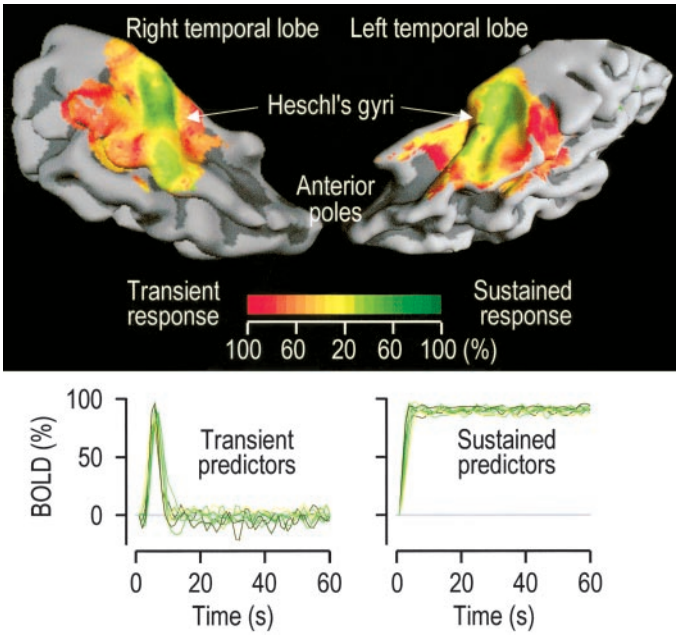

Fig. 3. (**Top**) The relative contribution map of transient and sustained BOLD signal sources across all subjects and trials with the corresponding signals as identified by temporal ICA. (**Bottom**) Signals represent intraindividual averages of the five trials used as predictors within a group multiple regression analysis (*31*). The functional map is projected on the reconstructed cortical surface of the temporal lobes of a standard brain template. Color coding indicates the relative contribution of the two predictor classes and suggests a spatial continuum between the temporal response patterns. The contribution of the sustained response type becomes less predominant as one moves from the core to the belt areas. There was no notable hemispheric difference in the extension of the predominantly transient and sustained responses.

Our data add to the evidence that the temporal decomposition of neural activity into transient and sustained patterns, or a continuum of them (*4*), may be a fundamental principle of deciphering auditory information. The mechanisms of upstream propagation of differential neural activity have only been partially unraveled. At the cortical level, the transformation into different temporal response types could be achieved by separate synaptic networks (*27*). The general rules, however, need to be viewed in light of the auditory network at large. In the thalamocortical circuitry, for instance, neural signals undergo radical reconstruction, with some properties preserving fidelity and others being transformed or generated anew in the auditory cortex (*28*). Temporal signal transformation appears to be a fundamental principle in the auditory system and could be related to different hierarchical levels of sound characterization. This hypothesis becomes particularly perspicuous considering the serial properties of auditory information.

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Supporting Online Material

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Representation of the Quantity of Visual Items in the Primate Prefrontal Cortex

Andreas Nieder,* David J. Freedman, Earl K. Miller

Deriving the quantity of items is an abstract form of categorization. To explore it, monkeys were trained to judge whether successive visual displays contained the same quantity of items. Many neurons in the lateral prefrontal cortex were tuned for quantity irrespective of the exact physical appearance of the displays. Their tuning curves formed overlapping filters, which may explain why behavioral discrimination improves with increasing numerical distance and why discrimination of two quantities with equal numerical distance worsens as their numerical size increases. A mechanism that extracts the quantity of visual field items could contribute to general numerical ability.

The ability to judge the relative quantity of items in the visual field is highly adaptive. Social animals such as primates can make decisions to fight or flee by judging the relative number of friends versus foes (*1–3*); in foraging, choosing a larger alternative can contribute to survival (*4*). These behaviors depend on the capacity to abstract information from sensory inputs and to retain it in memory, neural correlates of which are found in the prefrontal cortex (PFC) (*5*, *6*). To investigate the role of PFC neurons in representing visual quantity, we trained monkeys to judge whether two successive displays contained the same small number of items (Fig. 1A).

Picower Center for Learning and Memory, RIKEN-MIT Neuroscience Research Center, and Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, MA 02139, USA.

*To whom correspondence should be addressed: E-mail: nieder@mit.edu

Monkeys were trained with computer displays on which one to five dots could appear (Fig. 1B). We varied the exact physical appearance of the displays by randomly placing dots in 24 possible locations on a 5 × 5 matrix centered around the fixation target, on which monkeys maintained gaze. Each dot was also randomly varied among five different sizes (*7*). Monkeys watched two displays (first sample, then test) separated by a 1-s delay. They were trained to release a lever if the displays contained the same number of items. Average performance of both monkeys was significantly better than chance for all tested quantities (Binomial test, $P < 0.01$), with a decline when tested for higher quantities (*8*) similar to that seen in humans performing comparable tasks (Fig. 1C) (*9*).

To determine whether the monkeys solved the task by truly abstracting quantity rather than attending to low-level visual features, we used seven sets of control stimuli (Fig. 1B) (Table 1). Across these stimulus sets, the exact physical appearance of each numerical quantity varied widely. Even though monkeys were trained on the standard dots alone, they readily generalized (without additional training) to the control stimulus sets; performance was very similar across them (Fig. 1C). This suggests that monkeys were indeed judging quantity.

We recorded from 352 randomly selected neurons from the lateral PFC (Fig. 2A) of two monkeys (*7*). A third or more of them showed activity that varied significantly with the number of items in the sample display either during its presentation (131/352 or 37%) or during the memory delay [111/352 or 32%; analysis of variance (ANOVA), $P < 0.01$] (*10*). Five such neurons are shown (Fig. 2, B to F). Each cell shows peak activity for one of the visual quantities and a systematic drop-off of activity as the number of sample items varies from the preferred value. Many neurons (77/168) showed selectivity during both the sample presentation and the memory delay (Fig. 2, B and D); typically, neural preference was similar for both epochs (Pearson's correlation coefficient, $r = 0.56$, $P < 0.0001$) (*7*). We also recorded from the gyrus of the inferior parietal lobule (IPL) (area 7a). Only 7% (16/222) of IPL neurons were selective for quantity of visual stimuli. They will not be considered further in this report.

Neural activity also generalized across changes in the physical appearance of the sample displays. Neurons were tested with different combinations of both standard and control stimuli, and switching between them had little or no effect on neural activity. For example, the neurons (Fig. 2) showed remarkably similar activity to the standard or variable feature stimuli (Fig. 2B) and to displays with low or high density (Fig. 2C), with dots arranged in lines or shapes (Fig. 2D), with standard dots or those equating total area across numerosities (Fig. 2E), and with standard dots or those that equated the total circumference (Fig. 2F). Few of the quantity-selective neurons showed a significant effect of stimulus type (sample epoch, 17% or 22/131; delay, 13% or 14/111; two-way ANOVA, effect of stimulus protocol or interaction between stimulus protocol and quantity, $P < 0.01$). Of the 308 neurons tested with different combinations of standard and/or control stimuli, only a small proportion of the neurons were affected by stimulus type (sam-

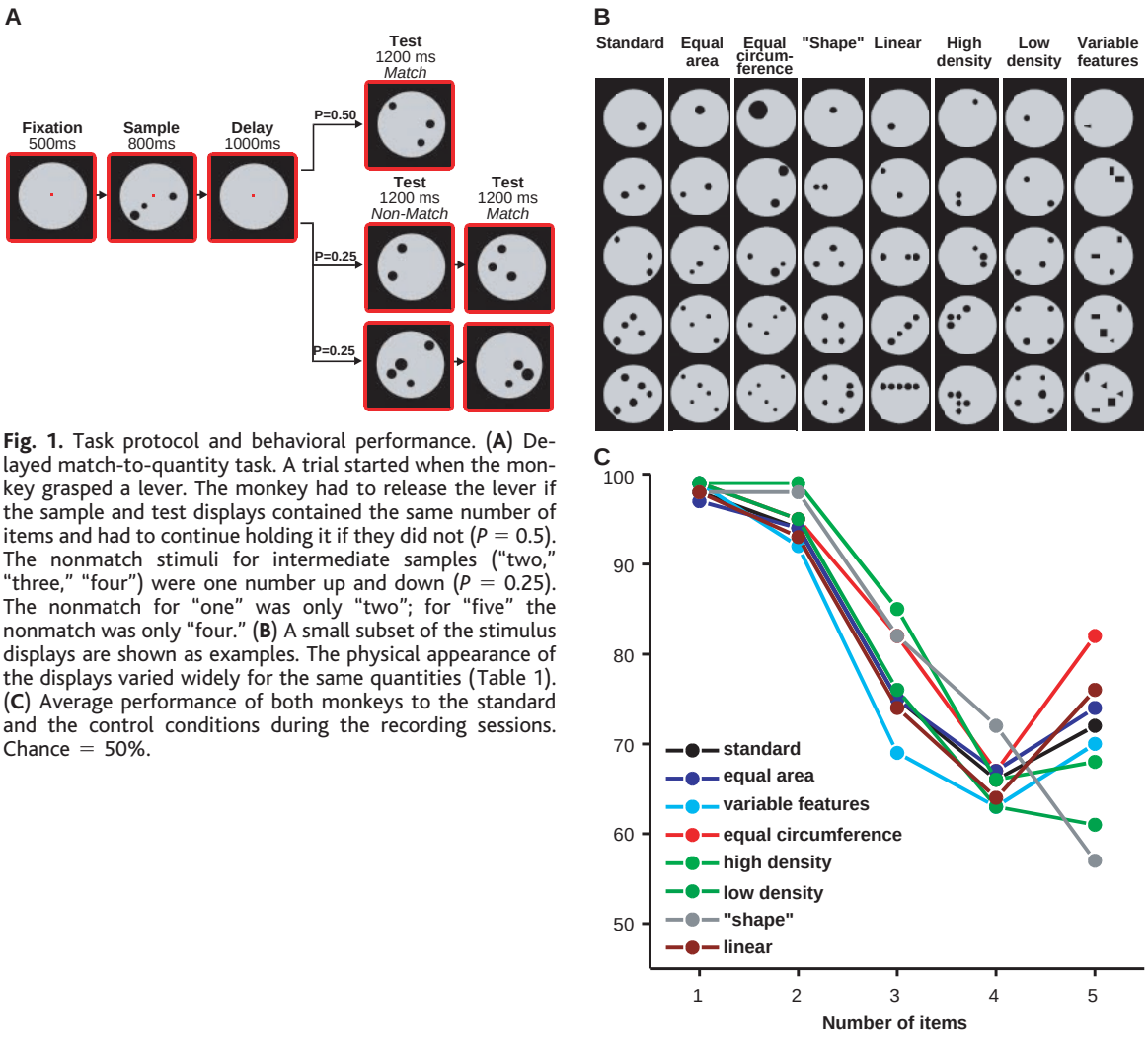

Fig. 1. Task protocol and behavioral performance. (**A**) Delayed match-to-quantity task. A trial started when the monkey grasped a lever. The monkey had to release the lever if the sample and test displays contained the same number of items and had to continue holding it if they did not ($P = 0.5$). The nonmatch stimuli for intermediate samples ("two," "three," "four") were one number up and down ($P = 0.25$). The nonmatch for "one" was only "two"; for "five" the nonmatch was only "four." (**B**) A small subset of the stimulus displays are shown as examples. The physical appearance of the displays varied widely for the same quantities (Table 1). (**C**) Average performance of both monkeys to the standard and the control conditions during the recording sessions. Chance = 50%.

Table 1. Stimulus protocols. For the shape category, three dots were arranged as triangle, four dots as quadrangle, five dots as pentagon. Randomized arrangement signifies a 5 × 5 matrix. Density was determined by calculating the average distance between the dots. For high-density stimuli, the dots had an average distance of <1.4° of visual angle (measured from center of the dots). For low-density stimuli, the items were arranged with an average distance of >2.5° of visual angle. Surface area, circumference, and density were evaluated with respect to concomitant changes in quantity.

Stimulus type	Spatial arrangement	Surface area	Circumference	Density	Item
Standard	Randomized	Increasing	Increasing	Increasing	Dots
Equal area	Randomized	Equal	Increasing	Increasing	Dots
Equal circumference	Randomized	Decreasing	Equal	Increasing	Dots
Linear	One-dimensional	Increasing	Increasing	Increasing	Dots
Shape	Triangle, quadrangle, pentagon	Increasing	Increasing	Increasing	Dots
High density	Randomized	Increasing	Increasing	Equally high	Dots
Low density	Randomized	Increasing	Increasing	Equally low	Dots
Variable features	Randomized	Increasing	Increasing	Increasing	Dots, ellipses, squares, bars, triangles

ple epoch, 12% or 36/308; delay interval, 7% or 21/308; two-way ANOVA, $P < 0.01$). Quantity-selective neurons also showed a high degree of correlation of their activity between tested stimulus protocols (sample epoch median correlation coefficient = 0.81; delay = 0.77) (*7*). Thus, the quantity of sample items was the dominant factor encoded by these neurons, not the physical appearance of the displays.

Neural activity in the PFC seemed to underlie a systematic, orderly representation of quantity; neurons showed peak activity to a specific quantity and a progressive drop-off as the quantity progressively varied (Fig. 2, B to F). To evaluate this across the population, we normalized the activity of each quantity-selective neuron and plotted its activity as a function of distance from its preferred quantity (*7*). On average, activity dropped off progressively with numerical distance (Wilcoxon signed ranks tests) for the sample (Fig. 3A) and the delay (Fig. 3B) intervals. The activation latencies for different quantities were similar ($P = 0.76$, Friedman test) (*11*).

Population neural filter functions were calculated by averaging the normalized activity for all neurons that preferred a given quantity. Neural activity formed band-pass filters with increasingly attenuated activity as distance from the preferred quantity increased (Fig. 3, C and D). To correlate these functions with behavior, we conducted additional psychophysical tests using a broad range of quantities as nonmatch stimuli. Monkeys made most errors for quantities that were adjacent to the cued quantity of dots and performed progressively better as numerical distance between two displays increased ("numerical distance effect") (*12*).

The average bandwidth of the neural filters increased with quantity (*7*) (i.e., on average, neurons became less precisely tuned as their preferred quantity increased) (Fig. 3, E and F). This same increase in bandwidth with increasing quantity is evident in network models of numerosity (*13*). It could be a neural correlate of the "numerical magnitude effect," the behavioral observation that it is harder to discriminate between two quantities of equal numerical distance as their magnitude increases (*12*). This was observed in our monkeys' behavior: For larger sample quantities, nonmatches had to be numerically more distant to reach a similar performance level as for small sample quantities (see behavioral data in Fig. 3, E and F) (*7*). Tuning curve shapes were asymmetric (a steeper slope for smaller quantities), but assumed a Gaussian shape when plotted on a logarithmic scale (*14*).

Further evidence that PFC neural activity contributed to behavior came from an examination of error trials. When monkeys made judgment errors, neural activity for the preferred quantity was significantly reduced to 84.8 and 72.1% of that observed on correct trials (100%) for the sample and delay epochs, respectively (*7*). As a result of this (and the orderly representation of

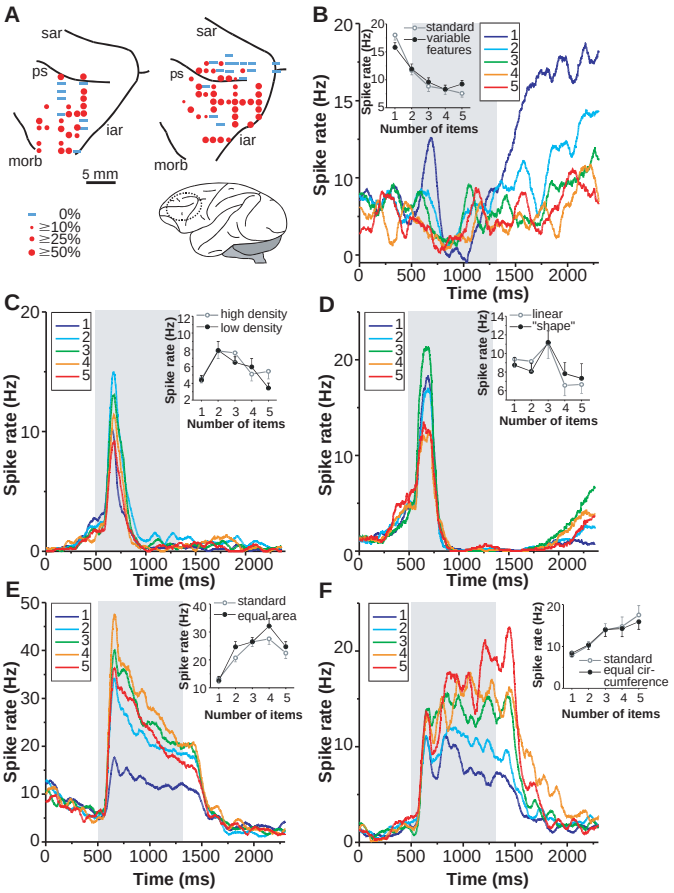

Fig. 2. Recording sites and neural responses. (**A**) Location of recording sites in PFCs of the two monkeys. The dot size reflects the proportion of selective units found at each recording site. iar, inferior arcuate sulcus; morb, medial orbital sulcus; ps, principal sulcus; sar, superior arcuate sulcus. There was no apparent topographical arrangement or clustering of neurons by their properties. (**B** to **F**) Responses (spike density functions) of five example neurons selective to different numbers of items. Each colored line shows the time course of activity for the five tested quantities. Gray shading represents the sample period (800 ms). The rate function insets indicate the mean activity of the neurons to each of the two stimulus protocols (error bars represent SEM) using the epoch (sample or delay) in which there was maximal quantity selectivity.

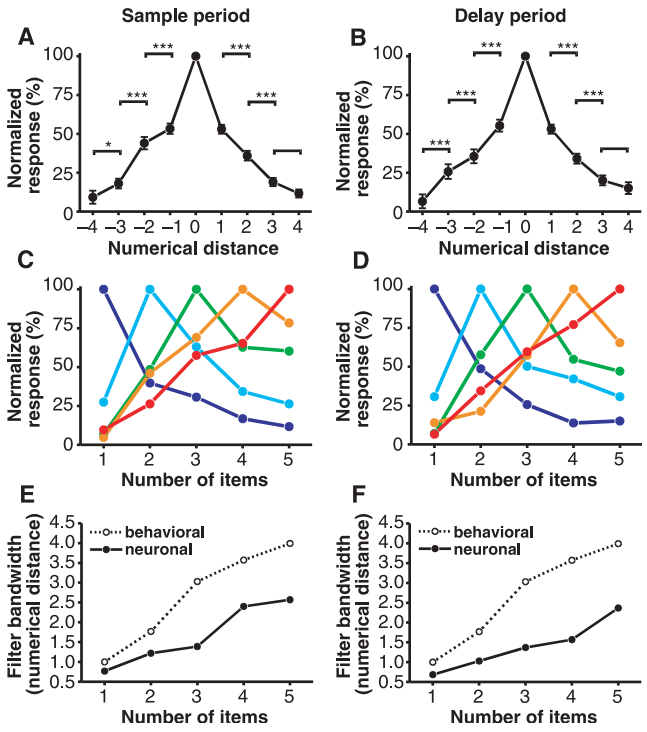

Fig. 3. Normalized response rates of selective neurons as a function of numerical distance. (**A** and **B**) Normalized spike rate during sample (A) and delay (B) epoch of all tested cells plotted against the numerical distance from the preferred number of items. Numbers closer to the preferred quantity elicited significantly higher spike rates (Wilcoxon matched-pairs signed-ranks test, *** = $P < 0.001$ and * = $P < 0.05$). (**C** and **D**) Normalized responses averaged for neurons preferring the same quantity for the sample (C) and delay (D) epochs. Colors are as in Fig. 2, B to F. (**E** and **F**) The average bandwidth of the neural filters for neurons preferring different quantities during sample (E) and delay (F) epochs. The same behavioral function is plotted in (E) and (F) for comparison with the neural data. Filter bandwidth increases for both behavior and neural activity with increasing quantity (though absolute values for neuronal and behavioral filter bandwidths are not directly related).

quantity), the activity on error trials elicited by a sample of a given quantity was more similar to that elicited by adjacent quantities on correct trials, especially during the delay (Fig. 3, A and B).

These results indicate that neurons in the lateral PFC can participate in high-level, abstract visual representations that can contribute to judgments of quantity. Many neurons were tuned for the number of items on a visual display but showed little change in activity to wide variations in the exact physical appearance of the displays. They seemed to preserve a systematic relation among different quantities; adjacent quantities evoked relatively similar activity and there was progressive drop-off as numerical distance increased. Neural activity seemed to form a bank of overlapping filters whose properties can explain the numerical distance and magnitude effect found in behavioral tests. Because monkeys (*15–17*) and other animals (*18–20*) are endowed with some rudimentary numerical competence, PFC activity may be a neural correlate for deriving the quantity information in a visual display.

This, of course, does not mean that the PFC is the only region where such information is represented. Human imaging and neuropsychological studies indicate involvement of both the frontal and parietal lobes in numerical ability (*21–25*). Neurons in a somatosensory-responsive area in the superior parietal lobe can keep track of the number of hand taps by a trained monkey (*26*); the authors reported few such neurons in the PFC. By contrast, our task examined judgments of visual quantity. Consistent with recent studies indicating that PFC neurons contribute to abstract visual categories (*5*, *6*), we found ample PFC neurons tuned to small numbers of visual stimuli (and a relatively small number in area 7a). Whether different brain areas contribute to different types of numerical abilities needs to be addressed with further experimentation.

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8. The improvement in performance for "five" is probably due to the "end-effect" (*27*). Four was the only nonmatch numerosity for sample numerosity five. Therefore, it was relatively easier for the monkeys to discriminate five items than to discriminate displays with four items.
9. Humans typically show a decrease in performance (an increase in response latency) for progressively larger quantities when asked to enumerate the quantity of items in a brief visual display (*27*, *28*). Our monkeys also showed an average increase in behavioral response latency of about 66 ms for each added item up to "four," but no additional increase for "five."
10. The quantity "one" was preferred by the modal group of neurons, but neural preference was equally distributed among the remaining quantities. The numbers of neurons that preferred each quantity were (sample period/delay period): 1, 54/38; 2, 17/23; 3, 13/10; 4, 20/17; 5, 27/23.
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Materials and Methods

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