The associative-semantic network for words and pictures: Effective connectivity and graph analysis

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ABSTRACT

Explicit associative-semantic processing of words and pictures activates a distributed set of brain areas that has been replicated across a wide range of studies. We applied graph analysis to examine the structure of this network. We determined how the left ventral occipitotemporal transition zone (vOT) was connected to word-specific areas. A modularity analysis discerned four communities: one corresponded to the classical perisylvian language system, including superior temporal sulcus (STS), middle temporal gyrus (GTm) and pars triangularis of the inferior frontal gyrus (GFi), among other nodes. A second subsystem consisted of vOT and anterior fusiform gyrus along with hippocampus and intraparietal sulcus. The two subsystems were linked through a unique connection between vOT and GTm, which were hubs with a high betweenness centrality compared to STS and GFi which had a high local clustering coefficient. Graph analysis reveals novel insights into the structure of the network for associative-semantic processing.

1. Introduction

Until recently, the vast majority of functional imaging data were based on univariate voxelwise comparisons between conditions. The maps of significant differences were often described as 'systems' or 'networks' but this commonly went beyond the actual data analysis. In the current paper we will apply a graph theoretical approach (Bullmore and Sporns, 2009; Buckner et al., 2009; He and Evans, 2010; Bullmore and Bassett, 2011) to characterize the network for associative-semantic processing. As a mathematical technique, graph theory has been known for long. Its application however to imaging data is of a more recent date and has steadily increased in popularity. Graph analysis has been applied to a number of imaging modalities: structural (He et al., 2007, 2008) and resting-state MRI (Nelson et al., 2010), diffusion-tensor imaging (DTI) (Gong et al., 2009) as well as task-related fMRI (Buckner et al., 2009). Compared to dynamic causal modelling (DCM) (Penny et al., 2004), graph analysis does not require the a priori definition of a restricted set of models (nodes, intrinsic feedforward and feed-

back connections, modulations) by the experimenter. The associative-semantic network consists of a large number of nodes and an even exponentially larger number of possible functional connections. Given the extent of the network and the significant lacunes that remain in our knowledge about its internal connectivity structure, graph analysis was optimally suited for this research purpose.

A highly consistent pattern of activation in functional imaging can be obtained when explicit associative-semantic judgments are compared to lower-level tasks such as visuoperceptual judgments of size for words and pictures (Vandenberghe et al., 1996; Vandenbulcke et al., 2005, 2007; Nelissen et al., 2007, 2011). Regions activated both for words and pictures include the left ventral occipitotemporal transition zone (vOT) (Vandenberghe et al., 1996; Buckner et al., 2000; Van Doren et al., 2010; Seghier and Price, 2011), left posterior middle temporal gyrus (Chertkow et al., 1997; Vandenbulcke et al., 2007; Whitney et al., 2011), the anterior temporal pole (Hodges et al., 1992; Vandenberghe et al., 1996; Rogers and McClelland, 2004), left ventral anterior temporal cortex (Jefferies and Lambon Ralph, 2006; Visser et al., 2012) and left anterior inferior frontal gyrus (Goldberg et al., 2007). Other areas are activated more during semantic processing specifically for words compared to pictures or vice versa. Such areas include the triangular and opercular part of the inferior frontal gyrus, the

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posterior third of STS for words (Vandenberghe et al., 1996; Vandenbulcke et al., 2007) and the right fusiform gyrus for pictures (Vandenbulcke et al., 2006; Thierry and Price, 2006). It also contains more domain-general (Binder et al., 2009) regions such as the inferior frontal sulcus (Wagner et al., 1997; Van Doren et al., 2010), middle frontal gyrus (Demb et al., 1995; Vandenberghe et al., 1996), and intraparietal sulcus. In this context, we use the term 'domain-general' to refer to cognitive processes that may not be exclusive for tasks involving language or semantic processing and that may be invoked during a wider variety of tasks, e.g. due to their role in selective attention or executive control. A similar distribution of activations has been reported across a wide variety of experiments of semantic processing (Binder et al., 2009). To our knowledge, this set of activations has not been analyzed mathematically at the systems level until now. The first aim of the current study was to apply a graph theoretical approach to this activity pattern to investigate the network structure.

At a more local level, we were mainly interested in how the junction between left ventral occipital and posterior inferior temporal cortex (ventral occipitotemporal transition zone (vOT)) is connected with the perisylvian word-specific system. vOT is activated across a wide variety of language (Cohen et al., 2000, 2002; Jobard et al., 2003; Price and Devlin, 2003, 2011; Démonet et al., 2005; Vinckier et al., 2007; Seghier and Price, 2011; Woodhead et al., 2011; Hellyer et al., 2011) as well as picture processing paradigms (Buckner et al., 2000; Price and Devlin, 2003, 2011; Seghier and Price, 2011). It lies at the transition between ventral occipital and ventral temporal cortex and contains the midfusiform gyrus (Seghier and Price, 2011; Price and Devlin, 2011; Woodhead et al., 2011; Hellyer et al., 2011). It overlaps with the visual word form area (Cohen et al., 2000, 2002; Vinckier et al., 2007). Its y coordinate (-58 ± 5 mm) lies slightly posterior to the basal temporal language area (-41 ± 6 mm) area, the anterior fusiform gyrus and the inferior temporal gyrus (Jobard et al., 2003; Démonet et al., 2005). It is neuroanatomically and functionally distinct from the ventral anterior temporal cortex that lies at a distance more anteriorly and has been implicated in multimodal processing of conceptual representations (Visser and Lambon Ralph, 2011; Visser et al., 2012). Rather than an anatomically or functionally well-delineated area, vOT is a conglomerate of areas fulfilling different functions, with a posterior–anterior gradient (Jobard et al., 2003; Démonet et al., 2005; Seghier and Price, 2011).

Many functional interpretations of vOT implicitly assume a connectivity pattern with the language network but this has not been directly tested empirically. For instance, if one considers vOT as an 'entry point' to the word-specific system (Démonet et al., 2005), one would expect functional connectivity between vOT and language-specific areas such as posterior STS. Likewise, if vOT integrates top-down predictions from the language system with bottom-up visual input (Price and Devlin, 2011) or reflects the interaction between the 'triangular network' of orthography, phonology and semantics (Woodhead et al., 2011; Hellyer et al., 2011), one would expect a high degree of connectivity with word-specific areas in posterior temporal or inferior frontal cortex. Alternatively, left vOT has also been implicated in more 'generic' functions (Van Doren et al., 2010, 2012). According to one hypothesis, it belongs to a long-distance feedback loop together with the inferior frontal sulcus that mediates visual short-term memory, enhancing perceptual identification, conscious perception and episodic memory encoding (Van Doren et al., 2010, 2012). According to a related hypothesis, based on a meta-analysis of reading studies (Jobard et al., 2003), it is implicated in segmentation and classification of visual stimuli in familiar units. The second aim therefore of the current study was to evaluate how vOT is connected with word-specific areas, such as STS.

2. Subjects and methods

2.1. Subjects

Thirty-three healthy elderly subjects, aged between 54 and 89 years of age (19 M/14 F; mean age 67.2 ± 8.5 years), without neurological or psychiatric history, participated. All were strictly right-handed, free of psychotropic or vasoactive drugs, had a normal structural MRI and scored within the published norms on a standard conventional neuropsychological assessment. This sample has already been published as control group for fMRI studies of language and semantic processing in primary progressive aphasia (Vandenbulcke et al., 2005), stroke (Vandenbulcke et al., 2006), amnestic mild cognitive impairment (Vandenbulcke et al., 2007) and Alzheimer's disease (Nelissen et al., 2007; Nelissen et al., 2011).

2.2. Experimental paradigm

Stimuli were projected onto a screen 28 cm in front of the subjects' eyes. The design of the fMRI experiment was factorial (Vandenberghe et al., 1996; Vandenbulcke et al., 2005, 2006; Nelissen et al., 2007). The first factor, task, had two levels: Associative-semantic versus visuoperceptual judgment. The second factor, input modality, also had two levels: Pictures versus printed words. The associative-semantic condition consisted of a modified version of the Pyramids and Palm Trees test (Hodges et al., 1992). During a trial, a triplet of stimuli was presented for 5250 ms, one stimulus on top (the sample stimulus) and one in each lower quadrant (the test stimuli). Subjects had to press a left- or right-hand key depending on which of the two test stimuli matched the sample stimulus more closely in meaning. A given triplet was presented in either the picture or the word format and this was counterbalanced across subjects. In the visuoperceptual control condition, a stimulus was presented in three different sizes. Subjects had to press a left or right-hand key depending on which of the two test stimuli matched the sample stimulus more closely in size on the screen. Two successive trials were separated by a 1500 ms interval. Each epoch, i.e. a block of trials of the same type, consisted of four trials (total duration 27 s).

Stimuli were presented at 3.8 deg eccentricity. The pictures were taken from the Snodgrass–Vanderwart set. Mean picture size was 5.6 deg and letter size 1.5 deg.

2.3. Image acquisition

A 1.5 T Siemens Sonata system (Siemens Medical Solutions, Erlangen, Germany) equipped with an eight-channel receive-only head coil (MRI Devices Corp., Waukesha, USA) provided a T1-weighted structural volume (coronal inversion recovery prepared three-dimensional gradient echo images; Inversion time 800 ms, TE/TR 3.93/1950 ms) as well as T2* echo-planar images (EPI) (42 sagittal slices; voxel size $3.6 \times 3 \times 3$ mm³; TE/TR 40/3000 ms). Usage of the GeneRalized Autocalibrating Partially Parallel Acquisitions (GRAPPAs) method (Griswold et al., 2002) maximized sensitivity for anterior temporal activity changes and minimized susceptibility artefacts. Scans were acquired between 2003 and 2007 (Vandenbulcke et al., 2005, 2006, 2007; Nelissen et al., 2007), prior to the development of Spin-Echo EPI as a means to reduce anterior temporal susceptibility artifact (Visser and Lambon Ralph, 2011; Visser et al., 2012). A total of 108 volumes were acquired during each run. Each run consisted of three replications of each of the four conditions. Subjects underwent four to six runs each.