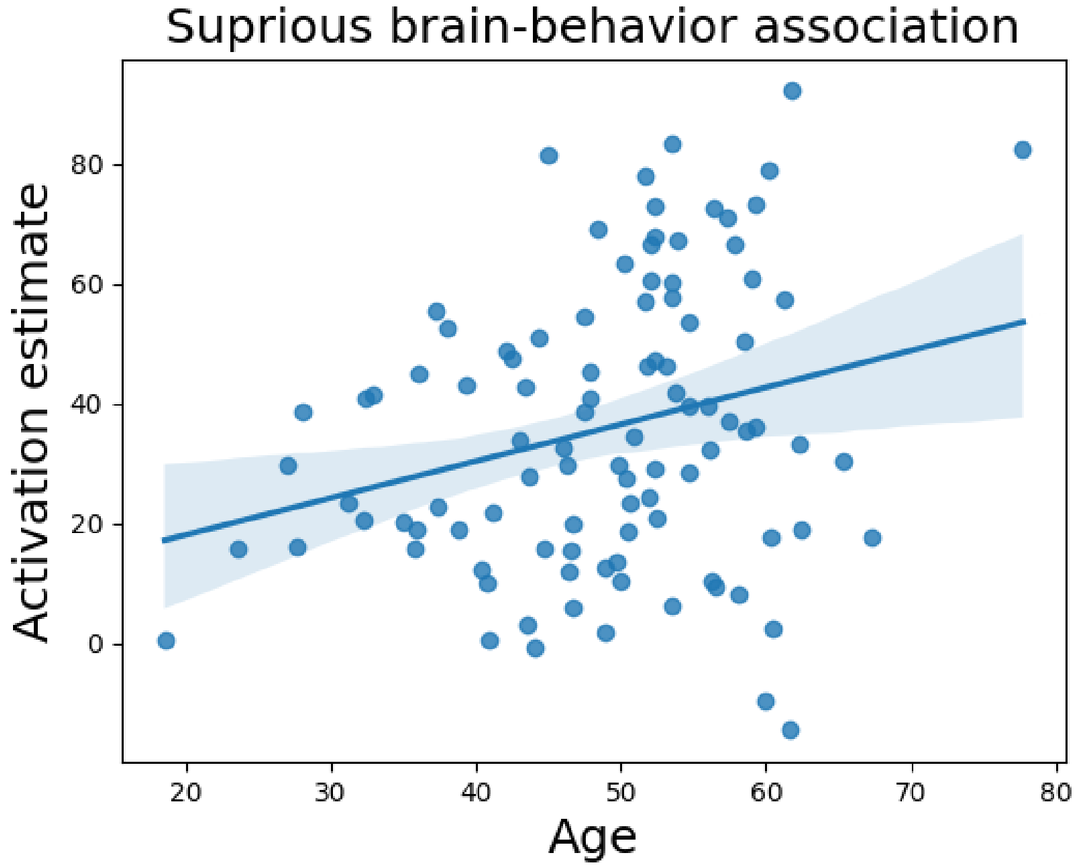
- Under the standard analysis approach (ignoring RT), if there are:
  - differences in the overall BOLD response (regardless of condition) across people
  - variability in the RT difference between conditions across people
- This can induce an artifactual correlation between activation (between-condition



Mumford et al, 2023

Spurious brain-behavior correlations

- When overall BOLD response (across all conditions) differs by some subject feature (e.g. age), then this can lead to spurious brain-behavior associations with that feature
  - Even when there is no true relationship between age and activation (condition differences) or RT!



Mumford et al, 2023

Can it be fixed by regressing out RT at the group level?

- No!
  - Simulations show that regressing RT out at the group level could actually *increase* the size of the spurious effect.

Without RT regressor in group model:

	t	p
Age	2.698	0.008

With RT regressor in group model:

	t	p
Age	7.163	0.000

Mumford et al, 2023

Solution: Model RT at the first level

Model name		Unconvolved regressor	Duration	Modulation
1	Constant Duration, no RT (ConsDurNoRT)		.1s	None
			.1s	None
2	RT Duration (RTDur)		RT	None
			RT	None
3	Constant Duration, RT (ConsDurRT)		.1s	None
			.1s	None
			.1s	RT*

← The standard model

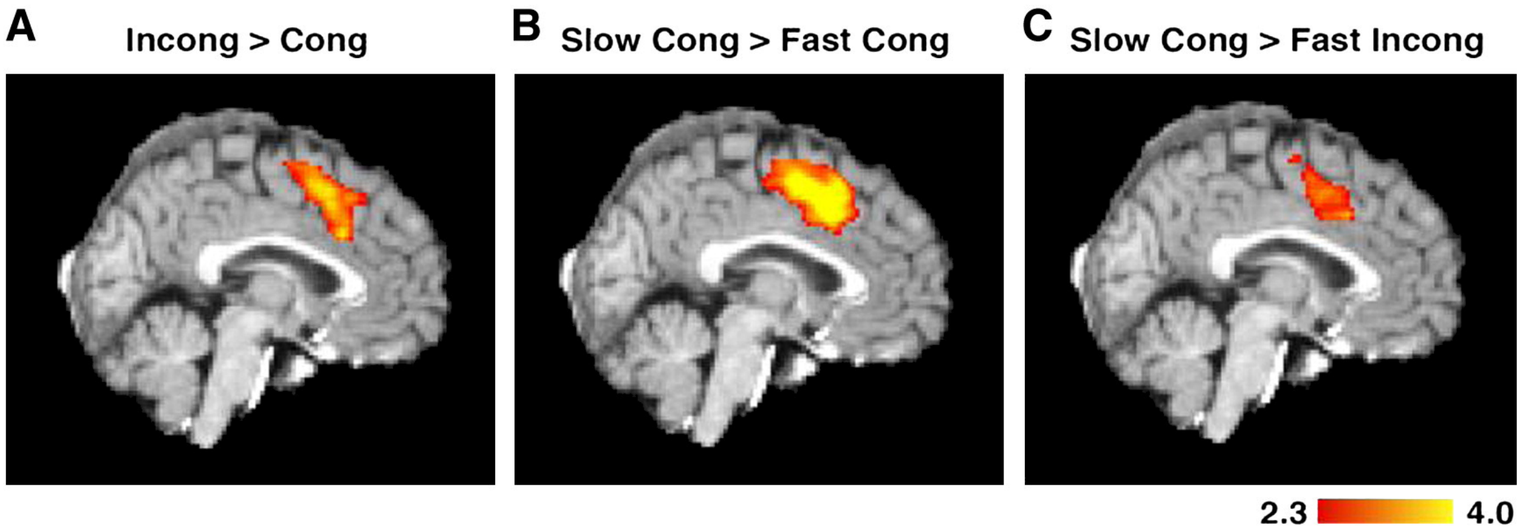
The Grinband et al. (2008) model

← The Mumford et al. model

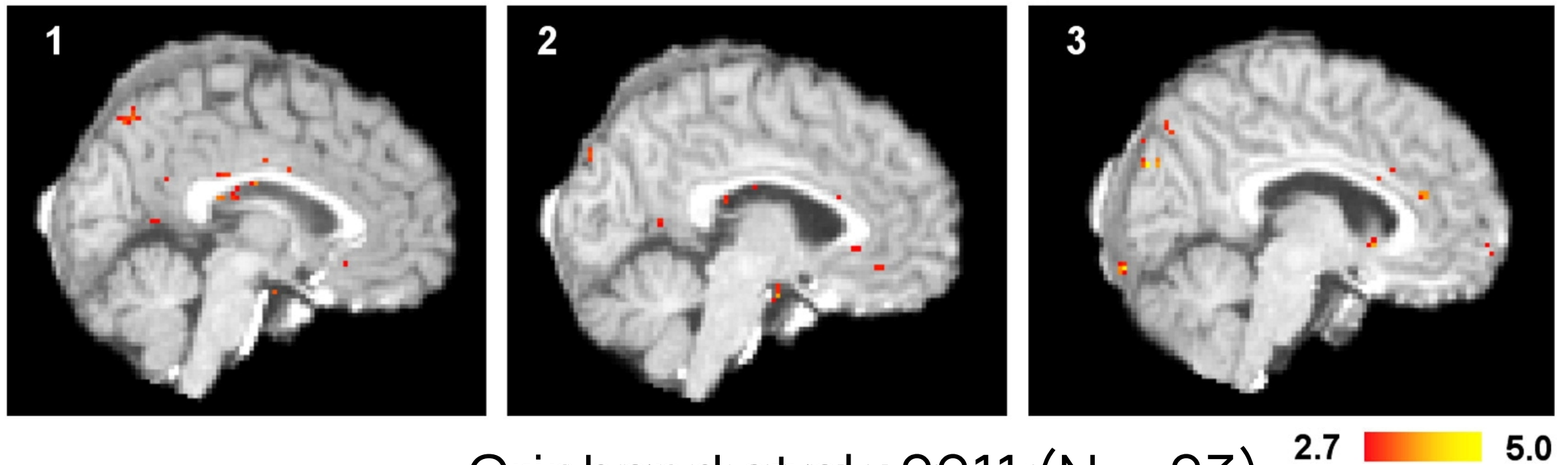
The Constant Duration + RT model allows quantification of the unique contributions of time on task and condition differences

Mumford et al, 2023

Are we throwing out the baby with the bathwater?



Activation for Stroop effect disappears after removing RT effect



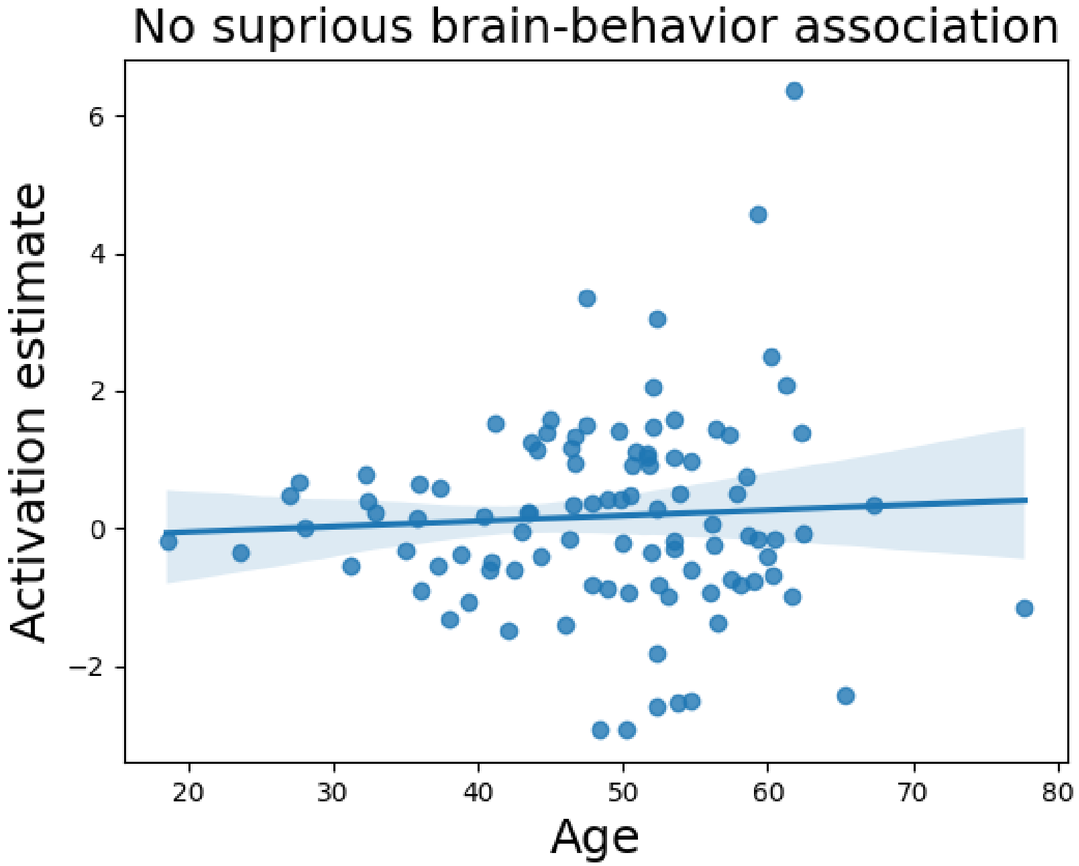
Grinband et al., 2011 (N = 23)

With sufficient power, we can find specific effects even after removing RT

Without RT modeling

With RT modeling

Modeling RT at the first level prevents suprious relations with RT and other correlates of BOLD response



Without first-level RT modeling:

	t	p
Age	2.698	0.008

With first-level RT modeling:

	t	p
Age	0.562	0.575

Mumford et al, 2023

Confound modeling is not a magic balm

- There is a general sense evident from brain-behavior association studies that regression can magically cure all that ails us
- Simply adding regressors will not fix many problems, and can cause others
  - Collider bias
    - When a confound regressor is a common effect of X and Y variables
  - Measurement error (Westfall & Yarkoni, 2016)

Conclusions

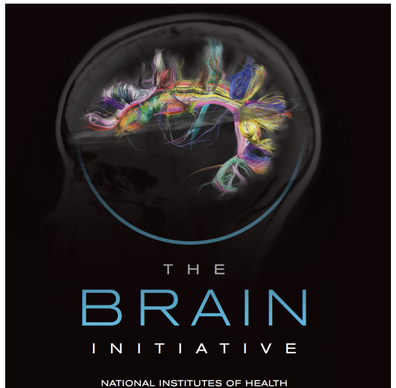
- Response time is a major potential confound for all task fMRI studies
  - Without adjustment, it is impossible to determine whether activations simply reflect time on task
- If response time effects are not modeled at the first level, they can result in sprious brain-behavior associations

Acknowledgments

The Poldrack Lab

Jeanette Mumford

Funding



NSF

NIH National Institute of Mental Health