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Duality of Function: Activation for Meaningless Nonwords and Semantic Codes in the Same Brain Areas

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Abstract

Studies of the neural substrates of semantic (word meaning) processing have typically focused on semantic manipulations, with less consideration for potential differences in difficulty across conditions. While the idea that particular brain regions can support multiple functions is widely accepted, studies of specific cognitive domains rarely test for co-location with other functions. Here we start with standard univariate analyses comparing words to meaningless nonwords, replicating our recent finding that this contrast can activate task-positive regions for words, and default-mode regions in the putative semantic network for nonwords, pointing to difficulty effects. Critically, this was followed up with a multivariate analysis to test whether the same areas activated for meaningless nonwords contained semantic information sufficient to distinguish high- from low-imageability words. Indeed, this classification was performed reliably better than chance at 75% accuracy. This is compatible with two non-exclusive interpretations. Numerous areas in the default-mode network are task-negative in the sense of activating for less demanding conditions, and the same areas contain information supporting semantic cognition. Therefore, while areas of the default mode network have been hypothesized to support semantic cognition, we offer evidence that these areas can respond to both domain-general difficulty effects, and to specific aspects of semantics.

Key words: difficulty effects, fMRI, MVP, reading, word recognition

Introduction

The question of how we derive meaning from symbols such as print has been a persistent source of fascination for millennia. Relatively recent methods for examining how the brain works to achieve this, particularly in the domain of functional neuroimaging, have yielded major advances. For example, we now know which brain areas are associated with semantic processing across multiple functional neuroimaging studies (Vigneau et al. 2006; Binder et al. 2009; Visser et al. 2010; Wang et al. 2010). But we also know that differences in task difficulty can

influence results that depend on contrasting different task conditions. Indeed, a recent study demonstrated a new level of influence of task difficulty effects, where differences in task difficulty led to a reversal of the typical pattern of activation for contrasting meaningful words and meaningless nonwords (Graves et al. 2017). Areas that typically respond to semantic information were found to activate more for meaningless nonwords than meaningful words. Such a result would presumably only be found if the putative semantic areas were responding to differences in difficulty between the contrasted conditions.

Here we sought to test whether areas responding to difficulty might also contain semantic representations. Specifically, we wanted to know whether areas that activate for meaningless nonwords compared to meaningful words might also be coding semantic information. If this were the case, it would be a direct demonstration of how domain-general difficulty effects can co-localize with domain-specific semantic representations. This distinction is important for interpreting what functions are being localized. Domain-general effects cut across domain-specific functions such as reading, mathematics, object naming, and recognition. So rather than being specific to a particular information or application domain, domain-general effects occur when one condition demands more cognitive resources than another. Indeed, the function of particular neural systems is often characterized as relating to either domain-general effects, or more domain-specific processes such as those associated with linguistic input (Blank and Fedorenko 2017). Here we test the conditions under which both of these effects may occur in the same neural systems in the same experiment, thereby offering a clear demonstration of the circumstances under which a particular set of brain regions may show duality of function.

In the experiment detailed below, the words are manipulated in terms of a semantic factor, imageability. These meaningful words are first compared to nonwords through a standard mass-univariate analysis, and then the presence of information for distinguishing high and low levels of imageability is tested using pattern-based analysis. In general, the motivation for using both univariate and multivariate analyses is that they may be sensitive to different aspects of word recognition (Cox et al. 2015). Univariate analysis is sensitive to overall differences in mean activation between conditions, as would likely occur with differences in overall difficulty between conditions such as identifying words and nonwords. Multivariate analysis, on the other hand, is sensitive to differences in distributed patterns of representation (Jimura and Poldrack 2012), as is expected to occur with differences in semantic factors such as imageability (Wang et al. 2013).

Imageability is the degree to which a word calls to mind sensory impressions. It has been widely used as a way to operationalize the distinction between abstract and concrete words. Abstract words tend to be of low imageability and contain relatively few semantic features, while concrete words are generally of high imageability and contain relatively more semantic features (Paivio 1991; Plaut and Shallice 1993). A number of groups have used this distinction to investigate the neural basis of semantics (Mellet et al. 1998; Kiehl et al. 1999; Jessen et al. 2000; Pexman et al. 2007b; Wang et al. 2010), including Binder et al. (2005), who made two bridging assumptions. One is that the verbal or language system on which low-imageability words are thought to rely is represented by most typical right handers within the left hemisphere. The other is that the sensory-based system engaged by high-imageability words can be represented in both hemispheres. Therefore, neural processing of low-imageability words should be primarily left-lateralized, while high-imageability words could take advantage of both hemispheres. Indeed, this is what Binder et al. (2005) found.

A possible confound, however, is that low-imageability words typically take longer to respond to than high-imageability words. This raises the possibility that the contrast between these word types was being driven by performance differences rather than, or in addition to, differences in semantic content. Indeed, in the same study, areas where activation correlated with longer

response time (RT) were largely the same as areas activated for low-imageability words, which was the condition involving longer RT (Binder et al. 2005). To attempt to find areas reliably activated across many studies for semantic processing, a large-scale meta-analysis was performed (Binder et al. 2009). Also included were studies that used a more general contrast of words compared to meaningless but pronounceable nonwords, called pseudowords. The rationale for including that contrast was that words and pseudowords share valid form information (orthography for written strings, phonology for written and spoken forms), but only the words have meaning. The meta-analysis also attempted to account for potential performance differences across conditions by only including studies that addressed such differences. The result was a set of areas associated with a strongly semantic condition (such as words or concrete/high-imageability words) compared to a weakly (or no) semantic condition (such as pseudowords or abstract/low-imageability words). This contrast revealed a set of areas largely similar to those activated previously for high-imageability words, including the angular gyrus (AG), a large swathe of middle temporal gyrus (MTG), dorsal prefrontal cortex, posterior cingulate/precuneus (PC), and parahippocampal gyrus (Binder et al. 2005). A subset of these areas in the AG, posterior MTG, and PC were also specifically associated with concrete words in another meta-analysis that focused on the concrete-abstract word distinction (Wang et al. 2010). Such consistency of putative semantic effects across numerous studies was taken as strong evidence for involvement of these areas in semantic processing.

Recently, we attempted to replicate the Binder et al. (2009) meta-analysis finding in a single study (Graves et al. 2017). It included two semantic contrasts that were well-represented in that meta-analysis: words – pseudowords (lexicality contrast), and high – low imageability words (imageability contrast). Following Binder et al. (2005), we operationalized concreteness/abstractness in terms of imageability. The imageability contrast partially replicated the standard result by showing activation for high-imageability words in the PC. The lexicality contrast, however, yielded a surprising result in that words activated the left inferior frontal junction (IFJ, an area at the intersection of the inferior frontal and precentral sulci) and supplementary motor area (SMA), areas overlapping the task-positive network (TPN; Fox et al. 2005). The TPN, similar to the multiple-demand network, is a set of brain areas that activates for resource-demanding tasks compared to less demanding conditions such as rest (Duncan 2010; Raichle 2015). Pseudowords, on the other hand, activated AG, anterior temporal lobe (ATL), ventromedial prefrontal cortex, and PC. These areas overlap the default-mode network (DMN, a set of areas that is negatively correlated with the TPN; Buckner et al. 2008; Raichle 2015) and are putative semantic areas (Binder et al. 1999, 2009). The participants in that study also showed poorer performance, in terms of RT and accuracy, on the words than pseudowords (pronounceable but meaningless letter strings). This suggests that the unexpected activation of the TPN for words and DMN for pseudowords reflected differences in difficulty rather than semantic content (Graves et al. 2017). A major implication of this result is that activation in DMN areas for words that had been interpreted as reflecting semantic processing might instead reflect difficulty effects. Or, if these areas respond to both difficulty and semantics, how could this be?

The current study addresses this question by examining how areas within the DMN that are key elements in the putative semantic network might show two very different types of responses: Activating for meaningless nonwords and

representing information for decoding words along a semantic dimension (in this case, high/low imageability). While there is much discussion of the brain carrying out multiple different kinds of processes in the same areas, there has been little direct demonstration of this (Price and Friston 2005; Poldrack 2010). The current study aims to help fill that gap.

Materials and Methods

Participants

Participants for functional magnetic resonance imaging (fMRI) were recruited from the Rutgers University-Newark community. Interested participants were initially asked to complete an online survey to determine eligibility. Right-handed native English speakers who reported no history of traumatic brain injury, psychiatric illness, recreational drug use, or claustrophobia were recruited from the database. Our sample consisted of 20 participants, 13 female, with an average age of 23.7 years ($SD = 3.8$). The Wechsler Test of Adult Intelligence (WTAR; Wechsler 2001) was administered to estimate verbal intelligence. Participants had a mean scaled WTAR score of 112.7 ($SD = 10.2$), where the population average is 100.

Stimuli

For the lexical decision task performed in the scanner, stimuli consisted of 180 words and 180 nonwords pronounceable in English. The words were of either high or low imageability and high or low meaning relatedness. The meaning relatedness manipulation showed minimal results. It was also not a focus of the current report and so will not be discussed further, except where necessary to clarify the details of the methods.

Imageability ratings were obtained from a compilation of 6 databases (Paivio et al. 1968; Toggia and Battig 1978; Gilhooly and Logie 1980; Bird et al. 2001; Clark and Paivio 2004; Cortese and Fugett 2004). Words were separated into high and low imageability by selecting those rated at the top and bottom 40% for imageability. The following additional measures known to affect lexical processing were collected: estimated word frequency (\log_{10} of the number of contexts in which each word stimulus occurs) from the SUBTLEX-US database (Brysbaert and New 2009), length in letters, 4 measures from CLEARPOND: average bigram (two-letter combination) and biphone (two-phoneme combination) frequencies, orthographic and phonological neighborhoods (Marian et al. 2012), number of meanings from WordMine2 (Durda and Buchanan 2006), and relatedness among those meanings (e.g., “show” has high relatedness, “bark” has low relatedness) from 3 sources (Durkin and Manning 1989; Azuma 1996; Azuma and Van Orden 1997). Stimuli selection procedures continued until high and low imageability words did not reliably differ (pairwise t -tests of $P > 0.05$) on these factors, resulting in 90 high- and 90 low-imageability words.

Nonword foils were also included, as necessary for the lexical decision task. They were of two types: Meaningless, pronounceable nonwords (pseudowords), and pseudohomophones (letter strings like “karv” that are not words but would sound like words if read aloud). The pseudoword/pseudohomophone distinction is not relevant to the analyses conducted here, and because there were also no reliable differences in accuracy and response times (RT) between these nonword types, we will refer to them collectively as “nonwords” for the remainder of the report. All nonwords were generated to consist of valid English trigrams using the ARC Nonword Database (Rastle et al. 2002). The nonword foils

were matched with words on length in letters, orthographic neighborhood, and bigram frequency.

Scan Session and Performance

Stimulus delivery was controlled and response times (RT) recorded using PsychoPy software (Peirce 2007). Words and nonword foils were displayed for 500 ms, separated by random inter-trial intervals ($M = 3432$ ms, $SD = 234$ ms) marked by a fixation cross. Participants were instructed to press a button as quickly and accurately as possible to indicate whether the target was a word or nonword. RT was calculated as the time from stimulus onset to initiation of the button press response, in milliseconds. Button presses were counterbalanced across participants to account for possible advantages or neural differences associated with a right versus left button press. A one-minute practice round was provided for participants to become accustomed to the appropriate response for words versus nonwords.

Stimulus schedules were generated and simulation tested for optimized detection power of planned contrasts according to a mixed event-related block design. Blocks contained 18 trials, with 9 words and 9 nonwords. Each block contained either high or low imageability words randomly intermixed with an equal number of nonwords, and each run consisted of 4 blocks. The event-related aspect of the design allowed for analyzing any trials with incorrect responses separately from those with correct responses. The blocked aspect of the design was optimized for multivariate pattern analysis (MVPA), as described below. Response accuracy and RT were analyzed with t -tests to test for differences in mean accuracy between high compared to low imageability words, and words compared to nonwords.

Image Acquisition and Analysis

Data were collected on a 3-T Siemens Magnetom TrioTim Scanner with a 12 channel head coil. A T1 high-resolution anatomical brain scan was collected for each subject, using a gradient echo sequence, with a TR of 1900 ms and a TE of 2.52 ms (matrix = 256×256 voxels, 176 contiguous 1 mm axial slices, field of view, FOV = 256 mm, flip angle = 9). Five runs of Blood Oxygen Level Dependent (BOLD) data were collected using a gradient-echo echoplanar imaging (EPI) sequence (TR = 2000 ms, TE = 25 ms, FOV = 208 mm, matrix = 64×64 , flip angle = 77). One hundred twenty six whole brain volumes ($3.25 \times 3.25 \times 3.00$ mm voxels), each consisting of 35 axial slices, were obtained for each run.

All images were preprocessed using the AFNI software suite (<http://afni.nimh.nih.gov/afni>; Cox 1996). For each participant, the first 6 images in each run were ignored due to initial saturation. Slice timing and motion correction were applied to the images. Additional noise covariates from the 6 motion parameters calculated during motion correction and the signal in the ventricles were entered as regressors of no interest. Regressors of interest were included for each word condition paired with each type of nonword, with Imageability, Relatedness, and Nonword background type (pseudoword, PW, or pseudohomophone, PH) as factors, using the AFNI program 3dDeconvolve. RT was included as a mean-centered regressor for each participant, and only correct trials were included in the main analysis. Trials with erroneous responses (wrong button pressed, no response, or RT more than 3 SDs from the mean) were modeled separately. The group analysis was subsequently conducted

with each individual's images for each condition. These images were spatially transformed to a standard reference space (Talairach and Tournoux 1988) using the AFNI script, @auto_tlrc, and smoothed using a 6 mm FWHM kernel. A brain mask excluding most white matter and cerebrospinal fluid was applied to all contrast images. A voxelwise threshold of $P < 0.01$, with a cluster correction of 805 μL (mapwise corrected $P < 0.05$), as determined by Monte Carlo simulation implemented in the AFNI program 3dClustSim, was used for all contrasts.

Next we used MVPA to test for possible representation of semantic information in areas activated by nonwords. To do this, we started with a set of areas from our previous study that, compared to the current study, showed very similar activation of DMN areas for nonwords (cf. cool colors in Fig. 1 with Fig. 2A, a binarized version of nonword activations from Graves et al. 2017, their Fig. 1A). The search space was restricted to the left hemisphere because the neural areas associated with semantic processing for words are generally larger on the left (Binder et al. 2009). Because this mask was based on areas of significant fMRI activation, it includes primarily gray matter, as shown in Figure 2A. No additional measures were taken to exclude white matter and cerebrospinal fluid. The timecourse for word event trials was extracted from these areas. Defining these based on an independent dataset avoids the possibility of logical circularity or "double-dipping" (Kriegeskorte et al. 2009). The impulse responses for the word stimuli were estimated by deconvolving the BOLD time series data using least-squares sum estimation (Mumford et al. 2012), as implemented in the AFNI program 3dLSS. This yielded a set of independent event impulse estimates for each participant. These events were placed in the same order for each participant, spatially transformed to atlas space as described above, and averaged to produce a mean participant dataset for use with MVPA.

A Gaussian Naïve Bayes (GNB) classifier, implemented in the PyMVPA software suite (Hanke et al. 2009), was trained using 6-fold leave-one-run-out cross-validation to determine whether participants were reading high or low imageability words. A mean accuracy rate of 75% was found to be reliable at $P < 0.05$. Significance was determined by comparison with a Monte Carlo simulation-derived null distribution on our data. We also sought to determine which areas within the mask were contributing most to classification accuracy by performing a searchlight analysis with a 3 mm radius, using the same GNB classifier as above. To mitigate the potential for false positives that arises from multiple comparisons across the 2405 voxels

in the mask, searchlight results were thresholded at 98% accuracy. While more principled approaches to correcting for multiple comparisons exist that derive an empirical null distribution for each searchlight (Stelzer et al. 2013), the current approach is computationally tractable and gives a descriptive sense of which voxels within the mask are contributing most to the classification. To check the specificity of results, we performed a second MVPA analysis using a different brain area mask. This mask was generated from the same prior study, but was based on areas activated for words compared to nonwords (Supplementary Fig. S2), which generally corresponded to TPN areas. These areas were also tested for the ability to classify words based on imageability.

Results

Behavioral Results

Behavioral data were first analyzed in terms of response times (RT). Words were recognized more quickly than nonwords. The mean RT for words was 698 ms, while the mean RT for nonwords (averaged across pseudowords and pseudohomophones) was 827 ms (item-wise $t = 27.5$, $P < 0.001$). There was no reliable difference between pseudowords (825 ms) and pseudohomophones (830 ms, item-wise $t = 0.7$, $P > 0.1$). There was also no reliable difference between words of high and low imageability. Both had a mean RT of 698 ms. There was also no main effect of nonword background on word recognition. Specifically, RT for words within blocks of pseudoword foils (696 ms) were not responded to significantly differently from words within blocks of pseudohomophone foils (700 ms, item-wise $t = 0.7$, $P > 0.1$).

Analyses of response accuracy data yielded broadly similar patterns to those above for RT data. Words were responded to significantly more accurately (97.1%) than nonwords (90.6%, item-wise $t = 11.5$, $P < 0.001$). No reliable differences emerged between pseudowords (90.5%) and pseudohomophones (90.6%, item-wise $t = 0.1$, $P > 0.1$), nor between words of high (97.2%) and low (96.9%) imageability (item-wise $t = 0.6$, $P > 0.1$). There was also no main effect of nonword background on word recognition accuracy. That is, words within blocks of pseudoword foils (97.2%) were not responded to significantly differently from words within blocks of pseudohomophone foils (96.9%, item-wise $t = 0.4$, $P > 0.1$).

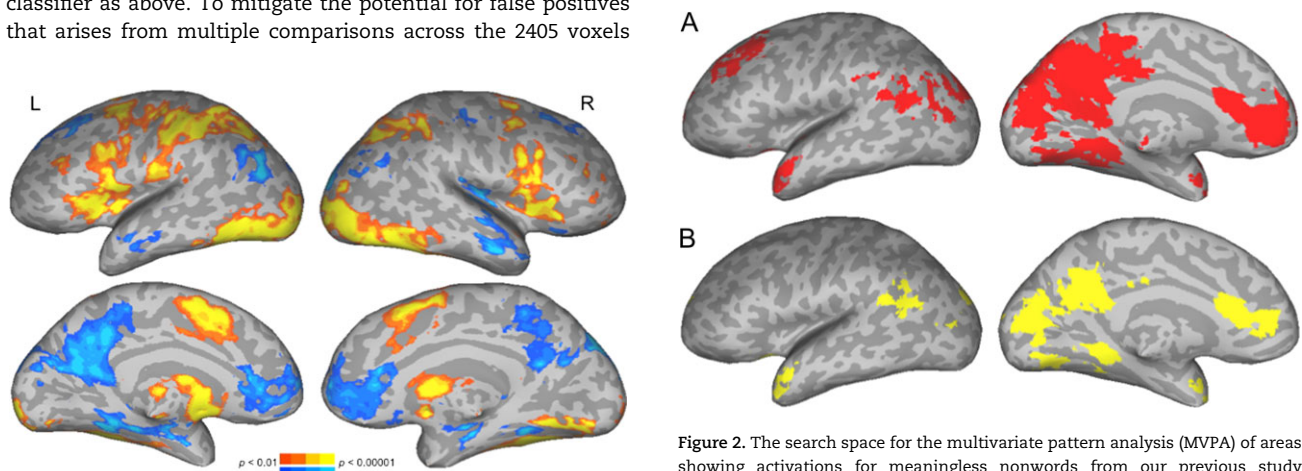


Figure 1. Direct contrast of words (warm colors) with nonwords (cool colors). Significant group activations are projected onto cortical surfaces in Talairach space. Lateral views are in the upper row, medial views in the lower row.

Figure 2. The search space for the multivariate pattern analysis (MVPA) of areas showing activations for meaningless nonwords from our previous study (Graves et al. 2017) is shown in the upper row (A). Areas within the search space contributing to the significant classification of words into high or low imageability at greater than or equal to 98% accuracy are shown in yellow in the lower panel (B).

Imaging Results

To test for overall differences between meaningful words compared to nonwords (pseudohomophones and pseudowords), we performed a direct contrast of words (warm colors in Fig. 1) to nonwords (cool colors in Fig. 1). The pseudoword and pseudohomophone conditions were collapsed into a single nonword condition because no activation differences were seen for blocks of words intermixed with pseudohomophone foils, compared to blocks of words intermixed with pseudoword foils. Also, a direct contrast of pseudohomophones and pseudowords yielded minimal activations for pseudohomophones only, in the right inferior frontal gyrus (Supplemental Fig. S1). For the word–nonword contrast, words activated the left inferior frontal gyrus and inferior frontal junction, precentral and postcentral gyri, intraparietal sulcus, ventral occipito-temporal and lateral occipital cortices, along with a similar but more spatially restricted set of areas on the right (warm colors in Fig. 1). Nonwords activated the bilateral anterior temporal lobe, angular gyrus, dorso-medial and ventro-medial prefrontal cortices, and posterior cingulate/precuneus (cool colors in Fig. 1). Coordinates for maximum activations shown in Figure 1 are provided in the Supplemental Materials (Table S1).

In terms of previously described networks, words activated regions largely overlapping the TPN, while nonwords activated regions largely overlapping the DMN. While these results are generally consistent with four previous studies (Fiebach et al. 2002; Bedny and Thompson-Schill 2006; Westbury et al. 2016; Graves et al. 2017), they run counter to many other previous studies that have directly contrasted words and nonwords (Démonet et al. 1992; Cappa et al. 1998; Henson et al. 2002; Binder et al. 2003, 2005; Mechelli et al. 2003; Rissman et al. 2003; Ischebeck et al. 2004; Kuchinke et al. 2005; Xiao et al. 2005; Orfanidou et al. 2006). Those previous studies generally showed words activating components of the DMN and nonwords activating components of the TPN. Because words and nonwords generally share form but only the words have meaning, those previous results led to the interpretation that a major function of the DMN may be semantic processing. On the face of it, our current results seem inconsistent with a semantic interpretation for the DMN, since it is the less meaningful nonwords that activated DMN areas. An alternate possibility is that semantic information is represented in DMN areas, but an imbalance in the level of difficulty between words and nonwords is leading to activation for words in TPN areas.

To test for the presence of semantic information in the DMN areas that are essentially identical to putative semantic areas, we performed an MVPA analysis on the activation timecourse for word events as described in the Methods section above. Note that these areas (Fig. 2A) showed activation for meaningless nonwords compared to words, where words were determined to be the more difficult condition based on performance data (Graves et al. 2017). High and low imageability words were distinguished with 75% accuracy (reliable at $P < 0.05$ by Monte Carlo simulation). To determine if some voxels contributed more than others to this classification, we performed a searchlight analysis using the same GNB classifier and training regime as above to map which voxels were showing the highest (98% or greater) classification accuracies. This revealed a large subset of areas distributed throughout the original mask, including from the ATL, AG, VMPFC, parahippocampal gyrus, PC, and cuneus (Fig. 2B).

To test the alternate possibility that this imageability classification result could have been obtained from TPN areas not

typically associated with semantic processing, we also trained the classifier to distinguish high from low imageability words using activation timecourses for words in TPN areas (shown in Supplementary Fig. S2). The areas were defined based on activations for words relative to nonwords from a previous study (Graves et al. 2017), and restricted to the left hemisphere to be comparable with the previous MVPA analysis for nonword-activated areas described above. This did not yield better than chance classification accuracy (58%, $P > 0.1$).

Discussion

This study examined the question of whether domain-specific processing of semantic information and domain-general difficulty effects can co-locate in the same set of brain areas. While such co-location has been assumed to occur (Price and Friston 2005; Poldrack 2010), direct demonstration of domain-specific effects of semantic processing in areas showing domain-general effects of difficulty has been scarce. We defined search spaces for MVPA based on our previous study showing that contrasting words with nonwords can yield activation for words in TPN areas and nonwords in DMN areas typically associated with processing meaningful letter strings (Binder et al. 2009; McNorgan et al. 2015). Essentially the same pattern of activation occurred in our current study, showing consistent results of univariate word–nonword contrasts across two independent data sets. Multivariate decoding of words along the semantic dimension of high/low imageability was successful for DMN but not TPN areas. This shows that DMN areas activated for nonwords relative to words can also contain semantic information, thereby demonstrating how effects of domain-general difficulty and domain-specific semantics can co-localize in the same set of brain areas.

In terms of difficulty effects, we should note that nonwords were more difficult than words in the current dataset, in that nonwords were associated with longer RT and lower accuracy than words. However, words were the more difficult condition in our previous (Graves et al. 2017) dataset, and again the results of the word–nonword contrast were essentially identical across the two studies. It is on this basis that we interpret nonword activation in the DMN/putative semantic areas as reflecting difficulty effects. The imageability classification, on the other hand, is unlikely to be related to difficulty effects, as performance was not different between high and low imageability words. Therefore, classification of words as being of high or low imageability should depend on semantic information, consistent with established cognitive and computational models (Paivio 1991; Plaut and Shallice 1993; Harm and Seidenberg 2004).

Regarding the lack of performance differences between levels of word imageability, this helps with interpretation of the fMRI results by removing the possible confound of performance differences. Other studies, however, have reported performance differences, with lexical decisions to high imageability words generally being faster than for low imageability words (Paivio 1991; Balota et al. 2004; Yap et al. 2012; Westbury et al. 2013). We think the lack of a performance effect for imageability in the current study comes from how we selected the word stimuli. High and low imageability words did not differ in two other semantic factors: Number of meanings and relatedness among those meanings. Although we are aware of no other studies that have controlled for both of these variables across levels of imageability, there is suggestive evidence that controlling for other semantic factors

can reduce the effect of imageability. Variance in lexical decision performance specifically attributable to imageability has been shown to attenuate with the addition of other semantic variables such as measures of affect and contextual co-occurrence (Westbury et al. 2013, 2016). Controlling for two other semantic variables may have attenuated effects of imageability on lexical decision performance in the current study as well.

We have also sought to better understand the neural basis of semantics by breaking it into its components, rather than treating it in a monolithic way. This was our original intention in manipulating both imageability and lexical semantic ambiguity (meaning relatedness) for our stimuli. However, as noted above, this additional manipulation produced largely negative results. In future work we hope to explore the neural basis of other promising semantic measures, like semantic diversity or semantic richness (Pexman et al. 2007a, 2008; Yap et al. 2011), possibly contrasting effects of these variables with effects of imageability, analogous to Westbury et al. (2016). Indeed, as Westbury et al. (2016) point out, semantics is likely to be a multi-component rather than monolithic construct, and the influence of uncontrolled aspects of semantics may account for inconsistencies across studies examining the neural basis of imageability effects. For example, many studies have shown activation for high greater than low imageability words in the bilateral AG and PC (Jessen et al. 2000; Binder et al. 2005; Sabsevitz et al. 2005; Graves et al. 2010; Lin et al. 2017). Others, however, have shown bilateral PC but not AG (Graves et al. 2017), left but not right hemisphere AG (Mellet et al. 1998; Wang et al. 2010; Westbury et al. 2016), or results in entirely different areas (Kiehl et al. 1999; Pexman et al. 2007b; Hauk et al. 2008). In addition to possibly uncontrolled aspects of semantics, another potential explanation for these inconsistencies across studies is that differences in difficulty and semantic content across conditions may be independently modulating many of the same brain areas.

Comparing Univariate and Multivariate Results

The univariate General Linear Model contrast between words and nonwords yielded results that were different from most previous fMRI results for this contrast (McNorgan et al. 2015). They were, however, so similar as to effectively replicate the results of this contrast from our previous study (Graves et al. 2017). Words activated largely TPN areas, while nonwords activated DMN areas. We then used a multivariate approach to determine that the areas activated for nonwords were also encoding semantic information. This raises the question, how could areas showing more activation for nonwords than words be encoding levels of imageability that are only defined for words? Our results suggest that the word–nonword contrast was dominated by differences in difficulty between the two types of stimuli, while DMN areas are indeed coding information more specifically relevant to words, in this case semantic information about their imageability.

In terms of the possible relationship between imageability and lexicality (word–nonword) effects, studies that do find a behavioral difference between levels of imageability typically find faster RTs for high imageability words, as noted above. Neural effects of high imageability words, when directly contrasted with low imageability words, often occur in the same areas as for nonwords, such as the AG and PC, that we have reported recently (Graves et al. 2017) and in the current study. This leads to the question of what the imageability distinction and nonword processing might have in common. While we do

not yet have definitive answers, one possibility is the generation of a stop signal for searching through a hypothetical semantic space, assuming the task is structured in such a way that information from semantic space is being used to make lexical decisions (for an example of an implemented computational model of lexical decisions based on traversal of semantic space, see Rodd et al. 2004). When comparing, for example, a low imageability word like “rate” with a nonword like “jate”, rate might have been encountered in sufficient contexts to seem generally familiar, even if it does not evoke the kind of sensory recall that aids recognition of high imageability words like “rose”. Such a low imageability word could elicit a more extended search of semantic space compared to a nonword that could be more readily identified as unfamiliar. This would be consistent with activation in the TPN reflecting active task engagement, and activation in the DMN corresponding to less task engagement, suggesting that difficulty differences between words and nonwords and imageability effects may be two aspects of the same underlying process.

Another possibility is that this model-inspired description of searching semantic space may apply to the DMN but not TPN. To falsify this possibility, difficulty effects and semantic effects would need to be so related as to be indistinguishable, so that DMN areas activated for nonwords in the lexicality contrast and TPN areas activated for words should both contain information sufficient to distinguish high from low imageability words. This was not the pattern seen in our data. Instead, only DMN areas were found to contain information sufficient to classify words based on imageability. We did not directly contrast the classification accuracies between the DMN and TPN areas, so discussion of the specificity of the DMN classification result is descriptive rather than statistical. Yet it is the case that DMN areas contained information for reliably classifying words based on imageability, while TPN areas did not. To summarize, the overall pattern suggests contrasting words with nonwords is susceptible to the influence of even small differences in difficulty between conditions. While this can lead to activation for meaningless nonwords in areas of the DMN that are often associated with semantic processing, the ability to use information in these same areas to classify words in terms of a semantic variable suggests that effects of difficulty and semantics co-localize particularly in areas of the default mode network.

Implications for Functional Networks

Relatively early work focusing on network-level analyses of brain function suggested that cortical function might largely be separated into two anticorrelated TPN and DMN networks (Fox et al. 2005; Raichle 2015). Subsequent work suggests the TPN may be divided into at least two functional networks. One is the frontoparietal control network (Dosenbach et al. 2007; Spreng et al. 2010). The exact definition of the other is less clear, but has been variously referred to as the salience network (Seeley et al. 2007; Uddin 2015; Shine et al. 2017), or the dorsal attention network (Spreng et al. 2010; Power and Petersen 2013; Ihnen et al. 2015). Our results show activation for words relative to nonwords in a set of areas that spans both the frontoparietal and salience/dorsal attention networks. Essentially the same set of regions has been shown to have functional coherence, with increasing activation associated with increasing domain-general processing demands, leading to its description as the multiple-demand network (Duncan 2010). Thus, while there is evidence for the existence of multiple functional networks

within the TPN, characterization of the TPN network as a set of multiple-demand regions distinct from the DMN appears to be the most useful level of description for the current results. There is also a great deal of speculation about the possible functional roles of the DMN. These include monitoring of internal states, declarative memory recall, mind wandering, and semantics (Buckner et al. 2008; Binder et al. 2009; Andrews-Hanna et al. 2010; Raichle 2015). To be clear, we are not suggesting that all brain function is divided into two discrete networks that trade off depending on task difficulty. Rather, we suggest that in these two lexical conditions, the DMN and TPN networks temporarily organize to handle differences in task difficulty across the conditions being compared. At the same time, because networks of brain areas are presumably optimized for representing particular kinds of information, we propose that such representations are maintained in parallel with any co-occurring effects of task difficulty.

Conclusion

As the field of cognitive neuroscience moves from its initial focus on strict localization of function toward a more network-focused approach to understanding structure–function relationships in the brain, one consistent assumption has been that multiple functions can occupy the same brain areas. Direct evidence for this, however, has been relatively scarce. Here we have demonstrated how domain-general effects of task difficulty can co-localize with domain-specific representations for semantics. One possible implication for future studies is that interventions targeting domain-specific or domain-general function could in principle focus on the same brain areas.

Supplementary Material

Supplementary material is available at *Cerebral Cortex* online.

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Notes

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