Deos the Bairn Not Raed Ervey Lteter by Istlef, but the Wrod as a Wlohe?

Kalanit Grill-Spector[1,*] and Nathan Witthoft[1]
[1]Department of Psychology and Neuroscience Institute, Stanford University, Stanford, CA 94305, USA
*Correspondence: kalanit@stanford.edu
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In this issue of *Neuron*, Glezer et al. find higher sensitivity to changes in real words than pseudowords in the left visual word form area (VWFA). Here we discuss the implications of their findings and the constraints they impose on neural coding in the lVWFA.

In the paper *Evidence for Highly Selective Neuronal Tuning to Whole Words in the "Visual Word Form Area,"* published in this issue of *Neuron*, Glezer and colleagues (Glezer et al., 2009) use an elegant manipulation to examine sensitivity to whole words in the left visual word form area (lVWFA). Using fMRI-A (Grill-Spector and Malach, 2001), they show that there is higher sensitivity to changes of a single letter in real words (RW, e.g., boat) than in pseudowords (PW, e.g., doat) that are pronounceable and have similar bigram frequency as real words. In the study, subjects were shown pairs of RWs or PWs that were either identical (e.g., "coat/coat"), varied by a single letter (e.g., "soat/poat"), or varied in all letters ("goat/fish") while performing an oddball orthographic task requiring finding an infrequently appearing sequence of letters. They found that the amplitude of response in the lVWFA was similar to pairs of different RWs and PWs and also was similarly reduced (i.e., adapted) to pairs of identical RWs and PWs. However, they found differences in the lVWFA's response to pairs of PW or RWs that differed in a single letter. For RWs, the lVWFA recovered from adaptation to the same level as for pairs of RWs that differed in all letters. In contrast, for PWs there was a gradual recovery from adaptation, in that responses for PW that differed in one letter were in-between the responses to identical PW pairs and PW pairs that differed in all letters. The authors supplement their region of interest analyses with a whole-brain analysis showing that these effects are largely restricted to the left occipitotemporal sulcus and that the results are not due to differences in semantic information across RWs changed by one

letter (as words that have related semantic information but different letters also cause a complete recovery of adaptation in the lVWFA). Thus, Glezer and colleagues interpret their findings as evidence for neurons tuned to whole words in the lVWFA.

In interpreting their data, the authors attempt to explain several phenomena: (1) the similar levels of responses in the lVWFA to pairs of completely different RWs or PWs, (2) the gradual recovery from adaptation for pairs of PWs changed by one letter as compared to pairs changed in all letters, and (3) the complete recovery from adaptation for pairs of RWs that differ in just one letter. They argue that their findings suggest that neurons in the lVWFA are sharply tuned to whole words, but also respond weakly to similar PWs. As a consequence, a RW produces a strong activation in a subset of neurons tuned to that specific word, whereas a PW produces a low activation across many neurons tuned to RWs that are similar to that PW. So for example, the word "firm" would strongly drive neurons tuned to that word, but not neurons tuned to words like "farm" or "form," even though they have highly similar orthography. At the same time, a pseudoword like "furm" or "ferm" would be expected to drive neurons tuned to all three of the real words, but weakly. In other words, the authors make two propositions: (1) the similar level of lVWFA responses to a RW or PW is an outcome of an aggregate of different response profiles across the neuronal population in a voxel: relatively few neurons that strongly respond to a specific RW or many neurons that respond to a lesser degree to a PW. And (2) that the tuning of these "word" neurons is different for RWs than PWs, meaning that they are sharply tuned to a RW, but not to a PW.

These results provoke several interesting questions. First, does their explanation of the putative neural tuning require additional mechanisms? As the authors indicate, fMRI measures the aggregate neural response across space (the voxel) and time (several seconds). Thus, any combinations of responses across time and space in a voxel that produce the same aggregate response cannot be distinguished with fMRI. Nevertheless, the proposition that tuning for RWs is sharper than PWs is a strong assumption and may not be necessary for explaining the present results. Prevailing models of neuronal response suggest that neurons respond to a stimulus as a function of the similarity between the neuron's optimal stimulus and the incoming stimulus. This predicts a similar level of response for "farm" and "furm" from a neuron tuned to "firm," as the level of response to a word is proportional to the number of overlapping letters appearing in the correct order between the word and the preferred word a neuron is tuned to. However, here "furm" drives the neuron, but "farm" does not, even though both have the same similarity to the optimal stimulus. An outstanding question is the mechanism that allows this change in response property to a RW and a PW to take place.

Another question is whether other models of neural responses can explain these results. One alternative model of the representation in the lVWFA is that neurons are tuned to actually occurring bigrams, trigrams, and quadragrams even though they may just be parts of words (Vinckier et al., 2007) (see Figure 1). Further, neural responses are driven by orthographic similarity. According to this scheme, both a RW and PW will generate a distributed response across multiple neural populations in a
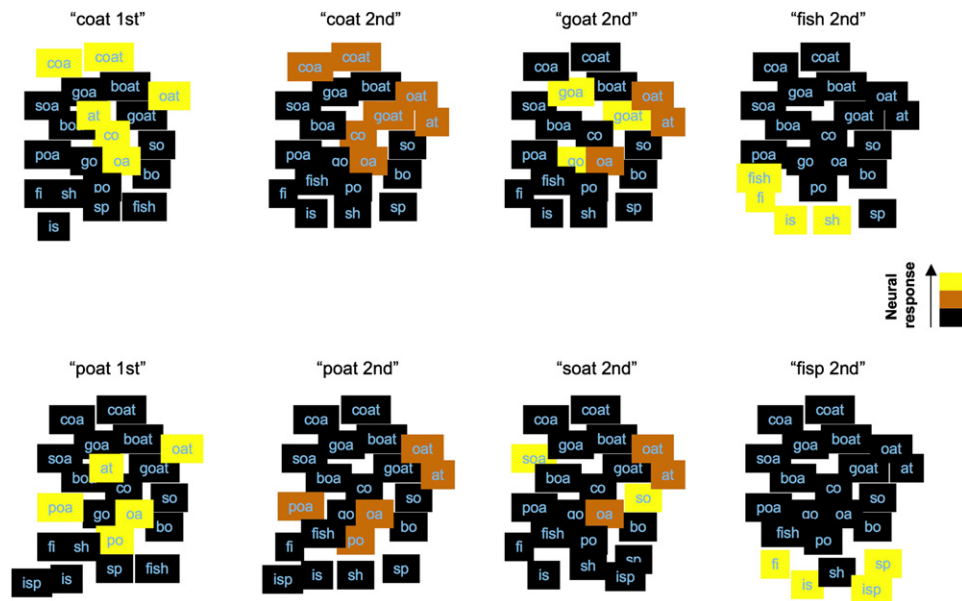
Figure 1. Toy Model of a Voxel Containing Neurons (Illustrated by the Boxes) that Respond to Bigrams, Trigrams, and Quadragrams
The top row illustrates putative responses to real words (RWs), and the bottom row illustrates responses to pseudowords (PWs). The neurons are colored by their response level, with black indicating no response, orange, low response (because of adaptation), and yellow, strong response (see color bar). In this toy model, the neuron will respond strongly if the exact letter string appears in the input word. A RW activates bigram, trigram, and quadragram neurons, while a PW activates only bigram and trigram neurons. The voxel's response is the aggregate response over all its neurons' responses across the first and second words in a trial. The first word (left) in each row illustrates the first word in a trial. The other panels illustrate different second words in a trial, according to the trial types in the experiment. When the second word is identical to the first, there is maximal adaptation and lowest signal. Note that when one letter is changed for the RW there is a higher signal than for the PW because there are neurons tuned to quadragrams of the RW, but not the PW. An outstanding question for this type of model is whether the response to a second real word that differs in one letter from the first one is different from or similar to the response to a second word that differs in all letters (two rightmost columns, top row).

voxel. When showing pairs of identical RWs or PWs, the same neural population will be activated by the first and the second word in a pair. Thus, there will be maximal adaptation. However, when changing a single letter, this model predicts differential profiles of recovery from adaptation for RW and PW pairs. For the RWs, the second word in a pair will strongly activate another subset of bigrams, trigrams, and quadragrams, but there is no quadragram that the second PW will activate maximally, yielding a lower overall response. Thus, this alternative suggests that the partial recovery from adaptation for a PW is not due to broader neural tuning to PWs than RWs, but due to lesser overlap between the PW and any other quadragram. However, this alternate model predicts lower signals (or some adaptation) for RW pairs that change in one letter compared to RW pairs that change in all letters (because there is lesser overlap between the first and second words in the latter case). Whether or not this is the case depends on several factors, including the relative level of response to an optimal stimulus compared to a nonoptimal stim-

ulus, and the number of neurons coding specific actually occurring orthographic sequences within a voxel (e.g., there may be more neurons in a voxel responding to "goat/goa/go" than "fish/is/sh," etc.). Note, however, that the authors attempt to control these factors by matching the bigram frequencies across PWs and RWs.

Finally, suppose the representation is of whole words—does the IVWFA code the letters in the word and their ordering or word shape? Behavioral studies of reading indicate that letter information, word shape, and semantic information independently contribute to reading speed, with letter information explaining about 62% of the variance in reading speed and word shape explaining about 16% of the variance (Pelli and Tillman, 2007). Thus, changing the letters in a word preserving its shape (e.g., changing "this" to "tbis") impedes reading more than changing the word shape (changing "this" to "tHis"). Previous fMRI-A studies showed that the IVWFA is insensitive to case or font (Dehaene et al., 2004, 2005). However, to our knowledge, no study has examined adaptation effects to word shape or compared the effects of

word shape and letter on the IVWFA's responses. It would be interesting to compare sensitivity to word shape and letter information, as behavioral data indicate higher sensitivity to the latter.

In sum, Glezer and colleagues present an intriguing finding and an interesting interpretation of word representation in the IVWFA. Future experiments will be informative for constraining the space of interpretations.

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