

Evidence of fronto-temporal interactions for strategic inference processes during language comprehension

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We investigated how readers strategically infer context-appropriate information on the basis of the presented text and their world knowledge during passage reading. In the main experimental condition, participants were instructed to read short passages and to predict the development of the situation described in each passage during reading. To accomplish this task, we assumed that participants need to draw strategic inferences relevant to the contexts. Comparing this condition with a passage-reading condition without prediction, we found out that the left anterior prefrontal cortex (aPFC) in Brodmann area 9/10 and the left anterior ventral inferior frontal gyrus (vIFG) in Brodmann area 47 elicited increased hemodynamic responses. These two regions are probably critical in coherence evaluation and in drawing strategic inferences. Additionally, we used dynamic causal modelling (DCM) to investigate the fronto-temporal interactions induced by the experimental conditions. Ten models with different plausible ways to modulate the connections between frontal and temporal regions were compared. The DCM results showed a consistent conclusion: The connectivity between the left posterior superior temporal sulcus (pSTS) and the left dorsal lateral inferior frontal gyrus (dIFG) were enhanced when participants made inferential predictions during reading. The results support the role of top-down influences mediated by the neural pathways between dIFG and pSTS in retrieving strategic inferences. With these findings we discuss functional roles of aPFC, vIFG and dIFG–pSTS connections in drawing strategic inferences.

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Introduction

The comprehension of spoken and written language not only requires the retrieval of the meaning of individual words and their syntactic and semantic combination but also demands real-world knowledge. Consider the following sentence (Potts et al., 1988): “No longer able to control his anger, the husband threw the delicate porcelain vase against the window.” Although not stated explicitly, readers may infer from their prior knowledge that the vase broke. This ability to draw inferences plays a crucial role in language comprehension. However, relatively little is known about the critical brain regions subserving these inference processes and how those regions interact with each other and with other language regions.

In many cases, readers are not aware of the generation of inferences during reading. Nevertheless, they are able to draw goal-directed or strategic inferences under their conscious control (Graesser et al., 1994; Graesser et al., 1993; Horiba, 2000; Kerns et al., 2004; Magliano et al., 1999; Rapp and Gerrig, 2006; van den Broek et al., 2001). For instance, readers drew more inferences during reading for “studying” than during reading for “entertainment” (Narvaez et al., 1999). Moreover, specific reading goals can alter the strength and the time course of these inferences. Consider again the above scenario about the angry husband. Predictive inferences, in this case “the vase broke”, are generally considered to be lacking immediately at the end of the sentence and thus take time to develop (Calvo and Castillo, 1998; Graesser et al., 1994). However, if readers are encouraged to predict the development of the situation described in the sentence, predictive inferences can be detected already at the end of the sentence (Allbritton, 2004; Calvo et al., 2006) and can be sustained much longer (McDaniel et al., 2001).

In this experiment, we used the reader’s ability to draw strategic inferences to investigate neural mechanisms of how readers infer context-appropriate information during reading. In the critical condition, namely the predictive-reading condition, we induced strategic inference processes by asking our participants to predict the development of the situation described in the text actively during reading. To contrast with this condition, we introduced the normal-reading condition in which we asked them to read and

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understand the text, but did not encourage predictive reading. We assumed that strategic inference processes are more intense during predictive reading than during normal reading. Additionally, we included a pseudoword-reading condition that served as a common baseline of the above mentioned passage-reading conditions.

According to discourse models of language comprehension such as the construction–integration model (Kintsch, 1998) and the immersed experienter model (Zwaan, 2004), inference processes are comprised of two key processes, namely, inference generation and information integration. Inferences can be generated automatically through word-association mechanism or through controlled retrieval processes (Cook et al., 2001; Myers and O'Brien, 1998). The controlled retrieval of inferences, the main focus of this study, probably involves frontal regions, which are associated with cognitive control, and temporal regions in which the semantic information and world knowledge are stored. This notion of fronto-temporal interactions in inference processes has been implied in a number of studies (Badre et al., 2005; Friederici, 2001; Gold et al., 2006; Kerns et al., 2004; Kuperberg et al., 2006; Mechelli et al., 2005; Oleser et al., 2007; Virtue et al., 2006; Wagner et al., 2001).

Furthermore, according to the above mentioned discourse models, the ultimate goal of text comprehension is to establish a coherent mental representation by integrating textual information and inferences. Previous fMRI studies indicated that information integration and coherence evaluation may be subserved by anatomical discrete frontal regions in the left hemisphere. Hagoort et al. (2004) showed that the left inferior prefrontal cortex, i.e., Brodmann area (BA) 45/47, elicited increased responses for both semantic and world knowledge violations, which indicates that the region is involved in information integration. Coherence evaluation seems to be associated with the left anterior prefrontal cortex. Ferstl and her colleagues conducted a series of fMRI and lesion studies (Ferstl and von Cramon, 2001, 2002; Ferstl et al., 2002) in which they asked participants to judge the coherence between two sentences in each trial. They observed increased responses in the left frontomedian cortex (BA 9/10) while participants were judging coherent sentence pairs relative to incoherent sentence pairs. They suggested that this region plays an important role in coherence evaluation.

Higher cognitive functions are likely to be realized by the interactions between several specialized brain regions (Friston, 1994). Drawing strategic inferences probably enhances fronto-temporal interactions. From the anatomical connections between frontal and the temporal lobes, we know that these interactions are mediated by means of at least two sets of neural pathways (Duffau et al., 2005). In the dorsal stream, the posterior temporal regions and the lateral frontal regions are connected by the arcuate fasciculi and the superior longitudinal fasciculi. In the ventral stream, the posterior and anterior temporal regions are connected by the inferior longitudinal fasciculi, and the anterior temporal regions are connected to the orbital frontal regions via the uncinate fasciculi (Catani et al., 2002; Crosson et al., 2005). Despite of the existence of the two sets of neural pathways in both hemispheres, the connections in the left dorsal stream seem to be dominant in language processing (Catani and ffytche, 2005; Mandonnet et al., 2007). To restrict the scope of this study, we mainly focused on the fronto-temporal interactions in the left hemisphere. The left dorsal stream interconnects three important language regions: the inferior frontal gyrus (IFG), the posterior superior temporal sulcus (pSTS) and the temporoparietal junction (TPJ) including the angular gyrus and the supramarginal gyrus. These regions and their connecting

pathways are probably engaged in different language functions (Bitan et al., 2005; Catani and ffytche, 2005; Nakamura et al., 2006; Tyler and Marslen-Wilson, 2007). For instance, Horwitz and Braun (2004) showed that the functional connectivity among IFG, TPJ and pSTS were enhanced in a narrative production task but were absent in the less linguistically demanding production task. Moreover, Bitan et al. (2005) showed that different effective connectivity patterns were observable when participants carried out rhyming and spelling judgment tasks. This implied that different regions and connections are recruited for various language tasks. However, very little is known about how inference processes modulate the interactions between brain regions, especially while reading everyday texts. Some brain regions seem to be critical for inference processes. Virtue et al. (2006) found activations in the left posterior superior temporal gyrus at coherence breaks during story reading. These were the points at which participants needed to generate inferences in order to understand the story. Some evidence indicated that word-level controlled semantic retrieval requires the involvement of both IFG and pSTS (Badre et al., 2005; Gold et al., 2006; Wagner et al., 2001). A similar mechanism may also be used in retrieving inferences, leading to the enhancement of interregional interactions between IFG and pSTS. Apart from IFG and pSTS, TPJ and the left anterior temporal lobe (aTL) also appear to be critical for inference generation. Activity of TPJ was shown to be involved in sentence-level semantic retrieval (Ferstl, 2007; Mason and Just, 2006; Price, 2000; Xu et al., 2005). When clarity of speech is reduced, which probably induces more top-down influences, Oleser et al. (2007) demonstrated functional connectivity enhancement between TPJ and left frontal regions. Moreover, in the model of speech processing proposed by Hickok and Poeppel (2007), TPJ is an essential component in the communication between frontal and temporal regions. Similar to TPJ, several researchers suggested that aTL is engaged in sentence-level comprehension (Beeman, 2005; Ferstl, 2007; Maguire et al., 1999; Humphries et al., 2001; Vigneau et al., 2006). In the framework of semantic processing in natural language, Beeman (2005) proposed that bilateral aTL detects, elaborates and refines higher order semantic relations, and IFG is responsible for the selection of competing activated concepts. According to this theory, the act of drawing strategic inference should enhance the interactions between aTL and IFG.

In the present study, we investigated the neural correlates of drawing strategic inferences by two complementary approaches. The first approach was to identify brain regions critical for drawing strategic inferences by contrasting the hemodynamic responses in the predictive-reading condition with those in the normal-reading condition. The second approach was to investigate the fronto-temporal interactions modulated by strategic inference processes using effective connectivity analysis (dynamic causal modelling, DCM, Friston et al., 2003). On the basis of the anatomical connections and the fMRI studies reviewed above, we constructed and compared 10 models with different plausible ways to modulate the connections among IFG, pSTS, TPJ and aTL (for details, see Figs. 1 and 2). The results provide useful information for refining theoretical notions in the field of higher level language processes.

Methods

Experimental design

Participants were asked to read short passages and respond to a lexical-decision task that occurred after each passage. Passages

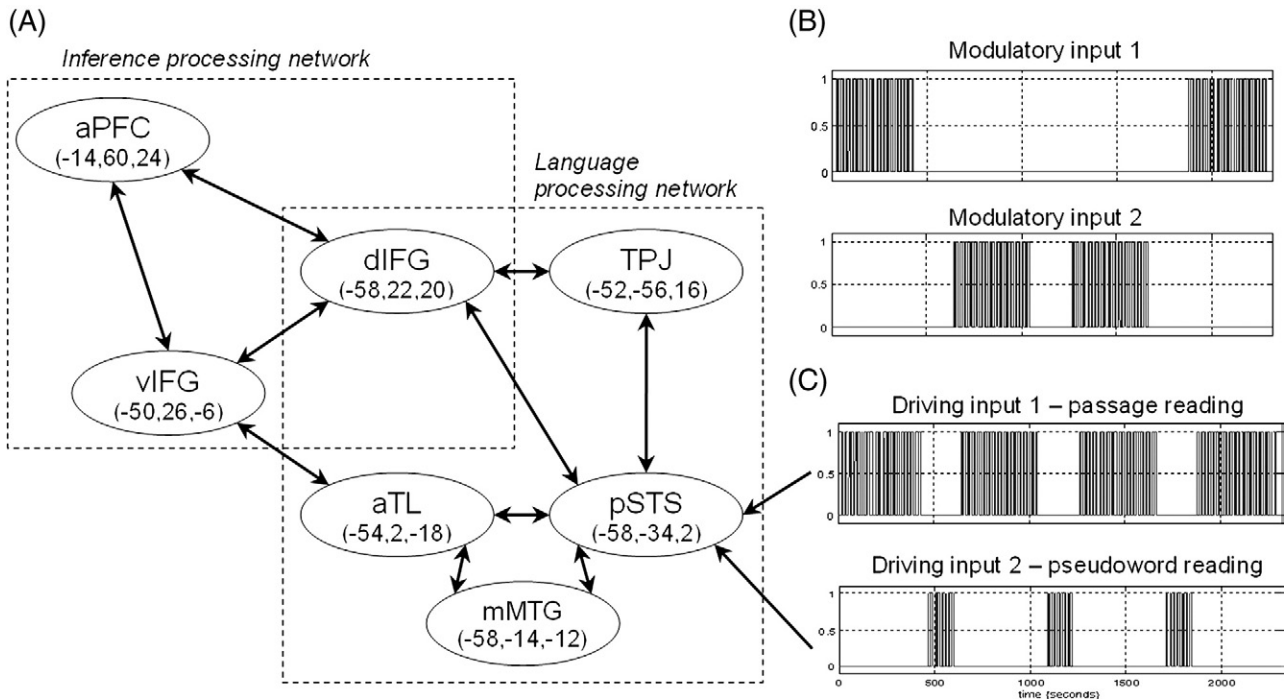


Fig. 1. The basic DCM structure in this study. (A) The schematic representation of the anatomical connections and the selected regions, namely anterior prefrontal cortex (aPFC), dorsal lateral inferior frontal gyrus (dIFG), anterior ventral inferior frontal gyrus (vIFG), temporoparietal junction (TPJ), posterior superior temporal sulcus (pSTS), middle portion of the middle temporal gyrus (mMTG) and anterior temporal lobe (aTL). The MNI coordinates of the selected regions are listed in brackets. For detailed information of the regions, please see the Results section. (B) The modulatory inputs, which corresponded to the predictive-reading and the normal-reading conditions. (C) The driving inputs which were assumed to influence pSTS directly.

were constructed in the way that the outcome of the situation described in each passage was predictable although it was not mentioned explicitly. This setting enabled us to manipulate the predictability of the target word in the lexical-decision task, i.e., the real target words of the task were either predictable or non-predictable. Thus, by comparing the response times for the predictable and non-predictable target words in the lexical-decision task, we were able to verify whether participants in the predictive-reading condition indeed predicted the development of the situation described in the text according to their world knowledge rather than simply associating irrelevant ideas. If participants actively predict the development of the situation described in the passage during reading in the predictive-reading condition, then the concept named by the predictable target word should be more prominent in the reader's mind and the lexical-decision task should be facilitated relative to the non-predictable target word. This facilitation effect should be weaker in the normal-reading condition because predictive inferences are not generated routinely (Calvo and Castillo, 1998). In other words, we expected an interaction effect between reading condition (predictive reading vs. normal reading) and target word type (predictable vs. non-predictable). In contrast to many behavioural studies using lexical-decision tasks for investigating inference processes, we did not include a control version for the predictive passages in the current experimental design because our study mainly focused on passage reading instead of lexical-decision latency. The advantage of this design is that every participant read exactly the same set of passages. For the sake of consistency, participants were also asked to respond to a lexical-decision task after each pseudoword sequence. Furthermore, to assure that participants read the passages and pseudoword

sequences carefully, in 25% of the total trials, a word-recognition task was presented after the lexical-decision task. Note that to recognize a pseudoword in the pseudoword-reading condition is more difficult than to recognize a real word in the passage-reading conditions. Therefore, we expected that the recognition accuracy in the pseudoword-reading condition would be relatively low but above chance level. To examine the hypothesis with regard to the behavioural responses of the tasks, we conducted a behavioural pre-study prior to the fMRI experiment.

Construction of stimuli

Ninety-six German passages were constructed. Thirty-two of them were translated and adapted for our German sample from the "predicting sentences" used in the study of McKoon and Ratcliff (1986), whereas the remaining 64 passages were constructed by the authors. Each passage consisted of 1 to 3 sentences describing an everyday event. The length of each passage was exactly 15 words. For each passage, a single word that depicted the implicit outcome of the described event was selected. These words were used as the predictable target words in the lexical-decision tasks. Furthermore, a non-predictable target word was selected and a pronounceable pseudoword was constructed for the stimuli of each lexical-decision task. The predictable and non-predictable target words did not differ significantly in length ($t_{95}=1.10$). The target words for the recognition task included a randomly selected content word from the passage and a common word that did not appear in any passage. Additionally, 24 pseudoword sequences were constructed. Each pseudoword sequence consisted of 15 pronounceable pseudowords. For the lexical-decision task following each pseudo-

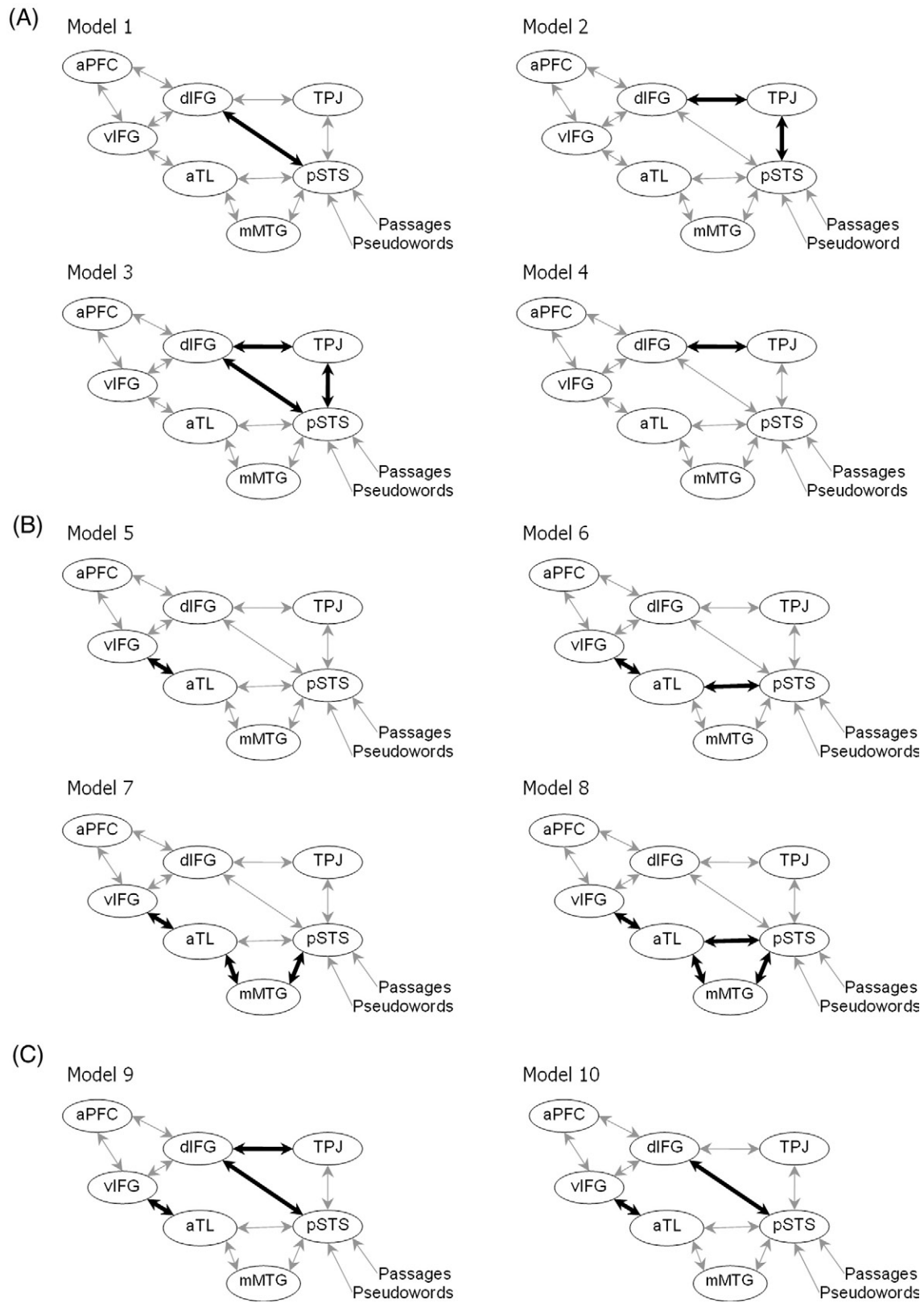


Fig. 2. The 10 models derived from the basic model (see Fig. 1). The connections modulated by the two modulatory inputs of predictive reading and normal reading are in bold. (A) Models with modulatory inputs at connections in the dorsal stream. (B) Models with modulatory inputs at connections in the ventral stream. (C) Models with modulatory inputs at connections in both dorsal and ventral streams.

Table 1
Text material samples and their target words in the lexical-decision task and the recognition task

Text	Lexical-decision task	Recognition task
	Target word	Target word
<i>Passage</i>		
Als die Boeing der steilen Bergwand immer näher kam, begannen die Passagiere laut zu schreien. (When the aeroplane came closer and closer to the steep mountain-face, the passengers began to scream loudly.)	Predictable: Absturz (crash)/Non-predictable: Liebster (sweetheart)/Pseudoword: Tennul	Bergwand/Tennis
<i>Pseudoword sequence</i>		
Geduldis ser jägur, süt dür Hihen grac. Dira pavanne wiader isaw eh sür svannund dep.	Real word: Borke (bark)/Pseudoword: Nochs	Dira/Eukf

word sequence, a target word was selected and a pronounceable pseudoword was constructed. Sample text materials are shown in Table 1.

Behavioural pre-study

Participants

Nineteen¹ (9 males, 10 females; mean age: 22; SD: 2) native German speakers were recruited. All of them were university students, right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971) and had normal or corrected-to-normal vision.

Stimulus presentation and tasks

The experiment consisted of 120 trials, 96 of them consisted of a passage and 24 of them consisted of a pseudoword sequence. Each passage and pseudoword sequence only appeared once in the entire experiment and every participant read exactly the same set of passages and pseudoword sequences. In each trial, participants needed to read either a passage or a pseudoword sequence and respond to a lexical-decision task. Additionally, in 25% of the total trials, the lexical-decision task was followed by a recognition task. The trials consisting of a passage were divided into 4 blocks, 24 trials each, and the trials consisting of a pseudoword sequence were divided into 3 blocks, 8 trials each. Each block of pseudoword-reading trials was arranged in between two blocks of passage-reading trials. In the beginning of a block of passage-reading trials, participants were asked to read the passages in the block using one of the two reading modes and respond to the subsequent lexical-decision and recognition tasks. For the predictive-reading condition, they were instructed to focus on the situation described in each passage and to predict the development of the situation actively, whereas for the normal-reading condition, they were instructed to read and understand the passages. In the beginning of a block of pseudoword-reading trials, they were instructed to read the pseudoword carefully and respond to the subsequent lexical-decision and recognition tasks. The sequence of reading conditions were counterbalanced in an ApBpBpA/BpApApB fashion, where “A” is predictive reading (24 trials), “B” is normal reading (24 trials) and “p” (8 trials) is pseudoword reading. The trials within a block were presented in random sequences. Participants were informed about the end of each block. The between-block interval was 15 s.

¹ In the pre-study, data from 16 participants were used in the analyses of lexical-decision latencies, i.e., data from 3 participants were excluded (for details, see the Results section).

Stimuli were presented on a 20-in. LCD screen using E-prime (Schneider et al., 2002). In the beginning of each trial, an asterisk was presented for 1000 ms. To remind participants as to which of the two reading modes should be used in the current block, the asterisk was red in the case of the predictive-reading condition; for the normal-reading condition and the pseudoword-reading condition, it was black. Subsequently, a passage or a pseudoword sequence was presented word by word. Each word was exposed for 450 ms and was followed by a 50-ms blank interval. Then, a question mark was presented for 1000 ms to cue the onset of the target word of the lexical-decision task. The maximum onset duration of the target word was 2500 ms, and it was erased once a response had been given. Participants needed to decide whether the target word was a real German word or a pseudoword and to provide a response by pressing the Y/N button of a response box. In 50% of the lexical-decision items, a real word was presented. Half of the real target words in the passage-reading conditions were predictable and the other half were non-predictable. To counterbalance the “yes”/“no” responses and the predictable/non-predictable target words in the lexical-decision tasks, four experiment versions were generated. Whenever there was a recognition task in the trial, a blue question mark was presented for 1000 ms after the lexical-decision task. Then, the target word of the recognition task was presented for a maximum of 2500 ms and was erased once the response had been given. Participants were requested to decide whether or not the target word had appeared in the passage or pseudoword sequence of the trial and to provide a response by pressing the Y/N button. The inter-trial interval was 4000 ms. The total time of a trial without a recognition task was 16000 ms, otherwise it lasted 19500 ms.

To allow participants to familiarize themselves with the reading conditions and the tasks, they were requested to participate in a training session consisting of 36 trials before the main experiment. The same procedure described above was used for training, only with different text materials.

fMRI study

Participants

Fifteen² (4 males, 11 females; mean age: 24; SD: 4) native German speakers, none of whom participated in the pre-study, gave informed written consent to participate in the experiment. All of them were university students, right-handed according to the

² In the fMRI experiment, data from 12 participants were used in the fMRI and DCM analyses, i.e., data from 3 participants were excluded. (for details, see the Results section).

Edinburgh Handedness Inventory (Oldfield, 1971), had normal or corrected-to-normal vision and did not have history of psychiatric, neurological disorder or claustrophobia.

Stimulus presentation and tasks

Exactly the same procedure as in the pre-study was executed (see above) except that the stimuli were projected on a screen in the MR cabin and viewed by participants via a mirror mounted in the head coil of the MRI scanner.

MRI acquisition

Functional images were acquired with a 3-T head scanner (Siemens Allegra) with birdcage head coil at the University of Regensburg. Participants were noise shielded by earplugs and headphones. Their heads were fixated by soft foam pads. Blood oxygen level-dependent (BOLD) responses were measured using a T2*-weighted echo planar imaging (EPI) sequence (echo time (TE)=30 ms; volume repetition time (TR)=1040 ms; resolution=3×3 mm²; number of slices=18, interleaved; slice thickness=4 mm; distance factor=10–20%; flip angle=62°). To achieve high temporal resolution in the functional scans, the most superior portion of the supplementary motor cortices, the motor cortices and the lower half of the anterior temporal lobes were not covered by the scan volume. These regions are unlikely to be important in language comprehension (Cabeza and Nyberg, 2000; Vigneau et al., 2006). At the end of the experiment, structural images of the whole brain were acquired using a T1-weighted MPRAGE sequence (TR=2250 ms; TE=2.6 ms; resolution 1×1×1 mm³).

Conventional fMRI data analysis

Data pre-processing and statistical analyses were conducted using SPM5 (Wellcome Department of Imaging Neuroscience, London, UK, <http://www.fil.ion.ucl.ac.uk/spm/>). Functional images of each participant were corrected for residual head motions, realigned to the first image and corrected for slice timing. Subsequently, all functional images were co-registered and normalized to the MNI-152 template and re-sampled to 2×2×2 mm³ spatial resolution. Spatial smoothing was applied to the functional images using an isotropic Gaussian kernel with a full-width half-max (FWHM) of 4 mm. A general linear model (GLM) was constructed for each participant in order to analyze the hemodynamic responses captured by the functional images. In each GLM, regressors were generated by convolving the canonical hemodynamic function with a boxcar function representing a particular section of the experiment. Three separate regressors were used to model the hemodynamic responses during predictive reading, normal reading and pseudoword reading. Fourteen regressors were used to capture the responses during lexical-decision tasks and during recognition tasks in different reading conditions and target word types. These regressors are not the interest of this study. Their main purpose was to prevent task-related responses from confounding with the responses induced by passage reading or pseudoword reading. Moreover, high-pass filter (1/128 Hz) was applied to remove low-frequency drifts. *T*-test contrasts between the reading conditions were calculated individually and averaged across participants using random-effect analysis. In this study, activations surpassing a voxel-level height threshold at $p < 0.0003$ ($t = 4.70$, uncorrected) and an extent threshold of $p < 0.05$ (corrected), which corresponding to a minimal cluster size of 15 voxels were considered to be significant unless otherwise specified.

DCM analysis

DCM enables us to estimate (i) intrinsic connectivity, i.e., the influences from the activities of the interconnected brain regions in the absence of external input, (ii) the modulation (enhancement or inhibition) of connectivity induced by experimental manipulations and (iii) the direct external influences on the regional activities (Friston et al., 2003). To identify which fronto-temporal connections are modulated by inference processes, we adopted the two-stage procedure implemented in the study of Stephan et al. (2007). In the first stage, using Bayesian model selection proposed by Penny et al. (2004) and Stephan et al. (2007), we selected the best among 10 models, which reflected different plausible ways to modulate the connections between frontal and temporal regions (for details, see Figs. 1 and 2). In the second stage, we compared the modulatory effects induced by the two reading modes in the best model using a classical second-level (between-subject) analysis, one-sample *t*-test that compared the corresponding estimates of the modulatory effects from the individual DCMs. The DCM module in SPM5 was used for the Bayesian model estimation and selection. The detailed procedures for defining DCMs, Bayesian model selection and second-level analysis of the modulatory effects are described below.

Regions selection and time series extraction. The selection of regions was based on the group-level results of the conventional fMRI data analysis. To identify the regions critical to inference processes, we considered the significantly activated clusters in the contrast between the predictive-reading condition and the normal reading condition at the predefined threshold (Fig. 3D) and at a lowered threshold (Fig. 3E). Three regions were selected, namely the anterior prefrontal cortex (aPFC, cluster 19 in Fig. 3D), the dorsal lateral inferior frontal gyrus (dlIFG, cluster 25b in Fig. 3E) and the anterior ventral inferior frontal gyrus (vIFG, cluster 20 in Fig. 3D). Their coordinates are shown in Fig. 1. For dlIFG, we chose the coordinate of a local maximum (cluster 25b in Fig. 3E) instead of the peak coordinate (cluster 25a in Fig. 3E) of this region because this coordinate overlaps with the dlIFG activation when we compared passage reading with pseudoword reading (see Fig. 3A). Thus, the activity around this coordinate can reflect the processes for inference processes and language comprehension in general. To simplify the model, an activated cluster (cluster 21 in Fig. 3D) in the anterior ventral inferior frontal region, which is located in the same Brodmann area as vIFG was not selected.

Regions involved in language comprehension were determined by the contrast between passage reading (predictive- and normal-reading conditions) and the pseudoword reading (see Fig. 3A). To reduce the complexity of the network, we only considered the activated clusters in the left hemisphere. Four regions were selected, namely the posterior superior temporal sulcus (pSTS, cluster 2 in Fig. 3A), the temporoparietal junction (TPJ, cluster 3 in Fig. 3A), the middle portion of the middle temporal gyrus (mMTG, cluster 4a in Fig. 3A) and the anterior temporal lobe (aTL, cluster 4b in Fig. 3A). Their coordinates are shown in Fig. 1. Please note that mMTG and aTL belong to the same cluster. The location of aTL is the most anterior local maximum of that cluster. This region was included because we postulate that the anterior temporal areas are involved in inference processes (for details, see the Introduction section). In the contrast in consideration, a small cluster in the anterior ventral inferior frontal gyrus (cluster 5 in Fig. 3A) was not included because its location is close to a selected region vIFG.

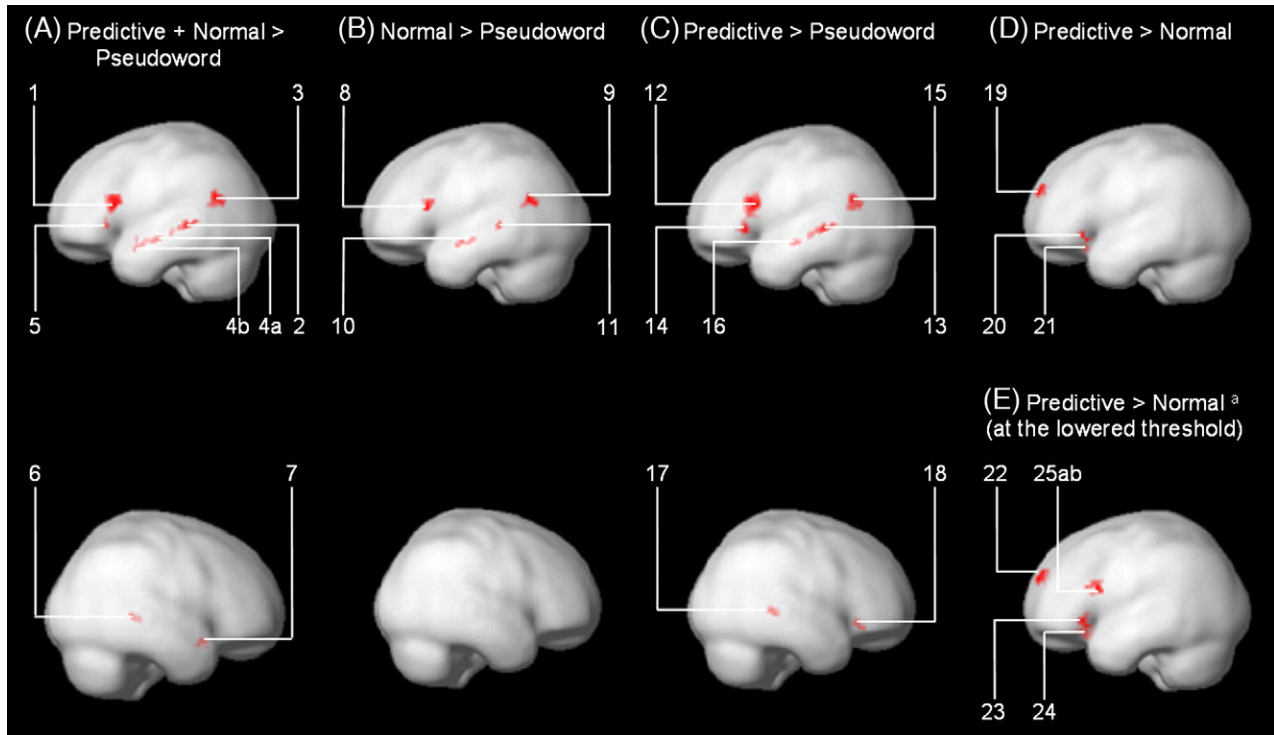


Fig. 3. Significant clusters in the comparisons between the reading conditions. (A) Contrasting predictive reading and normal reading with pseudoword reading. (B) Contrasting normal reading with pseudoword reading. (C) Contrasting predictive reading with pseudoword reading. (D) The direct comparison between predictive reading and normal reading. (E) The direct comparison between predictive reading and normal reading at the lowered threshold. The numbering of the regions corresponds to Table 4. ^aLowered threshold: The voxel-level height threshold at $p < 0.001$ ($t = 4.0$, uncorrected) and the extent threshold at $p < 0.05$ (corrected).

The region-specific time series were extracted and adjusted for confounds in the subject-level using SPM5. The locations of regions in each individual model were based on the peaks or the local maxima of the selected clusters in the group-level analysis. The time series were the first eigenvariate of all voxels within a 4-mm radius centred on each location and significant in the t -contrast comparing passage reading versus implicit baseline at voxel-level height threshold of $p < 0.01$ (uncorrected). The coordinates of the regions are given in Fig. 1. As the activations vary over subjects, if the voxel at the coordinate of a region was not significant at the subject-level, the centre of the region was shifted to the nearest significant voxel from the coordinate defined by the group-level analysis. In summary, 23 out of 84 (27%) regions defined in all 12 participants were not at their coordinates defined by the group-level analysis, but the maximum displacement between a region and its ideal coordinate was less than 2.6 mm. No region was overlapping with each other and the minimum edge to edge displacement between two regions was at least 10 mm.

Definition of anatomical connections. To specify plausible anatomical connections between the selected regions in DCM, we primarily used the evidence from diffusion tensor imaging (DTI) studies of humans. We first defined the long-range connections connecting the frontal and temporal regions and then the intra-lobe connections in the left hemisphere. The final network of connections specified in DCM is shown in Fig. 1A.

The long-range connections between dIFG and the posterior language regions, pSTS and TPJ seem to be interconnected by

three segments of white matter pathways (the arcuate fasciculus and the superior longitudinal fasciculus) in the dorsal stream (Catani et al., 2002; Catani and ffytche, 2005, Croxson et al., 2005 and Makris et al., 2005). We did not connect pSTS to vIFG because the arcuate fasciculus terminates predominantly in the dorsolateral prefrontal cortex instead of the ventral part of the cortex (Makris et al., 2005). Ventrally, evidence was shown that aTL and the orbital frontal gyrus including vIFG are connected via the uncinate fasciculus (Catani et al., 2002; Croxson et al., 2005). For intra-lobe connections, mMTG is likely to be connected to its neighbours pSTS and aTL in the left temporal lobe by U-shape short fibres, and the direct connections between pSTS and aTL seems to be connected by the inferior longitudinal fasciculus (Catani et al., 2002). In the frontal lobe, aPFC, dIFG and vIFG are probably interconnected according to primate studies (Petrides and Pandya, 1999, 2001). We assumed that all abovementioned connections are reciprocal. Further evidence for the network described above was provided from a comprehensive functional-anatomical model of language processing proposed by Friederici (2002) and Friederici and Kotz (2003). In their model, they indicated that functional connections exist between the posterior temporal regions and the inferior frontal regions, between the posterior and anterior temporal regions and between the inferior frontal regions and the anterior temporal regions. This model matches well with our proposed network.

Definition of driving inputs. A boxcar function representing the two passage-reading conditions, and a boxcar function representing the pseudoword-reading condition were defined as the driving

inputs. We assumed that the driving inputs influence pSTS directly, and the neuronal activity propagates from pSTS to other regions through the connections defined above. This assumption is based on the results from the anatomically constrained magnetoencephalography (aMEG) study from Marinkovic et al. (2003) in which the authors showed that activity of visual language processing spreads from the pSTS and the inferolateral temporal area to the other regions.

Definition of modulatory inputs. According to the above steps, a basic model was constructed which is shown in Fig. 1. To test whether and which fronto-temporal connections are enhanced by the two reading modes, we systematically derived 10 DCMs from the basic model by defining modulatory inputs at various connections. Two boxcar functions were used as two separate modulatory inputs in DCM (see Fig. 1B), which corresponded to predictive reading and normal reading. In Models 1–3 (see Fig. 2A), modulatory inputs were allowed to modulate all direct and indirect connections between pSTS and dIFG in the dorsal stream. In Model 4 (see Fig. 2A), modulation was with respect to the connections between TPJ and dIFG. In Models 5–8 (see Fig. 2B), modulatory inputs were allowed to modulate all possible sets of connections between pSTS and vIFG in the ventral stream. As the two reading modes may also modulate the fronto-temporal connections in both dorsal and ventral stream simultaneously, we included two models, Model 9 and Model 10 (see Fig. 2C) in which two different sets of connections could be influenced by the modulatory inputs. In Model 9, modulatory inputs could modulate all direct fronto-temporal connections in the dorsal and ventral streams. In Model 10, modulatory inputs could modulate the connections between dIFG and pSTS and the connections between aTL and vIFG. In all 10 models, we assumed that the modulatory inputs influence the bidirectional connections between the frontal and temporal regions. This assumption was made because frontal regions are very likely responsible for integrating different sources of information including inferences, as well as for coherence evaluation and for driving controlled semantic retrieval, as argued in the Introduction section. This implies that any feed-back effect such as controlled semantic retrieval also induces feed-forward effects in order to integrate the product of the feed-back effect into a coherent representation in the frontal regions during language comprehension.

Bayesian model selection. We followed the conservative model comparison strategy proposed by Penny et al. (2004). Accordingly, we approximated the evidence for each model with Akaike's and Bayesian information criteria (AIC and BIC) by which model accuracy and complexity are taken into account. Evidence for each model was compared by Bayes Factors (BF_{ij}). They were defined as the ratio between the estimated evidences for each of the two models, $BF_{ij} = (\text{evidence of model } i) / (\text{evidence of model } j)$. When $BF_{ij} > 1$, the data favour model i over model j , and when $BF_{ij} < 1$, the data favour model j over model i . We regard the evidence as consistent when both Bayes Factors computed by AIC and BIC

agree with each other and are larger than e (the natural exponent 2.72). As the above model comparison procedure is carried out on the subject level, to compare models in the group level, we used the method implemented by Stephan et al. (2007). Two indices were computed, namely group Bayes factor (GBF) and positive evidence ratio (PER). A group Bayes factor was computed by multiplying the individual Bayes factors. However, GBFs can be misleading if strong outliers are present. Therefore, we computed PER that counts the number of comparisons for which the BF passed the threshold for positive evidence for either of the compared models.

Second-level analysis of the modulatory effects. To test whether the modulatory effects of the two passage-reading conditions differ from each other in the best model, we performed a one-sample t -test (two-sided) to compare the corresponding estimates of the modulatory effects from the individual DCMs. These tests were carried out separately for each modulatory effect on each connection. We adopted a conservative statistical threshold of $p < 0.05$ with Bonferroni's correction.

Results

Behavioural data

Pre-study

One of the participants exhibited very low accuracy (<50%) in the recognition tasks. For two other participants, the mean response latency in the lexical-decision task was 60% slower than for the rest of the participants. The data sets of these three participants were excluded from further analysis. In total, data from 16 participants were included in the analyses to be reported.

Response accuracy. The mean accuracies of the lexical-decision task in the pre-study were 97% in the predictive-reading condition, 97% in the normal-reading condition and 96% in the pseudoword-reading condition. They did not differ significantly ($t_{15} < 1.4$, $p > 0.18$). The mean accuracies of the recognition task were 93% in the predictive-reading condition, 89% in the normal-reading condition and 74% in the pseudoword-reading condition. With respect to recognition accuracy, there was no significant difference between the two passage-reading conditions ($t_{15} = 1.5$, $p = 0.15$). As expected, the recognition accuracy in the pseudoword-reading condition was significantly lower than that in the passage-reading conditions ($t_{15} = 3.5$, $p < 0.01$).

Lexical-decision latency. We conducted two 2 (passage-reading condition: predictive-reading vs. normal-reading) \times 2 (target word type: predictable vs. non-predictable) ANOVAs of the mean response latencies of the correct "yes" responses, one based on subject variability (F_1) and one based on item variability (F_2). We used 2 criteria to remove outliers. First, lexical-decision latencies above or below 2.5 standard deviations from the mean of "yes"

Table 2
Pre-study: mean lexical-decision latency of "yes" responses (in ms)

Reading condition	Predictive reading		Normal reading	
	Predictable	Non-predictable	Predictable	Non-predictable
RT (SD)	675 (157)	751 (147)	678 (157)	712 (132)

Table 3
fMRI study: mean lexical-decision latency of “yes” responses (in ms)

Reading condition	Predictive reading		Normal reading		
	Target word	Predictable	Non-predictable	Predictable	Non-predictable
RT (SD)		581 (106)	669 (133)	582 (87)	622 (113)

responses in each of the two reading conditions were replaced (2.0%) by the mean in each condition separately. Second, lexical-decision latencies above or below 2.5 standard deviations from the mean of “yes” responses in both reading conditions were replaced (1.7%) by the overall mean of “yes” responses. In total, 3.7% data points were replaced. The mean lexical-decision latency of “yes” responses is shown in Table 2. The main effect of reading condition was not significant ($F_1(1,15)=1.26$, $p=0.28$; $F_2(1,95)=1.48$, $p=0.23$). The main effect of target word type was significant ($F_1(1,15)=11.57$, $p<0.01$; $F_2(1,95)=36.55$, $p<0.01$), as was the interaction effect between reading condition and target word type ($F_1(1,15)=5.08$, $p<0.05$; $F_2(1,95)=4.93$, $p<0.05$). In order to

gain more information with respect to the reading-condition \times target-word-type interaction effect, we conducted t -tests on the latencies in the two reading conditions. Separate comparisons indicated that the mean lexical-decision latency was significantly shorter for predictable than for non-predictable target words in the predictive-reading condition ($t_{15}=4.60$, $p<0.01$) but not in the normal-reading condition ($t_{15}=1.66$, $p=0.12$).

Behavioural data in the fMRI study

Two participants exhibited very low recognition accuracy (<67%) in one of the two reading conditions in the scanner. For one other participant, the mean response latency in the lexical-

Table 4
Significant clusters in the comparisons between the reading conditions and the regions selected for DCM

Structure/gyrus	Approximate BA	Side	MNI coordinates			Size (mm ³)	Z _{max}
			x	y	z		
<i>A. Predictive and normal reading > pseudoword reading</i>							
1. Dorsal lateral inferior frontal gyrus	44/45	L	-58	20	14	1104	4.83
2. Posterior superior temporal sulcus ^a (pSTS)	21/22	L	-58	-34	2	688	4.61
3. Supramarginal gyrus/posterior superior temporal gyrus ^a (TPJ)	22/39/40	L	-52	-56	16	968	4.56
4a. Middle portion of the middle temporal gyrus ^a (mMTG)	21	L	-58	-14	-12	368	4.12
4b. Anterior portion of the middle temporal gyrus ^{a,b} (aTL)			-54	2	-18		
5. Anterior ventral inferior frontal gyrus	47	L	-50	24	0	144	4.10
6. Posterior superior temporal sulcus	21/22	R	52	-36	0	256	4.62
7. Anterior superior temporal lobe	21/38	R	52	10	-16	152	4.43
<i>B. Normal reading > pseudoword reading</i>							
8. Dorsal lateral inferior frontal gyrus	44/45	L	-58	20	14	424	4.60
9. Angular gyrus/posterior superior temporal gyrus	22/39	L	-60	-60	20	623	4.34
10. Middle portion of the middle temporal gyrus	21	L	-58	-4	-14	208	4.02
11. Posterior superior temporal sulcus	21/22	L	-58	-34	-2	144	3.90
<i>C. Predictive reading > pseudoword reading</i>							
12. Dorsal lateral inferior frontal gyrus	44/45	L	-54	16	18	1440	5.08
13. Posterior superior temporal sulcus	21/22	L	-58	-34	-2	912	4.79
14. Anterior ventral inferior frontal gyrus	45/47	L	-50	26	0	664	4.74
15. Supramarginal gyrus/posterior superior temporal gyrus	22/39/40	L	-50	-56	16	1040	4.43
16. Middle portion of the middle temporal gyrus	21	L	-58	-14	-12	160	4.40
17. Posterior superior temporal sulcus	21/22	R	52	-36	-2	384	5.02
18. Anterior ventral inferior frontal gyrus	47	R	46	28	-10	224	3.99
<i>D. Predictive reading > normal reading</i>							
19. Anterior prefrontal cortex ^a (aPFC)	9/10	L	-14	60	24	400	4.75
20. Anterior ventral inferior frontal gyrus ^a (vIFG)	47	L	-50	26	-6	152	4.14
21. Dorsal lateral inferior frontal gyrus	47	L	-30	24	-18	144	4.02
<i>E. Predictive reading > normal reading at lowered threshold^c</i>							
22. Anterior prefrontal cortex	9/10	L	-14	60	24	624	4.75
23. Anterior ventral inferior frontal gyrus	47	L	-50	26	-6	336	4.14
24. Anterior ventral inferior frontal gyrus	47	L	-30	24	-18	520	4.02
25a. Dorsal lateral inferior frontal gyrus	44/45	L	-50	12	18	512	4.12
25b. Dorsal lateral inferior frontal gyrus ^{a,b} (dIFG)			-58	22	20		

^a A region selected for DCM.

^b A local maximum of the cluster. It was listed because its coordinate was used to define a region in DCM (for details, see the Methods section).

^c Lowered threshold: The voxel-level height threshold at $p<0.001$ ($t=4.0$, uncorrected) and the extent threshold at $p<0.05$ (corrected).

decision task was 60% slower than for the rest of the participants. The data sets of these three participants were excluded from further analyses. In total, data from 12 participants were included in the following analyses of lexical-decision latencies as well as fMRI and DCM analyses.

Response accuracy. The mean accuracies of the lexical-decision task during the fMRI data acquisition were 98% in the predictive-reading condition, 98% in the normal-reading condition and 97% in the pseudoword-reading condition. They did not differ significantly ($t_{11} < 1.6$, $p > 0.15$). The mean accuracies of the recognition task were 89% in the predictive-reading condition, 88% in the normal-reading condition and 73% in the pseudoword-reading condition. With respect to recognition accuracy, there was no significant difference between the two passage-reading conditions ($t_{11} < 1$, $p = 0.57$). As expected, the recognition accuracy in the pseudoword-reading condition was significantly lower than that in the passage-reading conditions ($t_{11} = 5.7$, $p < 0.01$).

Lexical-decision latency. We used the same criteria for identifying outliers as in the behavioural pre-study. In total, 4.0% data points were replaced. The mean latencies in each condition are displayed in Table 3. Data analyses were as in the pre-study, except that we included the sequences of reading conditions (2 levels) and experiment versions (4 levels) as 2 between-subject factors because the experiment in contrast to the pre-study was not fully counter-balanced. Fully counterbalancing the experiment would have required that the number of subjects is a multiple of 8. The main effect of reading condition was not significant in the subject analysis, but it was significant in the item analysis ($F_1(1,4) = 1.89$, $p = 0.24$; $F_2(1,95) = 5.12$, $p < 0.05$). The main effect of target word type was significant ($F_1(1,4) = 12.90$, $p < 0.05$; $F_2(1,95) = 23.65$, $p < 0.01$). The interaction effect between reading condition and target word type was significant ($F_1(1,4) = 13.88$, $p < 0.05$; $F_2(1,95) = 6.60$, $p < 0.05$). All other interaction effects were not significant ($F_1 < 5.4$; $p > 0.08$). Similar to the results in the pre-study, separate comparisons of the latencies in the two reading conditions indicated that the mean lexical-latency was significantly shorter for predictable than for non-predictable target words in the predictive-reading condition ($t_{11} = 3.91$, $p < 0.01$), but only marginally significant in the normal-reading condition ($t_{11} = 2.2$, $p = 0.05$).

Conventional fMRI data analysis

Compared to the results for the pseudoword-reading condition, the predictive-reading and normal-reading conditions together evoked increased responses in the superior and middle temporal lobe, the temporoparietal junction and the infer frontal gyrus in the left hemisphere (Fig. 3A, upper panel). The activations in the right hemisphere were clearly less extensive, only two clusters in the right posterior and anterior temporal regions were activated (Fig. 3A, lower panel). When comparing each reading condition against the pseudoword-reading condition separately, similar activation patterns were observed (Figs. 3B and C). The direct comparison between the predictive- and normal-reading conditions revealed three significant clusters in the left frontal lobe. One of them was located in the left anterior prefrontal cortex (BA 9/10), and two of them were located in the anterior ventral inferior frontal gyrus (BA 47). At a lowered threshold, voxel-level height threshold of $p < 0.001$ ($t = 4.0$, uncorrected) and extent threshold of $p < 0.05$ (corrected), one more cluster in the left dorsal lateral inferior frontal gyrus (cluster 25 in Fig. 3E) was revealed. This cluster overlapped with the activations of the dorsal lateral inferior frontal gyrus in all other contrasts (cluster 1 in Fig. 3A, cluster 8 in Fig. 3B and cluster 12 in Fig. 3C). Comparing normal reading with predictive reading, no significant cluster was found at the predefined or the lowered threshold. The detailed information with respect to the significant clusters is listed in Table 4.

DCM analysis

Table 5 lists the individual BFs of the pairwise Bayesian model comparisons between Model 1 and all other nine models. The results clearly indicated that Model 1 is the best model among the models in the comparisons. The evidence in favour of Model 1 was robust ($GBF > 10^{19}$) and highly consistent among participants. For the comparisons between Model 1 and any other models, at least 10 out of 12 participants showed positive evidence in favour of Model 1, but no single comparison showed positive evidence in favour of any other model besides Model 1.

In Model 1, only the bidirectional connections between dIFG and pSTS were allowed to be modulated by the modulatory inputs which corresponded to the two passage-reading conditions. The

Table 5
The participant-specific Bayes factors of the pairwise Bayesian model comparisons between the best model (Model 1) and all other 9 models

Subject	Model comparison								
	1 vs. 2	1 vs. 3	1 vs. 4	1 vs. 5	1 vs. 6	1 vs. 7	1 vs. 8	1 vs. 9	1 vs. 10
1	2.9E+02	2.9E+03	1.1E+01	4.4E+01	5.1E+02	1.2E+04	4.2E+05	3.1E+03	5.4E+01
2	1.3E+02	2.9E+03	1.3E+08	4.6E+04	1.5E+50	1.1E+04	6.2E+05	1.3E+03	3.2E+01
3	1.7E+03	1.1E+03	2.0E+02	6.2E+02	3.0E+51	4.2E+05	2.2E+07	1.5E+03	5.2E+01
4	2.6E+03	9.9E+03	5.2E+11	3.5E+12	5.2E+07	6.5E+15	2.1E+17	4.1E+03	4.9E+01
5	9.9E+01	3.3E+03	1.1E+00	1.5E+00	5.2E+69	4.0E+03	2.0E+05	2.8E+03	5.2E+01
6	2.2E+02	2.1E+03	5.0E+00	5.1E+00	8.1E+99	1.1E+04	4.8E+05	2.3E+03	5.1E+01
7	1.5E+03	4.4E+03	3.9E+01	5.5E+02	1.1E+90	3.2E+05	4.3E+06	8.0E+03	5.4E+01
8	3.7E+03	2.5E+03	7.8E+01	1.4E+02	3.1E+52	3.1E+05	1.3E+07	2.0E+03	4.2E+01
9	9.9E+01	1.6E+03	2.9E+00	2.8E+00	–	4.2E+03	1.4E+05	2.0E+03	4.5E+01
10	4.0E+02	2.3E+03	1.8E+01	4.1E+01	1.0E+118	3.0E+04	8.8E+05	2.6E+03	5.1E+01
11	2.3E+01	3.1E+00	2.6E+01	1.7E+02	9.1E+04	3.4E+05	4.7E+07	6.5E+01	4.7E+01
12	1.5E+02	1.7E+03	6.3E+00	2.4E+00	1.0E+39	5.6E+03	6.1E+04	7.2E+02	1.8E+01
GBF	3.0E+30	1.5E+38	2.3E+31	1.2E+32	1.6E+586	4.2E+65	2.3E+84	6.2E+38	5.1E+19
PER	12:0	12:0	11:0	10:0	11:0	12:0	12:0	12:0	12:0

“–” denotes that BIC and AIC approximations to the model evidence did not agree and no statement can be made.

Table 6
The participant-specific modulatory effects in Model 1 (in Hz)

Subject	pSTS → dIFG			dIFG → pSTS		
	Predictive reading	Normal reading	Difference	Predictive reading	Normal reading	Difference
1	0.19	0.02	0.17	0.14	-0.02	0.16
2	0.28	-0.04	0.32	0.20	-0.06	0.26
3	0.26	-0.03	0.29	0.10	-0.02	0.12
4	0.28	-0.09	0.37	0.11	-0.12	0.23
5	0.15	0.07	0.08	0.04	-0.03	0.07
6	0.17	0.08	0.09	0.07	0.00	0.07
7	0.21	0.17	0.04	0.20	0.08	0.12
8	0.24	-0.06	0.30	0.04	0.00	0.04
9	-0.01	0.10	-0.11	0.01	0.01	0.00
10	0.24	0.11	0.13	0.18	0.07	0.11
11	0.17	-0.01	0.18	0.07	-0.02	0.09
12	0.18	0.05	0.13	0.09	0.01	0.08
Mean	0.20	0.03	0.17	0.10	-0.01	0.11
SE	0.02	0.02	0.04	0.02	0.01	0.02
t_{11}	8.64	1.35	4.19	5.57	0.60	5.30
p	0.0000*	0.2047	0.0015*	0.0002*	0.5591	0.0003*

* Significant using Bonferroni correction for multiple tests (2 comparisons). The adjusted threshold is $p=0.025$.

individual modulatory effects on these connections are listed in Table 6. Predictive reading significantly enhanced the connectivity between dIFG and pSTS bidirectionally, whereas the modulatory effect of normal reading did not deviate from zero. The modulatory effects of predictive reading at both bidirectional connections between dIFG and pSTS were significantly larger than those effects of normal reading. Incorporating the results of Bayesian model selection with the second-level modulatory effects comparison, we can conclude that predictive reading enhanced the connections between dIFG and pSTS but did not enhance the other fronto-temporal connections in the comparisons.

Discussion

Our results show that increased responses in the anterior prefrontal cortex (BA 9/10), the inferior portion of the inferior frontal gyrus (BA 47) and the dorsal lateral inferior frontal gyrus (BA 44/45) in the left hemisphere are associated with the reader's active involvement in predicting the development of the situation described in the text during reading. The DCM analyses demonstrated that predictive reading primarily enhances the interactions between dIFG and pSTS. These three regions and the dIFG–pSTS connections seem to be particularly important for drawing strategic inferences. Below, we first discuss the methods used in this study. Then, based on our findings and what we know from previous imaging studies, we postulate a neural mechanism for drawing strategic inferences.

Experimental paradigm and DCM

The present study differs from previous brain imaging studies of higher level language processes in various aspects. The first difference is with respect to the experimental paradigm: In many previous studies, the effects of interest were studied by contrasting the effects induced by different types of text materials such as syntactically complex versus less complex texts, coherent versus incoherent texts, comprehensible versus incomprehensible texts, etc. One potential disadvantage of these paradigms is that it is often

difficult to determine which level of language processing is isolated in the comparisons (Okada and Hickok, 2006). Also, “degraded” text materials (e.g., incomplete, incoherent or incomprehensible texts) may even trigger more strategic inferences than “normal” texts (Keefe and McDaniel, 1993; McNamara et al., 1996; Kuperberg et al., 2006; Mason and Just, 2004; Obleser et al., 2007). In contrast, we kept the text materials fixed but encouraged strategic inferences during reading in our study. This allowed us to remove all activities related to lower level language processes and single out the higher level language processes. But this approach also has its caveats. A potential problem would be the difficulty to switch between reading modes, especially for participants to switch off the predictive-reading mode in the normal-reading condition. To assist participants to switch between the reading modes, we intentionally arranged a pseudoword-reading block in between two passage-reading blocks. Since it is very difficult to infer anything coherent from a pseudoword sequence, we expect that this forces participants to stop using the predictive-reading mode. Another drawback with this approach is that it may be difficult for an experimenter to control whether participants follow the instructions with respect to the given reading modes. Even if participants were to ignore the reading mode instructions, they could still perform the lexical-decision task and the recognition task perfectly. These potential problems would blur the distinction between the two reading modes. However, we are confident that they did not affect the present study substantially because the behavioural results obtained in the lexical-decision task, the physiological responses of fMRI and the connectivity analyses all reflected that there are clear differences between the two reading modes in the expected direction. In both pre-study and the behavioural results of fMRI experiment, we found significant reading-mode \times target-word-type interaction effects: The difference between the response times elicited by predictable and non-predictable target words was much larger in the predictive-reading condition than it was in the normal-reading condition. One may wonder why the difference between the passage-reading conditions was not evident for the predictable target words but rather for the non-predictable target words. A straightforward way to interpret the behavioural results is that the

predictive-reading mode slowed down the response times of non-predictable target words. Possibly, participants generated an expectation of the target word during predictive reading, and this expectation strongly mismatched with the meaning of the non-predictable target word, leading to an inhibitory effect in this case, whereas this inhibitory effect was absent or relatively weak for the predictable target word (cf. Fincher-Kiefer, 1995; Zwann et al., 2002). This implies that the resulting representation of the text, including the inferences that were drawn during reading, better matched the predictable than the non-predictable target word in the predictive-reading condition. Otherwise, the inhibitory effect on the non-predictable target word should also have been observed for the predictable target word. This relation between the resulting representation and the predictability of the target word does not hold true or was not as strong in the normal-reading condition, where participants presumably are less engaged in active inference processes. Based on previous research, an alternative interpretation may also be plausible. With a set of experiments similar to the ones in the present study, Allbritton (2004) showed that the predictive-reading mode increases response times for predictable and non-predictable target words in general. Although we did not find a significant main effect of reading mode, we cannot rule out the possibility that a similar effect as shown in Allbritton (2004) modulated the results in present study. It is possible that the effect that slowed down the response times in general in the predictive-reading condition was counteracted by the hypothesized facilitation effect on the predictable target word, resulting in a null difference between reading modes in this condition. If it was the case, the inhibitory effect on the non-predicted target word as well as the facilitation effect on the predicted target word may also play a role in the present results. Though we cannot be absolutely sure which effects were at the basis of the observed response-time pattern of the lexical-decision task, in either way discussed above, we can be sure that our reading-mode manipulation was effective: At least, the behavioural results indicated that participants drew inferences relevant to the predictable target words in the predictive-reading condition, but it was not necessary the case in the normal-reading condition. Moreover, this interpretation is supported by the results of the conventional fMRI analysis and DCM analysis in which more activity and stronger connectivity between regions were found in the predictive-reading condition than in the normal-reading condition.

Another point related to the experimental design is the construction of GLM. In a number of fMRI studies of inference processes (such as Ferstl and von Cramon, 2001; Kuperberg et al., 2006), the researchers investigated the hemodynamic responses induced by text reading together with those induced by a judgment task that followed text reading. As a result, inference processes and decision making could not be clearly delineated in those studies. In contrast, we concentrated on the responses during text reading in which no explicit judgment or behavioural response was required. Our results may thus better reflect brain responses in connection with natural language processing.

The third difference concerns the data analysis: In addition to using the conventional GLM data analyses to identify brain regions from the perspective of response magnitude, we applied effective connectivity analyses to investigate the interregional couplings during text reading. This perspective gave us further information with regard to mechanisms of drawing strategic inferences. For example, we found marked difference between predictive reading and normal reading in dIFG–pSTS connectivity, although the

activation levels of dIFG and pSTS did not differ significantly in both conditions at the predefined threshold. Our results demonstrate the importance of connectivity analysis in studying human cognition.

Functional roles the frontal regions in inference processes

The passage-reading conditions compared with the pseudoword reading condition elicited increased responses in pSTS, aTL, TPJ and IFG in the left hemisphere (Fig. 3A). The involvement of these regions in language processing has been observed repeatedly in many brain imaging studies (Bookheimer, 2002; Cabeza and Nyberg, 2000; Gernsbacher and Kaschak, 2003; Xu et al., 2005). Interestingly, we did not find significant activation in the posterior inferior temporal gyri, which are important in retrieving semantics (Hickok and Poeppel, 2004; Martin, 2007; Price, 2000). This may be due to the consistent correspondence between orthography and phonology in German language (Price, 2000). Three frontal regions, aPFC, vIFG and dIFG (at the lowered threshold), evoked increased responses in predictive reading relative to normal reading. Activity in aPFC was observed in previous studies exploring inference processes, for instance, Ferstl and von Cramon (2001) and Kuperberg et al. (2006). In the study of Ferstl and von Cramon (2001), participants were asked to judge the coherence between two sentences during reading. Presumably, participants had to draw inferences to bridge the sentences in a coherent manner in this task. The authors found increased activity in aPFC (BA 9/10) for coherent sentence pairs compared to incoherent pairs. In agreement with the general function role of aPFC proposed by Christoff and Gabrieli (2000) and Ramnani and Owen (2004), Ferstl and von Cramon (2001) suggested that the functional role of aPFC (BA 9/10) is to evaluate the coherence of the integration of various types of information such as presented text, inferred information and the general knowledge of readers. Coherence evaluation is crucial for integration processes because the results of coherence evaluation determine how the information should be integrated and updated in working memory (Kintsch, 1998; Zwaan, 2004). Following the above interpretation, one would expect that aPFC should always be engaged in text comprehension because coherence evaluation is one of the key processes in many text comprehension theories (Graesser et al., 1994; Kintsch, 1998). However, aPFC activity was not found consistently in the previous studies of text comprehension (Ferstl, 2007). Our results demonstrated that a major factor triggering aPFC activity is the reader's intention, i.e., whether a reader draws strategic inferences intentionally or not. We suggest that the functional role of aPFC in language processing is specific to evaluating the coherence of the strategic inferences with respect to the described situation instead of coherence evaluation in general.

Apart from aPFC, two significant clusters in vIFG (BA 47) were activated at the predefined threshold and a cluster in dIFG (BA 44/45) was activated at the lowered threshold in the contrast between predictive reading and normal reading. There is evidence that IFG is an anatomically complex region and is responsible for various functions in language comprehension (Matthews et al., 2003; Sakai et al., 2003). Hagoort (2005) suggested that the functional roles of IFG in language comprehension change gradually from semantic processing to syntactic processing and to phonological processing along with the anterior ventral portion (BA 47/45) to the posterior–dorsal portion (BA 45 and ventral part of BA 6). The study of Badre et al. (2005) tried to dissociate the

functional role of dIFG and vIFG (termed mid and anterior ventrolateral prefrontal cortex in their paper). Their results showed that dIFG mainly supports a generalized control process, which selects information among a set of competitors, whereas vIFG activations are sensitive to associative strength and contribute to controlled semantic retrieval. With respect to our findings, vIFG seems to be responsible for drawing inferences associated with the described situation. These inferences are probably selected, integrated with other information and maintained in dIFG (Hagoort et al., 2004).

In summary, the results of the conventional fMRI data analyses showed that activity in vIFG, aPFC and dIFG is critical for retrieving, evaluating and integrating strategic inferences respectively.

Top-down influences in inference generation

Our DCM results lead to a clear conclusion: The neural interactions between dIFG and pSTS are modulated by predictive reading. The importance of the interactions between the left inferior frontal areas and the left posterior temporal areas in language processing has been known since the 19th century (see review by Poeppel and Hickok, 2004), and this was also shown in recent studies using functional connectivity analyses (Hampson et al., 2002; Horwitz et al., 1998; Horwitz and Braun, 2004) and direct electrostimulation (Mandonnet et al., 2007; Matsumoto et al., 2004). However, the functions emerging from interregional interactions remain poorly understood. Most studies using connectivity analysis showed that the change of functional connectivity between regions was driven by external stimuli such as text comprehensibility (e.g., Homae et al., 2003; Hampson et al., 2002; Obleser et al., 2007) and text complexity (e.g., Horwitz and Braun, 2004). Our DCM results demonstrated that connectivity enhancement can be initiated by a top-down cognitive process even though the external stimuli remain constant. Specifically, we showed that bidirectional connectivity between dIFG and pSTS was enhanced when readers predict the development of the story during reading. This task can be interpreted as world knowledge retrieval, i.e., retrieval of relevant information based on the experience of the reader. It is conceivable that world knowledge retrieval is controlled by the same mental mechanism that is responsible for the process of controlled semantic retrieval proposed by Wagner et al. (2001). In their experiment, participants were asked to indicate which word from a group of target words was most semantically related to a cue word. They found stronger IFG responses when the participants compared weakly related words than when they compared highly related words. The authors argued that the bottom-up automatic word-association mechanism probably did not support the semantic retrieval when comparing weakly related words and suggested that the left inferior prefrontal cortex (BA 45/47) mediates a top-down bias to guide semantic retrieval in the left temporal areas. Badre et al. (2005) further demonstrated that the co-activation of the left frontal and temporal regions is related to controlled semantic retrieval. Kerns et al. (2004) reached a similar conclusion in an fMRI study using sentence materials as cues for word production. In their study, the authors demonstrated that the purpose of activity in the left prefrontal cortex (BA 9/46 and 45) is to maintain contextual information and to guide the selection of context-appropriate responses during word production. It is not unlikely that the top-down mechanism recruited in the word-level controlled semantic retrieval may also be employed in retrieving world knowledge

while drawing strategic inferences according to a complex mental representation of the text.

In conclusion, by incorporating the results from conventional fMRI analyses and effective connectivity analyses, we have shown that strategic inference processes involve a fronto-temporal network in the dorsal stream. The key components in this network include aPFC, dIFG, vIFG and the connection between dIFG and pSTS. We have postulated that vIFG is responsible for driving controlled semantic retrieval. Via dIFG–pSTS interactions, a top-down bias arises, which guides the temporal regions in activating and selecting lexical-semantic information. The role of aPFC is to evaluate the coherence of the representations maintained and integrated in dIFG.

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