Current Biology 18, 1483–1488, October 14, 2008 ©2008 Elsevier Ltd All rights reserved DOI 10.1016/j.cub.2008.08.054

Report

Prefrontal Neurons Predict Choices during an Auditory Same-Different Task

Brian E. Russ,[1] Lauren E. Orr,[1] and Yale E. Cohen[1,*]
[1]Department of Psychological and Brain Sciences
Center for Cognitive Neuroscience
Dartmouth College
Hanover, NH 03755

Summary

The detection of stimuli is critical for an animal's survival [1]. However, it is not adaptive for an animal to respond automatically to every stimulus that is present in the environment [2–5]. Given that the prefrontal cortex (PFC) plays a key role in executive function [6–8], we hypothesized that PFC activity should be involved in context-dependent responses to uncommon stimuli. As a test of this hypothesis, monkeys participated in a same-different task, a variant of an oddball task [2]. During this task, a monkey heard multiple presentations of a "reference" stimulus that were followed by a "test" stimulus and reported whether these stimuli were the same or different. While they participated in this task, we recorded from neurons in the ventrolateral prefrontal cortex (vPFC; a cortical area involved in aspects of nonspatial auditory processing [9, 10]). We found that vPFC activity was correlated with the monkeys' choices. This finding demonstrates a direct link between single neurons and behavioral choices in the PFC on a nonspatial auditory task.

Results

Behavioral Performance

Two rhesus monkeys participated in the same-different task (Figure 1A) that used morphed versions of the prototype spoken words *bad* and *dad* (Figure 1B). Figure 1C shows the behavioral performance of the two monkeys. The data shown in this figure were generated from all of the recording sessions reported in this study. The monkeys reliably reported that the 0%–40%-morph test stimuli were different than the reference stimulus and that the 60%–100%-morph test stimuli were the same as the reference stimulus. The monkeys' reports on the 50% morphs were, in general, intermediate between their reports on the lower-percentage and the upper-percentage morphs. The monkeys' performance during this task is consistent with a large literature of human and animal studies that tested the perceptual boundaries of human phonemes (*ba* and *da*) [11–15].

Neurophysiological Data

We recorded from 91 vPFC neurons while the monkeys participated in the same-different task (Figure 1A). For 53 of these 91 neurons, we collected blocks of data in which both *bad* and *dad* were the reference stimulus. In the other 38 neurons, we only collected blocks of data in which either *bad* (22 neurons) or *dad* was the reference stimulus (16 neurons). Of the 91 neurons, 67 were classified as "auditory" [16–18]; these neurons had reliably different firing rates during the 500 ms period that began with the test-stimulus onset than during the 500 ms period that occurred prior to the test-stimulus onset (t test, $p < 0.05$).

The response profiles of two vPFC neurons are shown in Figure 2. For the vPFC neuron in Figure 2A, when the test stimulus was a 0%–50% morph, this neuron had a high firing rate (cool-blue colors). In contrast, when the test stimulus was a 60%–100% morph, the neuron had a relatively lower firing rate (red/purple colors).

Which aspects of the task could this vPFC neuron be coding? Given that the stimulus-presentation dynamics in our same-different task are similar to that used in oddball tasks and stimulus-specific adaptation [2, 19], stronger "pop-out" vPFC responses might reflect the automatic detection [2] of uncommon test stimuli. Therefore, stronger responses could reflect test stimuli that are acoustically distinct from the reference stimulus (i.e., the 0%–80% morphs). However, because this neuron responds weakly to several of these test stimuli (see Figure 2A), its response pattern does not reflect the presence of acoustically distinct test stimuli.

Another neuron with a different type of response profile is shown in Figure 2B. Unlike the neuron in Figure 2A, this vPFC neuron had a low firing rate (cool-blue colors) when the test stimulus was a 0%–50% morph and a high firing rate (red/purple colors) when the test stimulus was a 60%–100% morph. This neuron's response profile, like that in Figure 2A, is also incompatible with the idea that vPFC neurons automatically signal the detection of acoustically distinct test stimuli with strong pop-out responses [2]: this neuron had a low firing rate when the reference and test stimuli were acoustically distinct. Relatively few neurons (n = 4/67) had response profiles like that shown in Figure 2B; most (n = 63/67) had response profiles similar to that shown in Figure 2A.

We hypothesize that vPFC activity, instead of correlating with the automatic detection of uncommon stimuli, might be correlated with the monkey's choices (behavioral reports; see Figure 1C). For the neuron in Figure 2A, stronger responses might reflect trials when the monkey reports that the reference and test stimuli are perceptually—as opposed to acoustically—distinct (i.e., different), whereas weaker responses might reflect trials when he reports that they are perceptually similar (i.e., the same). For the neuron in Figure 2B, weaker responses might code the trials when the two stimuli are the same and strong responses might code the trials when the stimuli are different. This hypothesis is tested directly by a series of population analyses in the next section.

Relationship between the Monkeys' Choices and Neural Activity

Does vPFC activity reflect what the monkeys *should* choose or does it reflect the monkeys' *actual* choices? For gaining insight into whether neural activity reflects what the monkey should choose, a neurometric analysis [20, 21] (see Supplemental Data, available online) was conducted. This analysis tests whether an ideal observer can use vPFC activity to predict the differences between test stimuli and whether this activity covaries with the monkeys' behavioral reports. However, as seen in the Supplemental Data, the results of the neurometric

*Correspondence: yec@dartmouth.edu

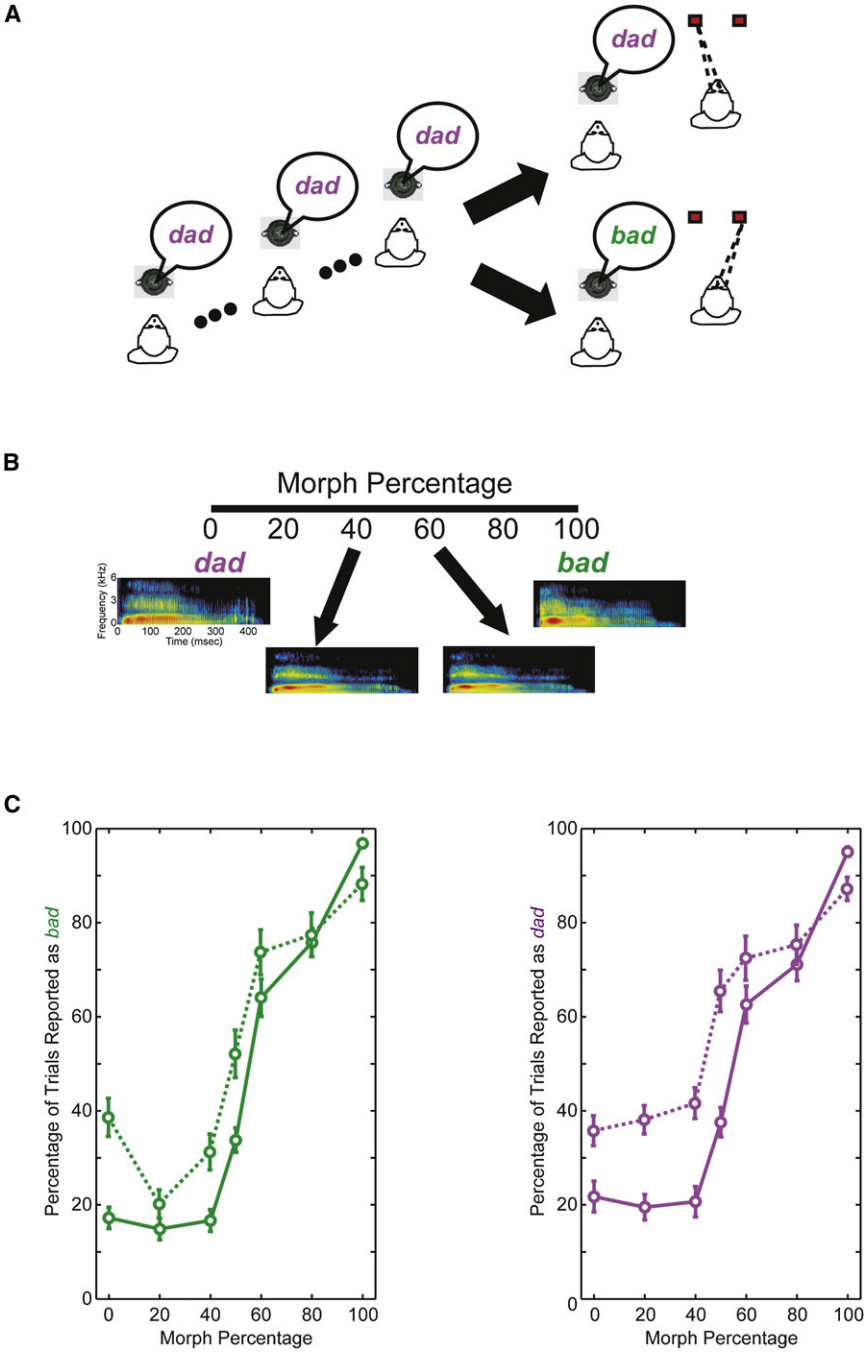

Figure 1. Same-Different Task and Behavioral Performance

(A) After two to four presentations of the reference stimulus, a test stimulus was presented. The reference stimulus was always one of the two prototype spoken words (*bad* or *dad*). The test stimulus was a morphed version of the prototypes. If the monkeys perceived that the reference and test stimuli were the same, they made a saccade to a leftward target. If the monkeys perceived that the reference and test stimuli were different, they made a saccade to a rightward target.

(B) Spectrographic representations of the prototype spoken words and of two of the morphs. In this example, the reference stimulus is *bad*. Consequently, it is the 100% morph, whereas *dad* is the 0% morph; see Experimental Procedures for more details. When the reference stimulus is the spoken word *dad*, the morph percentages are reversed (e.g., the 0% morph is *bad* and the 100% morph is *dad*). The axes for all of the spectrograms are seen in the leftmost spectrogram.

(C) The average performance of the monkeys from those recording sessions reported in this manuscript. The monkeys' performance is shown as a function of the reference stimulus: the prototype spoken word *bad* (left column) or *dad* (right column). A 0% morph means that the test stimulus was a different prototype than the reference stimulus (e.g., the reference stimulus was the prototype *bad* and the test stimulus was the prototype *dad*). A 100% morph means that the test and reference stimuli were the same (e.g., both were the prototype *dad*). Other values represent morphed stimuli between these two extremes. The data that are plotted with a solid line are from monkey H; the data that are plotted with a dashed line are from Monkey P. Error bars are standard error of the means.

analysis indicate that vPFC activity is not a good predictor of the test stimulus and, hence, is not a good predictor of what the monkey should choose.

To test the hypothesis that vPFC activity reflects the monkeys' actual choices, we calculated the choice probability (CP) [22–24]. On a neuron-by-neuron basis and using both successful and error trials, we first formed two distributions. One distribution contained the test-stimulus-period firing rates from trials when the monkey reported that the reference and test stimuli were the same. The second distribution contained the firing rates when the monkey reported that the stimuli were different. From these two distributions, a receiver-operating-characteristic curve was generated; the area under this curve is a neuron's CP [23]. The CP values from different neurons and from different variations of the analysis were grouped together to form different population distributions of the CP values; to minimize the differences between different neurons' firing rates, firing rates were normalized with a *Z* score.

If vPFC activity reflects the automatic detection of acoustically uncommon test stimuli, neural activity should not be modulated by the monkeys' choices. Under this hypothesis, the CP should equal 0.5. On the other hand, if vPFC activity reflects the monkeys' choices, the CP should be > 0.5 or < 0.5 if vPFC activity, on average, increases or decreases, respectively, when the monkeys report that the reference and test stimuli are different.

We first calculated the "grand" CP [24]. In this analysis, the "same" and "different" distributions were formed with the data generated from all of the potential test-stimulus morph values (i.e., 0%–100%). The data in Figure 3A represent the grand-CP values generated when the reference stimulus was *bad*, whereas the data in Figure 3B represent the grand-CP values generated when the reference stimulus was *dad*. The mean grand-CP values from both distributions were reliably greater than 0.5 (t test, $p < 0.05$). This result is consistent

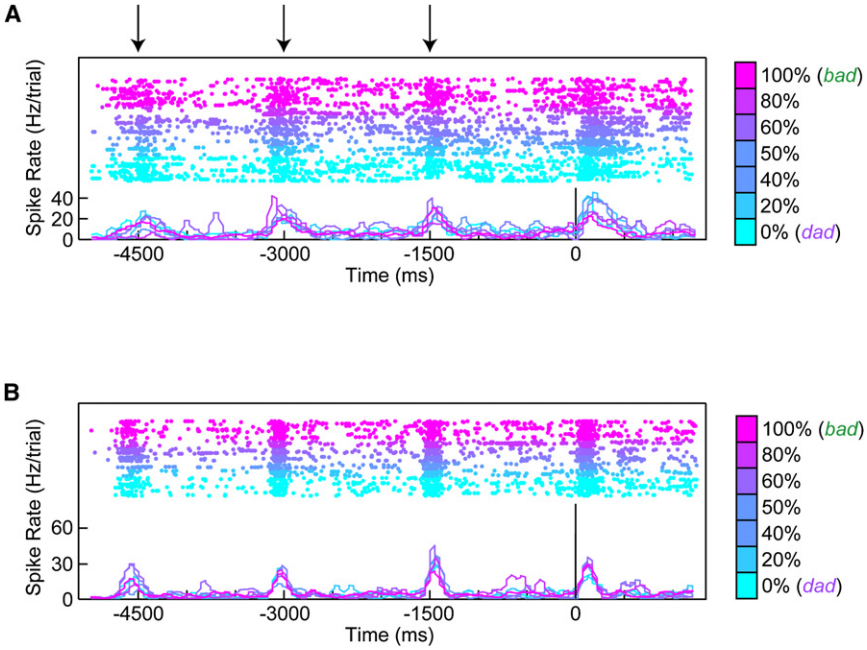

Figure 2. Examples of vPFC Activity during the Same-Different Task

In (A) and (B), the reference stimulus was the prototype spoken word *bad*. In each panel, the rasters and spike-density histograms are aligned relative to the onset of the test stimulus. The morph value of the test stimulus is indicated by color, as shown by the color bar: 0% morphs are the lightest blue color and 100% morphs are the purple color. When the test stimulus was a 100% morph, it was identical to the reference stimulus. The arrows in (A) indicate the approximate times of each of the reference stimuli. In these two panels, only successful trials are shown.

with the hypothesis that vPFC activity during the same-different task reflects the monkeys' choices.

This population-level result was also seen at the single-neuron level. When the reference stimulus was *bad*, 33 of the 56 neurons had grand-CP values reliably larger than 0.5 (permutation test, $p < 0.05$); this proportion of neurons is reliably greater than chance (binomial test, $p < 0.05$). Similarly, when the reference stimulus was *dad*, a significant proportion of vPFC neurons ($n = 26/55$; binomial test, $p < 0.05$) had grand-CP values that were reliably larger than 0.5 (permutation test, $p < 0.05$). We did not find a reliable population ($p > 0.05$) of vPFC neurons with significant CP values < 0.5.

Next, we considered whether the results of the grand-CP analysis might be biased by particular test-stimulus morph values. The CP values might have been biased toward large values during those trials when the monkeys' choices were "easy" (i.e., those trials when the reference and test stimuli were very different or identical) and there were few error trials. In contrast, the CP values might have been biased toward values equaling 0.5 during those trials when the monkeys choices were "hard" (i.e., those trials when the reference and test stimuli were moderately similar) and there were relatively more error trials.

To eliminate this possibility, we calculated the CP values from the neural data generated during "easy" trials (0%, 20%, 80%, and 100% morphs) and during "hard" trials (40%–60% morphs). The population distributions of these easy- (Figure 3C) and hard-CP (Figure 3D) values were both reliably greater than 0.5 (t test, $p < 0.05$). Thus, vPFC neurons code the monkeys' choices for both easy and hard morph values.

Finally, we examined, at the population level, the grand-CP time course. Figure 4A shows this analysis when the data were aligned relative to test-stimulus onset. As expected, when the reference stimuli were presented (i.e., time < 0), the mean CP value was not reliably different than 0.5. However, following test-stimulus onset, the CP increased and became reliably > 0.5. The average CP value remained > 0.5 after test-stimulus offset for another ~250 ms before returning to a value of 0.5.

To test how the grand CP is modulated before the monkeys report their choices, we realigned the data relative to the onset of the two LEDs. As seen in Figure 4B, the CP preceding LED onset remained elevated. Additionally, there was a slight increase in the CP after LED onset, correlating with the monkeys' saccade to one of the two LEDs. This CP increase was not wholly related to any potential spatial tuning of neural activity during the saccade period: saccade-related activity in our population of vPFC neurons was not, in general, spatially tuned (data not shown).

Control Analyses for Task-Dependent Activity

If vPFC activity reflects the automatic detection of acoustically uncommon stimuli, we would expect that vPFC activity would habituate with repeated presentations of the reference stimuli, as seen in stimulus-specific adaptation studies [19, 25]. We found that, on average, vPFC activity was not modulated by the number of reference stimuli and, hence, did not habituate (*bad*: $F(6,383) = 1.51$, $p > 0.05$; *dad*: $F(6,376) = 1.25$, $p > 0.05$). We also tested whether a vPFC neuron's response to the test stimulus was dependent on the number of reference stimuli. As the number of reference stimuli increases, the probability that the next stimulus is a test stimulus also increases. To test this possibility, we sorted the average test-stimulus firing rates as a function of the number of reference stimuli that preceded test-stimulus onset (see Figure S3). We did not find a main effect for the number of reference stimuli (*bad*: $F(2,1105) = 1.68$, $p > 0.05$; *dad*: $F(2,1082) = 0.43$, $p > 0.05$), but there was a main effect for the morph percentage on the test-stimulus firing rates (*bad*: $F(6,1105) = 29.83$, $p < 0.05$; *dad*: $F(1,1082) = 8.89$, $p < 0.05$); this latter result indicates that test-stimulus firing rates were modulated by the morph percentage, as seen in Figure 2. Finally, we asked whether the context in which the prototype stimuli were presented (i.e., as a reference or a test stimulus) modulated vPFC activity. To test this issue, we calculated, on a neuron-by-neuron basis, an index that quantified how similarly a neuron responded to a prototype when it was the reference stimulus versus when it was the test stimulus (top rows of Figures S4A and S4B). Given that these index-value distributions were not reliably different than zero (t test; $p > 0.05$), vPFC neurons, on average, responded comparably to a prototype when presented as a reference or a test stimulus. In contrast, when the reference and test stimuli were different prototypes (see the bottom rows of Figures S4A and S4B), the average index value was reliably

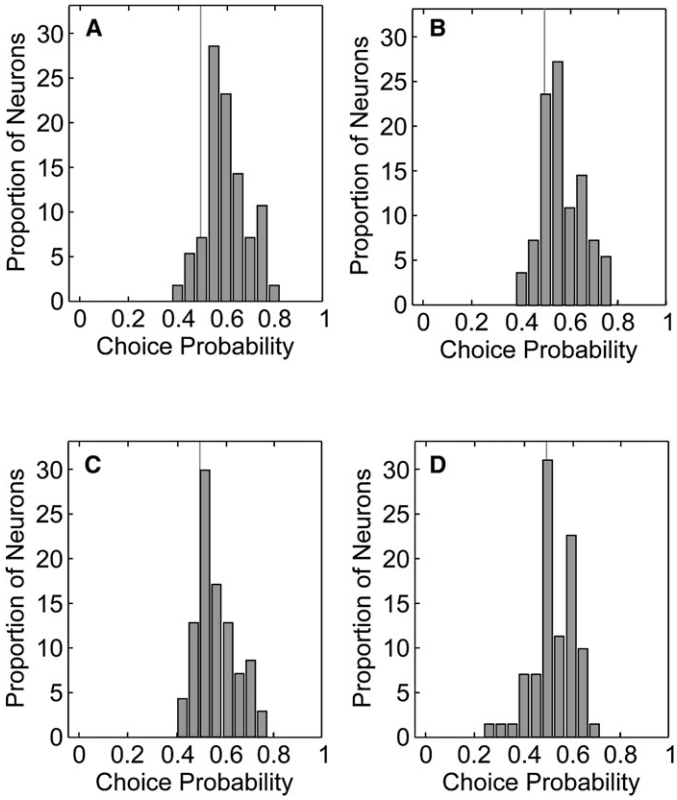

Figure 3. Choice Probability

The distribution of grand choice-probability values for each neuron in our population of vPFC neurons when (A) the reference stimulus is the prototype word *bad* and when (B) the reference stimulus is *dad*. Panel (C) shows the distribution of the CP values generated from those trials when the monkeys' decisions were "easy"; that is, those test-stimulus morphs that were very different or identical to the reference stimulus (i.e., 0%, 20%, 80%, and 100%). Panel (D) shows distribution of the CP values generated from those trials when the monkeys' decisions were "hard"; that is, those test-stimulus morphs that were moderately similar to the reference stimulus (i.e., 40%, 50%, and 60%). For panels (C) and (D), we grouped together data collected for the two different reference stimuli.

different than zero ($p < 0.05$), indicating that vPFC neurons responded differently to the two prototypes.

Discussion

Whereas it is clearly adaptive to detect uncommon or novel stimuli, it is not adaptive to respond to all of these stimuli, because this detection might divert key attentional and neural resources away from a critical task. Indeed, neural representations of uncommon stimuli are reduced as the attentional demands of an ongoing task increase [26–30]. Alternatively, attention can facilitate the detection of uncommon tones from the background [31, 32]. Thus, the perceptibility of uncommon stimuli is under considerable cognitive control and is not purely an automatic response.

Because the PFC plays a key role in executive function [6], it is natural to hypothesize that it might also contribute significantly to the adaptive processes that allow an animal to contextually respond to the presence of uncommon stimuli. The PFC might mediate this role through top-down mechanisms that flexibly modulate the neural circuits involved with the detection of novel stimuli [30, 33, 34]. Several lines of evidence support a role for the PFC in contextually dependent detection of uncommon or novel stimuli. Familiarity, for example, may be a modulating factor: when familiar stimuli, which are inherently not novel, occur in unfamiliar situations, they differentially modulate PFC neurons [35]. Second, PFC activity is correlated with decisions on the commonality of a stimulus and the subsequent reallocation of neural resources [36]. Third, using a delayed match-to-sample task that was similar, but not identical, to our same-different task, Miller and colleagues reported that PFC neurons are actively engaged in the decision-making process of whether two stimuli are the same or different [37]. Finally, the current data (see Figures 3 and 4) indicate that test-period vPFC activity reflects the monkeys' choices during a same-different task.

Conclusion

Previous work from our laboratory and that from others have suggested that the pathway leading from the primary auditory cortex to the superior temporal gyrus and, ultimately, to the vPFC is dedicated to processing the nonspatial aspects of auditory stimuli [9, 10, 16, 38]. However, because these studies did not test neural activity while monkeys were participating in an auditory behavior, it was not known whether the vPFC and other areas in this pathway are actively engaged in auditory cognition. Here, we demonstrate directly that the vPFC plays an important role in aspects of nonspatial auditory cognition: vPFC activity reflects the decision-making processes

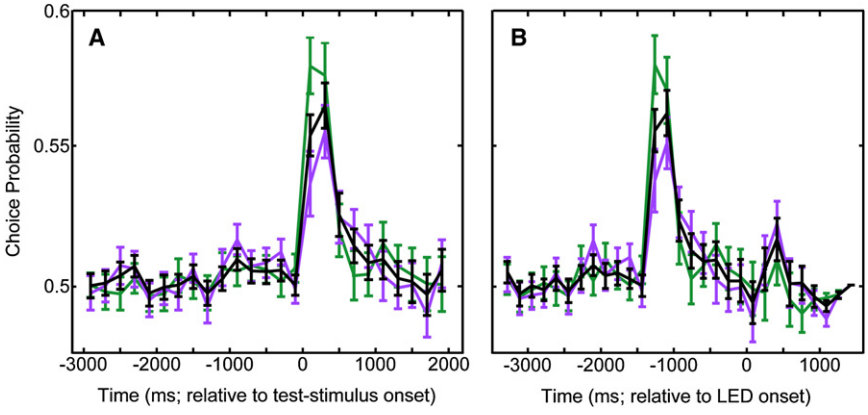

Figure 4. Time Course of Choice Probability

(A and B) The CP values were calculated from nonoverlapping 200 ms epochs of neural activity. The data in (A) are aligned relative to the onset of the test stimulus, whereas the data in (B) are aligned relative to the onset of the LEDs. In both panels, the data in green illustrate the CP values generated when the reference stimulus was *bad*, whereas the data in purple illustrate the CP values generated when the reference stimulus was *dad*. The data in black illustrate the CP values generated when the two reference stimuli were combined. The error bars represent the standard error.

that monkeys make during a nonspatial auditory task. Unfortunately, our data are too preliminary to offer insight into the mechanism of this decision-making process; though, future studies may be able to shed more light on these mechanisms. Finally, our results further emphasize the role of the PFC in the maintenance and retrieval of abstract rules [6–8, 39, 40] and are consistent with a more general literature describing a role for the PFC in decision making [41–44].

Experimental Procedures

We recorded from neurons in the vPFC from one male and one female rhesus monkey (*Macaca mulatta*). Under isofluorane anesthesia, the monkeys were implanted with a scleral search coil, a head-positioning cylinder, and a recording chamber. vPFC recordings were obtained from the male rhesus monkey's left hemisphere and from the female's right hemisphere. All recordings were guided by pre- and postoperative magnetic-resonance images of each monkey's brain. The Dartmouth Institutional Animal Care and Use Committee approved the experimental protocols.

Auditory Stimuli

The prototype stimuli were the spoken words *bad* and *dad*. In humans, these stimuli differ in their place of articulation. The prototypes were digitized recordings of an American adult female and were provided by Michael Kilgard. Morphed versions of the prototypes were created with the *STRAIGHT* [45] software package, which is run in the MATLAB (The Mathworks) programming environment. Morphing was accomplished by calculation of the shortest trajectory between the fundamental and formant frequencies of the two prototypes. Morphed versions of the two prototypes were created at 20%, 40%, 50%, 60%, and 80% of the distance along this trajectory. Spectrograms of the two prototypes and some of the morphed stimuli are shown in Figure 1.

Same-Different Task

As schematized in Figure 1, the task began with two to four presentations of a "reference" stimulus that was followed by the presentation of a "test" stimulus. The manner in which stimuli were presented in this task is similar to that seen in other studies of stimulus novelty, such as oddball tasks and stimulus-specific adaptation [2, 19]. The reference and test stimuli were 500 ms in duration, and the interstimulus interval averaged 1600 ms. The stimuli were presented from a speaker (Pyle, PLX32) that was in front of the monkey at a level of 70 dB SPL. The reference stimulus was always one of the two prototype words. The test stimulus was a morph of one of the two prototypes. The 100% morph was operationally defined to be the same prototype as the reference stimulus; therefore, the 0% morph was the other prototype. 500 ms after test-stimulus offset, two LEDs were illuminated. If the test stimulus was a 0%–40% morph, the monkeys were rewarded when they successfully reported that the reference and test stimuli were different by making a saccade to the LED that was 20° to the right of the speaker. If the test stimulus was a 60%–100% morph, the monkeys were rewarded when they successfully reported that the reference and test stimuli were the same by making a saccade to the LED that was 20° to the left of the speaker. When the test stimulus was a 50% morph, which has been shown to be a perceptual boundary [13, 14], the monkeys were rewarded randomly based on their overall performance level [46].

Recording Procedure

Single-unit extracellular recordings were obtained with tungsten microelectrodes (Frederick Haer & Co.) seated inside a stainless-steel guide tube. The electrode and guide tube were advanced into the brain with a hydraulic microdrive (Narishige MO-95). The electrode signal was amplified (Bak MDA-4I) and band-pass filtered (Krohn-Hite 3700,) between 0.6–6.0 kHz. Single-unit activity was isolated with a two-window, time-voltage discriminator (Bak DDIS-1). The time of occurrence of each action potential was stored for on- and offline analyses.

The vPFC was identified by its anatomical location and its neurophysiological properties [18, 47]. The vPFC is located anterior to the arcuate sulcus and Area 8a and lies below the principal sulcus. vPFC neurons were further characterized by their strong responses to auditory stimuli.

Once a neuron was isolated, the monkeys participated in blocks of trials of the same-different task. Because vPFC neurons respond broadly to a wide range of auditory stimuli [16], we did not tailor the reference and test stimuli to the neuron's response characteristics. In each block of trials, there were six trials in which the test stimulus was a 0% morph, six trials in which the test stimulus was a 100% morph, and two trials each of the remaining morphs. The test stimulus was chosen in a balanced, pseudorandom order. We report those neurons in which we were able to collect data from $\geq$ five successful blocks of trials using one prototype as the reference stimulus.

Supplemental Data

Supplemental data include Supplemental Experimental Procedures and four figures and can be found with this paper online at http://www.current-biology.com/cgi/content/full/18/19/1483/DC1/.

Acknowledgments

We would like to thank John Pezaris, Tony Zador, Anne Krendl, Jung Hoon Lee, and Heather Hersh for helpful comments on the preparation of this manuscript; Ashlee Ackelson and Selina Davis for excellent technical assistance; and Farshad Chowdhury and Lauren Wool for assistance with preliminary aspects of data collection. B.E.R. was supported by a National Research Service Award grant from the National Institute of Mental Health, of the National Institutes of Health (NIMH-NIH). Y.E.C. was supported by grants from NIMH-NIH and from the National Institute on Deafness and Other Communication Disorders, also of the NIH.

Received: June 20, 2008
Revised: July 29, 2008
Accepted: August 11, 2008
Published online: September 25, 2008

References

1. Ranganath, C., and Rainer, G. (2003). Neural mechanisms for detecting and remembering novel events. Nat. Rev. Neurosci. *4*, 193–202.
2. Näätänen, R. (1992). Attention and brain function (Hillsdale, NJ: Erlbaum).
3. Cohen, Y.E., Russ, B.E., and Gifford, G.W., III. (2005). Auditory processing in the posterior parietal cortex. Behav. Cogn. Neurosci. Rev. *4*, 218–231.
4. Gifford, G.W., III, Hauser, M.D., and Cohen, Y.E. (2003). Discrimination of functionally referential calls by laboratory-housed rhesus macaques: Implications for neuroethological studies. Brain Behav. Evol. *61*, 213–224.
5. Hauser, M.D. (1998). Functional referents and acoustic similarity: field playback experiments with rhesus monkeys. Anim. Behav. *55*, 1647–1658.
6. Miller, E.K., Freedman, D.J., and Wallis, J.D. (2002). The prefrontal cortex: categories, concepts, and cognition. Philos. Trans. R. Soc. Lond. B Biol. Sci. *29*, 1123–1136.
7. Bunge, S.A., Kahn, I., Wallis, J.D., Miller, E.K., and Wagner, A.D. (2003). Neural circuits subserving the retrieval and maintenance of abstract rules. J. Neurophysiol. *90*, 3419–3428.
8. Gabrieli, J.D., Poldrack, R.A., and Desmond, J.E. (1998). The role of left prefrontal cortex in language and memory. Proc. Natl. Acad. Sci. USA *95*, 906–913.
9. Rauschecker, J.P., and Tian, B. (2000). Mechanisms and streams for processing of "what" and "where" in auditory cortex. Proc. Natl. Acad. Sci. USA *97*, 11800–11806.
10. Russ, B.E., Lee, Y.-S., and Cohen, Y.E. (2007). Neural and behavioral correlates of auditory categorization. Hear. Res. *229*, 204–212.
11. Kuhl, P.K., and Miller, J.D. (1975). Speech perception by the chinchilla: voiced-voiceless distinction in alveolar plosive consonants. Science *190*, 69–72.
12. Kuhl, P.K., and Miller, J.D. (1978). Speech perception by the chinchilla: identification function for synthetic VOT stimuli. J. Acoust. Soc. Am. *63*, 905–917.
13. Kuhl, P.K., and Padden, D.M. (1982). Enhanced discriminability at the phonetic boundaries for the voicing feature in macaques. Percept. Psychophys. *32*, 542–550.
14. Kuhl, P.K., and Padden, D.M. (1983). Enhanced discriminability at the phonetic boundaries for the place feature in macaques. J. Acoust. Soc. Am. *73*, 1003–1010.
15. Eimas, P.D., Siqueland, E.R., Jusczyk, P., and Vigorito, J. (1971). Speech perception in infants. Science *171*, 303–306.

16. Russ, B.E., Ackelson, A.L., Baker, A.E., and Cohen, Y.E. (2008). Coding of auditory-stimulus identity in the auditory non-spatial processing stream. J. Neurophysiol. *99*, 87–95.
17. Gifford, G.W., III, MacLean, K.A., Hauser, M.D., and Cohen, Y.E. (2005). The neurophysiology of functionally meaningful categories: macaque ventrolateral prefrontal cortex plays a critical role in spontaneous categorization of species-specific vocalizations. J. Cogn. Neurosci. *17*, 1471–1482.
18. Cohen, Y.E., Russ, B.E., Gifford, G.W., III, Kiringoda, R., and MacLean, K.A. (2004). Selectivity for the spatial and nonspatial attributes of auditory stimuli in the ventrolateral prefrontal cortex. J. Neurosci. *24*, 11307–11316.
19. Ulanovsky, N., Las, L., and Nelken, I. (2003). Processing of low-probability sounds by cortical neurons. Nat. Neurosci. *6*, 391–398.
20. Britten, K.H., Shadlen, M.N., Newsome, W.T., and Movshon, J.A. (1992). The analysis of visual motion: a comparison of neuronal and psychophysical performance. J. Neurosci. *12*, 4745–4765.
21. Green, D.M., and Swets, J.A. (1966). Signal Detection Theory and Psychophysics (New York: John Wiley and Sons, Inc.).
22. Purushothaman, G., and Bradley, D.C. (2005). Neural population code for fine perceptual decisions in area MT. Nat. Neurosci. *8*, 99–106.
23. Britten, K.H., Newsome, W.T., Shadlen, M.N., Celebrini, S., and Movshon, J.A. (1996). A relationship between behavioral choice and the visual responses of neurons in macaque MT. Vis. Neurosci. *13*, 87–100.
24. Gu, Y., DeAngelis, G.C., and Angelaki, D.E. (2007). A functional link between area MSTd and heading perception based on vestibular signals. Nat. Neurosci. *10*, 1038–1047.
25. Reches, A., and Gutfreund, Y. (2008). Stimulus-specific adaptations in the gaze control system of the barn owl. J. Neurosci. *28*, 1523–1533.
26. Yucel, G., Petty, C., McCarthy, G., and Belger, A. (2005). Graded visual attention modulates brain responses evoked by task-irrelevant auditory pitch changes. J. Cogn. Neurosci. *17*, 1819–1828.
27. Yucel, G., Petty, C., McCarthy, G., and Belger, A. (2005). Visual task complexity modulates the brain's response to unattended auditory novelty. Neuroreport *16*, 1031–1036.
28. Sabri, M., Liebenthal, E., Waldron, E.J., Medler, D.A., and Binder, J.R. (2006). Attentional modulation in the detection of irrelevant deviance: a simultaneous ERP/fMRI study. J. Cogn. Neurosci. *18*, 689–700.
29. Sussman, E.S., Bregman, A.S., Wang, W.J., and Khan, F.J. (2005). Attentional modulation of electrophysiological activity in auditory cortex for unattended sounds within multistream auditory environments. Cogn. Affect. Behav. Neurosci. *5*, 93–110.
30. Mitchell, T.V., Morey, R.A., Inan, S., and Belger, A. (2005). Functional magnetic resonance imaging measure of automatic and controlled auditory processing. Neuroreport *16*, 457–461.
31. Muller-Gass, A., Stelmack, R.M., and Campbell, K.B. (2006). The effect of visual task difficulty and attentional direction on the detection of acoustic change as indexed by the Mismatch Negativity. Brain Res. *1078*, 112–130.
32. Doeller, C.F., Opitz, B., Mecklinger, A., Krick, C., Reith, W., and Schroger, E. (2003). Prefrontal cortex involvement in preattentive auditory deviance detection: neuroimaging and electrophysiological evidence. Neuroimage *20*, 1270–1282.
33. Wallis, J.D. (2007). Neuronal mechanisms in prefrontal cortex underlying adaptive choice behavior. Ann. N Y Acad. Sci. *1121*, 447–460.
34. Daffner, K.R., Scinto, L.F., Weitzman, A.M., Faust, R., Rentz, D.M., Budson, A.E., and Holcomb, P.J. (2003). Frontal and parietal components of a cerebral network mediating voluntary attention to novel events. J. Cogn. Neurosci. *15*, 294–313.
35. Matsumoto, M., Matsumoto, K., and Tanaka, K. (2007). Effects of novelty on activity of lateral and medial prefrontal neurons. Neurosci. Res. *57*, 268–276.
36. Schonwiesner, M., Novitski, N., Pakarinen, S., Carlson, S., Tervaniemi, M., and Naatanen, R. (2007). Heschl's gyrus, posterior superior temporal gyrus, and mid-ventrolateral prefrontal cortex have different roles in the detection of acoustic changes. J. Neurophysiol. *97*, 2075–2082.
37. Miller, E.K., Erickson, C.A., and Desimone, R. (1996). Neural mechanisms of visual working memory in prefrontal cortex of the macaque. J. Neurosci. *16*, 5154–5167.
38. Miller, C.T., and Cohen, Y.E. (In press). Vocalization Processing. In Primate Neuroethology, A. Ghazanfar and M.L. Platt, eds. (Oxford, UK: Oxford University Press).
39. Miller, E.K., and Cohen, J.D. (2001). An integrative theory of prefrontal cortex function. Annu. Rev. Neurosci. *24*, 167–202.
40. Johnston, K., and Everling, S. (2006). Neural activity in monkey prefrontal cortex is modulated by task context and behavioral instruction during delayed-match-to-sample and conditional prosaccade-antisaccade tasks. J. Cogn. Neurosci. *18*, 749–765.
41. Gold, J.I., and Shadlen, M.N. (2000). Representation of a perceptual decision in developing oculomotor commands. Nature *404*, 390–394.
42. Gold, J.I., and Shadlen, M.N. (2003). The influence of behavioral context on the representation of a perceptual decision in developing oculomotor commands. J. Neurosci. *23*, 632–651.
43. Schall, J.D. (2001). Neural basis of deciding, choosing, and acting. Nat. Rev. Neurosci. *2*, 33–42.
44. Kim, J.N., and Shadlen, M.N. (1999). Neural correlates of a decision in the dorsolateral prefrontal cortex of the macaque. Nat. Neurosci. *2*, 176–185.
45. Kawahara, H., Masuda-Katsuse, I., and de Cheveigne, A. (1999). Restructuring speech representations using a pitch-adaptive time-frequency smoothing and an instantaneous-frequency-based F0 extraction. Speech Commun. *27*, 187–199.
46. Grunewald, A., Bradley, D.C., and Andersen, R.A. (2002). Neural correlates of structure-from-motion perception in macaque V1 and MT. J. Neurosci. *22*, 6195–6207.
47. Romanski, L.M., and Goldman-Rakic, P.S. (2002). An auditory domain in primate prefrontal cortex. Nat. Neurosci. *5*, 15–16.