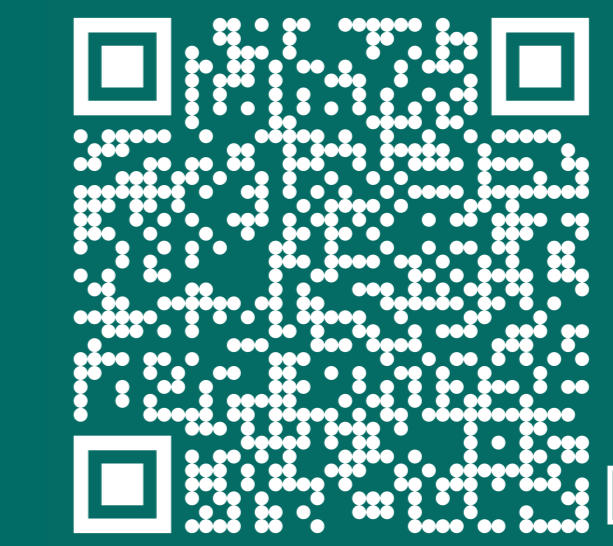


# Towards a Functional Future for the Cognitive Neuroscience of Human Aging

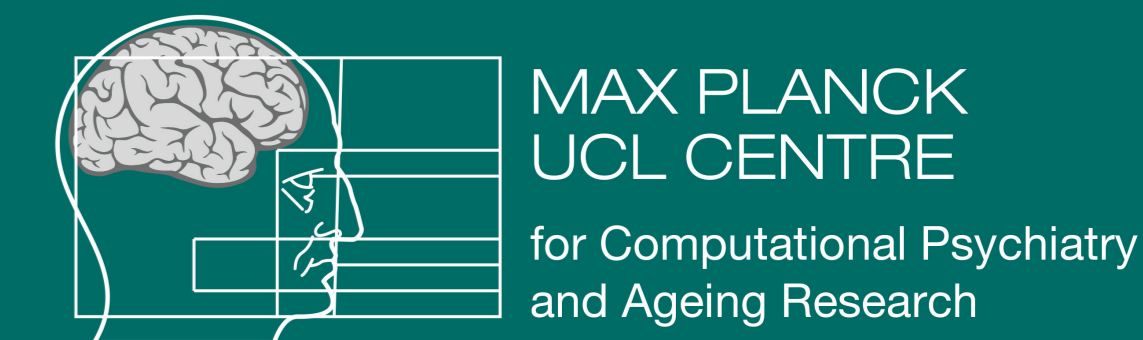
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## AGING RESEARCH INCREASINGLY TASK-INDEPENDENT

Increased reliance upon task-independent (structural and resting-state) neural investigations of cognitive aging.

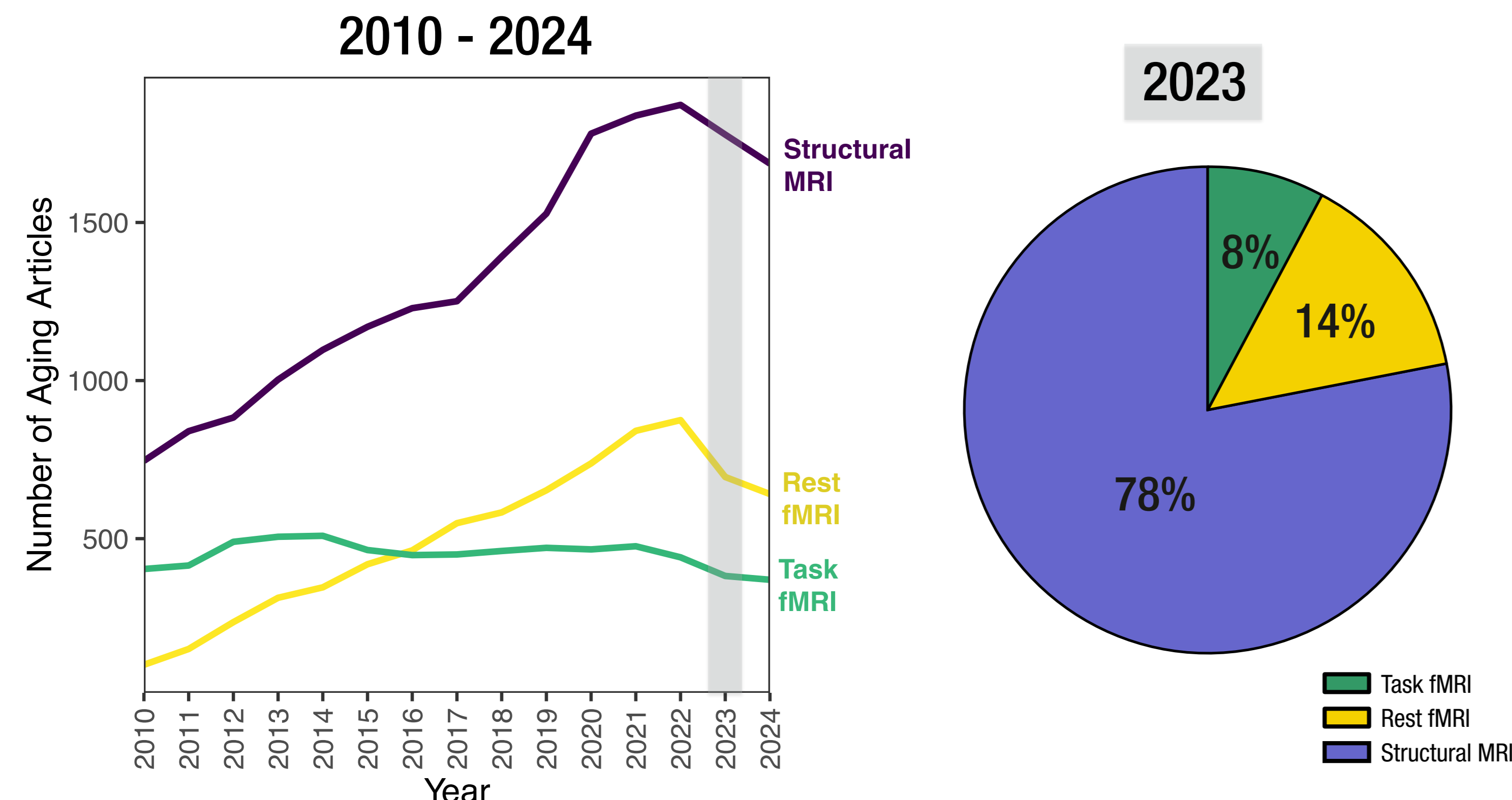


Fig. 1. Number of aging research articles per year, per modality. Indexed by Web of Science.

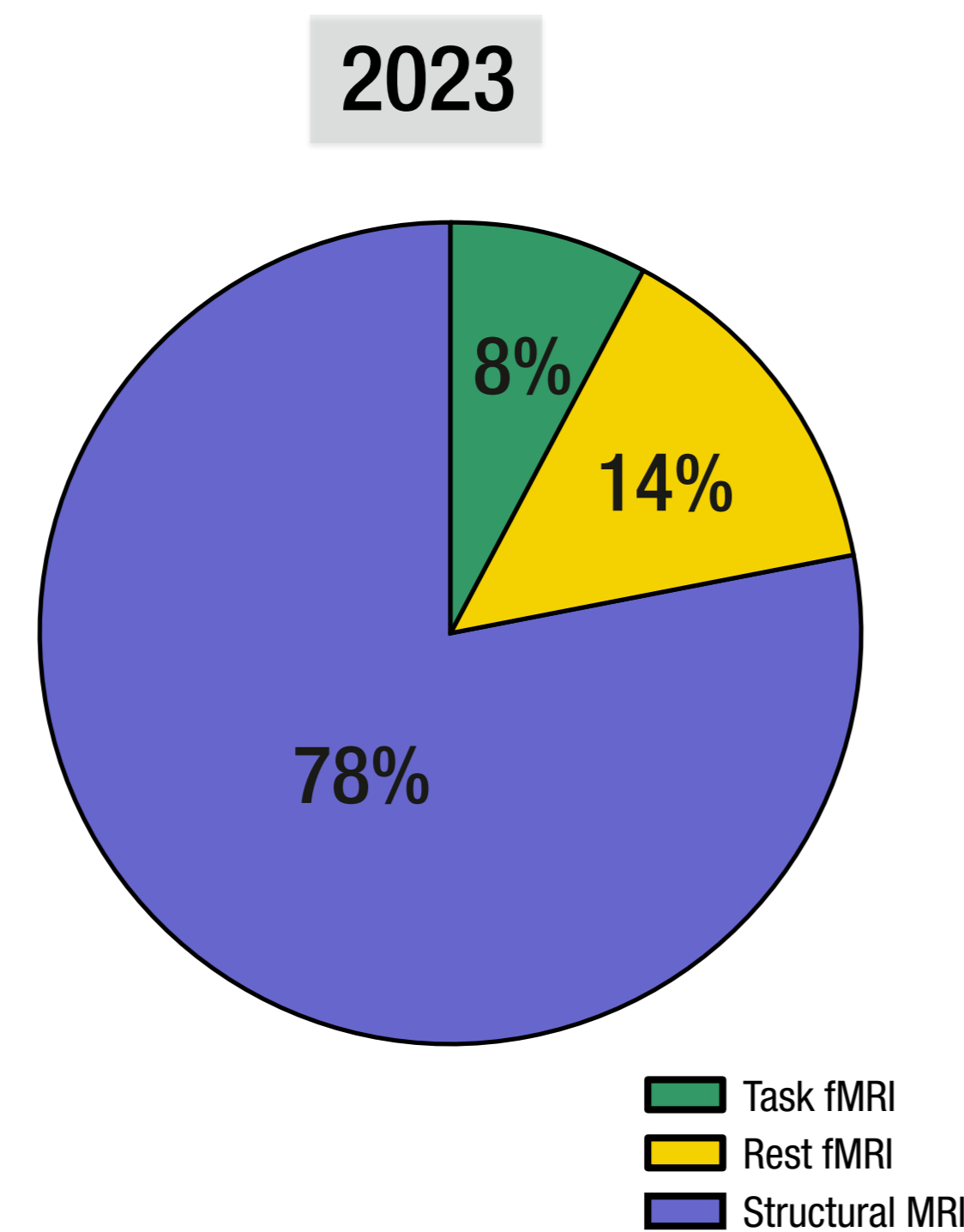


Fig. 2. Percentage of cognitive neuroscience of aging articles per modality in 2023.

Real-time functional imaging of cognition *in action* must become a primary focus of the field.

Inferences of behavioral relevance based on structure or rest *alone* are logically problematic.

Structure and resting-state should share variance with task-elicited function to establish their behavioral relevance in cognitive aging.

## THE SEARCH FOR CONVERGENCE

Do **structure (S)** and **task-related function (TF)** in a given brain region both relate to the same aging-related **behaviour (B)**?

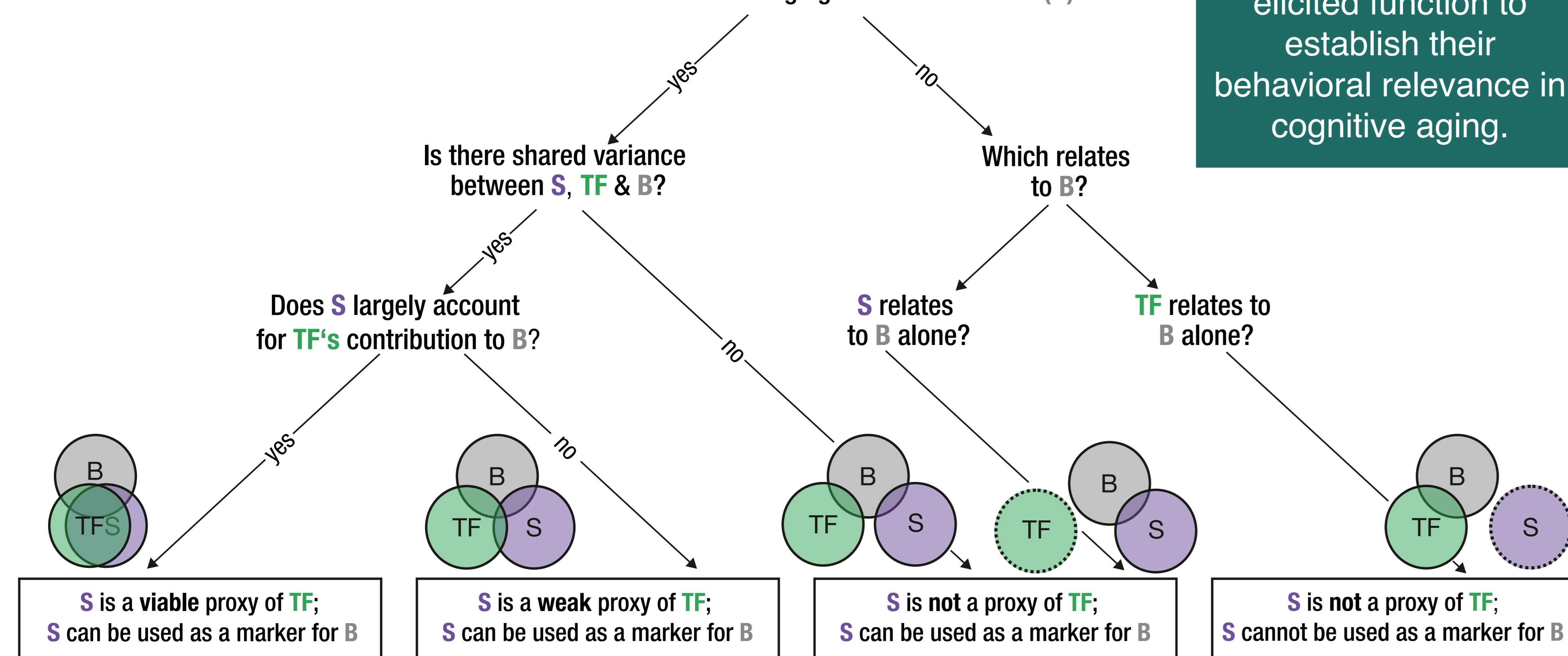


Fig. 3. Diagram of which conclusions can be drawn in the presence or absence of convergence between a task-independent modality and function.

## THE NEED FOR TASK-BASED FUNCTION

### 1. Prediction: task-based outperforms other modalities<sup>[2,3,4]</sup>

Fig. adapted from Makowski et al.<sup>[2]</sup>

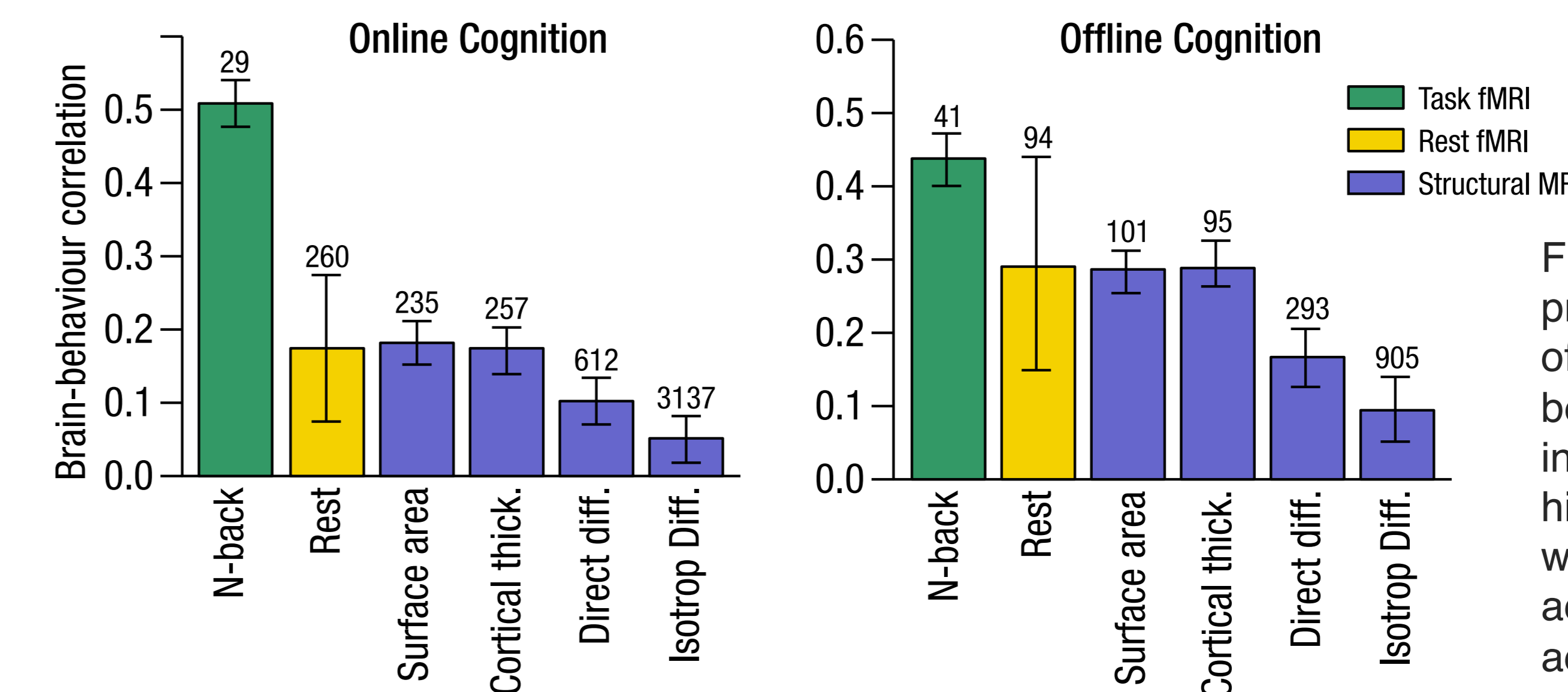


Fig. 4. Task-based fMRI better predicts online (working memory) & offline (NIH toolbox composite) behavior compared to other task-independent modalities – has the highest brain-behavior correlation with smallest sample size needed to achieve effect at 80% power. Figure adapted from Makowski et al.<sup>[2]</sup>.

### 2. Understanding cognitive processes

Structure and resting-state cannot capture functional dynamics of the aging brain as during experimentally-manipulated cognitive operations.<sup>[e.g.,5]</sup>

## THE COGNITIVE NEUROSCIENCE OF AGING NEEDS TO BE

### functionally-interrogated

How do brain representations change in aging? How are neural resources modulated by varying task demands? Task-based studies have stimulated development of most prominent cognitive neuroscience theories.

### multimodally-imaged

To gain greater mechanistic understanding of neural systems most sensitive to cognitive aging: ranging from subcortical to cortical, neurotransmitter to network, and balancing spatial and temporal resolution. e.g., combining fMRI with M/EEG, or dynamic PET & MRS.

### behavior-first

To understand the neural bases of cognitive changes, the latter must be comprehensively conceptualized, assessed, and modelled. e.g. computational modelling to parameterize time-resolved latent aspects of changing cognition.

## SOME OUTSTANDING CONSIDERATIONS

### Reliability of task-based functional neuroimaging?

What does reliability mean in the context of tasks and the context of aging? We need to distinguish reliability of the tool from what is taking place in the scanner.

Cognition is variable across situations (trials, conditions, tasks) & timescales (minutes, days, years). Practice effects are observed in longitudinal studies, and individual differences are known to increase with advancing age.

### Balancing breadth vs. depth?

Will yet another large cohort-level n-back task really help us understand the neural bases of cognitive aging? Can we imagine the typically resting state run being replaced by an additional task? Focus on fewer, well-thought-out, novel tasks in aging studies?<sup>[e.g.,6]</sup>

#### References:

[1] Mooraj et al. (2025). Towards a functional future for the cognitive neuroscience of human aging. *Neuron*.  
 [2] Makowski et al. (2024). Leveraging the adolescent brain cognitive development study to improve behavioural prediction from neuroimaging in smaller replication samples. *Cerebral Cortex*.  
 [3] Webb et al. (2020). Contributions of White Matter Connectivity and BOLD Modulation to Cognitive Aging: A Lifespan Structure-Function Association Study. *Cerebral Cortex*.

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 [6] Grill et al. (2024). Dopamine release in human associative striatum during reversal learning. *Nature Communications*.