

Network modulation during complex syntactic processing

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ABSTRACT

Complex sentence processing is supported by a left-lateralized neural network including inferior frontal cortex and posterior superior temporal cortex. This study investigates the pattern of connectivity and information flow within this network. We used fMRI BOLD data derived from 12 healthy participants reported in an earlier study (Thompson, C. K., Den Ouden, D. B., Bonakdarpour, B., Garibaldi, K., & Parrish, T. B. (2010b). Neural plasticity and treatment-induced recovery of sentence processing in agrammatism. *Neuropsychologia*, 48(11), 3211–3227) to identify activation peaks associated with object-cleft over syntactically less complex subject-cleft processing. Directed Partial Correlation Analysis was conducted on time series extracted from participant-specific activation peaks and showed evidence of functional connectivity between four regions, linearly between premotor cortex, inferior frontal gyrus, posterior superior temporal sulcus and anterior middle temporal gyrus. This pattern served as the basis for Dynamic Causal Modeling of networks with a driving input to posterior superior temporal cortex, which likely supports thematic role assignment, and networks with a driving input to inferior frontal cortex, a core region associated with syntactic computation. The optimal model was determined through both frequentist and Bayesian Model Selection and turned out to reflect a network with a primary drive from inferior frontal cortex and modulation of the connection between inferior frontal cortex and posterior superior temporal cortex by complex sentence processing. The winning model also showed a substantive role for a feedback mechanism from posterior superior temporal cortex back to inferior frontal cortex. We suggest that complex syntactic processing is driven by word-order analysis, supported by inferior frontal cortex, in an interactive relation with posterior superior temporal cortex, which supports verb argument structure processing.

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Introduction

Processing of complex syntactic structures demands more cognitive resources than the processing of relatively simple constructions, and this is associated with locally increased neuronal activation (Just et al., 1996; Stromswold et al., 1996; Caplan et al., 1998). Although reported patterns of activation foci modulated by experimental factors vary between studies, it appears that an important role in sentence processing is played by left-hemisphere inferior frontal cortex, in particular Broca's area (for a comprehensive and critical overview, see Rogalsky & Hickok (2011)). Debate on the precise functional role of (different parts of) this area is ongoing and hypotheses range from relying on specific structure-

building or linearization operations (Bornkessel-Schlesewsky et al., 2009; Grodzinsky & Friederici, 2006) to those relying on more general cognitive processes of representational conflict resolution (Novick et al., 2005) or the integration/unification of different types of information into the sentence context (Hagoort, 2005). It has also been claimed that Broca's area supports a working memory component that may underlie any of the above-named processes (Fiebach et al., 2005; Kaan & Swaab, 2002), though this appears to be specifically plausible for the pars opercularis (Rogalsky & Hickok, 2011). Whatever its precise functional role(s), inferior frontal cortex does not operate in isolation, but is part of a larger network involved in sentence processing (Keller et al., 2001). The form of this network, as well as its modulation through syntactic complexity, is still under investigation (see Friederici (2009)).

In addition to inferior frontal cortex, another important role in syntactic processing is played by left-hemisphere posterior superior temporal cortex, where activation has also been shown to increase with syntactic complexity in sentence processing, from early functional

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imaging studies onwards (e.g. Just et al., 1996; Ben-Shachar et al., 2003). It is quite possible that the specific contribution of the posterior superior temporal cortex to syntactic parsing is in thematic role assignment, based on verb argument structure, the extraction of 'actorhood', and/or order preferences with respect to the animacy of potential arguments (Bornkessel et al., 2005; Grewe et al., 2007; Shetreet et al., 2007). This is in line with effects of verb argument structure complexity observed in this area (Den Ouden et al., 2009; Thompson, et al., 2007; Thompson et al., 2010a). It has been suggested that Broca's area and posterior superior temporal gyrus together form a network that is responsible for thematic role assignment, a crucial aspect of complex sentence processing which, in English, relies on both the processing of word order and verb argument structure (Friederici 2009; Friederici et al., 2006).

In an fMRI study examining the neural correlates of syntactic processing and recovery from aphasia, Thompson et al. (2010b) showed a pattern of left-hemisphere activation associated with processing of complex syntactic structures, viz. object-cleft constructions (OC; 1a) compared to subject-cleft constructions (SC; 1b). Using an auditory verification task, in which auditory sentences and visual scenes were presented simultaneously, participants indicated by button-press (yes/no) whether or not the two matched. Sentence types included OC, SC, and simple actives (ACT) (60 trials per condition), pseudorandomly distributed over 4 runs (see Thompson et al. (2010b) for details).

1. a. It was the groom that the bride carried. (OC)
- b. It was the bride that carried the groom. (SC)

Unlike subject clefts, object-cleft constructions have a noncanonical word order (in English, an order other than subject–verb–object), and are deemed to be more complex based on formal syntactic theory (e.g. Chomsky, 1977, 1995; Bresnan, 2001), as well as on more general cognitive theories in which object clefts make greater demands on working memory (e.g. King and Just, 1991; Caplan & Waters, 1999; Gibson, 1998; Gordon et al., 2002). Whereas the contrast subtracting object-cleft activation levels from subject-cleft activation only revealed a small cluster of voxels in the left posterior insula, the opposite contrast revealed robust differential activation in a number of perisylvian left-hemisphere areas, including the inferior frontal, middle frontal and precentral gyri, the anterior insula, as well as the middle temporal, posterior superior temporal and angular gyri.

The areas identified by Thompson et al. (2010b) to be involved in processing complex sentences were similar to those reported in other studies (Just et al., 1996; Stromswold et al., 1996; Caplan et al., 1998, 2001; Caplan, 2001; Cooke et al., 2002; Ben-Shachar et al., 2003). However, the BOLD signal subtraction analyses performed in this and similar studies do not provide insights about connectivity and information flow between these areas. Functional and effective connectivity analyses are required to map the network structure between activated areas, that is, to ascertain which network nodes interact during complex syntactic processing. One particular purpose of the current investigation was to determine which of two cortical areas is a better candidate to provide the driving input to the 'syntactic network': (i) posterior superior temporal cortex, likely involved in verb argument structure processing, or (ii) inferior frontal cortex, with its suggested prime role in supporting sequential processing, complex structure building and decomposition, either directly or indirectly through a working memory component. If activation throughout the network turns out to be principally driven by posterior superior temporal cortex, this corroborates the view that sentence processing occurs bottom-up, starting with the lexico-syntactic analysis of prime components, viz., verbs. On the other hand, if the network is driven primarily by inferior frontal activation, this suggests that sentence processing starts from the analysis of the linear order of its lexical components into a hierarchical structure. Ultimately, these processes have to team up, in order to achieve a correct parse for complex sentences.

In this paper we reanalyzed the raw data from Thompson et al. (2010b) by performing a two-stage connectivity analysis: we first

used directed partial correlation (dPC) analysis as a hypothesis-free method to limit the model space and we then applied Dynamic Causal Modeling (DCM) to look at driving inputs and modulatory influences on the connections within the preselected models. dPC is a method that in principle allows for detecting effective connectivity, as discussed in Mader et al. (2008). This method has been used successfully by Saur et al. (2010), to investigate the networks underlying different aspects of auditory comprehension. Due to the comparably low temporal resolution of fMRI data the information about the connectivity structure has to be assumed to be contained in the instantaneous interactions. dPC does not depend on prior knowledge about the underlying network structure. It can be applied without assumptions about the network topology under investigation. The statistics that come with dPC analyses "decide" about the presence or absence of interactions, which can be used for the formulation of hypotheses about the network structure, as in the present study.

As a second step in our reanalysis of the Thompson et al. (2010b) data, we used Dynamic Causal Modeling (DCM; Friston et al., 2003) to further specify the preselected models. Through inference from local activation levels, DCM provides parameter estimates that reflect the effective strength and context-dependent modulation of connections between clusters of neurons (Stephan et al., 2010). The method has been used to investigate effective connectivity in areas such as task-related modulations of the network supporting speech comprehension (Leff et al., 2008), developmental changes within the phonological processing network (Booth et al., 2008), modulations of inferior frontal gyrus connectivity associated with lexical and phonological processing (Heim et al., 2009a) and altered connectivity in patients with primary progressive aphasia (Sonty et al., 2007).

One major concern in DCM is the *a priori* selection of models to be tested. The primary challenge is to reduce the number of relevant models that will be compared, based on theoretical, practical or other data-external considerations, beforehand. Without such a reduction, the number of possibilities is essentially unlimited, due to boundless combinations of different driving inputs, self-modulating nodes and multiple modulations on different connections. For this reason, we raised the cluster size threshold in the subtraction reanalysis of the Thompson et al. (2010b) data, in order to select only the most strongly activated peaks in the potential network, and we let our competing models be constrained by the outcome of the dPC functional connectivity analysis. Further restrictions on the model shape are discussed in Material and methods.

Through serial application of these three methods of data analysis (BOLD subtraction, dPC and DCM), we investigated (i) which of two competing hypotheses about the driving input to the network provided a better fit to the data, viz., models with driving input from posterior superior temporal cortex or from inferior frontal cortex, and (ii) which of the directional connections in the syntactic network is crucially modulated by the processing of complex syntactic structures.

Material and methods

Time series

The background to the fMRI experiment, as well as the participant, task and imaging information, have been published in detail in Thompson et al. (2010b). For further background, we refer the reader to that publication. The data of twelve right-handed volunteers ranging in age from 32 to 79 years (7 females, mean age 54), presented in Thompson et al. (2010b), were used to identify participant-specific activation peaks within a sphere of a 9 mm radius of the group activation peaks (based on the elevated cluster threshold). All second-level statistics were evaluated at a voxelwise significance threshold of $p < .05$, corrected for multiple comparisons per false discovery rate (FDR: Benjamini & Hochberg, 1995; Genovese et al., 2002). We used a cluster size threshold of 15 contiguous

voxels (405 mm^3), which was higher than the threshold used in the original analysis of the data, reported in Thompson et al. (2010b) (viz., 3 contiguous voxels (81 mm^3)). Time series from these peaks were extracted and served as input for the dPC and DCM analyses. Importantly, for the network analyses, we created new models in which we (i) concatenated the scans from the four separate runs and (ii) modeled the main effect of TASK (all three conditions, collapsing over matched and mismatched trials), parametrically modulated by the conditions OC and SC. In addition, main effects of the different runs were covaried out through the addition of three session regressors, including explicit modeling of the transitions between runs.¹ From these models, time series were extracted within a volume of interest of 6 mm radius from the participant-specific activation peaks and averaged over voxels.

dPC analyses

For computational details on the dPC method we refer to recent publications by Mader et al. (2008) and Saur et al. (2010). In short, dPC is an approach in the time domain quantifying Granger-causality, which enables a hypothesis-free exploration of networks in the sense that once the network nodes are defined, no further prior assumptions about the functional network structure are necessary (Eichler, 2005). Granger introduced the concept of instantaneous causality or instantaneous interaction. These interactions are bidirectional as the cause cannot be distinguished from the effect based on predictability. Owing to the temporal characteristics of the fMRI time series, with the dPC method we investigate such instantaneous interactions by using vector autoregressive processes. To eliminate scanner drift, a 3rd degree polynomial was fitted to each of the averaged time series. To allow comparison across the group of participants, resultant dPC values were divided by their levels of significance resulting in normalized dPC (dPC_{norm}) values. Group networks were computed by averaging these dPC_{norm} values across participants (mean dPC_{norm}). An interaction on group level was considered significant if the following condition was fulfilled: $(\text{mean } dPC_{norm} - 2 * \text{stdv}[\text{mean}]) > 1$.

Dynamic Causal Modeling

The result of the dPC analysis served as the basis for the models that were tested with DCM. That is, the intrinsic connections in our DCM models were defined by the results of the dPC analysis. We limited our comparisons to models with equal basic complexity, i.e. with equal bidirectional connectivity within the dPC output network, one driving input and one modulation of a unidirectional condition per model.

Based on earlier findings with respect to the different cortical areas involved in syntactic processing and the results from Thompson et al. (2010b), we tested two sets of models (in the same comparison): (1) those with a driving input onto posterior superior temporal cortex (posterior superior temporal sulcus (pSTS)) and (2) those with a driving input onto inferior frontal cortex (IFG). Our research interest was specifically aimed at the network modulation involved in the processing of syntactically complex sentences, hence we modeled modulations by the object-cleft condition only. Together, these considerations left us with 12 models that could be directly compared as to their model goodness (see Fig. 2).

For model selection, we used two methods that are often contrasted with each other (Stephan et al., 2009), but which each have their own merits. First, we performed a classic frequentist repeated measures ANOVA, with a 12-level factor *model*, using the subject-specific negative free energy (F) as log-evidence ratio approximations for each model. In

order to directly investigate the effect of the driving input node, we also conducted a 2×6 repeated measures ANOVA, with factors *input* and *modulation*.

Second, we used variational Bayesian Model Selection (BMS), a recent version of BMS currently implemented in SPM8, to present the ‘winner’ among our twelve competitors. The output of this comparison is a value for the exceedance probability and the posterior model probability of each model, each summing to 1 (or 100%). The exceedance probability value for a model k reflects the probability that k is a better fit to the data than any other model, of those tested. The posterior probability for a model k stands for the expected likelihood of obtaining model k , for any randomly selected subject. Because we basically compared two groups of models, with driving inputs onto two different network nodes, we also performed a family-level inference based on model space partitioning, using the SPM routine *spm_compare_families* (Stephan, et al., 2010).

Though both the frequentist (classical) and the Bayesian are based on the same single-subject model evidence approximation, i.e. the F value (negative free energy, F), they consider the problem of model selection from two different analytical points of view. In the frequentist approach we used an analysis of variance to test for differences in log-evidences over models relative to intersubject differences. In contrast, the Bayesian approach describes a hierarchical model, which is optimized to furnish a probability density on the models themselves by treating the model as a random variable. The frequentist approach tries to reject the null hypothesis that there are no differences in model evidence across models, whereas the Bayesian approach estimates the models’ probabilities and enables inference in terms of exceedance probabilities. Consequently, results between these methods might differ. On the other hand, if both methods converge in the same winning model, this may further underline the significance of the result.

Subject-specific estimates for the 8 parameters in the winning model were entered into eight one-sample t-tests, to test difference from zero. These parameters were the driving input, the strengths of the intrinsic connections between the nodes and the impact of the modulation onto the relevant connection.

We also performed post-hoc investigations into the relation between parameter estimates and our individual participants’ preference for the group’s winning model (G). In a first analysis, we calculated difference scores between each individual’s negative free energy (F) values for G and for either that participant’s winning model (if other than G), or the second-best model (in case G was optimal). The resulting F-difference scores are positive for individuals for whom model G is better than any other, and negative for those who have an alternative winner, i.e. it reflects the strength of that individual’s preference for group’s winning model G. We then performed Pearson correlations separately for each parameter estimate, as well as a regression analysis, between parameter estimates and F-difference scores. Secondly, we split up the participants into those for whom G was the optimal fit, versus those for whom one of the other 11 models was the winner. We then performed Mann–Whitney U-tests to see if these groups differed in the parameter values for each of the eight model variables.

Results

fMRI

The factorial re-analysis of Thompson et al.’s (2010b) fMRI data, with an elevated cluster size threshold ($k = 15$), revealed a significant main effect of sentence type, with no main effect of sentence–picture matching and no interaction of sentence type and sentence–picture matching. In further analyses, therefore, matched and mismatched stimulus trials were collapsed. The effect of sentence type was solely driven by the contrast of OC>SC, yielding four clusters of differential activation. Plotting of the data confirmed that for all these clusters, the effect was driven by OC sentences showing increased activation

¹ One participant only completed three of the four fMRI runs. For the analysis of this participant’s results, we adapted the statistical model, as well as the computation of time series for dPC and DCM, to include the correct number of runs (3) and regressors (2).

Table 1

Activation peaks and cluster extent for the contrast OC>SC, based on the factorial group analysis ($N=12$; $p<.05$, FDR corrected, $k>15$).

Contrast	Activation peak	Seed	BA	x	y	z	Cluster size	t-Max
OC>SC	LH inferior frontal gyrus, triangular part	IFG	9, 44, 45, 46	-54	18	18	44	4.91
	LH middle frontal gyrus (premotor cortex)	PM	6, 8, 9	-39	6	45	52	5.79
	LH posterior superior temporal sulcus	pSTS	21, 22	-57	-45	6	42	5.16
	LH anterior middle temporal gyrus	aMTG	21, 22, 38	-48	3	-21	15	5.16

Note: LH = left hemisphere; OC = object-cleft sentences; SC = subject-cleft sentences.

relative to SC sentences, rather than by decreases of activation in the SC condition relative to baseline (see Table 1 and Fig. 1A). The four clusters were centered around peak activations in the triangular part of the IFG, the posterior superior temporal sulcus (pSTS), premotor cortex (PM) and the anterior middle temporal gyrus (aMTG). The opposite contrast of SC>OC yielded no significant differential activation.

dPC

Within a 9 mm radius of the four group activation peaks for the contrast OC>SC, we determined participant-specific peaks for the same contrast (see Table 2). Although the activation peak in IFG for the group analysis was located in the *pars triangularis* (BA 45), it must be noted that in five of the twelve participants the individual IFG peaks within a 9 mm radius of these coordinates were located in the *pars opercularis* (BA 44). Likewise, the activation cluster with a peak in pSTS extended into the superior and to a lesser extent the middle temporal gyrus, while for five participants, the peak closest to the anterior MTG group peak was actually located in the temporal pole (BA 38). The raw data were extracted from these individual peaks, averaged over voxels within a 6 mm radius, and entered into the dPC analysis. Fig. 1B shows the results, with significant connectivity between aMTG-pSTS, pSTS-IFG and IFG-PM. These significant interactions defined the intrinsic connections in the 12 models that were compared using Dynamic Causal Modeling.

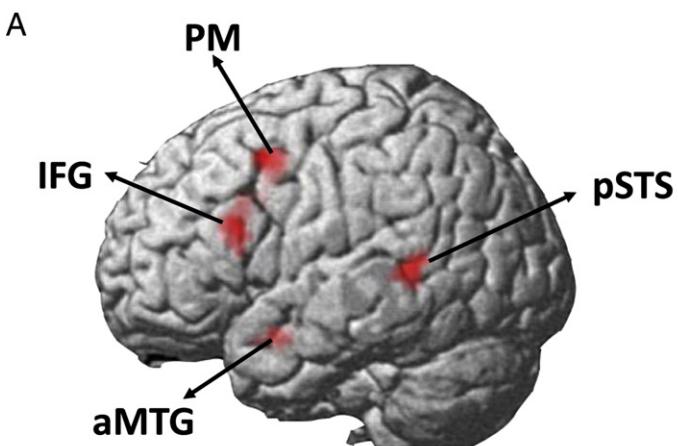


Fig. 1. (A) Rendering of the four clusters of voxels showing increased activation associated with processing of object-cleft sentences, relative to subject-cleft sentences ($N=12$; $p<.05$, FDR corrected, $k>15$). (B) Functional connectivity between four activation peaks, based on directed partial correlation (dPC) analysis. Mean dPC values are given for each significant interaction; two standard deviations of the mean (SDM) are given in brackets. An interaction was defined significant if the mean dPC value minus two SDM were larger than 1. Note: PM = premotor cortex; IFG = inferior frontal gyrus; aMTG = anterior middle temporal gyrus; pSTS = posterior superior temporal sulcus.

DCM

For each participant, the twelve models given in Fig. 2 were estimated. The average negative free energy (F) values for each model are plotted in Fig. 3. A repeated measures ANOVA, comparing these values across models, failed to meet the assumption of sphericity, as assessed with Mauchly's test ($X^2=672.3$; $p<.05$). Therefore, the degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\epsilon=.143$). The ANOVA (corrected for degrees of freedom) revealed a trend towards a main effect of *model* ($F(1.57,17.27)=3.111$; $p=.08$). Follow-up pairwise comparisons show that the model with the highest (i.e. less negative) F value, model #12, differed significantly from models #2, #3, #7, #8 and #9 (all $p<.05$).

In the 2×6 ANOVA on the F values, the 6-level factor *modulation* and the interaction between *input* and *modulation* failed to meet the assumption of sphericity as well ($X^2=186.4$ and $X^2=173.1$; $p<.05$), so degrees of freedom were again corrected using Greenhouse-Geisser estimates of sphericity for these effects ($\epsilon=.207$ and $\epsilon=.208$, respectively). Results showed a trend towards a main effect of *input* ($F(1,11)=3.816$; $p=.077$), driven by higher F values for the models with driving input onto IFG.

Variational Bayesian Model Selection showed model #12 to be the winner, with an exceedance probability of 84.8% (see Fig. 4) and a posterior model probability of 30% (see Fig. 5). The Bayesian comparison between the two groups of models with different driving inputs showed that the models with driving input onto IFG generally fit better to the data, with a group exceedance probability of 86.7% and a posterior model probability of 64%.

In summary, from the models that were tested, model #12, with driving input onto the IFG and modulation by object-cleft processing of the connection between IFG and the pSTS, is the model that best fit our data. Also, between models with different modulations, those with driving input onto IFG provide the better fits to the data, as compared to models with pSTS driving input.

Fig. 6 shows the winning model with the mean parameter estimates alongside the connections. The only parameter values that differed significantly from zero were for the connections from pSTS to IFG (+0.13; $p<.05$) and from pSTS to aMTG (+0.35; $p<.05$). Under an alpha level that is corrected for multiple comparisons ($\alpha=0.00625$), none of the connections are significantly different from zero (see also Table 3).

Visual observation of the subject-specific estimates for the various parameters revealed variation between subjects, not merely in the size of parameter estimates, but more crucially in the signs of the estimates.

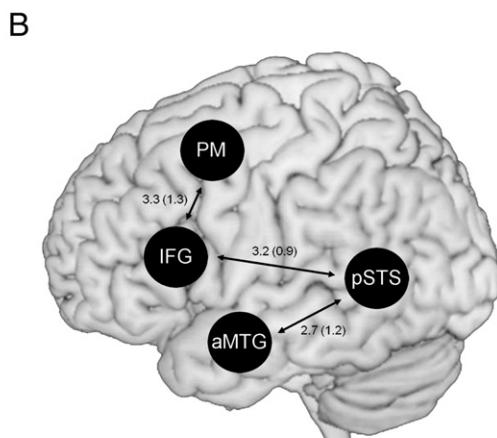


Table 2
Peak MNI coordinates for the four seed regions in the individual participants.

participants	Region			PM			pSTS			IFG		
	aMTG			x	y	z	x	y	z	x	y	z
1	-51	9	-15 ^a	-42	6	45	-54	-48	6	-54	18	15
2	-48	3	-15 ^a	-30	9	39	-63	-45	12	-48	15	24
3	-51	12	-18 ^a	-33	6	54	-63	-39	3	-51	21	24
4	-51	-3	-18	-33	6	45	-54	-39	3	-57	18	15
5	-54	3	-18	-33	6	39	-48	-45	9	-48	18	12 ^b
6	-51	-3	-15	-36	0	45	-51	-39	3	-57	15	24 ^b
7	-51	0	-21	-36	6	39	-57	-48	0	-54	18	9
8	-51	-3	-24	-30	6	54	-48	-45	9	-48	15	24
9	-54	9	-21 ^a	-36	9	39	-54	-36	3	-54	21	18
10	-54	3	-18	-39	3	51	-51	-48	9	-51	18	9 ^b
11	-45	0	-21 ^a	-30	6	54	-60	-39	3	-54	12	18 ^b
12	-54	6	-21	-36	6	42	-57	-39	9	-48	15	18 ^b

Where a particular connection between nodes was excitatory for some participants, it was inhibitory for others. The different 'directions', reflected in different estimate signs, lead to a mean that is relatively close to zero. In order to probe further into what may drive this variance between subjects, we investigated the relation between parameter estimates and our individual participants' preference for model #12, as expressed by difference scores in F values between individual's winning model and their 'runner up'. In all, #12 emerges as the optimal model for six of our twelve participants, with three showing an optimal data-fit with model #3, and another three showing preferences for models #6, #9 and #11, respectively (for models, see Fig. 2). Separate Pearson correlations show significant positive correlations between preference strength for model #12 and the parameter estimates for IFG-pSTS ($r(10)=.66$, $p=.01$), modulation of IFG-pSTS by OC ($r(10)=.42$, $p=.009$) and driving input onto IFG ($r(10)=.66$, $p=.009$), but a regression analysis shows that model preference for #12 is primarily driven by the parameter estimates reflecting the driving input onto IFG, without the other variables adding significant explanatory power. Driving input significantly predicted preference for model #12, ($\beta=.664$, $t(10)=2.81$, $p<.05$), and it explained a significant proportion of the variance in the strength of this preference ($R^2=.44$, $F(1, 10)=7.88$, $p<.05$).

Mann-Whitney U-tests were used to compare parameter values between the subjects for whom #12 was optimal and the subjects that had alternative winners. There was a significant positive effect for the parameter estimates reflecting the strength of the connections IFG-PM ($p=.037$), IFG-pSTS ($p=.037$), modulation of IFG-pSTS by the object-cleft sentence condition ($p=.004$), and the driving input onto IFG ($p=.01$). Only the positive effect of modulation of IFG-pSTS by OC survives correction for multiple comparisons ($\alpha=0.00625$).

Discussion

As reported by Thompson et al. (2010b), conventional fMRI analysis contrasting object-cleft and subject-cleft sentence processing revealed a left-lateralized group of perisylvian regions that showed increased activation associated with complex syntactic processing. Refined analyses of these data revealed four regions of significant activation located in the inferior frontal gyrus (IFG), premotor cortex (PM), posterior superior temporal sulcus (pSTS) and anterior middle temporal gyrus (aMTG), largely replicating results from earlier studies on the neural correlates of syntactic processing (Just et al., 1996; Stromswold et al., 1996; Caplan et al., 1998, 2001; Caplan, 2001; Cooke et al., 2002; Ben-Shachar et al., 2003).

It should be noted that, although the individual participants' seed points in IFG were centered around the group activation peak in the *pars triangularis* (BA 45), the group activation cluster extended to and included the *pars opercularis* (roughly, BA 44) and for some participants,

the local activation peak was indeed in the *pars opercularis*. We therefore refrain from making specific claims about the functional roles of the triangular versus the opercular part of Broca's area in complex sentence processing here. For the same reason, we exercise restraint with respect to specific claims about our posterior superior temporal *sulcus* seed point; this focal point was also part of a larger activation cluster, which extended over the posterior superior temporal cortex. As such, these seed points should perhaps better be considered as 'representative' of their larger regions, which is why we have continued to refer to these larger regions as inferior frontal cortex and posterior superior temporal cortex in the interpretation of our modeling results.

Subsequent dPC analysis of participant-specific time series showed a pattern of functional connectivity along the route aMTG-pSTS-IFG-PM, without specifying the direction of information flow, nor its locus of origin, in this network. We postulated bidirectional intrinsic connectivity throughout the network, while with respect to the locus of origin, we compared models in which the driving input of activation to the network was located in pSTS with models that had their driving input onto IFG. As noted in the introduction, the posterior superior temporal cortex shows activation associated with verb argument structure complexity and thematic role assignment, making this region a viable candidate for serving as a gateway to the complex syntactic processing network. Alternatively, activation in such a specialized network might be driven principally from inferior frontal cortex, which appears to support either the computation of complex/hierarchical syntactic constructions or at least the syntactic working memory component this involves. The models with IFG as the origin of driving input indeed turned out to fit better to the data than their rival models.

The model that best fit the data was the model that allowed for object-cleft processing to modulate the flow of information from the inferior frontal gyrus to the posterior superior temporal cortex, reflecting the importance of this connection in the parsing of complex syntactic structures. Within that model, group parameter estimates showed that the only connections with an independently significantly strong flow of activation both originated in the posterior superior temporal cortex (although these did not survive correction for multiple comparisons). With respect to the connection from pSTS to IFG, this likely reflects the interactive nature of the parsing process, with information flowing first from IFG to pSTS (based on the Bayesian identification of model #12 as optimal among its competitors), and on to anterior middle temporal gyrus from there, but certainly also flowing back to IFG, even resulting in strengthened effective connectivity. Connections between the IFG and premotor cortex appear to be inhibitory more than anything else, based on the negative mean parameter estimates in the winning model. With one of the smallest mean parameter estimate values, there is only very weak evidence for information flow from the PM region (back) to the IFG.

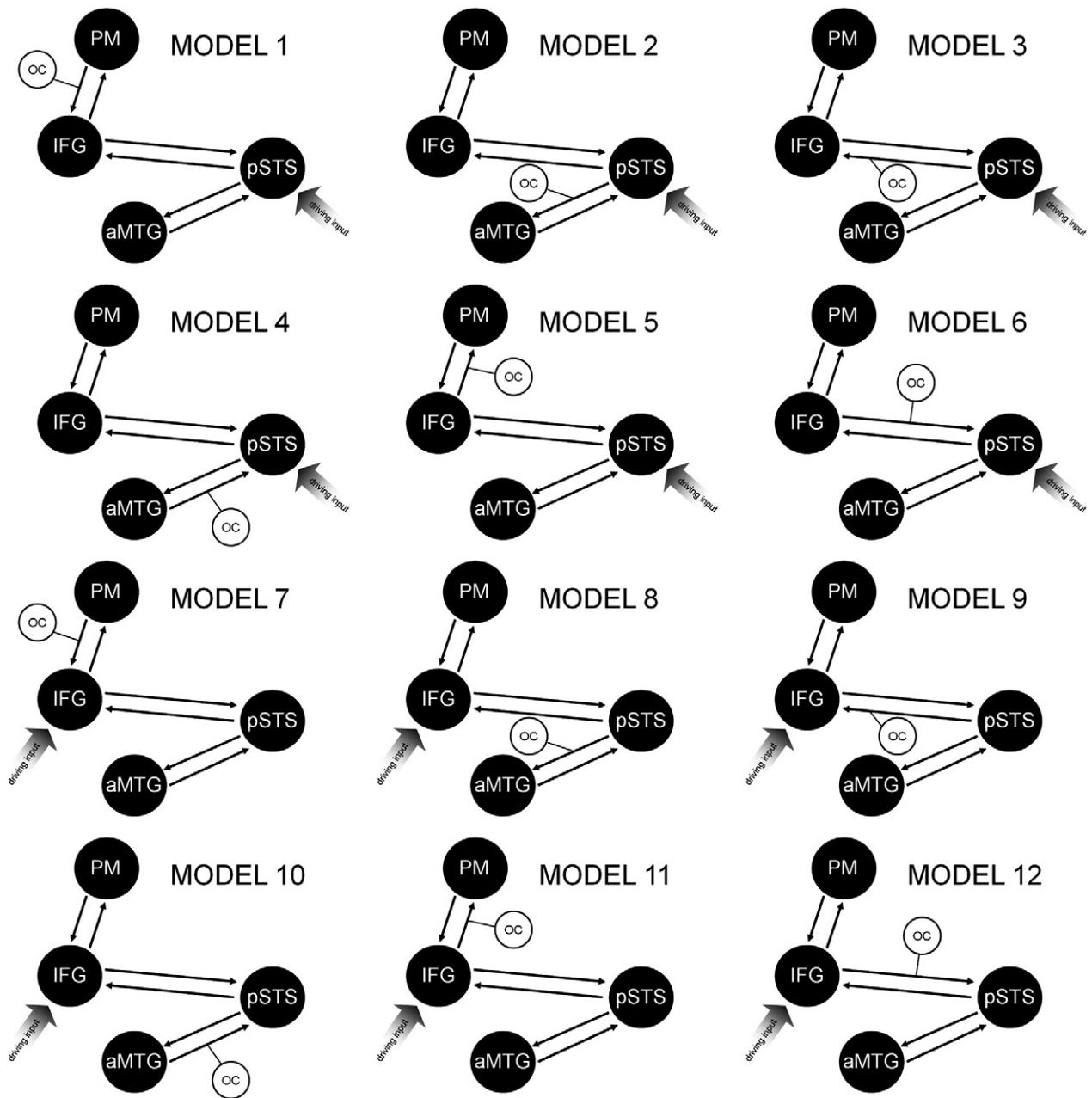


Fig. 2. The 12 DCMs that were compared. All have bidirectional connectivity between PM-IFG, IFG-pSTS and pSTS-aMTG. Models 1–6 have driving input on pSTS, while models 7–12 have driving input on IFG. Modulation by object clefts (OC) is tested on all connections. Note: PM = premotor cortex; IFG = inferior frontal gyrus; aMTG = anterior middle temporal gyrus; pSTS = posterior superior temporal sulcus.

These data, then, suggest that the driving force in the complex syntactic processing network is the syntactic computation that is supported by inferior frontal cortex. In this scenario, the sequence of lexical items, primarily asyntactic in nature, is fed to inferior frontal cortex and it is there that structure is assigned and syntactic complexity starts to be analyzed. The full parsing process is interactive between syntactic deconstruction and lexico-semantic operations (Tanenhaus & Trueswell, 1995; Ferreira, 2003; Kim & Osterhout, 2005). Crucially, sentence-structural information is conveyed to posterior temporal areas that support retrieval of verb argument structure information, so that thematic roles can be assigned on the basis of both these sources of information (Keller et al. 2001). At the same time, there is interaction between posterior temporal cortex and anterior temporal cortex, which has been associated with a role in morphosyntactic comprehension and the analysis of syntactic structure in sentence processing in lesion as well as functional neuroimaging studies (Dronkers et al., 1994; Humphries

et al., 2005; Newman et al., 2010). By contrast, there is some reason to assume that the premotor cortical activation observed in this network is perhaps less specific to syntactic complexity analysis. Hanakawa et al. (2002) report premotor cortex activation associated with tasks that involve general rule-based manipulations, similar to those likely involved in the parsing of complex syntactic stimuli (Christensen, 2010), or to those involved in “incongruity detection”, as suggested by Heim et al. (2009b). It is therefore conceivable that the premotor activation reported here, though functional within the network particularly involved in object-cleft processing, is more task-related than the activation in other parts of the network.

Both dPC and DCM are multivariate methods, so both methods might indeed be expected to provide identical results. The fact that the dPC analysis detects connections that are not detected by DCM is most likely due to the fact that DCM makes more assumptions about the system under investigation. Particularly, DCM discriminates

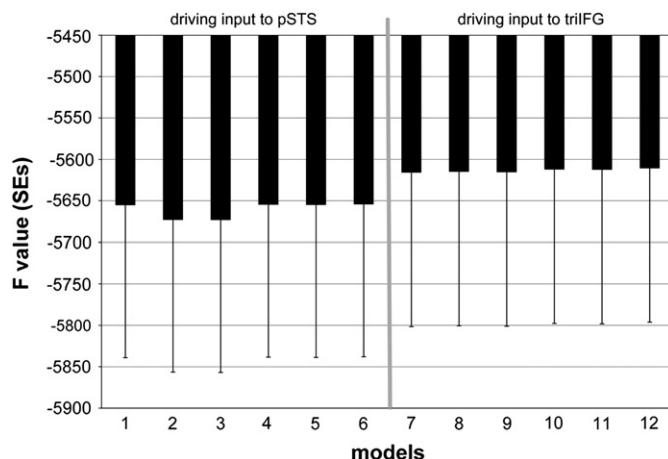


Fig. 3. Mean negative free energy (F) values, with standard errors (SE), for the 12 models. The left six models are those with driving input from posterior superior temporal sulcus (pSTS). The right six models have driving input from the inferior frontal gyrus (IFG).

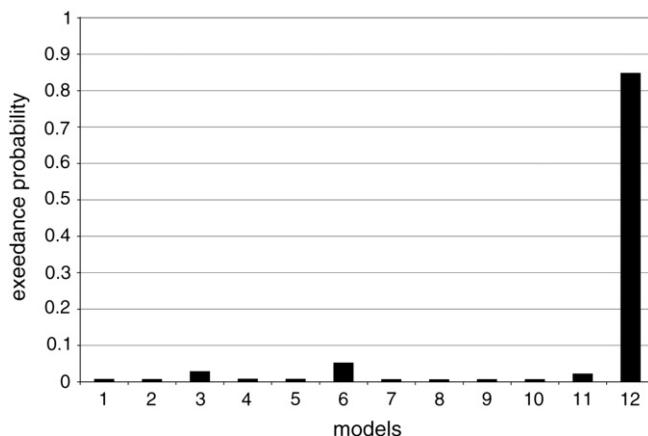


Fig. 4. Exceedance probabilities for the 12 models compared with variational Bayesian Model Selection.

between the directions of information flow. If this direction differs between subjects, as is the case in the present study, it is possible that a connection cancels out by averaging over the subjects.

Note that there are potential issues with respect to the sequential application of dPC and DCM on the same dataset. Kriegeskorte et al. (2009) addresses various pitfalls in systems neuroscience, related to using the same dataset for selection and testing of hypotheses and the danger of presenting circular results.² We have been careful to use dPC only as a means of constricting the number and type of possible models based on the four activation clusters. Crucially, all DCMs are equally in line with the output of the dPC analysis, so none of the models inherently fits the dPC outcome better than any of the others. The internal competition between the models is thus fought on an equal basis and the resulting winner is simply the one that forms the best fit to the data, better than any of the competitors we tested. Nevertheless, the models' actual parameter estimates are statistically correlated with the statistics used in the selection process, because the noise is correlated between the two analyses (since it is the same data). Although the exact magnitude of this effect is not known, it should ideally be corrected for in the DCM statistics, as also suggested by Kriegeskorte et al. (2009). Again, such a correction would not lead to a different winner from among the 12 models we tested, as they

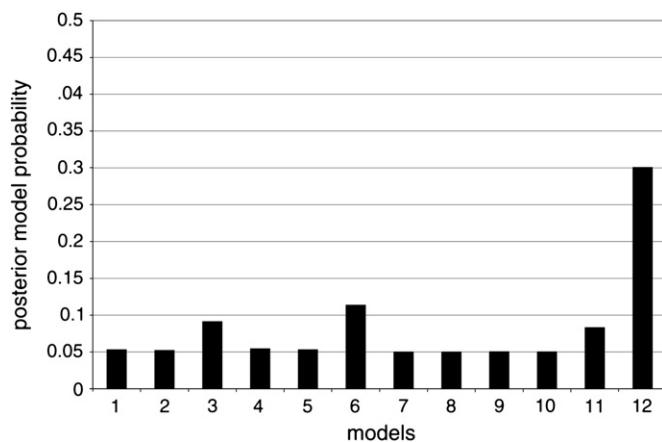


Fig. 5. Posterior model probabilities for the 12 models compared with variational Bayesian Model Selection.

were all equally correlated with the dPC outcome, but it would raise the statistical threshold for acceptance of the parameter values. This further accentuates that our winning model is not perfect or complete.

Considerable between-subject variation was found in the 'directionality' of information flow between the model connections. In any case, the interpretation of 'directionality' based on these parameter estimate signs is controversial, as the connections themselves are already specified in terms of a specific directionality. In the present case, we only tested models that have full interactivity between the connected nodes, but the picture that emerges is one in which this interactivity varies between individuals. Follow-up investigations into the relation between individual participant's model preference and parameter estimates for the variables in model #12 show positive effects of the parameter estimates for the driving input onto IFG, the connection IFG-pSTS and for the modulation of this connection by the complex OC sentences.

One related issue that needs to be addressed is the overall relatively weak evidence for the individual winning model compared to its closest competitors, as revealed by the absence of a strong main effect of the factor *model* in the frequentist analysis and by the low posterior probability value obtained through the Bayesian Model

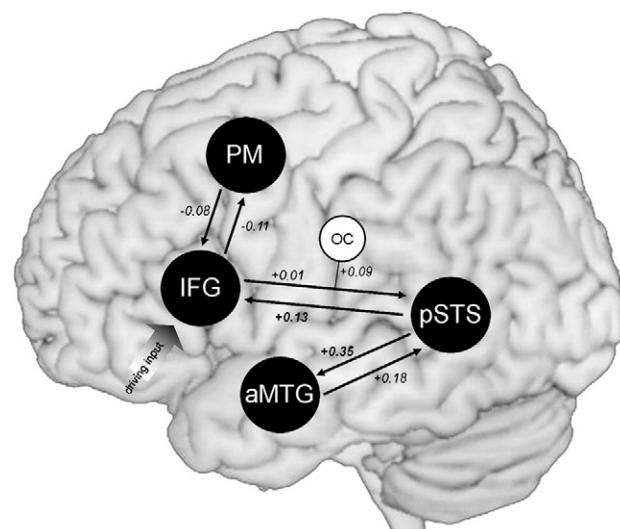


Table 3

Mean parameter estimates and their probability of being different from zero for model 12.

Connection/parameter	Parameter estimates	
	Mean	p
PM_trilFG	−0.078	.302
pSTS_aMTG	0.349	.024
pSTS_trilFG	0.131	.027
aMTG_pSTS	0.182	.152
trilFG_PM	−0.113	.365
trilFG_pSTS	0.012	.947
Modulation OC trilFG-pSTS	0.093	.199
Driving_input	1.235	.060

Selection, as well as by the considerable variance shown with respect to connection strengths in this group of participants. It should be clear that the DCM approach we have adopted in this study only reveals the best model from among a group of similar models that are inherently all imperfect. For example, the models of the network supporting complex syntactic processing tested here do not include associations with subcortical structures, while there is much evidence that such areas also play a functional role in the computation of sentence meaning, particularly in inhibitory and excitatory control of cortical networks (Ullman, 2001; Kotz et al., 2003; Snijders et al., 2010; David et al., 2011).

At this point, no paper model can truly reflect the highly extensive, complex and interactive neural network that underlies a higher cognitive function such as syntactic processing in the human brain. What one can do, however, is to limit the search space for the models and test specific hypotheses. We have done the first by limiting ourselves to strong activation peaks for a crucial syntactic fMRI contrast and by using a functional connectivity analysis to map the most likely basic network infrastructure between these peaks. We have done the second by testing whether the driving input to the resulting network was in one of two logically possible locations, based on previous activation studies and theoretical models of syntactic processing. As to which connection is primarily modulated by the processing of relatively complex sentences, we did not have an *a priori* hypothesis, hence we tested all possibilities within the infrastructure of our basic model. The reader should note that there is no mathematical or logical end to the degree of complexity that can be postulated in the models that are compared in a DCM analysis and we are fully aware that the network we present as the winning model is far from complete. In the present paper, we have chosen to be restrictive, rather than expansive, with respect to the model space investigated.

Conclusions

Successive application of three methods of neuroimaging data analysis was used to investigate the infrastructure of a neural network supporting complex syntactic processing, as well as the information flow within this network. A conventional BOLD fMRI subtraction paradigm investigating increased activation associated with the processing of object-cleft sentences relative to subject-cleft sentences revealed four major left-hemisphere peaks of activation, viz. in the inferior frontal gyrus, the premotor cortex, posterior superior temporal sulcus and anterior middle temporal gyrus. Directed partial correlation modeling showed evidence of functional connectivity between these four regions, such that the inferior frontal gyrus connected to premotor cortex and the posterior superior temporal sulcus, which in turn connected to the anterior middle temporal gyrus. Finally, using dynamic causal modeling, with both frequentist and Bayesian Model Selection, the driving input to this network was found to be located in the inferior frontal gyrus, rather than in the posterior superior temporal sulcus, while the primary modulation by complex sentence processing was on the connection between inferior frontal to posterior superior temporal cortex.

With no pretension to being either conclusive or exhaustive, these results add to current insights into the nature of the neural system that underlies complex sentence processing. The primary drive to this interactive system now appears to come from inferior frontal cortex, with a substantive role for its connection with posterior superior temporal cortex and a feedback mechanism from posterior superior temporal cortex back to inferior frontal cortex. In line with earlier research into the respective roles for these separate areas in syntactic processing, we suggest that syntactic structure-building and decomposition operations are supported primarily by the inferior frontal cortex, in an interactive relation with posterior superior temporal cortex, which supports thematic role assignment. Sentence processing does not start from analysis of pivotal verbs and their argument structure subcategorizations, but with structure building based on word order.

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