nature neuroscience

Spatial selectivity in human ventrolateral prefrontal cortex

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The functional organization of lateral prefrontal cortex is not well understood, and there is debate as to whether the dorsal and ventral aspects mediate distinct spatial and non-spatial functions, respectively. We show for the first time that recordings from human ventrolateral prefrontal cortex show spatial selectivity, supporting the idea that ventrolateral prefrontal cortex is involved in spatial processing. Our results also indicate that prefrontal cortex may be a source of control signals for neuroprosthetic applications.

Prefrontal cortex (PFC) is thought to provide the physiological basis for the multimodal integration and executive processing underlying goal-directed behavior[1,2]. Recordings from single units in monkey dorsolateral PFC show spatial selectivity with respect to eye movements[3], whereas human functional magnetic resonance imaging (fMRI) shows increased activation in this area when spatial working memory is in use[4]. In contrast, it has been proposed that ventrolateral PFC (vPF) is specialized for non-spatial processing, as it shows object selectivity in both monkeys[5,6] and humans[7]. However, this view of separate spatial and object processing areas in lateral PFC has been called into question by findings of spatial processing in monkey vPF[8] and by theoretical models that are able to account for experimental results without separate spatial and object processing domains[9].

To examine this issue, we recorded intracranial electroencephalographic (iEEG) activity during the performance of a memory reach task by three individuals who had electrodes implanted into vPF. Each subject had bilateral depth electrodes implanted through the inferior frontal gyrus (Brodmann's areas 45/47; **Supplementary Note** online). Our research protocol was approved by the institutional review board at Huntington Memorial Hospital, and informed consent was obtained from each individual. Subjects initiated each trial by placing their right hand on a central fixation stimulus. A target was then flashed at one of six locations, and this was followed by a short memory period. Subjects were instructed to make a reach to the location formerly indicated by the target when the fixation stimulus was extinguished.

Bilateral recordings from vPF typically showed spatial selectivity during the target presentation period (**Fig. 1a**,**b**). We observed selectivity both in the average evoked potential (**Fig. 1c**,**d**) and in the power spectrum (**Fig. 1e**,**f**). Approximately 200 ms after the target stimulus was presented, the neural activity diverged between trials with targets on the right and left (**Fig. 1c**,**d**). Notably, recordings from the right hemisphere showed effects with polarity opposite that of recordings from the left hemisphere. Subjects 2 and 3 showed spatial selectivity in vPF during target presentation (8 of 12 electrodes across the three subjects; $P < 0.01$). To assess the magnitude of selectivity, we calculated a selectivity index for each of these eight electrodes (selectivity index = 4.9 ± 1.5, mean $\pm$ s.d.; **Supplementary Note**).

We also observed spatial selectivity in vPF during the movement period (**Fig. 2a**,**b**). Again, we found that the polarity of the effect was

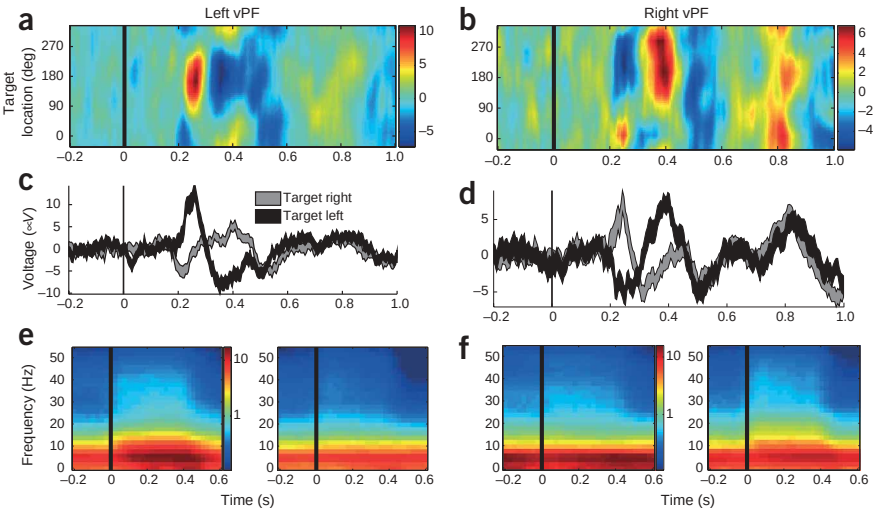

Figure 1 Human ventrolateral PFC shows spatial selectivity during target presentation. (**a**) Spatial selectivity during target presentation for an electrode in left vPF in subject 2. Target onset occurred at time $t = 0$. Color scale represents voltage. (**b**) Selectivity for an electrode in right vPF in the same individual. (**c**) Evoked potentials to targets presented to the right and to the left for the same electrode as in **a**. Error bars, s.e.m. (**d**) Evoked activity from right vPF (same electrode as in **b**). (**e**) Spectrograms plotting power as a function of time and frequency for targets presented to the left (left) and to the right (right) for the same electrode. Color scale represents log-power values. (**f**) Spectrograms calculated from activity in right vPF (same electrode as in **b**).

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Published online 13 March 2005; doi:10.1038/nn1424

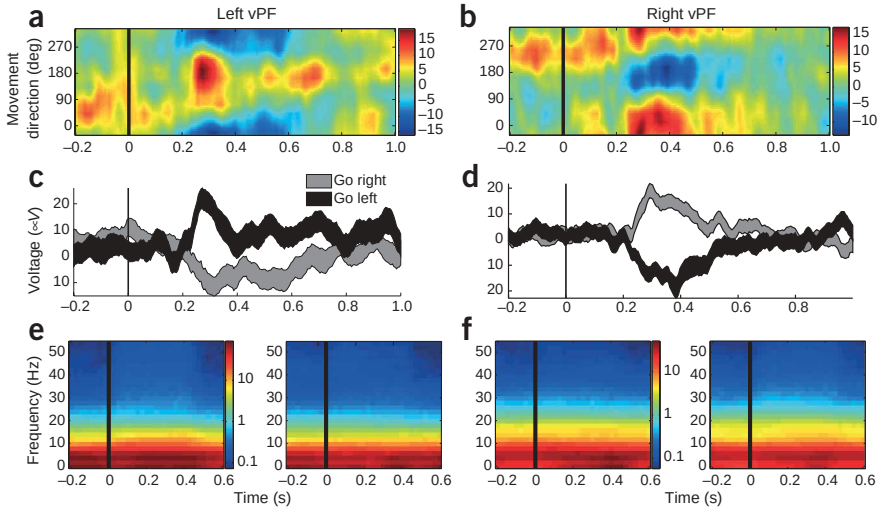

Figure 2 Human ventrolateral PFC shows spatial selectivity during the movement period. (**a**) Spatial selectivity during the movement period for an electrode in left vPF in subject 3. Movement signal occurs at time $t = 0$. Color scale represents voltage. (**b**) Selectivity for an electrode in right vPF in the same individual. (**c**) Evoked potentials during movements to the right and to the left for the same electrode as in **a**. Error bars, s.e.m. (**d**) Evoked activity from right vPF (same electrode as in **b**). (**e**) Spectrograms plotting power as a function of frequency and time for movements to the left (left) and the right (right). Same electrode as in **a**. (**f**) Spectrograms from right vPF (same electrode as in **b**).

reversed across the hemispheres, with positive-going potentials in left vPF, and negative-going potentials in right vPF, for trials requiring leftward movements (**Fig. 2c**,**d**). This pattern of effects was also apparent, to a lesser extent, in the power spectrum (**Fig. 2e**,**f**). Only subject 3 showed spatial selectivity during the movement period (4 of 12 electrodes across the three subjects; $P < 0.01$; selectivity index $= 4.5 \pm 1.3$).

We used the neural activity of subject 2 to decode the location of target presentation on each trial. Using a 300-ms moving window of evoked activity from either left or right vPF gave a decoding accuracy of 70–80% (**Fig. 3a**, solid and dashed lines), whereas using evoked activity from four bilateral electrodes in vPF increased decoding accuracy to 95% (**Fig. 3a**, dotted line). Using spectral activity between 5–45 Hz provided the same accuracy (**Fig. 3b**). In both cases, the accuracy increased with time starting at approximately 200 ms after target onset and reached peak accuracy at around 400 ms after stimulus onset.

Similarly, we were able to accurately decode the direction of movement in subject 3. Using a 300-ms moving window of evoked activity from the movement period in either left or right vPF provided a decoding accuracy of 70–80% (**Fig. 3c**). Decoding movement direction using two simultaneous bilateral recordings increased decoding accuracy to 95%. Spectral activity did not provide as good a decoding for movement direction as evoked activity did, reaching ~75% accuracy when we used two bilateral vPF recordings (**Fig. 3d**).

Here we report, for the first time, evidence for spatial selectivity in human vPF. As eye movements were not recorded during the performance of this task, we could not discriminate whether this selectivity pertains to visuospatial memory processing or to the planning of reaches or saccades. However, the present results are inconsistent with theories indicating only a non-spatial role for vPF[5–7]. Notably, these results do not rule out non-spatial processing in vPF. Rather, it is likely that both spatial and non-spatial processing take place there, as has been previously suggested[8,9].

The present results are consistent with evidence of a great deal of cross-talk and integration between the dorsal, action-based, and ventral, recognition-based pathways of the visual system[10]. It is also known that the monkey lateral intraparietal area, located squarely in the dorsal stream, encodes stimulus attributes such as color[11] and shape[12], when these attributes are important to the experimental task. Our results additionally suggest that ventral areas, typically thought of as object-processing areas, may encode spatial information as well.

Finally, there is increasing evidence in recordings from macaque that local field potentials (LFPs) from sharp-tipped electrodes can be used to accurately decode both movements[13] and movement plans[14]. Although iEEG recording samples a larger volume than sharp-tipped electrodes, the present results complement other studies indicating that iEEG records are sufficient to decode spatially tuned activity

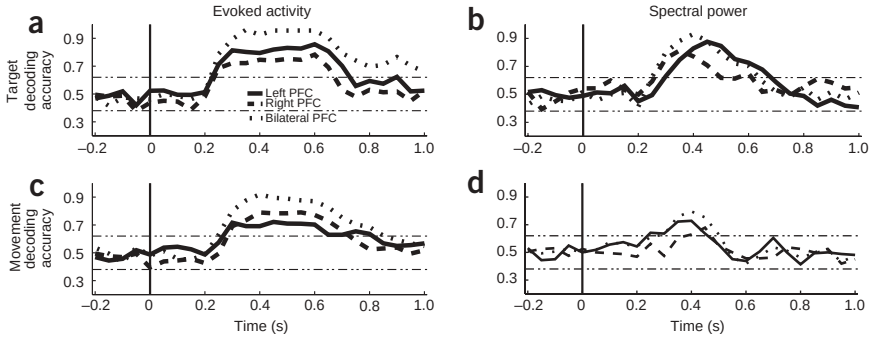

Figure 3 Using bilateral recordings improves decoding accuracy. (**a**) Classification accuracy for target location (left versus right) using evoked activity from electrodes in subject 2. Plots for left and right vPF show data from a single unilateral electrode, whereas the plot for bilateral vPF shows data from all four bilateral electrodes. Horizontal lines indicate upper and lower chance boundary ($P < 0.01$). (**b**) Classification accuracy for the target location using 5–45 Hz spectral power. Plots for left and right vPF show data from a single unilateral electrode, whereas the plot for bilateral vPF shows data from the two most lateral electrodes. Using additional electrodes did not improve the accuracy of the decoding. (**c**) Classification accuracy for movement direction (left versus right) using evoked activity from subject 3. Plots for left and right vPF show data from a single unilateral electrode, whereas the plot for bilateral vPF shows data from all four electrodes located bilaterally in vPF. (**d**) Classification accuracy for movement direction using 5–45 Hz spectral power. Plots for left and right vPF show data from a single electrode, whereas the plot for bilateral vPF shows data from the two most lateral electrodes. Using additional electrodes did not improve the accuracy of the decoding.

and may provide an additional method for deriving neuroprosthetic control signals[15].

Note: Supplementary information is available on the Nature Neuroscience website.

ACKNOWLEDGMENTS

We thank S. Musallam, A. Gail, B. Pesaran and H. Glidden for helpful discussion. The authors acknowledge support from the US Defense Advanced Research Projects Agency, National Eye Institute, the Boswell Foundation, Office of Naval Research and National Institute of Neurological Disorders and Stroke.

COMPETING INTERESTS STATEMENT

The authors declare that they have no competing financial interests.

Received 10 September 2004; accepted 15 February 2005
Published online at http://www.nature.com/natureneuroscience/

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