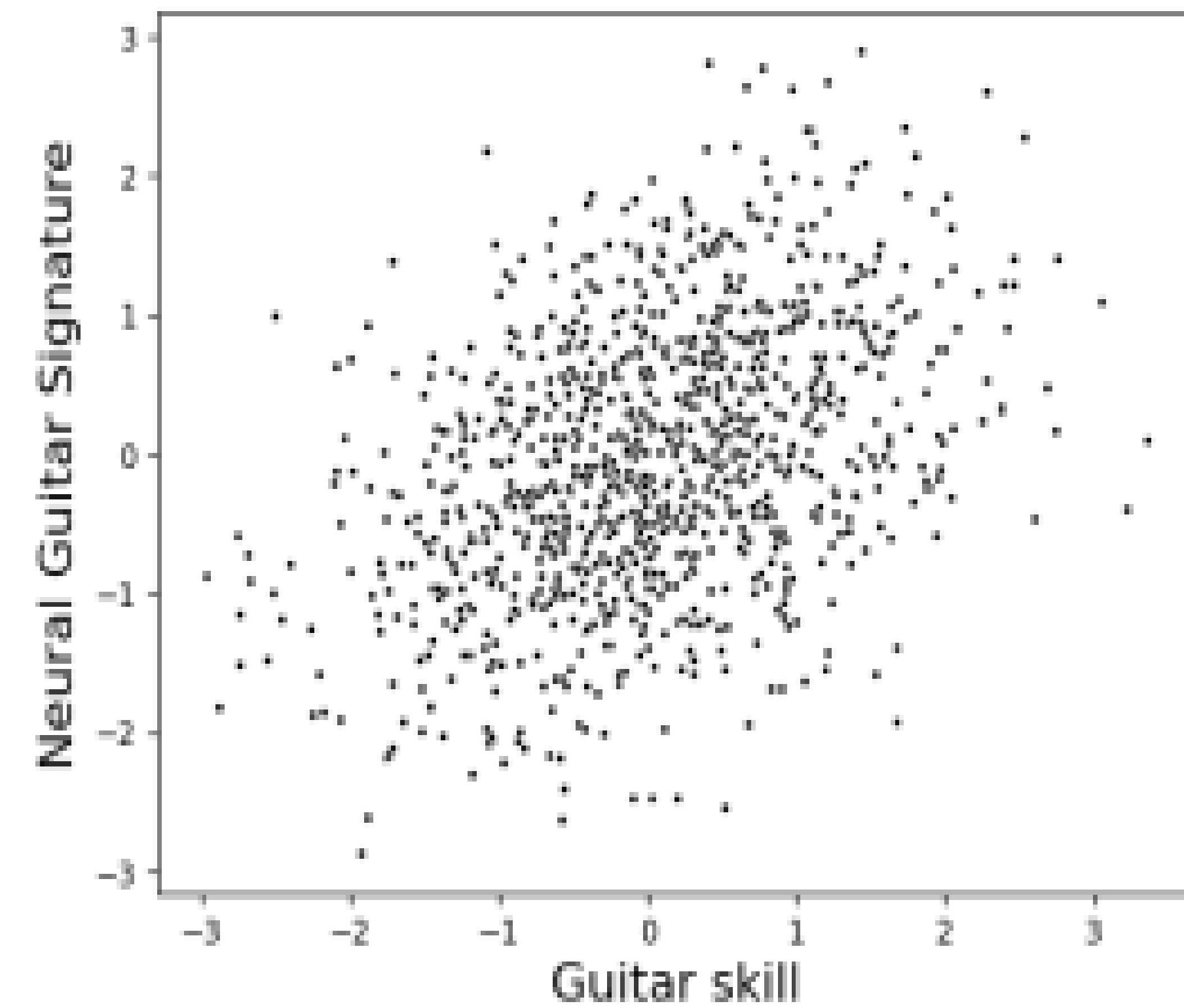
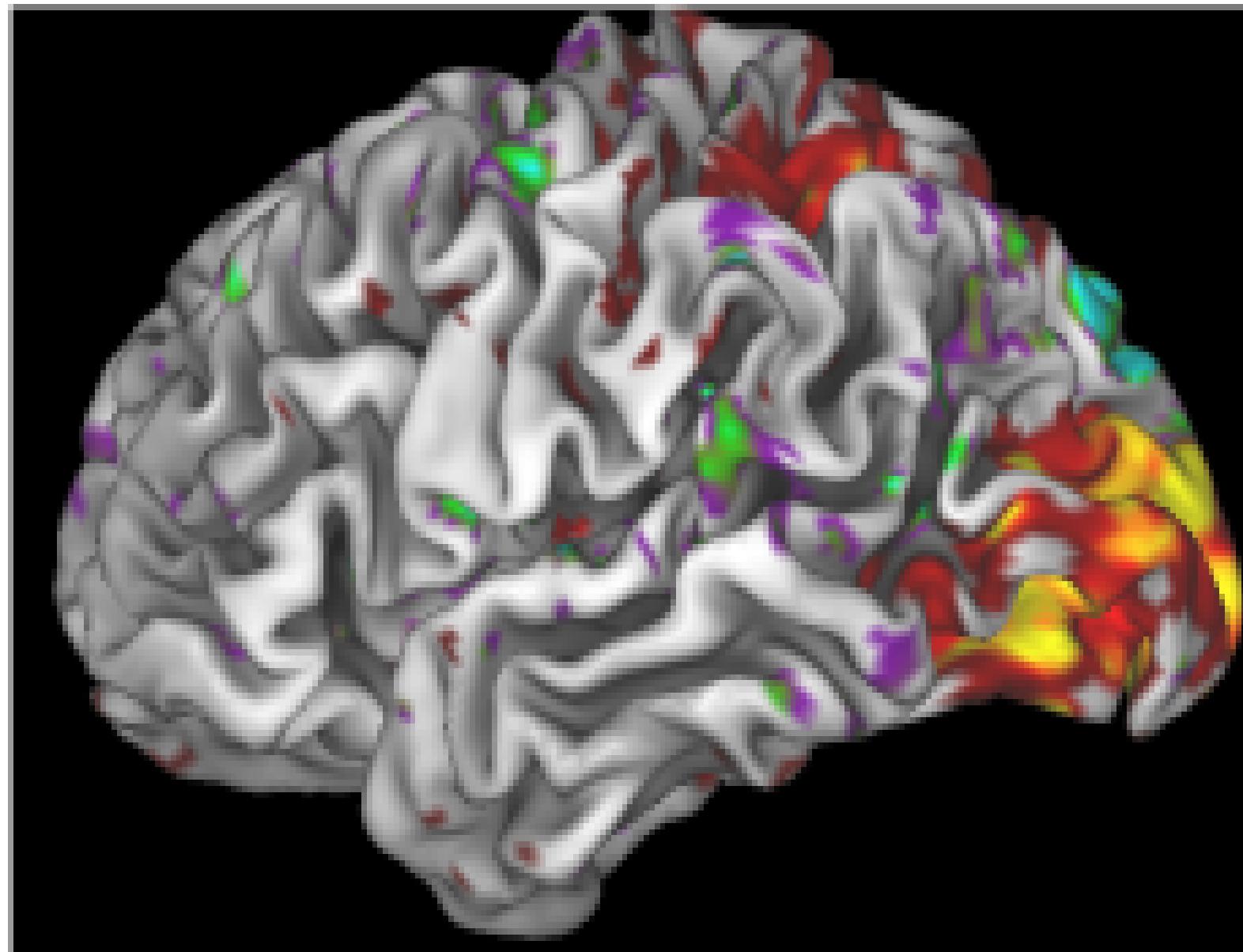


Improving the validity of brain-behavior associations

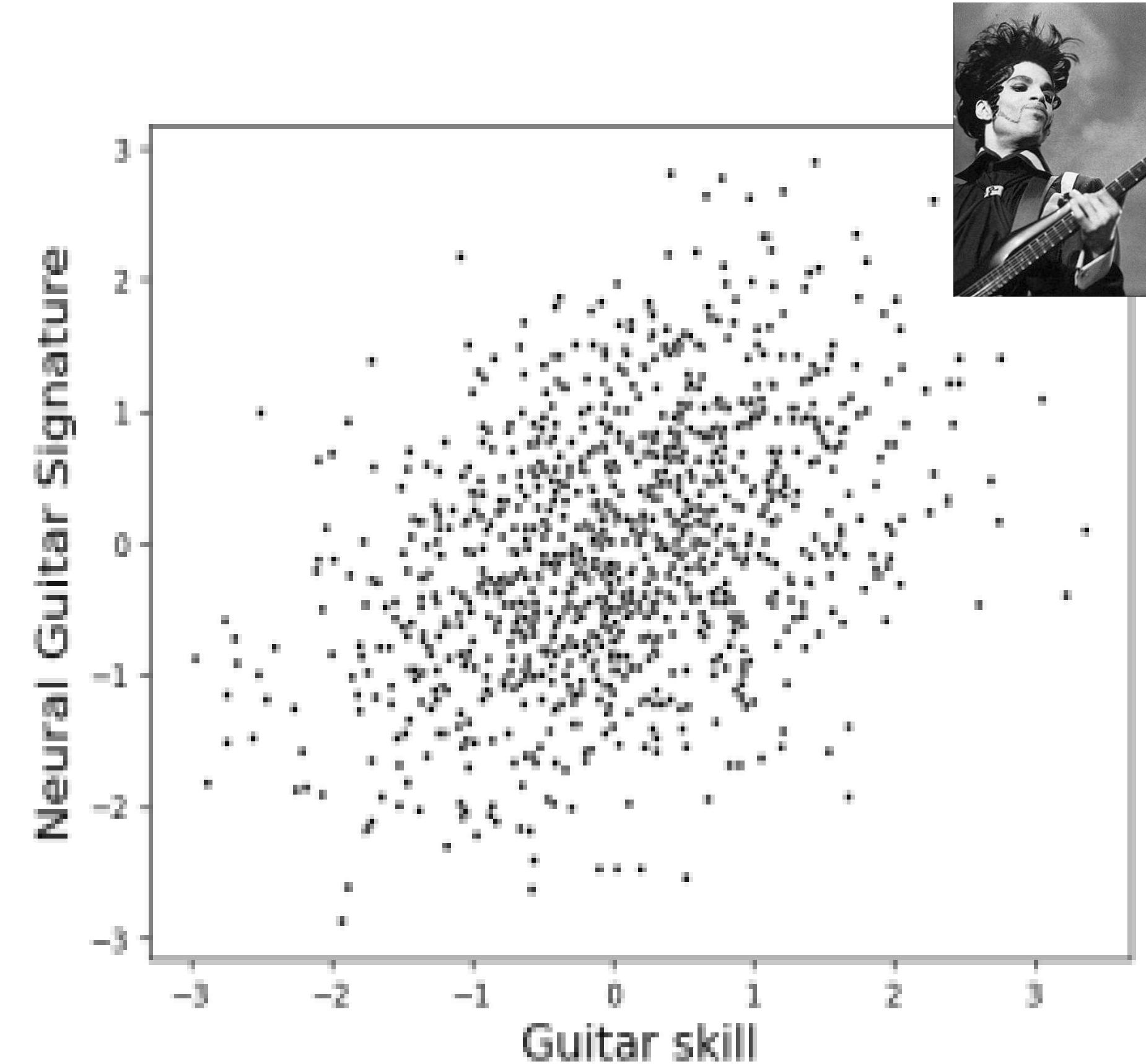
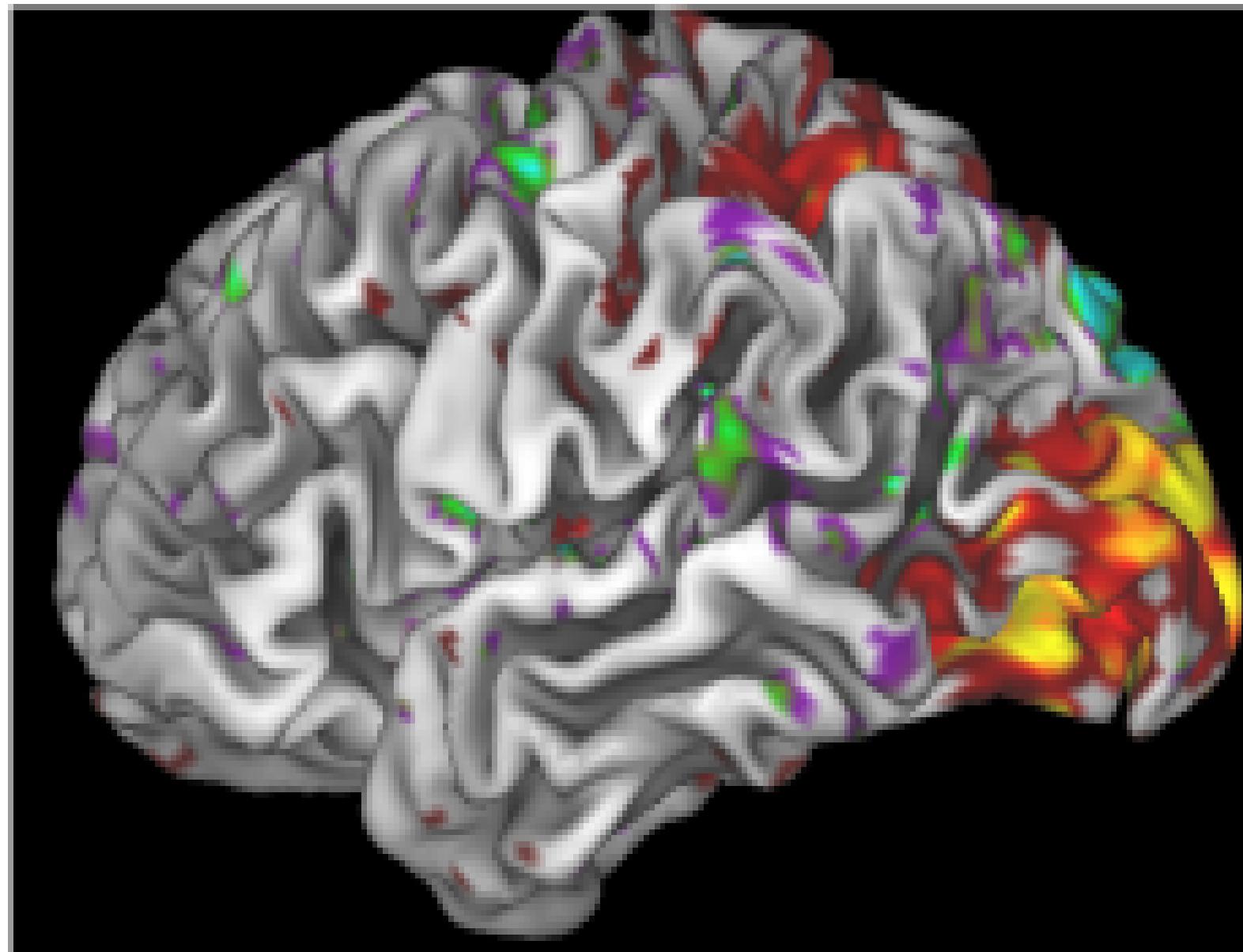
Russ Poldrack
Stanford University

What does a brain-behavior association mean?

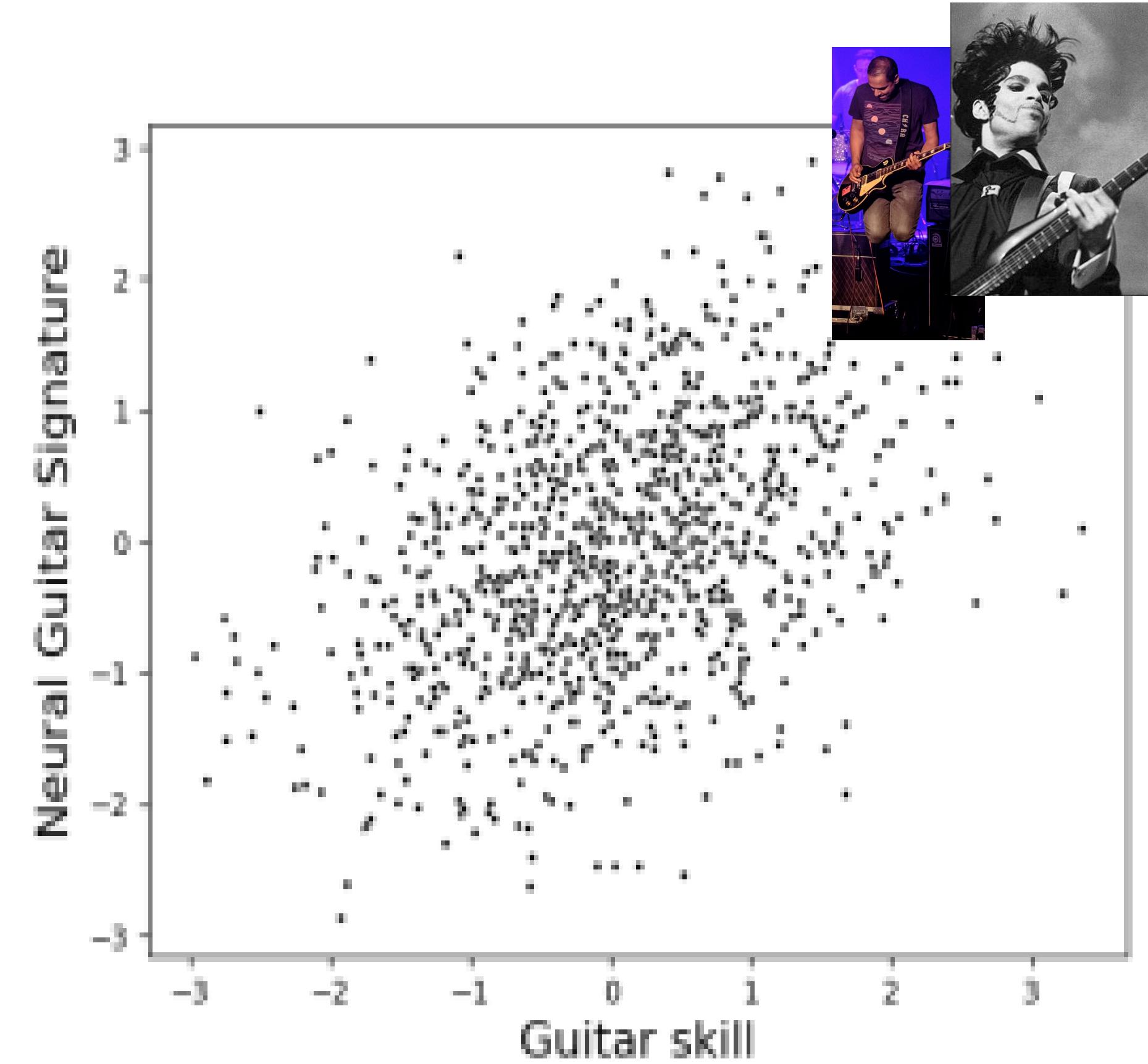
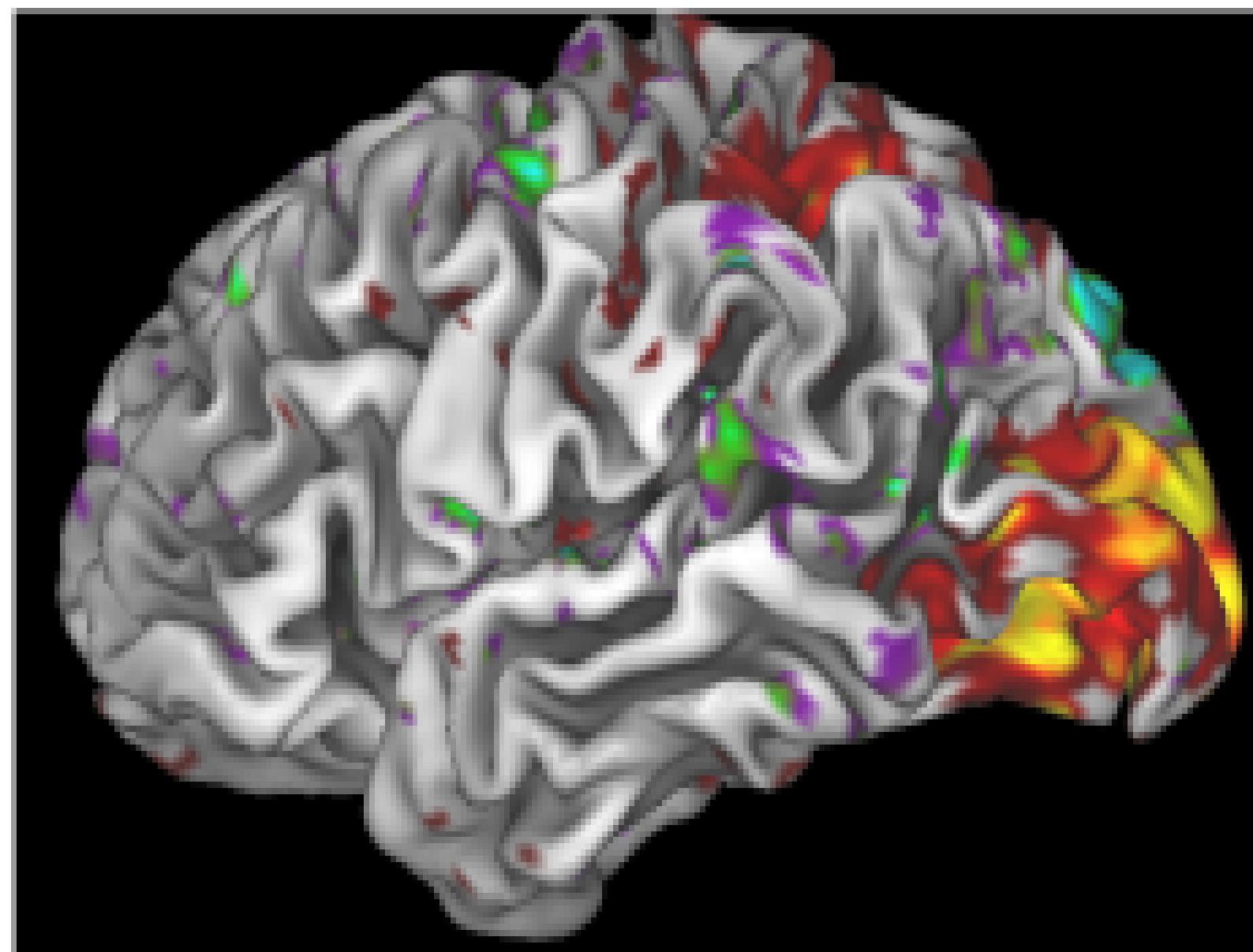
What does a brain-behavior association mean?



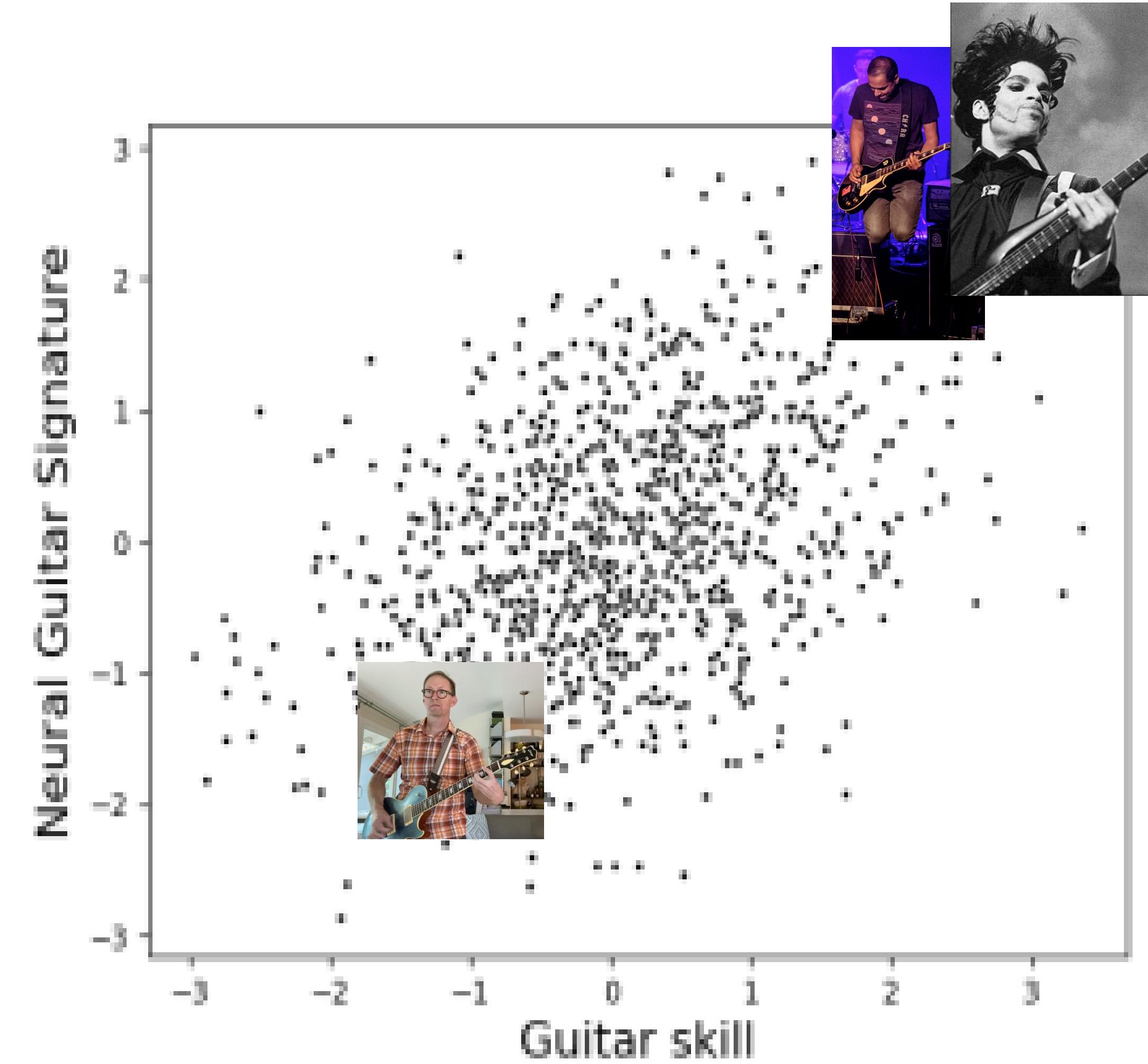
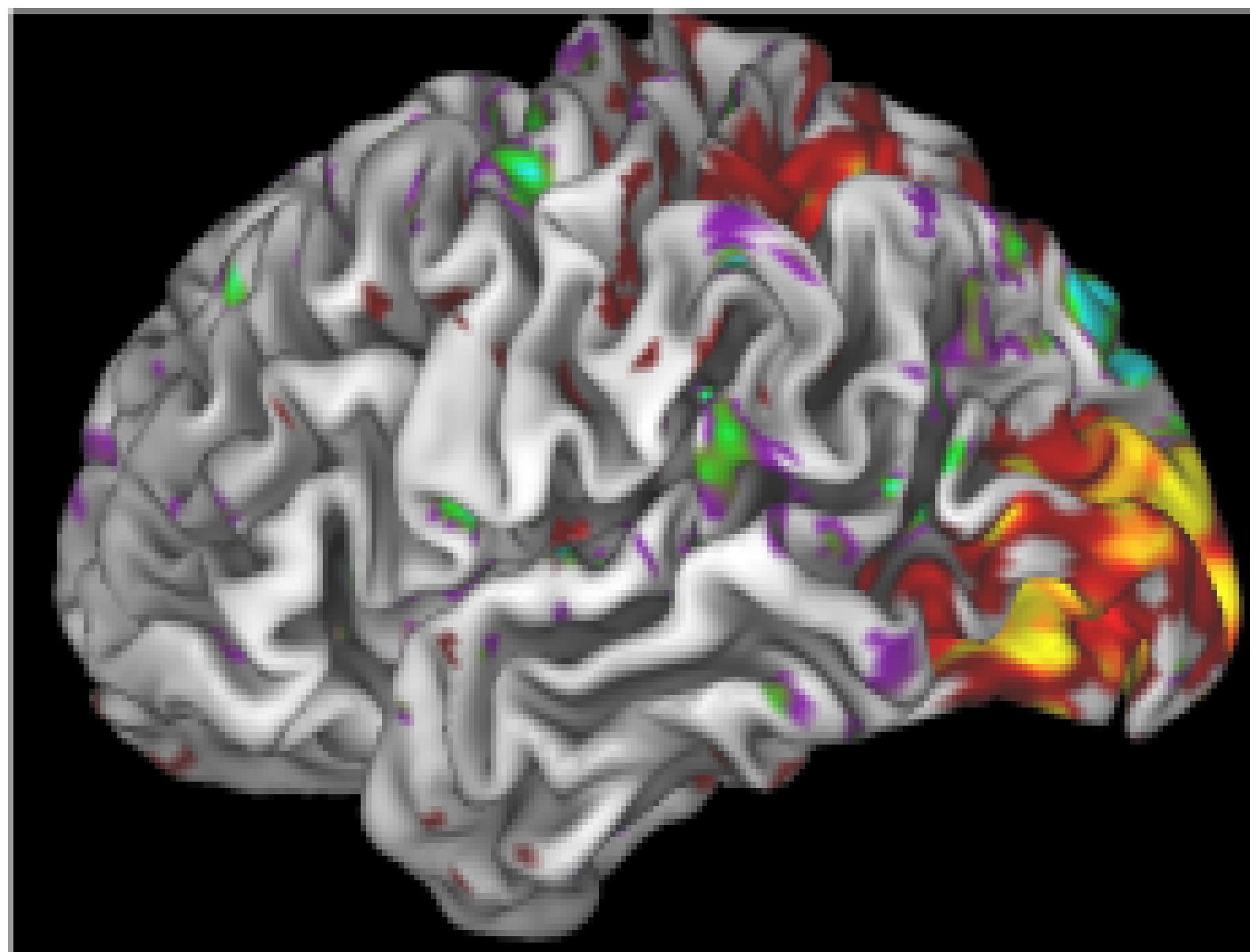
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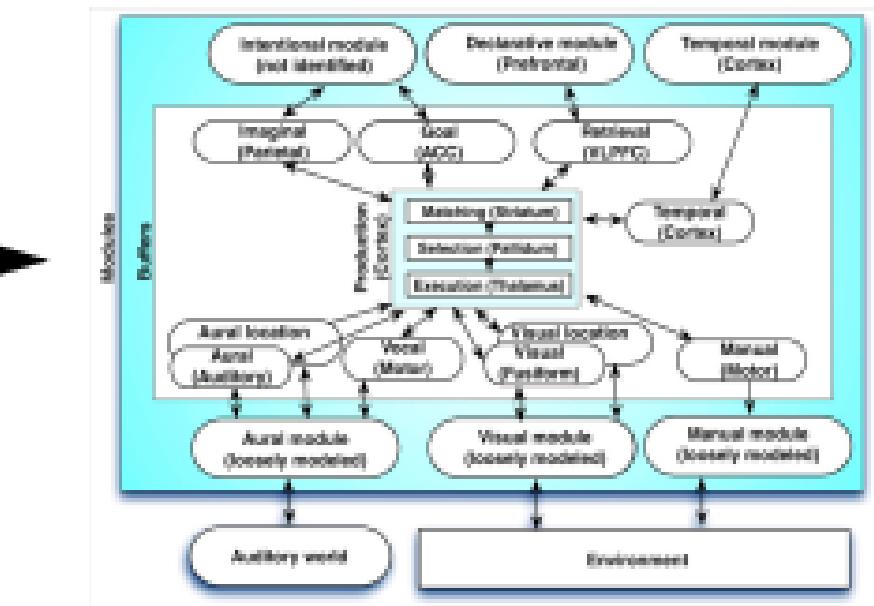
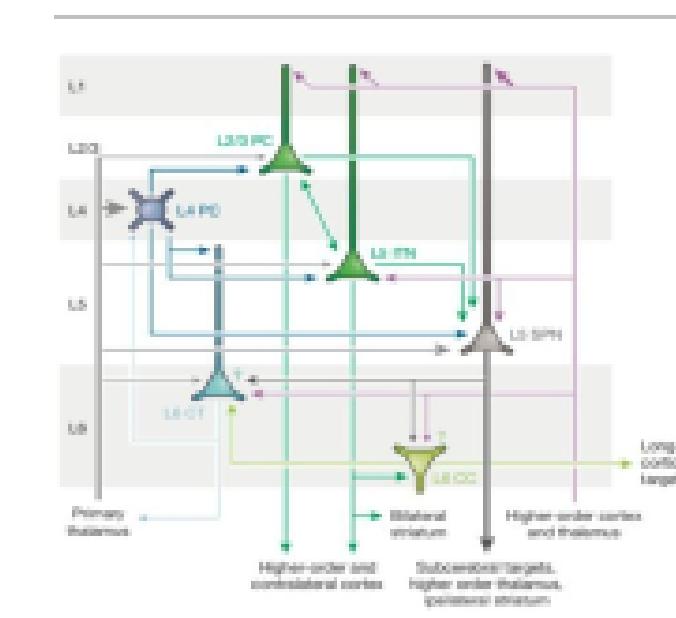


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What does a brain-behavior association mean?

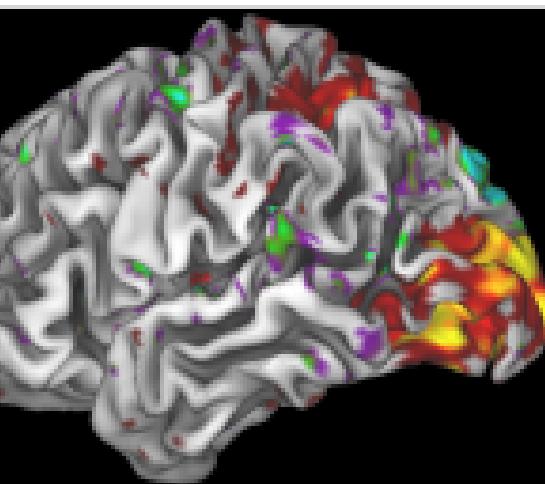




brain

cognition

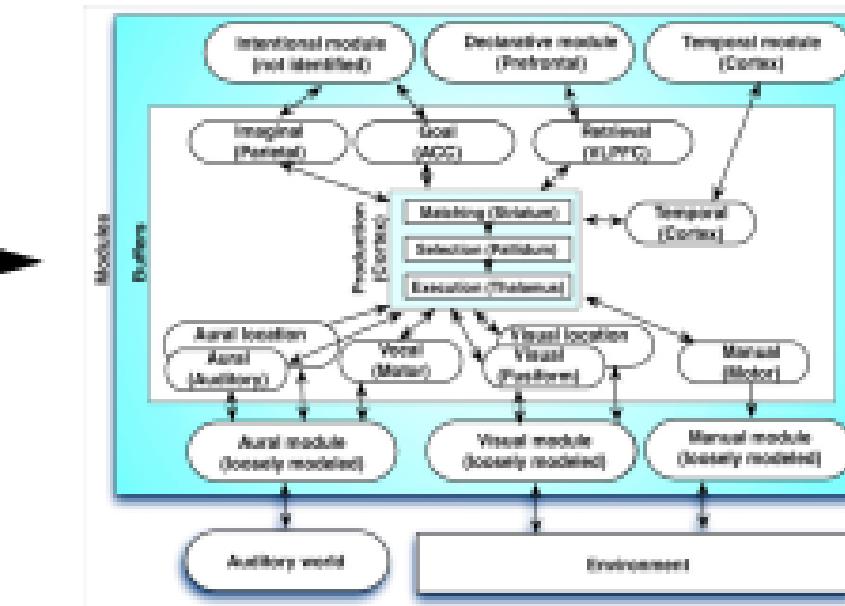
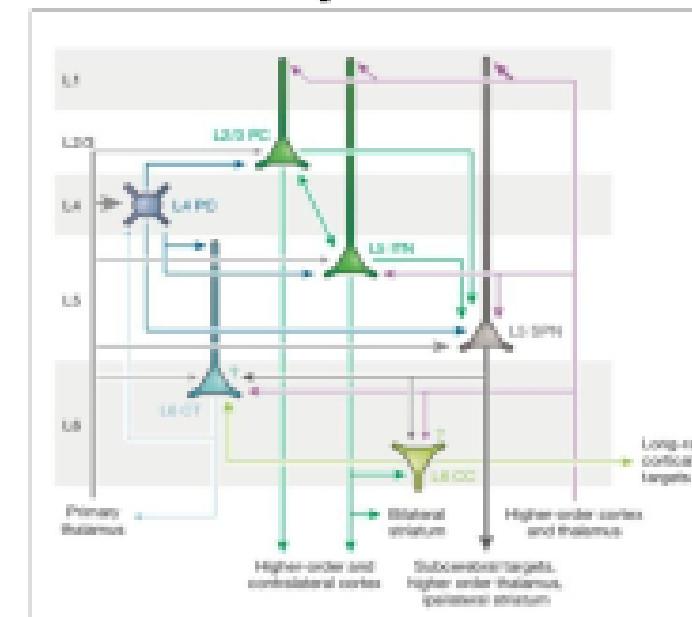
observed



fMRI

behavior

latent



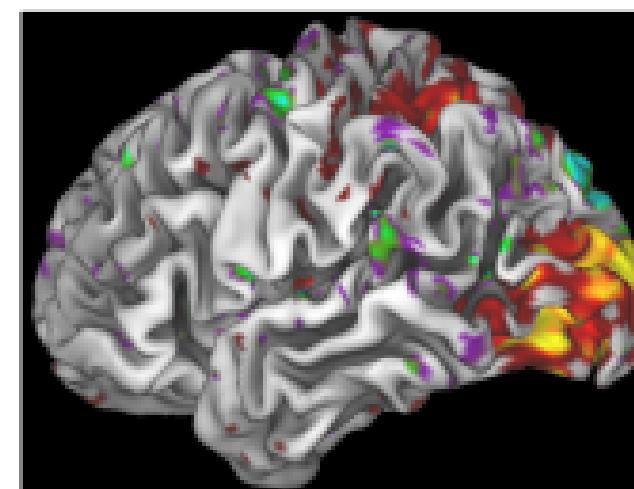
brain

cognition

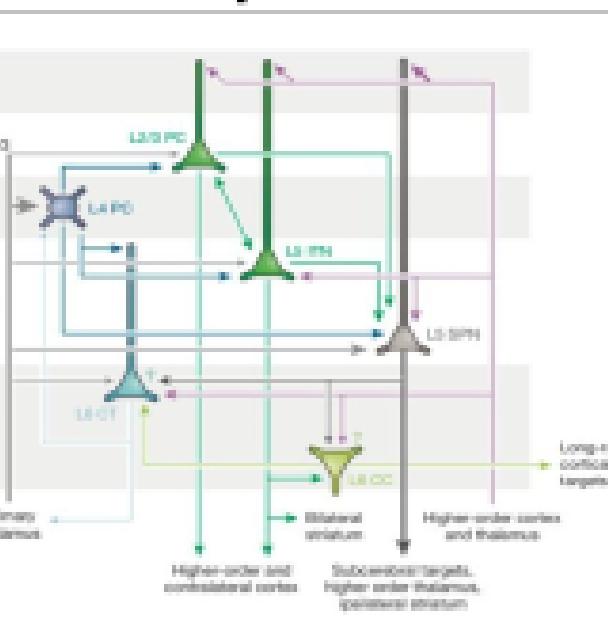
observed

fMRI

behavior

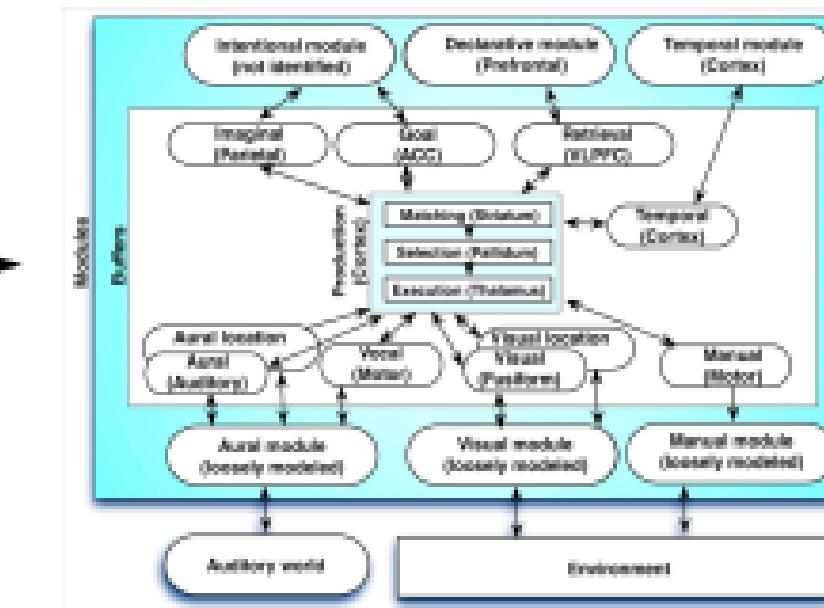


latent



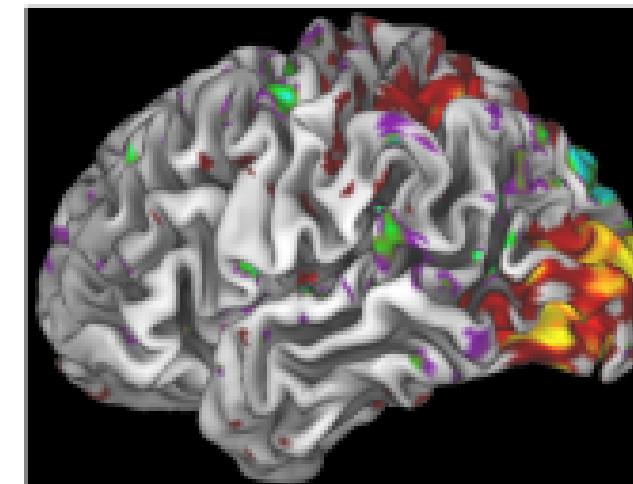
brain

cognition

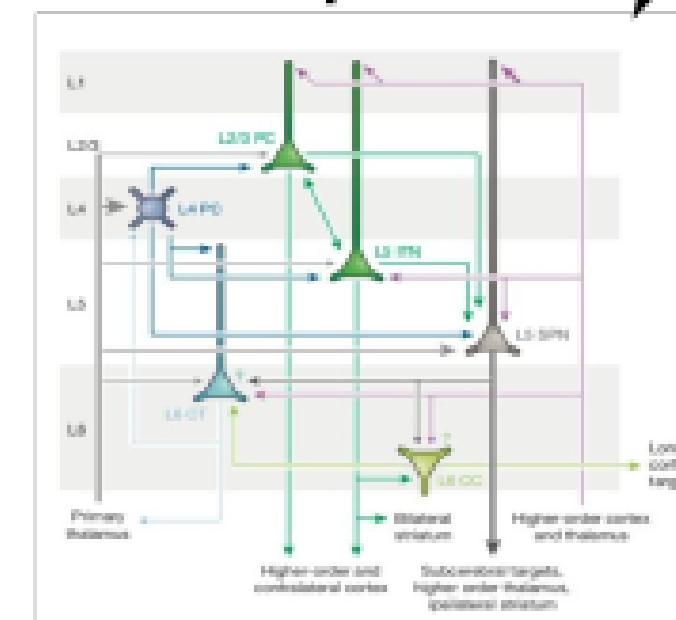


fMRI behavior

observed



latent



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

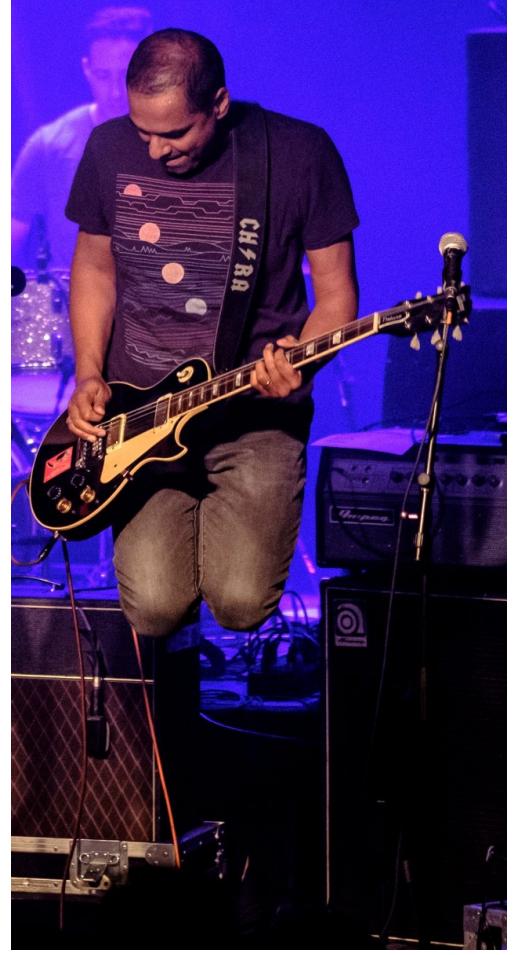
1. The Prius has a gas-electric hybrid engine (which uses surplus engine power to generate electricity which is then turned back into drive power) and regenerative braking (which captures energy that would otherwise be lost as heat).

Efficiency: A thought experiment

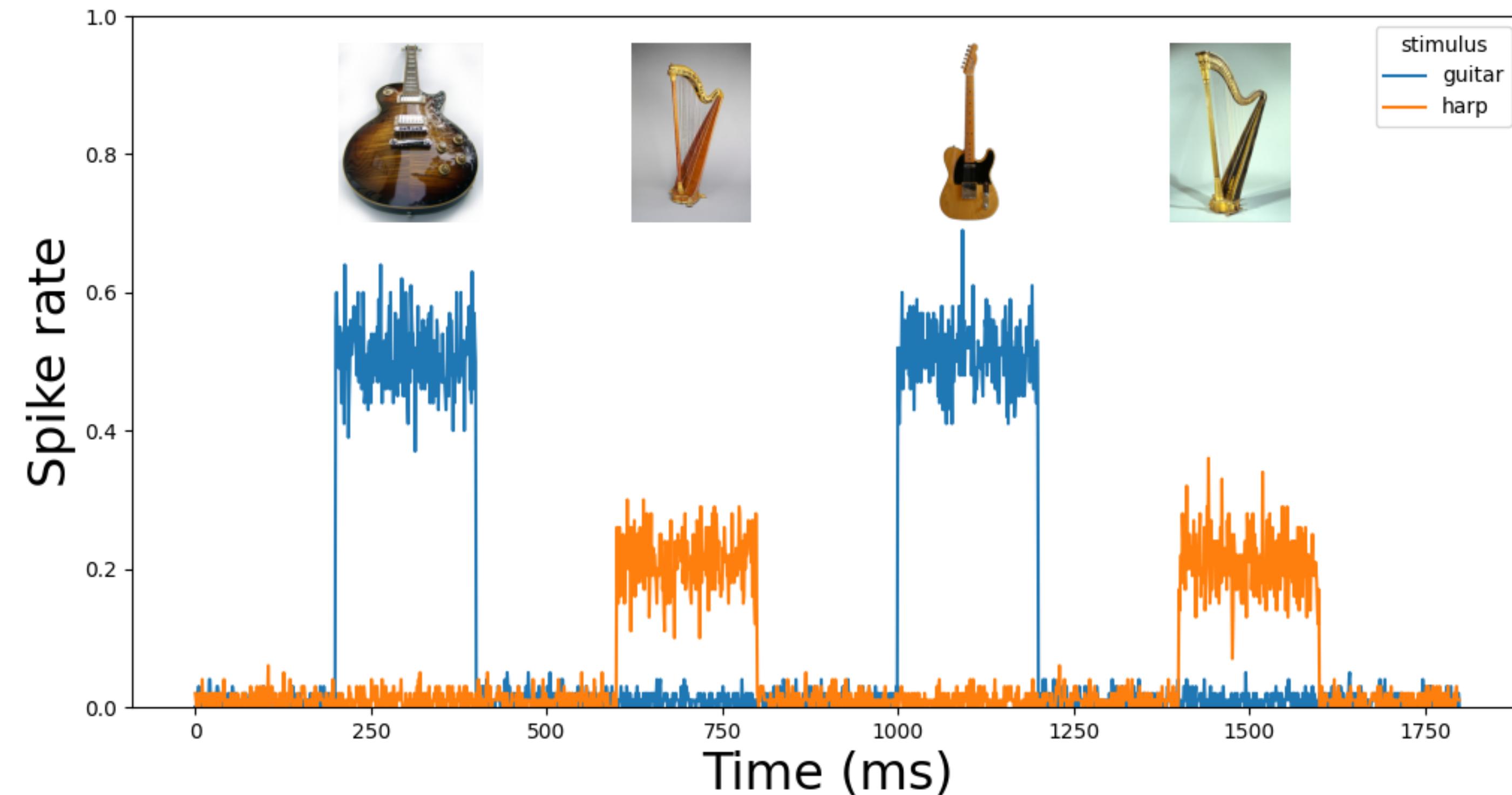
1. The Prius has a gas-electric hybrid engine (which uses surplus engine power to generate electricity which is then turned back into drive power) and regenerative braking (which captures energy that would otherwise be lost as heat).
2. The Prius is more efficient.

Explaining brain-behavior associations

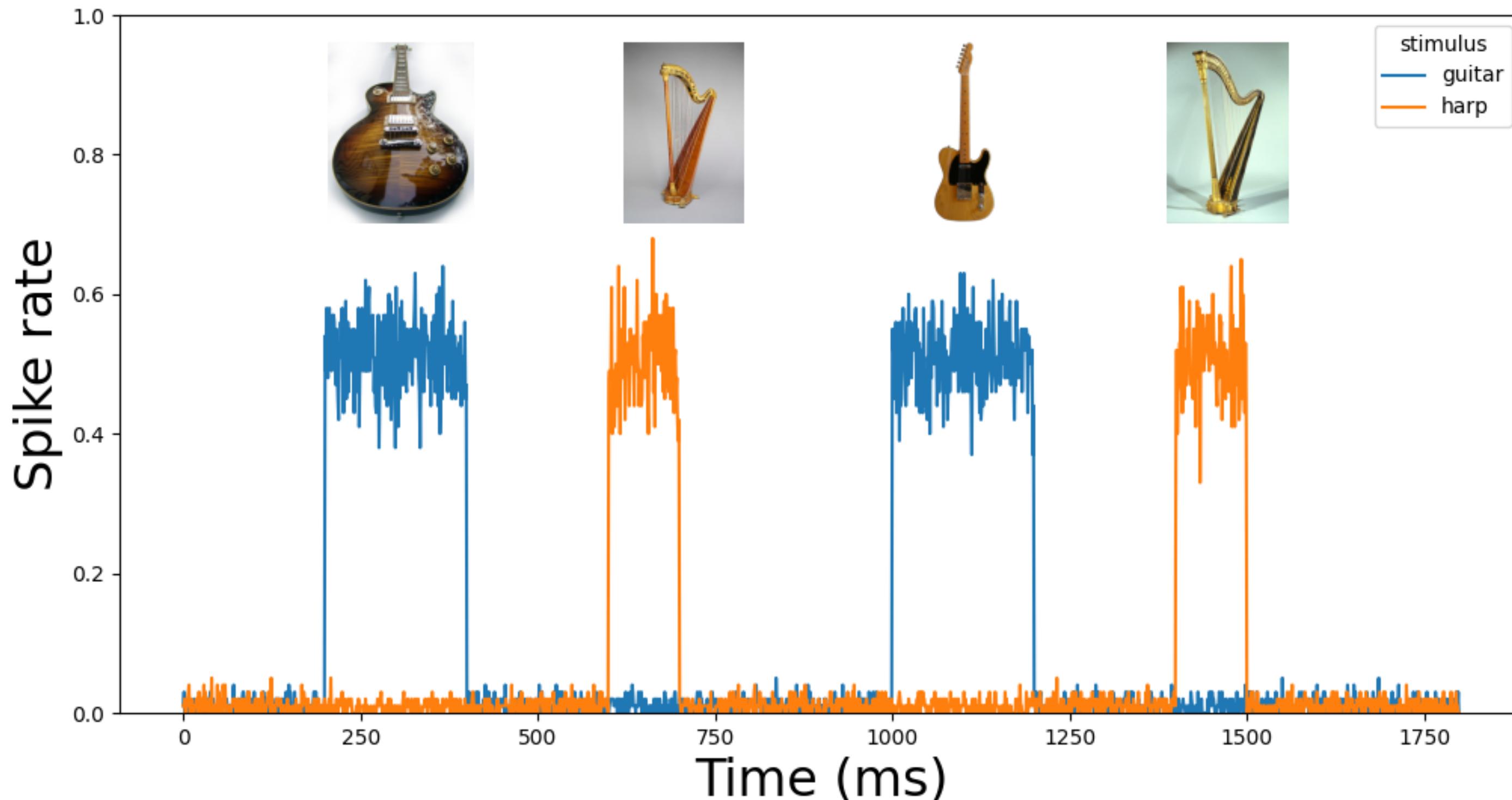
- “Efficiency” is a non-explanation
 - It simply renames the phenomenon
- What kinds of neural differences might actually explain these associations?
 - Different intensity of neuronal activity
 - Different duration of neuronal activity



Difference in intensity of neural activity

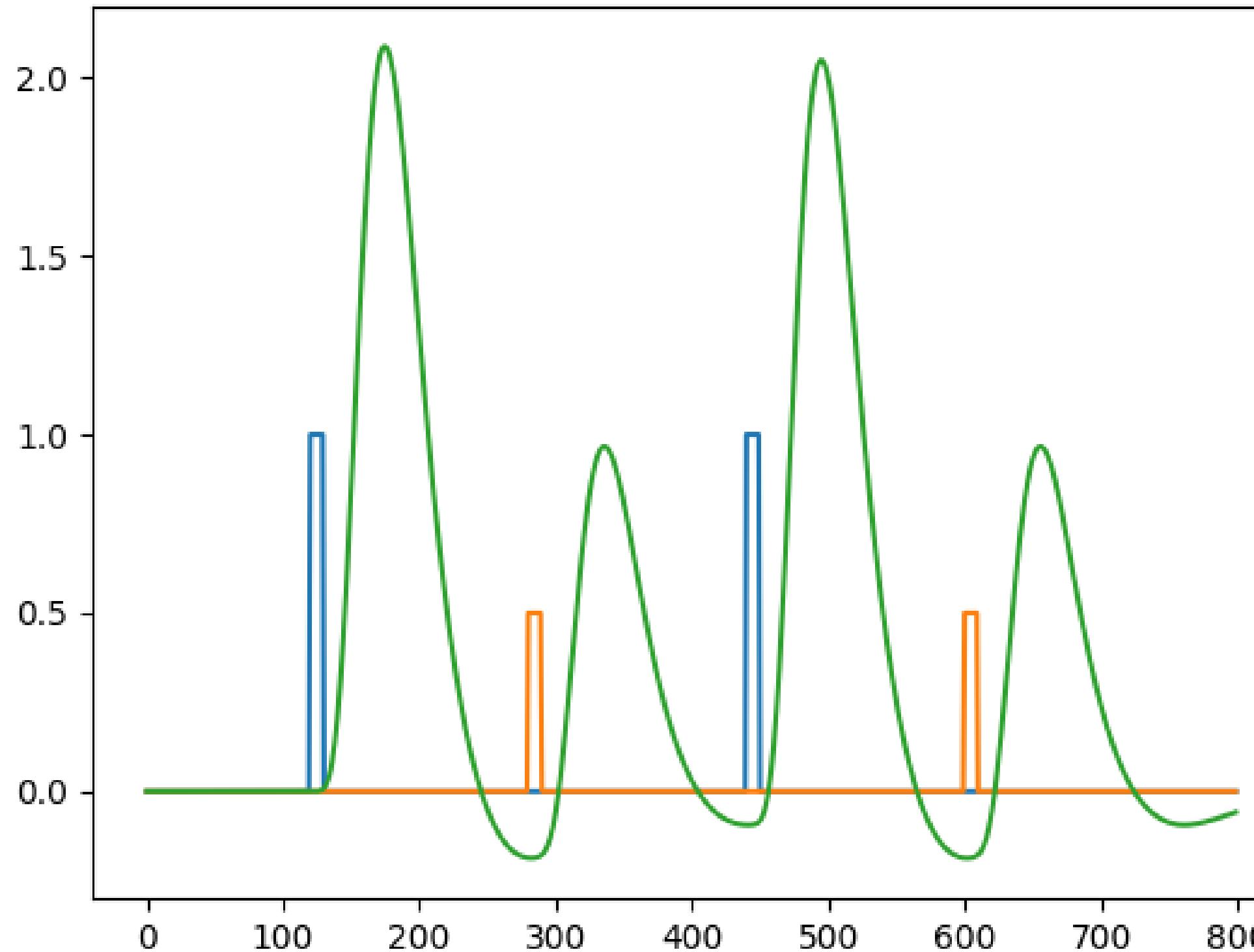


Difference in duration of neural activity

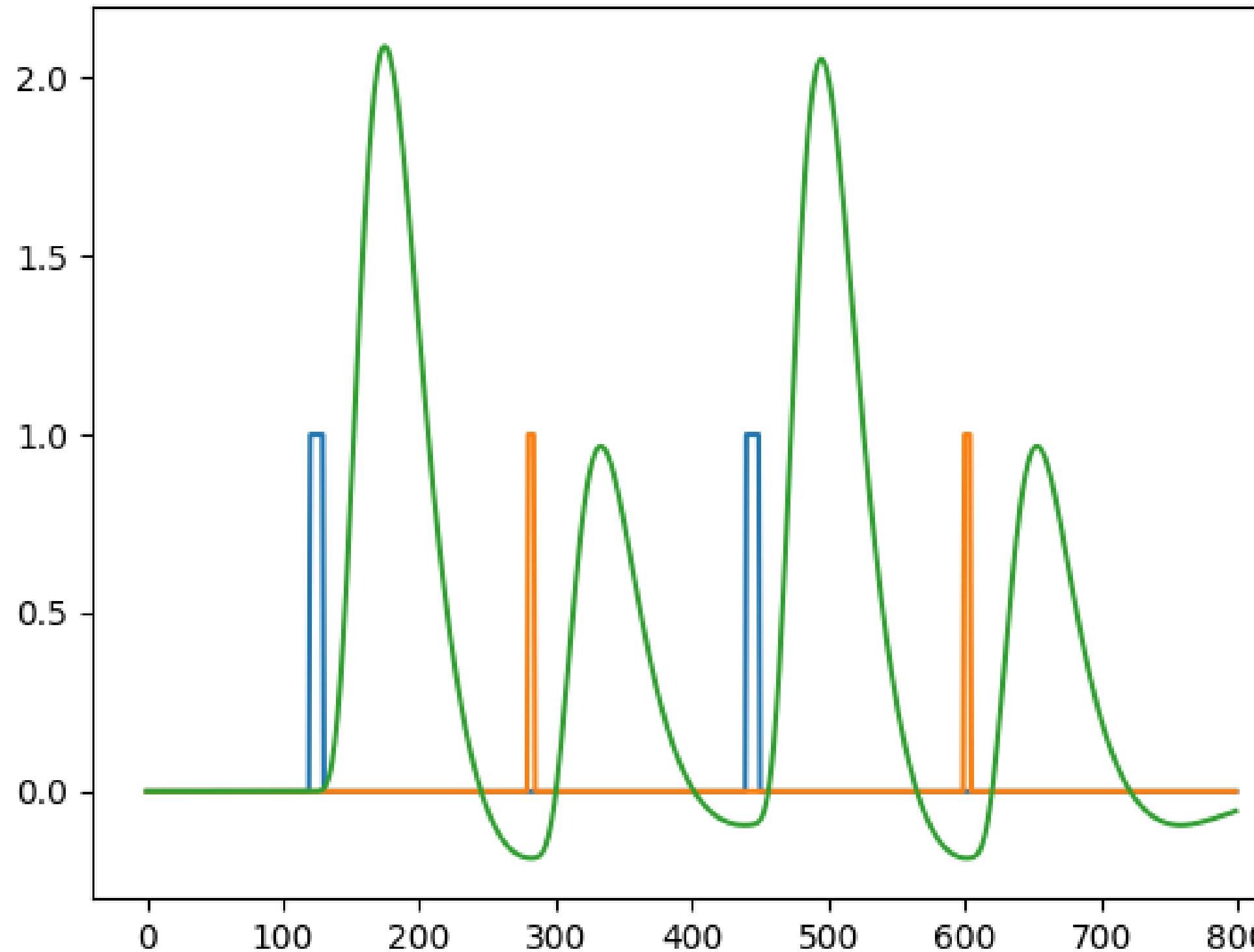


Changes in rate vs. duration of neural firing are
indistinguishable in fMRI

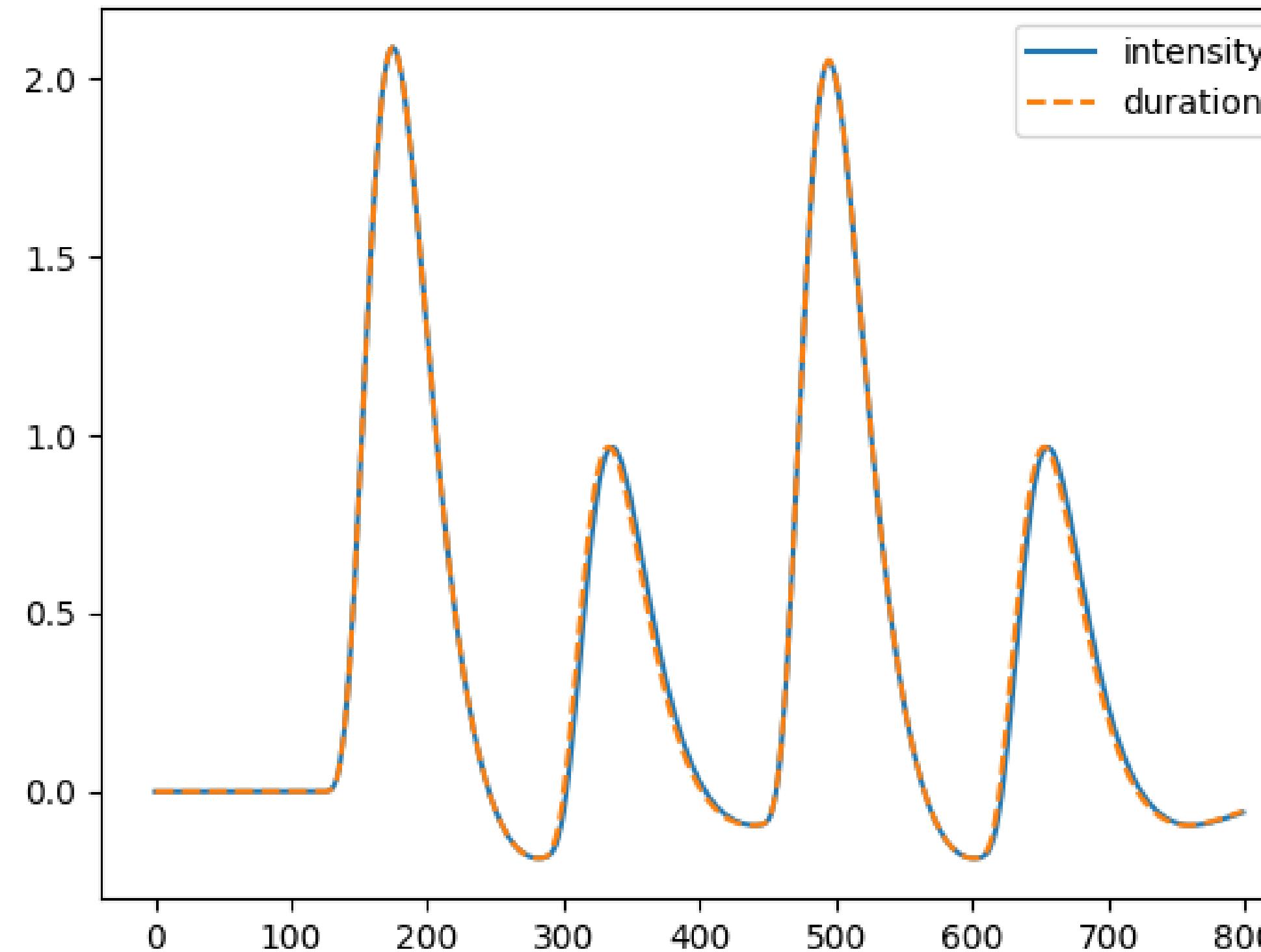
Same duration, different amplitude



Same amplitude, different duration



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

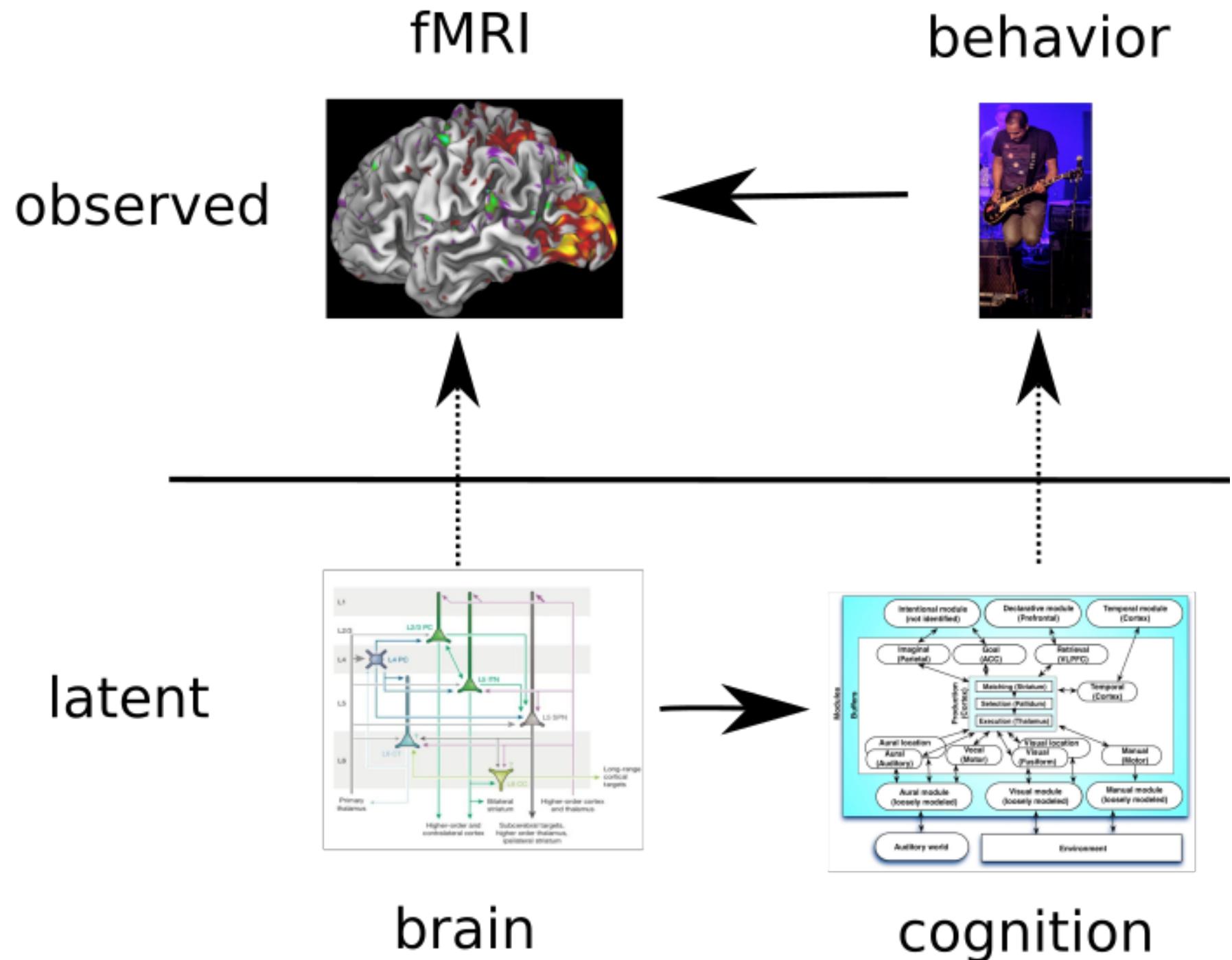


The response time paradox

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

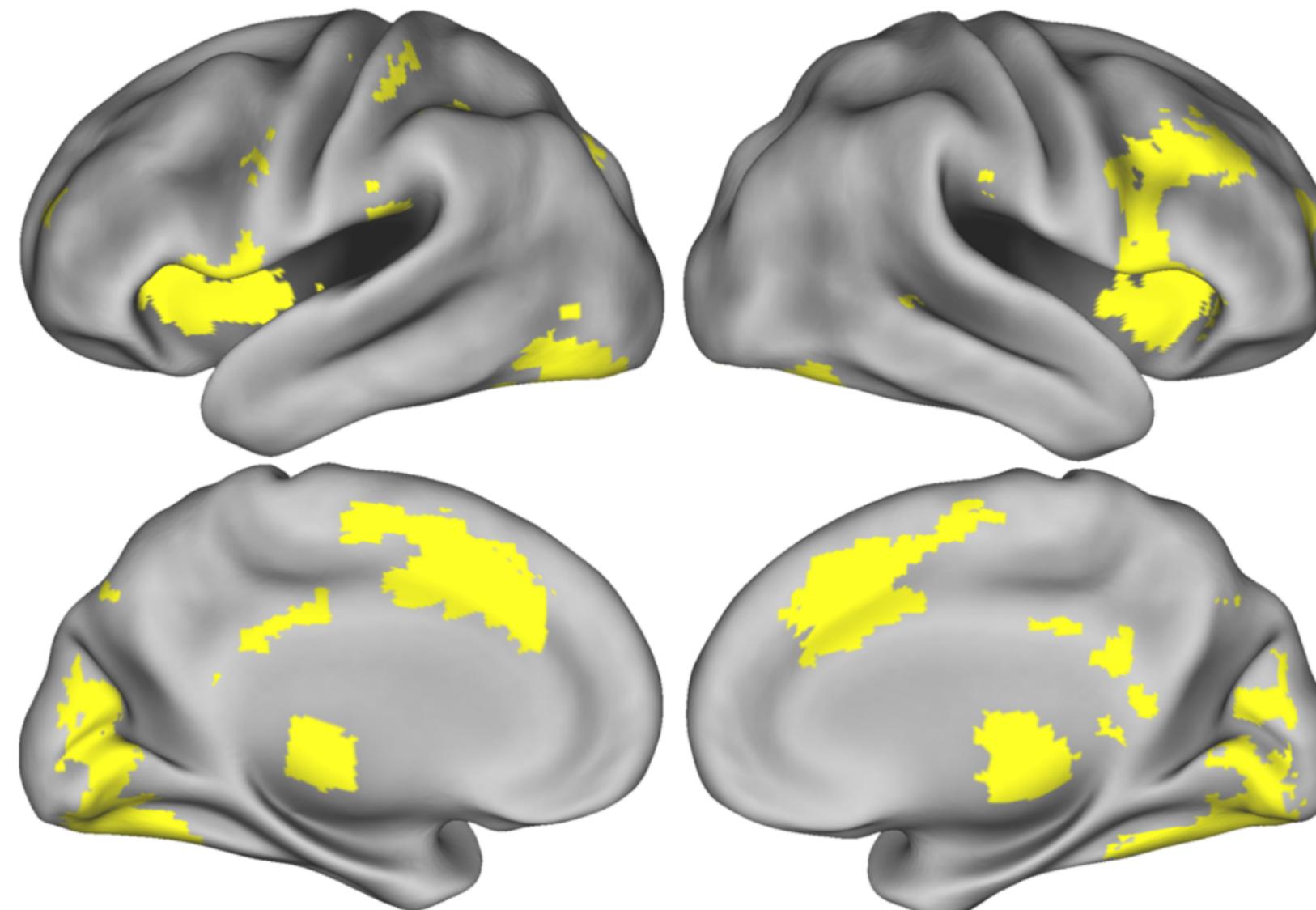
The response time paradox

- 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 due to a "time on task" confound
 - Known since Grinband et al. (2008)

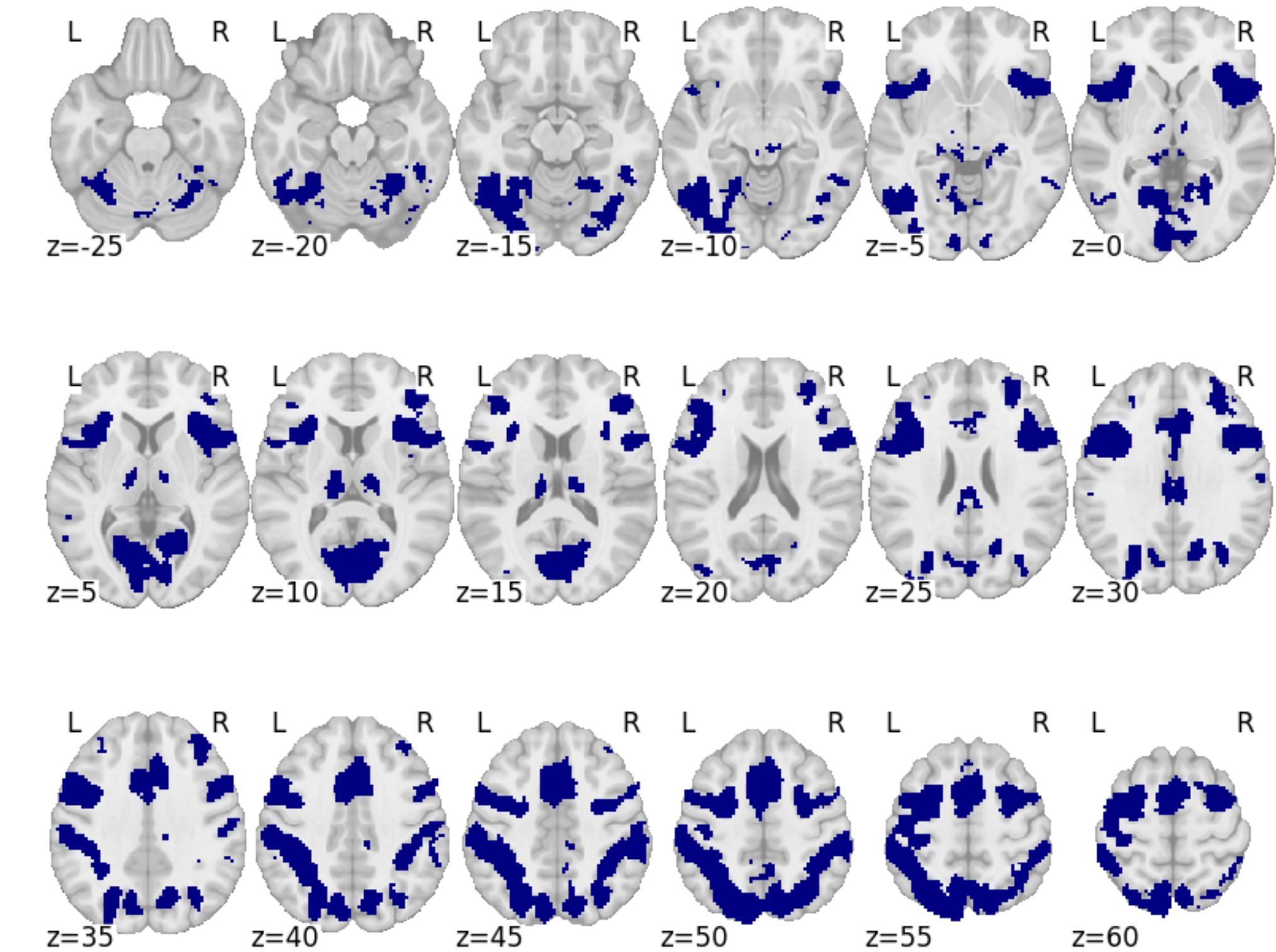


Response time correlates in fMRI are very strong

Conjunction across 4 tasks



Conjunction across 7 tasks

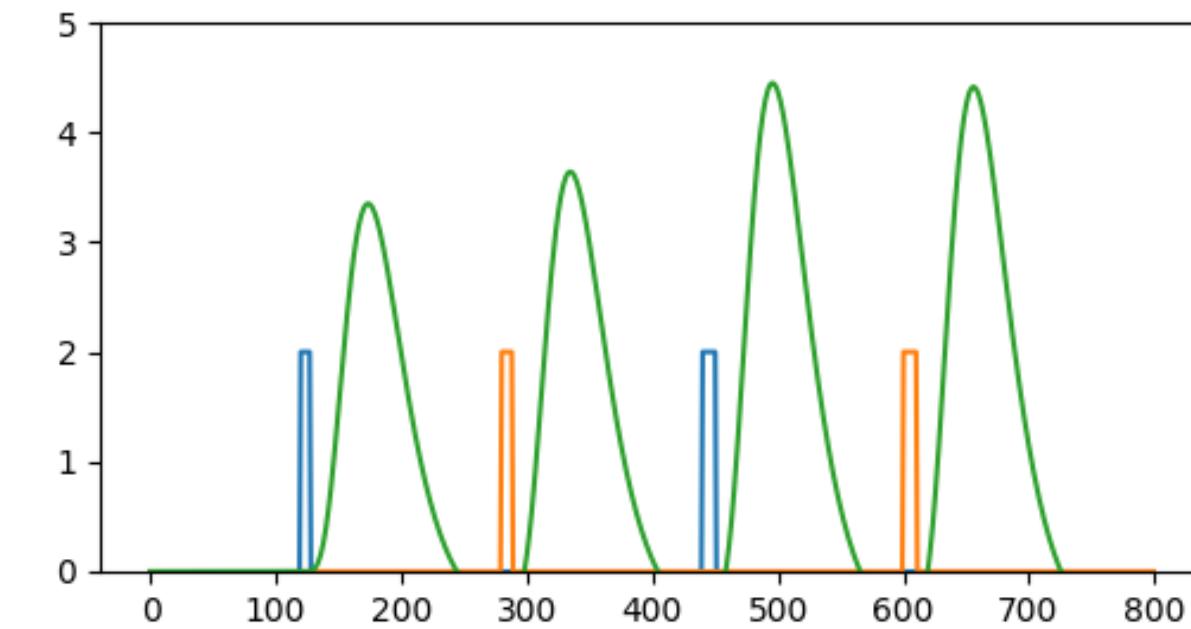
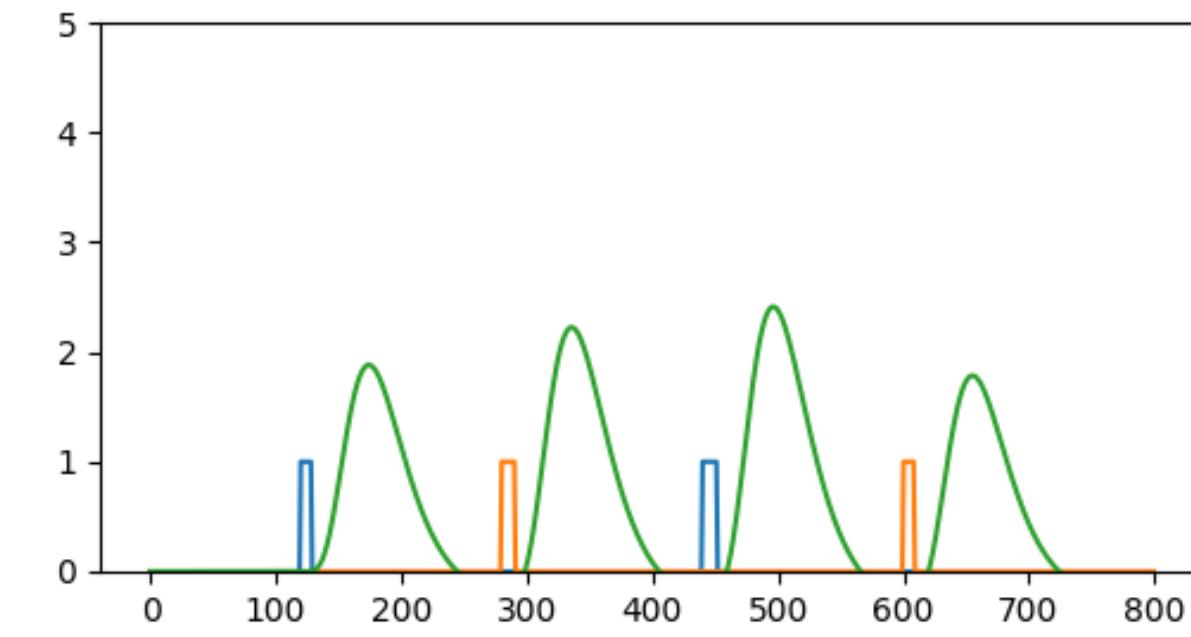


Yarkoni et al., 2009

Mumford et al, 2023

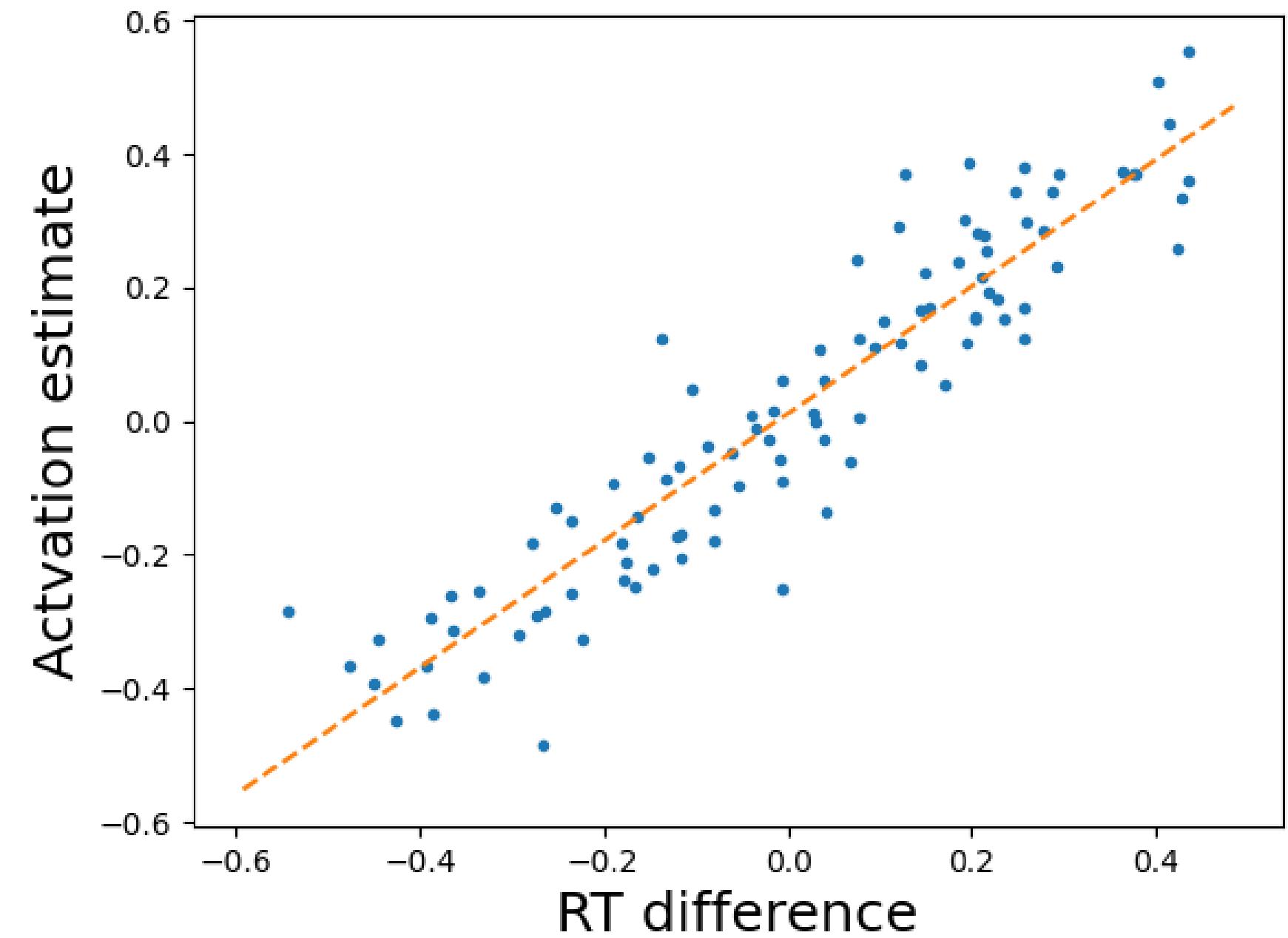
What about brain-behavior associations?

- 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



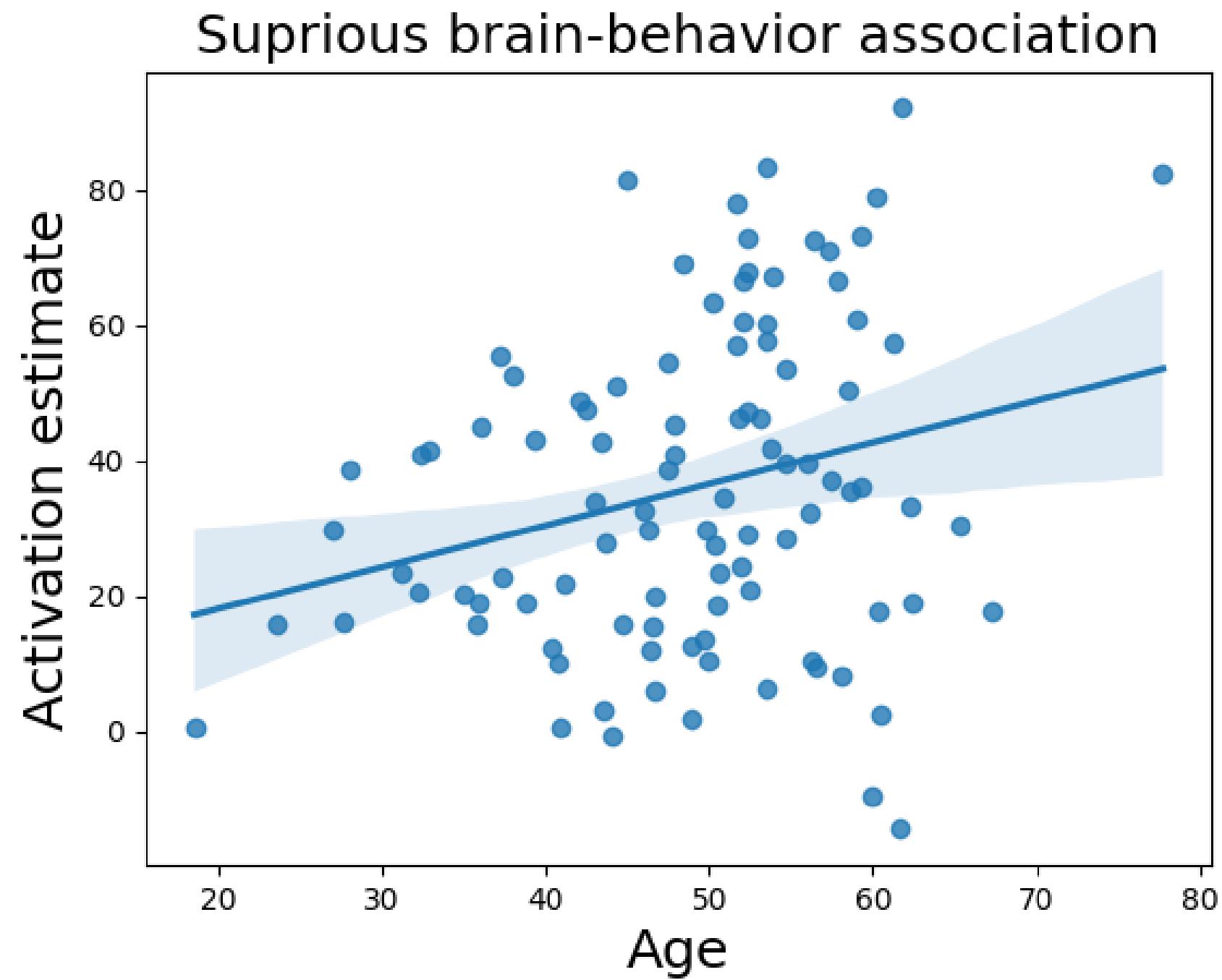
What about brain-behavior associations?

- 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 comparisons) and the RT difference.
 - Even if the average RT difference between conditions is zero across subjects!



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!



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.

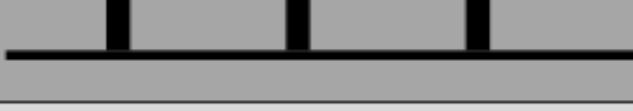
Without RT regressor in group model:

	t	p
Age	2.698	0.008

With RT regressor in group model:

	t	p
Age	7.163	0.000

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

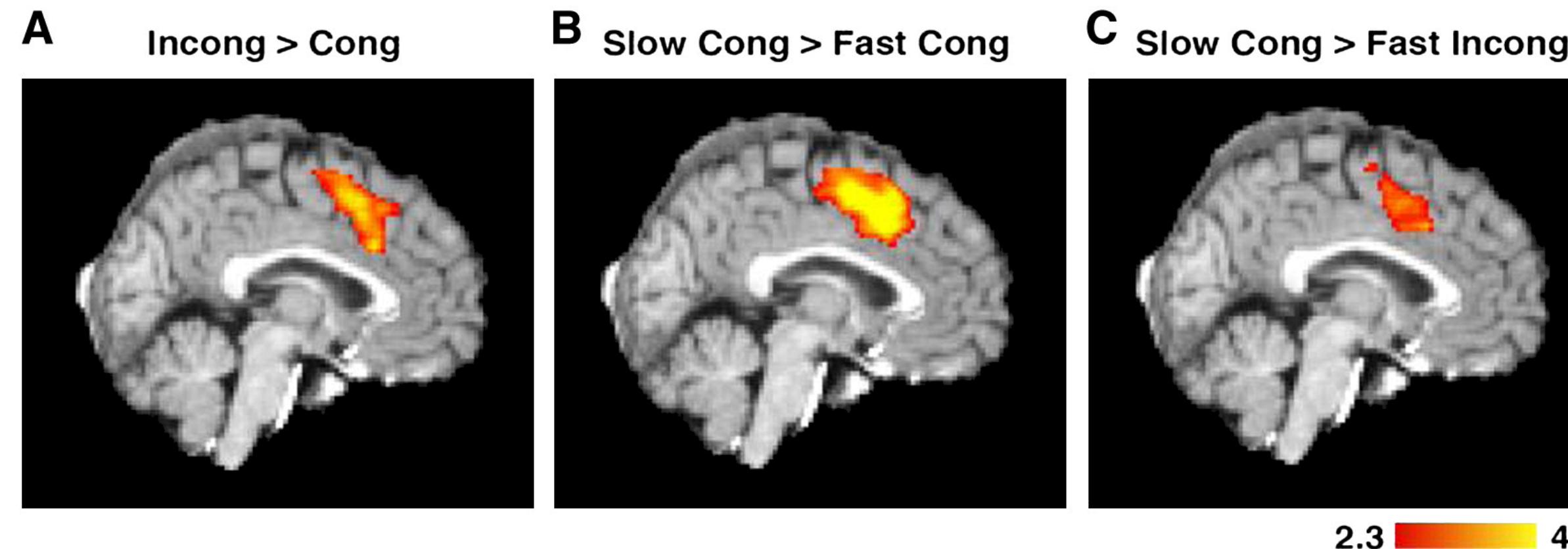
The Grinband et al. (2008) model

The Mumford et al. model

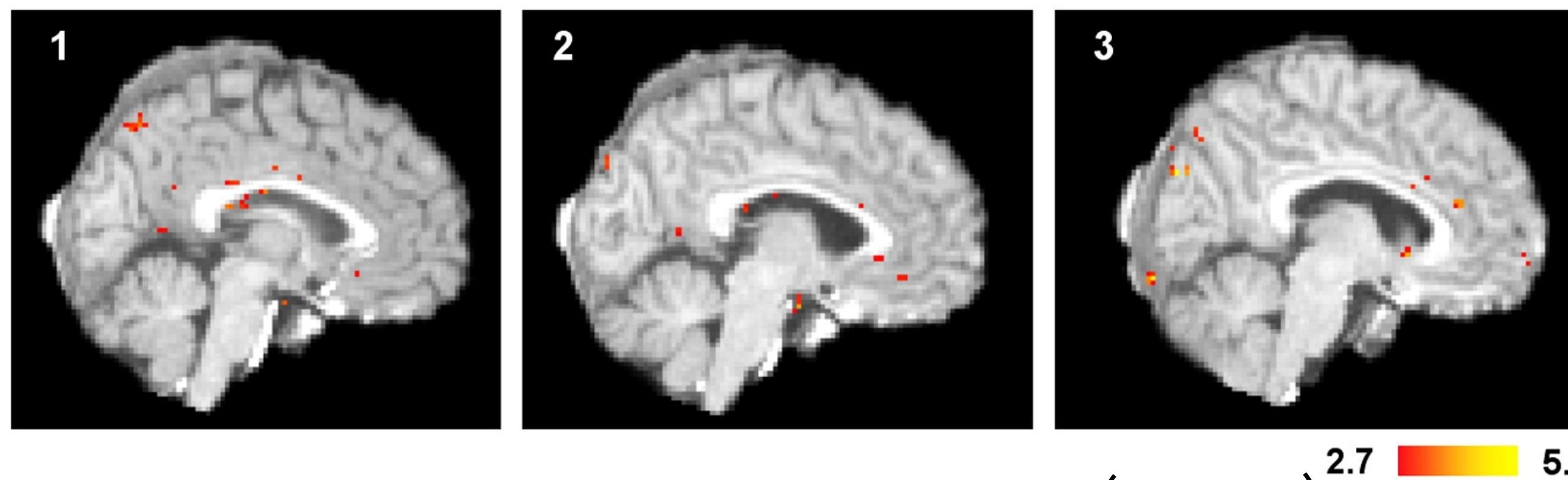
The Constant Duration + RT model allows quantification of the unique contributions of time on task and condition differences

Mumford et al, 2023

Are we throwing out the baby with the bathwater?

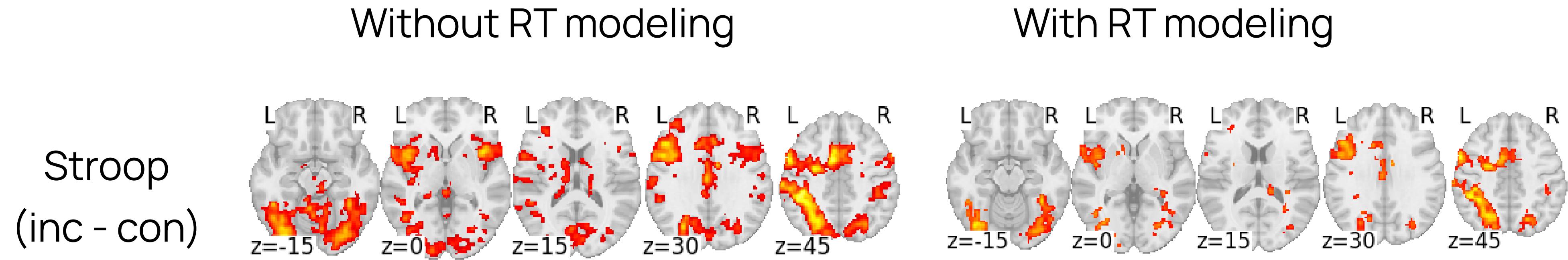


Activation for Stroop effect disappears after removing RT effect

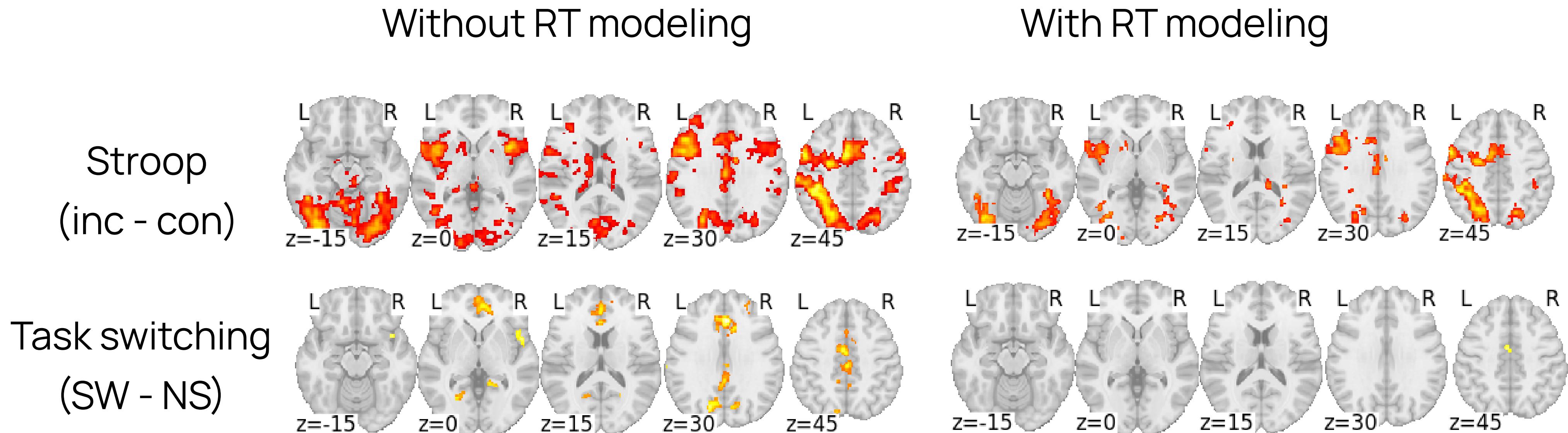


Grinband et al., 2011 (N = 23)

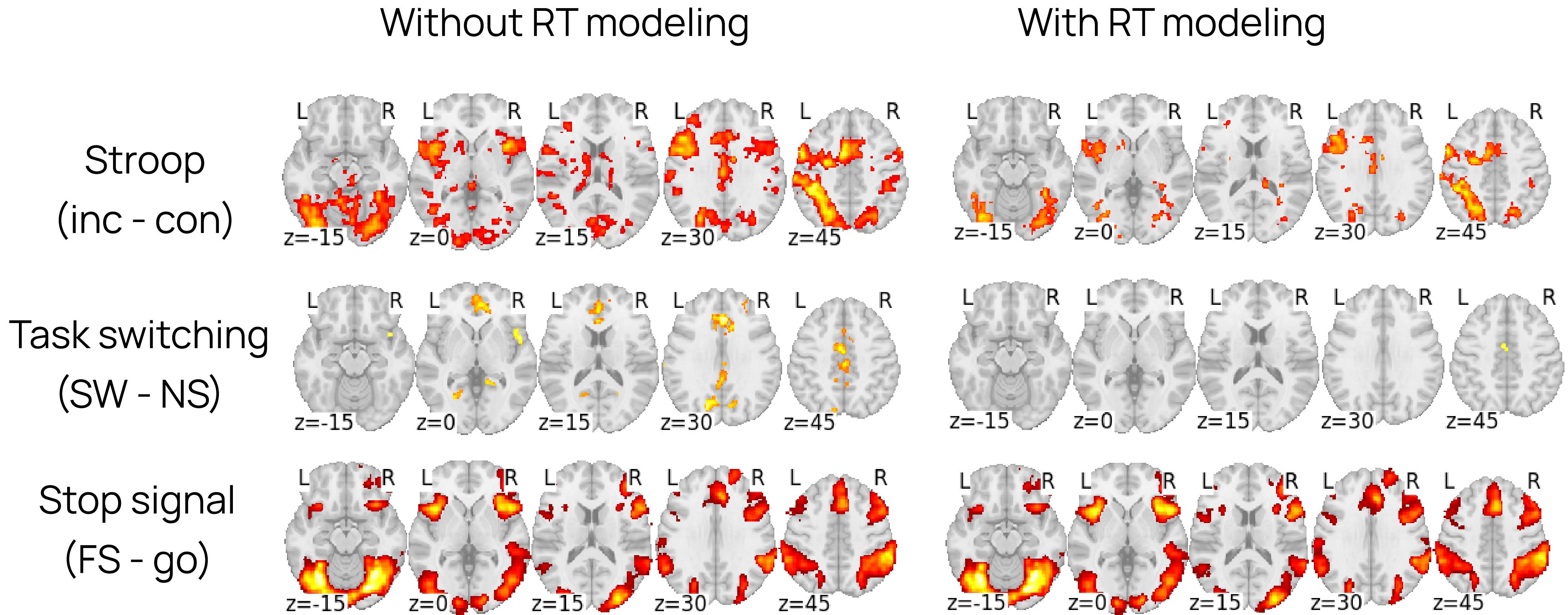
With sufficient power, we can (sometimes) find specific effects after removing RT



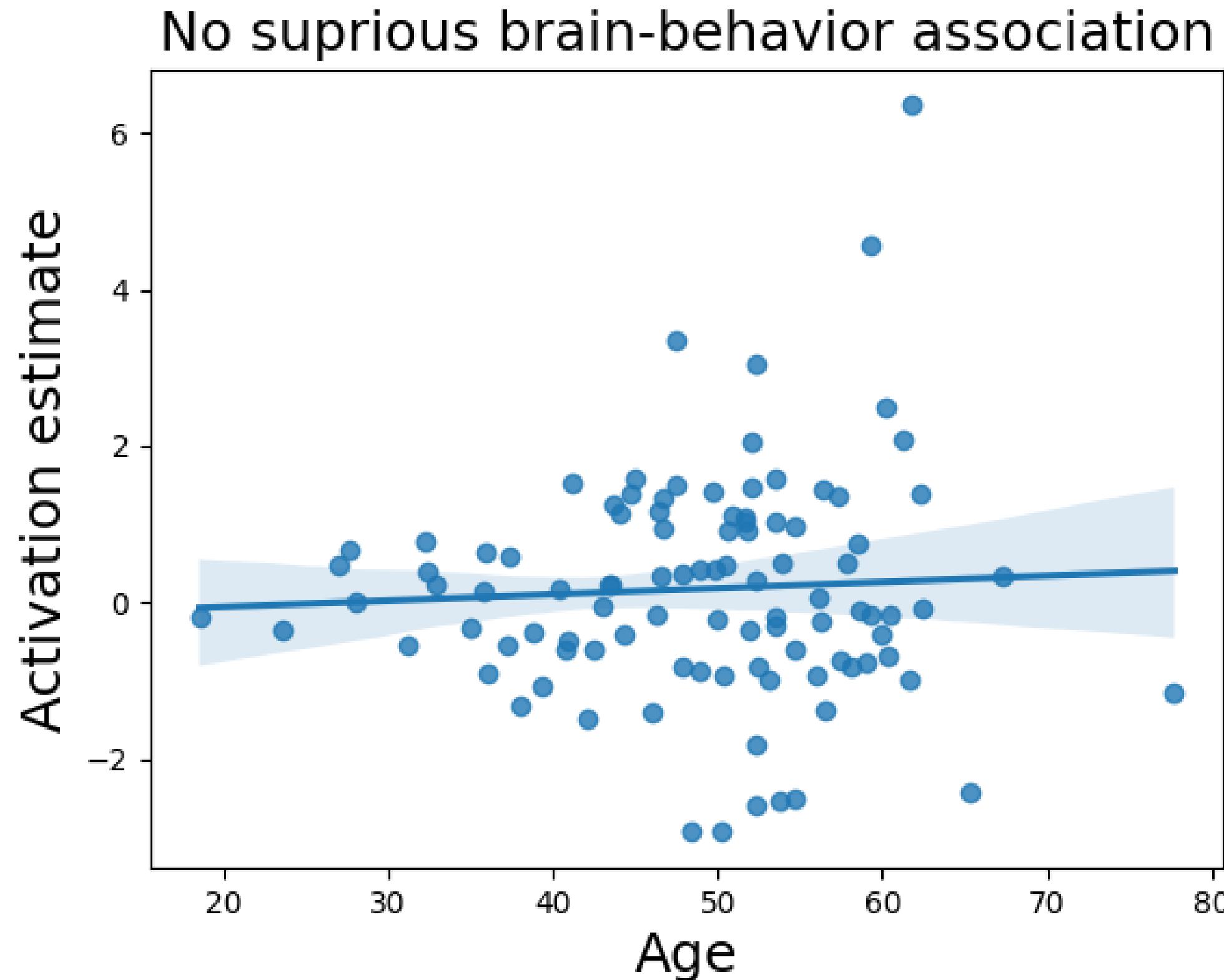
With sufficient power, we can (sometimes) find specific effects after removing RT



With sufficient power, we can (sometimes) find specific effects after removing RT



Modeling RT at the first level prevents spurious 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)
 - When confound variables are measured with error, including them can inflate error rates (sometimes to nearly 100%)
- We need a greater focus on causal justification for our statistical models (Wysocki et al., 2022; Kopal et al., 2023)



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 spurious brain-behavior associations
- This poses a major problem for large projects that share statistical results from first-level models that do not include RT

Acknowledgments

The Poldrack Lab



Jeanette Mumford



Funding

