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alone does not define what the functional role of this activity is, but rather that it interacts with other brain regions to control human behavior in the presence of self-related processing [6]. Prior research has shown that activity in the vmPFC upregulates activity in the left superior temporal sulcus, which is thought to reflect social attention. In particular, the strengths of neural coupling between the two regions can predict the biased responses to self-related stimuli in perceptual matching [7]. In parallel, neuropsychological studies have shown that brain damage over the vmPFC abolishes self-biases in memory, whereas brain damage in the dorsal attentional control network that spares the vmPFC causes abnormally large biases toward self-related information due to an exaggerated effect of strong attentional signals [8]. The evidence indicates that self-reference acts as a golden thread linking the vmPFC to other regions to create a specific neural circuit in the brain to support self-reference.

Lane and colleagues [2] propose that recording task-irrelevant resting state and pre-stimulus activity would yield insights into how the self performs this function by identifying the trajectory of the self with little experimental control. Such approaches do contribute to assessing the continuity of consciousness of the self, a topic that has been extensively discussed in cognitive neuroscience [9] as well as philosophy [3]. However, these methods alone are unlikely to pinpoint specific cognitive and neural responses associated with self-reference. By contrast, empirical manipulation provides a way to link self-processing to specific functional or neural processes [10]. For example, the function of self-reference in perception may be targeted by manipulating the luminance of stimuli while controlling other factors. Researchers reported that reduction of stimulus luminance was less detrimental to perceptual sensitivity of shapes associated with the self than shapes associated with others, suggesting that self-reference can enhance perception [11]. In our view, using various approaches (e.g., empirical manipulation, neural analysis during resting state) within a study would provide us with a better understanding the functions of self-reference that are intrinsic to perception and cognition over time [12].

Acknowledgments

The author dedicates this paper to the memory of Glyn W. Humphreys (1954–2016), especially Glyn's invaluable contribution to the theory of self-reference. It was an honor and a privilege to work with him. This work was supported by grants from the Wellcome Trust (WT 106164MA), the Economic and Social Research Council (ES/K013424/1), and the National Science Foundation (31371017).

[1]Department of Experimental Psychology, University of Oxford, Oxford OX1 3UD, UK

*Correspondence: jie.sui@psy.ox.ac.uk (J. Sui).

http://dx.doi.org/10.1016/j.tics.2016.04.005

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Spotlight

The Importance of Single-Trial Analyses in Cognitive Neuroscience

Mark Stokes[1,*] and Eelke Spaak[1]

Theories of working memory typically assume that information is maintained via persistent neural activity. By contrast, Lundqvist *et al.* report that single-trial delay activity is actually 'bursty'; the classic profile of persistent activity is an artefact of trial-wise averaging. Tackling brain–behaviour relationships at the single-trial level is an important future direction for cognitive neuroscience.

Classic models of working memory assume that information is stored via persistent neural activity [1]. Since the earliest neurophysiological experiments in awake, behaving primates [2], researchers have reported evidence that working memory is maintained via persistent delay activity in the prefrontal cortex (PFC). The idea is relatively simple: task-relevant mental representations are kept 'on line' by maintaining corresponding patterns of neural activity for as long as required.

As in most neurophysiological studies, however, classic evidence for persistent activity was essentially based on the results of many individual trials averaged together to form a putative 'representative' estimate of neural activity. Averaging across trials is important to improve the signal-to-noise ratio. If we can assume that each trial is a noisy sample of the true distribution, the average over trials should represent the signal we could expect from

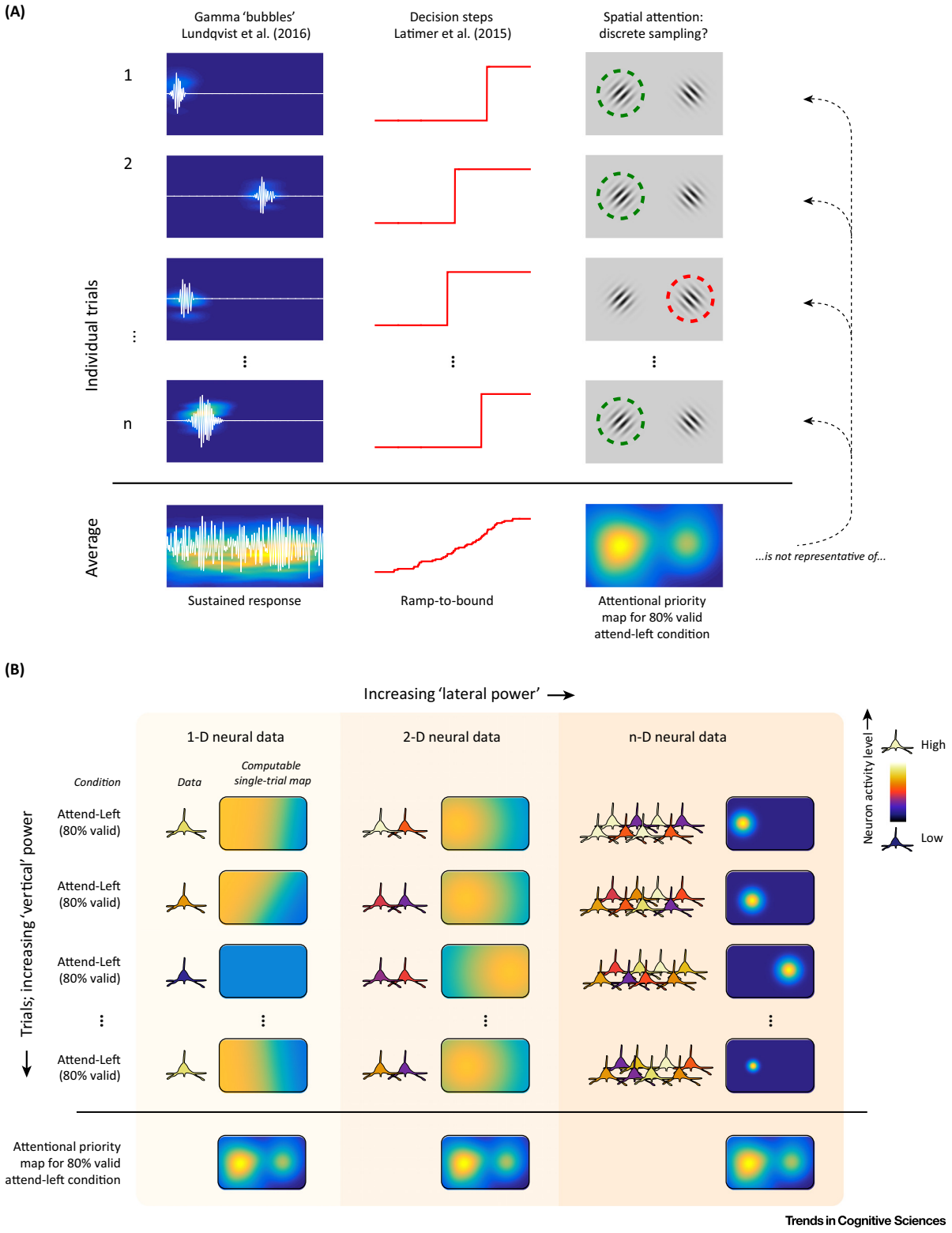

Figure 1. Unscrambling the Egg: Advances in Cognitive Neuroscience Will Critically Depend on Better Methods to Characterise Single-Trial Neural Dynamics. (A) Combining single trials through computing the mean does not necessarily result in a representative average. Left: Gamma-frequency 'bubbles' [3] (time–frequency representations of power, with traces superimposed) in the prefrontal cortex during individual trials of working memory maintenance activity. The average shows a familiar

(Figure legend continued on the bottom of the next page.)