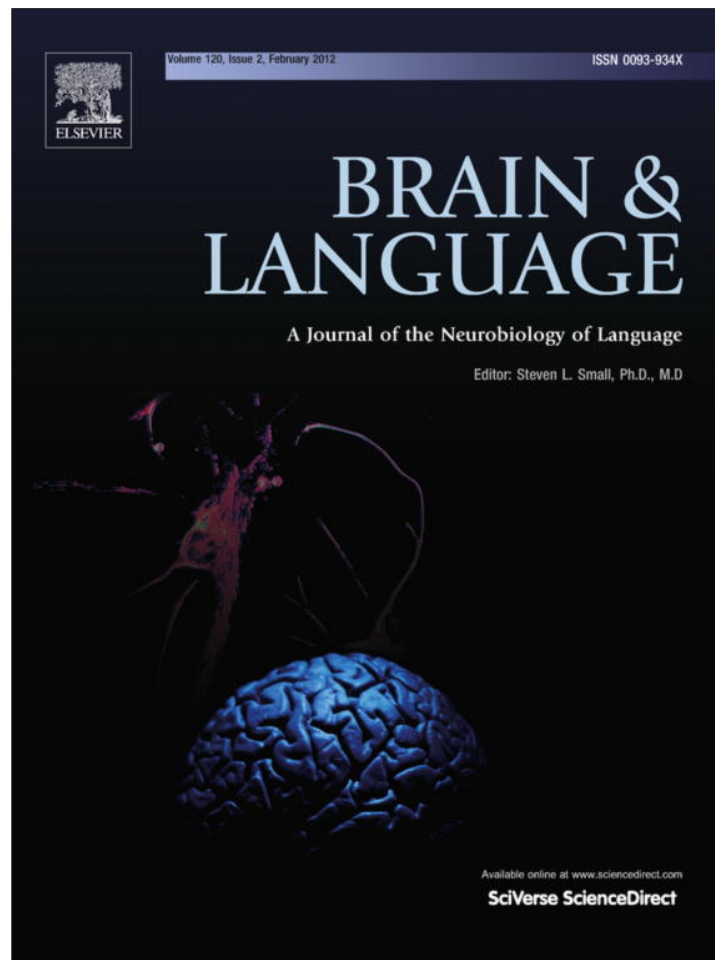


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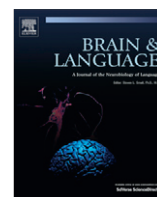
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Syntactic processing in the human brain: What we know, what we don't know, and a suggestion for how to proceed

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ABSTRACT

For every claim in the neuroimaging literature about a particular brain region supporting syntactic processing, there exist other claims implicating the target region in different linguistic processes, and, in many cases, in non-linguistic cognitive processes (e.g., Blumstein, 2009). We argue that traditional group analysis methods in neuroimaging may obscure functional specificity because of inter-subject anatomical variability (Fedorenko & Kanwisher, 2009). In Fedorenko, Hsieh, Nieto-Castanon, Whitfield-Gabrieli, and Kanwisher (2010) we presented a functional localizer that allows quick and reliable identification of key language-sensitive regions in each individual brain. This approach enables pooling data from corresponding functional regions across subjects rather than from the same locations in stereotaxic space that may differ functionally due to inter-subject anatomical variability. In the current paper we demonstrate that the individual-subjects functional localization approach is superior to the traditional methods in its ability to distinguish among conditions in a brain region's response. This ability is at the core of all neuroimaging research and is critical for answering questions of functional specialization (e.g., does a brain region specialize for processing syntactic aspects of the linguistic signal), which is in turn essential for making inferences about the precise computations conducted in each brain region. Based on our results, we argue that supplementing existing methods with an individual-subjects functional localization approach may lead to a clearer picture of the neural basis of syntactic processing, as it has in some other domains, such as high-level vision (e.g., Kanwisher, 2010) and social cognition (e.g., Saxe & Kanwisher, 2003).

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1. Introduction

Humans share with other species the ability to learn a mapping between strings of sounds and meanings (e.g., Kaminski, Call, & Fischer, 2004; Pepperberg, 2000; Savage-Rumbaugh et al., 1993). However, only humans can (a) combine these lexical-level representations in novel ways in order to convey how objects relate to one another in the world or to describe a state of one's own or another's mind, or (b) infer the relationships among elements in a string of words (cf. Gentner, Fenn, Margoliash, & Nusbaum, 2006; Ouattara, Lemasson, & Zuberbühler, 2009). Because this ability – syntactic processing – is one of the defining characteristics of our species, scientists have long sought to understand the cognitive and neural architecture of the system underlying it, as well as its relationship to other human cognitive abilities. In the current paper, we focus on the neural machinery supporting syntactic processing, with a particular focus on investigations using functional magnetic resonance imaging (fMRI), and we argue that a new

method – defining regions of interest functionally in individual subjects and then rigorously investigating the functional properties of these regions – may be promising for future investigations of this and related questions.

We begin with a brief summary of what is currently known about the neural basis of syntactic processing from neuroimaging studies, and we outline some of the questions that remain unresolved. We point out that all neuroimaging is premised on the ability to detect in the relevant brain region a differential response to conditions that differ in the cognitive operations they entail, so maximizing this ability (referred to here as “functional selectivity”) is of paramount importance in all functional imaging studies. We argue that traditional group analysis methods based on voxels defined in a common stereotaxic space may obscure functional selectivity because subjects differ from each other anatomically. We further argue that an individual-subjects functional localization approach presents a powerful complement to these traditional methods, and may lead to a clearer picture of the neural basis of syntactic processing, as it has in some other domains, such as high-level vision (e.g., Kanwisher, 2010) and social cognition (e.g., Saxe & Kanwisher, 2003). In support of this position, we directly compare the individual-subjects functional localization

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approach to the traditional approaches with respect to their functional selectivity, using a dataset from Fedorenko et al. (2010). We focus on regions that have been argued to be engaged in syntactic processing based on previous studies. Based on the higher selectivity observed in functionally defined subject-specific regions of interest (ROIs) compared to several kinds of standard group ROIs,¹ we conclude that functional localization in individual subjects holds promise for understanding the neural basis of language.

1.1. The neural basis of syntactic processing: What we know and what we don't know

Several brain regions have been consistently implicated in structural processing. We here briefly review the main candidates (see e.g., Kaan and Swaab (2002), Friederici and Kotz (2003), Grodzinsky and Friederici (2006), Bornkessel-Schlesewsky and Friederici (2007) and Caplan (2007), for reviews).

In a seminal finding, Carramazza and Zurif (1976) demonstrated that Broca's agrammatic aphasics have difficulty interpreting structures where the order of the noun phrases does not correspond to the typical order of thematic roles in English (for example, reversible passives like *The girl was chased by the boy*, where the sentence-initial noun phrase *the girl* occupies the position of a typical agent but is assigned the patient role by the verb phrase). Ever since this discovery, Broca's area has been a focus of investigations of syntactic processing. The traditional definition of this region includes opercular and triangular portions of the left inferior frontal gyrus, IFG (cf. Lindenberg, Fangerau, & Seitz, 2007, for an extensive discussion of the variability in what researchers refer to as "Broca's area" across neuroimaging studies). Regions in/around the left IFG have indeed been shown to respond more strongly to syntactically complex sentences across a number of studies (e.g., Ben-Shachar, Hendler, Kahn, Ben-Bashat, & Grodzinsky, 2003; Ben-Shachar, Palti, & Grodzinsky, 2004; Friederici, Fiebach, Schlesewsky, Bornkessel, & von Cramon, 2006; Grewe et al., 2005; Santi & Grodzinsky, 2007; Stromswold, Caplan, Alpert, & Rauch, 1996). However, other studies have implicated these regions in lexico-semantic processing (e.g., Hagoort, Baggio, & Willems, 2009; Hagoort, Hald, Bastiaansen, & Petersson, 2004; Rodd, Davis, & Johnsrude, 2005; Schnur et al., 2009) and phonological processing (e.g., Blumstein, Myers, & Rissman, 2005; Myers, Blumstein, Walsh, & Eliassen, 2009). Some have claimed that different portions of the left IFG support different aspects of linguistic processing (e.g., Buckner, Raichle, & Petersen, 1995; Fiez, 1997; Poldrack et al., 1999; Bokde, Tagamets, Friedman, & Horwitz, 2001; Burton, 2001, 2009; Dapretto & Bookheimer, 1999; Devlin, Matthews, & Rushworth, 2003; Gough, Nobre, & Devlin, 2005; Costafreda et al., 2006; Santi & Grodzinsky, 2007; Heim, Eickhoff, & Amunts, 2009), or even different aspects of syntactic processing (e.g., Friederici et al., 2006), but no consensus has yet been reached about what the relevant divisions are and what cognitive function(s) each sub-region supports (cf. alternative accounts that postulate broader cognitive functions to account for a range of findings; e.g., Novick, Trueswell, & Thompson-Schill, 2005; Duncan, 2001, 2010; Badre & D'Esposito, 2009).

Posterior temporal regions (posterior superior temporal gyrus/sulcus, STG/STS) have also been implicated in syntactic processing (e.g., Constable et al., 2004; Cooke et al., 2002; Hasson, Nusbaum, & Small, 2006; Schlesewsky & Bornkessel, 2004). Grodzinsky and Friederici (2006) in a recent review hypothesize that these regions may be critical for integrating incoming elements into the evolving structure. However, other studies have observed activations in these regions for non-syntactic language tasks (e.g., Graves,

Grabowski, Mehta, & Gupta, 2008; Hickok, Okada, & Serences, 2009; Noppeney, Phillips, & Price, 2004).

Another region that has been reported in a few studies to be sensitive to syntactic processing is located in the left anterior temporal lobe (ATL). For example, Noppeney and Price (2004) observed a decreased response in this region when participants read sentences with similar structures (see Friederici, Ruschenmeyer, Hahne, & Fiebach, 2003; Friederici, Wang, Herrmann, Maess, & Oertel, 2000a; Humphries, Binder, Medler, & Liebenthal, 2006; Humphries, Love, Swinney, & Hickok, 2005; Rogalsky & Hickok, 2009, among others). However, as with the other regions, syntactic processing is not the only cognitive function that has been observed to activate ATL structures. For example, Patterson, Nestor, and Rogers (2007) have argued that these structures support amodal conceptual representations, although some (e.g., Humphries, Willard, Buchsbaum, & Hickok, 2001) have argued that these regions are more engaged during sentence understanding than non-linguistic conceptual processing.

In summary, each of the regions that have been implicated in syntactic processing (including the regions mentioned above as well as some other ones) has also been implicated in other linguistic functions. Moreover, most of these regions have also been implicated in a variety of non-linguistic functions (e.g., see Duncan (2001, 2010), Lindenberg et al. (2007), Badre and D'Esposito (2009), Fadiga, Craighero, and D'Ausilio (2009), for reviews of tasks that activate lateral frontal cortices; see Hein and Knight (2008), for a review of tasks that activate STS/STG regions; see Olson, Plotzker, and Ezzyat (2007), for a review of findings on the role of left temporal pole structures in social/emotional processing). This situation has recently been synopsized in a review by Blumstein (2009), as follows: "The functional properties of language, that is, speech, lexical processing, and syntactic processing, appear not to be focally represented in one area of the brain; rather, each recruits a broadly distributed neural network or processing stream. Moreover, certain areas of the brain that have been associated with language processing appear to be recruited across cognitive domains, suggesting that while language may be functionally special, it draws on at least some neural mechanisms and computational properties shared across other cognitive domains."

In order to claim that a particular brain region R supports a particular cognitive function, it is necessary not only to formulate predictions about the kinds of cognitive operations that should result in activity in region R, but also to be able to explain why other kinds of cognitive operations result in activity in region R. Researchers usually take one of two approaches (see e.g., a recent debate between Grodzinsky and Santi (2008), and Willems and Hagoort (2009), in TiCS, for an illustration): (1) they focus on the cognitive function that is of most interest to them (e.g., syntactic processing) and do not attempt to reconcile their findings with contradictory findings from other studies, sometimes dismissing them on the grounds of methodological flaws or slightly different loci of the peaks of activations; or (2) they attempt to provide a unifying account that can explain all the available data. For example, as mentioned above, some researchers have explicitly argued that the left inferior frontal brain regions that have been implicated in syntactic processing are more functionally general. For example, Hagoort and colleagues (e.g., Hagoort et al., 2009) have put forward the *semantic unification* proposal, whereby the left IFG is responsible for constructing complex meanings out of simpler meaning units. Thompson-Schill and colleagues (Novick et al., 2005; Snyder, Feigenson, & Thompson-Schill, 2007; Thompson-Schill, 2005; see also Badre & Wagner, 2007) have argued that this region is critical for cognitive control abilities that are required to select the relevant representation among multiple competing representations. And Duncan (Duncan, 2001, 2010; see also Miller & Cohen, 2001) has argued that neurons located on the lateral surface of the frontal

¹ Throughout the paper, we use the term "standard group ROIs" to refer to cases where the same set of voxels in stereotaxic space is used across subjects.

lobes are general-purpose problem solvers and can be used to perform a wide range of goal-directed cognitive tasks.

To summarize, no brain region has so far been convincingly demonstrated to be *selectively* engaged in syntactic processing or a component thereof. This may be because such regions do not exist. In particular, it is possible that all the regions that support syntactic processing support other, linguistic or non-linguistic, functions. However, we believe that current methods may be obscuring the true functional architecture, whatever that may be, as argued next.

1.2. Potential limitations of the current methods and a possible solution

All neuroimaging methods depend fundamentally on the ability to detect in some region of the brain a differential response between conditions that differ in the cognitive operations they involve. The current standard practice in the field of neuroimaging of language entails performing a random effects analysis on the data with the activations reported in stereotaxic coordinates (e.g., Talairach or MNI). The main way to compare results across studies is to compare the locations of activations (often represented by activation peaks) in stereotaxic space. The most systematic comparisons involve meta-analyses of activation peaks from large numbers of studies (e.g., Bookheimer, 2002; Costafreda et al., 2006; Indefrey & Levelt, 2004; Kaan & Swaab, 2002; Lindenberg et al., 2007; Poldrack et al., 1999; Vigneau et al., 2006). The basic premise of these kinds of comparisons is that functional organization is sufficiently related to stereotaxic space, that this space provides a common ground for comparing results across studies, which is essential for accumulating knowledge about the functional architecture of the language system. However, because of inter-subject anatomical variability, functional regions may fall in different locations in stereotaxic space (see Saxe, Brett, and Kanwisher (2006) and Fedorenko and Kanwisher (2009), for reviews of the relevant literature and discussions of this and related issues). As a result, the responses across subjects extracted from the same location in stereotaxic space may underestimate selectivity of the underlying brain tissue.

Inter-subject anatomical variability has consequences for both voxel-based and standard-group-ROI-based analyses (where a fixed ROI, expressed as a set of voxels in stereotaxic space, is used across subjects; this includes both anatomically defined ROIs and functionally defined ROIs, or fROIs). In *voxel-based* analyses some subjects may not show an effect in a particular voxel. As a result, voxels that show an effect in only a small proportion of the subjects may not be detected, and in the voxels that do emerge, selectivity may be underestimated because averaging will include some subjects who do not show the effect (see also Appendix A). Similarly, in *standard-group-ROI-based* analyses individual subjects' activations may fall in slightly different locations relative to the ROI volume (which is fixed across subjects in common stereotaxic coordinates). As a result, selectivity may be underestimated because in each subject the ROI will include some voxels that do not show the effect.

The solution we offered in Fedorenko and Kanwisher (2009) involves functional localization of language-sensitive cortex in individual subjects (see Ben-Shachar et al., 2004; January, Trueswell, & Thompson-Schill, 2009; Neville et al., 1998; Rogalsky & Hickok, 2000, among others, for earlier attempts to use individual subjects' activation maps in the analyses). This approach consists of two steps. First, a contrast aimed at the cognitive process of interest is used to identify regions – in each individual brain – that support the relevant cognitive process. For example, a contrast between faces and objects is used to identify regions that are engaged to a larger extent in face processing than in object processing more

generally (Kanwisher, McDermott, & Chun, 1997). And second, hypotheses about the functions of these regions are tested by examining the response of these regions to various new conditions of interest.

In Fedorenko et al. (2010), we presented a localizer task that functionally identifies key language-sensitive regions in individual brains in a tractably short period of scanning (15–20 min). We used a contrast between sentences and pronounceable nonwords. This contrast targets brain regions engaged in processing word- and sentence-level meaning and should therefore include regions supporting lexico-semantic and syntactic processing. We demonstrated that a number of regions (including the “classical” regions in the left frontal and left temporo-parietal cortices) – each present in at least 80% of individual subjects – show a reliably stronger response to sentences than to nonwords. This response (a) replicates within and between subjects, (b) generalizes across different sets of materials and different tasks (see Osterhout, Allen, McLaughlin, & Inoue, 2002, for evidence of task-independence in ERPs; cf. Meyer, Friederici, & von Cramon, 2000; Plante, Creusere, & Sabin, 2002; Wright, Randall, Marslen-Wilson, & Tyler, 2010, among others, for evidence of task effects observed with linguistic materials in fMRI studies), and (c) generalizes from the visual to the auditory modality (see also Bedny, Dodell-Feder, Pascual-Leone, Fedorenko, & Saxe, *in press*), although some regions do show an overall stronger response to visual or auditory stimuli (see Fig. 8 in Fedorenko et al., 2010; see also Carpentier et al., 2001; Constable et al., 2004; Michael, Keller, Carpenter, & Just, 2001, for earlier investigations of modality effects in language processing; cf. Osterhout & Holcomb, 1993, for ERP evidence of similar responses to high-level linguistic manipulations across modalities). The ability to identify a set of regions in each individual brain in a short scan opens the door to a research program characterizing the response profiles of these regions in detail by examining their responses to various linguistic and non-linguistic manipulations, including investigations of questions concerning the role of these regions in syntactic processing (see Section 5 for a discussion of advantages and potential limitations of this method).

In order to make a convincing case for this approach, however, it is necessary not only to demonstrate its feasibility as we have done in Fedorenko et al. (2010), but also to show how it compares to existing approaches. This is the aim of the current paper. In particular, we evaluate whether selectivity – which is critical for dissociating responses of a brain region to different stimuli/tasks – is indeed higher in subject-specific fROIs than in several kinds of standard group ROIs defined using traditional stereotaxic-space-based methods.

1.3. Selectivity

Throughout the paper, we use the term *selectivity* to characterize the degree to which different conditions are distinguished in a region's response. This represents a property of a *region*, and it is related to our ability to perform reverse inferences, i.e., inferring a particular cognitive process or computation from activation within a region (Poldrack, 2006). We also talk about the selectivity of a *method* when discussing the ability of a method to appropriately characterize brain regions in terms of stimuli/tasks that these regions respond to vs. do not respond to.

Formally, *selectivity* refers to the ability to detect an effect A while discriminating against a non-present effect B:

$$S = \beta_A \cdot (1 - \alpha_B) \quad (1)$$

where β_A represents the sensitivity (power) to detect effect A at a false positive level α . This selectivity measure represents the joint probability of detecting an effect A which is present (the true positive rate for effect A) while not detecting an effect B which is not

present (the true negative rate for a null effect B). This selectivity measure is also known as the area under the curve (AUC), representing the area under the receiver operating characteristic (ROC) curve, and characterizing the *discrimination* ability of a statistical test (see Appendix A for a demonstration of how an increase in the size of the sample does not lead to an increase in selectivity, but rather decreases it).

As is clear from Eq. (1) above, higher selectivity results from maximizing the likelihood of true positives (finding an effect when it is really present, i.e., *sensitivity* in the traditional statistics terminology) while minimizing the likelihood of false positives (not finding an effect when it is not present, i.e., *specificity* in the traditional statistics terminology).

We use effect sizes (i.e., percent BOLD signal differences) as an indicator of a method's selectivity. Effect sizes are important in understanding the functional architecture of a system, because they relate to the notion of "theoretical" significance (beyond the level of statistical significance). For example, if a region responds higher to one stimulus than another, but the difference between the means for these two conditions is very small, it is unclear how theoretically significant such a difference is (see Kanwisher, 2010, for a discussion of theoretical vs. statistical significance).

We chose to use raw (unstandardized) effect sizes for two reasons. First, standardized measures of effect size (such as Cohen's d or Hedge's g) are more commonly used when the metrics of the measures being studied do not have an intrinsic meaning. However, percent BOLD signal differences are meaningful in the sense that they are related to the amount of neural activity (despite many ambiguities about the precise kind of neural activity entailed). And second, even more importantly, differences in standardized measures have two possible interpretations: the differences could be due to (1) differences in (unstandardized) effect sizes (what we are reporting in the paper), and/or (2) differences in standard deviations of the data across the different methods. This latter difference is more difficult to interpret. In particular, we are arguing that the underlying BOLD signal differences for each subject are being underestimated when group (fixed) ROIs are used, due to inter-subject variability in the loci of activation, which leads to averaging – in any given subject – over voxels that show a strong effect and voxels that do not. Our direct comparison of the methods based on their unstandardized effect size contrast differences better reflects this underestimation thereby providing a stronger rationale for using subject-specific fROIs. (For completeness, we also provide the standardized effect size measures in Appendix G.)

Underestimating selectivity has important consequences for investigations of the functional architecture of the language system. If the method we are advocating has higher selectivity, then it has a potential to reveal functional architecture that may be invisible or diminished when less selective (i.e., group-based) methods are used. For example, underestimating the selectivity of regions supporting syntactic processing may lead to wrong conclusions about (a) within-language specificity (i.e., specificity for syntax vs. other aspects of language), (b) domain specificity (i.e., specificity for syntax vs. non-linguistic cognitive processes), and, consequently, (c) the linguistic (or other) computations conducted in these regions.

2. General methods

In this section, we (a) describe the dataset that we'll be using for all the method comparisons presented here, and (b) provide a summary of the individual-subjects functional localization method that we recently developed. Other aspects of the methods, relevant to specific method comparisons, will be described in later sections.

2.1. The dataset

In the current paper we use a dataset (25 subjects) from a four-condition experiment, which used a blocked design and included sentences, word lists, jaberwocky sentences and pronounceable nonword lists (see e.g., Cutting et al., 2006; Friederici, Meyer, & von Cramon, 2000b; Hagoort et al., 1999; Heim et al., 2005; Humphries, Binder, Medler, & Liebenthal, 2007; Humphries et al., 2006; Indefrey et al., 2001; Mazoyer et al., 1993; Petersen, Fox, Snyder, & Raichle, 1990; Vandenberghe, Nobre, & Price, 2002, for studies using similar contrasts in traditional group-based investigations).^{2,3}

The sentences were 12 or 8 words long (two different sets of materials were used across two subsets of subjects to ensure generalizability across different sets of materials) and were created so as to include a variety of syntactic constructions. The word lists were created by scrambling the words across sets of sentences, so that "reconstructing" a sentence out of individual words in a word list was not possible. The jaberwocky sentences were created by replacing the content words (nouns, verbs, adjectives and adverbs) in the sentences by pronounceable nonwords that were matched to the words in length (in letters and syllables) and bigram letter frequency. Finally, the nonword lists were created by scrambling the nonwords across sets of jaberwocky sentences in a similar way to how words were scrambled in the word lists condition.

The largest contrast (sentences > nonwords) was used in Fedorenko et al. (2010) as the localizer contrast to define subject-specific functional ROIs. The word list and jaberwocky conditions were included in order to take a preliminary look at the question of whether any of the fROIs show a dissociation between syntactic and lexico-semantic processing.

2.2. The method: subject-specific functional ROIs

A detailed description of the method that we developed for defining subject-specific fROIs can be found in Fedorenko et al. (2010). We here provide a summary.

Because activations in many language tasks (including our localizer contrast) are quite distributed, the traditional subject-specific fROI definition procedure (e.g., Kanwisher et al., 1997; Tootell et al., 1995), where each individual map for the contrast of interest is examined and subsets of voxels are hand-selected, guided by macroanatomic landmarks, does not seem appropriate. Looking at the individual activation maps for various language tasks, it is often difficult to decide where the borders of a region are in any given brain, or what part of the activation counts as the "same" functional region across two brains. In order to reduce the potential subjectivity present in the traditional fROI definition procedure, we developed a novel method of fROI selection: Group-constrained Subject-Specific (GSS⁴) method.

In the GSS method, a set of thresholded activation maps from individual subjects are overlaid on top of one another. The topographical information in the resulting probabilistic overlap map

² The main results from this dataset are reported in Fedorenko et al. (2010). Detailed descriptions of the materials, procedure and other aspects of the experiment can be found there. The complete set of materials is available from <http://web.mit.edu/evelina9/www/funcloc/>.

³ This dataset contains data from two experiments with the same design. In the first experiment ($n = 12$) participants were engaged in a passive reading task, and in the second experiment ($n = 13$), in addition to the reading task, participants had to report whether a memory probe (word/nonword) that appeared after each sentence / word list / jaberwocky sentence / nonword list was present in the immediately preceding string. Because the results from the two experiments were similar, we collapsed the data in Fedorenko et al. (2010) and in the current paper.

⁴ This method was originally introduced with the abbreviation "GcSS".

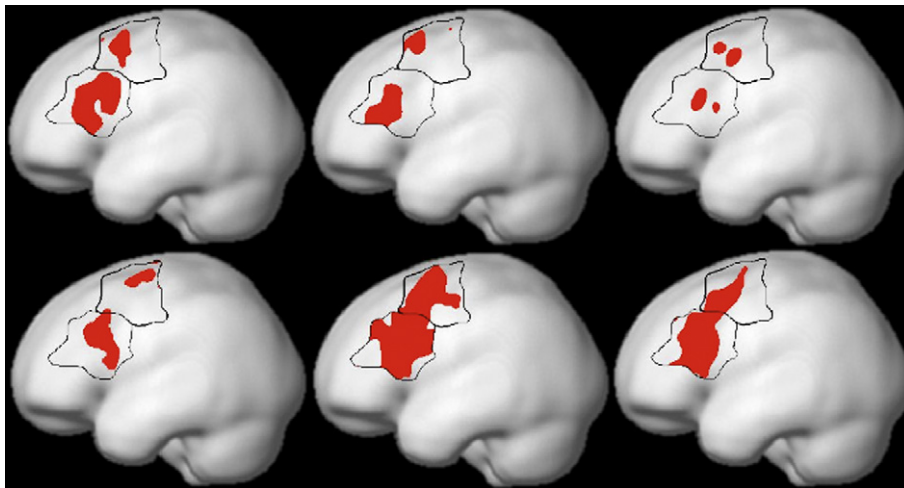


Fig. 1. Two sample fROIs (Left IFG and Left MFG) in six sample subjects. The borders of the group-level partitions are shown with a black outline and the subject-specific activations are shown in red.

is then used to divide the activation landscape into “partitions” (using an image parcellation algorithm) by identifying points of high inter-subject overlap and allowing for variation of individual activations around these high overlap points. In the critical step, the resulting group-level functional partitions are used to constrain the selection of voxels in individual subjects, i.e., individual subjects’ fROIs are defined by taking the intersection of the partitions and individual subjects’ thresholded activation maps. In the current version of the procedure, no constraints, such as e.g., contiguity, are placed on an individual subject’s voxels that fall within the borders of any given partition (future work may include refinements to this procedure). Fig. 1 illustrates this intersection procedure for a few sample subjects for two sample partitions (see http://web.mit.edu/evelina9/www/funcloc/funcloc_GcSS_analysis_flow.html, for a schematic illustration of all the steps). Having intersected the partitions with individual subjects’ activation maps, we selected a subset of “meaningful” fROIs that (1) are present in at least 80% of individual subjects, (2) show replicable responses within subjects and similar responses across subjects, and (3) respond more strongly to sentences than nonwords regardless of whether the stimuli are presented visually or auditorily (see Appendix B for a map showing the key group-level partitions identified in Fedorenko et al., 2010; these partitions, as well as an SPM toolbox for performing GSS analyses, are available for download from <http://web.mit.edu/evelina9/www/funcloc/>).⁵

Unlike the traditional group analyses based on the notion of inter-subject overlap at the voxel level, this method enables us to detect individual subjects’ activations that may land in similar but

largely/completely non-overlapping locations within a spatially constrained volume.

3. Results: Selectivity of GSS fROIs vs. standard group ROIs

For all of these analyses, we use the dataset from Fedorenko et al. (2010), described in Section 2.2. We extract the responses to the four conditions (sentences, words, jaberwocky and nonwords) from the different kinds of ROIs and compare the effect sizes observed in these ROIs for several key contrasts to those observed in our GSS fROIs (defined as described in Section 2.2).

We focus on three contrasts relevant to syntactic processing: (1) sentences > nonwords (our localizer contrast), (2) sentences > words, and (3) jaberwocky > nonwords. The effect sizes for these contrasts tell us how well the relevant pairs of conditions are distinguished in a region’s response (e.g., the size of the sentences > words effect tells us how well sentences and word lists are differentiated). Although none of these contrasts are designed to *isolate* syntactic processing exclusively, under any account of syntactic processing sentences should elicit a higher response than pronounceable nonwords and than words in regions supporting syntactic processing. Furthermore, according to most accounts, jaberwocky sentences should elicit a higher response than pronounceable nonwords because in the former but not in the latter, the order of nonwords, as well as the presence of function words in grammar-appropriate locations and functional morphology allows combining nonwords into more complex representations.⁶

The goal of the current investigation is not to answer the question of whether any brain regions specialize for syntax vs. other linguistic processes and vs. non-linguistic functions. This is a hard question that will require dozens of studies. What we do here is establish the individual-subjects functional localization approach as a method that’s optimally suited for answering this question eventually. In particular, we show this method’s superior ability

⁵ The brain regions identified with our localizer contrast are largely consistent with previous studies that have shown that left lateral frontal and temporal / temporoparietal regions respond strongly to sentence stimuli, and also more strongly to more linguistically rich stimuli (e.g., sentences) than to less linguistically rich stimuli (e.g., word lists or jaberwocky) (e.g., Indefrey et al., 2001; Humphries et al., 2007). However, the results of one study (Friederici et al., 2000b) are not consistent with our findings. In particular, Friederici et al. (2000b) failed to observe stronger activation in the left frontal regions for sentences relative to word lists, jaberwocky sentences, and nonword lists. It is unclear what the source of this discrepancy is. Because we (see also Bedny et al., in press) have now replicated the response profiles in the frontal and temporal regions across several studies (consistently finding the strongest response to sentences, weaker response to words and jaberwocky, and the weakest response to nonwords) and because these findings are also consistent with several other published reports, we think that the results reported in Friederici et al., 2000b are either not robust and therefore not replicated in similar studies, or are due to some study-specific properties which are different from all the other studies, although nothing stands out as an apparent difference based on a careful reading of the methods section of Friederici et al., 2000b.

⁶ It is worth noting that even if these conditions are met (i.e., the response to sentences is higher than to words and to nonwords, and the response to jaberwocky is higher than to nonwords), additional tests would then be required to better understand the role of the region in question in structural processing. Furthermore, in order to argue that a region is *selectively* engaged in syntactic processing, additional tests would be necessary to (a) demonstrate that this region is not engaged in other linguistic processes (e.g., phonological, semantic or discourse-level processes), and (b) demonstrate that this region is only sensitive to processing structure in language but not in other stimuli that may share some properties with language (e.g., music or action planning).

– relative to traditional, group-based, methods – to distinguish among conditions in a region's response (e.g., distinguishing between sentences and word lists). This ability is essential for addressing questions of functional specialization, which in turn lays the groundwork for understanding the computations performed by each brain region. (See Section 5 for other advantages that the individual-subjects functional localization method provides over the traditional group-based methods.)

We begin, in Section 3.1, by comparing the effect sizes in our subject-specific fROIs to those in standard group ROIs defined around activation peaks that have been argued to represent regions engaged in syntactic processing in several previously published studies. In Section 3.2, we examine the effect sizes in our subject-specific fROIs in relation to fROIs defined based on the group analysis of the same data. Finally, in Section 3.3, we examine two of our subject-specific fROIs (located in the left IFG) in relation to two anatomical ROIs: Brodmann areas (BAs) 44 and 45, defined using probabilistic cytoarchitectonic maps (Amunts et al., 1999). As discussed in Section 1, the left IFG (including BAs 44 and 45) is among the regions most frequently implicated in syntactic processing and is therefore of relevance here.

3.1. GSS fROIs vs. ROIs defined around activation peaks from the literature

3.1.1. Methods

In order to perform a relatively large-scale assessment of the selectivity of syntax-sensitive regions reported in the literature, we chose to work with ROIs defined around activation peaks from a recent meta-analysis (Vigneau et al., 2006). Vigneau and colleagues examined activation peaks from a set of 129 studies. They classified these peaks (a total of 729 peaks) into three broad categories: peaks reported for tasks involving phonological processing, peaks reported for tasks involving semantic processing, and – of most interest here – peaks reported for tasks involving syntactic/sentence-level processing (see Vigneau et al., 2006, p. 1415, for a description of the classification procedure). 160 of the 729 peaks were classified as syntactic/sentence-level peaks. These 160 peaks were further classified into five sub-categories based on the type of contrast used: (1) text comprehension (42 peaks), (2) sentence-level comprehension (72 peaks), (3) syntactic processing (43 peaks), (4) sentence completion (1 peak), and (5) mental imagery (2 peaks). The most relevant here is the third sub-category, which, for the most part, includes contrasts between more vs. less structurally complex sentences. (The other four sub-categories are less theoretically coherent, including a wide range of tasks involving sentences and texts.) In particular, most of these studies investigated constructions that either did or did not contain long-distance dependencies between words (e.g., Ben-Shachar et al., 2004; Constable et al., 2004; Cooke et al., 2002; Stromswold et al., 1996). Long-distance dependencies have been shown to lead to processing difficulty, compared to local dependencies, across a wide range of behavioral measures (e.g., Ford, 1983; Gibson, 1998; Gordon, Hendrick, & Johnson, 2001; Holmes & O'Regan, 1981; King & Just, 1991). Because it is possible to match constructions involving local vs. non-local dependencies for lexico-semantic properties, contrasts between them are commonly used to isolate syntactic processing or syntactic working memory in behavioral, neuropsychological and neuroimaging investigations.

To perform the analyses in this section, we first (a) defined spherical ROIs (6 mm in diameter) around each of the 43 syntactic peaks, and (b) extracted the response to the four conditions (sentences, words, jabberwocky and nonwords) from our dataset. We then selected the subset of these peaks that fell within one of our group-level partitions so that the data from these peaks would be comparable to the data from our new method. That constituted

29 peaks across 6 partitions (note that Vigneau et al. included only peaks in the left hemisphere in their meta-analysis). Finally, for each relevant partition, we compared the effect sizes in the ROIs defined around the syntactic peaks to those in the corresponding GSS fROI. We did this for each of our three contrasts: sentences > nonwords, sentences > words, and jabberwocky > nonwords. Before presenting the results, it is worth noting that these selectivity comparisons err on the conservative side because *all* the functional runs were used when estimating the responses in the peak-defined ROIs, whereas only the first run was used when estimating the response in GSS fROIs (the other runs were used for defining the ROIs).

3.1.2. Results

Across the three contrasts (sentences > nonwords, sentences > words, and jabberwocky > nonwords) and across different brain regions, the selectivity is higher in the fROIs defined with our GSS method than in nearby group ROIs defined around peak coordinates in stereotaxic space reported in earlier studies on syntactic processing. In particular, the differences in the magnitude of response to the conditions forming the contrasts above (e.g., the difference between the response to sentences and the response to word lists) are larger in the GSS fROIs compared to peak-defined group ROIs. The results are exemplified in Fig. 2 for two sample regions (see Appendix C, for a full set of detailed plots).

To quantify these differences in effect sizes, we used a Wilcoxon signed rank one-sided test comparing the GSS fROI effect size value to the corresponding distribution of peak-defined ROIs' effect size values. The results are summarized in Table 1. In three of the regions (IFG, IFGorb and MidPostTemp) the GSS fROI effect size is reliably higher than those of the peak-defined ROIs across all three contrasts. In the PostTemp region, the GSS fROI effect size is marginally higher than those of the peak-defined ROIs across the three contrasts. And in the remaining two regions (MFG and AntTemp) the effect size is only numerically higher, plausibly not reaching significance due a small number of peak-defined ROIs in those partitions.

In summary, these results demonstrate that GSS fROIs are more functionally selective than ROIs defined around activation peaks reported for syntactic contrasts in the previous literature. This was true across all three contrasts that involve syntactic processing. These results therefore suggest that analyses relying on GSS fROIs are promising for investigating questions of the functional architecture of the language system as they have more power to detect effects if they are present and to distinguish among conditions that are actually different.

3.2. GSS fROIs vs. standard group fROIs (defined in the same dataset)

3.2.1. Methods

In this section, we compare the selectivity of our GSS fROIs to that of fROIs defined based on traditional random-effects group analysis maps in the same subjects. For both kinds of ROIs, we used all but the first functional run in each subject to define the ROIs, and then extracted the responses from the first functional run, i.e., from a subset of the data that was not used for ROI definition (e.g., Kriegeskorte, Simmons, Bellgowan, & Baker, 2009; Vul & Kanwisher, 2009). To define our GSS fROIs, we intersected group-level partitions (see Appendix B) with individual subjects' activation maps for the sentences > nonwords contrast, as discussed in Section 2.2 and illustrated – for two sample partitions and six sample subjects – in Fig. 1 above. To define standard group fROIs, we intersected group-level partitions with the random-effects group analysis map for the same contrast (again, using all but the first functional run). Critically, in the group fROI analyses the same set of voxels in stereotaxic space was used for all subjects (i.e.,

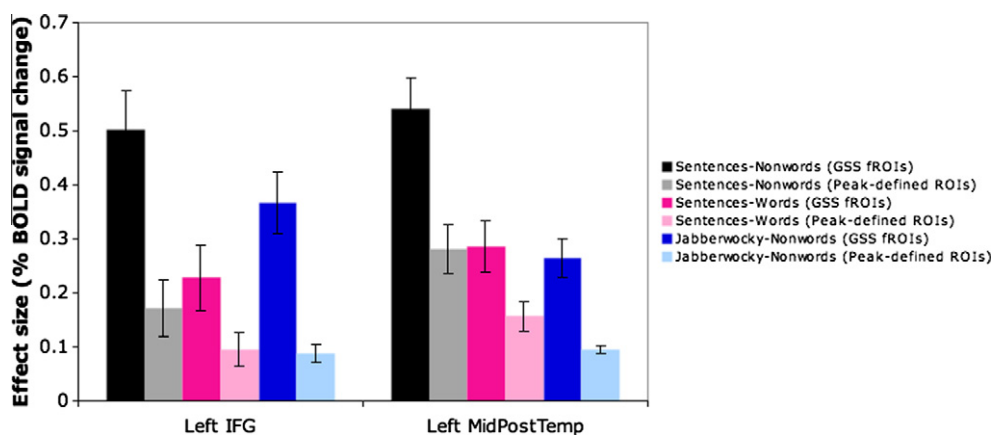


Fig. 2. Effect size comparisons between GSS fROIs (darker bars) and the ROIs defined around the syntactic activation peaks from several previously published studies that fell within the borders of the corresponding group-level partitions (lighter bars) for the sentences > nonwords contrast (black and grey bars), sentences > words contrast (pink bars), and jabberwocky > nonwords contrast (blue bars), for two sample regions (Left IFG and Left MidPostTemp).

Table 1

Results of Wilcoxon signed rank tests comparing the effect size values between GSS fROIs and peak-defined ROIs located within the corresponding partition.

	fROI	Number of peaks within partition	Sentences > nonwords	Sentences > words	Jabberwocky > nonwords
Left frontal regions	IFG	9	<.005	<.005	<.005
	IFGorb	7	<.01	<.05	<.01
	MFG	2	n.s.	n.s.	n.s.
Left posterior regions	AntTemp	1	n.s.	n.s.	n.s.
	MidPostTemp	6	<.05	<.05	<.05
	PostTemp	4	.06	.06	.06

the voxels that emerged in the group analysis for the sentences > nonwords contrast and fell within the borders of each relevant partition), whereas our method allows different voxels in stereotaxic space for each individual subject.

As discussed in Fedorenko et al. (2010), it is not obvious that the GSS fROIs would outperform group fROIs in this comparison. In particular, because the random-effects group fROIs include voxels that behave most consistently across participants, it is possible that these voxels would be most functionally selective. Therefore, the selectivity of group fROIs may be predicted a priori to be at least as high as that of subject-specific fROIs. This is not, however, what the results show. In Fedorenko et al. (2010) we already reported the results for the sentences > nonwords contrast. For each of the twelve regions we observed a reliably higher selectivity for the GSS fROIs compared to the group fROI. Here, we examined the selectivity of the GSS fROIs and group fROIs for the two functionally narrower contrasts that are relevant to syntactic processing: sentences > words, and jabberwocky > nonwords.

3.2.2. Results

For each of the three contrasts across brain regions, the selectivity was higher in GSS fROIs than in group fROIs (p -values < .0001). Looking at the individual regions, we see that numerically the effect is larger in GSS fROIs, compared to group fROIs, in every single region across the three contrasts. These results are presented in Fig. 3 (the results for the sentences > nonwords contrast are the same as those reported in Fedorenko et al., 2010, and are presented here for completeness). Moreover, in most of the regions, these differences in effect size values between GSS fROIs and group fROIs are significant (for example, we see a highly reliable difference across all three contrasts in the Left IFG and Left MidPostTemp regions). These results are summarized in Table 2. These results reflect the fact that in group ROIs, for each subject the averaging

includes some voxels that are not significant in that subject, due to inter-subject variability in the precise locations of activations.

Although the contrasts discussed here (sentences > nonwords, sentences > words, and jabberwocky > nonwords) are significant in most of the group ROIs, it is important to understand that smaller effect sizes mean that it would be generally more difficult to detect these (and other similar-size) effects. For example, while our dataset includes 25 subjects, typical imaging experiments where standard group analyses are used include on the order of 14–18 subjects. Therefore, some of these effects may not be detectable in such studies.

It is also worth noting that apart from the fact that GSS fROIs are characterized by higher selectivity, there is some variability among the regions in how selective they are (this variability is present in both GSS fROIs and group fROIs, but it is more pronounced in GSS fROIs, plausibly because the selectivity is overall higher allowing for more variation). Given how important selectivity of different brain regions is for understanding the neural architecture underlying human cognition, an interesting future line of research could be aimed at exploring this variability. In particular, understanding what properties of a region (such as e.g., its size, location in the brain, or spatial variability across subjects) predict the size of the effects observed in that region for various tasks may provide important insights. (For example, it is possible that language-sensitive regions located in the left hemisphere would show consistently larger effect sizes for language tasks than those in the right hemisphere.) In Appendix D we present some preliminary explorations of this question.

3.3. GSS fROIs vs. anatomical ROIs (BAs 44 and 45)

In this section, we compare two of our left frontal GSS fROIs (Left IFG and Left IFGorb) to two anatomical ROIs. In particular,

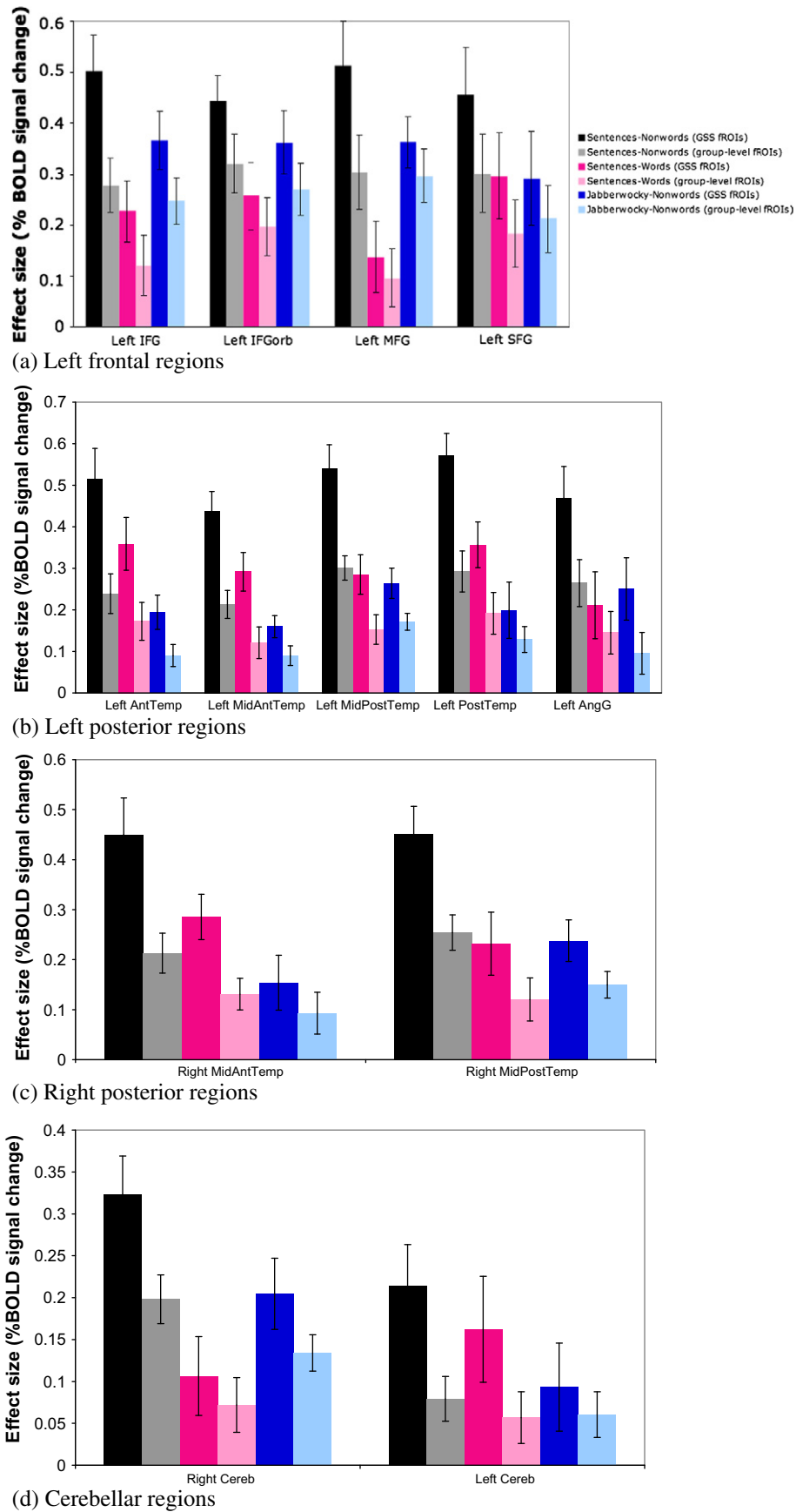


Fig. 3. Effect size comparisons between GSS fROIs (darker bars) vs. group fROIs (lighter bars) for the sentences > nonwords contrast (black and grey bars), sentences > words contrast (pink bars), and jabberwocky > nonwords contrast (blue bars).

Table 2Results of the *t*-tests comparing the effect size values between GSS fROIs and group fROIs.

	fROI	Sentences > nonwords	Sentences > words	Jabberwocky > nonwords
Left frontal regions	IFG	<.0005	<.001	<.0005
	IFGorb	<.05	n.s.	.055
	MFG	<.005	n.s.	n.s.
	SFG	<.005	<.05	<.05
Left posterior regions	AntTemp	<.0001	<.0005	<.01
	MidAntTemp	<.0001	<.0001	<.0005
	MidPostTemp	<.0001	<.0001	<.0005
	PostTemp	<.0001	<.0005	n.s.
	AngG	<.005	n.s.	<.05
Right posterior regions	MidAntTemp	<.001	<.0005	<.05
	MidPostTemp	<.0005	<.05	<.05
Cerebellar regions	Right Cereb	<.005	.090	.064
	Left Cereb	<.01	<.05	n.s.

we investigate Brodmann Areas 44 and 45, defined using probabilistic cytoarchitectonic maps (Amunts et al., 1999). These two Brodmann areas constitute Broca's region, which is one of the main candidates for the seat of syntactic processing, as discussed in the Introduction.

3.3.1. Methods

We first discuss the methodology of using probabilistic cytoarchitectonic maps more generally, since this tool is relatively new to the field of neuroimaging of language. Then, we discuss the relationship between BAs 44 and 45 and our two GSS fROIs located in the left IFG.

3.3.1.1. Probabilistic cytoarchitectonic maps. Although locations of cytoarchitectonic areas (typically Brodmann areas) are commonly estimated in neuroimaging studies based on the sulcal and gyral anatomy, these estimates are imperfect because of high inter-subject variability in the locations of different cytoarchitectonic zones relative to macroanatomic landmarks (e.g., Amunts & Willmes, 2006; Amunts et al., 1999; Zilles et al., 1997). Several years ago, Zilles and colleagues (Amunts et al., 1999; Schormann & Zilles, 1998; Zilles, Schleicher, Palomero-Gallagher, & Amunts, 2002) embarked on an ambitious project where the borders of cytoarchitectonic areas were delineated in ten post-mortem human brains. These brains were first scanned at high resolution. Then, each brain was thinly sliced and each target cytoarchitectonic zone was delineated in the relevant set of slices in each brain. Finally, the delineated sections in the relevant slices were aligned with the MR volume of the brain. Normalizing these ten brains into a common space then enabled the researchers to create probabilistic cytoarchitectonic maps, i.e. representations of the percent of subjects who show a given Brodmann area in each voxel of the normalized (MNI) space. So far, thirteen Brodmann areas have been delineated, and probabilistic maps for these areas are now publicly available. Among the first were Brodmann areas 44 and 45 (Amunts et al., 1999).

These cytoarchitectonic maps are a powerful tool as they bring us one step closer to being able to detect structure below the level of sulci/gyri in fMRI. Some researchers (e.g., Grodzinsky, 2010; cf. Fedorenko & Kanwisher, 2011) have argued that these maps are an ideal way to answer questions of functional specialization in the human brain, because (a) they represent cytoarchitecture which has been long assumed (e.g., Brodmann, 1909) and, based on the animal work, shown to correspond to function (e.g., Iwamura, Tanaka, Sakamoto, & Hikosaka, 1983; Matelli, Luppino, & Rizzolatti, 1991; Rozzi, Ferrari, Bonini, Rizzolatti, & Fogassi, 2008), and (b) they contain information about the variability present across individual brains.

We agree that these maps provide an excellent tool for use in fMRI, allowing a much more precise estimation of the location of cytoarchitecture relative to macroanatomy. However, we also think that some of the problems inherent in the traditional group analyses affect these maps, as well. In particular, due to large variability in the locations of these areas across subjects, maps for adjacent areas exhibit substantial overlap (for example, 43.0% of BA44 voxels also belong to BA45, and 51.3% of BA45 voxels also belong to BA44). As a result, deciding which cytoarchitectonic area a given voxel belongs to is non-trivial. It can be done using high thresholding levels for the cytoarchitectonic maps, i.e., including – for each BA – only voxels that are present in most of the 10 brains.⁷ However, this thresholding inevitably leads to a loss of information about the variability in the underlying anatomy, which is what these maps are trying to capture in the first place.

An alternative is to calculate for a target functional cluster of interest the probability that any given voxel in that cluster would be labeled as belonging to a particular cytoarchitectonic area (e.g., Santi & Grodzinsky, 2007). This is done by (a) extracting – for each voxel in the functional cluster – the probability of that voxel being in a given Brodmann area, and (b) averaging the values across all the voxels in the cluster. This approach provides useful information about the degree to which functional activations land within a particular Brodmann area. However, no standards have yet been set for what probability values are sufficiently high in order to claim that a functional cluster lands within the borders of a particular Brodmann area. Setting an absolute stringent threshold seems too arbitrary, so quantitative methods for this kind of an assessment need to be developed. These methods would presumably take into account the size of the functional cluster, the variability in the locations of individual Brodmann areas for the target area, the extent of overlap between the target Brodmann area and adjacent Brodmann areas, the topography of the functional cluster relative to the topography of the target Brodmann area, etc. For example, given the substantial overlap between areas BA44 and BA45, it may be necessary to determine the minimum difference in probability values between these two areas that would be convincing in claiming that a functional cluster corresponds to e.g., BA45 and not BA44. The degrees of freedom currently present in this process make any claims about the relationship between functional activations and these probabilistic cytoarchitectonic areas

⁷ For reference, here is information on the overlap between BA 44 and BA45 across different thresholds (the first number represents the percentage of BA44 voxels that also belong to BA45, and the second number represents the percentage of BA45 voxels that also belong to BA44; *n* is the threshold in terms of the minimal number of subjects for whom a voxel corresponds to the relevant BA): *n* > 0: 43.0, 51.3; *n* > 1: 41.4, 46.4; *n* > 2: 27.6, 40.7; *n* > 3: 25.3, 25.4; *n* > 4: 20.5, 17.8; *n* > 5: 12.6, 6.9; *n* > 6: 4.1, 1.7; *n* > 7: 0.4, 0.0; *n* > 8: 0.0, 0.0; *n* > 9: NA, 0.0.

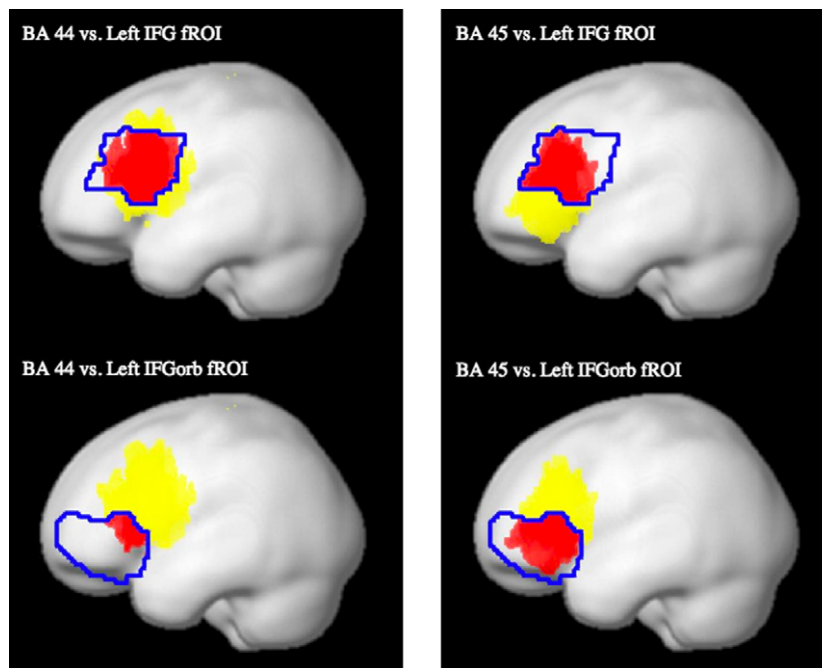


Fig. 4. The relationship between Amunts et al. (1999) probabilistic cytoarchitectonic maps (shown in yellow) for BA 44 (left panel) and BA 45 (right panel) and our group-level partitions (shown with blue contours) for Left IFG (top) and Left IFGorb (bottom). Overlap is shown in red.

difficult to interpret (see Eickhoff et al., 2007, for a discussion of issues in assigning activations to cytoarchitectonic areas and a possible solution).

3.3.1.2. BA44 and BA45 vs. Left IFG and Left IFGorb fROIs. We here focus on two of our GSS fROIs: the ones that overlap with the two relevant Brodmann areas. Fig. 4 demonstrates the relationship between the group-level partitions corresponding to our IFG regions (Left IFG and Left IFGorb) and BA44 and BA45. As can be seen from the figure, our left IFG partition overlaps with both BA44 and BA45 (which overlap with each other considerably, as discussed above), and the left IFGorb partition overlaps with BA45, but almost not at all with BA44 (see Appendix E for more information on the degrees of overlap).

In comparing the selectivity of the Brodmann areas to that of our GSS fROIs, we used (a) all the voxels in each BA map, and (b) only the voxels that are present in nine out of ten⁸ brains in Amunts et al.'s analysis (i.e., only high-overlap voxels)⁹ in order to see whether the results might look clearer at a higher threshold. In addition, we intersected the probabilistic maps with individual subjects' activation maps (again, using all but the first functional run) and defined subject-specific ROIs in the same way as we did using group-level partitions in our GSS method. This was done in an attempt to examine selectivity in a different kind of *subject-specific* fROIs. As discussed in Fedorenko et al. (2010), group-level functional partitions are only one way to constrain the selection of subject-specific voxels. Other possibilities are to constrain subject-specific ROIs with boundaries of macroanatomical structures with respect to each individual subject's anatomy (the current standard in the fROI method in high-level vision studies), boundaries of macroanatomical structures derived from probabilistic atlases (e.g., Rademacher et al., 2001; Westbury, Zatorre, & Evans, 1999), or functional constraints derived

in some different way (e.g., by using the borders of a fROI reported in another study). Using probabilistic cytoarchitectonic maps is yet another possibility (modulo the limitation that such maps only exist for a subset of cytoarchitectonic areas so far).

In order to make the results comparable across these different kinds of ROIs, even for the extraction of responses from the BA ROIs (where no data were used for defining the ROIs), we used the data from the first run only.

3.3.2. Results

The results for the three contrasts (sentences > nonwords, sentences > words, and jabberwocky > nonwords) are presented in Fig. 5.

Across all three contrasts the effect sizes are much larger in either of the two GSS fROIs (5b), compared to either way of defining the anatomical ROIs based on the probabilistic cytoarchitectonic maps (all voxels or just high-overlap voxels), 5a. In the comparison between the *Left IFG* GSS fROI and (i) BA 44 all voxels, (ii) BA 45 all voxels, (iii) BA 44 high-overlap voxels, and (iv) BA 45 high-overlap voxels, we see reliably larger effects for the sentences > nonwords contrast (p -values: <.0001, .0001, .001, .0001), for the sentences > words contrast (p -values: <.0001, .0001, .05, .001), and for the jabberwocky > nonwords contrast (p -values: <.0001, .001, .01, .001). Similarly, in the comparison between the *Left IFGorb* GSS fROI and (i) BA 44 all voxels, (ii) BA 45 all voxels, (iii) BA 44 high-overlap voxels, and (iv) BA 45 high-overlap voxels, we see reliably larger effects for the sentences > nonwords contrast (p -values: <.0001, .0001, .01, .0001), for the sentences > words contrast (p -values: <.001, .001, .01, .01), and for the jabberwocky > nonwords contrast (p -values: <.001, .001, .01, .001).

In addition, setting the differences in selectivity aside, it is worth noting that although some of the syntactic contrasts are significant in the BA ROIs (e.g., the difference between sentences and nonwords is significant in each of the BAs in the analysis with all the voxels (in both areas $p < .02$) and in BA45 in the analysis of high-overlap voxels ($p < .02$)), these significance levels would not survive any reasonable correction for multiple comparisons. (See

⁸ Because in BA44 there is no single voxel where all ten subjects overlap (in the MNI space; see Fischl et al., 2008, for better alignment results in the spherical space), we used the 9/10 threshold for both BAs.

⁹ Because the responses to the four conditions were similar across different thresholds (see Appendix F), we only considered the two extreme thresholds here.

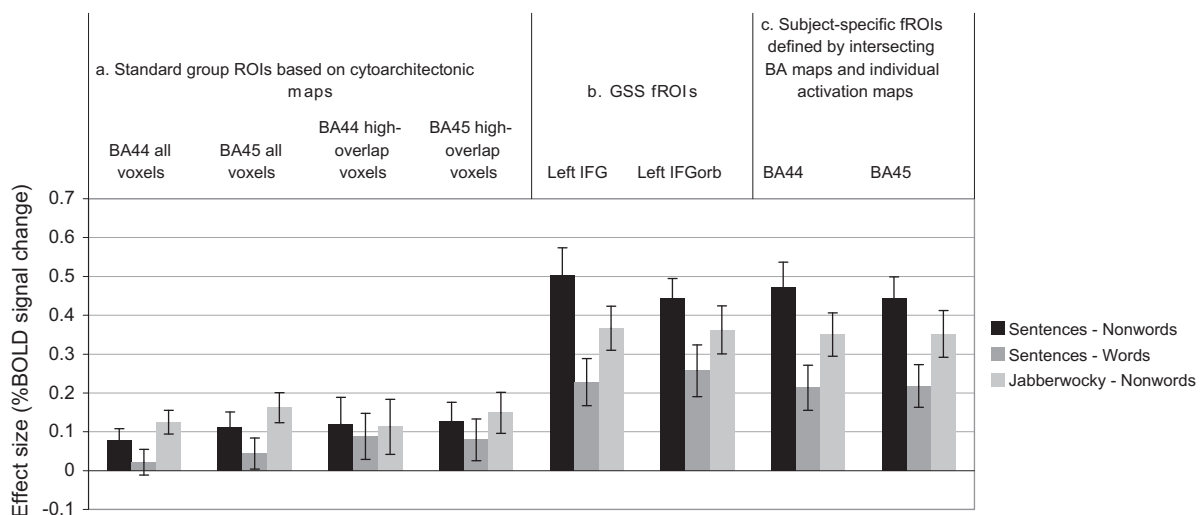


Fig. 5. Effect size comparison for BA44 and BA45 defined in two different ways using Amunts et al.'s (1999) probabilistic cytoarchitectonic maps (a); two GSS fROIs (Left IFG, and Left IFGorb) (b); and subject-specific fROIs created by intersecting the BA maps with individual activation maps (c).

Appendix F for response magnitudes for the four conditions and a further discussion of the response profiles of the BA ROIs.)

Is the higher power of the GSS fROIs compared to the BA ROIs due to a difference between our group-level functional partitions and the BA maps, or is it due to the importance of intersecting any kind of spatial constraint (functional or anatomical) with individual subjects' activation maps? In Fig. 5c we show the results for ROIs defined by intersecting individual subjects' activation maps with the BA maps. The selectivity of these ROIs is comparable to that observed for GSS fROIs (in fact, none of the differences in effect sizes between the GSS fROIs and the subject-specific ROIs defined using the BA maps are significant). This result suggests that it is not the specific partitions that are important for selectivity but rather the intersection of these partitions with each individual subject's localizer activations.

4. Summary of Sections A–C

In Sections A–C, we compared the selectivity of our GSS fROIs to different kinds of standard group ROIs where the same set of voxels in stereotaxic coordinates is used across subjects, and we have shown that GSS fROIs indeed have higher selectivity than the ROIs in each of the alternative methods considered. This strengthens our claim that the individual-subjects functional localization approach is optimally suited for investigating questions of functional specialization and holds promise for uncovering functional architecture in the language system that may have been invisible to other methods. And to the extent that we discover – in future work – overlap between e.g., syntactic processing and other aspects of language, or between syntactic processing and some non-linguistic task, using this more selective method, we will be more confident that what we have discovered is true multi-functionality, rather than a false positive resulting from averaging across adjacent but functionally distinct regions.

5. Discussion

The goal of this paper was to test whether the individual-subjects functional localization method not only presents a viable alternative to the traditional methods used in the neuroimaging of language community, but whether it is superior to those methods in its ability to differentiate among conditions in language-sensitive brain regions. We directly compared the

individual-subjects functional localization approach and several traditional approaches, focusing on regions implicated in syntactic processing. The GSS fROIs exhibited higher selectivity than (a) ROIs defined around the activation peaks from previous studies that have claimed to identify syntax-sensitive regions, (b) fROIs defined on the group analysis maps of the same data, and (c) anatomical ROIs defined using probabilistic cytoarchitectonic maps.

As discussed in Section 1, important questions about the neural architecture supporting syntactic processing currently remain unanswered. These questions concern the nature and degree of functional specialization of brain regions for syntactic processing vs. (a) other aspects of linguistic processing, and (b) non-linguistic cognitive tasks that may involve similar representations or computations. Answers to these questions are of interest in their own right, and further provide a necessary foundation for the ultimate goal of characterizing the computations conducted in these regions. Although we have not yet answered these questions, we have here demonstrated that the standard stereotaxic-space-based methods may not be ideally suited for investigating questions of functional specificity. In particular, in order to uncover potential functional dissociations, the most sensitive available method should be used, such that the chances of revealing such dissociations would be maximized, while the chances of observing spurious overlap would be minimized. We have shown that the traditional, group-based, methods underestimate selectivity, compared to the individual-subjects functional localization approach. We therefore conclude that functional localization in individual subjects holds promise for future investigations of syntactic processing, as well as for the domain of language more generally. In particular, by investigating the responses of language-sensitive regions – defined in individual subjects – to linguistic and non-linguistic manipulations, we can arrive at a detailed characterization of each region and start generating hypotheses about the kinds of representations each region stores or manipulates and the kinds of computations it performs.

In addition to demonstrating higher selectivity of our GSS fROIs, relative to several kinds of standard group ROIs, we wanted to elaborate more generally on the informativeness/usefulness of activation peaks reported in stereotaxic space given that we are making an argument for the need to define regions under investigation functionally in individual subjects. Perhaps the most obvious way to assess the usefulness of activation peaks in stereotaxic space would be to examine their *replicability*. This could be done by selecting a small set of studies from the literature and

attempting to replicate their findings using the same exact experimental protocol and the same scanning and analysis procedures, in order to examine the locations of activations across different versions of the same study. Activation peaks in stereotaxic space only have value to the extent that they represent some stable property of the surrounding neural tissue in that space. If this is the case, then an exact replication of a study should result in activations landing in very similar stereotaxic locations. If differences in the precise locations of activations across studies are sufficiently large, this already poses a problem for the current methods. In particular, given that the extent of this kind of variability is unknown in most cases¹⁰ (or at least is not quantified), it is unclear whether activations reported, for example, for two different tasks and landing in similar locations should be interpreted as activity of the same functional region or distinct adjacent regions. Without formally established criteria for such decisions, researchers are in danger of being affected by their theoretical biases in interpreting such patterns of activation.

An alternative way to evaluate the informativeness of activation peaks reported in stereotaxic space is to examine the responses of fROIs defined around these peaks to some conditions in new datasets. Such analyses would assess the *generalizability* of the peaks. The logic is as follows: if a particular location in stereotaxic space (e.g., an activation peak) represents a region that supports some cognitive function, then neural tissue surrounding this location should respond to various new stimuli/tasks in ways consistent with the hypothesized function. For example, it is reasonable to expect that a region argued to support auditory processing (based on e.g., a contrast between listening to tones and looking at gratings) would respond more strongly to music or speech sounds compared to e.g., pictures of objects. Because we already had the data on the response of the fROIs defined around the peaks meta-analyzed by Vigneau et al. to the four conditions in our dataset (sentences, words, jabberwocky and nonwords), we took a preliminary look at this question. The results were disappointing. For example, among the syntactic ($n = 43$) and sentence-level ($n = 72$) fROIs only a little over half respond to sentences reliably stronger than to nonwords/words at the most liberal threshold. This result is disturbing especially given that the contrast between sentences and nonwords/words is quite large (cf. a contrast between more and less complex sentences). If neural tissue around these peaks does not show even the most rudimentary characteristics that would be expected of regions that these peaks are argued to represent, then how can we treat these peaks as meaningful and rely on them in comparing results across studies, which is essential for accumulating knowledge about the functional profiles of language-sensitive cortex? In order to build on the results of previous studies, we need some reason to believe that the same functional regions are being characterized across studies. The GSS fROI approach provides one way to do this.

Note that in advocating the use of fROIs defined in each subject individually, for the study of the functional architecture of the language system, we are *not* arguing that other methods, or data based on them, should be discarded. Rather we see the individual fROI method as complementary in many ways to the standard group analyses (see Fedorenko et al., 2010, for additional discussion). For one thing, the construction of the best localizers (still very much work in progress) relies on some form of group analyses to find the regions characterized by highest inter-subject overlap. In addition, functional dissociations found with group analyses –

as long as they are replicable – remain very powerful, as these phenomena are found despite the tendency to underestimate selectivity in group analyses.

Before concluding, it is important to point out some limitations inherent in the individual-subjects functional localization approach and to discuss how these limitations can be addressed (see also Fedorenko et al., 2010). There are two primary concerns with interpreting the results obtained using the fROI method: (1) coverage, and (2) response profile ambiguity. First, it is possible that the localizer selected to identify brain regions of interest is not inclusive enough and some key region(s) are left out. With respect to this issue, our localizer includes many of the regions previously implicated in linguistic processing. As a result, even though it is possible that we are not including some important language-sensitive regions, a detailed characterization of the ones that we do capture will significantly advance our understanding of how language is implemented in the brain. (Besides, whole-brain analyses, which should always be used to supplement fROI-based analyses, will tell us if some systematic activations outside the borders of the fROIs are missed. If such activations are observed, additional new fROIs should be considered.)

And second, response profiles of functionally defined fROIs are often ambiguous. For example, a response profile where an ROI responds similarly strongly to two conditions is consistent with both (a) true multi-functionality, and (b) functionally distinct sub-regions within the ROI that respond to each of the conditions. Similarly, a response profile where an ROI does not respond to some condition could be observed when only a small proportion of voxels in that ROI respond to that condition. These concerns can be addressed by supplementing the fROI analyses with whole-brain analyses. Whole-brain analyses may detect activations outside the borders of the fROIs as well as non-homogeneous activations within the fROIs. Furthermore, in our recent work we developed analysis tools that enable examining subsets of voxels within individual subjects' fROIs that may have distinct functional profiles (these analysis tools are currently available by request and will soon be made available from <http://web.mit.edu/velina9/www/funcloc.html>). In cases where some functionally distinct subsets of voxels are discovered within a fROI, new fROI definitions should be considered that would divide some of the fROIs into smaller regions of analysis.

Coming back to the question of the neural basis of syntactic processing, although we remain agnostic as to whether any machinery exists in the human brain that is specialized for processing structural aspects of the linguistic signal, we believe that traditional methods – used in the vast majority of previous studies – have faced important limitations in providing a clear answer to this and related questions. In particular, group-based investigations (a) underestimate selectivity by not taking into consideration variability in activation loci across subjects; (b) are rarely replicated making it difficult to decide which findings are real and which may be spurious; and (c) do not provide an easy way to compare results across studies, thereby slowing down the process of knowledge accumulation about the functional profiles of key language-sensitive regions. The individual-subjects functional localization approach circumvents these problems. In addition to its superior ability to distinguish among conditions in a brain region's response, as demonstrated in the current paper (see also Saxe et al., 2006), the subject-specific fROI approach (i) always includes a partial replication of the results of previous studies (by showing similar responses to the localizer conditions in a subset of the data not used for ROI definition), and (ii) provides a reliable way to refer to the same functional region across individuals and studies, leading to faster progress in discerning the function(s) of brain regions.

To conclude, maybe all language-sensitive regions indeed support multiple aspects of language and/or some non-linguistic

¹⁰ Because of the expense associated with fMRI, there are very few “pure” replications, which would be important for quantifying the variability in the precise locations of activations for the same functional contrasts. (Critically, replication attempts would help eliminate spurious findings from consideration and strengthen our beliefs in a subset of findings that have a real empirical basis.)

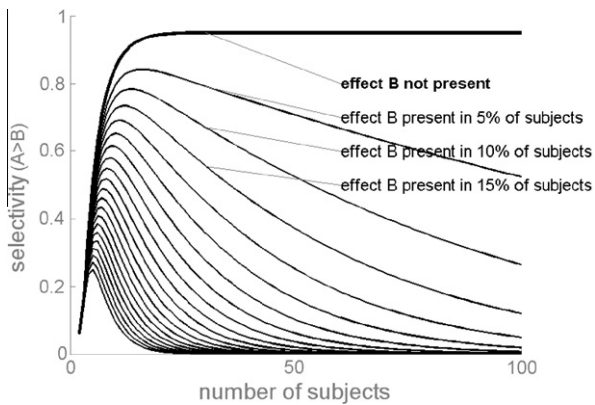


Fig. A1. Reduced selectivity with increasing number of subjects in the presence of inter-subject variability in the loci of activation. In this example we computed the selectivity (Eq. (2)) to detect an effect A (with $\delta_A = 1$, and $\alpha = .05$) against a second effect B, when the effect B is not present (thick top line), as well as when the effect B is present only in a small proportion of subjects (thin lines) due to “leakage” from nearby areas in the presence of inter-subject variability in the loci of activation.

cognitive operations (e.g., Blumstein, 2009). If so, we will find stronger evidence of such multi-functionality and will be able to better characterize it by examining overlap effects at the individual-subject level. It is also possible, however, that stunning functional specificity has simply remained hidden in previous studies. If so, the approach advocated here stands a good chance of finding it.

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Appendix A. The relationship between sample size and selectivity

In the presence of inter-subject variability in the loci of activation, effect B might be present within a group-level ROI for a small proportion of subjects (due to “leakage” from nearby regions where effect B could be present). In these cases *selectivity* takes the general form:

$$S = \beta_A \cdot (1 - \beta_B) = T(\delta_A \cdot n^{1/2} + T^{-1}(\alpha)) \cdot (1 - T(\delta_B \cdot n^{1/2} + T^{-1}(\alpha))) \quad (2)$$

where β_B represents the sensitivity (power) to detect the effect B at the same false level α , δ_A and δ_B are the signal-to-noise ratios of the effects A and B, respectively, within the ROI, and T represents the cumulative distribution function of the t -statistic. Eq. (2) reduces to Eq. (1) (see Section 1.3) when effect B is not present within the ROI voxels (when considering $\delta_B = 0$, leading to $\beta_B = \alpha_B$). Even when effect B is present in a small proportion of subjects its effect on selectivity can be quite marked (see Fig. A1), and it typically leads to decreasing levels of selectivity with increasing number of subjects (because the group-level analyses will now find a population-level significant effect B at voxels where only a small proportion of subjects truly show this effect).

Appendix B. Functional group-level partitions

See Fig. B1.

Appendix C

See Fig. C1.

Functional group-level partitions

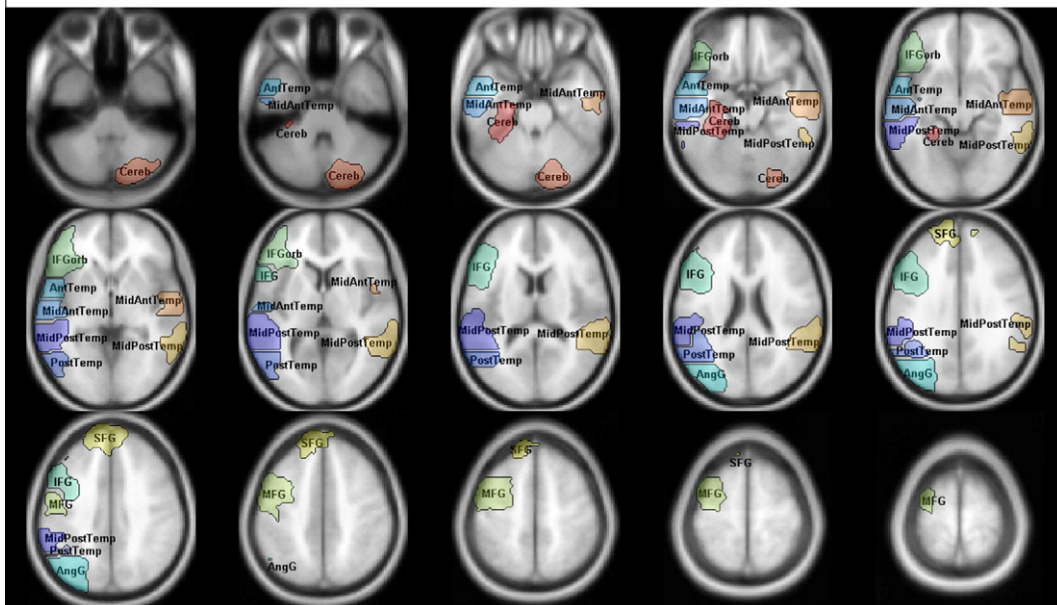


Fig. B1. Functional group-level partitions that are used to constrain the selection of subject-specific voxels in the GSS fROI method.

Effect size comparisons between GSS fROIs and the ROIs defined around the syntactic activation peaks from a number of previously published studies that fell within the borders of the corresponding group-level partitions.

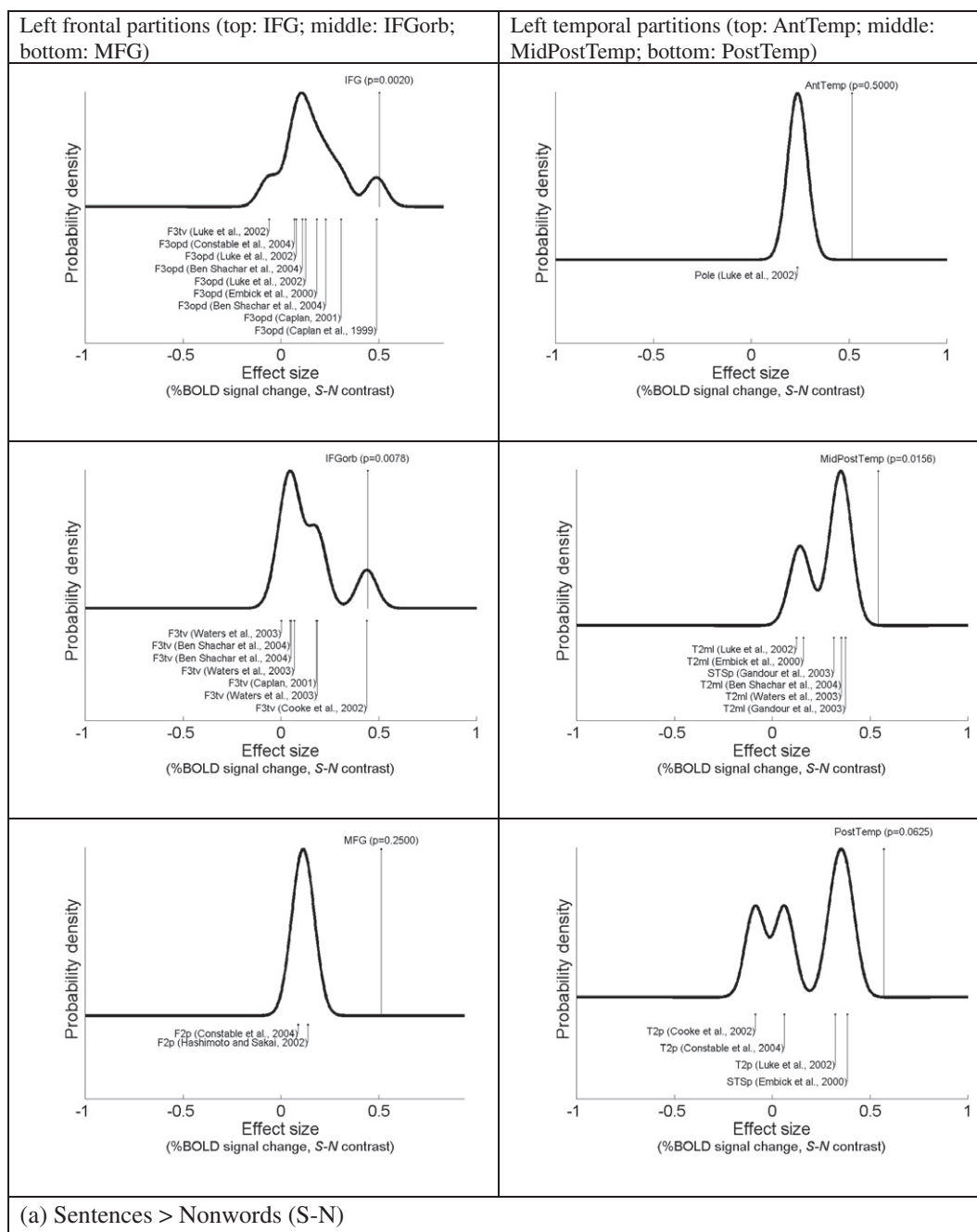


Fig. C1. Effect size comparisons between GSS fROIs and the ROIs defined around the syntactic activation peaks from a number of previously published studies that fell within the borders of the corresponding group-level partitions. The effect sizes for peak-defined ROIs are shown with arrows in the lower part of each plot. For each peak-defined ROI we provide information on the study where the peak was reported, and, for completeness, the cluster to which the peak was assigned in Vigneau et al.'s (2006) clustering analysis (e.g., F2p; see Vigneau et al., for details). For ease of visualization of the differences between average effect sizes for peak-defined ROIs and GSS fROIs for each partition and for each contrast, smoothed probability density plots were generated using kernel density estimation (Parzen, 1962) with bandwidth .05% BOLD signal change (the bandwidth parameter is comparable to the “bin-width” parameter in the more common histogram plots and controls the amount of smoothing). The effect sizes for the GSS fROIs are shown with the arrow in the upper part of each plot.

Appendix D. An initial exploration of factors that plausibly affect variability in selectivity among the different language-sensitive brain regions

We here consider two factors that plausibly affect the degree of selectivity of our language-sensitive regions: (1) functional stability of a region, and (2) size of a region. With respect to both factors,

we focus on our main contrast: sentences > nonwords. Also, although we are mostly interested in the variability in selectivity among the GSS fROIs, we consider group-level fROIs (investigated in Section 3.2) because some factors may differentially affect selectivity for these two kinds of fROIs. In this way, we expect to dissociate differences in selectivity among fROIs from differences in selectivity among methods.

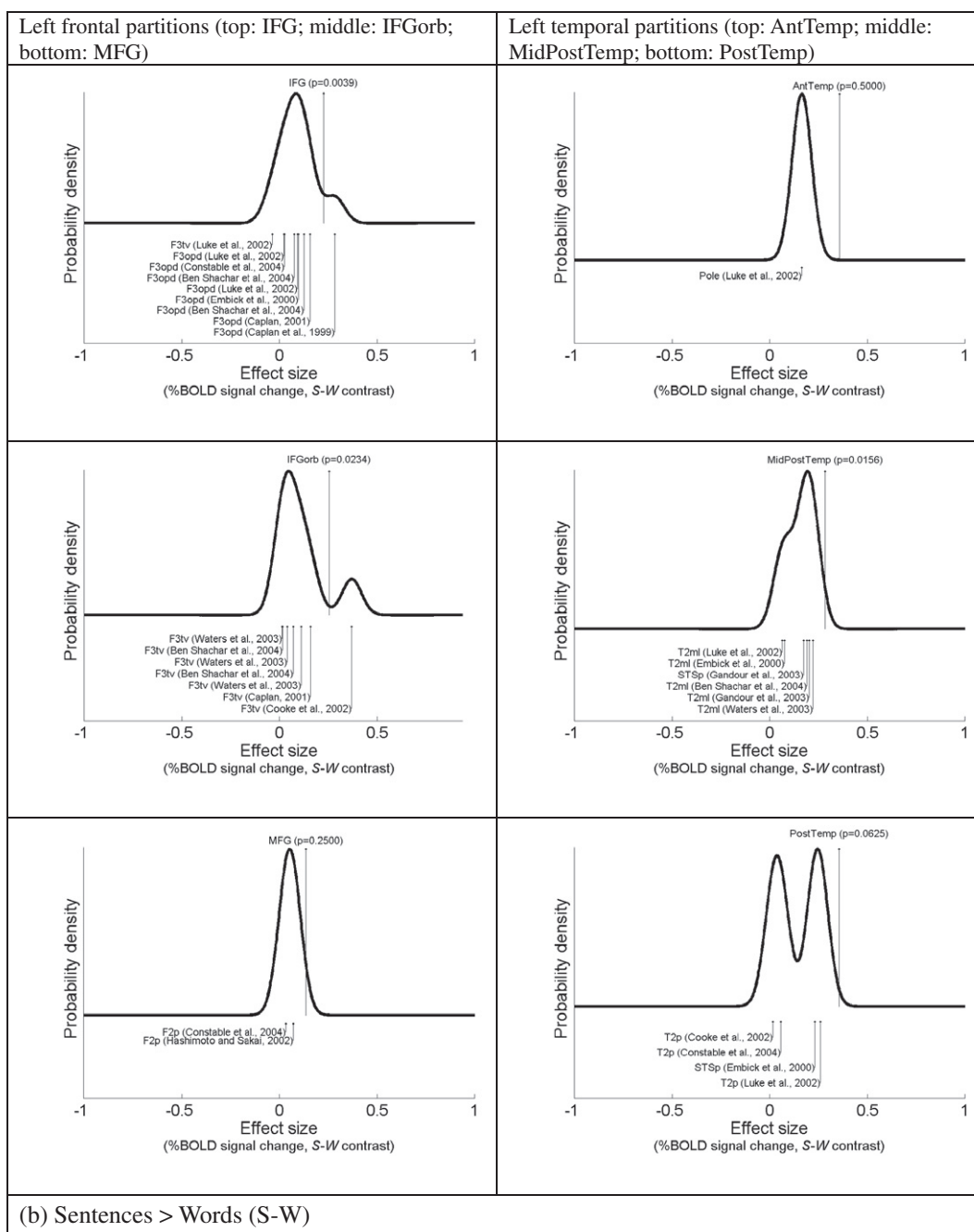


Fig. C1 (continued)

D.1. Functional stability

To estimate functional stability within a region, we computed correlation values across all voxels in each functional partition between odd and even runs (for the sentences minus nonwords contrast) (Fedorenko et al., 2010). For each region, we averaged these values across subjects. Functional stability in the patterns of differential response within a region can be expected to relate to the degree of selectivity within this region. In particular, if the selectivity of a region is low, the patterns of differential response can be expected to be weaker and also show reduced functional stability (either because of true differences in the loci of differential responses, or because of higher relative contributions of noise sources compared to these weaker differential effects).

Furthermore, regarding the selectivity of the different methods, because the GSS method relies on the ability to consistently detect subject-specific loci of activation we are interested in determining whether the improvements in selectivity of the GSS method are limited to those areas showing high functional stability or extend to regions showing a wider range of functional stability values.

The associations between selectivity (indicated by S-N effect sizes) and functional stability (indicated by within-subject S-N spatial correlations) are shown in Fig. D1. Functional stability is a good predictor of the degree of selectivity among the different regions, when considering both GSS fROIs ($r = .85$, $T(10) = 5.11$, $p < .001$), as well as group-level fROIs ($r = .75$, $T(10) = 3.61$, $p = .005$). This finding corroborates our expectation that the functional stability of an area is strongly associated with its selectivity.

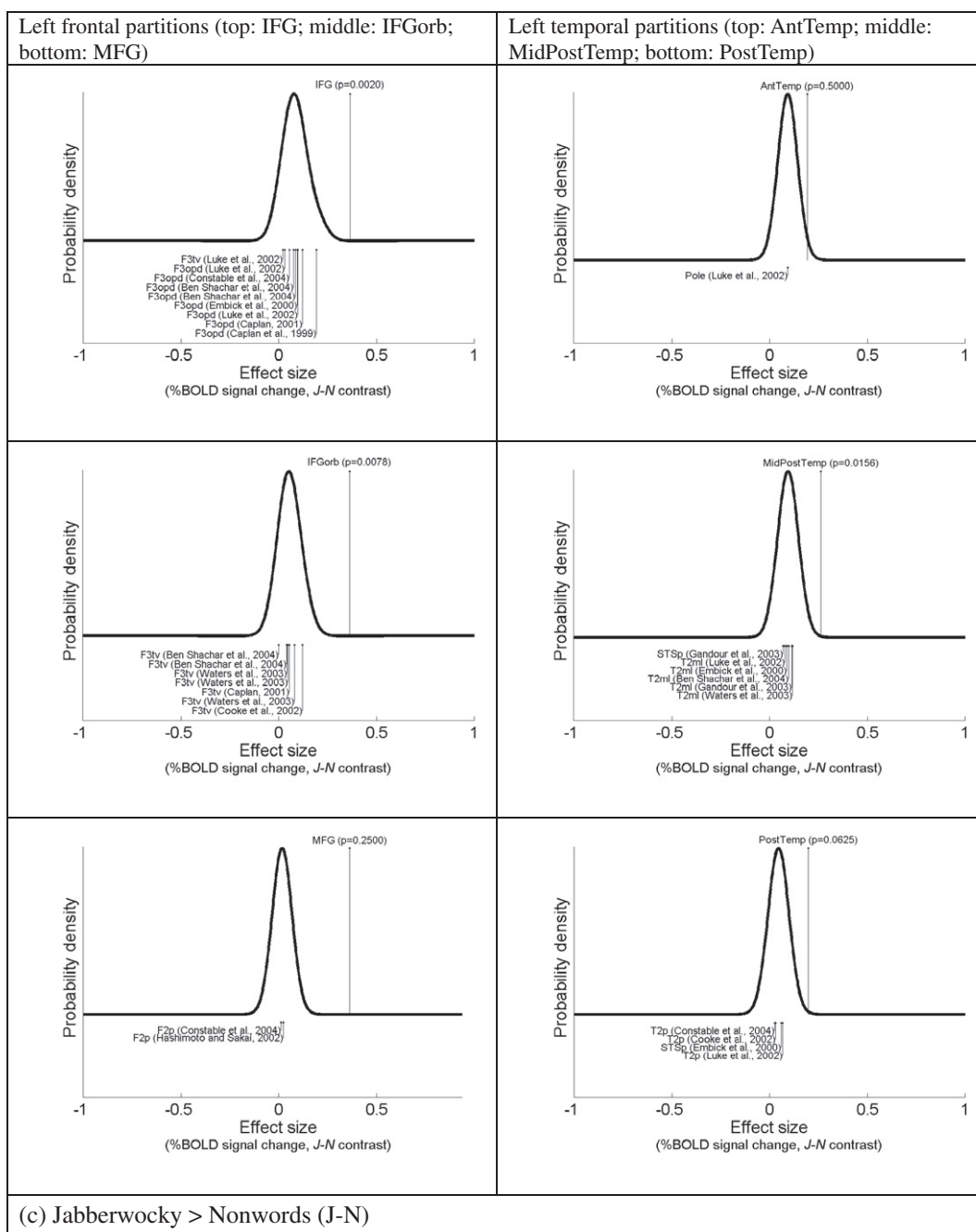


Fig. C1 (continued)

When considering the selectivity of the different methods, the improvements in selectivity when using GSS fROIs compared to group-level ROIs, while modulated by functional stability (ANCOVA effect of *functional stability*, $T(10) = 2.45$, $p = .034$), extend to the entire range of observed functional stability values (ANCOVA main effect of *method* controlled at the level of the minimum observed functional stability value (.24), $T(10) = 4.52$, $p = .001$). This finding is interesting because it indicates that, although the comparative improvements in selectivity of the GSS fROI method are *more marked* for those areas showing high levels of functional stability, the improvements are manifested for a wide range of levels of functional stability. In particular, if there is a minimal level of functional stability necessary for the GSS fROI method to outperform the group-level fROI method, this minimal level is well below

the range of functional stability values observed in the current study (minimal level below .09, $p < .05$).

D.2. Size

When considering a set of regions of different sizes around a fixed anatomical location, Poldrack (2006) found an inverse association between ROI size and selectivity. To our knowledge, it is not known whether this association extends to comparisons among different areas. Investigations of possible associations between selectivity and ROI size can guide the definition of appropriate units of analyses that would offer maximal selectivity. Regarding the selectivity of the different methods, because the GSS method tends to produce on average smaller ROIs in our sample than the

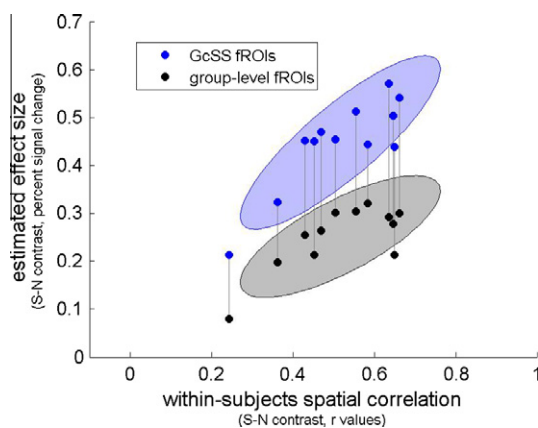


Fig. D1. Functional stability (estimated using within-subject spatial correlations) as a predictor of variability in the selectivity of the different language-sensitive regions.

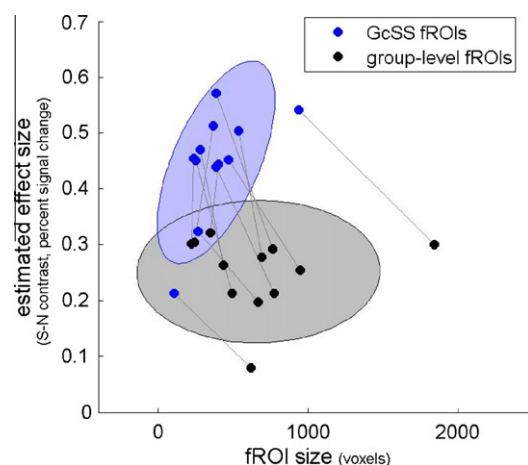


Fig. D2. Size as a predictor of variability in the selectivity of the different language-sensitive regions.

group-level method we are interested in determining if the improvements in selectivity of the GSS method are in some way related to the decrease in ROI size (when comparing the selectivity of the same regions).

The associations between selectivity and ROI size are shown in Fig. D2. When considering the selectivity of different regions, ROI size was positively associated with selectivity for GSS fROIs ($r = .75$, $T(10) = 3.61$, $p = .005$) but not for group-level fROIs ($r = .02$, $T(10) = 0.05$, $p = .96$). This finding could indicate a true association between ROI size and selectivity (across the language-sensitive regions) that is revealed by the GSS fROI method. Alternatively, it could indicate a selectivity dependency of the GSS fROI method that would result in selectivity improvements only for large ROIs (although this possibility is not supported by the additional between-method comparisons below). Further analyses and replications would be needed to better characterize the nature of this association.

When considering the selectivity of the different methods, the improvements in selectivity when using GSS fROIs compared to group-level ROIs were only marginally associated with the corresponding decreases in ROI size ($r = -.25$, $T(10) = -0.83$, $p = 0.43$). The associations were weakly negative indicating that while the improvements might be partially related to the associated decreases in ROI size (ROI size decreased on average from 670 voxels

in group-level fROIs to 380 voxels in GSS fROIs), in agreement with Poldrack (2006), this effect does not fully account for the observed improvements in the GSS fROIs selectivity (only 6% of the variance in selectivity values is explained by the reduction in ROI sizes). In addition, improvements in selectivity were only weakly modulated by baseline group-level ROI size (ANCOVA effect of ROI size, $T(10) = 1.34$, $p = .21$), or by target GSS ROI size (ANCOVA effect of ROI size, $T(10) = 1.63$, $p = .13$), and they extended to the entire range of observed ROI size values (ANCOVA main effect of method controlled at the level of the minimum observed ROI size value (103 voxels), $T(10) = 7.12$, $p < .001$). These results indicate that the GSS fROI method outperforms the group-level fROI method for the entire range of observed ROI sizes. In addition they indicate that the improvements in selectivity, when comparing the two methods, are only weakly modulated by ROI size. This suggests that the observed association between ROI size and selectivity for the GSS fROIs does not result from a possible better performance of this method for large ROIs (cf. we could expect better performance for small ROIs due to the relatively larger effect of inter-subject variability in the loci of activation in these cases), but rather could be a true association for these regions that is revealed by the GSS fROI method but not apparent when using group-level fROIs.

Given how important selectivity of different brain regions is for understanding the neural architecture underlying human cognition, future work may be aimed at (a) investigating these factors further with respect to language-sensitive regions by examining other linguistic and non-linguistic contrasts, (b) investigating the generalizability of these factors by examining their effects on selectivity of regions in other domains, and (c) exploring other factors that may affect selectivity, such as location or spatial variability across subjects.

Appendix E

E.1. Quantifying the overlap between BAs 44/45 and our IFG fROIs

In order to quantify the amount of overlap between the two anatomical ROIs used in Section 3.3 (BA44, BA45), on the one hand, and two of our fROIs located in/around the left IFG (Left IFG, Left IFGorb), on the other hand, we computed the probability of each of the two fROIs falling within the borders of either BA44 or BA45, as described in Section 3.3. For completeness, we computed these values for both (a) GSS fROIs, and (b) group-level fROIs (used in Section 3.2). For GSS fROIs, the probability was computed for each subject's fROI and then the values were averaged. The results are presented in Table E1.

Appendix F

F.1. Response profiles of BA 44 and BA 45 with respect to the four conditions

We here present the responses to the four conditions in our dataset (sentences, words, jabberwocky and nonwords) in the

Table E1
Estimates of the probability that our functional ROIs (Left IFG and Left IFGorb) fall within BA44 vs. BA45.

fROI	P of being within	
	BA44	BA45
Left IFG (GSS)	.19 (.01)	.16 (.02)
Left IFGorb (GSS)	.01 (.002)	.08 (.01)
Left IFG (group-level)	.23	.19
Left IFGorb (group-level)	.02	.12

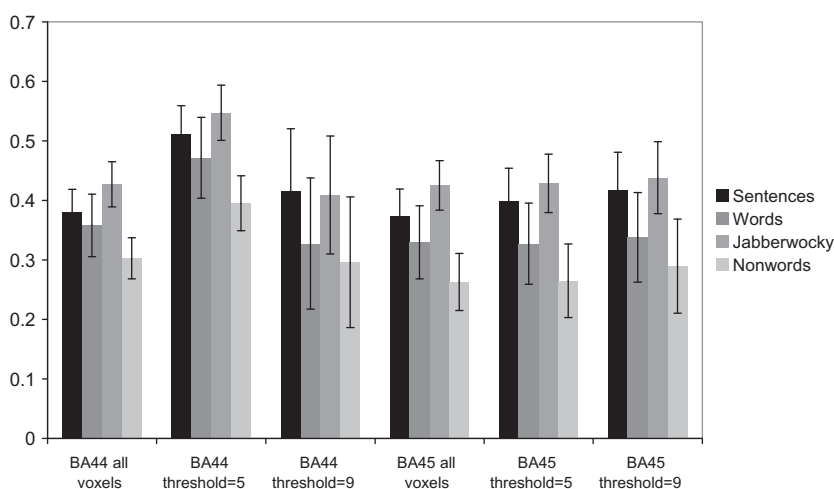


Fig. F1. Responses of BAs 44 and 45 to the four conditions in our dataset, using different threshold levels to define the ROIs. Error bars represent standard errors of the mean, computed across subjects.

Table G1

Effect sizes for the GSS fROIs.

fROI	Sentences > nonwords	Sentences > words	Jaberwocky > nonwords
Left frontal regions			
IFG	1.43	0.75	1.30
IFGorb	1.81	0.81	1.22
MFG	1.21	0.40	1.49
SFG	1.05	0.76	0.69
Left posterior regions			
AntTemp	1.50	1.20	1.00
MidAntTemp	1.91	1.28	1.23
MidPostTemp	1.92	1.20	1.45
PostTemp	2.16	1.32	0.60
AngG	1.29	0.55	0.69
Right posterior regions			
MidAntTemp	1.38	1.41	0.63
MidPostTemp	1.69	0.77	1.19
Cerebellar regions			
Right Cereb	1.53	0.49	1.05
Left Cereb	0.96	0.57	0.40

Table G2

Effect sizes for the peak-defined ROIs (syntactic peaks from Vigneau et al., 2006) [Results section 3.1].

fROI	Sentences > nonwords	Sentences > words	Jaberwocky > nonwords
ROIs for peaks within the IFG partition			
Ben-Shachar et al. (2004) F3opd	0.30	0.41	0.41
Ben-Shachar et al. (2004) F3opd	0.66	0.56	0.55
Caplan (2001) F3opd	0.97	0.57	0.69
Caplan et al. (1999) F3opd	1.22	0.85	0.74
Constable et al. (2004) F3opd	0.34	0.18	0.38
Embick et al. (2000) F3opd	0.60	0.49	0.46
Luke et al. (2002) F3opd	0.36	0.43	0.46
Luke et al. (2002) F3opd	0.36	0.12	0.24
Luke et al. (2002) F3tv	-0.14	-0.10	0.10
IFGorb			
Ben-Shachar et al. (2004) F3tv	0.31	0.60	0.01
Ben-Shachar et al. (2004) F3tv	0.24	0.15	0.33
Caplan (2001) F3tv	0.68	0.78	0.27
Cooke et al., 2002 F3tv	0.84	0.86	0.38
Waters et al. (2003) F3tv	0.32	0.21	0.24
Waters et al. (2003) F3tv	0.01	0.08	0.31
Waters et al. (2003) F3tv	0.68	0.45	0.51
MFG			
Constable et al. (2004) F2p	0.41	0.21	0.11
Hashimoto and Sakai (2002) F2p	0.43	0.32	0.21
AntTemp			
Luke et al. (2002) Pole	1.23	0.84	0.60
MidPostTemp			
Gandour et al. (2003) STSp	0.87	0.89	0.51
Ben-Shachar et al. (2004) T2 ml	1.79	1.55	0.76
Embick et al. (2000) T2 ml	0.62	0.49	0.49
Gandour et al. (2003) T2 ml	1.53	1.16	0.77
Luke et al. (2002) T2 ml	0.52	0.34	0.44
Waters et al. (2003) T2 ml	1.61	1.37	0.64
PostTemp			
Embick et al. (2000) STSp	0.88	0.96	0.31
Constable et al. (2004) T2p	0.35	0.48	0.20
Cooke et al. (2002) T2p	-0.31	0.11	0.17
Luke et al. (2002) T2p	0.87	1.14	0.39

Table G3

Effect sizes for the group-level fROIs [Results section 3.2].

	fROI	Sentences > nonwords	Sentences > words	Jabberwocky > nonwords
Left frontal regions	IFG	1.05	0.41	1.07
	IFGorb	1.10	0.70	1.05
	MFG	0.84	0.33	1.12
	SFG	0.79	0.56	0.64
Left posterior regions	AntTemp	1.01	0.76	0.67
	MidAntTemp	1.26	0.64	0.76
	MidPostTemp	2.05	0.86	1.69
	PostTemp	1.18	0.76	0.83
	AngG	0.94	0.57	0.38
Right posterior regions	MidAntTemp	1.07	0.83	0.45
	MidPostTemp	1.44	0.56	1.12
Cerebellar regions	Right Cereb	1.36	0.44	1.23
	Left Cereb	0.59	0.37	0.44

Table G4

Effect sizes for the anatomical group-level ROIs and for individually defined fROIs using the probabilistic cytoarchitectonic maps to constrain the selection of voxels in individual subjects [Results section 3.3].

	fROI	Sentences > nonwords	Sentences > words	Jabberwocky > nonwords
Anatomically defined group-level ROIs	BA 44 all voxels	0.51	0.13	0.81
	BA 45 all voxels	0.55	0.22	0.84
	BA 44 high-overlap voxels	0.53	0.30	0.56
	BA 45 high-overlap voxels	0.35	0.30	0.32
Subject-specific fROIs (BA maps are used to constrain the selection of individual voxels)	BA 44	1.44	0.73	1.25
	BA 45	1.59	0.80	1.17

two anatomical ROIs used in Section 3.3 (BA 44 and BA 45). We performed the extraction using three different thresholds in the probabilistic maps for each BA: (a) all the voxels in each map, (b) only the voxels that are present in five out of ten brains, and (c) only the voxels that are present in nine out of ten brains (highest-overlap voxels). If either or both of these areas support syntactic processing, then they should show a higher response to sentences than to words, and a higher response to jabberwocky than to nonwords. The results are presented in Fig. F1.

For the jabberwocky > nonwords contrast, consistent with these regions' engagement in syntactic processing, we see significant effects in BA 45 at all three thresholds (p -values: <.001, <.005, and <.01), and in BA44 at the two more liberal thresholds (p -values: <.001, <.005, n.s.). However, for the sentences > words contrast there are no significant effects at any threshold for either BA.¹¹ Without a reliably higher response to sentences than to words, it is difficult to interpret the effect observed for the jabberwocky > nonwords contrast. Even the reliable effects for the former contrast are small, and overall, the conditions are not well differentiated.

The lack of a reliable difference between the sentences and the words conditions is surprising given that (1) this is a large contrast (cf. contrasts between syntactically complex and syntactically simpler sentences used in the previous studies), (2) the sample size is relatively large ($n = 25$), and (3) these regions are among the prime candidates for syntactic processing. Based on these data, one would be hard pressed to argue for the role of these regions in syntactic processing, leave alone some narrow aspect of syntax (e.g.,

Grodzinsky & Santi, 2008). However, it is not the case that we think that these regions play no role in syntactic processing. Rather these results underscore, once again, the importance of using subject-specific functional ROIs instead of standard group ROIs that are the same across subjects. As reported in Section 3.3, both of the GSS fROIs in the left IFG (as well as subject-specific fROIs defined by intersecting the BA maps with individual activation maps) strongly differentiate between the sentences and the words conditions. This suggests that the analyses reported here underestimate selectivity (plausibly for the reasons discussed throughout the paper), and are therefore not optimal for addressing questions of the functional architecture of the language system.

Appendix G

G.1. Standardized effect sizes for all the ROIs discussed in the paper

See Tables G1–G4.

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¹¹ It is worth noting that the fact that these BAs do not show dissociable functional profiles with respect to this set of conditions does not mean that it is not possible to obtain such a dissociation in principle. In fact, several published papers report dissociations between activations observed in BAs 44 vs. 45 (e.g., Binkofski et al., 2000; Horwitz et al., 2003; Heim et al., 2005; Santi & Grodzinsky, 2007; Heim et al., 2009).

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