

With these findings, there now appears to be a rough framework for dissociating the neural basis of detection theory parameters: while choice sensitivity may rely on neocortical sensory encoding (Luo and Maunsell, 2015), choice criterion may rely on subcortical circuits, including the SC. Though tentative, this broad hypothesis will serve as a clear guide for future studies. The results also raise several new questions. For example, is the criterion signal in SC inherited from upstream structures, or is it computed locally, perhaps relying on cross-hemisphere communication? Also, which specific SC output pathways are important for setting behavioral criterion following stimulation? Outputs from SC are widespread, spanning from the diencephalon down to the midbrain, providing numerous means by which SC activity could influence criterion calculations or associated plasticity mechanisms.

In summary, Crapse et al. (2018) make a compelling case for the role of SC in deci-

sion making: behavioral manipulations of the choice criterion induce parallel changes in choice representations in SC, and physiological manipulations of SC induce parallel changes in choice criterion. Furthermore, the behavioral and neural data are unified under the same well-understood model, facilitating a clear mapping between algorithmic- and implementation-level accounts of choice behavior. This depth of understanding is the ideal in systems and behavioral neuroscience, and this paper in as an exemplar of how it can be achieved.

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## Memory, Numbers, and Action Decision in Human Posterior Parietal Cortex

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**Human lateral PPC demonstrates rich, functional heterogeneity across its subregions, including during mnemonic and numerical decision tasks. In this issue of *Neuron*, Rutishauser et al. (2018) report striking local heterogeneity within a small patch of anterior IPS at the neuronal level during memory-based decisions.**

The human lateral posterior parietal cortex (PPC)—inclusive of the superior parietal lobule (SPL), intraparietal sulcus region (IPS), angular gyrus (AG), and supramarginal gyrus (SMG) (Figure 1A), i.e., a substantial proportion of human neocortex—is engaged in a large variety of cognitive tasks, such as spatial attention, perceptual decision making, visual

categorization, and saccadic eye movements (Hyvärinen, 2012). Data over the past two decades indicate that PPC functions also contribute to two other cognitive domains: episodic memory (Wagner et al., 2005) and numerical cognition (Nieder and Dehaene, 2009). In each of these domains, there is evidence that specific subregions of PPC demonstrate

distinct functional responses, pointing to a multi-component model of PPC functional organization. For example, extensive fMRI data from recognition memory tasks (Figure 1B) indicate that the blood-oxygen-level-dependent (BOLD) signal in (1) lateral IPS monotonically increases with the perceived strength that a test probe is old, being weakest when the



subject is certain the probe is new and strongest when certain the probe is old; (2) SPL/medial IPS increases with decision uncertainty, being stronger when subjects are less confident in their memory decision; and (3) AG increases with decision certainty, being stronger when subjects are highly confident the probe is old and, to a lesser extent, new.

In this issue of *Neuron*, Rutishauser et al. (2018) report unique recognition memory data from intracortical recordings in two tetraplegic subjects who were chronically implanted in the most anterior edge of the SPL (human homolog of anterior intraparietal area), in a small 4 × 4 mm patch equivalent to the area measured with one to two fMRI voxels or one to two intracranial EEG macroelectrodes (Figure 1A). In both subjects, the recorded patch fell medial to the anterior extent of IPS (hereafter aIPS), close to somatomotor areas. This patch of aIPS—which fMRI had identified as important for imagined reaching and grasping actions (Aflalo et al., 2015)—was implanted to enable the subject to control an external robotic hand via a neuroprosthetic brain-machine interface. Subjects in this study performed an “old-new” memory task in which they first studied visual images, and ~36 min later, their memory for the images was probed. On the recognition test, subjects encountered studied and novel images and indicated whether each probe was “old” or “new.” Importantly, relying on the well-established mapping between behavioral expressions of confidence that a test probe is old and the underlying strength of mnemonic evidence, subjects indicated their decision confidence when responding (1 = new confident; 2 = new probably; 3 = new guess; 4 = old guess; 5 = old probably; 6 = old confident). Of central interest was whether the firing rates of neurons in this patch of human aIPS vary as a function of memory strength, decision confidence, or some combination of the two.

Strikingly, Rutishauser et al. (2018) report that the firing rates of some recorded neurons varied with perceived memory strength (putative “memory selective neurons” [MS neurons]), whereas the firing rates of (predominantly different) neurons varied with decision confidence (putative “confidence selective neurons” [CS neurons]). Firing rates of MS neurons varied with subjective memory experi-

ence (either the perception of novelty or of familiarity), regardless of whether the memory decision was correct or incorrect and, critically, with memory strength (operationalized as decision confidence) only for the preferred mnemonic class (either novelty or familiarity). By contrast, CS neurons differentiated high- and low-confidence decisions (increasing firing rates for either lower- or higher-confidence responses), regardless of whether the probe was perceived as novel or familiar. Thus, these rare recordings at single-unit spatial resolution from a small patch of aIPS revealed that the firing rates of some neurons putatively track decision uncertainty (which, at the resolution of fMRI, has been observed in SPL and medial IPS; Figure 1B), others putatively track decision certainty (which fMRI has observed in AG; Figure 1B), others track the strength of perceived familiarity, and yet others track the strength of perceived novelty (these latter findings lack a clear parallel in the fMRI literature, which has reported a monotonic increase in lateral IPS signal over the entire range of perceived familiarity; Figure 1B).

Given the exceptional nature of Rutishauser et al. (2018)’s aIPS findings during recognition memory, one might ask how they relate to prior electrophysiological evidence about this region’s functional responses during other tasks, such as numerical processing. For instance, we have consistently seen a selective increase in high-frequency broadband (HFB) activity, a proxy for averaged multi-unit activity, in the aIPS region when humans perform simple arithmetic tasks (Daitch et al., 2016; Dastjerdi et al., 2011, 2013) (Figures 1C and 1D). Interestingly, in an equation like “2 + 3 = 5” (with each item appearing consecutively), there is little, if any, change in the HFB signal when the first digit or the “+” operator is shown, but HFB surges after the second (“3”) and the third (“5”) digits, suggesting a role for the parietal region in the process of choosing the response based on numerical evidence. Could the “memory” and “confidence” effects observed by Rutishauser et al. (2018) reflect, at least in part, the fact that perceived memory strength and decision confidence had to be mapped to actions through numerical categories? To report memory and decision confidence, their subjects had to

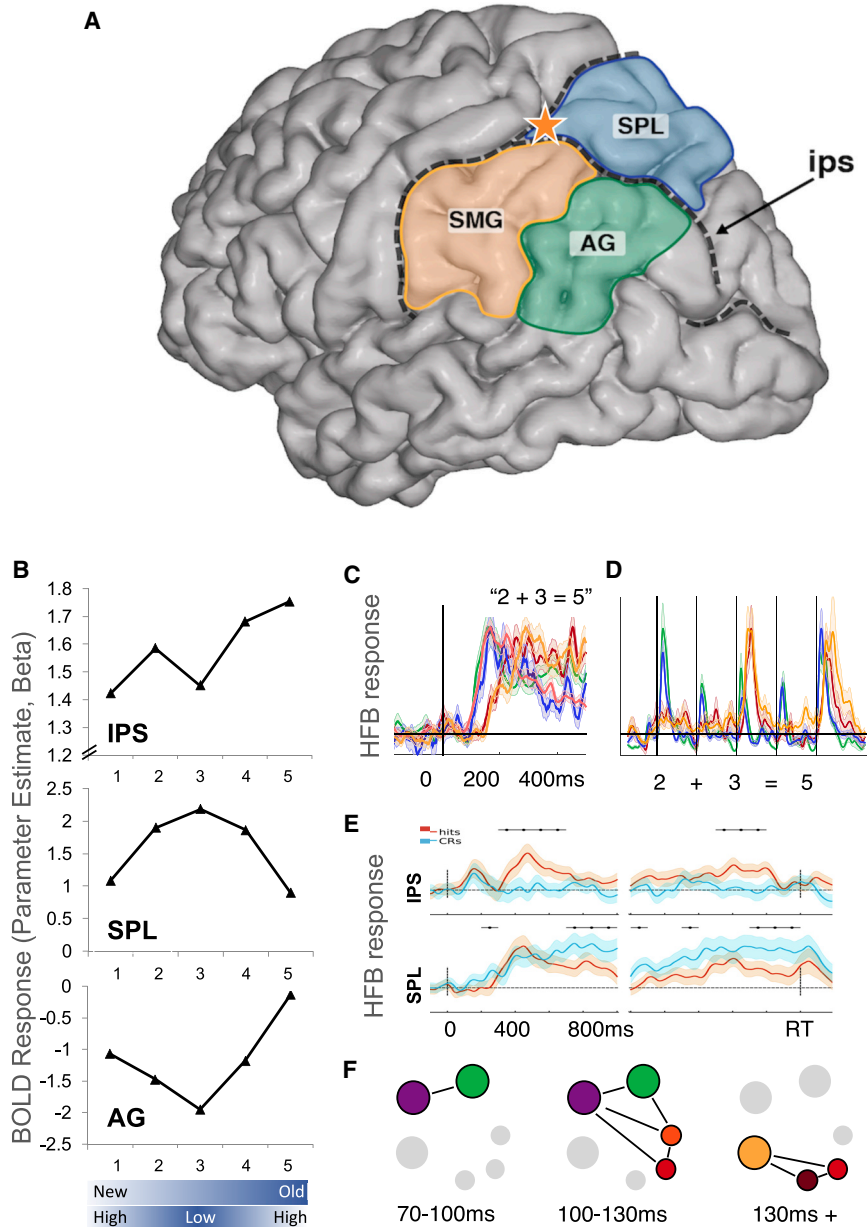
say a number: 1, 2, or 3 for varying confidence “new” and 4, 5, or 6 for varying confidence “old.” Moreover, because the subjects performed quite well on the memory task, the probability of selecting each verbal action was not uniform: the vast majority of verbal responses were either “1” or “6” (corresponding to new confident and old confident) (see Figure 1D in Rutishauser et al., 2018).

To examine whether aIPS neural firing rates could be explained by subject’s numerical choice, Rutishauser et al. (2018) had their subjects perform a second task in which, on each trial, they were shown a number (1 to 6) and, after a 1 s delay, were cued to verbally report back the number. Here, the number on each trial was randomly selected from only six options, and thus numbers presumably appeared with an approximately equal probability across trials. Analyses of firing rates in this task revealed putative “number selective neurons” in which firing differentiated between whether the subject was about to choose from 1–3 or from 4–6 but did not further differentiate between the numbers within each range. Moreover, most MS neurons that varied with memory strength during recognition did not also differentiate between the same choices (1–3 versus 4–6) during the number task and vice versa (see Figure 5F in Rutishauser et al., 2018).

The differences between the action distributions in the memory and number tasks (highly non-uniform versus uniform) leave open the possibility that the firing rates of CS neurons in aIPS track response probability and action selection demands, with some neurons firing more for higher-frequency responses and others firing more for lower-frequency responses. More intriguingly, Rutishauser et al. (2018)’s data raise the exciting possibility that the firing rates of the two populations of MS neurons also track response probability but in a manner that is gated by the decision categories of perceived familiarity and perceived novelty.

Two other observations may further bear on whether neurons in this patch of aIPS mediate the transformation of memory evidence to choice of action.

First, the MS neurons reported by Rutishauser et al. (2018) demonstrated differential firing relatively late during memory trials (>550 ms post-stimulus).



**Figure 1. Posterior Parietal Cortex, Memory, and Numerical Cognition**

(A) Lateral parietal cortex can be divided into two major divisions using the post-central sulcus (vertical dashed line) as a landmark: the primary somatosensory cortex and the posterior parietal cortex (PPC), anterior and posterior to the sulcus, respectively. The PPC itself can be divided into two major anatomical subdivisions using the intraparietal sulcus (ips) as a landmark: the superior and inferior parietal lobules with these subdivisions: SPL, superior parietal lobule; AG, angular gyrus; SMG, supramarginal gyrus; and the cortex within the ips and immediately surrounding it is known as the IPS region. The area of recording in Rutishauser et al. (2018) is shown with orange star (aIPS region).

(B) During recognition memory, fMRI data reveal three distinct PPC BOLD response profiles that vary with perceived memory strength and decision confidence (here, ranging on a five-point scale from (1) high confidence “new” to (5) high confidence “old” decisions). Lateral IPS activity monotonically increases with perceived memory strength, SPL and medial IPS activity is greater during lower- versus higher-confidence memory decisions, and AG activity is greater during high confidence “old” responses and, to a lesser extent, high confidence “new” responses. Adapted from Hutchinson et al. (2015).

(C) Exemplar HFB time courses during a simple addition condition at sites in different inferior temporal cortical subregions (green, fusiform visual region; red and dark brown, posterior inferior temporal gyrus, pITG subregions known to be selectively engaged in processing numerical symbols) and two PPC subregions (purple, SPL; light orange, aIPS) studied by Daitch et al. (2016). The HFB time course at each site is scaled by its own maximum. The shaded area represents the SE across trials for each condition. Note that

Extant data indicate that (1) memory-strength-dependent signals emerge in the human medial temporal lobe within 150–300 ms (Gonsalves et al., 2005) and (2) above-chance familiarity-based memory decisions can be expressed by healthy adults well prior to 550 ms (Hintzman et al., 1998). Moreover, the scalp-EEG parietal “old/new” effect (greater positivity for strong hits versus correct rejections) onsets within ~400 ms (Rugg and Curran, 2007), and our group has observed that HFB activity in IPS selectively increases during high-confidence correct rejections as early as 300 ms, with this effect persisting until ~200 ms prior to expression of the memory decision (Figure 1E) (Gonzalez et al., 2015). Collectively, these data suggest that the later onsetting MS neurons in this patch of aIPS may not be central to “mnemonic evidence accumulation” per se, but instead may relate to memory-guided action selection processes.

Second, two prior publications by Andersen’s group (which report data from one of the same two subjects in the present *Neuron* article) provide interesting clues for interpreting the evidence from Rutishauser et al. (2018)’s study, as they also suggest that this patch of aIPS plays a functional role in memory-guided action. In one of the reports, aIPS neurons changed their firing rates when the subject imagined a continuous reaching movement to a spatially cued target after a delay period (Aflalo et al., 2015). In the other, aIPS neurons were engaged when the subject

the ITG and aIPS sites respond after the fusiform visual regions and SPL sites.

(D) HFB time course at each site as in (C) (scaled by each site’s own maximum). The shaded area represents the SE across trials for each condition. Note that the aIPS site responds more to the second digit than to the first digit.

(E) Stimulus-locked (left) and response-locked (right) HFB time courses for high-confidence hits and high-confidence correct rejections (CRs) for the IPS and SPL sites studied in Gonzalez et al. (2015). Gray bars indicate significant differences between Hits and CRs (\* $p < 0.05$ ; Bonferroni corrected; the shaded area represents the SE across trials for each condition).

(F) Sequence of coupling between the brain regions in Daitch et al. (2016)—same colors as in (C) and (D)—with earlier ITG-SPL loops engaged in visual processing/attention and later loops engaged in the arithmetic function/choice selection. Note how different nodes are engaged at different time windows, yet all within a quarter of a second.

chose one of six imagined actions to perform, and the activity of as few as 50–75 units was sufficient to achieve 90% coding of action choice (Klaes et al., 2015).

Rutishauser et al. (2018)'s groundbreaking study raises the possibility that the aIPS region may be a critical node where multiple PPC computations based on decision-relevant evidence (here, mnemonic, but in other contexts possibly perceptual or numerical) lead to action choice—even though aIPS neurons may not partake in the coding of action execution itself. As PPC function emerges, in part, from complex across-region neural dynamics with different information exchanges at different temporal windows (Figure 1F), as well as through interactions with broader neural systems, future studies that leverage simultaneous recordings with high spatial and temporal resolution across different nodes of neural networks bode well for continued theory building and hypothesis testing.

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## Phase-Amplitude Coupling: A General Mechanism for Memory Processing and Synaptic Plasticity?

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In this issue of *Neuron*, Helfrich et al. (2017) demonstrate that phase-amplitude coupling (PAC) between slow oscillations and spindles is crucial for memory consolidation, and shifts in its phase relationship may explain age-related deficits in memory performance. These results also suggest a more general function of PAC in synaptic plasticity.

Hierarchical cross-frequency phase-amplitude coupling (PAC) of neuronal oscillations, in which the phase of slower oscillations modulates the amplitude of faster ones, has been proposed as a general mechanism supporting the en-

coding, storage, and retrieval of information (Fell and Axmacher, 2011). During slow-wave sleep (SWS), the interplay

