The Picture of the Linguistic Brain: How Sharp Can It Be? Reply to Fedorenko & Kanwisher

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Abstract

What is the best way to learn how the brain analyzes linguistic input? Two popular methods have attempted to segregate and localize linguistic processes: analyses of language deficits subsequent to (mostly focal) brain disease and functional Magnetic Resonance Imaging (fMRI) in health. A recent *Compass* article by Fedorenko and Kanwisher (FK, 2009) observes that these methods group together data from many individuals through methods that rely on variable anatomical landmarks and that results in a murky picture of how language is represented in the brain. To get around the variability problem, FK propose to import into neurolinguistics a method that has been successfully used in vision research – one that locates functional Regions Of Interest (fROIs) in each individual brain. In this note, I propose an alternative perspective. I first take issue with FK's reading of the literature. I point out that, when the neurolinguistic landscape is examined with the right linguistic spectacles, the emerging picture – while intriguingly complex – is not murky, but rather, stable and clear, parsing the linguistic brain into functionally and anatomically coherent pieces. I then examine the potential value of the method that FK propose, in light of important micro-anatomical differences between language and high-level vision areas and conclude that as things stand the method they propose is not very likely to bear much fruit in neurolinguistic research.

1. Two Opposite Positions

Fedorenko and Kanwisher (2009; FK henceforth) have recently made a new methodological proposal for the neuroimaging of language: disappointed at the murky picture they see emerging from neurolinguistic studies and aware of individual variation that is said to permeate the neuropsychology of language, they rely on successful insights from vision and propose a new method to improve the anatomical resolution at which language can be partitioned into its neural component parts. At issue is the right method to detect effects in the brain through fMRI. Neurolinguistic studies typically use two analytic approaches, one based on Whole Brain Volume (WBV) search and the other on anatomical Region Of Interest (aROI) search. WBV sets up a stimulus contrast (e.g., between two sentences, or two words with different properties), builds an image of the brain's activity for each stimulus type, and searches for regions where the brain's response to one stimulus type is stronger than to the other. This method charts activation levels for every single brain voxel (the little cubical volume units into which the brain image is divided) in a quest for regions that evince differential signal intensity for the different stimulus types. This search is exhaustive, but also costly: as activation levels are repeatedly compared across the multitude of brain voxels, the results must be corrected for possible error due to multiple statistical comparisons.[1] Corrections reduce statistical power which, according to FK, threatens to render real effects undetectable.

The second common method, aROI, limits the search space to the relevant brain parts, in order to minimize repeated comparisons and subsequent corrections. For that, anatomical landmarks are used, and these vary across individuals. Current practices average results across subjects in group studies, and as individual brains vary, a resulting fuzzy picture should come as no surprise. These problems, FK argue, have brought neurolinguistics to a dead end, evident from a recent series of meta-analyses, which show that linguistic tasks activate large parts of the brain and that different aspects of language are not separable neurologically.

FK propose a fresh start through an alternative strategy: to begin the investigation by identifying pertinent *functional* (as opposed to anatomical) landmarks in each individual brain (functional Regions of Interest, fROIs henceforth), inside which further searches for structure can proceed. These fROIs abstract away from individual differences in brain anatomy, getting around the variability problem and solving much of the problem of reduced statistical power. FK's proposal, then, aims to get at the heart of the putative problem. It marks a departure from current practice and, as such, should be carefully examined.

As I see it, FK express their disappointment with the current state of affairs through 3 claims:

- Shifty Anatomy: The anatomical structure of the 'language' regions is shifty and varies greatly across individual brains.
- Variable Experimental Outcomes: Results of language experiments in focally brain-damaged aphasic patients and in fMRI with healthy adults are highly variable.
- Elusive Functional Anatomy of Language: we are unable to single out a brain region that is either necessary or sufficient for linguistic functioning, nor is there a brain region that is exclusively dedicated to language.

In other words, variable anatomy renders group analyses uninformative, which leads to variable outcomes of group studies.[2] In light of the gloomy picture they see, FK make a constructive proposal: use individual fROIs in neuroimaging studies of language as a way to sidestep variability and provide a clearer picture of brain/language relations. The fROI method would reliably localize the true functional regions of interest in each individual participant, from which the signal can then be extracted in its maximal intensity. The Kanwisher team pioneered the successful differentiation between important functional modules of higher human vision in fMRI (Kanwisher et al. 1997, *passim*) and so FK suggest to import this method into the study of language.

It is true that the anatomy of the main language regions is variable; certain empirical inconsistencies in the extant database may be spotted as well. It is important to realize, however, that the move FK propose is not the necessary conclusion, even on a pessimistic reading of the literature. In this note, I hope to provide arguments for an alternative perspective, suggesting the following:[3]

- Questionable Meta-Analyses: FK's analysis is based on problematic meta-analyses, which collapse disparate methods, materials, and contrasts are collapsed, and which contain functional distinctions that may not be expressed neurologically.
- Stable Functional Anatomy of Language: When tasks, stimuli and contrasts are held constant, a much clearer picture emerges, exhibiting robust and consistent linguistic effects across subjects, groups and studies in both the lesion and the imaging literatures.

- Constrained Anatomical Variation: The brain's language regions are anatomically variable alright; but this variability is neither boundless nor mysterious. For the language regions, it is encoded in cytoarchitectonic probability maps – the best currently available anatomical localization tool, which parcelates regions into smaller areas, while taking variability into account. We harness these maps to understand brain/language relations. No such cytoarchitectonic parcelation exists for the fusiform gyrus, the large brain region where the fROI approach has been used effectively.

These observations will lead to the suggestion that the fROI method is not presently appropriate to the study of brain/language relations.

2. Meta-analyses Present an Incoherent and Unstable Picture

The core of FK's empirical demonstration is formed by three meta-analyses (Ojemann 1991; Vigneau et al. 2006; Lindenberg et al. 2007). Vigneau et al. pool together reports that probed 'syntactic processing,' 'phonology' and 'semantics' and localize their peaks on a template brain.[4] The results are disappointing. Notably, activations resulting from 'sentence processing' tasks, once considered the core function of Broca's region, are spread all over the left hemisphere, and moreover overlap with those obtained in phonological and semantic tasks.

Lindenberg et al. are more focused anatomically. Concentrating on Broca's region, they analyze results of PET, fMRI and MEG studies of language, by grouping peaks of activation[5] obtained by frequently used linguistic tasks.[6] This meta-analysis revealed little structure in the designated region: it identifies three distinct activation clusters but does not distinguish between activation peaks of studies that tapped different functions. What has been celebrated as the central language region, then, appears to be multi-functional.

Finally, Ojemann (1991) studies the cerebral representation of naming skills in a large number of neurosurgical patients through intra-operative brain stimulation that blocks function. Hoping to localize naming, he finds it to be variable and spread out.

These surveys, together with inconsistencies in the production/comprehension performance contrast in Broca's and Wernicke's aphasia, indicate to FK that indeed, the cerebral representation of language is vastly distributed. Putting these disturbing results together with observations on the variable anatomy of the language regions, they conclude that current approaches have failed.

Should such gloomy conclusions be drawn? Perhaps, but we should ask whether FK's review can serve as a basis for it. The next section considers the possibility that the inconsistencies FK observe result from incorrect choices made by these meta-analyses. It raises two questions regarding these meta-analyses: Were the studies grouped together similar (section 3.I.)? Did they carve language mechanisms into neurologically relevant components (section 3.II.)?

3. Poor Choices and Uneven Comparisons: A Critique of the Meta-analyses

3.1. POOLING APPLES AND ORANGES TOGETHER

Language is complex and connects to big chunks of cognition. A careful meta-analysis must therefore group results of tests that are expected to be on a par, in order to compare their cortical localization. This cannot be said here: Vigneau et al. (2006) group experiments by linguistic 'level' (syntax, semantics, phonology) while ignoring the contrasts that

were employed. This is simply mistaken: regional fMRI activations are only interpretable if the *contrasts* between experimental conditions are considered – a contrast between a condition that features words and one that features silence is obviously different from a contrast between two word types, even though both contrasts contain words. A concrete example might help: Vigneau et al.'s sentence processing meta-analysis groups 'syntax' experiments. It considers a study syntactic if it contains sentence stimuli. Scott et al. (2000) and Ben-Shachar et al. (2004) used sentence stimuli and are therefore included. But an examination of the contrasts each employed reveals little similarity (Table 1):

It is difficult to see how these two studies can be related, because different goals dictated different contrasts: Scott et al. focused on speech and intelligibility, employing a 'natural sentences' condition and three others that were derived from it – one intelligible and 2 unintelligible (p. 2401). Their main contrast had to do with speech intelligibility, as they were interested in brain regions for speech, not syntax (indeed, no information on the syntactic properties of the sentence stimuli is provided). Ben-Shachar et al. (2004), by contrast, sought to localize subcomponents of syntax and compared natural auditory sentences in Hebrew that featured different word-order configurations. Their main contrast had to do with syntax, not speech (indeed, no information on the acoustic properties of the speech signal is provided). No perspective I am aware of would expect the results of these two studies to bear any systematic relation to one another, let alone be similar, because *in functional imaging, the results we interpret pertain to contrasts, not stimuli.*

A 'syntax experiment', then, is not one that contains stimuli that have a syntax but one that contains syntactic *contrasts*. As Table 1 shows, this dictum was not followed by Vigneau et al., which must have contributed to the fuzziness of the picture their meta-analysis produced. Other parts of this meta-analysis suffer from the same problem. And thus, if

Table 1. Conditions, stimuli, and main contrasts of two studies categorized as ''syntactic'' by Vigneau et al. (2006). Activations are different, but so are the contrasts.

	Condition	Example contrast	Resulting peaks
	Scott et al. 2000 experiment on speech intelligibility		
a.	Sp natural sentences	**a+b+c – d**	Left STG, left ST S
b.	VCo intelligible, vocoded speech		
c.	RSp Unintelligible, ''alien sounding,'' ''rotated'' speech, involving spectral inversion of the original speech	**a+b – c+d**	Right STG
d.	RVCo Unintelligible, noise-vocoded rotated speech, ''sounds like intermittent fluctuating static... not at all like speech''		
	Ben Shachar et al. 2004 experiment on word-order in syntax		
a.	Base form S V O_1 O_2 Dani gave the red book to the professor from Oxford	**b+c – a+d**	Left and right Heschl complex, Left and right STS
b.	Topicalized direct object O_1 S V_O_2 The red book Dani gave to the professor from Oxford		
c.	Topicalized indirect object O_2 S V O_1_ To the professor from Oxford Dani gave the red book		
d.	Dative shifted S V O_2 O_1 Dani gave to the professor from Oxford the red book		

functional distinctions are blurred, how can a clear and undistorted picture of the functional anatomy emerge?

Another meta-analysis FK discuss is Lindenberg et al.'s, who analyzed the results of 119 articles that used a variety of language tasks and looked for activations in an aROI that is defined by Amunts et al.'s 1999 cytoarchitectonically based definition of Broca's region. The studies that entered into the meta-analysis are not listed, most unfortunately. The details remain opaque and not much can be confidently asserted. Moreover, the absence of discussion of what constitutes a type of task that is included in the meta-analysis, and the rough description of the tasks, leaves one unsure about how exactly this meta-analysis was constructed.

The disappointing fuzziness FK see may thus be due to reasons other than theirs: *it is not the anatomy that is to blame, but the decision to group studies that make unrelated functional distinctions*. When studies that focus on disparate phenomena are glossed over, as seems the case in both Vigneau et al. and Lindenberg et al., need we wonder that the resulting peaks for phonology, syntax and semantics are vastly widespread (and overlapping)?

3.2. focusing on distinctions that may not have neurological relevance

Ojemann (1991) also obtained murky results from picture naming, concomitant to intra-operative brain stimulations, which are supposed to disrupt subjects' performance. Stimulations throughout large portions of the left hemispheres can disrupt naming. FK conclude that 'Some of this variability... plausibly has to do with the complexity of the task… However, any residual functional variability is an expected consequence of underlying anatomical variability' (p. 849). But this conclusion does not follow. The disrupted task may be related to language, but also, to much more: at the very least, successful naming requires scene analysis, and word-to-picture matching, in addition to word retrieval and production, as FK themselves acknowledge. Ojemann's naming map, then, hardly serves as relevant evidence for language-related variability in brain-representation, contrary to his widely publicized claim.[7]

4. An Alternative Picture: Stable Generalizations at a Fine-grained Syntactic Level

The great 19th Century neurologists and their followers used activities/modalities as basic functional units of language – production and comprehension, reading and writing, repetition and naming.[8] FK point out correctly that this division is not empirically justified, as language comprehension and production are not neurologically separable. This has indeed been recognized for over 30 years,[9] leading many to move away from the comprehension/production duo toward a more detailed and linguistically informed componential analysis of the neurology of language.

Newer approaches first focused on linguistic levels, redefining the language centers as cross-modally composed of syntax, semantics and phonology.[10] This redefinition led to new discoveries; but before long, empirical inconsistencies arose (e.g., Linebarger et al. 1983). For some, the conclusion was to give up generalization and focus on case studies (Caramazza 1986); others explored the possibility that the neurological components of language would be found through finer-grained analyses that require rather subtle linguistic distinctions.[11] This perspective bore fruit, in my view, first in aphasia and later in neuroimaging. As the neuroimaging literature – and most of FK's discussion – is concerned with the neural substrate of receptive mechanisms, I focus here on sentence comprehension.[12]

4.1. STABILITY IN APHASIA

Goodglass (1968) was the first to document a grammatically selective aphasic deficit in sentence reception. He discovered that in Broca's aphasia, comprehension accuracy of semantically reversible passive sentences was lower than the (near-normal) comprehension of actives. Caramazza and Zurif (1976) then found a similar deficit for certain types of relative clauses, a result that has withstood multiple replications and extensions. Increasingly refined research methods enriched the database to comprehension scores on varieties of construction types in languages as varied as Chinese, Japanese, Korean, Hebrew, Spanish, English, Dutch and German and in various tasks.[13] Timed tasks led to convergent results.[14] Details aside, it is quite clear today that the sentence-level deficit in at least Broca's aphasia – and with it our view of the functions of Broca's region – is highly selective and that its description must include syntactic variables. Relative clauses have figured rather centrally in this collective research project, so let me zoom in on these. Consider the following array, that lends itself to a two-dimensional factorial design, pitting site of Movement (or Canonicity) and place of Embedding as factors. It has been repeatedly used in aphasia comprehension experiments:

Studies with aphasic patients are logistically hard to conduct, and the number of patients per study is typically small. Fortunately, multiple experiments have used the array in Table 2 with clinically diagnosed Broca's aphasics, creating a rich database through repeated testing with the same comprehension task (binary-choice, 'who-did-what-to-whom', sentence-to-picture matching) and with stimuli that have similar properties – depicted scenes, from which all semantic and contextual cues are removed.[15] Drai and Grodzinsky (2006) reanalyzed these studies to obtain a broader quantitative view. Our analysis may thus be usefully compared to the meta-analyses FK reviewed.

We only used studies that report raw individual patient scores, so that these could be analyzed directly (and secondary meta-analyses could thereby be avoided). Our 2 × 2 factorial design let us test (i) how much variability there is between patients and (ii) whether despite noise, structure can be discerned in these data along any of the dimensions (i.e., columns and rows in Table 2). Studies included did not always feature the same number of trials per condition, and so we represented each patient's score as a 99% Confidence Interval (CI, $p < 0.01$) on his/her mean (% correct), as visualized in Figure 1.

Figure 1A shows that patients' scores on both Center Embedded and Right Branching constructions are highly variable and that the Embedding contrast (rows of Table 2) fails to distinguish between the two types, as both red (Center Embedding) and black (Right Branching) lines display a similar random pattern. This failure is confirmed by group statistics. Should we conclude that no syntactic distinctions are found for these patients'

Table 2. A factorial design in which 2 dimensions are manipulated: Movement site or ±Canonicity in the columns (where Movement, depicted by the link, is either from subject or from object position of the blue relative clause), and place of Embedding (the position of the relative – Center Embedding vs. Right Branching) in the rows.

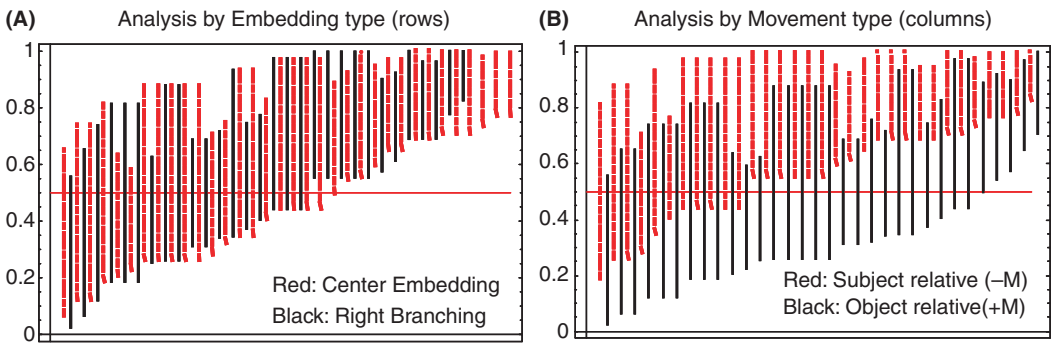|	Movement from Subject ('canonical' word-order)	Movement from Subject ('non-Canonical' word-order)
CE	I. The boy [who _ is chasing the tall girl] is Dan	II. The boy [who the tall girl is chasing __] is Dan
RB	III. Dan is the boy [who __ is chasing the tall girl]	IV. Dan is the boy [who the tall girl is chasing __]

Fig 1. Comprehension performance of Broca's aphasic patients on Center embedding vs. Right ranching relative clauses (n = 32). Each full black or perforated red line represents a p<.01 confidence interval on a single patient's performance on a given sentence type, on a 0-1 proportion-correct scale. A long line implies a case with few trials (hence a broad CI); a short line implies many trials. A horizontal red line marks chance level; if crossed by a CI, chance performance cannot be ruled out (Drai & Grodzinsky, 2006). A. A test of the hypothesis that Embedding position (a k a sentence complexity) matters for comprehension performance in Broca's aphasia failed to discern structure. B. A test of the hypothesis that position of extraction (Movement site) matters for comprehension performance discerned clear structure (adapted from Drai & Grodzinsky, 2006).

performances and that Broca's region evinces no 'pure' distinction at the syntactic level? That would be hasty, for Figure 1B presents a very different picture. It displays the same performance scores, but this time, partitioned along the columns of Table 2 (the ±Movement contrast). It is easy to see that (i) individual variation is smaller in each column (=color), as most individuals are above chance in the subject-extracted sentences (red), and at chance on object-extraction (black, +Movement) and (ii) the Movement dimension distinguishes performances, as Performance$_{+Movement}$ < Performance$_{-Movement}$. Group statistics show a highly significant difference. You may pick your favorite explanation for these results, and yet the punch line of this exercise remains the same: *the brain makes very fine linguistic distinctions, exhibiting robust structure at the group level, but only when appropriate units of analysis are used.*

Drai and I have given the same treatment to other contrasts that were repeatedly tested in several languages with 69 Broca's aphasic patients and obtained similar results. Here, I restricted myself to the relative clause illustration, for the sake of clarity and brevity.

Convergent cross-methodological results are also available: classical Cross-Modal-Lexical-Priming studies have been conducted on many parts of the array in Table 2, with healthy and aphasic adults. Healthy subjects show priming for the filler at the gap: e.g., on hearing sentence IV (*Dan is **the boy**$_{filler}$ *1 who the tall girl is *2 chasing __ gap*3*) and being asked to make a lexical decision on a word related to *the boy*, they show priming (relative to an unrelated word) if asked to make the judgment at point *1, priming is diminished at *2, but revived in *3 (Nicol and Swinney 1989). This pattern, taken to indicate that a displaced constituent (*filler*) is re-activated at its *gap*, is not observed in Broca's aphasic patients.[16] A real-time processing perspective, then, further underscores the involvement of Broca's region, lending further support and coherence to the picture from comprehension.

This presentation is far from full-proof: while clear regularities in the performance of Broca's aphasic patients are identified, similar work with other patient groups who suffer other lesion types awaits to be done. Moreover, lesion size, shape and position are obviously not within the experimenter's control, and with the possibility

of physiological and cognitive compensatory mechanisms, many unknowns are still out there to be discovered. And so, while extant data do not let us conclude that we've spotted the sole and precise locus of syntactic movement, the striking regularity above is no small matter, strongly suggesting that *even relatively gross stroke-induced lesions display functional specificity of a kind that the meta-analyses which FK reviewed completely missed*. I think that such regularity calls for an explanation, invites further exploration and shouldn't be ignored.

4.2. STABILITY IN FMRI

A related approach has been taken with fMRI in health. Similar to aphasia, early imaging studies of sentence comprehension used subject/object pairs of relative clauses and found activations in left Broca's region.[17] These contrasts (and others related to them) have been used in several recent studies. Activations in Broca's region and in Wernicke's region (bilaterally in some cases) are consistently found.[18] The regularity demonstrated by these recent works speaks to FK's quest for more statistical power through the fROI method: these group studies produced effects through whole-brain volume (WBV) searches, which in many cases were sufficiently robust to survive corrections for multiple statistical comparisons. Importantly, these studies used sentence stimuli whose duration ($\sim$3–6 s) is longer than the typical vision stimuli (<1 s) and hence noisier. Note that the contrasts in many of these experiments touch on subtle linguistic distinctions, which may also hinder robustness in the fMRI signal. Nevertheless, clear effects are obtained, seemingly holding across modalities, tasks, materials and analytic methods[19] and are strong enough to create a reasonably clear picture. In fact, this group of studies is one of the few which did cluster nicely in Vigneau et al.'s meta-analysis.

Though parts of Table 2 were tested in fMRI, the complete array was not explored until recently. Andrea Santi employed an adaptation paradigm, with a design that followed the footsteps of Kourtzi and Kanwisher (2001) study of object identification (Santi and Grodzinsky in press). The result: the anterior part of Broca's region (Brodmann's 45) adapts to Movement, but not Branching location; its posterior part (Brodmann's 44) and what can roughly be called Wernicke's region adapt to both factors; and interestingly, no brain region adapts to Embedding location along. These results – and their striking consistency with the picture from aphasia – suggest an even more specific perspective, with functional subdivisions *within* Broca's region.

The picture for the language regions, then, is intriguingly complicated, but far from gloomy. A class of regularities (which I hope can be understood) is observed, and these seem to manifest a degree of linguistic finesse that should be looked at carefully.

There seems to be an additional lesson here: if that is how seriously our brain respects grammatical distinctions, how can we expect regularity to emanate from meta-analyses that attempt to localize activations for gross distinctions such as 'phonology, semantics, syntax, lip reading, finger movement, working memory' (Lindenberg et al. 2007)'? In light of what we have seen, a positive result in such meta-analyses – a regular relation between these arbitrarily lumped tasks and anatomical location – would be quite surprising.

As I see it, the excitement about the discovery of the Fusiform Face Area (FFA, Kanwisher et al. 1997; *passim*) arose precisely because it broke high-level vision into category-specific, ecologically coherent components, showing that the brain respects functional distinctions that are finer than mere object recognition (Malach et al. 1995). Similarly, if language processing has coherent neurological underpinnings, as everyone

seems to agree, it is hard to see how these can be discovered without a detailed compo-nential analysis of language. Yet, FK are silent on the model that guides their exploration. A perceptual analogue to their discussion of language might thus be the perception of scenes of any kind – landscapes, houses, faces, car races and parades – surely the opposite from what they intend.

5. Navigating the Linguistic Brain with Maps and Atlases

5.1. BRAIN TOPOGRAPHY AND CYTOARCHITECTURE

FK attribute the instability of neurolinguistic results to anatomical variability in the language regions. We should see how variable the anatomy actually is and whether what we know about it is useful. A quick tour of neuroanatomical problems and methods might help.

The quest for methods to parcelate cortex began in the 19th century, with the hope of finding structure in cortical tissue that would be physiologically relevant (Amunts and Zilles 2006). Realizing the limitations of topographic parcelation visible to the naked eye, anatomists turned to microscopic analyses of cortical slices, in search of structure. Micro-scopic observations focused on 'cytoarchitecture': cell morphology and packing-density, and the character of the laminar structure of cortex. Cytoarchitectonic regularity was seen across small regions, terminating abruptly. Points of sudden change in pattern were called cytoarchitectonic borders. Correlations between cytoarchitectonic patterns and myelina-tion patterns seen in white matter (through observations on the myelin sheath of neurons) further supported the cytoarchitectonic approach, as Brodmann (1908/2006) recalled in a historical review.

Brodmann's implicit hypothesis was that cytoarchitecture reflects connectivity patterns, which in turn determine function (Amunts and Zilles 2006). On this view, cytoarchitec-tonic borders demarcate the end of one functional unit and the beginning of another. As the cytoarchitectonic approach suggest anatomical modularity, it should be quite relevant to modular perspectives on cognition: once cytoarchitectonic borders are found, correla-tions between the areas they delimit and function are expected. Moreover, cytoarchitec-tonic borders correlate with those marked by (recently developed) receptor architectonic mapping techniques, which chart the cortical distribution of different neurotransmitter receptors (a likely functional index).[20] Cytoarchitectonic borders therefore seem to be good candidates for functional parcelation of cortical tissue.

When moving to MRI, this type of map carries a practical problem: the resolution of current MRI technology is not sufficient for the identification of cytoarchitectonic bor-ders in a regular brain image. These borders can only be identified on actual, dissected brains (and that through intense effort). A blob on an MR image can thus only be local-ized by visual inspection of the brain's topography, as revealed by those macrostructural landmarks evident in an image (sulci and gyri). But as these do not correlate with the cytoarchitecture, how do we get around the individual variation problem?

Talairach and Tournoux's (1988) brain atlas proposed an interesting solution. It estab-lished a coordinate system that helps normalize every brain to a common topographic reference space. However, aware of the limitations of topography, and the importance of cytoarchitectonic borders, Talairach & Tournoux encoded Brodmann's (1909) map, which parcelates cortex into 43 distinct areas, into their atlas, by projecting his cytoarchitectonic borders onto their reference space (Zilles and Amunts 2010). Each voxel could now be identified by its 3D coordinates and their associated 'Brodmann Area' (BA). Brodmann's

long-forgotten map was thus revived, as Talairach & Tournoux's atlas became a major reference for the MR imaging community, which started using it for functional localization.

5.2. CYTOARCHITECTONIC VARIABILITY AND PROBABILITY MAPS

This usage was somewhat naïve. Early mappers believed that pointing to a BA number really localized their clusters. Some were unaware that Brodmann had likely mapped only one hemisphere of one human brain, as part of his herculean cross-species cytoarchitectonic brain mapping effort.[21] Others did not know that Brodmann's Areas were projected onto the *surface* of Talairach's brain, while two-thirds of cortex are hidden inside sulci.

Present day anatomical projects – topographic, cytoarchitectonic and receptor-based – attempt to correct these errors. They analyze multiple brains, thanks to ideas, technologies and rich financial and human resources that our forefathers did not possess. In this context, Amunts et al. (1999) and Tomaiuolo et al. (1999) have focused on Broca's region, which consists of 2 'Brodmann Areas': 44 and 45. Amunts et al. draw the cytoarchitectonic borders of this region in 10 postmortem brains as part of the Jülich Brain Mapping Project, whereas Tomaiuolo et al. chart its posterior part (Brodmann's 44) by marking sulcal borders in 3D-reconstructed MR images of 50 healthy brains. In both cases, individual variation is found, as FK aptly point out.

Should this variability lead to a murky picture that is a result of weakened effects in fMRI group studies? FK claim it does. And yet, we have seen that robust and consistent group results *are* often obtained, when the right linguistic units are chosen, and kept constant across studies that are compared.

Moreover, the whole idea behind these brain mapping projects (that have indeed brought anatomical variability in Broca's and other regions to the limelight) is to use what we know about this variation in order to localize group results *modulo* the variability. Thus, both Amunts et al. and Tomaiuolo et al. do not only chart variability; they offer localization tools that take variability into account – *probability maps*. The 10 brains of the former, and the 50 of the latter, are superimposed on a template brain, which enables researchers to co-register their activation clusters with these maps in a common reference space, and so determine their location at the best currently available resolution. Quite a few group results have been evaluated against these maps (in fact, Amunts et al.'s map serves as the anchor against which Lindenberg et al. 2007 evaluate variability in the localization of Broca's region).

5.3. CYTOARCHITECTONIC PROBABILITY MAPS AND FMRI RESULTS IN SYNTAX

As a concrete example, consider Figure 2A – a slice of Amunts et al.'s probability map for the anterior portion of Broca's region (*a k a* Brodmann's Area 45) in both cerebral hemispheres. There is considerable variability, but also cohesion: shapes, volumes, positioning and general location of the different BA 45s are not wild, certainly not up to a point which would preclude group statistics (on the current resolution of fMRI). When we co-register group results with these maps, we accomplish localization at the best currently available resolution.

To illustrate, consider a group result and its probability map localizer: Santi and Grodzinsky (2007a,b) conducted a parametric study that compared the brain's reaction to sentences that contain two different syntactic relations – Movement and Reflexive Binding (e.g., *John loves the woman who David pinched* vs. *John knows Mary pinched herself*). As the
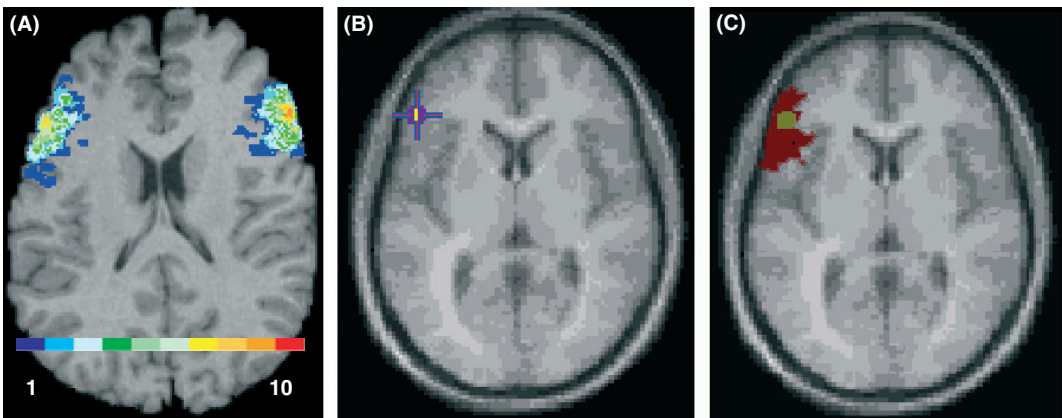
Fig 2. A. The cytoarchitectonic borders for Brodmann's Area 45, marked for 10 *post mortem* brains and normalized to a single template. The degree of overlap per voxel is color coded. The resulting variability is visible – there is hardly a voxel on the left hemisphere in which all 10 brains overlap (courtesy of Katrin Amunts). B. The cluster of voxels in which a Movement distance parameter produced significantly higher activation than a Binding distance parameter in Santi & Grodzinsky's (2007) group study. C. Co-registration of the map in A with the cluster in B shows that the activation is well within Brodmann's Area 45.

comprehension of both types requires the linking of two non–adjacent positions, the idea was to see whether they tap different memory resources. Details aside, although the difference between the two types appears minimal, group analyses clearly demonstrated a group Movement effect (2B) inside BA 45 (2C). Note that this is one example of quite a few.[22] And so, while the way I have portrayed the current state–of–affairs obviously glosses over certain problems, the weight of the evidence suggests that the picture is not as murky as FK's review suggests and that the challenging intricacies it presents should not lead to the abandonment of this picture we have for a fresh start, but rather, to a joint effort to understand this picture and move ahead.

6. Broca's Region vs. The Fusiform Gyrus – An Exercise in Functional Anatomy

The success of the fROI approach in vision, FK argue, suggests that it should be carried over to language. Important differences between the two domains and their respective anatomy seem to cast doubt on this idea: the language regions are parcelated into a number of areas by probability maps, but no such maps exist for the fusiform gyrus – locus of the face area. Brodmann's Area 21, which contains the fusiform, has not yet lent itself to cytoarchitectonic parsing, remaining one of the largest cytoarchitectonically uniform chunks in the human brain.

The rich internal structure of Broca's region, by contrast, has led several researchers to entertain the intriguing possibility that it supports different linguistic functions.[23] As we have seen, some fMRI experiments are beginning to make such distinctions, with crucial use of probability maps that provide the necessary resolution.

The study of high-level vision currently lacks this type of tool. The fusiform gyrus constitutes a single, large, cytoarchitectonic area, and the position of functional units within it may be truly shifty – the Kanwisher group compares the anatomical status of the face area to the Gulf Stream, which is geographically unstable although it gives clear signs of life (Saxe et al. 2006). The fROI strategy seems suitable to this anatomical

realm,[24] but not to the language domain, where a better understood micro-anatomy helps to discover fine function/structure relations.

7. Modular Multi-functionality of the Language Regions

The clarity of the picture for language should not blur the sight of potential pitfalls: some language regions may support Working Memory (Smith & Jonides, 1999, *passim*), and it has been claimed that Broca's region hosts no syntactic functions, e.g. 'semantics' (Willems & Hagoort, 2009) and even aspects of 'mental imagery' (Binkofski et al. 2000). This apparent multi-functionality has led FK to argue that no brain region is either necessary or sufficient for language processing, let alone syntax.

I wonder how many of these results would withstand careful scrutiny.[25,26] But even if some do, it is important to realize that the current debate remains unaffected. Everyone seems to follow a research program that seeks structure by delineating the functions of a brain region and exploring each independently. We assume that the functions of each region are independent, until a theory that unifies them is proposed. This approach, which allows regional multi-functional modularity, is in line with the one that Saxe, Brett and Kanwisher (2006) recommend: study functions separately from a coherent theoretical perspective, hope that higher-resolution devices and maps are in the making, but first pursue each separately, and then try to understand how they relate to one another.

To underscore this point, consider the columnar structure of primary visual cortex (V1), long known to carry two discrete specializations that overlap anatomically: orientation columns (responsible for the identification of lines with specific orientations in each receptive field) and ocular density columns (neuronal aggregates that determine which eye is the dominant one for each receptive field). These two systems partially overlap in the same cortical piece (Hübener et al. 1997). The highly structured modularity of each of these two overlapping systems is not questioned. Quite the contrary: this fact has led researchers in vision to try to *understand* the nature of this overlay, in order to see whether these two systems interact, and if so, how and why (E.g., Swindale et al. 2000).

8. Selecting a Functional Localizer Task

FK have already embarked on an experimental journey into language with the fROI method. Critical to success is a suitable functional localizer task. They report their preliminary attempts. Their first two tried to obtain a significant effect in each individual subject for contrasts that had previously produced group results: A subject/object relative contrast used in past studies (e.g., Stromswold et al. 1996 in PET, Just et al. 1996 in fMRI) and a task invoking 'a dissociation between syntactic and semantic processing' that had likewise produced group effects (Dapretto and Bookheimer 1999) did not lead to results at the individual level. We are not told why these two experimental paradigms were selected, what the benefits of success would have been and why FK think they failed.

The third attempt was successful (see Fedorenko & Kanwisher, 2009a). Two contrasts activated a voxel cluster in every individual subject: (i) a contrast between 'word lists and pronounceable non-word lists (targeting regions involved in processing word-level meanings) and (ii) the contrast between sentences and word lists (targeting regions involved in processing sentence-level meanings).' We are not told whether there was a group result, although FK say that 'these regions appear in anatomically similar locations

across participants, suggesting that we are looking at the 'same' regions in different brains.' (p. 855). No details on the loci of these regions are provided, and as the word 'same' is put in quotes, it is difficult to know what FK intend: if there was substantial anatomical overlap, why didn't they use probability maps to quantify it, like we do in groups studies? If there was no such overlap, why imply that the same anatomical region is involved?

Moreover, the contrast used for the determination of fROIs is of central importance. In language, just like in vision, the selection of the functional contrast that works for each individual is the crucial move: *unless we understand the character of the functional contrast used as a delimiter and the rationale for its significance, it is hard to say why it, and nothing else, is the right method to discover the language-relevant fROI.*

FK do not discuss this issue, so one can only try to make a guess: variability in their localizer task may emanate from the different strategies subjects may employ when they see a meaningless sequence of words and/or phonemes. Some subjects may tune out, whereas others may be desperately attempting to make sense of what they hear. The voxels targeted by this contrast may thus vary across subjects according to the effort each decided to exert, and until the connection between effort and language is made unclear, the significance of the functional localizer cannot be assessed.

9. Taking Stock

In this note, I tried to show that neurolinguistic studies that combine micro-anatomical methods produce a reasonably stable picture of the anatomy of language, which is quite different from that of high-level vision. If you accept these conclusions, are you still willing to make the move FK recommend? Should we revert to the fROI method, in order to increase statistical power? I am not sure, as this move would make us abandon the picture we have, and in addition lose precious anatomical information which cytoarchitectonic probability maps (available for language but not high-level vision) provide. And so, while there is always more than one path *en route* to scientific discovery, and new ideas are always welcome, I cannot see convincing arguments that the methodology FK propose is what we need.

Short Biography

Yosef Grodzinsky is Professor and Canada Research Chair in Neurolinguistics at the Department of Linguistics, McGill University, where he is also Associate Member of the Department of Neurology/Neurosurgery. As well, he is Adjunct Professor at the Department of Speech, Language and Hearing Science, San Diego State University. He obtained a B.Sc. at The Hebrew University of Jerusalem in 1981 and a Ph.D. in Cognitive Science at Brandeis University in 1985, under the supervision of Noam Chomsky, Merrill Garrett and Edgar Zurif. He was then an A.P. Sloan postdoctoral fellow at the Center for Cognitive Science, MIT. From 1987 to 2001, he was Professor of Psychology at Tel Aviv University and Research Professor of Neurology at the Aphasia Research Center, Boston University School of Medicine. His research interests include syntax, semantics, language acquisition, aphasic syndromes and functional neuroimaging. In 2007, he received the Humboldt Senior Researcher Award, which enhanced his collaboration with the Institut für Medizin, Forschungszentrum Jülich and the Max-Planck Institute for Brain and Cognitive Science in Leipzig. His current research program focuses on the development of brain maps for syntax and semantics through fMRI studies in health, and in focal and

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Notes

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[1] Statistical comparisons seek to determine whether sampled quantities (e.g., MRI signal intensities recorded in a voxel on a pair of stimuli) should be viewed as drawn out of different pools (or distributions). Assertion A, that two quantities are different, requires specific assumptions about the character of the distribution of these quantities. Also, A follows from statistical comparisons which are associated with a degree of certainty. If A has over 95% chance to be true (on standard assumptions), it is taken to have a 'significant' degree of certainty (is significant at $p < 0.05$). But even this seemingly high level leaves a 5% chance to the possibility that A is false, and the quantities at issue were actually sampled from the same pool. If a single comparison is made, one might be willing to live with this possibility. But if multiple comparisons are conducted (say, over 20 at $p < 0.05$), then at least some assertions about a significant outcome are most likely false. To remedy this situation, corrections make significance harder to obtain as the number of comparisons increases. WBV fMRI analyses compare signal intensity in each of the many brain voxel. Corrective measures are therefore necessary.

[2] See the review in Kaan and Swaab (2002) for a somewhat similar conclusion.

[3] Some of the above points are reminiscent of points made in debates in neuropsychology in the 1990s (e.g., Caramazza 1986; Zurif et al. 1989) and a more recent debate on fROI in neuroimaging (Friston and Henson 2006; Friston et al.; Friston et al. 2006 Saxe et al. 2006). Indeed, in some instances, I merely rehash others' arguments.

[4] Their tables (pp. 1416–1417) break down these linguistic levels into sub-components (e.g., phonological studies are listed by task – reading, listening and discriminating syllables, letters, or pseudo-words), but these sub-components are not used for the map that FK reproduce, which only distinguishes between studies of phonology, syntax and semantics, each of which is widely scattered over large portions of cortex..

[5] an activation cluster consists of a group of contiguous voxels which reached significance on some test. The peak of a cluster is that voxel which scored highest on that test and can be viewed as the best representative of the cluster modulo the contrast at issue.

[6] These tasks are 'semantic', 'syntactic', 'phonological', 'lip-reading', 'finger movement' and 'working memory'.

[7] Ojemann's figure, which FK display, received wide circulation, as it was reproduced in the Science section of the New York Times when his article was published.

[8] See Lichtheim 1885; Geschwind 1970.

[9] Zurif and Caramazza 1976; Caramazza and Zurif 1976; Schwartz et al. 1980; Grodzinsky 1984, 1986.

[10] Blumstein 1973; Zurif 1980; Berndt and Caramazza 1980.

[11] Kean 1980; Friederici et al. 1982; Grodzinsky 1984, 1986, 1990; Shapiro and Levine 1990; Shapiro et al. 1993; Swinney and Zurif 1995; Hickok and Avrutin 1995; Zurif 1995; Friederici and Frazier 1992; Friedmann and Grodzinsky 1997, among others.

[12] However, it should be noted that the linguistic approach has led to interesting results and a lively debate in the domain of language production as well (e.g., Kean 1980; Grodzinsky 1984; Lonzi and Luzzatti 1993; Friedmann and Grodzinsky 1997; Friedmann 2006, and much subsequent literature).

[13] E.g., Schwartz et al. 1980, 1987; Ansell and Flowers 1982; Friederici and Graetz 1987; Shapiro and Levine 1990; Hagiwara and Caplan 1990; Grodzinsky et al. 1993; ; Shapiro et al. 1993; Hickok and Avrutin 1995; Mikelič et al. 1995; Beretta et al. 1996, 2001; Law 2000; Burchert et al. 2001, 2003; Friedmann and Shapiro 2003; Ruigendijk et al. 2006; Vasić et al. 2006; Garraffa and Grillo 2007.

[14] Zurif et al. 1993; Swinney and Zurif 1995; Shapiro et al. 1993; Poirier et al. 2009.

[15] Caramazza and Zurif 1976; Grodzinsky 1989; and Sherman and Schweickert 1989 in English; Law 2000 in Chinese; Friedmann and Shapiro 2003 in Hebrew; Burchert et al. 2001 in German.

[16] Zurif et al. 1993; Swinney and Zurif 1995; Shapiro et al. 1998; although see McKoon G. and Ratcliff 1996, for an alternative view.

[17] Just et al. 1996; Stromswold et al. 1996.

[18] Much related work on various aspects of syntax has been done in recent years, e.g., Röder et al. 2002; Cooke et al. 2001; Ben-Shachar et al. 2003, 2004; Fiebach et al. 2005; Bornkessel et al. 2005; Friederici et al. 2006; Santi and Grodzinsky 2007a,b; Caplan et al. 2002; Shetreet et al. 2009. Seeking to be brief and focused, I won't discuss here.

[19] E.g., Bornkessel et al. 2005; Fiebach et al. 2005 or Friederici et al. 2006 for comprehension of visually presented sentences as in; Ben-Shachar et al. 2003, 2004; Santi and Grodzinsky 2007a,b for grammaticality judgment of auditory stimuli; question answering, as in Ben-Shachar et al. 2004, among others.

[20] Eickhoff et al. 2007; Zilles and Amunts 2009.

[21] Amunts et al. 1999; Zilles and Amunts 2010.

[22] Cf. Heim et al. 2008; Makuuchi et al. 2009; a similar, probability-map-based treatment is currently given to lesions by Amunts, Pieperhoff, Love, Shapiro & Grodzinsky, in preparation.

[23] Friederici 2004; Grodzinsky and Friederici 2006.

[24] Kanwisher et al. 1997; O'Craven and Kanwisher 2000; Hemond et al. 2007.

[25] See Grodzinsky and Santi (2009) for a discussion of the results Willem & Hagoort present.

[26] An oft-cited paper is Binkofski et al.'s (2000) mental imagery study, where a 'self-observation' imagery condition, in which subjects were asked to imagine that they are looking at themselves moving a finger, activated left BA 44 (among other areas) when compared to rest. No other contrast in this imagery experiment activated this area. Binkofski et al. took this result to indicate that BA 44 is not only linguistic but is also involved in 'higher-order forelimb' motor control, in a manner akin to mechanisms that control speech.

FK take this conclusion to indicate that Broca's region is multi-functional. Perhaps, but note that the condition at issue involves the most complex and longest verbal instructions. This may be the reason for the activation, because *comparisons were always made to the rest condition*. Other imagery studies of hand movement do not activate BA 44 (e.g., Wolbers et al. 2003; Buccino et al. 2004; Urgesi et al. 2007), they exclude Broca's region.

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