DEEPER INSIGHTS INTO THE ROLE OF BROCA'S REGION IN LANGUAGE PROCESSING BY CONNECTIVITY ANALYSIS

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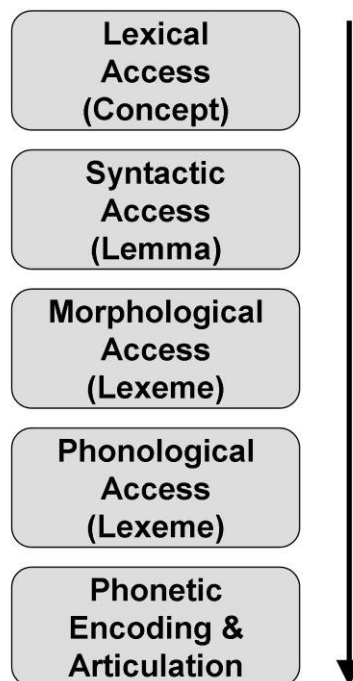
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Abstract: The "Decade of the Brain" had major influence on our understanding of the functional neuroanatomy. Based on PET, fMRI, MEG and other neuroimaging techniques, numerous papers on "neural correlates of ..." have been published. In the wake of this explosion of papers came novel techniques to meta-analyse the wealth of data, which further improved our knowledge on structure-function relationships in the brain. We now know that very few brain areas are specialised for one particular function, but rather, like Broca's region, are organised in fashions described as "networks" by some authors. The notion of a network, however, implies more than coincidental activation: It implies understanding of the interplay of the network nodes. Statistical software packages for the analysis of neuroimaging data thus provide us with novel approaches to investigate the connectivity within networks functionally and causally. The present talk demonstrates the development in using connectivity analyses for better understanding the functional neuroanatomy of language processing. We demonstrate how the combination of the Jülich cytoarchitectonic probabilistic brain atlas in combination with connectivity analysis provides insights into the dynamics within the language network around Broca's region that exceeds the traditional GLM approach, since connectivity analysis may detect subtle differences which are not tapped by simple region-wise comparisons of amplitudes of the hemodynamic response function.

1   Introduction

Language production relies on a series of processing stages (e.g. Levelt et al., 1999). After initial retrieval of the lexical concept, processing goes to the *lemma* level at which syntactic features (e.g. word category) are stored. Next, the *lexeme* level is accessed which contains form-related aspects such as morphological information or the phonological and phonemic structure of the word. Finally, the phonetic gestures and speech motor programmes are retrieved and initiated in order to articulate the word (Figure 1).

Stages of Word Production
after Levelt et al. (1999)

Lexical
Access
(Concept)

Syntactic
Access
(Lemma)

Morphological
Access
(Lexeme)

Phonological
Access
(Lexeme)

Phonetic
Encoding &
Articulation

Figure 1 – The serial language production process after Levelt et al. (1999).

At the neural level, these different processing stages are supported by distinct brain regions which are involved in either the cognitive or the motor aspects of language. Of major importance is Broca's region in the left inferior frontal cortex, consisting of cytoarchitectonic areas 44 and 45 (Amunts et al., 2004). The present paper illustrates the functions of areas 44 and 45 of Broca's region as parts of different neural circuits for the language production process.

2   Cognition vs. Articulation

Neuroimaging studies of language production (Bookheimer et al., 2000; Indefrey et al., 2001; Petersen et al., 1988; Wise et al., 1999) as well as lesion studies (Dronkers et al., 1996) hint at the involvement of the left insula in the motor aspects of articulation (Dronkers et al. 1996), whereas cortical region, in particular Broca's region, support rather cognitive processes at the lemma and lexeme level. In order to address this question in one experiment, Heim et al. (2002) directly compared lexical vs. articulatory processes. Based on Levelt's model of language production, three experimental conditions were included which, by pair-wise comparison, allow distinguishing brain region supporting cognitive aspects from those involved in articulatory-motor processes.

During picture naming (NAME), lexical access, phonological code retrieval and articulation were involved. In the articulatory baseline condition (BASE), subjects repeatedly said "jaja" when seeing a smiley, which involved simply articulation but no lexical processing. Finally, a resting baseline (REST) was included to compare to BASE. Comparing NAME > BASE thus revealed lexical processing regions, including left areas 44 and 45 and the left inferior temporal cortex but not the insula. In contrast, BASE > NAME activated left insula, Rolandic operculum, and premotor cortex. Together, these data support the functional distinction between neural systems involved in lexical processing vs. articulation, demonstrating that Broca's region is rather a cognitive than an articulation region.

Building upon these findings, Eickhoff et al. (2009) further investigated the functional interaction of area 44 in Broca's region and regions subsequently transforming phonological information into spoken output. First, a quantitative meta-analysis of 19 neuroimaging studies of speaking was conducted using the Activation Likelihood Estimate Algorithm (ALE; Turkeltaub et al., 2002). This analysis yielded the significant involvement of area 44, insula, cerebellum, basal ganglia, ventral premotor cortex, and primary motor cortex (M1). Next, dynamic causal modelling (DCM; Friston et al., 2003) was applied to test how these regions were functionally connected. The model best explaining the data featured area 44 in Broca's region as the cognitive region from which activation first proceeded to the left insula. From here, cerebellum and basal ganglia were targeted in parallel, with both projected to the premotor cortex. From there, finally, activation propagated to M1.

Relating this network to behavioural data additionally revealed two distinct functional modules within the articulation network. The connections from the insula to cerebellum and basal ganglia were particularly modulated by the fact that speaking had to be prepared; in contrast, the intrinsic connections from the basal ganglia and cerebellum to the premotor cortex were correlated with the speech rate as a measure of actual articulatory effort. These patterns are in line with the notion that the insula-cerebellum-basalganglia network supports articulatory planning, whereas the cerebellum-basalganglia-premotor network is rather involved in the execution of articulatory gestures. Such distinction relates to the clinical syndromes of apraxia-of-speech (with planning difficulties) vs. dysarthria (difficulties with the execution of articulation).

3 Dissociation of Areas 44 and 45 in Broca's Region

Having established the fact that Broca's region only feeds into, but is not part of, the articulation network, we set out to investigate the particular functions of cytoarchitectonically defined areas 44 and 45 of Broca's region. Based on suggestions from earlier neuroimaging studies, we first tested whether areas 44 and 45 support phonological vs. semantic processing, respectively.

3.1 Semantic vs. Phonological Processing?

A meta-analysis of verbal fluency tasks (Costafreda et al., 2006) suggests a functional dissociation of areas 44 and 45 for phonological vs. semantic processes, respectively. However, neither were the localisations based on objective cytoarchitectonic maps, nor did the studies included in the meta-analysis directly test both fluency tasks against each other. In order to bridge these gaps, Heim et al. (2008; 2009a) had subjects perform a semantic, a phonological, and, in addition, a syntactic fluency tasks, localised the activations by means of the cytoarchitectonic atlas (Amunts et al., 2004; Eickhoff et al., 2005), and conducted DCM connectivity analyses on the data. The observed results did not provide evidence for the Costafreda account, but suggested a different picture. First, all fluency tasks recruited both areas 44 and 45, which speaks against a simple functional specialisation. Second, however, the connectivity

patterns of areas 44 and 45 with M1 revealed novel insights into the functionality of these areas. I appeared that area 45 received input from both the semantic and the phonological task, suggesting a domain-independent access to lexical items in whatever context. Activation then propagated into area 44, which received additional phonological input. This pattern is in line with the suggestion that area 44 supports the access to the lexeme level once a lexical entry has been retrieved. Most importantly, area 44 inhibited activation in area 45, indicating that, while the phonological code is being retrieved, no new lexical entry should be accessed in a verbal fluency task. Such distribution of functions in areas 44 and 45 is best described in terms of Gold et al. (2005) as „domain preference" rather than „domain specificity".

3.2   Lexical vs. Phonological Processing!

The two studies thus suggest the involvement of area 45 in lexical retrieval in general, and of area 44 in phonological processing more specifically. To further test this hypothesis, data from a brain activation study (Heim et al. 2005b) were again analysed with DCM (Heim et al. 2009b). The original activation study revealed that the involvement of areas 44 and 45 in visual pseudoword vs. word processing depends on the task context. Whereas area 44 (and the left ITG) showed stronger activation for pseudowords than words independently of the task (phonological decision on the first phoneme vs. lexical word-pseudoword decision), area 45 was only involved in lexical but not in phonological decisions. Subsequent DCM analysis showed that this pattern is due to the fact that the connection between ITG (early lexical access) and area 45 is modulated by the task context, and is up-regulated during lexical decisions. This pattern is in line with our suggestion that area 45 is involved in lexical access in general and area 44 in phonological processing (i.e., grapheme-to-phoneme conversion in the present experiment).

3.2   Area 44 and Syntax

The question arises whether the observed functional distinction between areas 44 and 45 is limited to phonological processing vs. lexical retrieval. Earlier studies using cytoarchitectonic maps (Indefrey et al., 2001, 2004) also suggested a role of area 44 in syntactic processing. Accordingly, a series of studies on syntactic processing (Heim et al. 2005a; 2006; 2009c; 2010) and a literature survey (Heim, 2008) were conducted to answer this question. In two parallel studies using written words (Heim et al., 2005) or to-be-named pictures (Heim et al., 2006), we demonstrated that decisions about a noun's syntactic gender (masculine, feminine, or neuter in German) leads to increased activation in area 44. Likewise, the presentation of nouns with a gender-marked determiner that fails to match the noun's gender (*das Baum instead of *der Baum* – the$_{masc}$ tree) yielded higher activation in area 44 than the correct determiner-noun pairings. This result was consistent in the visual and the auditory modality.

These findings were further corroborated by a series of studies that used gender repetition priming instead of meta-linguistic decisions (Heim et al., 2009c; 2009d). In a picture naming task (Heim et al. 2009c), items were presented in blocks in which all nouns had the same gender (priming blocks) or mixed genders (non-priming blocks). Again, area 44 showed a syntactic gender effect. Likewise, when using written distractor words that did or did not match the gender of the to-be-named picture (Heim et al. 2009d), an effect in area 44 was found.

Finally, in order to include studies from other labs that had not used the cytoarchitectonic atlas, the peak coordinates reported for syntactic processing in these studies were analysed with the cytoarchitectonic atlas (Heim, 2008). Also in this review, there was a clear convergence of peaks in area 44; additional recruitment of area 45 could be attributed to additional selection

demands, a notion which is in line with our account that area 45 is involved in lexical selection.

4 Conclusion

The data presented here suggest a functional specialisation of areas 44 and 45 in Broca's region which goes beyond earlier accounts. This novel insight is to large extent driven by the use of DCM connectivity analysis. A tentative summary model has recently been proposed by Heim (2010), which is depicted here in Figure 2. The model bears some resemblance with one that was published in parallel by Price (2010), and which is based on partly overlapping studies from the literature. Interestingly, the model contains aspects of syntactic processing neither present in the model by Price (2010), nor that by Indefrey & Levelt (2004). Finally, it is worth noting that connectivity analysis on brain imaging data may mirror theoretical or network-simulation research and may thus inform integrated models of speech production, which build on both neuroimaging data and computer simulations (Kröger & Heim, 2011) to better explain the complex processes underlying the retrieval and articulation of human speech sounds and its disorders.
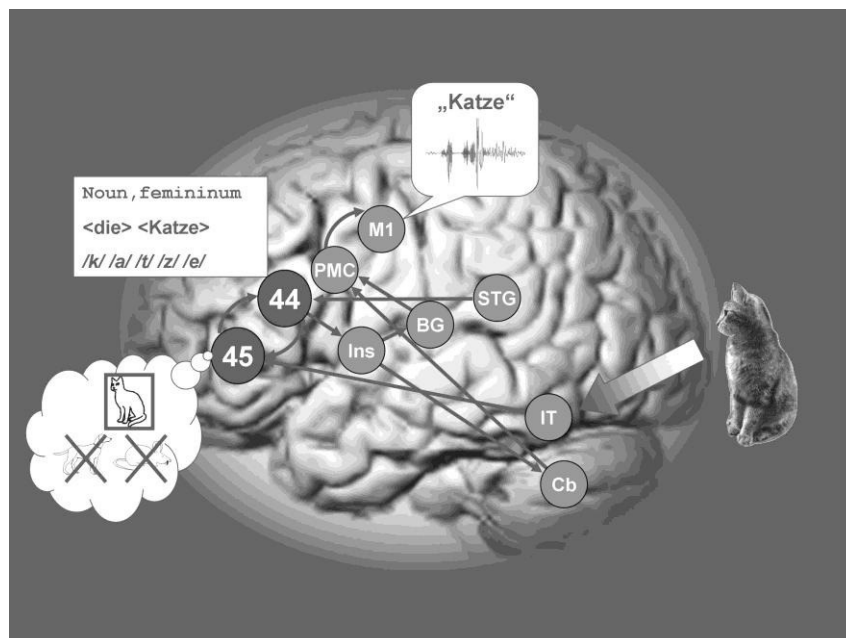
Figure 2 – A neurocognitive model of the language production process based on the neuroimaging and connectivity data reported in this paper. Note the central role of areas 44 and 45 in Broca's region for the selection and combination of lexical information within a network with visual and speech-motor regions.

5 Acknowledgements

6 References

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