network that generates it. This synchrony-enhancing effect of LFPs generated by physiological activity is a novel and interesting finding, but it should be noted that the significance of synchrony in cortical network function has itself been questioned (Shadlen and Movshon, 1999). Thus, the skeptic might argue that one epiphenomenon merely enhances another and dismiss this ''cortical soliloquy'' as a meaningless mumble. Nevertheless, these exciting results provide new insight into how cortical networks organize and regulate their own activity, and, by establishing this field effect, Fröhlich and McCormick have opened a new chapter in the exploration of the function of network synchrony.

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A Roadmap to Brain Mapping: Toward a Functional Map of Human Parietal Cortex

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In this issue of *Neuron*, Nelson and colleagues report a novel parcellation of human lateral parietal cortex based on task-induced response profiles and resting-state functional connectivity. Their findings inform current debates about the contributions of parietal cortex to cognition, including the retrieval of episodic memories.

What is the function of the parietal lobe in human cognition? Asking neuroscientists and cognitive psychologists this question would likely generate a wide range of answers. Responses might include such functions as attention, action intention, spatial perception, decision making, numerical cognition, working memory, and even long-term (episodic) memory retrieval. That the functions ascribed to the parietal lobe—more specifically, lateral parietal cortex—are vast and seemingly disparate has motivated efforts to carve the region at its anatomical and functional joints. While considerable progress has been made using architectonic methods in the postmortem human (Figures 1A and 1B) and nonhuman primate, initial functional parcellations of human lateral parietal cortex have been coarse grained. For example, a dorsal/ventral axis of parietal organization has been proposed based on studies of attention (e.g., Corbetta et al., 2008), episodic memory retrieval (e.g., Cabeza et al., 2008; Wagner et al., 2005), and resting-state functional connectivity (e.g., Fox and Raichle, 2007). While these initial functional parcellations have yielded important insights, continued advances in understanding lateral parietal function likely require specification of finer-grained organizational structure. In this issue of *Neuron*, Nelson et al. (2010) take a significant step along the road toward a fine-grained functional parietal map, revealing six functionally distinct regions in human lateral parietal cortex. Their findings may help resolve seemingly conflicting accounts of parietal function, including current debates about how the region supports retrieval of episodic memories (Cabeza et al., 2008; Hutchinson et al., 2009; Vilberg and Rugg, 2008; Wagner et al., 2005).

In their study, Nelson et al. partitioned the left lateral parietal cortex using a sophisticated approach that iterated

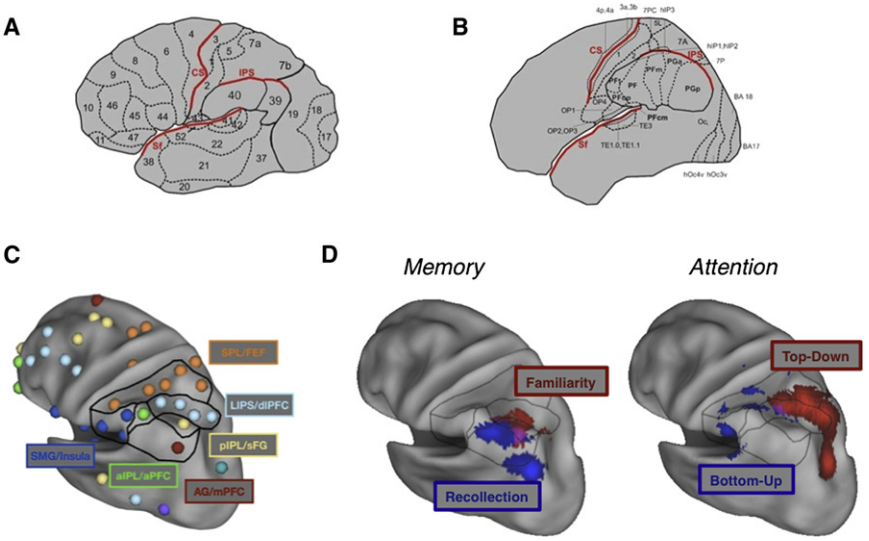

Figure 1. Anatomical and Functional Parcellations of Lateral Parietal Cortex
Schematics of proposed subdivisions of human parietal cortex based on (A) Brodmann's map and (B) a recent cytoarchitectonic atlas (modified from Caspers et al., 2008; CS, central sulcus; Sf, sylvian fissure; IPS, intraparietal sulcus). (C) Nelson et al.'s parcellation of human parietal cortex (FEF, frontal eye fields; dlPFC, dorsolateral prefrontal cotex; sFG, superior frontal gyrus; mPFC, medial prefrontal cortex; aPFC, anterior prefrontal cortex). (D) (Left) Activation likelihood estimation (ALE) map of parietal regions sensitive to item familiarity (red) and recollection (blue) (based on studies reviewed by Vilberg and Rugg, 2008). (D) (Right) ALE map of regions thought to index top-down (red) and bottom-up (blue) attention (based on studies reviewed by Hutchinson et al., 2009), with the Nelson et al. boundaries projected onto the maps.

between local task-based functional MRI (fMRI) and global connectivity, based on resting-state fMRI and large-scale network analysis. They began by recording blood-oxygenation-level-dependent (BOLD) fMRI responses as subjects simply fixated for several minutes at a time. Under such "resting-state" conditions, activity in neural regions tends to fluctuate, with correlated signal fluctuations between particular sets of regions being thought to reflect distinct resting-state networks (Fox and Raichle, 2007). By examining resting-state functional connectivity (rs-fcMRI), Nelson et al. aimed to identify which lateral parietal subregions belonged to distinct "intrinsic" networks. To do so, they created a grid of seeds spanning the left lateral parietal surface, and for each seed calculated how its resting-state activity profile correlated with that of other brain regions. By computing the dissimilarity of the global connectivity profiles for neighboring parietal seeds, the authors determined the likelihood of a functional border falling at each seed. This approach revealed an initial set of bounded parietal regions with 15 spatially coherent peaks that spanned the superior parietal lobule (SPL), intraparietal sulcus (IPS), inferior parietal lobule (IPL), supramarginal gyrus (SMG), and angular gyrus (AG).

The authors next turned to task-based BOLD data to characterize the activity profiles of the 15 parietal peaks. To do so, they extracted task-induced time courses from spherical regions-of-interest (ROIs) centered at the peaks, using data collected in six studies of episodic retrieval. Across various retrieval tasks and stimulus types, two axes of functional differentiation emerged. First, along an approximately anterior/posterior axis, Nelson et al. observed that activity in posterior parietal ROIs (IPS, IPL, and AG in Figure 1C) varied depending on whether subjects recognized studied items (hits) versus identified novel foils (correct rejections), whereas anterior parietal ROIs (SMG and SPL in Figure 1C) showed no such "retrieval success" effects. Second, within posterior ROIs, distinct "retrieval success" profiles were observed in a dorsal and a ventral ROI (in IPS and AG, respectively), with an ROI in between (pIPL) showing an effect that resembled an average of the IPS and AG patterns. This dorsal/ventral dissociation is broadly consistent with prior studies of episodic retrieval (Wagner et al., 2005), which have repeatedly demonstrated that the profile of "retrieval success" effects differs in IPS and AG (see below).

At this point, the dual windows onto parietal functional differentiation suggested that the region might be parcellated into as many as 15 or as few as 3 regions. To further characterize the connectional profile of the parietal ROIs identified with rs-fcMRI, Nelson et al. turned to graph-theoretic analyses of the rs-fcMRI data to specify the whole-brain connectional topography of lateral parietal regions. To do so, they first identified regions most strongly correlated with each parietal ROI and then analyzed the connectional structure of the full set of regions. This analysis indicated that the initial 15 ROIs appear to be components of at least four distinct large-scale parietal-cortical networks (or neural "communities"), parcellated into SMG, SPL, IPS, and AG networks. Strikingly, while this rs-fcMRI analysis was entirely independent of the task-based data, the parcellation according to network membership obeyed both the anterior/posterior parietal boundary between regions sensitive versus insensitive to episodic retrieval success, as well as the dorsal/ventral distinction between retrieval success effects in IPS and AG. Given this convergence, along with the hint in the task-based data that further functional differentiation may exist (i.e., between AG and pIPL), Nelson et al. then examined whether a finer parcellation emerges when restricting rs-fcMRI network analysis to either the retrieval-sensitive (AG and IPS) or the retrieval-insensitive (SMG and SPL) networks. While further differentiation was not apparent in the latter, this analysis revealed that the retrieval-sensitive parietal networks might further divide into four networks. In this manner, six functionally separable parietal regions were obtained (Figure 1C). In a final step, Nelson et al. returned to the retrieval data and demonstrated that, of the parietal-cortical networks showing retrieval success effects, the parietal and extraparietal components of each "community" demonstrated similar retrieval-related time courses. This finding suggests that network membership at rest is predictive of task-evoked responses.

Nelson et al.'s approach is a powerful extension of earlier studies that combined

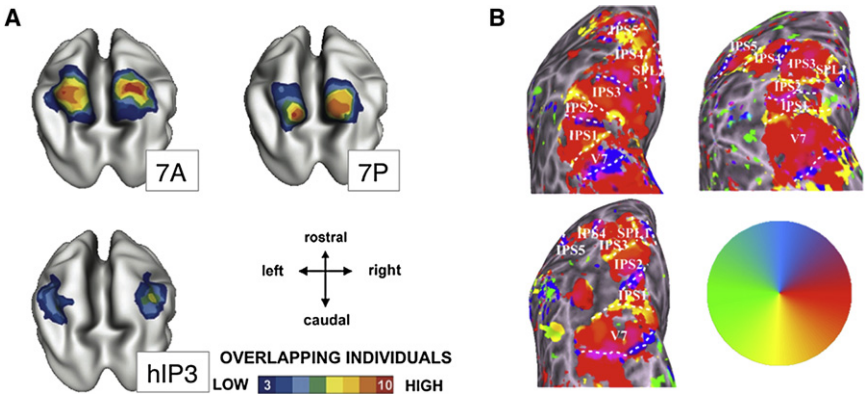

Figure 2. Individual Variability of Anatomical and Functional Subregions of Parietal Cortex
(A) Probabilistic maps of cytoarchitectonic overlap across ten individuals for three parietal subregions (7A, 7P, and hIP3) (modified from Scheperjans et al., 2008).
(B) Functionally defined maps coding retinotopic spatial attention from the inflated left hemispheres of three subjects (top row and bottom left). Color wheel indicates corresponding aspect of contralateral visual space (modified from Konen and Kastner, 2008).

rs-fcMRI and task-based fMRI to characterize specific lateral parietal regions. For example, using rs-fcMRI, Vincent et al. (2006) demonstrated that AG functionally couples with hippocampal seeds and, using task-based episodic retrieval data, demonstrated that AG activity is modulated by event recollection. Moreover, rs-fcMRI techniques in isolation have previously revealed at least three different intrinsic networks involving lateral parietal cortex: a dorsal fronto-parieto-occipital network involving SPL, a more ventral fronto-parietal network involving SMG, and a hippocampal-cortical network involving AG (Vincent et al., 2008). Nelson et al., on the other hand, began with hundreds of seeds distributed across lateral parietal cortex and used boundary identification and network analyses to differentiate multiple subregions of lateral parietal cortex, including those with differential sensitivity to episodic retrieval outcomes. In so doing, they identified six distinct parietal subregions, as well as many of the extraparietal structures that form the functional networks with which these subregions communicate.

While the authors' parcellation scheme constitutes a more detailed partitioning of human lateral parietal cortex than previously attained by rs-fcMRI and/or retrieval-based functional imaging, it does not reach the level of granularity evident in architectonic maps (Figure 1B). This may partially be a consequence of the latter methods being conducted at the individual-subject level rather than the group level. High across-subject variability in the location of particular architectonic regions in parietal cortex (Figure 2A) may pose challenges when attempting finer-grained functional parcellation using group-level data. Indeed, recent within-subject retinotopic mapping studies provide evidence for at least six discrete representations of attended visual space in dorsal parietal cortex (Figure 2B). Thus, a large swath of parietal cortex that has been difficult to partition in group-level analyses appears to comprise multiple retinotopically organized sectors in individual subjects. Future application of the parcellation methods of Nelson et al. to *individual-subject* data might provide powerful leverage on whether even further subdivisions exist in lateral parietal cortex. Additionally, these methods could be used more broadly to finely map other cortical regions, such as prefrontal cortex or the medial temporal lobe (MTL). In fact, given recent rs-fcMRI evidence of hippocampal-AG coupling (Vincent et al., 2006), the integrated approach of Nelson et al. could provide a finer-grained understanding of how particular MTL regions interact with particular parietal-cortical networks during episodic remembering. A further application of the Nelson et al. approach for fine mapping of cortical regions could be to additionally include knowledge of the *structural connectivity* profile of regions (for a combined rs-fcMRI and structural connectivity approach to parietal mapping, see Uddin et al., 2010).

The findings of Nelson et al. bear on current debates about parietal contributions to cognition, including the relationship between parietal correlates of attention and memory. While the ubiquity of lateral parietal activity in studies of episodic retrieval has been hypothesized to reveal the role of attention during attempts to remember (Cabeza et al., 2008), a recent meta-analysis of the retrieval and attention literatures conducted by our lab seems to challenge this view (Hutchinson et al., 2009). We found the dorsal and ventral parietal regions that demonstrate retrieval effects to at least partially dissociate from the dorsal and ventral parietal regions implicated in "top-down" and "bottom-up" attention. Nelson et al.'s findings appear consistent with this perspective, as the dorsal attention and retrieval effects in our meta-analysis appear to approximately correspond to their SPL and IPS/pIPL regions, respectively; likewise, the ventral attention and retrieval effects appear to correspond to their SMG and AG/pIPL regions, respectively (Figures 1C and 1D). While within-subject comparisons of parietal retrieval and attention effects are needed to fully resolve this debate, the compelling findings of Nelson et al. are the latest to highlight the richness of lateral parietal functional organization.

It remains an open question as to whether the anterior regions that Nelson et al. observed to be insensitive to retrieval success (SPL and SMG) are truly insensitive to memory outcomes or whether a finer-grained parcellation of *memory behavior* would reveal differential activation according to memory outcomes. To definitively address this question, one needs to delineate memory states at a finer grain than the comparison of hits versus correct rejections–e.g., between recognition based on recollection versus item familiarity (Wheeler and Buckner, 2004) or differences in recognition confidence. Finally, their findings will inform future efforts to understand how lateral parietal mechanisms contribute to episodic memory more broadly, including how the computations of particular dorsal and ventral parietal structures impact the

encoding of events into memory (Uncapher and Wagner, 2009).

Nelson et al.'s findings are part of a rising tide of data documenting a mosaic of distinct areas in human parietal cortex, which vary in their local functional properties as well as their global connectivity. The authors' efforts to parcellate parietal cortex complement related efforts to delineate occipito-temporal visual areas, wherein distinct areas are thought to have unique cytoarchitecture, anatomical connectivity, and functional properties. Continued examination of parietal heterogeneity using convergent techniques promises to ultimately reveal a fine-grained human parietal functional map, which will prove invaluable for understanding the neural bases of many aspects of cognition, from attention to memory and beyond.

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Genome Variation and Complexity in the Autism Spectrum

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A large international consortium reports in *Nature* on the diversity of genomic changes in families with autism spectrum disorders. Inherited and de novo mutations affecting many genes were discovered implicating disruption to postsynaptic and cellular signaling processes.

Autism spectrum disorders (ASDs) embrace a combination of behavioral phenotypes impacting on cognitive, social, and motor functions. The genetic basis of ASD, originally revealed in twin and family studies, is now being investigated on a genome-wide level using recent technological advances, resulting in the discovery of a multiplicity of putative driver mutations in neuronal and neurodevelopmental genes, including postsynaptic genes (Pinto et al., 2010 [a recent issue of *Nature*]). Understanding how this complex genetic etiology disrupts biochemical mechanisms and influences the spectrum of behavioral phenotypes in individuals may lead to new therapeutic avenues and insights into the molecular basis of human social interactions.

With the inexorable progress toward whole genome sequencing, mutations ranging in size from a single nucleotide to deletions and insertions of contiguous regions will be measured in each and every gene for all diseases. Many rare diseases of the nervous system are caused by a mutation in single genes, and there are "complex" diseases that have their basis in mutations affecting many genes. Prominent among these complex diseases are ASD, schizophrenia, and bipolar disease (Carroll and Owen, 2009). While it is only a matter of time before we have a definitive description of the genomic variation in ASD individuals using whole genome sequencing, an international consortium has reported the genomic variation at a lower resolution in individuals and families with ASD (Pinto et al., 2010). This report, building on earlier studies, provides new evidence that changes in the function of many genes, arising by rare inherited and de novo mutations, underlie the behavioral phenotypes of ASD.

The study surveyed the genome for deletions or insertions (extra copies of genomic DNA) greater than 30 kb in size