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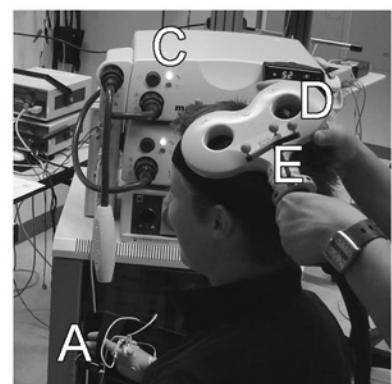
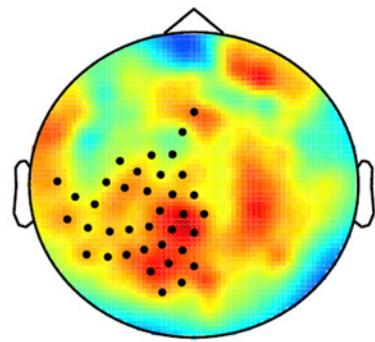
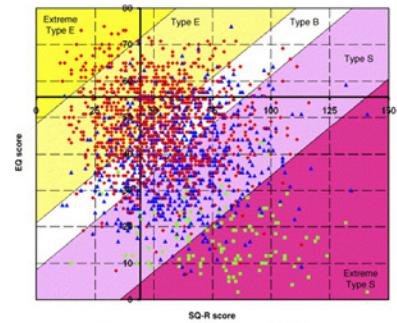
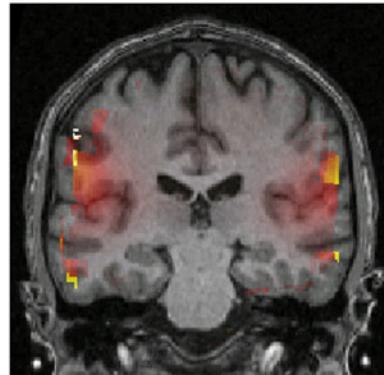


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Dear readers,

It is a pleasure to introduce the third issue of Nijmegen CNS, Proceedings of the Cognitive Neuroscience Master of the Radboud University. This journal has been run by students since the start two years ago. It aims at being a scientific journal of high quality reflecting the research that is being carried out by the students of the research master Cognitive Neuroscience at the Radboud University. To reach this goal, all of the theses have gone through a peer-review procedure after which only the best studies were selected for the printed version of the journal. This was done according to the criteria of importance, quality and originality. The abstracts of the theses that have not been selected can be found at the end of this issue. Furthermore, all complete theses that have been submitted in this and previous years can be found in the online version on the website www.ru.nl/master/cns/journal.

Both the field and the research master Cognitive Neuroscience encompass a wide variety of disciplines and methods. This is elegantly illustrated by the six selected articles that cover the fields of psycholinguistics, neurocognition, perception and action. Among the techniques that were used were fMRI, electrophysiology and TMS. The research has been carried out at different research institutes including the F.C. Donders Centre for Cognitive Neuroimaging, the Nijmegen Institute for Cognition and Information (NICI), the Radboud University Nijmegen Medical Centre and the Max Planck Institute for Psycholinguistics. This is indicative of the wide variety of research questions addressed by the exciting field of cognitive neuroscience in general and of the work the students are doing in this programme in particular.

Finally, I would like to note that this journal would not have been possible without the help of many, including the authors who submitted their thesis and the advisory board that helped us publish this first issue with the new board. In addition we are grateful to the reviewers that helped us greatly with judging the quality of the articles and commenting on them, the old editorial boards that have paved the way for us, and of course you, our readers.

On behalf of the editorial board, I thank you for showing interest in what we are doing and for reading this journal. We hope that you will enjoy this issue.

Best regards,
Bernard Bloem
Editor-in-Chief



From the Institute Director

It is with pride that I introduce the third issue of Nijmegen CNS, the Proceedings of the Cognitive Neuroscience Master. The aim of our master programme is to learn students how to become a good researcher and a member of the scientific community. Both require having good ideas and communicating these ideas. The most important way in which we communicate our ideas and research is by publishing in peer reviewed journals. As a scientific community we are also responsible for quality control. We evaluate and judge each others work. A scientist thus has to play multiple roles as a member of the scientific community. As such, our masters' journal is an important instrument in our programme. As students you learn to play these different roles by doing, both what it means to publish your research and what it means to evaluate the research quality of your peers. This issue again is a testimony of the high quality of our students and the level of professionalism that they have achieved in running this journal. I have a number of journal copies in my office, which I hand out with pride to colleagues from all over the world. Without exception, they are impressed by the presence of these Proceedings and by their quality. The journal also serves as an instrument that motivates the teachers. If this is what our students produce, then we better go all out in teaching them how to get even better. In my view, our masters programme has become a great success. The different institutes involved are now preparing a graduate school in cognitive neuroscience, which is a natural next step in establishing a complete educational package for our most talented students. We also will integrate our research efforts even more than in the past. These are developments that will be beneficial for our students as well. With all this good news I hope that the editors of the journal will be motivated to continue producing issues of the same high quality as the first three.

Prof. dr. Peter Hagoort
Director F.C Donders Centre for Cognitive Neuroimaging
& Max Planck Institute for Psycholinguistics.

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The mere exposure effect in artificial grammar learning: Implications for dyslexia studies

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Several studies have reported an association between dyslexia and implicit learning deficits and it has been suggested that the weakness in implicit learning observed in dyslexic individuals can be related to sequential processing and implicit sequence learning. In the present paper, we review the current literature on implicit learning and dyslexia. We present a novel forced-choice structural mere exposure artificial grammar learning paradigm and characterize this paradigm in normal readers in relation to the standard grammaticality classification paradigm. The objectives of the present study were to investigate the behavioural equivalence of the forced-choice preference classification compared to grammaticality classification in artificial grammar learning. It can be argued that preference classification is a more optimal measure of the outcome of implicit acquisition since in the preference version participants are kept completely unaware of the underlying generative mechanism, while in the grammaticality version, the subjects have at least in principle been informed about the existence of an underlying complex set of rules at classification (but not during acquisition). We used a balanced ACS design and the factors grammaticality (grammatical/non-grammatical) and ACS (high/low) were independently controlled in a 2 x 2 factorial design. Based on the mere exposure effect, we predicted that the development of preference will correlate with the grammaticality status of the classification items. In addition, we characterize the effects grammaticality (grammatical/non-grammatical) and associative chunk strength (ACS; high/low) on the classification tasks (preference/grammaticality). The results confirm our prediction. Finally, we discuss the suitability of this task for further investigation of the implicit learning characteristics in dyslexia.

Keywords: artificial grammar learning, structural mere exposure effect, dyslexia, inferior frontal cortex, basal ganglia

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1. Introduction

During the acquisition of reading and writing skills, the child creates the ability to represent aspects of the phonological component of language by an orthographic representation and relate this to a visuographic input-output code. This is typically achieved by means of a supervised learning process (i.e., teaching), in contrast to natural language acquisition, which is largely a spontaneous, non-supervised, and self-organized acquisition process (Petersson, 2005a; Petersson, Ingvar, & Reis, 2007, in press). Aspects of language can also be an object of meta-linguistic awareness: the intentional and explicit control over aspects of phonology, syntax, semantics, discourse, as well as pragmatics, and children gradually create explicit representations and acquire processing mechanisms that allow for reflecting and analyzing different aspects of language use (Karmiloff-Smith, Grant, Sims, Jones, & Cuckle, 1996). When children subsequently learn to read, this also has repercussions on the phonological representations of spoken language (Morais, 1993; Petersson, Reis, Askelöf, Castro-Caldas, & Ingvar, 2000; Petersson, Reis, & Ingvar, 2001; Ziegler & Goswami, 2005). Learning to read involves both explicit as well as implicit processes; typically children initially learn grapheme – phoneme mappings explicitly after which they apply and continue to learn how phonology is mapped onto its written representation implicitly (Gombert, 2003; Petersson & Reis, 2006; Ziegler & Goswami, 2005). Karmiloff-Smith (1992) proposed that cognitive development relies on implicit/procedural learning mechanisms to initiate the set-up of a new stage of representational development. A deficit in implicit acquisition mechanisms might therefore impact negatively on the acquisition of reading and writing skills and therefore affect literacy acquisition. Dyslexia is rarely studied within the framework of learning and a deficit in implicit learning might contribute to difficulties associated with dyslexia (Howard, Howard, Japikse, & Eden, 2006). Recently, Howard et al. (2006) provided evidence suggesting that the weakness in implicit learning observed in dyslexic individuals might be narrowed down to paradigms that involve sequential processing and argued that the implicit sequence learning deficit in dyslexia is associated with selective deficits in the fronto-striatal-cerebellar circuits that underlie implicit sequence learning. Recently it has been shown that fronto-striatal circuits are involved

in sequence processing after implicit grammar acquisition (Forkstam, Hagoort, Fernandez, Ingvar, & Petersson, 2006; Petersson, Forkstam, & Ingvar, 2004).

1.1 Implicit learning

Humans are equipped with acquisition mechanisms that extract structural regularities implicitly from experience without the induction of an explicit model (Reber, 1967, 1993; Stadler & Frensch, 1998). This capacity was explored in the seminal work of Reber (1967), showing that humans can successfully classify strings generated from an implicitly acquired artificial grammar and proposed that this process is intrinsic to natural language acquisition. Following this suggestion, it has been argued that artificial grammar learning (AGL) is a relevant model for investigating aspects of language learning in infants (Gomez & Gerken, 2000), exploring differences between human and animal learning relevant to the narrow faculty of language (Hauser, Chomsky, & Fitch, 2002), language learning in adults (Friederici, Steinhauer, & Pfeifer, 2002; Petersson et al., 2004), and we suggest that it can serve as a device for investigating the implicit aspects of structure learning related to reading and writing acquisition. Reber (1967) suggested that humans can acquire implicit knowledge of the underlying structure through a statistical learning process and that the acquired knowledge is put to use during grammaticality classification. Reber (1967; but see Reber, 1993) argued that implicit learning mechanisms abstracted ‘rule-based’ knowledge and more recent studies seem to suggest that dual mechanisms might be at play (Forkstam et al., 2006; Knowlton & Squire, 1996; Meulemans & Van der Linden, 1997). Following Reber (1967) and Seger (1994), Forkstam & Petersson (2005) adapted four proposed defining characteristics of implicit learning: (1) limited explicit access to the knowledge acquired; subjects typically cannot provide a sufficient explicit account of what they have learnt; (2) the nature of the knowledge acquired is more complex than simple associations or simple exemplar-specific frequency counts; (3) implicit learning does not involve explicit hypothesis testing but is an automatic (incidental) consequence of the type and amount of processing performed on the stimuli; (4) implicit learning does not rely on declarative memory mechanisms that engage the medial temporal lobe memory system.

1.2 Dyslexia: An implicit learning deficit?

Developmental dyslexia (DSM IV) is commonly defined as a reading disability, a deficit in learning to spell and write, occurring in children despite normal intelligence, no sensory or neurological impairment and conventional instruction and socio-economic opportunity (Dilling, Mombour, & Schmidt, 1991; Habib, 2000; Shaywitz, 1998). Dyslexia is rarely studied in the framework of the contemporary learning literature (Howard et al., 2006). Learning to read involves both explicit as well as implicit processes; children initially learn the grapheme – phoneme correspondence explicitly, typically in a supervised manner, after which they apply and continue to learn them implicitly in an unsupervised manner (Gombert, 2003). A deficit in implicit learning might contribute to difficulties associated with dyslexia, but the literature on implicit learning and dyslexia has yielded mixed results (Howard et al., 2006). Most studies of implicit learning in dyslexics have investigated serial reaction time (SRT) types of tasks and there are to our knowledge only two studies that investigate artificial grammar learning (AGL). For a recent review of these experimental tasks see Forkstam and Petersson (2005).

An important weaknesses of all studies of implicit learning in dyslexics to date is that they lack a developmental design (Goswami, 2003). Another weakness of some of the studies is that they report null-findings. In the context of small study samples and not always carefully controlled experimental designs, these null-findings are difficult to interpret and it is not unlikely that the absence of significant results reflect a lack of statistical power and the outcome of potential confounding factors. On the other hand, the mixed literature on implicit learning and dyslexia might suggest that it is not enough to investigate simple implicit acquisition tasks or just to contrast implicit and explicit learning.

Vicari et al. (2003) reported deficient implicit learning in dyslectic children in a visuo-motor SRT-type tasks that used sequences of colours. They also included a test of declarative (explicit) memory capacities. Their main finding suggests that individuals with developmental dyslexia are impaired in the acquisition of implicit sequence knowledge, while there was no significant difference between the dyslexia and control groups in terms of explicit sequence learning. Some studies have reported null-findings on similar SRT-type tasks (Kelly, Griffiths, & Frith, 2002; Waber et al., 2003) and Rüsseler et al. (2006) questioned the implicit learning deficit in dyslexia based on these and their

own null-findings. In Rüsseler et al. (2006), the dyslexic subjects performed at consistently longer response times (RTs) on the SRT-task compared to the normal controls, though the difference did not reach statistical difference. This was also the case in Kelly et al. (2002). Importantly, in a follow-up study, Vicari et al. (2005) used the classical SRT-task as well as an implicit mirror drawing test, and showed that the children with developmental dyslexia were impaired on both tasks. Their SRT results suggest a deficit in sequential learning and that the deficit does not depend on the material to be learned (with or without motor sequence of response action) but only the implicit character of task. These behavioural findings were further replicated in a fMRI study on adult dyslexics (Menghini, Hagberg, Caltagirone, Petrosini, & Vicari, 2006). Consistent with this perspective, both Stoodley et al. (2006) and Howard et al. (2006) provided further evidence that the implicit learning deficits observed in dyslectic individuals can be narrowed down to paradigms that involve sequential processing. Stoodley et al. (2006) found a significant differences in implicit learning between good and poor readers on the SRT-task. In addition, the dyslexia group showed less of an RT decrease on the repeated sequence, while the RTs were similar to that of the control group on the random trials. Recently, Sperling et al. (2004) argued that poor implicit learning could hinder the establishment of good phonological processing as well as learning orthographic–phonological representations, while Gombert (2003) proposed that children with dyslexia have a phonological deficit that prevents normal implicit learning of linguistic regularities and, hence, interferes with reading development. Howard et al. (2006) showed that adult dyslexics are impaired on implicit acquisition in an alternating (higher-order) SRT-task in which sequential dependences exist across non-adjacent elements. They compared the performance on the alternating SRT-task with the performance on a simple spatial context learning task in which the global configuration of a display cues the location of a search target. Their results suggest that college students with a history of dyslexia are impaired in implicit higher-order sequence learning but unimpaired in spatial context learning. They also argue that evidence from patient, functional neuroimaging, and transcranial magnetic stimulation investigations suggest that sequence learning depends on fronto-striatal-cerebellar circuitry and that the acquisition of non-adjacent higher-order sequential regularities calls on fronto-striatal-cerebellar circuitry whereas spatial contextual learning depends on medial temporal lobe structures (Chun & Phelps, 1999;

Howard et al., 2006; Packard & Knowlton, 2002a). The fMRI results of Menghini et al. (2006) suggest that implicit learning deficit in dyslexia is associated with a level of activation in higher cerebellar and parietal regions. They speculate that automatization is required to achieve reading fluency and that the cerebellum might be important for the development of automaticity. However, it is important to note that the development of automaticity does not necessarily overlap with implicit learning. Automaticity can arise from repetitive application of explicit, conscious procedures, over and over again, until adequate performance is achieved (Cohen, Dunbar, & McClelland, 1990; Cohen, Servan-Schreiber, & McClelland, 1992; Logan, 1988; MacLeod & Dunbar, 1988; Petersson, Elfgrén, & Ingvar, 1997; Petersson, Elfgrén, & Ingvar, 1999; Petersson, Sandblom, Gisselgård, & Ingvar, 2001). Howard et al. (2006) also reported significant positive correlations between measures of reading ability and accuracy based implicit acquisition measure. Importantly, they were able to rule out several non-specific explanations for their results, including a general cognitive or attention deficit, task difficulty, or age, and established that deficits in implicit sequence learning occur even when explicit learning can be ruled out. They emphasize that dyslexics do not suffer from a general implicit learning deficit, but that this deficit is specific to sequential processing, highlighting the importance of sequence complexity (i.e., the level of structure present in the sequences), consistent with the findings of Vicari et al. (2005; 2003).

1.3 Implicit artificial grammar acquisition

The artificial grammar used by Reber (1967), here and subsequently referred to as the Reber grammar, is an example of a right-linear phrase structure grammar which generates a rational language (Perrin & Pin, 2004). This type of grammar represents the simplest formal model that captures the idea of the ‘infinite use of finite means’ (Petersson, 2005b;

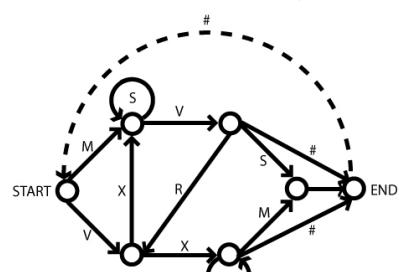


Figure 1. The transition graph representation of the Reber grammar which was used to generate the grammatical strings in the present study (cf., Reber & Allen, 1978).

Petersson, Grenholm, & Forkstam, 2005). The Reber grammar, like any right-linear phrase structure grammar, can be implemented in a finite-state architecture (Figure 1; Petersson, 2005), and we used this grammar in the present study as a generator of the stimulus material. The finite-state machine can be viewed both as an explicit generating mechanism or as a recognition device for a formal language (e.g., Davis et al., 1994). It should be noted that the term ‘language’ is technical and does not entail anything but that a formal (or artificial) grammar represents a specification of a mechanism that generates (or recognizes) certain types of sequential structural regularities (Petersson et al., 2004). It is also important to note that the finite-state architecture is not limited to capture local substring dependencies but that this architecture can also incorporate long-distance dependencies (as long as there is a fixed finite upper bound for these dependencies, cf., Petersson, 2005b; Petersson et al., 2005).

The typical artificial grammar learning (AGL) experiment includes an acquisition phase followed by a grammaticality classification. During the acquisition phase, participants are engaged in a short-term memory task using an acquisition sample of symbol sequences generated from an artificial grammar. Subsequent to the acquisition phase, subjects are informed that the symbol sequences were generated according to a complex system of rules and they are asked to classify new items as grammatical or not based on their immediate impression (guessing based on ‘gut feeling’). The subjects typically perform reliably above chance (Forkstam et al., 2006; Petersson et al., 2004), and it can be concluded that participants have acquired knowledge about aspects of the underlying generative structure. It is assumed that the classification performance is based on implicit acquisition mechanisms because subjects are typically unable to provide sufficient reasons to motivate their classification decisions (Forkstam et al., 2006; Forkstam & Petersson, 2005; Stadler & Frensch, 1998). An alternative way of assessing the implicit acquisition of an artificial grammar is the structural mere exposure version of AGL. This version is based on the mere exposure effect, which refers to the finding that repeated exposure to a stimulus induces an increased preference for that stimulus compared to novel stimuli (Zajonc, 1968). The mere exposure version might be a more sensitive measure of implicitly acquired knowledge because the participants are never made aware of the existence of an underlying generative mechanism.

1.4 Dyslexia and artificial grammar acquisition

Much less is known about the implicit acquisition of artificial grammars in dyslexics. To date only two studies on dyslexia have been conducted using this paradigm. Rüsseler et al. (2006) used a short acquisition session and report null-findings only in terms of correct responses on the grammaticality classification task; no baseline classification was included in the experiment, and they did not control for local sub-string regularities (i.e., ACS-type information, cf., below). Although there was no significant difference between the dyslectic and normal readers, the dyslectic subjects performed at a lower level (mean number of correct responses) on the classification task. In an interesting study by Pothos and Kirk (2004) the artificial grammar of Knowlton & Squire (1996) was used in two AGL tasks of equal formal complexity but with different stimulus format in a between-subject design: in one of the tasks (geometric-shapes-embedded AGL task) the stimuli were created so as to encourage whole stimulus perception, de-emphasizing the constituent elements, while in the other task (geometric-shapes-sequential AGL task) the constituent elements were emphasized by presenting them serially. Pothos and Kirk (2004) controlled for local sub-string regularities (i.e., ACS) but did not manipulate this dimension experimentally. The dyslexia group performed equally well on “grammaticality” classification in both tasks, and the non-dyslectic group performed as well as the dyslexia group on the visual-embedded but less well on the visual-sequential task. These findings were interpreted as indicating that the dyslectic participants were less able to process the individual stimulus elements, suggesting that dyslectic individuals are sometimes prevented from adopting an explicit strategy, which would have interfered with the implicit acquisition mechanisms supporting geometric-sequential AGL, consistent with recent work associating dyslexia with problems in focused attention and attention shifting. Thus, Pothos and Kirk (2004) proposed that competent real world learning is achieved via an interaction of implicit and explicit learning processes.

In summary, there is a cumulating series of investigation of implicit learning in dyslexia and taken as a whole, these studies suggest that there are aspects of implicit learning that might operate at sub-normal levels in dyslectic individuals. The lack of a developmental design in these studies (Goswami, 2003) prevents us from making any conclusions

concerning the causal role of an implicit acquisition deficit in dyslexia; this phenomenon might be an outcome of dyslexia rather than a cause, similar in character to the many parallel findings between the dyslexic and illiterate brain (Petersson et al., 2007, *in press*; Petersson & Reis, 2006; Petersson, Reis et al., 2001). A few tentative conclusions are however warranted: (1) dyslexia does not seem to be associated with a general implicit learning deficit; (2) the implicit learning deficit observed does not seem to be related to non-specific factors like general cognitive or attention deficit, task difficulty, or age; (3) the implicit acquisition deficit seems to be related to sequence processing, which is likely related to sequence complexity (i.e., the level of structure present in the sequences, for a short review see Petersson (2005b) and a comprehensive review see Davis et al. (1994)); (4) the implicit learning deficit in dyslexia can be observed when explicit learning is intact.

1.5 Objectives

In the present study we characterize a new forced-choice structural mere exposure AGL paradigm in normal readers based on preference classification. We compare this preference classification paradigm with the standard grammaticality classification paradigm. We predict, based on the mere exposure effect (Zajonc, 1968), that the development of preference will start to correlate with grammaticality. In order to achieve these objectives, we used a balanced associative chunk strength (ACS) design (Forkstam et al., 2006; Meulemans & Van der Linden, 1997). In the balanced ACS design, the factors grammaticality status (grammatical/non-grammatical) and ACS (high/low) are independently controlled in a 2 x 2 factorial design. It has been argued that a sensitivity to the level of ACS is a reflection of statistical fragment-based learning mechanism while a sensitivity to the grammaticality status of the items, independent of ACS, is related to an implicit structure-based acquisition mechanism. Moreover, it is not implausible that learning based on ACS reflects explicit declarative memory mechanism involving the medial temporal lobe (Forkstam et al., 2006; Lieberman, Chang, Chiao, Bookheimer, & Knowlton, 2004), while implicit learning of grammaticality status independent of ACS reflects a procedural learning mechanism involving the basal ganglia and the prefrontal cortex (Forkstam et al., 2006). In this study, the subjects participated in one implicit acquisition sessions per day for five days;

symbol strings were presented visually one letter at a time, which requires temporal integration of information. Before the first acquisition session on the first day, subjects participated in a baseline preference classification task. Finally, after the last acquisition session on the 5th day, subjects performed a preference classification and then the standard grammaticality classification task. In summary the objectives of the present study were to investigate the behavioural equivalence of the forced-choice preference classification to the standard grammaticality classification task and to explore the effects of the factors grammaticality status (grammatical/non-grammatical) and ACS (high/low) on the classification task (preference/grammaticality). In the discussion section, we argue that these AGL paradigms are suitable for further investigation of the implicit learning characteristics in dyslexia.

2. Methods

2.1 Participants

Thirty two right-handed (16 females, mean age \pm SD = 22 ± 3 years; mean years of education \pm SD = 16 ± 2) healthy Dutch university students volunteered to participate in the study (part of larger fMRI project; data not shown). They were all pre-screened and none of the subjects used any medication, had a history of drug abuse, head trauma, neurological or psychiatric illness, or a family history of neurological or psychiatric illness. All subjects had normal or corrected-to-normal vision. Written informed consent was obtained from all participants according to the Declaration of Helsinki and the local medical ethics committee approved the study.

2.2 Materials

We generated 569 grammatical (G) strings from the Reber grammar (5-12 consonants from the alphabet [M, S, V, R, X]; see Figure 1). For each item we calculated frequency distribution of 2 and 3 letter chunks for both terminal and complete string positions in order to derive the associative chunk strength (ACS) for each item (cf., Knowlton & Squire, 1996; Meulemans & Van der Linden, 1997). Then iteratively, we randomly selected 100 strings, generating an acquisition set which were comparable in terms of 2 and 3 letter chunks to the complete string set. Subsequently we generated the non-grammatical

(NG) string, derived from each remaining G string by a switch of letters in two non-terminal positions, and these were selected to match the G strings in terms of both terminal and complete string ACS (i.e. collapsed over order information within strings). Finally, in an iterative procedure, we randomly selected 3 sets of 60 strings each from the remaining G strings, in order to generate the 3 classification sets consisting of 50% G and NG strings, as well as 50% high and low ACS strings relative to ACS information in the acquisition set and independent of grammaticality status. Thus the stimulus material included an acquisition set and two classification sets (all sets were disjoint). The classification sets were used for the 2 x 2 factorial design of the classification task. Thus each classification set consisted of 30 strings of each string-type: high ACS grammatical (HG), low ACS grammatical (LG), high ACS non-grammatical (HNG), and low ACS non-grammatical (LNG).

2.3 Experimental procedure

The subjects were informed that they were to participate in a short term memory experiment on the first day. The complete experiment included 5 days with an acquisition session each day. An initial preference classification (PC) test was performed before the first acquisition session on the first day (AGL1). A second preference test was performed after the last session on the 5th day (AGL2). After the AGL2 the grammaticality instruction was introduced (AGL3). During both acquisition and classification sessions, each string was centrally presented letter-by-letter on a computer screen (2.7 - 6.9 s corresponding to 5-12 letters; 300 ms letter presentation duration, 300 ms inter-letter-interval) using the Presentation software (<http://nbs.neurobs.com>).

2.3.1 Implicit acquisition task

During each acquisition session, all subjects were presented with the 100 acquisition strings, (acquisition set) on a computer screen (presentation order randomized for each acquisition session). When the last letter in a string disappeared the subject was instructed to immediately reconstruct the string from memory by typing on a keyboard in a self-paced fashion. No performance feedback was given and only positive examples (i.e., grammatical strings) were presented during acquisition. The acquisition phase lasted approximately 20-40 minutes.

2.3.2. Classification tasks

The classification task consisted of a yes/no forced-choice procedure, and the subjects were instructed to make their choice based on their immediate impression ('gut feeling'). On the first day, the subjects were given the preference classification instruction (AGL1); they were instructed to classify novel strings as preferable or not (likeable/pleasant or not) and that there was no right or wrong response. The subjects were given the same preference instruction on the last day (AGL2). After the AGL2 participants were informed about the grammatical nature of the strings and were instructed to classify new strings as grammatical or not (AGL3). During classification on day 1 and 5, the participants were presented with novel letter strings from the classification set in the same way as during acquisition. During a classification session 30 strings were presented one at a time on a computer screen. After a 1 s pre-stimulus period the strings were presented for 3 s, followed by a 1 s motor preparation delay period. The subject then had 2.5 s to make their classification decision and push the corresponding key with their left or right index finger, based on the preference. The classification sets and string presentation order were balanced over subjects. Each classification session was split in two in order to balance response finger within subject, each lasting approximately 20 minutes. The stimuli were presented via an LCD-projector, projecting the computer display onto a semi-transparent screen that the subject comfortably viewed through a mirror device. At the end of the experimental procedure on day 5, participants were presented a generation task and then a 31-item fragment completion task. In the generation task, participants were instructed to generate 10 letter strings that they regarded as grammatical; in the fragment completion task they were instructed to complete each item with the letter they thought would render the string grammatical.

2.4 Data analysis

Repeated measures ANOVA was used for the analysis of the data, unless otherwise stated (statistical software package SPSS). A significance level of $P < 0.05$ was used. Scores were based on hit- and endorsement rates. The hit rate is defined as the sum of all hits (accepted grammatical strings) and correct rejections (rejected non-grammatical strings). The endorsement rate is defined as the number of all strings classified as grammatical independent of the actual grammaticality status (cf., Forkstam et al., 2006; Meulemans & Van der Linden, 1997).

3. Results

On the baseline preference classification (AGL1; i.e., before any exposure to the grammar) subjects classified at the expected chance level ($50 \pm 7\%$ correct, $T(31) = 0.42$, $P = 0.67$). Consistent with previous findings the overall correct classification performance was clearly above chance on preference (AGL2; $65 \pm 14\%$ correct, $T(31) = 5.7$, $P < 0.0001$) and grammaticality classification (AGL3; $73 \pm 16\%$ correct, $T(31) = 7.7$, $P < 0.0001$). Thus, subjects classified items reliably above chance on both the preference classification (AGL2) and the grammaticality classification (AGL3) tasks. The classification performance improved after the grammaticality instruction was provided ($F(1,31) = 8.8$, $P = 0.006$).

3.1 Classification performance - hit rates

The analysis of hit rate showed that the subjects were sensitive to the grammaticality status of the items ($F(2,62) = 26$, $P < 0.0001$). In particular, the participants classified the grammatical strings correctly more often (AGL2 > AGL1), and the hit rate increased further on the AGL3 task compared to both AGL1 and AGL2. Specific contrast

Table 1. Endorsement rates over grammaticality and ACS levels. Percentage of items endorsed (i.e., item classified as grammatical independent of actual grammaticality status) by condition (grammatical/non-grammatical x high/low associative chunk strength (ACS) status; mean performance level and standard deviation).

AGL1		AGL2		AGL3	
		High ACS	Low ACS	High ACS	Low ACS
G	53 (15) %	45 (18) %	73 (16) %	62 (20) %	82 (20) %
NG	51 (21) %	48 (13) %	41 (22) %	34 (17) %	32 (22) %
					27 (21) %

G = grammatical; NG = non-grammatical; ACS = associative chunk strength.

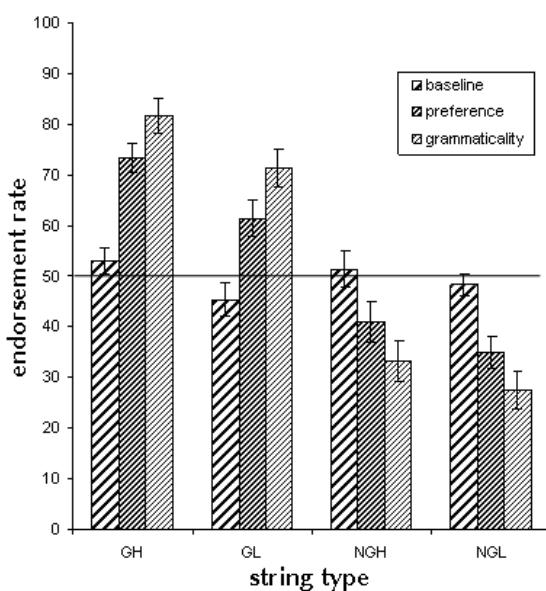


Figure 2. Endorsement rates over grammaticality and ACS levels. The endorsement rates (i.e., item classified as grammatical independent of actual grammaticality status) as a function of grammaticality status as well as associative chunk strength (GH: grammatical high ACS strings, GL: grammatical low ACS strings, NGH: non-grammatical high ACS strings, NGL: non-grammatical low ACS strings). The endorsement rate of grammatical vs. non-grammatical items increases as a function of repeated acquisition for both high and low ACS strings. Error bars correspond to standard error of the mean.

comparisons revealed that the group improved its classification performance for LG strings ($F(2,62) = 15.6$, $P < 0.0001$) and LNG strings ($F(2,62) = 17.8$, $P < 0.0001$) after the grammaticality instruction (AGL3) in comparison both to AGL2 and AGL1, while the classification performance for HNG strings improved in comparison only to AGL1 ($F(2,62) = 10.8$, $P < 0.0001$).

3.2 Classification performance - Endorsement rates

We then analyzed the performance data in terms of endorsement rate (i.e., items classified as grammatical independent of actual grammaticality status). Both grammaticality and ACS influenced the endorsement rate (Table 1, Figure 2 and 3). A repeated measures ANOVA with task (AGL1/2/3), grammaticality (G/NG), and ACS (H/L) as within factors, showed significant main effects of grammaticality ($F(1,31) = 47$, $P < 0.0001$) and ACS ($F(1,31) = 18$, $P < 0.0001$), while the main effect of task type was non-significant ($F(2,62) = 1.4$, $P = 0.25$). In addition, there was a significant interaction between task and grammaticality ($F(2,62) = 37$, $P < 0.0001$), while the interaction between task and ACS

was non-significant ($F(2,62) = 0.48$, $P = 0.57$). This shows that grammaticality is the main contributor to the increased classification performance between the baseline and the two classification tasks following implicit acquisition of the grammar, and suggest that subjects implicitly acquired knowledge about the underlying grammar after 5 days of acquisition. Moreover, there was a significant interaction between grammaticality and ACS ($F(1,31) = 8.9$, $P < 0.05$). Post-hoc analysis revealed that this interaction was due to the overall difference in classification performance of AGL2/3 compared to the baseline performance (AGL1) as well as the comparison between AGL2 and AGL3. No other interactions reached significance ($P > 0.9$).

In greater detail, preference classification (AGL2) was significantly affected by grammaticality ($F(1,31) = 31.7$, $P < 0.0001$) and ACS ($F(1,31) = 15.4$, $P < 0.0001$). These effects were also observed in grammaticality classification (AGL3; grammaticality, $F(1,31) = 61.6$, $P < 0.0001$; ACS, $F(1,31) = 13.6$, $P < 0.001$), while the interaction between grammaticality and ACS was not significant on either task (AGL2: $F(1,31) = 3.8$, $P = 0.059$; AGL3: $F(1,31) = 2.6$, $P = 0.11$).

We further investigated the effects of grammaticality, following Chang and Knowlton who argued that ACS might not be a useful cue for the low

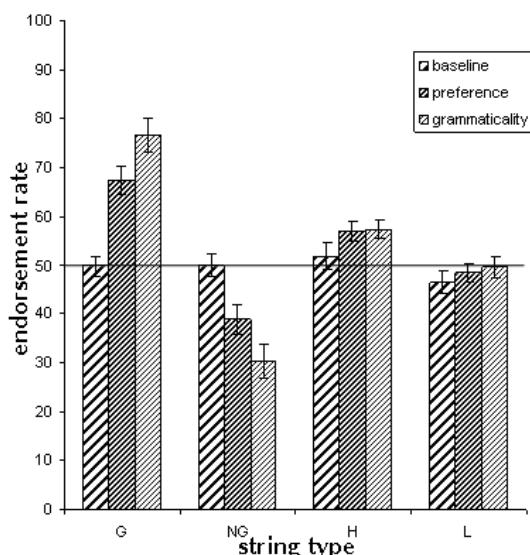


Figure 3. Endorsement rates over grammaticality and ACS main factor categories. The endorsement rates (i.e., item classified as grammatical independent of actual grammaticality status) as a function of grammaticality status (G = grammatical strings, NG = non-grammatical strings) as well as associative chunk strength (H = high ACS strings, L = low ACS strings). The endorsement rate for grammatical vs. non-grammatical items, but not for high vs. low ACS items, increases as a function of repeated acquisition sessions. Error bars correspond to standard error of the mean.

ACS items but that correct performance on these items has to be based on knowledge of structural regularities rather than local substring familiarity. Similarly to Lieberman et al., we found no effects of grammatical status for both high and low ACS strings on the baseline test (AGL1; GH vs. NGH: $F(1,31) = 0.42$, $P = 0.52$; GL vs. NGL: $F(1,31) = 0.65$, $P = 0.43$) while we observed significant effects for preference classification (AGL2; GH vs. NGH: $F(1,31) = 34$, $P < 0.0001$; GL vs. NGL: $F(1,31) = 24$, $P < 0.0001$) and grammatical classification (AGL3; GH vs. NGH: $F(1,31) = 59$, $P < 0.0001$; GL vs. NGL: $F(1,31) = 55$, $P < 0.0001$). We also observed a significant effect of ACS for both grammatical and non-grammatical strings during preference classification (AGL2; GH vs. GL: $F(1,31) = 22$, $P < 0.0001$; NGH vs. NGL: $F(1,31) = 4.04$, $P = 0.05$). However, for grammatical classification, ACS only had an effect on the grammatical strings (AGL3; GH vs. GL: $F(1,31) = 21$, $P < 0.0001$) but not on the non-grammatical strings (NGH vs. NGL: $F(1,31) = 2.9$, $P = 0.09$).

In addition, we compared GL vs. NGH based on the argument that this contrast maximally tax structural vs. substring knowledge; if grammatical status is used for classification, the acceptance of a GL item would crucially depend on the grammatical status of the item, while if substring knowledge is used, the low ACS status would promote a rejection decision. In contrast, if substring knowledge is used for classification, the acceptance of HNG items would depend on the high ACS status, while if grammatical status is used, the grammatical status would indicate a rejection decision. As predicted, we found a significant advantage for GL over NGH strings in both preference classification (AGL2; GL > NGH: $T(31) = 3.28$, $P = 0.003$) and grammatical classification (AGL3; GL > NGH; $T(31) = 5.82$, $P < 0.0001$). Taken together, these results show that grammatical status independent of ACS is used for structural generalization in classifying novel strings and provide support for the notion that grammatical structure other than substring familiarity or fragment features is used for successful classification.

3.3 Signal detection and bias - Analysis of the d-prime and beta values

The subjects showed a stable d-prime effect in discriminating between grammatical (G) and non-grammatical (NG) strings (except in the baseline AGL1 test; mean d-prime values: AGL1 = 0.006, AGL2 = 0.94; AGL3 = 1.53; AGL2 > AGL1:

$T(31) = -4.91$, $P = 0.0001$; AGL3 > AGL2: $T(31) = -2.95$, $P = 0.006$, AGL3 > AGL1: $T(31) = -7.63$, $P = 0.0001$). No significant response bias was found (mean beta-values: AGL1 = 1.02; AGL2 = 1.01; AGL3 = 1.17; all $P > 0.6$). However, participants showed no d-prime effect in discriminating between high and low ACS strings (mean d-prime values: AGL1 = 0.15, AGL2 = 0.22; AGL3 = 0.21; all $P > 0.66$). In other words, no difference in the ability to discriminate between high and low ACS was found. In addition, no significant response bias was observed (mean beta-values: AGL1 = 0.99; AGL2 = 0.98; AGL3 = 1.00; all $P > 0.8$). We also investigated the behavioural data for training effects on day 5 by dividing each classification task (preference/ grammatical) into four separate blocks for each task. The statistical analysis yielded no differences in the performance between the four blocks within each classification task.

3.4 Subjective reports

During each classification session (AGL1/2/3) each subject was asked to rate their level of attention, distraction, engagement, boredom, and perceived difficulty (VAS ratings four times evenly distributed over each session). There was no significant difference on these measures except for a small increase in the level of attention (AGL1: 7.9 ± 1.1 ; AGL2: 7.9 ± 1.1 ; AGL3: 8.3 ± 1.0 ; $F(2,58) = 9.2$, $P = 0.0001$) and the participants also rated grammatical classification as more difficult than preference classification (AGL1: 3.4 ± 2.3 ; AGL2: 3.2 ± 2.3 ; AGL3: 4.8 ± 2.8 ; $F(2,62) = 8.96$, $P = 0.001$) despite the fact that their performance improved. Most participants reported that the stimuli presented in the classification tasks were similar to what they saw during the acquisition sessions and they noticed some regularity in the stimulus during the acquisition task (typically that the strings would start with M or V). All participants (but one) reported only vague criteria for their preference and grammatical decisions (which would apply equally to all item-types).

3.5 Fragment completion and generation performance

A fragment completion and a generation task were administered after the last grammatical classification AGL3. In the fragment completion task, the participants had to fill in a missing letter in 31 strings that they had never encountered before.

All participants scored significantly above chance levels (20%; mean correct completions = $74 \pm 16\%$). We found a statistically significant correlation between the number of correct completions and the percentage of correct responses on both classification tasks (AGL2: $P = 0.025$; AGL3: $P = 0.013$). In the generation task, the participants were asked to generate 10 grammatically correct strings; 27 participants could generate grammatically correct strings (mean = 5.3 ± 3.7). The generated strings were categorized as: new (correct grammatical strings that were never presented to the participants); exact copies (correct grammatical strings that were not new but already presented during the acquisition sessions) and copies with more or less repeated trigrams (correct grammatical strings that were not new because if a repeated substring was deleted then they would also have been presented already; for example, a participant would write MSVRXVRXVRXVS and if some but not all of the VRX's are deleted then the string was part of stimuli of the acquisition sessions). According to this classification, participants generated on average 2.3 new grammatical strings and 2.3 exact copies. A significant correlation was found between the generation of grammatical items and the percentage of correct responses on AGL3 ($P = 0.0001$) but not on AGL2. The rating of perceived performance did not correlate with the percentage of correct responses on AGL3 (participants were asked to rate this only after AGL3).

4. Discussion

The artificial grammar learning paradigm has been used as a model of several aspects of language acquisition and implicit learning. In this experiment we modified the original version of the paradigm by investigating both grammaticality and preference classification. It can be argued that preference classification might be more optimal in characterizing the outcome of implicit acquisition since in the preference version participants are kept completely unaware of the underlying generative mechanism, while in the grammaticality version, the subjects have at least in principle been informed about the existence of an underlying complex set of rules at classification (but not during acquisition). The results of the present study showed that the participants implicitly acquired knowledge about

the underlying artificial grammar since participants performed well above chance levels on both preference (AGL2) and grammaticality classification (AGL3) in comparison to baseline classification (AGL1). Participants improved their performance in AGL3 compared to AGL2. Thus the instruction type did influence the final classification proficiency. However, this difference is quantitative rather than qualitative in nature since all effects significant in grammaticality classification (AGL3) were already significant in preference classification (AGL2), as well as the reverse; only the pattern of results was strengthened in AGL3 compared to AGL2. We found that being informed about the existence of an underlying generative mechanism the utilization of ACS did not increase in grammaticality classification and the significant effect of LG vs. HNG was already present in preference classification (AGL2; LG > HNG). These results suggest that grammaticality status independent of ACS is used for structural generalization in classifying novel strings and provide support for the notion that grammatical structure other than local sub-string regularities is to a large extent used for classification. Thus, the abstraction of grammatical structure takes place during implicit artificial grammar acquisition. This can be seen especially in the quantitative performances between the two classification tasks that takes place without an increase in the use of ACS-type information. Furthermore, the use of a preference classification baseline ensures that the effects observed in the classification task are actually due to information learned during the acquisition phase. Subjective reports also suggested that the participants did not utilize an explicit rule-searching strategy but that their classification decisions were reached by guessing based on gut feeling. In addition, the subjective ratings of perceived performance did not correlate with the actual classification performance. These results show that preference and grammaticality classification are equivalent in terms of behavioural effects and strongly support the notion that humans can implicitly acquire knowledge about a complex system of interacting rules by mere exposure to the acquisition material that also can be effectively put to use (Reber, 1967). In other words, preference starts to correlate with the grammaticality status of the classification items without any explicit awareness of the underlying generative mechanisms as predicted by the mere exposure effect (Zajonc, 1968).

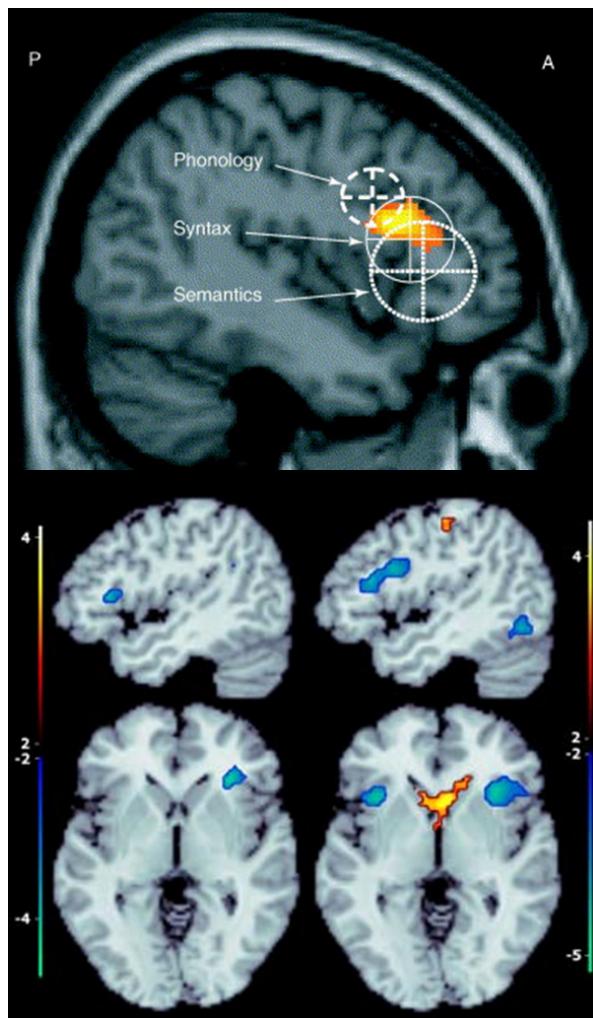


Figure 4. Top: Regions related to phonological, syntactic, and semantic processing (cf., Bookheimer, 2002, and Hagoort, 2005). Bottom Left: Activation related to artificial syntactic violations (Petersson et al., 2004). Bottom Right: Regions active in artificial grammatical vs. non-grammatical items in red and non-grammatical vs. grammatical in blue (Forkstam et al., 2006).

4.1 Dual mechanisms in implicit artificial grammar acquisition

Additional support for the implicit character of AGL comes from lesion studies on amnesic patients. Knowlton and Squire (1996) investigated amnesic patients and normal controls on the original AGL task as well as a transfer version of the task. The patients and their normal controls performed similarly on both AGL versions while the amnesic patients could not explicitly retrieve complete strings or any substring information. Knowlton and Squire (1996) argued that AGL depends on implicit acquisition of both abstract (i.e., ‘rule-based’) and exemplar-specific information, the latter indicated by the acquisition of distributional information of local sub-string regularities (i.e., ACS-type information). The acquisition of long-distance dependencies,

as opposed to local substring dependencies, has been demonstrated both in visuomotor sequence learning and in AGL (Poletiek, 2002). Moreover, it is known that infants can rapidly acquire and generalize over local sequential regularities and several studies have shown rapid (on the order of 2 – 10 min) ‘rule-abstraction’ (Marcus, Vijayan, Bandi Rao, & Vishton, 1999), AGL (Gomez & Gerken, 1999), and transition probability acquisition capacities in artificial syllable sequences (Saffran, Aslin, & Newport, 1996) in infants. It is also clear from these studies that distributional information of local sequential regularities are acquired and used for grammaticality classification in addition to implicit abstraction of grammatical structure (Forkstam et al., 2006; Meulemans & Van der Linden, 1997).

4.2 Artificial grammar learning and functional neuroimaging

A number of functional magnetic resonance imaging (fMRI) studies have investigated implicit (e.g., Forkstam et al., 2006; Lieberman et al., 2004; Petersson et al., 2004; Seger, Prabhakaran, Poldrack, & Gabrieli, 2000) and explicit learning of material generated from artificial grammars (e.g., Fletcher, Buchel, Josephs, Friston, & Dolan, 1999; Strange, Henson, Friston, & Dolan, 2001). In the explicit learning studies (e.g., Fletcher et al., 1999; Opitz & Friederici, 2003; Strange et al., 2001), the experimental task can be characterized as explicit problem solving with performance feedback (Petersson et al., 2004). In this set-up, the participants are explicitly instructed to try to extract the underlying rules based on feedback (“trial-and-error search”). To overcome the explicit nature of the acquisition task in these experiments, we have, as in this study, investigated grammaticality classification task after implicit acquisition without performance feedback in which the participants only are exposed to positive examples (i.e., well-formed strings, Forkstam et al., 2006; Petersson et al., 2004). The latter two studies showed that artificial syntactic violations activated Broca’s region (left Brodmann’s area (BA) 44/45; Figure 4). In Forkstam et al. (2006), the activated frontal regions were more extensive and also included right homotopic regions. Importantly, the left inferior frontal region (BA 45) was the only frontal region which was selectively sensitive to grammaticality but not to the level of associative chunk strength (ACS).

This lends support for the suggestion that the left inferior frontal cortex (BA 45) has a specific role in processing structural regularities (Petersson

et al., 2004). This is also consistent with recent results showing that the left prefrontal cortex subserves structured sequence processing (Figure 4, Bookheimer, 2002; Hagoort, 2005).

A recent study (Lieberman et al., 2004) using a similar AGL paradigm as Forkstam et al. (2006) also reported that the caudate nucleus was sensitive to grammaticality (Figure 4). Here the basal ganglia support the procedural aspects of processing. In this context, it is of interest to note that the basal ganglia learning system (Packard & Knowlton, 2002b) and the medial temporal lobe memory system (Squire & Zola-Morgan, 1991) might interact in complex ways, both competitively (Poldrack et al., 2001) as well as cooperatively (Voermans et al., 2004).

Neural systems supporting procedural learning and important for on-line governing of the parsing process, is thought to depend on recurrent networks implemented in cortico-striatal loops (see e.g., Luciana, 2003; Nelson & Webb, 2003). Classifications of G items correlated with the activation of the caudate nucleus when contrasted with NG items. Moreover, the opposite contrast of comparing classifications of NG vs. G items correlated with activation of the left inferior frontal region. In terms of laterality of the corticostriatal circuits, both the caudate and the inferior frontal region were active bilaterally during processing of grammaticality. The observed selective sensitivity to grammaticality, as opposed to ACS, in the left inferior frontal BA 45 suggests a left-lateral bias in the use of corticostriatal circuits for processing sequence structure.

4.3 Artificial grammar learning: implications for dyslexia

As noted in the introduction, very little is known about the AGL in dyslectic subjects. Based on the tentative conclusions outlined in the introduction, we would like to suggest that the AGL paradigm is a suitable device for further investigation into the implicit learning characteristics in dyslexia. In particular, since the implicit acquisition deficit observed in dyslexia seems to be related to sequence processing and to

sequence complexity (i.e., the level of structure present in the sequences, the use of the artificial (formal) language framework for defining and precisely quantifying sequence complexity seems highly relevant (Cutland, 1980; Davis et al., 1994; Hopcroft, Motwani, & Ullman, 2000). Structural complexity can be systematically varied in artificial grammars, thus making it possible to experimentally

manipulate the level of structure available in the stimulus material in a precise and quantitative manner (Petersson, 2005b; Petersson et al., 2005). The AGL paradigm is modality and material independent, which allows for experimental investigation into the role of material, sensory modality, as well as cross-modality transfer effects (e.g., results on pure tone-and syllable sequences suggest that performance is higher for syllables compare to pure tone sequences, $P = 0.01$, and while grammaticality classification was significant for both types of sequences on day 5, $P < 0.001$, implicit acquisition effects for preference classification on day 5, was only observed for the syllable group, $P = 0.01$, cf., Fáisca, Bramão, Forkstam, Reis, & Petersson, 2007). Moreover, issues related to temporal- and spatial integration can be investigated (e.g., Forkstam et al., 2006; Petersson et al., 2004; Pothos & Kirk, 2004) and importantly it is possible to separate the effects related to local sub-string regularities from those of structure abstraction in a precise manner. Finally, sequence processing after implicit artificial grammar acquisition is known to involve fronto-striatal loops as well as the cerebellum (Forkstam et al., 2006; Lieberman et al., 2004; Petersson et al., 2004). This is particularly relevant given the proposed fronto-striatal-cerebellar circuit deficit in dyslexics (Howard et al., 2006).

Ziegler & Goswami (2005) argue that atypical development of reading skills can arise from variations in the initial conditions or constraints on learning, or from variations in the training environment, or from an interaction between the two. They suggest that explicit access to phonemes is not readily available prior to reading and that all major theories of reading acquisition argue that gaining access to phoneme-size units is a crucial step for the beginning reader of an alphabetic language (Ziegler & Goswami, 2005). A major cause of the early difficulty of reading acquisition is that phonology and orthography initially favor different grain sizes and that structural regularities present in the lexicon of spoken word forms may form the basis of incidental/implicit learning about phonology (Ziegler & Goswami, 2005). Building on an implicit foundation of phonological knowledge, learning to read involves both explicit as well as implicit processes; typically children initially learn grapheme–phoneme mappings explicitly after which they apply and continue to learn how phonology is mapped onto its written representation implicitly (Gombert, 2003; Petersson & Reis, 2006; Ziegler & Goswami, 2005). Ziegler & Goswami (2005) suggest that it is these explicit processes and their potential interactions with the more implicit aspects of lexical processing

that are missing from the models. Awareness of sounds at the smallest grain size (phonemes) does not develop automatically as children get older and the discovery of the phoneme as a psycholinguistic unit depends largely on direct instruction in reading and spelling (Ziegler & Goswami, 2005). Therefore, in order to fully understand non-optimal reading and writing development it might be necessary to investigate not only implicit acquisition or explicit learning mechanisms but also their interaction.

4.4 Conclusion

In this paper we reviewed the literature on implicit learning and dyslexia and tentatively concluded that: (1) dyslexia does not seem to be associated with a general implicit learning deficit; (2) the implicit learning deficit observed in dyslexia does not seem to be related to non-specific factors like general cognitive or attention deficit, task difficulty, or age; (3) the implicit acquisition deficit seems to be related to sequence processing, which is likely related to sequence complexity; (4) the implicit learning deficit in dyslexia can be observed when explicit learning is intact. We also characterized a novel forced-choice structural mere exposure artificial grammar learning paradigm in normal readers in relation to the standard grammaticality classification paradigm. We explored the outcome of an acquisition mechanism capable of extracting structural regularities from experience in an implicit fashion from positive examples alone and without any external supervision or feedback. The results showed that preference and grammaticality classification are equivalent in terms of behavioural effects and strongly support the notion that humans can implicitly acquire knowledge about a complex system of interacting rules by mere exposure to the acquisition material that also can be effectively put to use.

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Oscillatory activity during somatosensory working memory maintenance

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In the current study magnetoencephalography was used to investigate oscillatory activity involved in somatosensory working memory maintenance. A delayed-match-to-sample paradigm was applied, using median nerve stimulation. Based on our findings we propose that somatosensory working memory maintenance is subserved by bilateral secondary somatosensory cortex, and reflected by sustained gamma band activity. Furthermore, we have demonstrated an increase in alpha band power over posterior areas and ipsilateral primary somatosensory cortex. Given that these regions were not required for the task, we interpret this alpha activity to reflect an inhibitory mechanism. Hence, we suggest that the observed somatosensory alpha plays a similar role as posterior alpha. Further research is needed to unravel the exact interplay between primary and secondary somatosensory areas and possible other regions involved in somatosensory working memory.

Keywords: somatosensory, working memory, MEG, oscillations, alpha, gamma

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1. Introduction

Working memory refers to the short-term maintenance of information that is no longer present in the environment (Baddeley, 2003). On the level of brain dynamics, it has been proposed that oscillatory activity produced by cell assemblies plays an essential role in the retention of stimuli in working memory (e.g. Jensen, 2006; Lisman & Idiart, 1995; Tallon-Baudry & Bertrand, 1999).

Oscillatory activity in humans can be non-invasively studied with magnetoencephalography (MEG), a brain imaging technique with a millisecond temporal resolution (Hämäläinen et al., 1993). However, cross-talk due to the mixing of signals from two or more brain sources at the sensor level often makes it complicated to spatially disentangle brain regions involved in cognitive processing. Therefore, we investigated working memory in the somatosensory system in which primary and secondary sensory areas are sufficiently far apart (cf. Simões et al., 2003), making it a suitable system for disentangling the roles of primary and secondary sensory areas.

Traditionally, it has been thought that the primary somatosensory cortex (SI), which contains a somatotopic representation of the contralateral body half, mainly contributes to stimulus representation and discrimination, whereas the secondary somatosensory cortex (SII), which holds bilateral somatotopic representations, plays a role in somatosensory memory and integration (Hernandez et al., 2000; Romo et al., 2002; Romo & Salinas, 2003; Simões et al., 2003). However, recent work in humans has shown transient involvement of SI in a working memory task (Harris et al., 2002): a TMS pulse applied to contralateral SI during the early period of retention disrupted somatosensory memory. Performance was not affected by TMS later into the retention interval or when applied to the ipsilateral SI. The authors concluded that initially retention of the stimulus takes place in both contralateral SI and bilateral SII, after which it is limited to SII. SI involvement in early working memory maintenance was confirmed by an fMRI (functional magnetic resonance imaging) study on vibrotactile working memory in humans, whereas SII involvement could not be established (Preuschhof et al., 2006). These findings in human subjects are somewhat at odds with the previous work in monkeys (Romo & Salinas, 2003); nevertheless, it seems apparent that SI and SII are involved in working memory maintenance.

It is thought that sustained gamma band activity

directly reflects the neuronal correlate of maintained working memory representations. Several studies, both in monkeys (Pesaran et al., 2002) and humans (Jokisch & Jensen, 2007; Tallon-Baudry et al., 1998), showed sustained gamma band activity during the retention interval in a visual delayed-match-to-sample task. Similar results were found in auditory and audiospatial working memory tasks in humans (Kaiser et al., 2003; Lutzenberger et al., 2002). As previous working memory research has mainly focused on the visual and auditory domains, it is interesting to see whether the somatosensory areas show similar activity in the gamma range, speaking to a general working memory mechanism. Hence, we hypothesize that increase in gamma activity in the somatosensory areas reflects the maintenance of somatosensory information.

Further, increase in posterior alpha activity has been shown in several studies on working memory for various modalities (Jokisch & Jensen, 2007; Krause et al., 1996; Tuladhar et al., 2007). However, the functional role of increased posterior alpha oscillations is still under debate. There are broadly three different interpretations, proposing that: (i) posterior alpha reflects cortical idling, a standby mode of the brain keeping it ready to be engaged (reviewed in Pfurtscheller et al., 1996), (ii) posterior alpha plays an active role in memory maintenance (Palva & Palva, 2007), and (iii) posterior alpha reflects inhibition or disengagement of (visual) regions not necessary for the task (Cooper et al., 2003; Jensen et al., 2002). The somatosensory working memory task does not require retention of any visual information; hence visual regions are not engaged in this task. We propose that if posterior alpha reflects inhibition of visual regions, this should result in a greater posterior alpha increase during the retention interval when comparing correct with incorrect trials. Better disengagement of non-relevant areas reduces interfering inputs, which is expected to lead to better memory performance.

Previous somatosensory studies demonstrated that somatosensory alpha (classically referred to as mu) is reduced contralaterally in response to unilateral tactile stimulation (e.g. Bauer et al., 2006; Crone et al., 1998). This suggests that somatosensory alpha plays a similar role as posterior alpha, which is well known to be suppressed with visual stimulation (Adrian & Matthews, 1934). However, a study investigating the effect of prestimulus oscillations on performance in a somatosensory detection task, found different effects for posterior and somatosensory alpha. Posterior alpha power was linearly related to psychophysical performance,

whereas a parabolic relationship was found for contralateral somatosensory alpha (Linkenkaer-Hansen et al., 2004). It remains unclear which role somatosensory alpha plays in working memory maintenance. We propose that if somatosensory alpha plays a similar role as posterior alpha, this should result in alpha increase in ipsilateral SI (and alpha decrease in contralateral SI) during working memory maintenance.

To summarize, we hypothesize that sustained gamma activity reflects somatosensory working memory maintenance, and that alpha band rhythms reflect functional inhibition of non-relevant areas. To test these hypotheses we have applied a somatosensory delayed-match-to-sample task to investigate working memory in healthy human subjects.

2. Methods

2.1 Subjects

23 healthy subjects (18-31 years of age, 11 female, 12 male) participated in the experiment after giving written informed consent. All subjects had normal or corrected-to-normal vision and were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971). Four subjects were excluded from further data analysis because of failure of performing the task above chance level (2 subjects) or showing artifacts in their recordings due to the median nerve stimulation (2 subjects).

2.2 Recording

Ongoing brain activity was recorded (sampling frequency 1200 Hz) using a whole-head MEG system with 151 axial gradiometers (VSM/CTF systems, Port Coquitlam, Canada). The subject's head location relative to the MEG sensors was measured before and after each session using marker coils placed at the nasion and the left and right ear

canals. In addition, structural MR images of the subjects' brains were acquired using a 1.5 T Siemens Magnetom Sonata system. During MR acquisition, the same earplugs were used but now with a drop of Vitamin E in place of the coils, to allow for co-registration of the MRI and MEG data. Stimuli were delivered with a constant current median nerve stimulator (Digitimer Ltd, Hertfordshire, UK).

2.3 Experimental paradigm

The experimental paradigm is presented in Figure 1. Subjects could practice the task before the start of the recording. Median nerve stimulation was set to 50% of the motor threshold level as established prior to the recordings. The task was a delayed-match-to-sample paradigm, in which a sample was presented to the right wrist, followed by a 2 s retention interval after which a probe was presented either to the right or the left wrist. Subjects had to indicate whether the probe stimulus was of higher or lower frequency than the sample, by pushing a button with the left or right foot. Each sample consisted of a 1 s long series of pulses with frequencies ranging from 7 to 10 Hz; the subsequent probe was either 1 Hz slower or faster than the corresponding sample, leading to a task difficulty that allowed for a substantial number of incorrect trials while still getting performance levels above chance. Each sample-probe pair was presented 16 times, amounting to 352 trials. The response was triggered by a question on the screen that also indicated which foot-button corresponded to which answer (higher/lower), so that response side and answer were counterbalanced. Subjects had 4 s to respond, and were asked to always respond unless completely unsure. No feedback was given. Each trial was preceded by 2.1 s baseline.

2.4 Data analysis

Performance on the memory task was analyzed by calculating percentage correct. Subjects that did not perform above chance level (50%) were discarded.

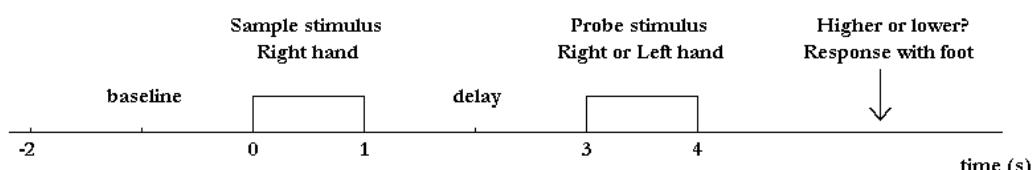


Figure 1. Design of the somatosensory memory task. In this delayed-match-to-sample paradigm, the sample consisted of a series of pulses with frequencies ranging from 7 to 10 Hz and was always presented to the right wrist; the probe was 1 Hz slower or faster than the corresponding sample and presented either to the right or left wrist. Subjects had to indicate whether the probe stimulus was of higher or lower frequency than the sample.

Data analysis of the MEG data was performed using the Matlab-based Fieldtrip toolbox, developed at the FC Donders Centre (<http://www.ru.nl/fcdonders/fieldtrip/>). The trials from the memory session were divided into correct and incorrect, depending on the response given. Trials with no response or more than one response were discarded. Partial artifact rejection was performed to reject those segments of the trials containing eye blinks, muscle artifacts or SQUID jumps. Only trial segments longer than 2 s were accepted for further analysis. For the sensor level analysis an estimate of the planar gradient was calculated for each sensor, which makes interpretation of the sensor-level data easier, as the maximal activity typically is above the source (Hämäläinen et al., 1993).

A time-frequency analysis was performed using an FFT (multi)taper approach with sliding time windows, for low and high frequencies separately. For low frequencies (2-34 Hz) we used an adaptive time window of 4 cycles length combined with a Hanning taper. For high frequencies (35-130 Hz) we applied a fixed time window of 0.2 s and ± 15 Hz smoothing, using 5 orthogonal Slepian tapers. The power was baseline corrected using a 0.2 s baseline period (-0.5 to -0.3 s) before stimulus presentation.

In order to perform statistics on the time-frequency data, normalization to z-scores was performed. This was done to control for differences in variance and noise between the two conditions, among others due to the large difference in trial numbers. To do this, the variance of the power in each time-frequency-channel bin was estimated (for each subject). Subsequently, t statistics were calculated for each time-frequency-channel combination compared to a collapsed baseline (-0.5 to -0.3 s). The resulting t values were transformed into z-scores and pooled across subjects (cf. Bauer et al., 2006).

All subsequent statistical tests were performed on these z-transformed power values. To establish whether the difference between correct and incorrect conditions was significant, we performed a cluster-based nonparametric randomization test (Maris & Oostenveld, 2007). By clustering neighbouring sensors that show the same effect, this test controls for multiple comparisons. As cluster-level test statistic we used the sum of the t-statistics of the sensors within a cluster. By randomizing the data across the two conditions and recalculating the test statistic 3000 times, we obtained a reference distribution to evaluate the statistic of the actual data. Separate tests were performed for low frequency (alpha: 8-12 Hz) and high frequency (gamma: 80-110 Hz) effects. The frequency boundaries were

consistent with those reported in literature (Bauer et al., 2006; Gross et al., 2007; Ihara et al., 2003) and confirmed by visual inspection of the averaged time-frequency representations (TFRs). Data points were averaged within frequency bands. The analysis window was set to the retention interval (2 s). We performed a randomization test averaging over time points to find effects present during the entire retention interval, and a subsequent randomization test without averaging over time to detect transient effects (which e.g. would be expected for SI contribution).

To localize the sources of oscillatory activity we applied a beamforming approach, using an adaptive spatial filtering technique (Dynamic Imaging of Coherent Sources, DICS) (Gross et al., 2001). For source reconstruction we used the data as measured from the axial sensors, not the planar gradients. The DICS technique uses cross-spectral density matrices, which were obtained by applying a multitaper FFT approach. The time windows and frequencies for analysis were based on the previously acquired TFRs. Data pieces obtained after partial artifact rejection were all at least 1 s long. Since there were substantially more correct than incorrect trials, a random selection of correct trials was made to get an equal number of trials for both conditions. Lead fields were calculated from forward head models based on each subject's anatomical MRI (Nolte, 2003). The brain volume of each individual subject was divided into a grid with a 1 cm resolution. Using the cross-spectral density matrices and the lead fields, a spatial filter was constructed for each grid point, and the spatial distribution of power was estimated for each condition in each subject. The relative power difference between conditions was calculated ((correct-incorrect)/incorrect) and the source reconstruction of this difference was overlaid on the subject's individual MRI scan. Subsequently, anatomical and functional data were spatially normalized to the MNI template (International Consortium for Brain Mapping, Montreal Neurological Institute, Canada) using SPM2 (<http://www.fil.ion.ucl.ac.uk/spm>). After spatial normalization the source reconstructions were averaged across subjects.

3. Results

3.1 Behavioural results

Behavioural performance over all subjects was $73 \pm 7\%$ correct on average (19 subjects), which was

significantly above chance level (50%) performance ($t(18) = 14.51$; $p < 0.01$). Error trials (multiple button presses) and no-response trials were excluded from the analysis. Two subjects were discarded because of poor behavioural performance. Side of the probe stimulus (ipsi- or contralateral to the sample stimulus) did not influence performance ($t(18) = 0.42$; $p = 0.68$).

3.2 Gamma band activity

Time-frequency representations (TFRs) of power for the combined planar gradients were

calculated for the correct and incorrect conditions separately. Spectral analysis of the higher frequencies showed modulation of gamma band activity during the retention interval. Gamma power (80-110 Hz) increased substantially for correct but not for incorrect trials in left and right somatosensory regions (Fig. 2). Furthermore, there seemed to be a difference in posterior gamma activity. To assess the significance of these modulations, a cluster-based randomization test was performed, averaging over frequencies (80-110 Hz) and time (the retention interval). This statistical test showed that gamma activity was significantly increased in the retention

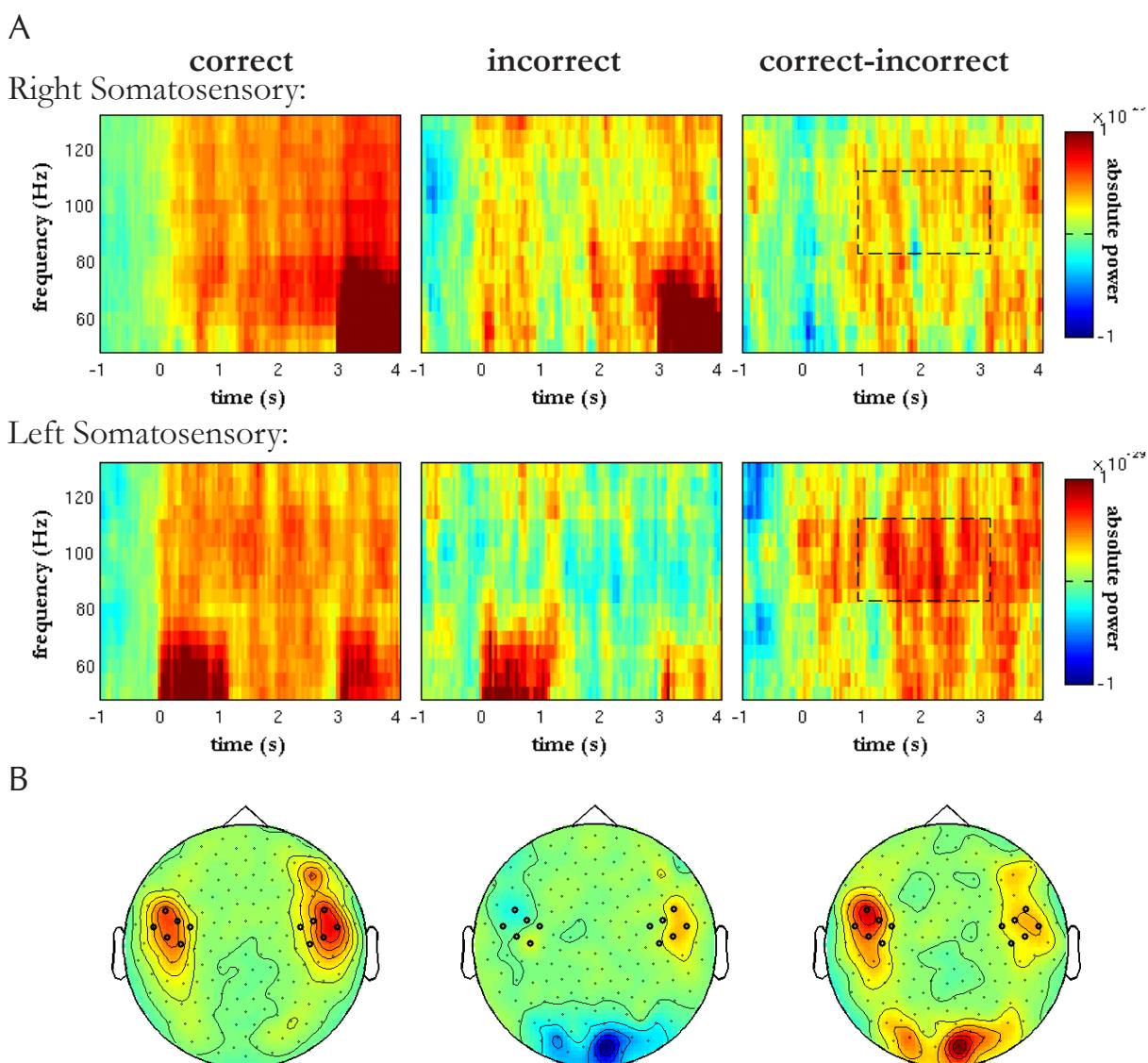


Figure 2. Gamma activity during the retention interval (time = 1-3 s). (A) Showing TFRs for right somatosensory (first row) and left somatosensory channels (second row); from left to right for correct trials, incorrect trials, and the difference calculated as correct-incorrect. (B) Topographic plots showing gamma activity (80-110 Hz) averaged over the retention interval, dots indicating the channels used for the TFRs above. All plots are showing power values, absolute baseline corrected (baseline: -0.5 - 0.3 sec). Note: Figures for gamma shown here are based on 17 subjects, whereas the statistical analysis was based on 19 subjects. For plotting purposes, 2 subjects were left out because of very high, lateralized gamma power that distorted the absolute power grand averages (i.e., including these 2 subjects in the grand averages, gives plots that do not correspond with statistical results, as z-scores correct for outlying power values, hence this lateralized activity is not reflected in the statistical results).

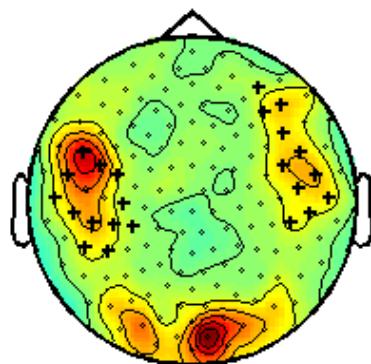


Figure 3. Statistics for gamma power (averaged over time). Topographic plot for gamma power (80-110 Hz) averaged over the retention interval, for correct vs incorrect. Significant channels (correct>incorrect) are marked with +. Showing group average power values, absolute baseline corrected (baseline: -0.5 to -0.3 s). Colorbar see fig. 2.

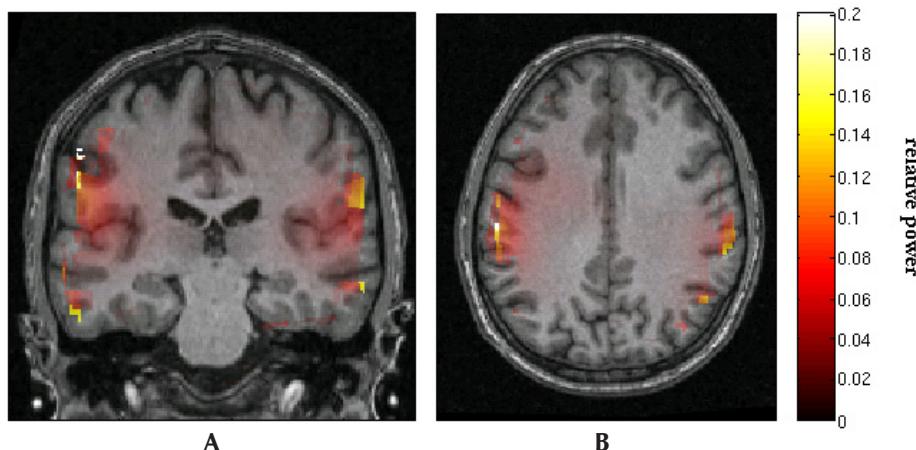


Figure 4. Coronal (A) and transverse (B) slices showing gamma power source reconstructions obtained using beamforming. Grand average across 6 subjects (preliminary data). Showing correct versus incorrect, relative difference (calculated as: (correct-incorrect)/incorrect). Gamma activity in these subjects is located in left and right SII.

interval for correct versus incorrect conditions ($p<0.01$) in the left and right somatosensory areas (Fig. 3). No significant results were obtained for the posterior gamma activity. These results were confirmed with a similar statistical test, now without averaging over time. Several significant clusters ($p<0.05$) including both left and right somatosensory channels were found throughout the retention interval (data not shown).

Due to overlapping pick up of sensors, SI and SII cannot be disentangled at the sensor level. To disentangle the source of the somatosensory gamma effect we applied a beamforming approach. The spatial distribution of gamma power was estimated for correct and for incorrect conditions for each subject for the entire retention interval (1-3 s at 95 ± 15 Hz). The source reconstruction of the relative difference between correct and incorrect was overlaid on the individual MRI for each subject, spatially normalized and averaged across subjects. Here we present preliminary source localization results based on 6 subjects that showed strong somatosensory gamma (Fig. 4). For these subjects, the beamforming results showed that the bilateral gamma activity was located in left and right SII.

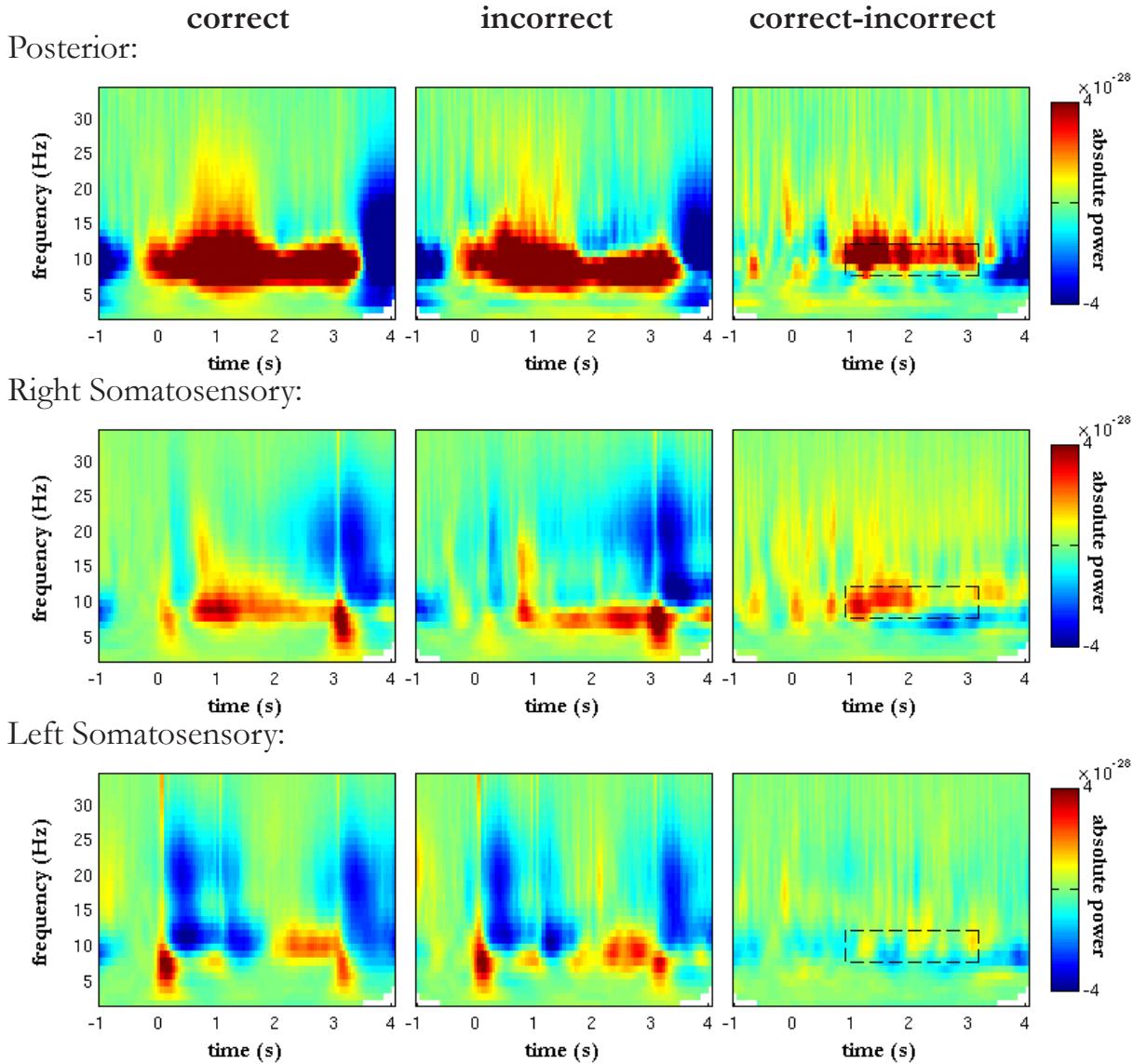
3.3 Alpha band activity

Spectral analysis of the lower frequencies showed modulation of alpha activity (8-12 Hz) in the retention interval¹. Both for correct and incorrect trials, alpha power increased over posterior areas during the retention interval (Fig. 5). This alpha increase was stronger for the correct trials than for incorrect, as can be seen in the TFR for the difference (calculated as correct - incorrect). To assess the significance of this difference, a cluster-based randomization test was performed, averaging over frequencies (8-12 Hz) and the retention interval (1-3 s). This statistical test showed that alpha activity was significantly increased in the retention interval for correct versus incorrect conditions ($p<0.01$) over posterior channels (Fig. 6).

Although weaker than the posterior alpha, right somatosensory channels clearly showed an increase in alpha power during the retention interval, both for correct and incorrect conditions. This increase

¹ Please note that due to the choice of 4 cycle time windows (see Methods), we can not fully assess activity in frequency ranges lower than 7 Hz. Nevertheless, for illustrative purposes these frequencies are included in the figures.

A



B

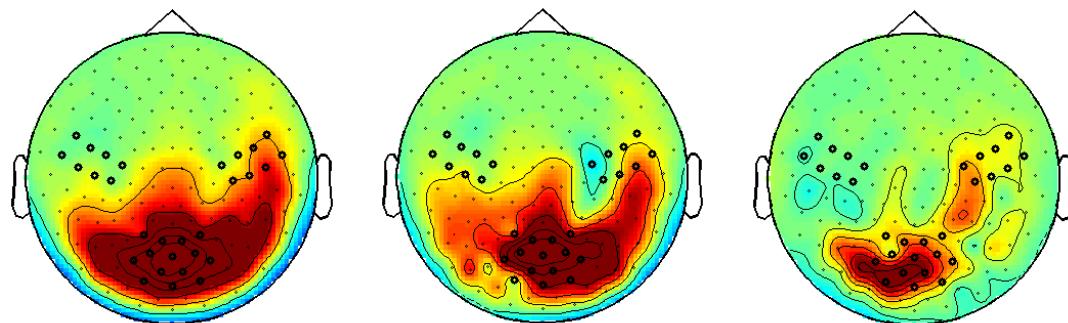


Figure 5. Alpha activity during the retention interval (time = 1-3 s). (A) Showing TFRs for posterior (first row), right somatosensory (second row) and left somatosensory channels (third row); from left to right for correct trials, incorrect trials, and the difference calculated as correct-incorrect. (B) Topographic plots showing alpha activity (8-12 Hz) averaged over the retention interval, dots indicating the channels used for the TFRs above. All plots are showing power values, absolute baseline corrected (baseline: -0.5 -0.3 sec).

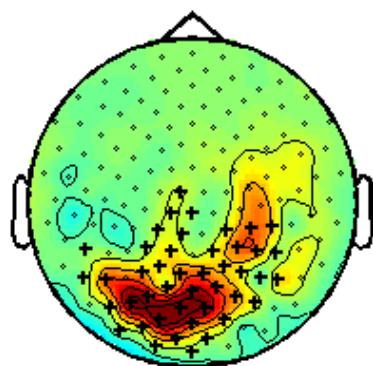


Figure 6. Statistics for alpha power (averaged over time). Topographic plot for alpha power (8-12 Hz) averaged over the retention interval, for correct vs incorrect. Significant channels (correct > incorrect) are marked with +. Showing group average power values, absolute baseline corrected (baseline: -0.5 to -0.3 s). Colourbar see fig. 5.

was stronger for correct trials, especially during the first second of the retention interval (Fig 5). Left somatosensory channels showed an initial decrease of alpha during the retention interval, both for correct and incorrect trials, followed by an increase in alpha power. Comparing the two conditions showed no clear effect (Fig. 5). To test for significance of these more transient somatosensory alpha effects, we performed another randomization test, similar to the one described before but now without averaging over time. Two significant clusters were found ($p<0.01$ and $p<0.05$), separated in time (first

cluster: 1 to 2.05 s, second cluster: 2.3 to 3 s). The channels included in these clusters vary over time points. Alpha activity was significantly increased early in the retention interval (1-2.05 s) for correct compared to incorrect conditions ($p<0.01$) in right somatosensory regions (Fig. 7A). No significant results were obtained for left somatosensory activity. Furthermore, both significant clusters contained posterior sensors (Fig. 7), confirming the previously presented results.

In order to establish the source of the right somatosensory alpha as observed on sensor level, we applied beamforming to the averaged power over the first second of retention. For each individual subject we used an optimized alpha frequency, based on the previous TFRs. Probably due to the relatively strong posterior alpha activity, it was not possible to localize the right somatosensory source in all subjects. Figure 8 shows the grand average over all subjects. Although small, a prominent source was located in right SI.

4. Discussion

In the current study MEG was used to investigate oscillatory activity involved in somatosensory working memory maintenance. A delayed-match-

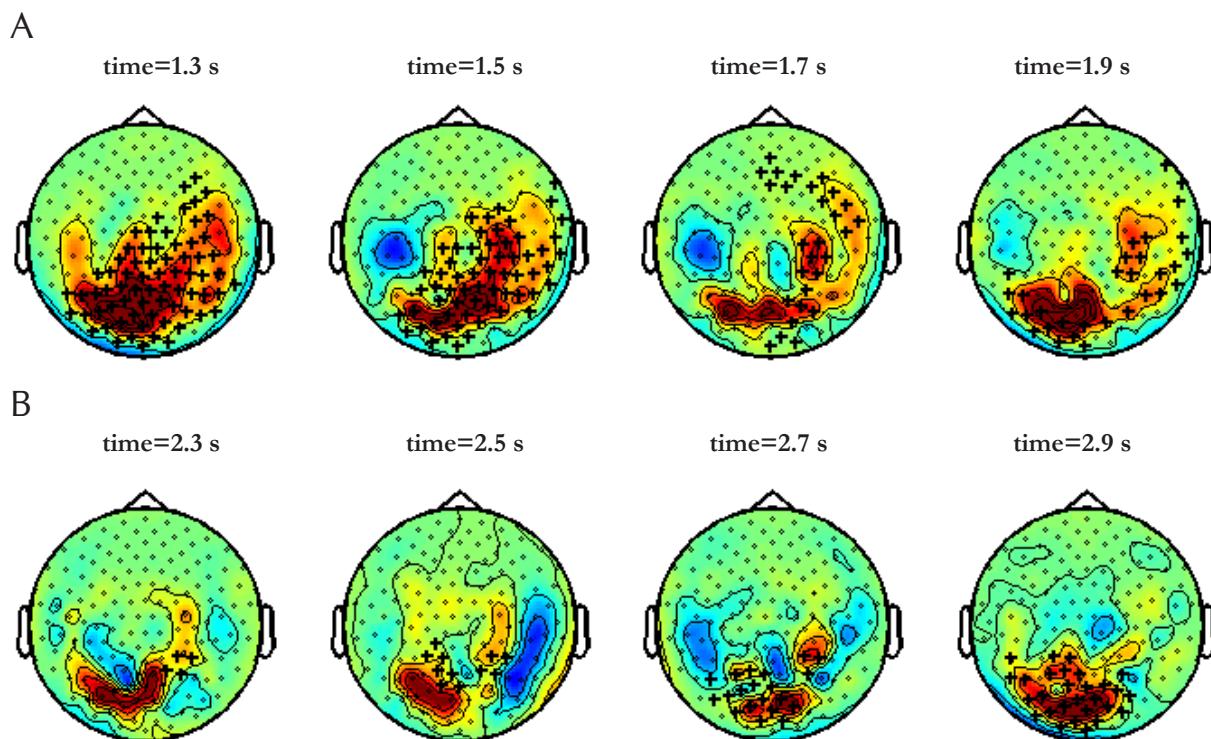


Figure 7. Statistics for alpha power (not averaged over time). Topographies showing significant channels (indicated by +), for time points during the retention interval (presented with 0.2 s steps). Significant clusters include both posterior and somatosensory channels for the first second of retention (A) and mainly posterior channels for the second part (B). Colorbar see fig. 5.

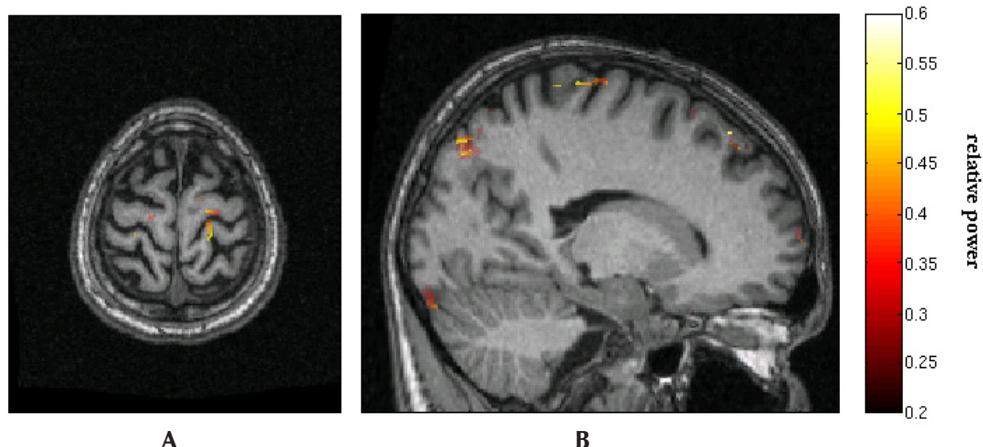


Figure 8. Transverse (A) and sagittal (B) slices showing alpha power source reconstructions obtained using beamforming. Grand average for all 19 subjects (preliminary data). Showing correct versus incorrect, relative difference (calculated as: (correct-incorrect)/incorrect). Somatosensory alpha activity is located in right SI.

to-sample paradigm was applied, using median nerve stimulation. We found an increase in gamma activity in bilateral somatosensory areas, reflecting working memory maintenance. Furthermore, we demonstrated increased alpha band activity over ipsilateral SI and over posterior areas, which are regions not required for the task at hand.

The behavioural results show that side of the probe stimulus (ipsi- or contralateral to the sample stimulus) did not influence performance. This finding confirms previous research showing a laterality effect (ipsilateral comparisons being faster) for short but not for long retention intervals (Harris et al., 2001; Harris et al., 2002), which suggests a bilateral representation of the stimulus after the early (~ 1 s) period. Further support for bilateral retention of the stimulus is given by our gamma band results.

4.1 Gamma activity reflects working memory maintenance

Our results show modulation of gamma band activity (80–110 Hz) over somatosensory areas during the working memory retention interval. Trials during which the stimulus was correctly maintained, showed an increase in gamma power that was significantly higher than the gamma activity in incorrect trials. Preliminary source localization results show that somatosensory memory maintenance takes place in bilateral SII.

Given the location of this effect, we propose that the increased gamma activity in correct trials directly reflects working memory maintenance. In incorrect trials, the subject failed to keep a representation of the stimulus, reflected by lower gamma activity over somatosensory regions. These results are in line with

previous research on working memory in the visual and auditory modalities, showing sustained gamma band activity to reflect the actual maintenance of the working memory representation (Jokisch & Jensen, 2007; Kaiser et al., 2003; Lutzenberger et al., 2002; Pesaran et al., 2002; Tallon-Baudry et al., 1998). To our knowledge, the current study is the first to show bilateral gamma activity in a somatosensory working memory task. We propose that sustained gamma band activity reflects the mechanism of working memory maintenance independent of modality.

Our preliminary source localization results are in line with previous work showing SII involvement in somatosensory memory and integration (Harris et al., 2001; Harris et al., 2002; Hernandez et al., 2000; Romo et al., 2002; Romo & Salinas, 2003). This is compatible with the idea of working memory requiring a central executive, supplemented by modality-specific peripheral storage systems (Baddeley, 2003). Here we show that for maintenance of somatosensory information, the somatosensory regions (probably bilateral SII) function as such a storage system.

4.2 Posterior alpha activity reflects inhibition

We show that alpha power increased in posterior areas during working memory maintenance. The posterior alpha power increase was present during the entire retention interval and significantly stronger for correct than for incorrect trials. As visual areas were not needed during the retention period, we interpret this alpha increase to reflect active functional inhibition of non-relevant areas, leading to better memory maintenance.

This is in line with previous research proposing

that alpha activity reflects inhibition of the visual stream (Cooper et al., 2003; Jensen et al., 2002; Jokisch & Jensen, 2007; Tuladhar et al., 2007). However, at this point we cannot fully exclude the alternative hypothesis, that posterior regions are actively involved in working memory maintenance, reflected by posterior alpha increase (Palva & Palva, 2007).

4.3 Somatosensory alpha activity reflects inhibition

The alpha band increase in right somatosensory areas was significantly stronger for the correct condition compared to the incorrect, during the first second of the retention period. Given the preliminary source localization results the alpha increase in the right somatosensory region can mainly be attributed to SI. As the sample stimulus was always presented to the right wrist and the probe stimulus could be presented to either side, right SI was never needed during the initial part of the task, but could be for the second part. Hence, it seems beneficial to inhibit right SI during the first half of retention and then to disinhibit it during the second half, before the upcoming probe. This confirms our disengagement hypothesis also for somatosensory areas.

For left somatosensory we see an initial decrease in alpha power, which, given that left SI was always needed for the initial stage of memory maintenance (Harris et al., 2002), would reflect engagement (or absence of disengagement) of this region. There was no significant difference between correct and incorrect trials for this effect. This suggests that regarding alpha, memory performance mainly depends on the ability to actively disengage non-relevant areas. Furthermore, these results do not confirm the finding that intermediate alpha power is optimal for performance (Linkenkaer-Hansen et al., 2004).

The ipsilateral somatosensory alpha increase confirms our predictions regarding alpha activity as a general mechanism for disengagement of areas not relevant for the task. We extend this beyond posterior regions and propose that alpha plays a role in actively disengaging both posterior regions and others, as we show here for primary somatosensory cortex. Our results are in conflict with the interpretation of alpha activity as an idling mechanism (Pfurtscheller et al., 1996) or playing an active role in working memory maintenance itself (Palva & Palva, 2007), as we see alpha increase in regions not necessary for performing the task, and an absence of this increase

in the relevant areas.

An fMRI study looking into BOLD (blood oxygen level dependent) changes following unilateral tactile stimuli to the fingers, found a positive BOLD response in contralateral SI, and a negative BOLD response in ipsilateral SI. This deactivation in response to ipsilateral somatosensory stimulation was localized to area 3b of SI (Hlushchuk & Hari, 2006). Several neuroimaging studies looking into the relation between the BOLD response as measured by fMRI and neural oscillations as measured by EEG/MEG, show that gamma band activity correlates positively with the BOLD response (Logothetis et al., 2001; Niessing et al., 2005), whereas posterior alpha band activity correlates negatively with BOLD (Goldman et al., 2002; Laufs et al., 2003; Moosmann et al., 2003). Hence, (if the same relationship holds for somatosensory alpha and BOLD) our results showing an alpha increase in ipsilateral SI are in line with the previous fMRI findings. Furthermore, our gamma results are also in agreement with fMRI studies showing contralateral SII activation following somatosensory stimulation (Del Gratta et al., 2002; Maldjian et al., 1999).

4.4 Conclusion

Based on our findings we propose that somatosensory working memory maintenance is subserved by bilateral secondary somatosensory cortex, and reflected by sustained gamma band activity. Furthermore, we have demonstrated an increase in alpha band power over posterior and ipsilateral primary somatosensory regions. Given that these regions were not required for the task, we interpret this alpha activity to reflect an inhibitory mechanism. Hence, we suggest that the somatosensory alpha we observed plays a similar role as posterior alpha.

However, the exact interplay between SI, SII and possible other regions involved remains unclear, as well as the means of functional connectivity between these areas. Further analysis of our data and subsequent research are required to unravel the exact mechanisms of somatosensory working memory.

In this paper, we presented preliminary beamforming results. We are planning on continuing this analysis and hope to reliably show the source reconstructions of the observed sensor effects, confirmed by statistics on source level. Furthermore, to clarify the interactions between regions and oscillations involved, analysis of functional connectivity will be applied.

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The time course of word category ambiguity processing: an MEG study

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Although it has been settled that the left posterior temporal region and the left inferior frontal gyrus (LIFG) are associated with language processing, their role and their interaction have not been understood thoroughly. Hagoort (2005) proposed the former to underpin the retrieval of single word information and the latter the creation of the syntactic structure. Supportive evidence for this hypothesis was found in a functional magnetic resonance imaging (fMRI) experiment on noun/verb ambiguous words (Snijders et al., 2007). The poor temporal resolution of fMRI, however, left the question unanswered whether, besides its role in constructing the syntactic structure, the LIFG is involved directly in the competition between ambiguous alternatives or in the resolution of the ambiguity. To address this issue, the present magnetoencephalography experiment was set up using the same manipulation. The enhanced event related field amplitude at the disambiguating word suggests that the role of the LIFG be related to the resolution of the ambiguity. On the other side, competition between alternative interpretations is not excluded. The increased power in the higher-beta (20–22 Hz) in the time window 150–500 ms indicates that ambiguity processing entails competition at the ambiguous word.

Keywords: word class ambiguity, beta frequency, syntactic processing

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1. Introduction

Consistent findings have linked syntactic processing to a network encompassing the left inferior frontal gyrus (LIFG) and the left temporal gyrus (Caplan, 2001; Vigneau et al., 2006). However, the specific role of these brain regions is poorly understood. Recently Hagoort (2005) proposed a model in which these two areas underlie two different stages in language processing with the left temporal cortex being associated with the retrieval of single word information and the LIFG with the unification of this information into a coherent representation. Notably, this framework specifies the unification of all the linguistic information, from phonological to semantic elements, and it is based on a computationally explicit syntactic model (Vosse & Kempen, 2000).

Some evidence in favor of this account has been presented by Snijders et al. (2007) in an fMRI study exploiting ambiguous words in sentence and word sequence context. Ambiguity has been a critical manipulation in a number of studies and many theories have tried to account for its effect in language comprehension, with varying degrees of success. Using a particular case of ambiguity, word class ambiguity, Snijders et al. (2007) succeeded in disentangling the distinct contribution of the left temporal regions and the LIFG in ambiguity processing, in line with the principles described by Hagoort (2005). Although successful in identifying the areas involved in the different aspects of syntactic processing, the study was not so successful in tracking their temporal development, due to the intrinsic limitations of any fMRI experiment.

By taking advantage of the high temporal resolution of magnetoencephalography (MEG) and by using the same manipulations of Snijders et al. (2007), the present experiment will measure these temporal dynamics and the interplay between the involved areas.

1.1 The MUC model

Hagoort (2005) described a function-oriented linguistic model which consists of three components: Memory (which underpins the retrieval of the word forms), Unification (which supports the composition of a coherent representation) and Control (which accounts for the communicative intentions and the extralinguistic factors); hence the acronym MUC. These functionally separate components interact to bind single word information together into a

meaningful representation, combining phonological, syntactic, semantic and extralinguistic elements. The syntactic parsing underlying the MUC model is derived from the Unification Space Model, an explicit computational model proposed by Vosse and Kempen (2000) and based on a lexicalist grammar.

1.1.1 Syntactic framework

In the Unification Space Model (Vosse & Kempen, 2000), the syntactic framework of the MUC model, there is no other rule than the unifying operation (also compare Jackendoff, 2002, p. 180), while all the syntactic information is stored in the lexical frames of the single words. The lexical frame, formed by a three-layer structure, defines the structural environment of the target word, as, in Figure 1, the lexical frame of the word *sees* specifies the potential attachments. The role of the unification function is to combine the lexical frames into a syntactic tree as they enter the unification space and to measure the strength of the unification links of the alternative structural configurations over time, so that, for example, the lexical frames of *woman* and *sees* are unified in a suitable structure. In the case of multiple potential attachments, the winning structure is defined by lateral inhibition among the possible alternatives. The parsing is successful when the lexical frames of a particular configuration form a syntactic tree in which all the conditions (e.g. agreement or word order constraints) are best fulfilled.

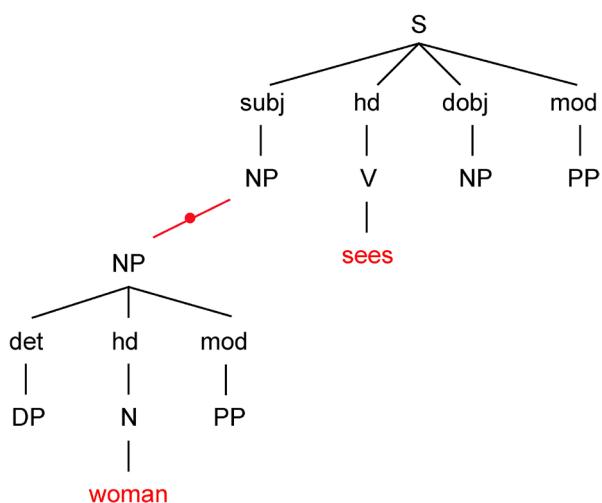


Figure 1. The lexical frame of the word *sees* defines the potential attachment of a Noun Phrase (NP) in the first position. The unification function selects the appropriate position for the attachment of the lexical frame of the word *woman*. NP:Noun Phrase, S:Sentence, det:determiner, dobj:direct object, hd:head, mod:modifier, subj:subject.

1.1.2 Memory

Within the framework of the MUC model (Hagoort, 2003, 2005), the lexical frame of an incoming word is retrieved from the mental lexicon (Levelt, 1992) and this process is considered to be supported by the left posterior temporal cortex. Whereas there is growing agreement that the word-specific syntactic information is stored in the mental lexicon (Jackendoff, 2002; MacDonald, Pearlmuter, & Seidenberg, 1994; Vosse & Kempen, 2000), the hypothesis that this region underlies the retrieval of lexical frames is supported by the role of this area in syntactic processing (Damasio, Grabowski, Tranel, Hichwa, & Damasio, 1996; Indefrey & Cutler, 2004; Ullman, 2001).

1.1.3 Unification

The anatomical area that is related to the unification space in which lexical frames are bound together has been indicated to be the left inferior frontal gyrus (LIFG, defined as Brodmann areas 44/45/47 by Caplan, 2001). The LIFG is implicated in constructing the syntactic structures of sentences (Caplan, Alpert, Waters, & Olivieri, 2000) and its suitability for the unification function derives from its ability to hold information on-line (Miller, 2000) and to select between competitive representations (Thompson-Schill, D'Esposito, & Kan, 1999; Thompson-Schill, Bedny, & Goldberg, 2005).

1.1.4 Control

The third component reflects those elements that contribute to the communicative goals but that are not of a linguistic nature, such as attentional control in turn-taking or language selection in bilingualism. This component is thought to be supported by a network of areas including the anterior cingulate cortex and the dorsolateral prefrontal cortex (Hagoort, 2005). The following discussion and the present experiment will not address the role of this component.

1.2 Ambiguity

The relation between the Memory and the Unification components and their neural substrates, the left posterior temporal cortex and LIFG respectively, will be investigated here exploiting word class category ambiguity instead of using the long-established but unnatural syntactic violation

manipulation. Experimental material based on violations contains by definition ungrammatical sentences and participants may soon become aware of the artificial trait of the sentences. In contrast, the material of the present experiment is composed of all legitimate and grammatically correct sentences.

Furthermore, ambiguity is so pervasive in natural languages that readers hardly ever notice it (Altmann, 1998). Examples of ambiguity can involve the syntactic structure of the sentence (*Two Sisters Reunited After 18 Years in Checkout Counter*) or the multiple meanings of a word (*Iraqi Head Seeks Arms*). The former type of ambiguity is called syntactic as it deals with the organization and the relations of the words in the sentence (Altmann, 1998) while the latter is referred to as lexical (Hagoort & Brown, 1994; Simpson, 1984) or semantic (Lee & Federmeier, 2006) ambiguity. In certain contexts, the distinction can be useful, although some authors (MacDonald et al., 1994; Traxler, Pickering, Clifton, & Van Gompel, 2000 among others) maintain that the two ambiguities are solved by the same mechanisms.

1.2.1 Syntactic ambiguity

Syntactic ambiguity is paradigmatically explained by the *garden path* effect (Bever, 1970), where reading times over the whole ambiguous sentence *The boat floated down the river sank* are significantly longer than for a similar, unambiguous sentence (like *The boat ridden down the river sank*). As consistent as this effect is, its explanations are very divergent. Syntax-first models assume that in the first instance only one interpretation is pursued, contextual information is not used immediately and longer reading times are due to the subsequent reanalysis (Ferreira & Clifton, 1986; Frazier & Rayner, 1982; Frazier, 1987; Pritchett, 1992); constraint-based models claim that, while one continuation is preferred, the other interpretations are still activated and reading difficulty arises from the on-going competition (MacDonald et al., 1994; McRae, Spivey-Knowlton, & Tanenhaus, 1998; Vosse & Kempen, 2000). Models that include a reanalysis stage differ in whether they assume that the same alternative is always chosen during the first reading (*fixed-choice* models, Frazier, 1987) or whether this varies across readers (*variable-choice reanalysis* models, Traxler, Pickering, & Clifton, 1998; Van Gompel, Pickering, & Traxler, 2000).

Van Gompel et al. (2000) proposed a two-stage reanalysis model, the *unrestricted race model*, to account for the *ambiguity advantage* effect, where globally ambiguous sentences (as *The son of the driver with the moustache was pretty cool*) are read faster than

unambiguous related sentences (as *The driver of the car with the moustache was pretty cool*, Traxler et al., 1998; Van Gompel, Pickering, & Traxler, 2001). In this model, alternative interpretations compete at the same time but only the analysis that is completed first is chosen. If the chosen analysis becomes inconsistent with later information, reanalysis occurs. However, despite the claims of Van Gompel, Pickering, Pearson, and Liversedge (2005), the *ambiguity advantage* effect does not represent evidence against competition models (Vosse & Kempen, 2007); in fact, Green and Mitchell (2006) proposed an implementation of a competition model (McRae et al., 1998) to account for the *ambiguity advantage* effect.

1.2.2 Lexical ambiguity

Lexical ambiguity has been the crucial manipulation to grasp the nature of the mental lexicon (Simpson, 1984). There is evidence that, without a biasing context, the multiple senses are activated in parallel and lexical competition has been measured with crossmodal priming paradigm (Tanenhaus, Leiman, & Seidenberg, 1979), reading times (Rayner & Duffy, 1986), neuropsychological investigations (Swaab, Brown, & Hagoort, 1998) and event-related potentials (Swaab, Brown, & Hagoort, 2003). In a lexical decision task, Azuma and Van Orden (1997) reported facilitation for semantically ambiguous words, an effect explained by Rodd, Gaskell, and Marslen-Wilson (2002) as the result of the presence of many related senses, in contrast to the reported inhibition for words with many unrelated meanings (see also the related MEG experiment, Beretta, Fiorentino, & Poeppel, 2005).

Furthermore, there is considerable agreement that both frequency (Rayner & Duffy, 1986; Simpson, 1984) and context (Duffy, Morris, & Rayner, 1988; Tabossi, 1988) play a decisive role in determining which meaning is chosen and how fast this occurs, although it is still subject of debate whether unselected meanings are nevertheless active (Mac- Donald et al., 1994; Swaab et al., 2003) or not (Glucksberg, Kreuz, & Rho, 1986; Simpson, 1981; Simpson & Krueger, 1991; Van Petten & Kutas, 1987).

The question whether ambiguous words have a special neural representation has been tested by Federmeier, Segal, Lombrozo, and Kutas (2000). After reporting that nouns and verbs have different neural topography, they showed that word class ambiguous words, even in disambiguating contexts, elicit a distinct event related potential (ERP) component: a slow frontal negativity. This component is thought

to be due to the resolution of semantic ambiguity (Lee & Federmeier, 2006).

1.2.3 The present experiment

The present MEG experiment exploits a special case of lexical ambiguity, namely noun-verb ambiguous words to create syntactically ambiguous sentences. In Dutch, there are quite a few word class ambiguous words (as *sprongen*, meaning both *jumps*, plural noun, and *jumped*, verb in simple past) and the preceding context may not bias one reading over the other. Up to *Want deze sprongen... (Because these jumps/jumped...)*, both the noun and the verb readings of *sprongen* are possible and the two continuations (*Want deze sprongen zijn niet zonder risico, Because these jumps are not without risk*, or *Want deze sprongen dagelijks in het koude meerje, Because these jumped everyday in the cold lake*, see Table 1) are legitimate. The word after *sprongen*, however, disambiguates towards one reading of the ambiguity. At that point, only one interpretation is correct and the word class category of *sprongen* is unequivocally manifest.

The ambiguity effect will thus be obtained by comparing the MEG signal elicited by the ambiguous word with the signal elicited by an unambiguous alternative. Besides the ambiguity effect, we will include an orthogonal manipulation, referred to as grammaticality, i.e. the ambiguous word and the unambiguous alternative will be presented either within a sentence or as element of a scrambled word sequence. In this way, the experiment will be based on a 2 x 2 factorial design with Grammaticality and Ambiguity as main effects.

1.2.4 Grammaticality

Sentences are expected to elicit a larger response over both frontal and temporal areas than scrambled word sequences. The frontal increase in activity is due to the involvement of the LIFG in the unification of single word lexical frames into a coherent sentential configuration, while the list of words does not need to be integrated in a unitary representation. For a similar contrast, sentences in comparison to random word lists, Bastiaansen, Magyari, Schoo, and Hagoort (2007) reported a sustained event related field (ERF) activity over left temporal regions and increased power in the theta (4–8 Hz) and in the lower-beta (13–18 Hz) frequency bands.

1.2.5 Ambiguity

When an ambiguous word is read, two lexical frames are retrieved from the mental lexicon, one associated with the noun and the other with the verb reading (Vosse & Kempen, 2000). We therefore expect larger activity in the left temporal region in the time window shortly after the presentation of the ambiguous word. In particular, time-frequency analysis may reveal to be selectively sensitive to this manipulation. The retrieval of lexical-semantic information has been found to be related to theta frequency power changes. Open class words elicit larger theta power than closed class words (Bastiaansen, Van Der Linden, Ter Keurs, Dijkstra, & Hagoort, 2005) and theta synchronization has different spatial distributions for abstract and concrete nouns (Weiss, Müller, & Rappelsberger, 2000). Power changes in the theta frequency band could hint at a modulation of the lexical retrieval, due to the ambiguity effect.

1.2.6 Grammaticality and ambiguity

The key prediction concerns the interaction between grammaticality and ambiguity. In the sentence context, ambiguous words are not only associated with two lexical frames, but they also increase the unification load since two syntactic structures compete until the ambiguity is resolved. Sentences containing an ambiguous word are the most difficult to unify, so they should elicit the largest effect, in correspondence of the LIFG, where unification occurs, and the left temporal cortex, where lexical frames are maintained active.

The results from a previous fMRI experiment (Snijders et al., 2007) on similar material support these hypotheses. Sentences led to stronger activation in frontal and temporal regions than word sequences, the ambiguity contrast was significant in the left posterior temporal areas and the region of interest analysis on LIFG showed a clear interaction effect in the predicted direction. However, the sluggishness of the hemodynamic response defies any effort to understand the temporal dynamics of the involved areas and the aim of the present MEG experiment is to overcome this limit. In particular, determining the temporal characteristics of the interaction effect represents the fundamental goal of the present experiment, in order to clarify whether the interaction effect in the LIFG is to be related to competition at the ambiguous word or to ambiguity resolution at the disambiguating word.

2. Methods

2.1 Participants

Thirty-two native Dutch speakers (mean age: 21.8 years; range 18–25, 16 women) recruited through the subject database of the F.C. Donders Centre for Cognitive Neuroimaging, Nijmegen, participated in the study. Participants were right-handed, without any non-removable metal in the body and without any history of neurological disease or language-related impairments. Participants provided written consent according to the Declaration of Helsinki and they were paid for their collaboration. Six additional participants were measured but discarded because of machine failure (three occasions) and excessive head movement.

2.2 Material

The stimulus material was constructed on the basis of two main manipulations: the critical word could have been either category ambiguous (A) or unambiguous (U) and could have occurred in a meaningful sentence (S) or in a scrambled word sequence (W). Furthermore, we distinguished between a noun (N) or a verb (V) reading of the ambiguous word in the sentence or of the unambiguous word. Therefore, there were eight (23) conditions: SAn, SAv, SU_n, SUv, WAn, WAv, WU_n, WUv. Examples are given in Table 1.

2.2.1 Ambiguous words

Ambiguous critical words had to be both a noun and a verb (and not to belong to any other category), have a noun-ratio (noun frequency divided by summed frequency) between 0.25 and 0.75 (the average was 0.5) and a summed frequency belonging to the upper 95% of all words in the corpus. Two corpora, CELEX (Baayen, Piepenbrock, & Van Rijn, 1993) and CLEF (Van der Beek, Bouma, Malouf, & Van Noord, 2002) were consulted and both had to give concordant results on all the criteria.

2.2.2 Ambiguous sentences

The initial part of the sentence, including the critical word, was constructed in such a way that both readings of the critical word were legitimate and equally plausible. Noun-ratio was assessed with a pre-test on 38 participants who had to complete sentences on the basis of the ambiguous beginning.

Table 1. Example of one experimental item with the critical word **sprongen** in the eight conditions.

SAn:	Sentence Ambiguous (noun reading) Want deze sprongen zijn niet zonder risico. <i>Because these jumps (n/v) are not without risk.</i>
SAv:	Sentence Ambiguous (verb reading) Want deze sprongen dagelijks in het koude meertje. <i>Because these jumped (n/v) everyday in the cold lake.</i>
SUn:	Sentence Unambiguous (noun reading) Want deze medicijnen zijn niet zonder risico. <i>Because these medicines (n) are not without risk.</i>
SUv:	Sentence Unambiguous (verb reading) Want deze zwommen dagelijks in het koude meertje. <i>Because these swam (v) everyday in the cold lake.</i>
WAn:	Word sequence Ambiguous (matched with SAn) cijfers alles sprongen ook aan weg die <i>ciphers all jumps/jumped (n/v) also at way the</i>
WAv:	Word sequence Ambiguous (matched with SAv) in uit sprongen alle het kooplui heer allerei <i>in out jumps/jumped (n/v) all the trader lord diverse</i>
WUn:	Word sequence Unambiguous (matched with SUn) cijfers alles medicijnen ook aan weg die <i>ciphers all medicines (n) also at way the</i>
WUv:	Word sequence Unambiguous (matched with SUv) in uit zwommen alle het kooplui heer allerei <i>in out swam (v) all the trader lord diverse</i>

Only beginnings whose ratio of noun endings divided by all endings were between 0.2 and 0.8 (average = 0.46) were used for constructing the experimental items. After the ambiguous word, two endings were added, one for the noun and one for the verb reading, taking care that the ambiguity was resolved for each sentence in the word following the critical word. Noun and verb sentences were matched on length. Sentences consisted of 6 to 12 words, with an average of 8.5 words per sentence. The critical word occurred in the second (39 times), third (33 times) or fourth (8 times) position of the sentence.

2.2.3 Unambiguous sentences

For every sentence, we constructed two suitable, unambiguous alternatives for the ambiguous critical word (as a noun and as a verb) that fitted the constructed sentences (called SUn and SUv, see Table 1). A part of the alternative words was taken from the CLEFcorpus by matching the syntactic environment of the critical word. For critical words for which no alternative could be found in the corpus, the alternatives were hand-picked. Ambiguous and unambiguous words were matched on (summed) word form frequency and length.

2.2.4 Word sequences

Words in the word sequences (WAn, WAv, WUn, WUv) were matched in frequency, length and syntactic category with the words from the sentence conditions. For each sentence, every word (except the critical word) was exchanged for a different word matched for frequency, length and syntactic category. Subsequently, the order of all words in the sequence (except the critical word) was randomized, with the constraint that two words could not have the same order of the corresponding words in the original sentence. Sequences were checked on lack of local grammaticality and were mixed again if three or more consecutive words formed a coherent sentence fragment. In all the conditions, none of the non-critical words could have elicited lexical or syntactic ambiguity.

2.2.5 Versions

The whole experimental material was composed of 80 experimental items in the eight conditions, thus the total amounts to 640 experiment sentences. The 80 experimental items were divided in four groups matched for frequency of the ambiguous and unambiguous critical words. Items from these four groups were assigned to condition pairs in the first two of the three blocks in which the experiment was divided. The condition pairs consisted of SAn-WUv, SAv-WUn, SUn-WAv and SUv-WAn and were chosen because neither the critical word nor any other words were repeated. Additionally, to increase the number of trials per condition in the third block the critical words from the first block were repeated, swapping the condition pairs to minimize any possible priming or memory effect. In this way, we obtained eight balanced versions, in which the eight conditions had the same number of items (30). We took care that every version was assigned to two male and two female participants.

2.3 Procedure

Stimuli were presented visually in serial presentation mode using Presentation software (Version 9.13, www.neurobs.com). The font was 'Times New Roman' with an angle of 2° at 50 cm from the screen. Every word was on the screen for 300 ms, with a 300 ms interword- interval. At the beginning of each sentence/word sequence, a visual fixation cross of 2 seconds showed when the participant could blink, followed by a 1.2 second long

blank screen. Experimental sentences/sequences were pseudorandomized and mixed with 96 fillers, 60 of which contained a meaningless consonant string (e.g. “grpsd”). This material was presented in clusters of five sentences or word sequences. Before each cluster, the word “*Zinnen*” (“Sentences?”) or “*Woorden*.” (“Words?”) appeared on the screen for 1.5 seconds to inform the participants of the type of incoming cluster. This device was intended to prevent subjects from attempting spurious unification of the scrambled word sequences.

Participants were instructed to read the words on the screen carefully and attentively. The control task was assigned to the participants that had to respond to the consonant strings in the fillers as quickly as possible by pressing a button. This control task kept the participants awake and was used to assess their responsiveness by measuring the reaction times to the control words. A short practice session preceded the experiment to test whether the participant had not misunderstood the task and whether the position was comfortable.

During the experiment, the electromagnetic signal of the brain was measured using a whole-head MEG system (Omega 2000; VSM/CTF Systems, Port Coquitlam, British Columbia, Canada) installed at the F.C. Donders Centre for Cognitive Neuroimaging, with 151 axial gradiometers at a sampling rate of 600 Hz, with participants in supine position in a magnetic shielded room. Electrooculogram (EOG) was recorded from electrodes above and below the eye and at the right and left temples. The head position relative to the MEG sensor array was measured at the beginning, at the end and before the third block using three reference coils (at the nasion and in the two ear channels). These landmarks became useful for the off-line realignment with the anatomical scans acquired with the MRI (Hämäläinen, Hari, Ilmoniemi, Knuutila, & Lounasmaa, 1993). In a separate session, a full-brain anatomical MRI image of each participant were acquired on a 1.5 T Siemens Sonata scanner (Siemens, Erlangen, Germany), using a standard T1-weighted sequence.

2.4 Data analysis

Data were analyzed using FieldTrip software package (<http://www.ru.nl/fcdonders/fieldtrip/>), a Matlab toolbox (The MathWorks, Natick, MA) that has been developed at the F.C. Donders Centre for Cognitive Neuroimaging. The main analysis was conducted on a 2 x 2 design, with sentences versus word sequences (Grammaticality) and ambiguous versus unambiguous words (Ambiguity) as main

effects, collapsing the noun and verb readings of the critical words into one category so that we obtained 60 trials for each condition. To investigate whether the effect of ambiguity was different for sentences and for word sequences, we compared ambiguous versus unambiguous sentences and ambiguous versus unambiguous word sequences.

Individual trials were time-locked at the critical word and included the 200 ms preceding and the 1500 ms following the critical word. All the trials were screened for artifacts (eye blinks, vertical and horizontal eye movements, muscle activity, jumps in the recording sensors) both by an artifact detection algorithm and by visual inspection. Trials in which participants inadvertently pressed the button were discarded too.

Using the anatomical MRI scan, data of individual subjects were realigned according to a standard head position to allow for grand-averaging (Knösche, 2002). Planar gradients of the MEG field distribution were calculated using a nearest-neighbor method (Bastiaansen & Knösche, 2000, applied by Jokisch & Jensen, 2007; Osipova et al., 2006). The horizontal and vertical components of the planar gradients approximate the signal measured by the MEG systems with planar gradients. This method is particularly useful for the interpretation of the field topography because planar gradients have typically the largest amplitude above the source (Hämäläinen et al., 1993).

2.4.1 Event Related Field analysis

Trials were bandpassfiltered between 0.5–30 Hz and baseline-corrected with the 200 ms preceding the critical word. The single-subject mean amplitude was calculated at each time point of the artifactfree trials. The grandaverage over all participants was then used for the statistical testing.

2.4.2 Time frequency analysis

Power spectra of all the trials were computed on a sliding time window using the multitaper approach applied to short sliding windows (Percival & Walden, 1993; Mitra & Pesaran, 1999) and then averaged across conditions (Jokisch & Jensen, 2007; Osipova et al., 2006). For the low frequencies (2–40 Hz), we applied an adaptive time window of four cycles per frequency ($\sim T = 4/f$) and an adaptive smoothing of $\sim f = 1/\sim T$. Statistical analysis was conducted on four frequency bins in the theta (4–6 Hz), alpha (8–12 Hz), lower-beta (14–18 Hz) and higher-beta (20–22 Hz) ranges, based on previous findings (see

Bastiaansen & Hagoort, 2006, for a review). For the high frequencies (20–90 Hz), we used a fixed time window length (400 ms) and a frequency smoothing of ~ 15 Hz, employing 11 tapers. A DFT filter with 5 s of sample padding was used to clear the data of the 50 Hz component, that is due to electrical interference. Frequency bins were not used in the statistical analysis of high frequency because there was no a priori knowledge of the frequencies of interest.

2.4.3 Statistical test

Differences between conditions were tested using a nonparametric randomization test (Maris & Oostenveld, 2007; Nichols & Holmes, 2002). This test controls the Type-I error rate due to multiple comparisons using a clustering approach. The two-sided *t*-statistics were computed for all the sensor-time point pairs (or sensor-frequencytime point triples for the high-frequency analysis) and spatially and temporally contiguous data points whose *p*-value was smaller than .05 were clustered together. The cluster-level test statistics was defined from the sum of the *t*-values of the data points comprising each cluster. The Type-I error rate was controlled for by evaluating a cluster-level test statistics for all the clusters under the randomization null distribution of the maximum cluster-level test statistic. The null distribution was computed by randomly swapping the condition assignment within every subject and by calculating the test statistics for the new set of clusters. A reference random distribution of the cluster-level statistics was created from 2000 random draws. The *p*-value was estimated according to the proportion of the randomization null distribution exceeding the observed cluster-level test statistics.

3. Results

3.1 Event Related Fields

3.1.1 Grammaticality main effect

The direct comparison between sentences and word sequences, where the ambiguous and unambiguous conditions were collapsed, exhibits two significant clusters ($p < .001$), spanning from 140 ms up to the end of the time window, and distributed over 148 sensors in total. In particular, the first cluster begins at 140 ms from left sensors, then move towards the right hemisphere up to 872 ms. In a similar fashion, the second cluster becomes

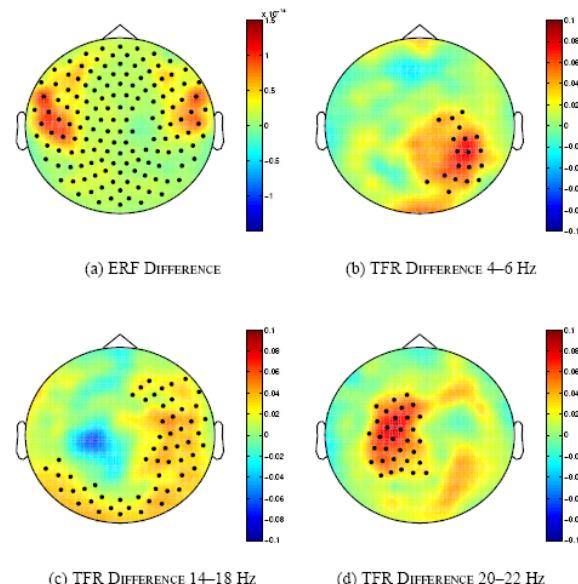


Figure 2. Comparison between sentences and word sequences. Panel a shows the difference between the ERF amplitudes of the two conditions for the first cluster (140–872 ms). The other three panels plots the logarithm of the ratio of the power between the two conditions: Panel b for the cluster in the theta band (400–800 ms), Panel c for the first cluster in the lower-beta band (0–550 ms) and Panel d for the cluster in the higher-beta band (950–1350 ms). Black dots indicate significant sensors.

significant at 735 ms mainly over left sensors and then moves towards the right side, up to the end of the time window, 1500 ms. The consistency of the scalp topography over time suggests common generators, being the areas with the largest difference bilaterally below the temporal and, to lesser extent, frontal sensors. Figure 2, panel a, shows the ERF difference in the time window of the the first cluster (140–872 ms) and black dots indicate the spatial distribution.

3.1.2 Ambiguity main effect

The main effect of ambiguity was tested comparing ambiguous and unambiguous critical words, collapsing sentence and word sequence conditions together. No significant cluster was found in the time window of the ambiguous word but there was a main effect of ambiguity between 1098–1353 ms ($p = .033$). However, this significant effect was due entirely to the sentence ambiguous condition, as the temporal and spatial characteristics of the two effects are almost identical.

3.1.3 Ambiguity within sentences and word sequences

The comparison between ambiguous and unambiguous sentences was not significant in the time

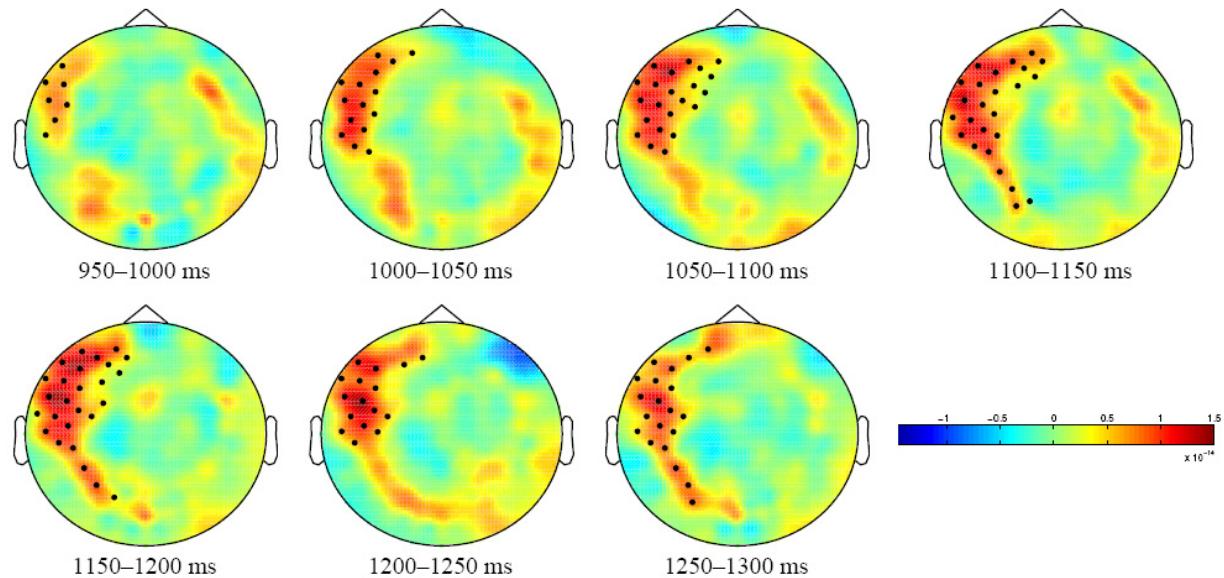


Figure 4. Topography of the amplitude difference between ambiguous and unambiguous sentences in bins of 50 ms. Black dots indicate sensors that are significant in at least one time point within the plotted 50 ms.

window of the ambiguous word ($p = .702$ between 420–485 ms) but was significant between 982–1300 ms (i.e. 382–700 ms after the disambiguating word, $p = .002$). Figure 3 illustrates the temporal evolution of the ERF amplitude for all the significant channels, the red filled space shows the temporal extension of the significant cluster. The spatial distribution of the same cluster over time is shown on Figure 4, where black dots indicate sensors that are significant at least at one time point in the bins of 50 ms. For the word sequences, the corresponding comparison for ambiguous and unambiguous conditions did not present any significant cluster (lowest $p = .106$).

3.2 Time frequency analysis

3.2.1 Grammaticality main effect

Sentences elicited a larger activity than word sequences in the theta (4–6 Hz), lowerbeta (14–18 Hz) and higher-beta (20–22 Hz) frequencies. In particular, in the theta range, the effect was significant over right posterior temporal sensors between 400–800 ms ($p = .039$, Figure 2, panel b) and, in the higher-beta range, it was significant over left parietal sensors between 950–1350 ms ($p = .021$, Figure 2, panel d). In the lower-beta range, two clusters emerged. The first one between 0–550 ms ($p = .007$, plotted in Figure 2, panel c) and the second one between 1000–1300 ms ($p = .025$). Both had an almost identical distribution, including frontal, temporal and occipital areas mainly in the right hemisphere. In the alpha frequencies (8–12 Hz), the fourth band we tested, the effect was not significant ($p = .088$).

3.2.2 Ambiguity main effect

In none of the frequency bands of interest was there a main effect of ambiguity (for the theta frequencies the smallest cluster had $p = .613$, for alpha $p = .095$, for lower-beta $p = .162$ and for higher-beta $p = .152$).

3.2.3 Ambiguity within sentences and word sequences

For the comparison within sentences, ambiguous words elicited a larger activity in the high-beta frequency band (20–22 Hz) than unambiguous words in the time window 150–500 ms ($p = .011$).

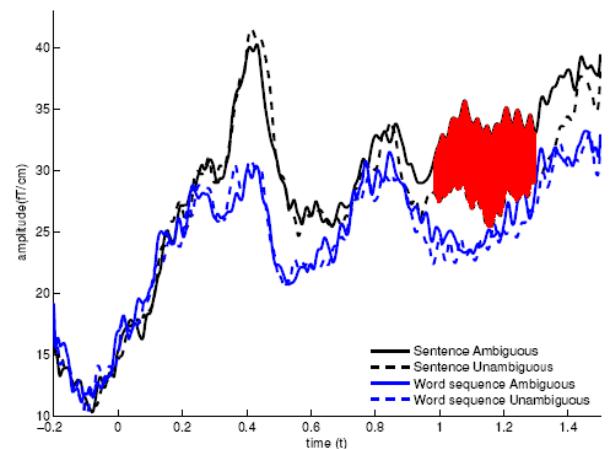


Figure 3. ERF amplitude for ambiguous and unambiguous sentences, averaged over significant sensors. The critical word (ambiguous/unambiguous) was presented at 0 ms and the following word (the disambiguating word for the ambiguous sentence condition) at 600 ms. The red filled space indicated the time span of the significant cluster (987–1300 ms). The word sequence conditions are given for comparison.

The activity is localized over left parietal and temporal sensors as illustrated in Figure 5. The direct comparison between ambiguous and unambiguous word sequences was not significant (lowest $p = .119$, at the lower-beta band, 14–18 Hz).

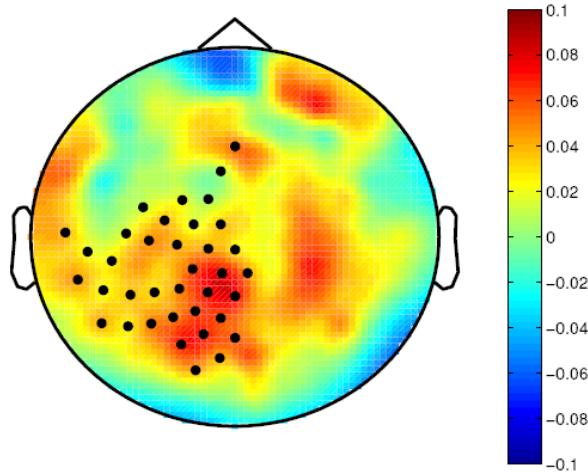


Figure 5. Difference between ambiguous and unambiguous sentences in the high-beta frequency band (20–22 Hz), between 150–500 ms plotted as the logarithm of the ratio of the power between the two conditions. Black dots indicate significant sensors.

3.2.4 High-frequency analysis

The same comparisons were tested in the high-frequency band (20–90 Hz), however, it was impossible to identify any significant cluster. The null result in the high-frequency band is rather disappointing, but it can be explained by the low signal to noise ratio inherent to the time-frequency analysis and by the time jitter to which induced high-frequency activity for higher cognitive processes is susceptible and which in turn could have been canceled out by averaging over a large number of subjects (Tallon-Baudry & Bertrand, 1999).

3.3 Post-hoc tests

3.3.1 Neutral versus slightly biased context

To test the hypothesis of some models (Van Gompel et al., 2005; Vosse & Kempen, 2000, among others) that perfectly balanced ambiguous words increase the processing difficulty in comparison to context-biased ambiguous words, we divided the ambiguous sentence condition in two groups, according to the preferences expressed in the pre-test. In the pre-test, a sentence-completion task, we assessed the noun-ratio for each ambiguous beginnings and only ambiguous words with a noun-ratio between 0.2 and 0.8 were used in the experiment. For this post-hoc test, two groups of

ambiguous sentences were used. The balanced group was formed by ambiguous words with a noun-ratio between 0.3 and 0.7, while the slightly biased one had a noun-ratio smaller than 0.3 or larger than 0.7.

Although the difference of the ERF amplitude between the two groups was very small, it was possible to pinpoint a small trend that was not significant if only averaging in the time window 300–500 ms after the ambiguous word, but that became significant after averaging in that time window over left temporal sensors, where the effect was expected ($p = .024$).

3.3.2 Noun versus verb reading

To examine whether nouns and verbs have different neural representation, we compared the noun and verb reading of the two unambiguous conditions (sentences and word sequences, so SU_n vs. SU_v and WU_n vs. WU_v). The same comparison for the ambiguous conditions (as, for example, in Federmeier et al., 2000) was not informative in our case, because the critical word was intended to be ambiguous in respect to the noun/verb reading. Nouns were associated with a larger ERF amplitude than verbs mainly over left temporal regions averaging over the 300–500 ms time window ($p = .002$, see Figure 6 for the scalp topography). The same comparison for word sequences did not yield any significant result ($p = .36$).

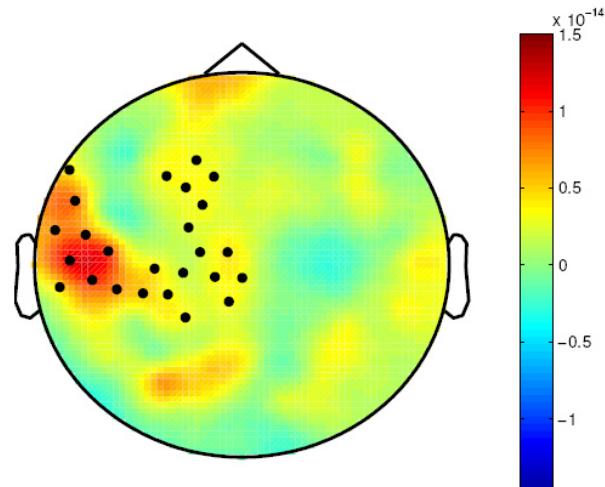


Figure 6. Comparison between unambiguous nouns and unambiguous verbs for the sentence condition in the time window 300–500 ms. Black dots indicate significant sensors.

4. Discussion

The present experiment builds on a previous fMRI experiment (Snijders et al., 2007) which

showed that noun/verb ambiguous words in a non-biasing context are associated with larger activity than unambiguous ones in the left inferior frontal gyrus and in the left posterior middle temporal gyrus, in accordance with the predictions of the MUC model (Hagoort, 2003, 2005). The present MEG experiment, aimed at overcoming the fMRI-related poor temporal resolution, revealed a strong ERF over left fronto-temporal sensors at the disambiguating word. Although the ERF amplitude was not modulated at the ambiguous word, the time-frequency analysis revealed an increase in high beta power (20–22 Hz) right after the presentation of the ambiguous word. Furthermore, similarly to the findings of Snijders et al. (2007), sentences presented a larger sustained activity, as higher ERF amplitude than scrambled word sequences and increased activity in the theta (4–6 Hz), lower-beta (14–18 Hz) and higher-beta (20–22 Hz) frequency bands.

4.1 Findings

4.1.1 Grammaticality

During sentence comprehension, single word information has to be retrieved from the mental lexicon and maintained on-line during the unification and the building of the syntactic structure. This was associated with an ERF sustained activity over left temporal and frontal regions, as the comparison between sentences and word sequences in our experiment indicated (see Figure 2, panel **a**). Furthermore, the right-hemisphere homologue areas showed an ERF sustained activity as well, although of smaller amplitude. In general, these results correspond to the fMRI activation regions for the same comparison in Snijders et al. (2007): LIFG, left middle temporal gyrus and both temporal poles. Sustained ERF amplitude for sentences was also reported by Bastiaansen et al. (2007) while the left-dominant bilateral activity has been confirmed by a number of studies (Bottini et al., 1994; Just, Carpenter, Keller, Eddy, & Thulborn, 1996; Kuperberg et al., 2000), with the proposal that the right-hemisphere is involved in semantic processing (Jung-Beeman, 2005).

The time-frequency analysis of the grammaticality effect highlighted a power increase in the theta (4–6 Hz), lower-beta (14–18 Hz) and higher-beta (20–22 Hz). This is perfectly consistent with the hypotheses put forward by Bastiaansen and Hagoort (2006) that theta frequencies are related to the retrieval of single word information and lower-beta frequencies to syntactic unification. This suggestion has been

corroborated by a number of studies addressing the role of theta in the lexical retrieval (Bastiaansen, Van Berkum, & Hagoort, 2002a, 2002b; Bastiaansen et al., 2005; Hald, Bastiaansen, & Hagoort, 2006; Röhm, Klimesch, Haider, & Doppelmayr, 2001; Weiss et al., 2000), the role of beta in syntactic processing (Haarmann, Cameron, & Ruchkin, 2002; Schoo, 2005; Weiss et al., 2005) and their combined role in sentence comprehension (Bastiaansen et al., 2007). The topography for the three frequency bands (Figure 2, theta is shown in panel **b**, lower-beta in panel **c** and higher-beta in panel **d**) is rather puzzling and its interpretation arduous due to the extremely small number of language studies using TFR on MEG data and to the inconsistency of topographies of oscillatory dynamics across studies (Bastiaansen & Hagoort, 2006). Nevertheless, the right posterior temporal distribution of the theta frequency band for MEG data is to be found in Bastiaansen et al. (2007) for the similar comparison between sentences and random word lists, while the beta power change over the right hemisphere was also reported by Weder (2003) for semantic violations in sentence context.

4.1.2 Ambiguity

We were not successful in identifying the main effect of ambiguity. The direct comparison between ambiguous and unambiguous words, collapsing sentences and word sequences together did not yield significant results in the ERF or TFR analysis and the only significant cluster in the ERF analysis is in fact the watered-down consequence of the interaction effect at the disambiguating word. This is, however, perfectly consistent with the fMRI findings. Snijders et al. (2007) reported that only the right striatum was exclusively sensitive to ambiguity, while other areas, including the left posterior middle temporal gyrus, showed, besides the main effect, a significant interaction with grammaticality. Because the magnetic signal falls off with the square of the distance and stronger and more superficial sources were also affected by the interaction effect, the main effect of ambiguity was undetectable with the MEG experiment.

4.1.3 Grammaticality and ambiguity

The interaction effect between grammaticality and ambiguity was in the direction of an increased activity for ambiguous sentences. This increased activity manifested itself in two ways: as higher power for higher-beta frequency band in the time window

of the ambiguous word and as larger amplitude in the ERFs in the time window of the disambiguating word. We suspect that the fMRI activity reported by Snijders et al. (2007) is to be related to the ERF amplitude. In fact, for both the grammaticality and the interaction effects, the scalp topography of the ERFs, and not that of any of the frequency bands, is consistent with the activated areas of the fMRI experiment.

On the basis of this observation, we can infer that the interaction effect reported in the fMRI experiment for the LIFG is the consequence of processes occurring at the disambiguating word: Figure 7 shows the ERF amplitude at the critical word (Panel a) and at the disambiguating word (Panel b) over significant channels, as in Figure 5, and the contrast estimates for the fMRI activity in the LIFG (Panel c). While the ERF amplitude at the critical word shows only a main effect of grammaticality, the activation patterns of the fMRI contrast estimates and the ERF amplitude at the disambiguating word are strikingly similar. In the light of this observation, we can infer that the activity associated with the interaction effect reported by Snijders et al. (2007) is to be found in the time window 400–700 ms after the presentation of the disambiguating word.

Besides the ERF effect at the disambiguating word, ambiguous sentences showed an increased power in the higherbeta frequency band in the time window of the ambiguous word (150–500 ms). The time window and the topography (see Figure 5) suggests that this effect can be associated with ambiguity processing occurring after the presentation of the ambiguous word. Effects in this frequency band for ambiguity processing have not been reported before, most probably because most electrophysiological studies uses only timelocked averaging methods (Pfurtscheller & Lopes da Silva, 1999) and analysis of oscillatory activity in psycholinguistic studies has only recently been more widely performed (Bastiaansen et al., 2002b).

4.2 Ambiguity in sentences: the MUC model

While the grammaticality effect showed a substantial sustained activity that can be easily related to the retrieval and the unification of lexical frames, the comparison of ambiguous versus unambiguous sentences elicited a more intricate pattern of transient activity as a consequence of the ambiguity processing. In fact, ambiguity processing involves several syntactic steps, occurring within short periods

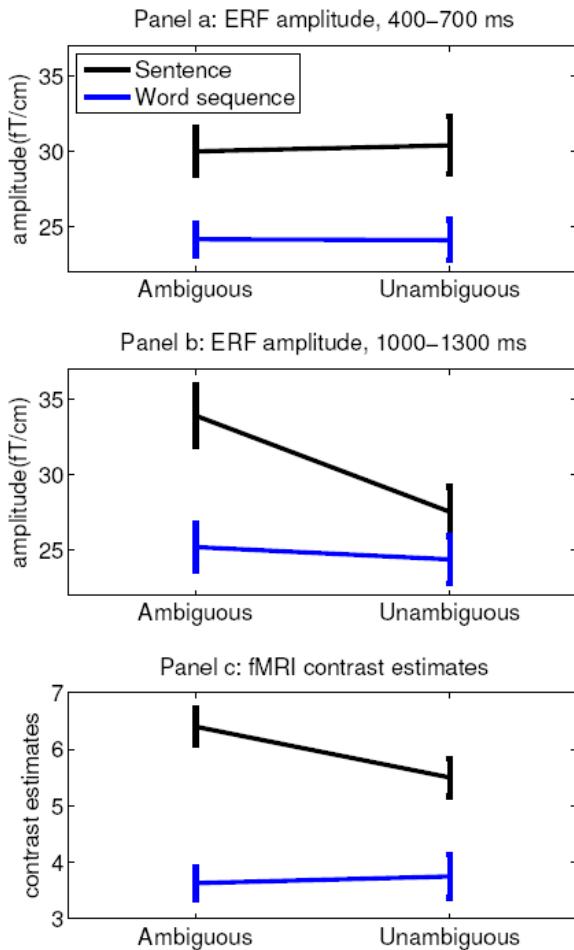


Figure 7. Comparison between the effects measured with MEG and fMRI in the four conditions: black lines for sentences and blue ones for word sequences, in both the ambiguous and unambiguous conditions. Mean ERF amplitude over sensors as in Figure 5 in the time window of the critical word (Panel a) and of the disambiguating word (Panel b). Panel c shows the fMRI contrast estimates in the LIFG (Snijders et al., 2007). Vertical lines indicate standard error for both the ERF amplitudes and the fMRI contrast estimates.

of time and quickly evolving over the sentence. As described by the Unification Space model (Vosse & Kempen, 2000), the syntactic framework of the MUC model (Hagoort, 2005), the main stages ambiguity processing undergoes are the retrieval of the lexical frames, the competition among alternatives and the selection of the context-relevant interpretation. Despite the lack of vast literature, it is possible to advance some hypotheses on the neural correlates of these stages on the basis of the findings of the present MEG study.

4.2.1 Retrieval of lexical frames

There is growing evidence that the retrieval of lexical frames is associated with power changes in

the theta band (4–7 Hz, Bastiaansen & Hagoort, 2003; Bastiaansen et al., 2005; Weiss et al., 2000). Because the Unification Space model predicts that for the ambiguous word two lexical frames had to be retrieved from the mental lexicon, we could have expected to find power increase in the theta band due to the ambiguity effect within sentences. However, no significant modulation in that frequency band was detected. This could be due to the transient nature of the lexical retrieval, which probably lasts only a few hundred milliseconds, shorter than the time window used in the TFR analysis for the theta frequencies (4–6 Hz), which was between 666 and 1000 ms (the length of the adaptive time window was equal to four cycles per frequency, see Methods). This is an intrinsic limitation to any frequency analysis on transient effects in the low-frequency range, because the temporal resolution is limited by the length of the oscillation. This limitation, however, does not apply to sustained activity, as in the case of grammatical contrast, in which a theta power modulation was found.

4.2.2 Competition and lateral inhibition

After having been retrieved, the two lexical frames engage in a competition through lateral inhibition between the two alternative unification links. It is reasonable to assume that this process can be associated with the increased power in the higher-beta frequency (20–22 Hz). Although there are no studies that relate this frequency band to any specific function, the syntactic functional role of beta frequencies (Bastiaansen & Hagoort, 2006), the time window in which this effect is significant (150–500 ms after the ambiguous word) and the distribution over left temporal and parietal regions (see Figure 5) corroborate the idea that the increased power in the higher-beta frequency is linked to ambiguity processing. Unfortunately, on the basis of the present study it is not possible to address the issue whether the higher-beta activity reflects competition tout court or lateral inhibition between alternatives.

Moreover, one element that points to the presence of competition is the small modulation of the ERF amplitude found over temporal sensors in the post-hoc test between balanced and slightly biased contexts. In the time window of the ambiguous word, perfectly balanced beginnings have a larger ERF amplitude than slightly biased beginnings, suggesting that the intensity of the competition, fiercer for perfectly balanced ambiguous sentences, is reflected in the strength of the activity over temporal regions.

4.2.3 Selection

The competition among the lexical frames is resolved when only one candidate remains active and the resulting interpretation is selected. In our material, the selection of the context-relevant interpretation could not have occurred at the ambiguous word, because at that point both interpretations (the noun and verb readings) were equally plausible. The only moment in which only one candidate was ultimately determinate was at the disambiguating word and only then did the selection of the relevant interpretation within the unification component occur.

This process manifests itself as larger ERF amplitude for ambiguous than for unambiguous sentences in the time window between 382–700 ms after the presentation of the disambiguating word. Furthermore, the comparison with the results from the fMRI experiment for the same contrast (Snijders et al., 2007, see Figure 7) suggests that the area underlying this effect is the LIFG. Indeed this is the area that Hagoort (2005) indicated as the neural substrate of the unification component, where the selection of the relevant alternative and the binding of the single word information into a coherent representation take place.

The temporal evolution of this effect is particularly revealing (Figure 4). In the time window 400–700 ms after the presentation of the disambiguating word, activity is initially restricted to a small region of the left frontal and anterior temporal cortex and it subsequently embraces a larger part of the frontal cortex and of the temporal regions. While the frontal activity is to be related to the LIFG and, functionally, to the selection of the relevant interpretation, the increased ERF amplitude over temporal region likely corresponds to the interaction effect found by Snijders et al. (2007) at the left posterior middle temporal gyrus. The concomitant activation of this area with that of the LIFG in both the MEG and the fMRI experiments confirm the suggestion that the temporal cortex is involved in maintaining online the lexical frames, when these are selected by the unification function.

4.3 Ambiguity in sentences: other perspectives

4.3.1 Reanalysis models

The data of the present experiment can be interpreted on the basis of other syntactic models. The *garden path* model (Frazier, 1987) could offer

an explanation of the ERF results as presented in Figure 3. When encountering the ambiguous word, the parser pursues only one of the two noun/verb readings while the other is set aside. When, however, the first analysis becomes incompatible with subsequent information, reanalysis occurs, indicated by processing costs as longer reading times (Frazier & Rayner, 1982) or, as in our case, larger ERF amplitude after the disambiguating word.

There is, however, some evidence in our experiment that can not be easily explained by the *garden path* model: the increased power in the higher-beta frequency band in the time window of the ambiguous word. In that model and its elaborated variant, the construal model (Frazier & Clifton, 1997), the syntactic structure is constructed following the two principles of minimal attachment and late closure, and it is not affected by the nonpreferred interpretation. Whether or not the effect in the higher-beta frequencies reflects competition, it is clear that the nonpreferred reading does have an influence on the ambiguity processing and this can not be accounted for by the structural principles of the *garden path* model.

A similar reanalysis approach, the *unrestricted race model* (Van Gompel et al., 2000), incorporates competition among syntactic structures, although its explanation is not fully compatible with our results either. In contrast to the *garden path* model, the *unrestricted race model* assumes that “the different analyses of syntactic ambiguity are engaged in a race” and predicts that “when the ambiguity is biased, the construction of [one] analysis is facilitated” (Van Gompel et al., 2005, p. 285). This implication is suggested by the post-hoc test on biasing context effect. The perfectly balanced ambiguous beginnings elicited a larger ERF amplitude at the critical word than the slightly biased context, a facilitation effect due to the bias in the context. Although the unrestricted race model assumes that multiple analyses are constructed in parallel, Van Gompel et al. (2005) insisted that this “does not increase processing difficulty” (p. 285). As a matter of fact, the increased power in the higher-beta frequencies indicates the opposite. Processing difficulties, whether due to competition or not, occur when an ambiguous word is presented.

4.3.2 N400/P600

It remains an open question whether the effect that we observed at the disambiguating word can be related to any of the other EEG language-related components, N400 (Kutas & Hillyard, 1980) or

P600 (Hagoort, Brown, & Groothusen, 1993; Osterhout & Holcomb, 1992). In the ERP literature, the N400 component, an ongoing negativity peaking at ~400 ms after the critical word, is considered to be an index of the difficulty of retrieving stored conceptual knowledge associated with the word, while the P600, a large positivity starting at ~500 ms and lasting for half a second, is usually elicited by syntactic anomalies (Kutas, Van Petten, & Kluender, 2006).

The vast ERP literature on these linguistic components is unfortunately of little help for our data. ERP polarity and scalp topography cannot be compared with the MEG field distribution and the temporal characteristics of the effect we observed (382–700 ms) are compatible with both accounts. In fact, the effect at the disambiguating word is too late and long-lasting to be a typical N400-component and it is too early for being a P600 effect (which has been consistently reported to begin after 500 ms, Coulson, King, & Kutas, 1998). Furthermore, these two components have very close, perhaps partially overlapping, neural generators (Halgren et al., 2002; Service, Helenius, Maury, & Salmelin, 2007) and the spatial resolution of the present MEG experiment is not sufficient to tell them apart. Consequently, it is impossible to reliably relate the effect at the disambiguating word with those language-related components.

4.3.3 ERF at the ambiguous words

The lack of modulation of the ERF amplitude at the ambiguous word is in apparent contradiction with some studies on ambiguity that have reported a modulation of the electrophysiological signal at the ambiguous word (Beretta et al., 2005; Federmeier et al., 2000; Lee & Federmeier, 2006; Pylkkänen, Llinás, & Murphy, 2006; Swaab et al., 2003). However, the first three of these studies exploited noun/noun ambiguity instead of the noun/verb ambiguity we used. Besides, two of them (Beretta et al., 2005; Pylkkänen et al., 2006) included a lexical decision task on the ambiguous words and in Swaab et al. (2003) the ambiguous word, on which the analysis was conducted, was primed on its dominant or subordinate meaning. So, in these three studies, participants became soon aware that the critical manipulation included lexical ambiguity, while hardly any participant from our study, inquired in a postexperiment questionnaire, reported to have noticed the ambiguity manipulation.

In an ERP experiment on noun/verb ambiguity, Federmeier et al. (2000, see also Lee & Federmeier,

2006) showed that ambiguous words, in comparison to their unambiguous counterparts, were associated with a slow frontal negativity beginning at 150 ms and continuing up to 900 ms and suggested that this effect was to ascribe to the resolution of semantic ambiguity. Our experimental data are, however, not comparable to those of Federmeier et al. (2000) and of Lee and Federmeier (2006) because, as explained by the authors, in those studies ambiguity detection and semantic disambiguation were triggered by the same word and occurred in overlapping time window, while in our study they were activated by two separate words.

Nevertheless, our results replicated part of the findings of Federmeier et al. (2000), which reported an enhanced N400 effect for unambiguous nouns in comparison to unambiguous verbs in the time window 250–450 ms. The post-hoc test for unambiguous words in sentence context indicated that nouns elicited a larger response in the 300–500 ms time window than verbs, localized mainly over left temporal regions, as Figure 6 shows. Based on its temporal and spatial characteristics, this effect can be related to the ERF component M350, thought to be the magnetic equivalent of the N400 (Halgren et al., 2002; Pylkkänen & Marantz, 2003).

4.4 Conclusions

The results of the present experiment show that sentences elicit higher sustained activity in the ERF amplitude and in the theta (4–6 Hz), lower-beta (14–18 Hz) and higherbeta (20–22 Hz) frequency bands than word sequences. The comparison between ambiguous and unambiguous sentences indicates enhanced power in the higher-beta frequency band (20–22 Hz) in the time window of the ambiguous word (150–500 ms) and a larger ERF amplitude after the disambiguating word (382–700 ms) than corresponding unambiguous sentences.

Within the framework of the MUC Model (Hagoort, 2005), it has been possible to relate those effects to the syntactic stages involved in sentence comprehension and ambiguity resolution, respectively. In particular, the sustained activity for the sentences is caused by the retrieval and the continuous unification of the lexical frames into a coherent sentential representation. Ambiguity processing within sentences, on the other side, reveals an intricate pattern of activation at the ambiguous word in the form of lexical retrieval and competition and at the disambiguating word in form of selection of the context-relevant interpretation. Competition at the ambiguous word is reflected in

the increased power in the higher-beta frequencies while the selection is associated with the larger ERF amplitude after the disambiguating word and, on the basis of the findings of Snijders et al. (2007), with higher activation in the LIFG.

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Reinvestigation of neuronal synchronization during a contour grouping task

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The problem of how the single elements which are encoded in the early stages of visual processing are grouped together to form a coherent percept, is still a matter of debate. One possible mechanism that has been proposed to solve this ‘binding-problem’ is that neurons which encode features of the same object synchronize their discharges. Another hypothesis suggests that perceptual binding is achieved by modulation of the firing rates rather than by temporal correlation between spikes. A recent study by Roelfsema et al. (2004) provided evidence for the latter view. The authors found that synchrony in the primary visual cortex (V1) of monkeys did not correlate with contour grouping while the covariation of firing rates did. Similar results were obtained for the analysis of selective attention. However, as we will show, the cross-correlation method that was used for the analysis of neuronal synchronization is not optimally suited for the investigation of high-frequency neuronal activity. We therefore reanalyzed the very same data by means of an optimized approach which comprises multitaper spectral analysis and cluster-based randomization testing. Here, we demonstrate that neuronal synchronization in the high-frequency range does correlate with both, perceptual binding and attention. Moreover, due to the experimental design by Roelfsema and colleagues these findings rebut a number of previous objections regarding the role of high-frequency synchrony in visual perception.

Keywords: perceptual binding, selective attention, neuronal synchronization, covariation of firing rates, cross-correlation, multitapering, cluster-based randomization statistics.

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1. Introduction

Synchronization of oscillatory neuronal activity in the gamma-frequency range (30-100 Hz) has been related to many cortical and cognitive functions, such as synaptic plasticity (Buzsaki, 2006), cortico-cortical and cortico-spinal communication (Fries, 2005; Schoffelen et al., 2005), attention (Fries et al., 2001) and has even been proposed to be a neural correlate of consciousness (Crick, 1994).

However, neuronal synchrony in the gamma-band came into the spotlight of debate most prominently when it was proposed as a possible solution for the so called ‘binding-problem’: In early stages of visual processing, every individual neuron captures only a small part of the visual scene. But to analyze the scene as a whole, the local features encoded by individual neurons must be bound together in such a way that they form coherent object representations which can be segregated from one another. How the brain solves this problem is still a matter of debate, but there are two major hypotheses. The binding-by-synchronization hypothesis states that neurons, that encode features which belong to the same object, synchronize their discharges, while neurons that respond to different objects do not (Singer & Gray, 1995; von der Malsburg, 1999; von der Malsburg & Schneider, 1986). Although there is a considerable amount of evidence supporting this idea (Castelo-Branco et al., 2000; Engel et al., 2001; Engel & Singer, 2001; Gray et al., 1989; Woelbern et al., 2002), the binding-by-synchronization hypothesis has also been challenged by studies whose results argue for an alternative hypothesis (Lamme & Spekreijse, 1998; Thiele & Stoner, 2003). This second hypothesis holds that perceptual binding is accomplished by the modulation of firing rates of single neurons, rather than by their temporal synchronization (Lamme et al., 2000; Shadlen & Movshon, 1999).

One recent study favoring this binding-by-rate-modulation hypothesis is by Roelfsema and colleagues (2004). The authors recorded multi-unit activity (MUA) in the primary visual cortex (V1) of three monkeys while the animals were performing a curve-tracing task in which they had to indicate which of two curves was connected to the fixation point (Fig.1). In order to complete this task successfully, all curve segments encoded by the single neurons in V1 have to be bound together into two different objects, one representing the target and the other the distracter curve. This experimental setup distinguishes itself from earlier studies in that the recordings where obtained from awake

behaving monkeys instead of anesthetized animals. Moreover, while the stimuli changed over trials, the content of the single receptive fields (RFs) remained constant (Fig.1). This eliminated the possibility that effects might arise due to varying stimulation of the RFs, rather than reflecting perceptual binding or attention. Roelfsema and his co-workers then compared the activity of neurons when their RFs fell on the same curve with their activity when their RFs fell on different curves. They found that synchrony did not correlate with perceptual binding, while the covariation of the neurons’ firing rates did. Similarly, synchrony between RFs did not depend on whether they were attended (i.e. located on the target curve) or not, while the amount of rate covariation was significantly enhanced by attention. However, it must be noted that the authors used the cross-correlation method to investigate neuronal synchronization (for a description of this method see Challis & Kitney, 1990). Although cross-correlation is a popular and generally reliable method for the analysis of synchrony between signals, it can lack sensitivity with regard to certain properties of neuronal activity in the gamma range. First of all, neuronal activity is generally characterized by power spectra of the form $1/f^\alpha$, where f denotes the frequency and α denotes a variable exponent. This means that the amplitude of the signal component decreases with increasing frequency f (Buzsaki, 2006; McCoy, 1998). Therefore, when two signals are cross-correlated, synchronization of the gamma-components might be obscured by the comparatively large amplitudes of low-frequency activity. While this problem can easily be solved by high-pass filtering the signal, the presence of noise imposes a greater difficulty, especially when the noise has similar or larger amplitude than the signal component of interest. One possible solution would be to smooth the signals before correlating them. But since smoothing in the time domain acts like a low-pass filter it can not be done extensively without loosing the high-frequency components. Another drawback is that cross-correlation – while reliably picking up synchrony at individual frequencies – turns out to be suboptimal for investigating effects that spread out over a broader frequency range but are rather weak at each particular frequency itself.

In view of these method-inherent problems and given that the data in Roelfsema et al. (2004) showed a tendency ($p<0.2$) towards increased synchrony during contour binding, we hypothesized that by using a more optimized approach we might be able to demonstrate that neuronal synchronization does indeed depend on perceptual organization and

selective attention. We therefore reanalyzed the very same data that were used in the study by Roelfsema and colleagues (2004) utilizing frequency-domain methods that are better suited for the analysis of broad-band high-frequency synchronization. The advantage of such spectral analyses over cross-correlation is that they are not biased by amplitude size and mean firing rates (Jarvis & Mitra, 2001). Moreover, by applying multiple orthogonal tapers on the time-series and averaging their respective spectral estimates, the variance can be considerably reduced (McCoy, 1998; Percival & Walden, 1993). This multitaper method also has the benefit that the spectral estimators of a broader frequency-band are concentrated into a single frequency-bin and the spectral analysis becomes optimized to effects that are weak but broad in frequency space (Jarvis & Mitra, 2001). Finally, analysis in the frequency domain allows applying statistical methods that are fitted to the characteristics of neurophysiological data and therefore are more sensitive to neuronal activity than conventional statistical tests (Maris et al., 2007).

2 Methods

2.1 Materials

All data presented here were originally recorded for a study published by Roelfsema et al. (2004) and were kindly made available by the authors.

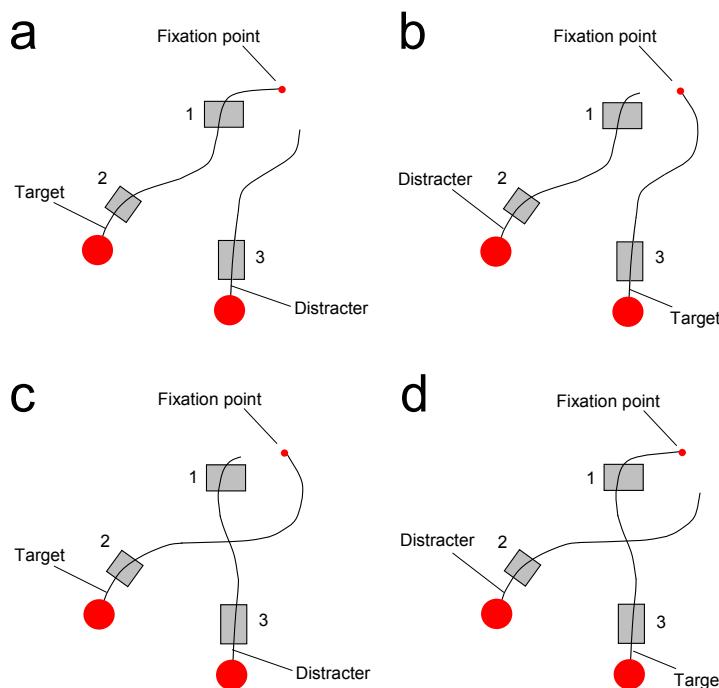


Figure 1. Examples of the four stimulus categories which were presented randomly interleaved during the curve-tracing task: (a) parallel, attended left (PL); (b) parallel, attended right (PR); (c) crossed, attended left (CL) and (d) crossed, attended right (CR). In each trial the monkeys had to indicate which of the two large red circles at the end of the curves was connected to the fixation point. The gray rectangles represent the receptive fields (RFs) of three multi-unit recording sites in primary visual cortex. When the curves cross each other, the grouping changes while the content of the RFs remains fixed.

For the data analyses we used Matlab in combination with FieldTrip, an open source toolbox for neurophysiological data analysis (available from <http://www.ru.nl/fcdonders/fieldtrip/>).

2.2 Experimental procedures

Three macaque monkeys were trained in a curve-tracing task. After the monkeys had successfully learned the task, electrodes were implanted chronically in area V1 in order to record multi-unit-activity (MUA) during task performance. Each of the recorded channels corresponded to a particular receptive field (RF) in the monkeys' visual range.

For details about the recording procedures and materials see Roelfsema et al. (2004).

2.3 Behavioural task

Each trial started as soon as the monkey began fixating within a $1^\circ \times 1^\circ$ window centered on a 0.3° red fixation point. After an initial fixation period of 300 ms, two curves were presented, one of them connecting a red circle to the fixation point (target curve) and the other one also ending in a red circle, but unconnected to the fixation point (distracter curve) (Fig.1). Subsequently the monkey had to maintain fixation for another 600 ms, then the fixation point disappeared and the monkey had to indicate the target by making a saccade to the red circle on the end of the curve in question.

The stimuli used for the task can be subdivided

into four different basic conditions, which were presented randomly interleaved:

- The curves run parallel to each other with the target curve ending on the left circle (PL, Fig.1a).
- The curves run parallel to each other with the target curve ending on the right circle (PR, Fig.1b).
- The curves cross each other with the target curve ending on the left circle (CL, Fig.1c).
- The curves cross each other with the target curve ending on the right circle (CR, Fig.1d).

In the original study by Roelfsema and colleagues (2004) the parallel conditions were further differentiated with respect to the degree of task difficulty, which in turn was determined by the proximity of the target and distracter curves. Since task difficulty was not of interest for the present analysis, the trials within the parallel conditions were collapsed over the different difficulty levels.

2.4 Data selection and preprocessing

For our analysis we selected only those datasets, which contained the four stimulus categories described above (PL, PR, CL and CR) and included those RF-pairs that fell on the same curve in the parallel conditions and on different curves in the crossed conditions, or vice versa (Fig.1). One of the Monkeys was trained exclusively in another version of the task and was therefore excluded from the analysis.

As the rectified channels in the original datasets were recorded at different sampling frequencies (10000/9 Hz and 10000/11 Hz respectively), all data were resampled at a sampling frequency of 900 Hz and converted into a FieldTrip compatible format.

All correct trials were then extracted from the data and cut to an equal length of 800 samples. This corresponds to a signal length of approximately 889 ms per trial, including a pre-stimulus period of 300 ms (270 samples) and a post-stimulus period of about 589 ms (530 samples).

Since we were concerned that different amounts of trials within the conditions (PL, PR, CL, CR) might introduce a bias into the comparisons bound vs. unbound and attended vs. unattended, respectively, we determined the condition with the least number of trials and randomly subselected the same number in the other conditions, thus obtaining an equal amount of trials for all conditions. Datasets that contained less than 50 correct trials per stimulus category were discarded.

To make sure that the RFs did not exhibit synchrony effects caused by physical proximity rather than by functional relation and to obtain an optimal

signal-to-noise ratio, we examined all channels with regard to their response properties. Channel pairs with overlapping RFs were excluded from the analysis, as were channels/RFs that did not show a significant response to stimulus onset. For each RF we also investigated whether they showed similar response amplitudes to the parallel and the crossed stimulus conditions, respectively. Any substantial differences in amplitude between the parallel and the crossed conditions would indicate that the presence (or absence) of any effects is likely to be induced by a different stimulation of the RF, rather than reflecting true attention or binding effects. Therefore all channels that showed such a difference were discarded. In order to test for channel responses and response differences, the average response (over trials) for each channel was computed separately for the crossed (CL and CR) and the parallel conditions (PL and PR). The resulting two sign×ls (Signal_{parallel} and Signal_{crossed}) were then baseline-corrected by subtracting the average value of the pre-stimulus interval and normalized by dividing both signals by the overall maximum response. If the two signals differed more than 40% of the overall maximum response at any point, the channel was excluded from further analysis. This procedure is able to test the channel responses with respect to baseline, to channel noise and to condition related differences at the same time. It is summarized in equation1:

$$\left| \frac{\text{Signal}_{\text{parallel}} - \text{Baseline}}{\text{MaxResponse}} - \frac{\text{Signal}_{\text{crossed}} - \text{Baseline}}{\text{MaxResponse}} \right| < 0.4$$

(Equation 1)

After the data and channel selection, we obtained a total of 63 channel pairs from two monkeys. This is roughly in accordance with the type and amount of data used for the analysis of synchrony in the original experiment (59 channel pairs from two monkeys). However, for the analysis of neuronal synchrony during visual attention, Roelfsema and colleagues (2004) also included datasets in which the monkeys performed other variations of the task resulting in a total number of 143 channel pairs from three monkeys. By contrast, we restricted all our analyses to the datasets that were also used in the investigation of perceptual binding.

2.5 Spectral analysis

To investigate the time courses of power and coherence in the gamma-frequency range (>30 Hz), we computed the respective time-frequency

representations (TFRs) by applying multitapered FFTs on 150 ms data segments sliding in 16.66 ms steps.

Therefore, in intervals of 0.0166 s, each trial was cut into overlapping data segments of 0.15 s length. Subsequently, we analyzed each of the segments using multitapers, which involves the multiplication of the signal with a set of discrete prolate spheroidal sequences (Slepian functions) (Mitra & Pesaran, 1999). As a result, the spectral estimators of a broader and well-defined frequency band are averaged and concentrated into a single frequency bin, thus reducing the variance (McCoy, 1998). In this way the signal-to-noise ratio is enhanced and the power- and coherence estimates become more sensitive to neuronal activity that is spread over a wider frequency range, as it is typical for high-frequency activity. The total amount of spectral smoothing is given by K^*1/T , with K corresponding to the amount of tapers applied and T being the signal length. $1/T$, also known as the Rayleigh frequency, determines the spectral resolution and thus the bin-width in the frequency domain. Accordingly, the application of 5 tapers on each segment resulted in a spectral smoothing of ± 16.66 Hz around the center of each frequency bin.

After the multi-tapering, all segments were Fourier transformed and their power- and cross-spectra were computed according to:

$$S_{xy}(f) = F_x(f) \times F_y(f)^* \quad (\text{Equation 2})$$

where $F_x(f)$ and $F_y(f)$ represent the Fourier-spectra of signal x and y at frequency f , while the asterisk (\cdot^*) denotes the complex conjugate. Accordingly, S_{xy} denotes the cross-spectrum for all $x \neq y$. When $x = y$, S_{xy} becomes S_{xx} or S_{yy} and denotes the powerspectrum of the respective signal. The power- and cross-spectra were then averaged over tapers and the coherence was computed according to:

$$\text{Coh}_{xy} = \frac{| \langle S_{xy} \rangle |}{\sqrt{\langle S_{xx} \rangle \times \langle S_{yy} \rangle}} \quad (\text{Equation 3})$$

where $\langle \cdot \rangle$ denotes the mean across trials.

The analysis of the lower frequencies (8–30 Hz) was performed in a very similar manner as the one for the high-frequencies (>30 Hz), with the exception that we used a longer window (250 ms) to segment the trials and a single hanning-window instead of multi-tapers for the spectral smoothing.

2.6 Stimulus induced changes in power and coherence

For each channel, we investigated the change in power and coherence with respect to stimulus onset according to:

$$\text{PC}\Delta = \frac{(\text{PC-Baseline})}{\text{Baseline}} \times 100 \quad (\text{Equation 4})$$

Where PC represents the power and coherence respectively, $\text{PC}\Delta$ denotes the change of PC with respect to baseline in percent, and Baseline denotes the average Power or Coherence of the pre-stimulus interval.

2.7 Synchrony and perceptual binding

To investigate the role of neuronal synchrony in perceptual binding, we evaluated the coherence of each channel pair when its channels were bound (i.e. their respective RFs fell on the same curve; Fig.1a) and compared it with the coherence of the same pair when its channels were unbound (i.e. the respective RFs fell on different curves; Fig.1c). This can be achieved by taking the difference $\text{Coherence}(\text{bound}) - \text{Coherence}(\text{unbound})$, so that the resulting values will indicate a positive correlation between neuronal synchrony and perceptual binding if they are significantly higher than 0 and a negative correlation if they are significantly lower than 0.

However, the magnitude of the sample coherence depends on the sample size, i.e. the more trials, the smaller the sample coherence, which might introduce a bias to this comparison. Moreover, conventional statistical tests rely on a normal distribution of the spectral estimates of the tapered time series. This property does not apply to coherence estimates, because by definition coherence values are bounded by zero and one and any distributions with a mean close to those values will be skewed. Yet, these problems can be circumvented by computing Z-spectra of coherence differences, which are more normally distributed and corrected for sample size. Another concern was that standard methods that correct for multiple comparisons (e.g. Bonferroni) do so at the expense of sensitivity, especially to effects that occur over a broader time- and frequency range. We therefore applied cluster-based randomization testing, which accounts for the multiple comparisons problem without losing sensitivity and without making assumptions about underlying distributions. A detailed description of the rationale and the

advantages of cluster-based randomization testing of coherence differences is given in Maris et al. (2007).

For the abovementioned reasons, we computed the Z-spectra for the difference in coherence between the bound and the unbound conditions for each frequency bin in each channel pair. The complete formula is given by

$$Z(f) = \frac{(\text{Tanh}^{-1}(x_1)-1/(2nt_1-2))-(\text{Tanh}^{-1}(x_2)-1/(2nt_2-2))}{\sqrt{(1/2nt_1-2)+1/(2nt_2-2)}} \quad (\text{Equation 5})$$

with x_a representing the coherence in condition a, nt representing the number of tapers and Tanh^{-1} being the inverse hyperbolic tangent.

Subsequently the Z-spectra were pooled over all channel pairs corresponding to

$$Z_N = \frac{\sum_{n=1}^N (Z_n)}{\sqrt{N}} \quad (\text{Equation 6})$$

where Z_n denotes the Z-spectrum of channel pair n and N denotes the total number of channel pairs. Accordingly, Z_N represents the difference-spectrum which contains the pooled Z-statistics of the coherence difference between the bound and the unbound conditions for each time-frequency bin.

In order to correct this difference-spectrum for multiple comparisons, we performed a cluster-based non-parametric permutation test. Therefore we selected all time-frequency bins in the spectrum whose pooled coherence Z-statistic exceeded a value of ± 1.96 , which corresponds to a two-sided p-value of 0.05. The selected time-frequency bins were then grouped on the basis of time-frequency adjacency, that is, neighboring bins were combined into a cluster. To evaluate the significance level for each of the observed clusters, the coherence Z-statistics within each cluster were summed and tested against a reference distribution, which we obtained in the following way: For a random subset of channel pairs, the two conditions in equation 5 were exchanged, which is equivalent to swapping the sign of the values in the channel pair's z-spectrum. The spectra of all channel pairs were then again pooled over the total number of pairs and clustered as described above. Repeating this procedure a large number of times produces a distribution of observations under the null-hypotheses and finally, by investigating how many of these random permutations contain a cluster with the same or a higher Z-score than the

ones observed in the actual data, the p-value of the latter can be determined.

A last concern with regard to the binding contrast was that in general there were more channel pairs bound in the parallel stimulus conditions, than in the crossed conditions. Since the target and distracter curves are more difficult to disentangle when they are crossed, as compared to when they run parallel, we were concerned that this imbalance might introduce a difficulty effect which in turn could bias the true binding effect. Consequently, we repeated the same analysis as described above, but this time taking the coherence difference between the parallel and crossed conditions and, in contrast to all our other analyses, selecting those channel pairs ($N=49$), which were bound in all conditions. If this comparison would yield similar effects or tendencies as the binding analysis above, we would have to be concerned that our findings regarding perceptual binding are biased by task difficulty.

2.8 Synchrony and attention

The analysis of neuronal synchrony for attended and unattended stimuli was performed in a very similar manner as the contrast between bound and unbound conditions: For each channel pair we determined the coherence in the conditions when the pair was attended (i.e. both RFs fell on the target curve, Fig.1) and compared it to its coherence when it was non-attended (i.e. both RFs fell on the distracter curve, Fig.1). As was done for the bound-unbound contrast, we then computed the pooled Z-statistics for the difference in coherence between the two conditions (attended – unattended) and performed a cluster-based randomization test in order to test for statistical significance.

3. Results

3.1 Stimulus induced changes in power and coherence

As illustrated in the top panel of Fig.2, the overall power in the high frequencies (30-100 Hz) starts to increase shortly after stimulus onset, reaching its peak at around 120 ms and then decreases again with the activity being most sustained between 50 and 90 Hz.

The time course of the overall coherence (Fig.2 bottom) shows a transient increase around the time of stimulus onset, followed by a general decrease

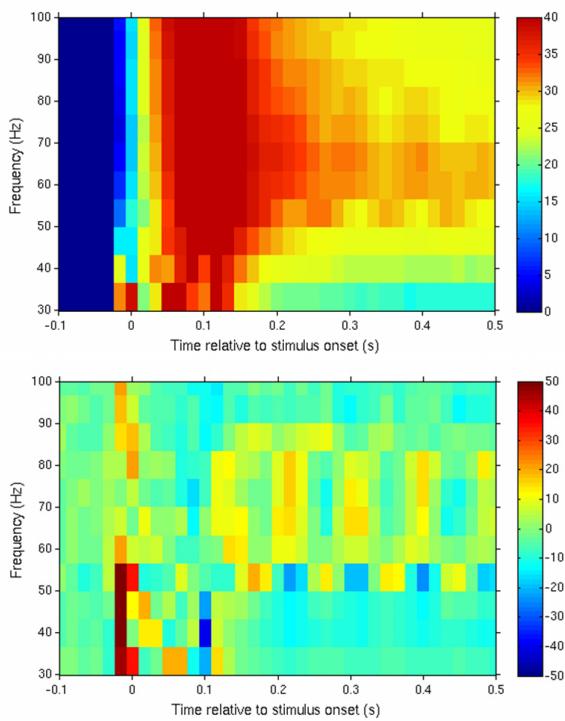


Figure 2. Stimulus locked changes in overall power (top) and coherence (bottom). The colour scale corresponds to the change relative to baseline in percent.

beyond baseline level, which reaches the minimum at around 100 ms. The fact that the transient coherence increase already appears about 20 ms before stimulus onset in the TFR is a result of the time-window length of 150 ms which also picks up coherence changes that occur up to 75 ms later. The same analysis performed on the pre-stimulus interval only (i.e. from -0.3 to 0 s relative to stimulus onset) showed no such effect.

Interestingly, we found in both, the power and the coherence, the values of the frequency band between approximately 55 and 85 Hz to be modulated with a frequency of about 11 Hz. Moreover, the frequencies adjacent to this frequency range (i.e. approx. 50-55 Hz and approx. 85-90 Hz) are also modulated, but with a 180° phase difference. Analyzing the power and the coherence for both monkeys separately revealed that these high frequency modulations are caused by the neuronal activity in only one of the monkeys while the data recorded from the other monkey showed no such modulations.

In the lower frequency range (8-30 Hz) we also observed a stimulus induced increase of power and coherence of about 100 ms to 150 ms length (data not shown). However, after this interval the values return to baseline-level. We therefore conclude that the modulations in the gamma-band are not caused by an increase of low-frequency power or coherence in the time range in which these modulations were observed.

3.2 Synchrony and perceptual binding

Our analysis of the relationship between synchrony and perceptual binding did reveal a significantly higher coherence for channel pairs when their RFs fell on the same curve as compared to conditions when their RFs fell on different curves. This finding suggests – in contrast to the results of the original study – that neuronal synchrony does correlate with perceptual binding.

The effect becomes significant ($p < 0.05$) between about 300 ms and 420 ms and in a frequency range from approximately 35 Hz to 55 Hz (Fig.3 top). Frequencies below 30 Hz did not show any significant effects (data not shown).

As described in the methods section, we were concerned that the binding effect might be biased by a difference in task-difficulty between the parallel and crossed conditions. The check-up analysis that addressed this problem revealed no significant effects. Moreover, in this control analysis, the time-frequency range in which the binding effect had been found, did not show a tendency in either direction. This indicates that task-difficulty does not bias the results of the binding contrast.

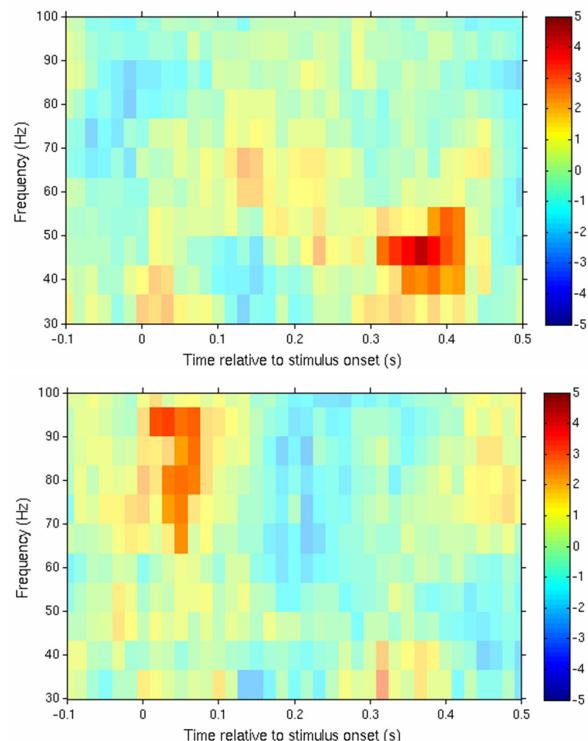


Figure 3. Time-frequency representations of the difference in coherence during perceptual binding (bound – unbound; top) and attention (attended – unattended; bottom). The colour scale corresponds to the z-transformed coherence differences pooled over all channel pairs. The significant time-frequency bins are shown in their original colours, while the colours of the insignificant ones are attenuated by a white 50%-transparency mask.

3.3 Synchrony and attention

The investigation of coherence within attended and unattended channel pairs showed that when attention is directed towards a given pair of RFs, the synchrony between them increases, thus indicating that visual attention correlates with neuronal synchronization in V1.

However, in contrast to perceptual binding, the enhanced synchronization between attended channels becomes significant ($p < 0.05$) earlier in time (10-80 ms) and in a higher frequency range (64-98 Hz). This is shown in Fig.3 (bottom). As in the analysis of synchrony during perceptual binding before, we could not observe any significant effects in the low frequency range.

4. Discussion

Roelfsema and his colleagues showed that firing rate modulation and covariation in area V1 depend on visual attention and perceptual organization. By contrast, their analysis of neuronal synchronization with cross-correlation did not yield any significant results (Roelfsema et al., 2004). However, using spectral analysis techniques optimized for detecting high frequency synchronization we were able to show that neuronal synchrony in area V1 does correlate with both, perceptual binding and attention. This demonstrates that frequency-methods comprising multitapering and cluster-based randomization testing are more sensitive in analyzing neuronal activity in the gamma-range than correlation measures in the time-domain.

The observation of high frequency synchronization correlating with perceptual binding and attention provides valuable evidence for a functional role of gamma-synchrony since the experimental setup of Roelfsema et al (2004) addresses issues that were not accounted for in previous studies. Firstly, the recordings were obtained from awake monkeys during task performance, while earlier studies mostly used anesthetized animals being passively exposed to the stimulus (Eckhorn et al., 1988; Gray et al., 1989; Singer & Gray, 1995). The latter studies were often criticized as their results could not directly be linked to visual awareness because the animals could not report their percept by overt behaviour (Lamme et al., 2000). Secondly, although the stimulus changed over trials, the content of the single RFs was held constant. Thus, the possibility that the observed effects might be due to a varying stimulation of

the RFs, rather than reflecting perceptual binding or attention, can be dismissed. Thirdly, previous work that linked neuronal synchronization to perceptual binding is often based on the use of collinear stimuli (Gray et al., 1989), which means that the line segments stimulating the RFs have the same orientation. On the other hand it is known that horizontal fibers in V1 connect cells with the same orientation tuning more extensively than cells with dissimilar orientation preferences (Gilbert & Wiesel, 1989; Ts'o et al., 1986). Therefore it was hypothesized that synchrony between neurons that are stimulated collinearly might reflect direct anatomical connections, rather than a neural correlate of feature grouping (Lamme et al., 2000). However, given that in the study by Roelfsema and colleagues (2004) most of the line segments falling on different RFs had dissimilar orientations, this objection can be ruled out. Taken as a whole, these features of the experimental design strengthen our findings regarding the correlation between neuronal synchronization and visual awareness and degrade many of the concerns and objections that have been raised in the past.

In view of the results of both, the study by Roelfsema et al. (2004) and the present one, the question of how the binding problem is ultimately solved by the brain remains to be resolved. On the one hand, the findings of the original study suggest that modulation of neuronal spiking frequency is directly related to perceptual binding. Still, the covariation of firing rates, which is put forward as the main argument for this perspective, can only be evaluated across different trials. For this reason, rate covariation cannot reflect a binding mechanism per se, but rather might be the result of binding-by-rate enhancement on a single trial level (Roelfsema et al., 2004). On the other hand, the results presented here clearly show that neurons encoding contours of the same object tend to synchronize their discharges, thus supporting the binding-by-synchronization hypothesis. Nevertheless, a recent study with a very similar paradigm and analysis procedure as the ones used here casts doubt on the generality of neuronal synchrony as a binding mechanism (Palanca & DeAngelis, 2005). Although the authors were able to show that in area MT the gamma-band synchrony in local field potentials (but not between spikes) was significantly enhanced when features were grouped, they concluded that "these changes in gamma band synchrony are small relative to the variability of synchrony across recording sites and do not provide a robust population signal for feature grouping" (Palanca & DeAngelis, 2005). Still, in how

far these results are comparable to our data can not be answered directly, since the data in our study were recorded in area V1 during task performance, whereas Palanca and DeAngelis recorded in area MT during passive stimulus exposure. Furthermore, we did find enhanced temporal correlation between spikes while Palanca and DeAngelis (2005) did not. This might indicate that the synchrony effects we found might be even more pronounced in local field potentials than in the multi-unit activity we analyzed but since our data did not include recordings of local field potentials, this presumption remains hypothetical.

Similar to the findings regarding perceptual binding, our results and the ones of Roelfsema et al. (2004) show that both, neuronal synchrony and the spiking rate are significantly enhanced by visual attention. This is in line with previous research on humans and animals (Bichot & Desimone, 2006; Bichot et al., 2005; Fries et al., 2001; Motter, 1993; Muller et al., 2000; Taylor et al., 2005), but to the best of our knowledge we are the first to show attentional synchrony effects in intracortical V1 recordings of awake animals during task performance.

Altogether these findings raise new questions about the neuronal mechanisms underlying visual perception and how they relate to each other. One study that addresses this kind of problem was recently published by de la Rocha et al. (2007). Investigating cortical neurons in vitro, they were able to show that even when the correlation of the input signals was held constant, the temporal correlation between the output spikes increased with the firing rate. This finding sheds a new light on the relation between the rate and the temporal correlation of spiking activity, suggesting that these two fundamental mechanisms may be linked more tightly than generally assumed. However, even in this light it is not possible to fully explain our findings and in particular the early synchrony effect that goes along with visual attention. This effect becomes significant between approximately 10 and 80 ms after stimulus onset while the firing rates in the attended and unattended conditions do not significantly differ before 200 ms (Roelfsema et al., 2004). Therefore the neuronal synchronization here cannot be a result of increased neuronal firing rates.

Another question that arises from the time courses of the attention and binding effects is how these two effects are related. While the late occurrence of the binding effect is in line with the view that top-down cognitive processes usually do not emerge before 150–300 ms after stimulus onset (Buzsaki, 2006), the earliness of the attention effect is rather surprising. Intuitively, one would assume

that the line segments have to be bound together before attention can be directed towards only one of the two curves. Accordingly the binding-related synchrony should be observed before or at least not later than attentional synchrony. But contrary to this intuition, we found that neuronal synchronization correlating with perceptual binding occurs more than 200 ms after the attentional synchrony effect. Consequently one may conclude that information about affiliations of line segments at this stage could be conveyed by firing rate modulations. But as we pointed out before, the firing rates of neurons in the attended and unattended conditions, respectively, do not start to diverge significantly until 200 ms relative to stimulus onset (Roelfsema et al., 2004). Thus, the possibility that rate modulation serves as a kind of bottom-up binding mechanism must also be dismissed. An alternative explanation could be that attention is directed towards a certain spatial location in which the trace of the target is expected rather than towards the target curve per se. In this case it should be possible to observe even higher attentional synchronization for conditions in which the target and distracter curves are arranged spatially remote and clearly distinct from each other. The investigation of this possibility will require further analysis.

In summary, the results of our study combined with the findings of Roelfsema and colleagues (2004) suggest that both, firing rate modulation and neuronal synchronization are directly related to perceptual binding and visual attention. However, whether the two mechanisms are epiphenomena of the same neural processes or two separate mechanisms that fulfill different aspects of visual perception remains speculative and will have to be answered by future research.

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Preparation of movement direction in the human motor cortex

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Behavioural studies using delayed response paradigms have shown that providing prior information about an upcoming movement shortens reaction times (RTs). Single cell recordings in monkeys have revealed that during such tasks, directional precues induce direction specific encoding in the motor cortex. Here, we used transcranial magnetic stimulation (TMS) to seek neurophysiological evidence of direction encoding in humans. Participants made thumb movements in five directions during a delayed response task in which movement direction was precued. TMS pulses were given during the delay resulting in evoked movements (TEMs) of the thumb. The direction of the TEMs provides a measure of the net excitability for the entire thumb. We hypothesized that the directional precue would modulate the direction of the TEMs during the delay so that the direction of the TEM would correspond to the direction of the precue. Additionally, we measured motor evoked potentials (MEPs) of the abductor pollicis brevis (APB), the first dorsal interosseous (FDI) and the flexor carpi radialis (FCR) to assess corticospinal excitability. We found that participants were faster to respond when there was a delay between the directional cue and the response signal than when there was not, suggesting motor preparation took place during this delay. Contrary to our hypothesis, TEMs moved away from the target during the delay period while MEP amplitudes decreased in all muscles. We take this as evidence that global inhibition at the corticospinal level prevents premature movements during the delay. Since inhibition is stronger in the direction of the target, TEMs move away from the target. During the RT, there was no further modulation of the TEMs. The MEP data showed that excitability of the projections to the APB and FCR returned to baseline, whereas the excitability of the FDI stayed reduced. This might reflect a mechanism called surround inhibition, which aids in the selection of voluntary movements.

Keywords: motor planning, direction encoding, motor cortex, human, TMS

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1. Introduction

1.1 Motor preparation

When people want to make even a simple movement, many parameters of this movement are planned before execution. This is referred to as motor preparation and has been extensively studied using delayed response paradigms. In these paradigms, participants are first presented with a precue that conveys specific information about the movement they are about to make (e.g. with which hand or how far). This precue is then followed by a visual signal indicating that the movement has to be executed. The period between the two signals is called the preparatory delay. If preparation occurs during this delay, it should result in a reduced reaction time (RT) compared to a situation in which participant did not receive prior information. Such reductions in RT are interpreted as indicating that participants are able to use the information they have about a movement to prepare their response before execution.

1.2 Encoding of movement direction in monkeys

There is strong evidence that the reduction in RT observed in delayed response tasks is the result of encoding certain parameters of a movement during a preparatory delay. One of these parameters is movement direction. Single cell recordings in the motor cortex during preparation studies in monkeys (Tanji & Evarts, 1976) revealed that precueing the direction of an upcoming movement differentially evokes preparatory neuronal activity in precentral pyramidal tract neurons that fire preferentially for the direction of the upcoming movement. Also, individual motor cortical neurons behave differently for different movement directions (Georgopoulos et al., 1988). They show a greater increase of firing rate for movements in their preferred direction compared to movements in the non-preferred direction. Furthermore, this preference is already apparent in the preparatory delay of a precueing task, at least 680-720 ms before the onset of any movement (Georgopoulos et al., 1989). These data support the idea that the direction of an upcoming movement can be encoded well in advance of execution.

1.3 Encoding of movement direction in humans

Behavioural studies provided evidence that movement direction is also encoded during a

preparatory delay in humans. For instance, precueing the direction of a required movement reduced the RTs for that movement (Rosenbaum, 1980). Additionally, when participants were restricted in the time they could prepare hand movements to two possible targets, they frequently moved in the wrong direction (Ghez et al., 1997). The proportion of movements in the correct direction increased when the time between the presentation of the cue and the forced movement onset was increased. Importantly, when the correct direction was precued, the number of errors was significantly reduced suggesting that the direction of the movement was planned in the preparatory delay.

1.4 TMS as a tool to study motor preparation

Transcranial Magnetic Stimulation (TMS) is a non-invasive method used to focally excite neurons in the brain. When a TMS pulse is delivered over the motor cortex, motor evoked potentials (MEPs) can be recorded from various muscles. The size of these MEPs is a reflection of corticospinal excitability. Corticospinal excitability has been shown to increase when the probability that a response is required increases (van Elswijk et al., 2007). An increase in corticospinal excitability can be quite selective. In an experiment by Tomberg (1995), participants were required to extend their index finger either alone or simultaneously with the three long fingers. Each of these movements requires the activation of a different extensor muscle. Prior to the movement, corticospinal excitability only increased for muscles specifically involved in the planned movement. Interestingly, corticospinal excitability for the non-involved muscle decreased, suggesting active inhibition of one movement by the other.

Changes in cortical movement representations can also be made visible using TMS. Classen and colleagues (1998) stimulated the motor cortex to induce a twitch in the thumb, termed a TMS evoked movement (TEM). For many participants, the TEM was always in the same direction. Participants then made voluntary movements in the direction opposite to the preferred direction for approximately 20 minutes. Following this training, TEMs were in the trained direction rather than the participants original preferred direction. This change was thought to reflect experience based modulation of motor cortex excitability.

1.5 TMS as a tool to measure direction encoding

Already, some experimental evidence suggests that TMS could be used to examine direction coding in the motor cortex. Sommer et al. (2001) looked more specifically at the encoding of direction during the reaction time. In this experiment, subjects reacted to a cue that indicated whether they should move their thumb downward or to the left. Analysis of TEMs indicated that participant's movements were deflected in the direction of the intended movement. The temporal window in which this effect occurred began no earlier than 214 ms after the go cue. This result clearly demonstrates that TMS can be used to probe directional information coded in the motor cortex during movement planning. However, motor preparation should be seen as a cognitive process that is separate from the actual motor execution in time as well as in neuronal activity. Delayed response paradigms have clearly established behavioural effects on reaction times. And because preparation and execution are separated in time, they are very well suited for probing pure movement preparation (Riehle, 2005). As Sommer and his colleagues did not use a delayed response paradigm, they only investigated the period after the participants had seen the response signal, which could encompass both movement preparation and movement initiation.

1.6 Current study

In this study we sought neurophysiological evidence for coding of movement direction in humans. To achieve this, we combined Sommers' paradigm (Sommer, 2001) with a delayed response paradigm (Rosenbaum, 1980) to study the TEMs of the thumb during the preparatory delay of a precue task. Additionally, we measured MEPs to assess corticospinal excitability.

We hypothesized that in humans, just as in monkeys, precueing the direction of an upcoming thumb movement would lead to a modulation of motor structures during a preparatory delay and that this would result in measurable changes in behaviour, TEMs and MEPs. Specifically, we hypothesized that precueing the direction of an upcoming movement would lead to direction related preparatory activity and therefore to reduced RTs. More importantly, we hypothesized that this preparatory motor activity would influence the direction of TEMs in the delay period between the precue and the go cue. Lastly, we used the pattern of MEP changes in the different muscles to measure facilitatory and inhibitory

changes in cortical excitability during direction-related preparation.

2. Methods

2.1 Participants

16 volunteers participated in the experiment for monetary compensation. The participants (5 male, 11 female) had a mean age of 24.1 (range 20-30 years). All participants were right-handed with a mean Oldfield handedness score of 93.0 (range 60-100) (Oldfield, 1971). All participants had normal or corrected to normal visual acuity and no one was colour-blind. Participants were screened for a history of neurological illness or neurosurgery and for metal or electronic implants. All participants gave written informed consent prior to the start of the experiment. The protocol was approved by the local ethics committee in accordance with the declaration of Helsinki.

2.2 Procedure and Task

2.2.1 Experimental set-up

Participants had to perform two tasks: a precue task and a cue task. In the precue task, the participant received prior information about the direction of the upcoming movement in the form of a red square presented at one of five positions (Figure 1). Direction of TEMs of the thumb measured with accelerometers and size of MEPs of the abductor pollicis brevis (APB) of the right hand, the first dorsal interosseous (FDI) of the right hand and the flexor carpi radialis (FCR) of the right arm were recorded as dependent variables.

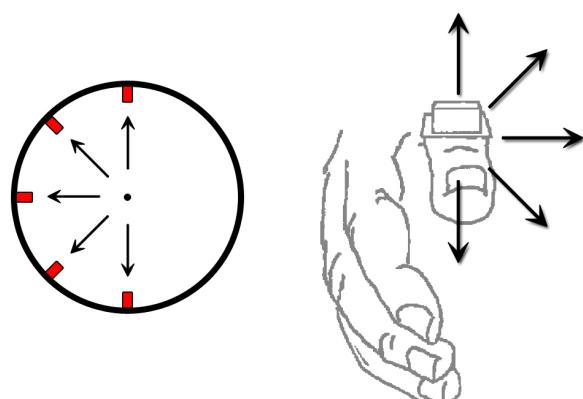


Figure 1. Participants made movements in one of five possible directions indicated by the red marks in the circle on the left. The drawing on the right shows the position of the right hand and the directions of the movements corresponding to the directions on the circle.

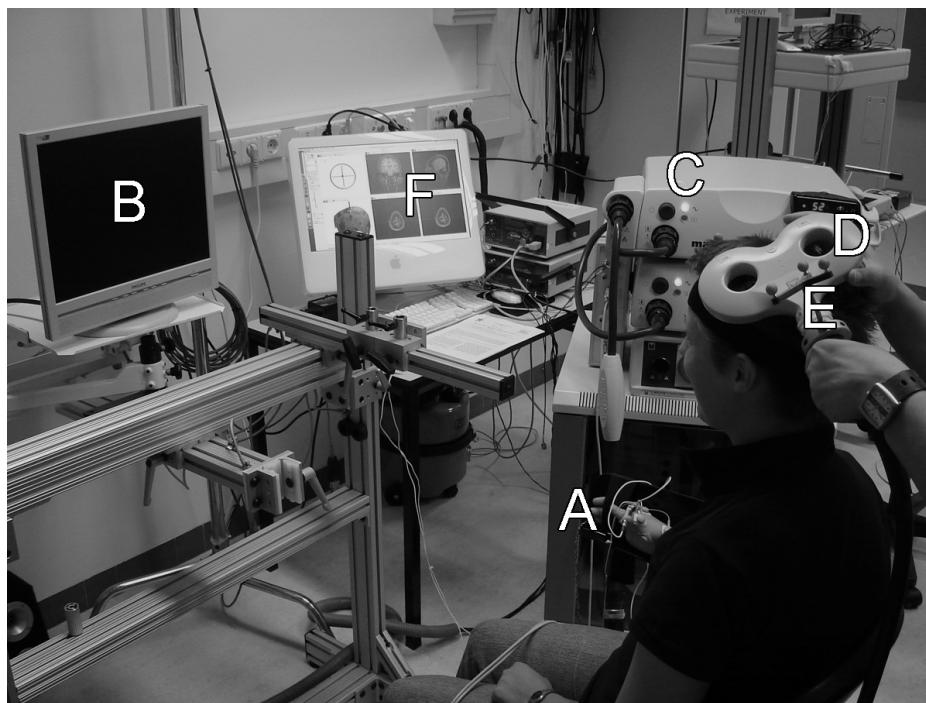


Figure 2. Experimental set-up. A. Arm fixed in semi-pronated position (see Figure 4 for detailed picture), B. Monitor for stimulus presentation, C. TMS stimulator, D. Figure-of-eight coil, E. Trackers to monitor coil position. Similar trackers were placed on the participant's head with a headband (one is just visible on the frontal right side of the head). A camera above the monitor picked up both trackers. F. Brainsight monitor to view the position of the coil in respect to the head.

Participants were seated in a chair in front of a computer screen on which all stimuli (Presentation, Neurobehavioral Systems, Inc., Albany CA) (set up, see Figure 2). To restrict movement as much as possible, the right arm and hand were fixed in a semi-pronated position using a custom-made armrest with two Velcro straps fitted across the underarm and hand (Figure 4). Importantly, participants were able to move their thumb freely to generate the required movements. Participants were instructed to keep their muscles completely relaxed at all times except when making the required movements.

2.3 Cue task

In a cue trial, three successive signals were represented on the circle (Top-right Figure 3). A warning signal (1100 ms) was followed by an arrow (100 ms) which served as the directional cue indicating the required direction of the upcoming movement. Immediately following the directional cue, a response signal indicating that the participant had to make a quick thumb movement in the direction of the cued target (80% green Go-cues) or withhold their movement (20% red No-Go-cues) was presented. Because the response signal followed directly after the directional cue, little or no directional preparation could take place before the response signal was shown. After each trial, the participant received feedback on the

direction of the movement he made or whether he correctly withheld his response. Since data from the cue task were only used to calculate RTs, no TMS was given in these blocks. The task consisted of two blocks of forty trials separated by a short break.

2.4 Precue task

A precue trial (Top-left Figure 3) differed from a cue trial in that the directional cue was provided 500 milliseconds earlier than in the cue task. The latency between the onset of the warning signal and the response signal was 1200 milliseconds in both tasks. Using TMS, direction coding was probed during and following the resulting delay between the directional cue and the response signal. A single TMS pulse was applied in 280 out of the 360 trials. If a magnetic pulse was given, it was at one of four possible time points. Either A) before the directional cue, B) in the middle of preparatory delay, 300 ms before the response signal, C) at the end of the preparatory delay, 100 ms before the response signal, or D) 250 ms after response signal (Bottom Figure 3). Generally, 250 ms after the response signal was well before the RT. If this was not the case, the trial was discarded. Since trials from all conditions are still identical at time point A, it was used as a baseline measure. Forty stimulations occurred at this time-point. Eighty stimulations were given at all

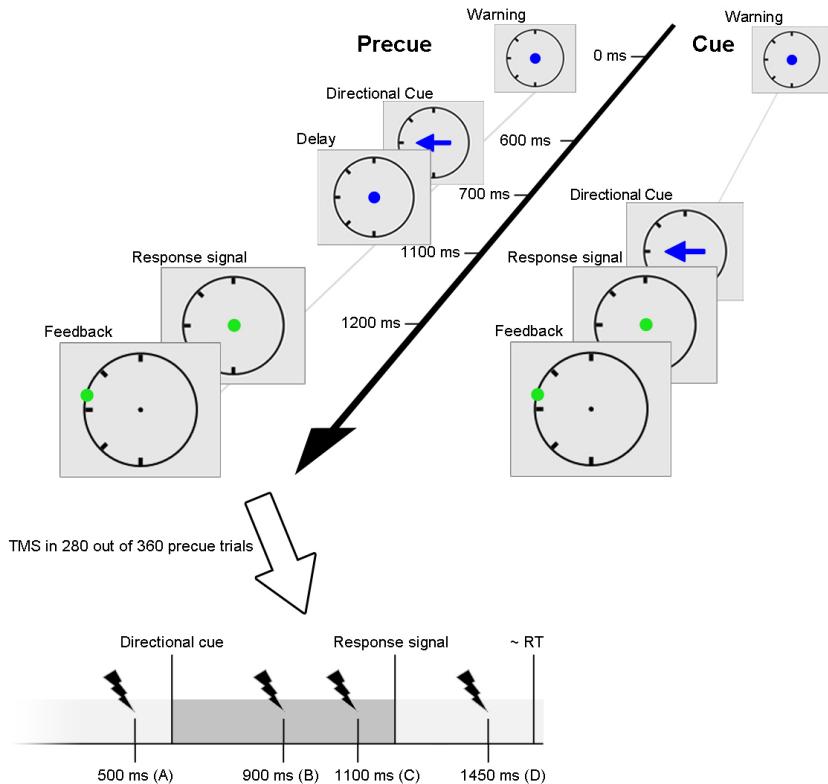


Figure 3. Left: Precue trial. Right: Cue trial. Note that the directional cue in the precue trials was presented 500 ms earlier than in the cue trials resulting in a preparatory delay of 500 ms. A single TMS pulse was given in 280 out of 360 precue trials. The timing of the pulses is shown at the bottom left of the figure. The preparatory delay is indicated in dark grey.

other time points. Feedback was only given on the eighty trials without TMS stimulation because the twitch induced by the TMS pulse prevented accurate feedback on the direction of the following voluntary movement. On TMS trials, “XXX” indicated that no feedback was provided. The task consisted of nine blocks of forty trials. Each block was followed by a short break with a longer break after the fifth block.

2.5 Practice session

One or two days before the test session, participants practiced the required movements and relaxing the muscles in between the movements. Acoustic feedback of the EMG signal from the APB was provided to aid relaxation. First, two blocks of 30 trials in which the targets appeared in predictable order (practice task) were administered. Participants were required to make a thumb movement in the direction of the target as soon as it was cued. Second, participants practiced the precue task in three blocks of 40 trials. There was no TMS in the practice session. Third, the cue task was practiced in three blocks of forty trials. If necessary, extra practice blocks were added to make sure participants were able to make the movements and quickly relax the muscles adequately. After the practice blocks, participants unfamiliar with TMS received a few stimulations to prepare them for the following day and get them familiarized with the sensation.

On the test day, the practice task was repeated (two blocks of thirty trials). Also, the precue task was practiced with the TMS pulses during the trials until the experimenter judged the performance as adequate.

2.6 Thumb movements

Thumb movements were measured with two uni-axial ISOTRON accelerometers (model 256-100 Endevco, San Juan Capistrano, CA) orthogonally mounted in a custom made plastic ring. The ring was placed around the proximal phalanx of the right-hand thumb in such a way that abduction or adduction movements were represented by one accelerometer and flexion or extension movements by the other (Figure 4).

2.7 Transcranial Magnetic Stimulation

TMS was delivered using a figure-of-eight shaped coil (diameter 70 mm) connected to a Magstim BiStim2 stimulator (Magstim Company, Whitland, UK). The coil was positioned tangentially on the left hemiscale with its handle pointing backward at an angle of about 45 degrees from the midsagittal axis (see Figure 2). The optimal position to place the coil was identified using a pulse sufficiently strong to evoke small movements of the thumb. Movement threshold was defined as the lowest stimulator output

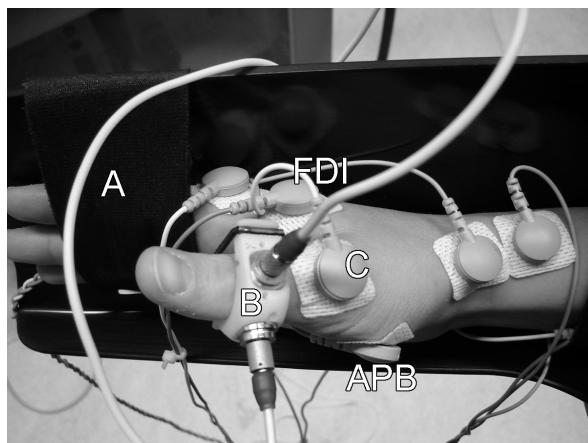


Figure 4. A. The arm was fixed in a custom made armrest with Velcro straps. B. Movements were measured with accelerometers mounted orthogonally in a plastic ring. C. EMG was measured with self-adhesive EMG electrodes. The active electrodes for the APB and FDI are indicated. The electrodes measuring FCR are not visible in the picture.

that evoked movements with an acceleration of at least $0.9 \text{ m}\cdot\text{s}^{-2}$ in at least five out of eight successive stimulations. Stimulation intensity was slightly above this threshold to ensure an evoked response on the majority of the trials. The average stimulation intensity was $49 \pm 10\%$ of the maximum stimulator output. During the experiment, the location of the coil with respect to the participants' head was monitored using Brainsight (Rogue Research, Montreal, Canada) (see Figure 2) and adjusted after every block and whenever the deviation from the optimal stimulation position was larger than 5 millimeters.

2.8 Electromyography

Surface electromyographic activity (EMG) was recorded using 20 mm Ag-AgCl self-adhesive surface electrodes (Kendall-LTP, Chicopee, MA). Electrodes were placed on the APB of the right hand to measure a muscle mainly involved in making the required movements, the FDI of the right hand to measure a hand muscle not or minimally involved in thumb movements and the FCR of the right underarm to measure a not or minimally involved distant muscle (Figure 4). Electrodes were placed in a “belly-tendon” arrangement, following standard skin preparation.

2.9 Acquisition

The acceleration signals and EMG signals were continuously monitored. EMG signals were amplified with a gain of 250 using an EKIDA amplifier (EKIDA, Halmstadt, Germany); acceleration signals were acquired with a gain of 10. Both signals were

anti-aliasing filtered at 1000 Hz and digitized (range $\pm 5\text{V}$, resolution $0.15 \text{ m}\cdot\text{s}^{-2}$ /bit for acceleration and $0.61 \mu\text{V}$ /bit for EMG, sampling rate 5000 samples/s/channel) by a CED Power1401 interface (Cambridge Electronic Design Ltd, Cambridge, UK). Data was recorded on a PC running Spike2 software (Cambridge Electronic Design Ltd, Cambridge, UK).

2.10 Data Processing and Analysis

2.10.1 Pre-processing

Data were processed off-line using MATLAB (The MathWorks Inc., Natick, MA) using the Fieldtrip toolbox ([hwww.ru.nl/fcdonders/fieldtrip](http://www.ru.nl/fcdonders/fieldtrip)). The acceleration and EMG data were cut into epochs beginning 1.2 seconds before the response signal and ending 0.8 seconds after the response signal.

The accelerometer data were lowpass filtered using a standard bidirectional filter with a cut-off at 100 Hz. The EMG data were bandpass filtered using a forward filter between 10 and 500 Hz. Forward filtering was done to prevent leakage from the MEP into the pre-trigger period, which could result in false detection of pre-activation of the muscles. The forward filtering leads to a small phase shift in the data. Since no latencies were calculated on the EMG signal, this shift had no consequences for the results.

2.10.2 Analysis

To determine the movement latency and direction, a peak detection algorithm found the first peak of acceleration in the amplitude of the resultant of the two accelerometer signals (Figure 5). In the TMS-trials, the algorithm was applied to the period following the TMS pulse to find the first peak of acceleration of the TEM. This time point defined the latency of the TEM. In the no-TMS trials, the algorithm was applied to the period following the response signal to find the first peak of acceleration of the voluntary movements. RTs were defined as the time between the response signal and the first peak of acceleration of the voluntary movements. For both the voluntary movements and the TEMs, the angle of the resultant of acceleration signals at the time of the first peak of acceleration was taken as the direction of the movement.

The deviation of the TEM to the target was defined as the difference between the angle of the target and the angle of the movement. All deviations were expressed as an absolute value in degrees.

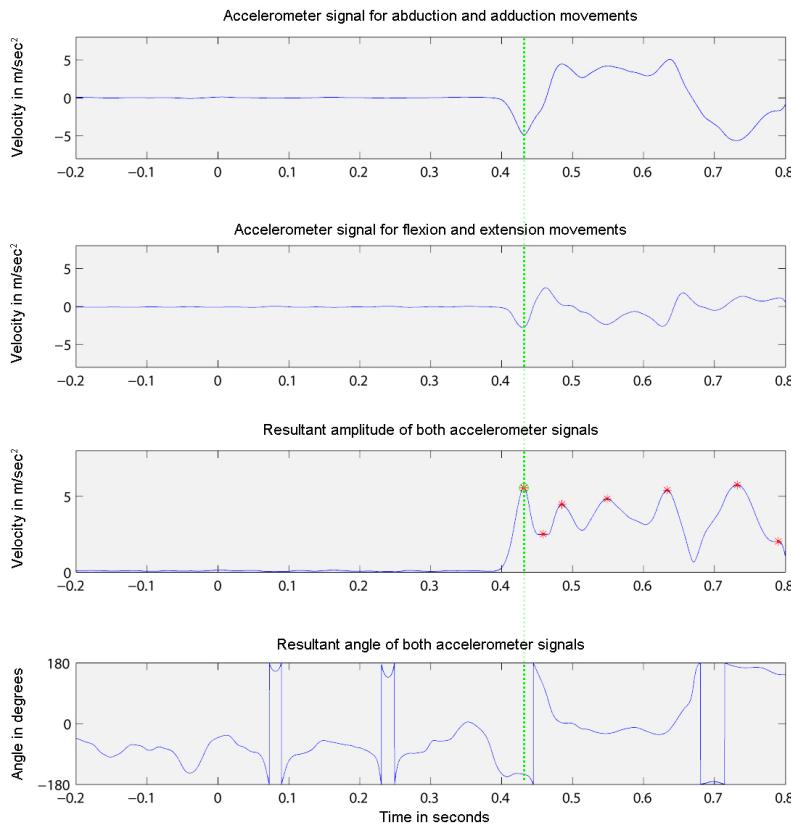


Figure 5. Acceleration signals from two orthogonal accelerometers (top two figures) were combined into a resultant. A peak detection algorithm selected peaks in the amplitude of the resultant (red stars in 3rd figure from top). The green line through the first peak indicates the end of the RT (Response signal was presented at 0 ms). The angle of the resultant at this time (bottom figure) is taken as the movement angle.

Deviation from target could therefore range from 0 (movement exactly on target) to 180 (movement in the exact opposite direction) degrees. The MEP amplitude in the EMG was quantified as the peak-to-peak amplitude of the EMG signals within 10 to 50 ms after the TMS pulse.

2.10.3 Trial rejections

To make sure participants were at rest during the critical period of each trial, a pre-stimulus EMG trace of all measured muscles was inspected. For TMS-trials this critical period was the 100 ms before the TMS pulse. For the no-TMS trials, it was the 100 ms period before the response signal. Trials in which the pre-stimulus EMG of any of the measured muscles had a root mean square value higher than 10 μ V were discarded. Furthermore, TMS trials where the latency of the detected first peak of acceleration deviated more than 10 ms from the mode of the detected peaks were also discarded because they likely reflect voluntary movements rather than TEMs. Lastly, no-TMS trials with RTs that deviated more than 2 SDs from the mean were discarded. This provides a better estimate of the mean RT. Under these strict criteria, a total of 19.3% of all trials were removed.

2.10.4 Statistical testing

To test whether giving prior information about

the direction of an upcoming required movement resulted in shorter reaction times, a repeated measures ANOVA was done with reaction times as the dependent variable and task (cue, precue) as within subjects factor.

Next, to test whether the direction of TEMs changed over the different time points, a repeated measured ANOVA with angular deviation of the thumb movement from the cued direction as the dependent variable was conducted. TMS stimulation time (A, B, C, D, see Figure 3) was entered as a within subjects factor. If main effects were significant, planned comparisons were done in which the angular deviations to the target were compared to those at baseline (time point A). Additionally, the deviations at time point C were compared to those at D. This was done because the time between time point C and D is the transition between preparation and movement execution.

The effect of TMS stimulation time on the MEP amplitudes was first tested in a repeated measured ANOVA with MEP amplitude as the dependent variable and muscle (APB, FDI, FCR) and TMS stimulation time (A, B, C, D) as within subjects factors. If the muscle*time interaction was significant, a separate repeated measures ANOVAs was done for each muscle. The contrasts that were tested were the same as for the deviations. All values reported are mean \pm SE.

3. Results

3.1 Reaction Times

Average reaction times for each direction are shown in Figure 6. Participants responded faster in the precue task than in the cue task ($F(1,15)=10.091$, $p=.006$). The average reaction time in the precue task was 422 ± 23 ms and in the cue task 470 ± 17 ms.

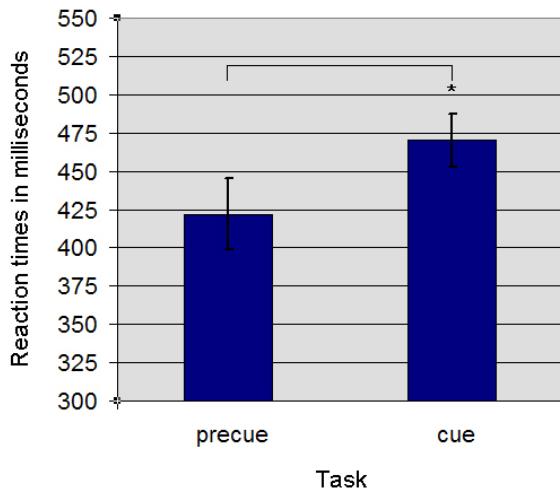


Figure 6. Reaction times were significantly shorter in the precue task than in the cue task. This suggests motor preparation took place in the preparatory delay.

3.2 Direction of movements

3.2.1 Voluntary movements

Participants were able to accurately execute movements in all directions. On average, voluntary movements deviated only 9.8 ± 1.8 degrees from the target (Figure 7) and there was little overlap between voluntary movements in response to the different cues.

3.2.2 TMS trials

Deviations were collapsed across the different cued directions because the number of significant comparisons was negligible considering the number of degrees of freedom when taking the five possible directions into account. The deviations of the TEMs from the target are displayed in Figure 8.

The deviation to the target did change as a function of time ($F(3,13)=4.403$, $p=.024$). Contrary to our hypothesis, the deviation from the target did not decrease during the delay. Rather, the deviation at the end of the delay was larger than the baseline deviation ($F(1,15)=11.355$, $p=.004$). Specifically,

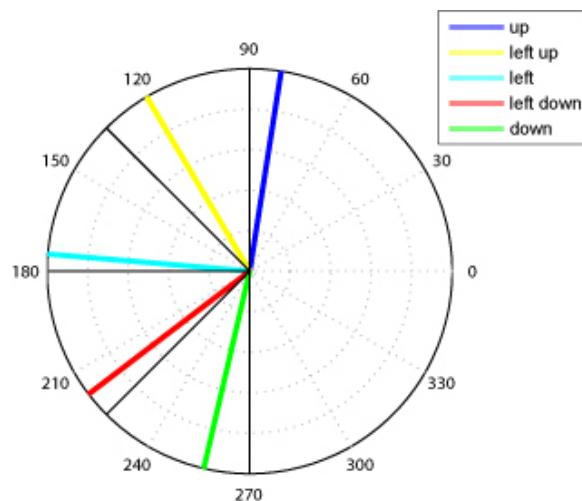


Figure 7. Average movement vectors for voluntary movements in the five different directions. The targets are indicated by the black lines.

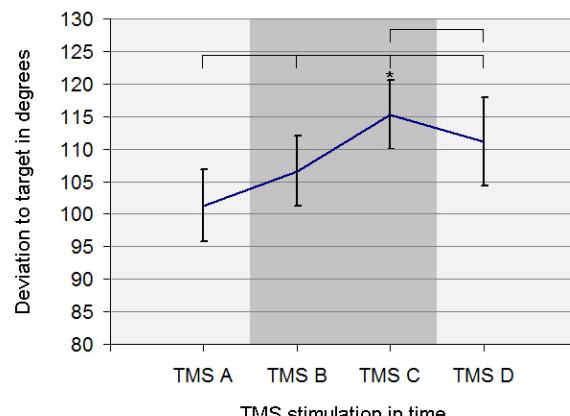


Figure 8. Deviations from target of the TEMs as a function of TMS applied at four different time points. Deviations increased in the preparatory delay (dark grey shaded area) from time point A to time point C. They did not change any further after the go cue.

the deviation from the target at time point C was 115.2 ± 5.3 degrees which was larger than the deviation of 101.3 ± 5.5 degrees recorded at time point A. Deviations at time points B and D were not significantly different from those at time point A (for both, $p>.1$). Also, there was no significant difference between angular deviations recorded at time point C and D ($F(1,15)=0.463$, $p=.507$).

3.3 MEP amplitudes

MEP amplitudes were expressed as a percentage of the mean MEP amplitude over all time points within each muscle. Since the modulations in MEP amplitude over time were not the same for all muscles ($F(6,10)=4.798$, $p=.015$), a separate ANOVA was done for each muscle. All muscles showed an effect

of TMS stimulation time on MEP amplitudes (APB: $F(3,13)=4.063$, $p=.031$, FDI: $F(3,13)=10.785$, $p=.001$, FCR: $F(3,13)=3.835$, $p=.036$).

As can be seen in Figure 9, MEP amplitudes decreased in all muscles during the preparatory delay. For the APB, the decrease of the MEP amplitudes from time point A ($116.0 \pm 7.5\%$) to time point B ($103.7 \pm 4.3\%$) almost reached significance ($F(1,15)=4.294$, $p=.056$). At time point C, MEP amplitudes were significantly smaller ($82.1 \pm 4.7\%$) than at time point A ($F(1,15)=8.977$, $p=.009$). MEP amplitudes in the FDI were smaller than amplitudes at time point A ($126.9 \pm 4.5\%$) at time point B as well as at time point C. At time point B the amplitudes decreased to $110.1 \pm 2.4\%$ ($F(1,15)=21.916$, $p=.000$). At time point C the amplitudes were $90.7 \pm 2.6\%$ ($F(1,15)=34.835$, $p=.000$). There was also a decrease of MEP amplitudes during the preparatory delay in the FCR. Amplitudes at time point B ($100.2 \pm 2.2\%$) and time point C ($92.6 \pm 2.2\%$) were smaller than at time point A ($111.83 \pm 4.5\%$) ($F(1,15)=9.795$, $p=.007$ and $F(1,15)=9.016$, $p=.009$ respectively).

In the RT, MEP amplitudes in the APB ($105.9 \pm 6.1\%$) and the FCR ($100.9 \pm 3.1\%$) showed an increase compared to the end of the preparatory delay ($F(1,15)=7.925$, $p=.013$ and $F(3,13)=3.835$, $p=.036$ respectively). They were not significantly different than baseline ($F(1,15)=0.771$, $p=.394$ and $F(1,15)=2.582$, $p=.129$ respectively). MEP amplitudes in the FDI did not show this increase from the end of the preparatory delay to the RT. MEPs at time point D ($83.0 \pm 3.7\%$) were as large as those at time point C ($F(1,15)=2.791$, $p=.116$) and smaller than those at time point A ($F(1,15)=32.837$, $p<.0001$).

4. Discussion

In this study we used a delayed response task to test for modulation of motor preparation by directional cues in humans. In monkey studies, directional encoding was indeed found during the preparatory delay of a precue task (Tanji & Evarts, 1976). And research done in humans indicates that directional encoding takes place during the response period of a cue task (Sommer, 2001). Here, asked whether directional encoding is also present earlier in a task, i.e. during the preparatory delay. However, we did not find evidence for this hypothesis: TEMs at the end of the preparatory delay were even further away from the target than they were at the time of baseline measurements (Figure 8). At first sight, this might seem inconsistent with the evidence for preparation encoding in monkeys who showed preferentially increased neural activity in response to a precued direction (Tanji & Evarts, 1976). However, we will argue here that the increase in deviation to target at the end of the preparatory delay can be understood in the context of corticospinal inhibition needed to counteract cortical facilitation which prevents premature movements.

4.1 Behavioural results

There was a clear difference between the RTs of both tasks. RTs in the precue task were almost 50 ms shorter than in the cue task. Although participants were instructed to make the required movement as quickly as possible, the RTs for both tasks were quite long compared to those previously reported in similar studies. For example Sommer et al.(2001) reported a mean RT of 304 ms compared to a mean

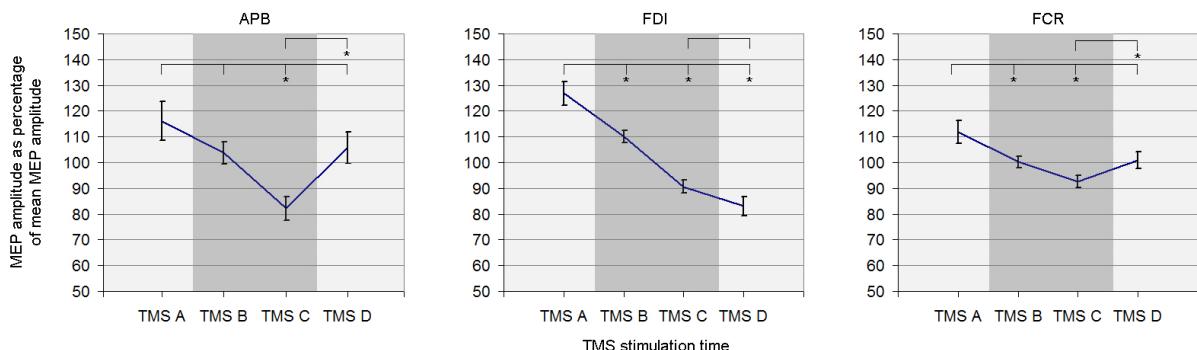


Figure 9. MEP amplitudes as a percentage of the mean MEP amplitude over all time points within each muscle. During the preparatory delay (dark grey shaded areas), MEP amplitudes decreased in all muscles. MEP amplitudes of the APB and FCR increased in the time between the go cue and movement onset while they did not in the FDI. Significant differences compared to time point A are indicated by an * in the bottom comparison. Significant differences between C and D are indicated by an * in the top comparison.

RT of 470 ms in our cue task. One explanation for this discrepancy is that there were five instead of two possible targets in our task. Another possibility is that since participants received visual feedback on the accuracy of movements but not on the speed, they might have focused more on making the movements accurately at the expense of making them quickly. Nevertheless, the fact that participants were 50 ms faster in the precue task than in the cue task is strong evidence that preparation did take place.

4.2 Global inhibition during preparation

During the preparatory delay, MEP amplitudes decreased in all measured muscles (Figure 9). This is in line with several previous studies that found MEP amplitude depression in the period from the warning signal to the go cue of simple RT tasks (Hasbroucq et al., 1997; Touge et al., 1998) and the preparatory delay of a precue task (Hasbroucq et al., 1999). It has been suggested that the decrease of MEP amplitudes can be interpreted as a general inhibition of corticospinal excitability to prevent premature movements (Touge et al., 1998). This notion was further supported by the observation that during a preparatory delay, cervical interneurons in monkeys were inhibited more than they were excited. Modulation was more frequent in interneurons with functional linkage to the muscle than in interneurons without such connectivity (Prut & Fetz, 1999).

In humans, manipulation of the amount of possible time preparation also seems to lead to modulation of cortical facilitation as well as corticospinal inhibition (Davranche et al., 2007). In this experiment, participants were required to produce isometric pressure on a button with both thumbs until a response signal (at a latency of either 2500 or 500 ms) indicated with which thumb a larger isometric press had to be produced. The onset of a response signal was more difficult to estimate the longer the delay with the result being decreased motor preparation and longer RTs. Because there was isometric pressure during the delay, MEPs obtained in the flexor pollicis brevis were followed by a silent period (SP) in the EMG reflecting the recruitment of inhibitory interneurons. With increased preparation, MEP amplitude decreased indicating a decrease in corticospinal excitability. At the same time, the SP became shorter indicating a decrease in inhibition at the cortical level. It is possible that this reduction in corticospinal excitability was necessary to allow for the cortical excitability to increase without resulting in overt movements.

It has been suggested that MEP-amplitudes

decrease are artefacts resulting from the predictability of the TMS pulses (Takei et al., 2005). It is, however, unlikely that our results can be explained by the fact that the pulses were given at four pre-set time points since the modulation of the MEP amplitudes over time was not the same for all muscles. MEP amplitudes in the APB and FCR returned to baseline after the response signal. Stimulation at time point D was just as predictable as at the other time points. Furthermore, reduction in MEP amplitudes was also found in a study where only a few pulses were given at each time point (McMillan et al., 2006), making it unlikely participants could anticipate them.

4.3 Differential disinhibition during RT

After the response signal, the MEP amplitudes of the APB and the FCR increased while the MEPs of the FDI remained suppressed. The selectivity of increased corticospinal excitability fits well with the results by Tomberg and his colleagues (1995) who found increased corticospinal excitability only in the muscle involved in the upcoming movement. Many other studies also report corticospinal excitability of the prime mover increasing to well above baseline just before movement onset (e.g. Davranche et al., 2007; McMillan et al., 2006). In our study, MEP amplitudes returned to, but did not exceed baseline. It is likely that this is because time point D was only at around 60% of the average RT. In another study that looked at the MEP amplitude during the RT of a task where wrist flexions or extensions were precued, MEPs in the FCR returned to baseline after approximately 40% of the average RT. At 100% of the average RT, the MEP amplitude had rapidly increased to about 300% of baseline (McMillan et al., 2004). Corticospinal excitability probably developed in a similar manner in our study.

The FDI had to remain suppressed to ensure a thumb movement without involvement of the index finger. This might have been achieved through a mechanism called surround inhibition. Surround inhibition contributes to the selection of voluntary movements by exerting inhibition on the non-involved muscles. This inhibition is exerted at the supraspinal level and is necessary to counteract the global increase in spinal excitability (Sohn & Hallett, 2004).

Here, Surround inhibition was less pronounced in the FCR although it should be noted that the increase in MEP amplitude from time point C to D was only 9% in the FCR compared to 33% in the APB. This could be because the FCR is further away from the APB than the FDI in effect making

suppression less critical to movement selection. Another possibility is that the co-contraction of the FCR was bigger than that of the FDI. Stinear and Byblow (2003) reported decreased MEP amplitudes of the APB during index finger flexions but only in those participants that could flex their index finger without activating the APB.

4.4 TEMs reflect inhibition

As TEMs can be taken as a measure of the net excitability of all the thumb muscles (McMillan et al., 2006), the movements away from the target during the delay suggest that the net inhibition in the direction of the cued direction was slightly larger than the overall global inhibition found with the MEPs. The fact that a previous study failed to find any evidence for event preparation during a preparatory delay (Hasbroucq et al., 1999) could be because MEPs cannot capture the interplay of all the involved muscles as the TEMs can. At around 60% of the RT, the deviations of the TEMs to the targets were the same as at the end of the preparatory delay. At this time, the MEP amplitudes of the APB had returned to, but not exceeded, baseline. A change of movement direction in the direction of the target can be detected from the time at which increased excitability can be detected (Sommer et al., 2001). It is therefore possible that TEMs did not yet move towards the target at time point D because the corticospinal excitability had not yet exceeded baseline.

4.5 Conclusion

Our data expand the evidence for global corticospinal inhibition during the preparatory delay in cued response paradigms. Inhibition was largest in the direction of the precued movement suggesting that especially premature movements that direction were being prevented. Disinhibition during the RT was most prominent in the movement-related muscle. Inhibition probably has to be fully lifted before TEMs move in the direction of a precued target.

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A neural and behavioural investigation of inter-subject variability in establishing communicative actions

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If established communication systems cannot be used, most people rapidly create novel systems to explain their intentions. However, for this human faculty, significant differences have been found in how quickly two people can create new, shared communicative actions. One hypothesis, explaining this variability, proposes that the capacities of two individuals independently influence the establishment of a communication system. Another hypothesis proposes that the similarities between interacting individuals influence it. In this study, these hypotheses were tested using the Tacit Communication Game in which two persons were engaged in learned and novel communicative actions. The behavioural and neural responses (fMRI) were compared to psychometric tests investigating the cooperative attitude and the fluid intelligence of individuals. The results of this study indicate that the individual abilities, but not the similarities, influence success when establishing communicative actions. The brain structures involved in the intention recognition of novel communicative actions are the right temporoparietal junction and the right superior temporal sulcus. The posterior cingulate and the right and left intraparietal sulcus appear to get more involved when the intentions underlying novel communicative actions become clear.

Keywords: joint action, communication, inter-subject variability, ToM, MNS, functional MRI

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1. Introduction

Translating intentions into meaningful actions is an ability that humans rely on in social situations. This ability developed over generations providing us with communication systems consisting of rules and conventions (Clark, 1997; Millikan, 1984; Millikan, 2004; Tomasello, 1999). Although these developed over long periods of time, if necessary humans can rapidly establish a new functional communication system to explain their intentions. For example, pidgin languages develop in situations of acculturation to enable an efficient communication when societies using different languages have to interact (Kottak, 2002). To rigorously investigate and manipulate the development of such communication systems, people should be in a controlled experimental setting where they have to cooperate, but cannot communicate using conventional systems. Galantucci (2005) developed such a task using a game in which two people, unfamiliar to each other, had to communicate by a graphic medium that disrupts the use of common symbols, in order to achieve a joint goal. De Ruiter and colleagues (2007) used the Tacit Communication Game (TCG) in order to investigate the emergence of a new communication system. In the TCG, two players had to reproduce a spatial configuration of two simple geometric shapes that only one player knew. This player could only communicate to the other about where and how he had to position his shape by means of moving his own token. Both studies showed that most pairs were able to quickly establish a new way to communicate. (Galantucci, 2005; Noordzij et al., 2007; De Ruiter et al., 2007). Galantucci (2005) found that most participants continuously integrated new information with the knowledge that they had already acquired. He also showed there was large inter-subject variation in the ability and the approach used to set up a new communication system. Some participants were able to create an effective communication very rapidly, while others did not seem capable of establishing any sufficient communication system (Galantucci, 2005). This could indicate that some individuals have problems translating intentions into novel understandable actions and vice versa. This raises the question what the personal differences are that lead to the large inter-subject variability found during establishment of a successful communication system. It has been suggested that the large inter-subject variation in successfully setting up a communicative action is related to the cooperative attitude of individuals

(Steels, 2006). However it could also (in part) be explained by their ability to deal with complex spatial problems.

In the current study, the Tacit Communication Game (TCG) was used to investigate the individual differences that influence the establishment of communicative actions. Using this task, we were able to compare a previously established communication system (pre-trained) to a situation in which a new communication system had to be learned (De Ruiter et al., 2007; Noordzij et al., 2007). To investigate the relationship between the variability in this task and ability to establish novel communicative actions, we measured the subjects' cooperative attitudes and their spatial capacities using particular psychometric tests. To measure the subjects' cooperative attitude we tested their empathizing and systemizing abilities (Saxe & Baron-Cohen, 2006) and their affinity for complex thought (Cacioppo et al., 1984). Their spatial capacities were assessed using a fluid intelligence test (Raven, 2000). In addition, the inter-subject variation could correlate with the involvement of different cerebral processes. To investigate this, the participants played the TCG while they were both lying in an MR scanner to obtain behavioural and BOLD data.

Empathy refers to the ability to identify other's feelings and emotions and to respond to these in an appropriate way. The Empathizing Quotient (EQ) can be used to measure empathy (Baron-Cohen & Wheelwright, 2004). Individuals high in systemizing are superior at tasks such as map-reading and mathematics and interpret the behaviour of others as a set of rules that are followed (Baron-Cohen et al., 2005). This can be measured using the Systemizing Quotient Revised (SQ-R) (Wheelwright et al., 2006). It can be suggested that individuals higher in empathizing have a higher cooperative attitude and therefore might be more successful than individuals higher in systemizing in establishing communicative actions. On the other hand, a pair that has similar empathizing or systemizing abilities might be better capable to understand each other, leading to a higher cooperative attitude and an increased performance when establishing communicative actions.

The affinity for complex thought can be measured using the need for cognition scale (NCS). A person should have a good self-regulation in order to gain an appropriate understanding of the intentions within a particular context. This means that he should have vast knowledge and be flexible in the choice of learning strategies, be motivated, and have good control over attention (Evans et al., 2003). It has been suggested that the higher the need for

cognition traits of an individual, the more capable this person is in understanding intentions, because he explores the received information to gain more knowledge about the underlying messages (Cacioppo et al., 1984; Evans et al., 2003). This suggests that individuals high in need for cognition have a higher cooperative attitude, because they have more affinity with thinking about the problem, and might be more successful in establishing novel communication systems.

An individual's fluid intelligence can be investigated using the Raven's progressive matrices. Two components of cognitive capacity are assessed with this measure, the eductive and reproductive abilities. The eductive ability is applied when trying to find meaning in confusion and when dealing with (spatial) complexity. The reproductive ability refers to the capacity to handle and to use information that was made apparent and communicated by another person (Raven, 2000). This could indicate that individuals with a high score on the Raven's test will be better than others when learning communicative actions.

The cerebral processes involved in human intention recognition could be described by two streams within the social neuroscience literature; the Theory of Mind (ToM) and the Mirror Neuron System (MNS). The ToM proposes that humans employ conceptual knowledge to make inferences about the content of another's mental state. The MNS refers to the areas involved in the understanding of actions by means of mapping the actions of others onto our own motor system.

We expect that particular brain regions belonging to the ToM network will show a larger involvement in situations where a communication is learned compared to situations in which an already established communication is applied. These brain areas are the right and left temporoparietal junction (TPJ), right posterior superior temporal sulcus (pSTS) and the posterior cingulate (PC) (Saxe & Powell, 2006; Saxe & Wexler, 2005; Saxe et al., 2004; Gallagher & Frith, 2003). It has been shown that especially the right TPJ, but also the left TPJ and the PC, are active when people try to reason about the thoughts and beliefs of others. These areas are not active when reasoning about other social information, such as individual physical feelings (Saxe & Powell, 2006; Samson et al., 2004). It is suggested that the right TPJ reflects the attribution of thought to another person and the establishment of a coherent model about that persons mind, without any link to the subject's own mental situation (Saxe & Wexler, 2005). Research on autism has shown that these patients, compared

to a normal population, have a lower activation of the TPJ when attributing mental states to animated shapes (Castelli et al., 2002). The superior temporal sulcus (STS) is a brain area that has been found to be involved in the understanding and production of intentional messages. It is suggested that the right pSTS is involved in intentional action representation and in the planning of an (novel) action that has an intentional message for another person (Saxe et al., 2004; Noordzij et al., 2007). Further, it has been proposed that the STS is engaged in action prediction, especially when revising these predictions after a violation (Sebanz et al., 2006).

Areas of the MNS have been shown to be involved in the understanding of intentions and this activity is modulated by cognitive empathy. The mirror neuron areas of the inferior frontal cortex demonstrated a greater activity which was modulated by an emotional empathy measure when watching grasping actions with a context, than when watching grasping actions without context or when watching only the contexts (Iacoboni et al., 2005; Kaplan & Iacoboni, 2006). It has been argued that the MNS in humans is not only an action recognition mechanism, but also supports a simulation-based model of others' intentions while they perform everyday goal-oriented actions (Iacoboni et al., 2005). According to the shared manifold hypothesis of intersubjectivity (Gallese, 2003) the large range of 'mirror matching mechanisms' within the brain enable us to experience others as similar human beings and through that detect similar sensations, actions and emotions in others. The shared manifold enables us to ascribe intentions to and communicate with others through shared cognition and consensus (Gallese, 2003).

The main question of this study was: which aspects of two interacting individuals lead to the successful establishment of a communicative action? According to Galantucci (2005) and Steels (2006) one person can disturb the intention translation and recognition process. This could indicate that the individual abilities of the participants are the most important factors within this process. Gallese (2003) argued that the shared manifold enables us to recognize intentions and communicate successively, because to do this we need to perceive similar sensations and emotions. This indicates that the similarities between the participants could be the most important influence during the establishment of communicative actions. If the capacities of the two interacting individuals independently have an influence, we hypothesize that the performance of a pair on the TCG will be affected by the intention understanding and production abilities of each

person. In this situation we expect that a high score on the EQ, low on the SQ-R, high on the NCS and high on the Raven's test of the Sender and/or the Receiver will lead to an increased score on the TCG. The ToM areas are believed to be involved in making inferences about the context of another's mental state. Following the first hypothesis, individuals with a great capacity to understand intentions and with that to make inferences about another's mental states should have a higher activation at these areas than others when establishing novel communicative actions. If the shared manifold of intersubjectivity applies, we hypothesize that when the pair has comparable scores on the psychometric tests they will have the best performance on the TCG. Following Gallese (2003) and the second hypothesis, the more the psychometric scores and with that the mental states of the participants are alike, the higher the MNS involvement should be in the establishment of novel communicative actions.

2. Materials and methods

2.1 Participants

The 54 participants were male students (18 -27 years), right-handed with normal or corrected to normal vision. We recruited only males to control for gender related influences. By means of emails and flyers, students were invited to complete two questionnaires, the EQ and SQ-R, on an online website. The information provided by the students

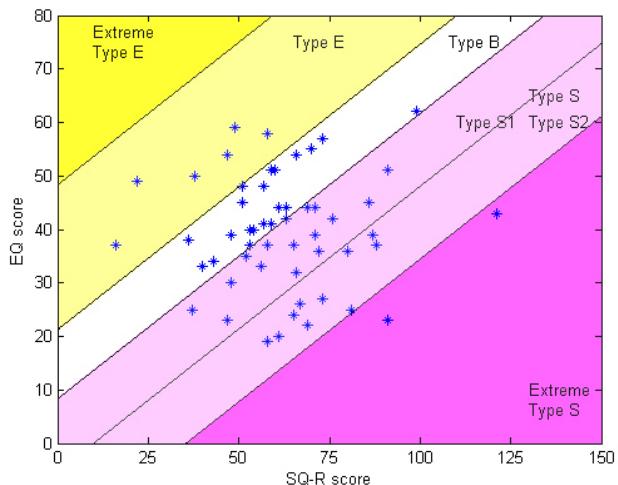


Figure 2. The EQ and SQ-R scores of the participants with the boundaries of the different brain types according to Wheelwright et al. (2006) and one extra boundary that was used in this study. The extra boundary is located exactly in the middle of brain type S and created two groups from brain type S, namely brain type S1 and brain type S2.

at this website was protected according to the Dutch Personal Data Protection act. 285 students filled in the questionnaires at the website. If a student had prior knowledge about the questionnaires, he was excluded from the selection. The participants of the experiment were selected out of the 285 students that responded at the website. The selection was done in order to obtain an appropriate spread over the EQ and SQ-R spectrum and following from that in the subjects' empathizing and systemizing abilities. According to Baron-Cohen (2005), persons that are stronger in empathizing have a type E brain; persons that are stronger in systemizing have a type S brain. People that have equivalent abilities in empathizing and systemizing have a balanced (B) brain (see Figure 1). This can be measured by the EQ and the SQ-R. In addition, persons that are superior in empathizing or systemizing have an extreme form of the type E and type S brain, respectively (Baron-Cohen et al., 2005). The EQ and SQ-R scores of the participants are shown in Figure 2. The participants were quasi-random assigned into 27 pairs, who were partners during the experiment. The purpose of this assignment was to create pairs with all possible combinations of brain types. The subject pairs did not know each other before hand. All participants gave informed consent according to the institutional guidelines of the local ethics committee (CMO region Arnhem-Nijmegen, Netherlands). For participation the students received a financial payment or credits related to a course.

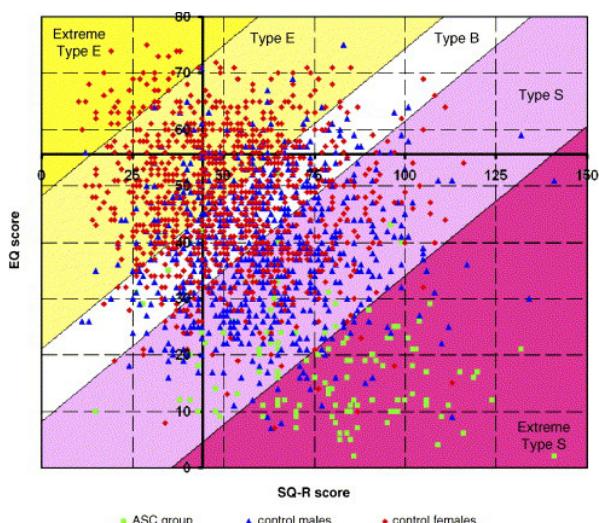


Figure 1. The EQ and SQ-R scores of all the participants of the study by (Wheelwright et al., 2006) with the distinction of the different brain types. Detailed information on the construction of the brain type boundaries can be found in the article of (Wheelwright et al., 2006)

2.2 Questionnaires

Four different kinds of psychometric questionnaires were used during this experiment; the EQ, the SQ-R, the Raven's test and the NCS. The format of the questionnaires was forced choice. Details on the construction of the EQ and SQ-R can be found in (Baron-Cohen & Wheelwright, 2004) and (Wheelwright et al., 2006). The NCS consisted of 18 statements. Details on the construction of the NCS can be found in Cacioppo et al (1984). All three questionnaires were translated to Dutch. The Raven's test consisted of 36 items and the participants had 20 minutes to work on them. With the use of an example item, it was explained to the participants that they needed to find the missing design of a particular sequence of designs.

2.3 Design and materials

The experiment consisted of a training session, an fMRI session, the Raven's test and the NCS in consecutive order. The 30-minutes training session familiarized the participants with the proceedings of the TCG and made sure that they had already learned a communicative rule before they started with the fMRI session. The 50-minute fMRI session included an anatomical scan of ten minutes. During the fMRI session, the participants played the TCG while they were scanned simultaneously. To investigate the establishment of a communicative actions, a situation with the already established communicative rule was compared with a situation in which communicative rule had yet to be established.

2.3.1 Experimental set up

During the training session, the participant-pair sat at opposing sites of a table each facing their own 19-inch computer monitor. The participants could not see each other and were wearing sound-proof head sets to avoid communication. Logitech hand-held controllers were used to move a token over the screen. The four face buttons were used for movements to the left, right, up and down, two shoulder buttons to rotate the token clockwise and counter-clockwise and another shoulder button was used as a start and end button. The game was programmed using Presentation version 10.1 and was run on a Windows XP personal computer.

During the fMRI session each subject lay supine in the bore of the MRI scanner. Head movements were minimized by an adjustable padded head

holder. They could move their token over the screen by means of a MR-compatible hand-held controller. The buttons used were the same as during the training period. The functional images were acquired using a Siemens (Erlangen, Germany) 1.5T and a Siemens (Erlangen, Germany) 3T MRI system. Standard head coils were used for radio frequency transmission and signal reception.

2.3.2 The training session

The training session consisted of an individual training and two trainings in which the participants played together. This session was performed outside the scanner. First, the participants got the individual training to get familiarized with the controller and the basics of the TCG. Second, during the first combined training the participants were introduced to the set-up of the game. Last, the participants were introduced to the communicative aspect of the TCG and they had to establish a communicative rule for a particular set of trials; the easy trials.

During the individual training the participant saw a triangle with a rotation at a certain location on the game board, i.e. nine squares arranged in three rows and three columns. After the participant pressed the start button a triangle that pointed upwards appeared in the center of the game board. The participant had to match this triangle to the location and rotation of the triangle that was shown before. After he made a correct match, a new position was shown. The participant had to complete 40 trials.

During the second training the participants were introduced to the set-up of the game and the principle behind the goal configuration. A participant was either the Sender or the Receiver and he kept this role during the remainder of the game. During this training the participants could both see the so called goal configuration (see Figure 3 #3) at the beginning of the trial. The participants needed to match their own token with the position and orientation indicated by the token of the same shape and colour at the goal configuration. The tokens could have three different shapes; a circle, a triangle or a rectangle. After the Sender pressed his start button the goal configuration disappeared and the Sender could move his token to the desired position. After 5 seconds the Receiver could move his token to the desired position. The pair received feedback on whether they matched their tokens correctly to the goal configuration. The participants received written instructions. They were introduced to the set up of the game and explained that they had to use their tokens to match those of the goal

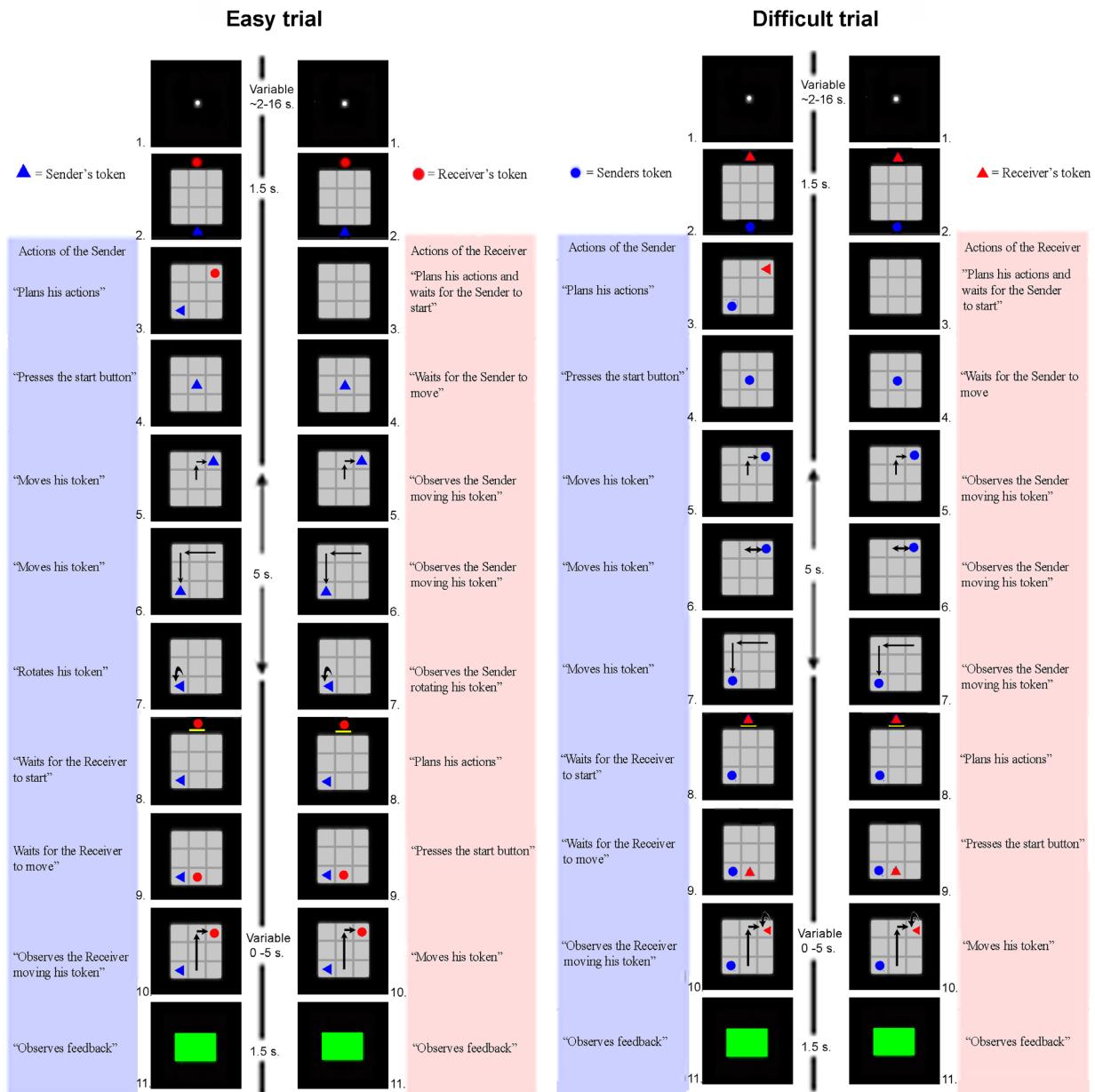


Figure 3. A timeline showing the different steps of the game and the actions of the Sender and the Receiver for the easy and the difficult problem. The Sender saw the images at the left of the timeline and the Receiver those at the right. The Sender's actions are indicated at the left column and the Receiver's actions at the right column. At #2 the game board and the tokens appeared. After 1.5 seconds the subjects saw the goal configuration, which consisted of two tokens inside the game board (#3). The participants had unlimited time to look at the goal configuration, but after the Sender pressed the start button, all tokens disappeared and the Sender's token appeared in the center of the game board (#4). The Sender had five seconds to move his token to the desired position within the game board (#5-7). A yellow bar under the Receiver's token indicated that the five seconds had passed and the Receiver could start to move (#8). The Receiver had unlimited time to think, but when he pressed his start button, his token appeared at a random location on the game board, but not at the goal position of both the Sender's and the Receiver's token (#9). After the first move, the Receiver had 5 seconds to move to the desired position (#10). When the Receiver finished within five seconds, he could end his turn by pressing the start button. The participants received visual feedback about their performance (#11). A green rectangle indicated a correct match with the goal configuration, a red rectangle an incorrect match.

configuration. The Sender was instructed that he should use enough time before pressing start, to make sure that the Receiver knew where to position his token. The pair was told to construct as many good goal configurations as possible and to be within that condition as quick as possible. They were not allowed to look at or speak with the other player

during the game.

During the third training, the participants were introduced to the communicative aspect of the TCG and they established a communicative rule for the easy trials (see Figure 3 easy trial). The set-up was the same as the second part of the training except for one major difference; only the Sender could see the

goal configuration. This meant that the Sender had to communicate to the Receiver what the location of the Receiver's token was and when they both had a triangle, also what the rotation of the Receiver's token was. The Sender could only do this by means of moving his own token around the game board. The participants completed at least 25 trials. If they made a mistake during the last ten trials, they had to complete ten extra trials until they had ten correct trials sequentially. The instructions for this part were also in written form and again different for the two players. The pair was informed about the changes in this training session with respect to the prior session. The Sender was instructed to think carefully about how to move and rotate his token before pressing the start button. It was also emphasized that they should both have their tokens at the correct end position in order to get a good feedback.

2.3.3 The fMRI session

During the fMRI session the pair played a version of the TCG consisting of easy and difficult trials, while the Sender lay in the 3T MRI scanner and the Receiver in the 1.5T MRI scanner. The players received a short written instruction with the most important points of the third training. These points were: only you/the Sender can see the goal configuration, after pressing start you have five seconds to move, press the start button after you finish moving (for the Receiver), the location and rotation of the token need to be correct, try to get as many trials correct and be within that condition as quick as possible. To be able to look at the establishment of new shared communicative actions, it was necessary to compare a situation with an already established communicative rule (the easy problem) with a situation in which communicative rule was yet to be established (the difficult problem) (see Figure 3). The easy trials of this session were comparable to the easy trials of the third part of the training. During the difficult trials the Sender

also had to indicate the location and rotation of the Receiver's token with his own token. Crucially, the shape of the Sender's token contained less rotation possibilities as the shape of the Receiver's token.

The fMRI session contained 84 trials. Half of these trials consisted of the easy problem, and the other half of the difficult problem. Not more than either three easy or three difficult trials were presented sequentially. There were four different shape combinations for the easy and for the difficult trials (see Figure 4). For the easy trials, the presentation of the shape combinations was intermixed. For the difficult trials, the shape combinations were presented in succession. When a pair solved four difficult trials from one shape combination consecutively, it was assumed that the pair had learned a communicative rule for that trial type. This would mean that it was not possible any more to measure the establishment of a communicative rule with that shape combination. Therefore this shape combination was excluded from the presentation. The resulting difficult shape combinations were still presented to the pair in succession. If a pair solved three of the difficult shape combinations, they remained with the final, the fourth, shape combination.

2.4 Behavioural data analyses

Each correctly answered item of the Raven's test counts as one point. For each statement of the NCS a maximum of seven points can be obtained, half of the statements are scored reverse. Each statement of the EQ scores two points if the empathic behaviour is confirmed strongly by the participant and one point if it is confirmed slightly. The control items did not receive points. Each statement of the SQ-R scores two points if the systemizing behaviour is confirmed strongly by the participant and one point if it is confirmed slightly. The points are summed for each test and these count as the score obtained for that test.

The mean accuracy values and the changes of the accuracy values over the trials were both considered as an indicator of the behaviour during the game reflecting the performance of the different pairs. The mean accuracy of each pair was analyzed using repeated-measures ANOVA (threshold, $p < .05$) with the factor problem (easy/difficult). By means of linear regression analyses with as dependent variable mean accuracy over all the pairs for each problem and as independent variable trial numbers, the change over the trials could be investigated. Linear regression analyses were also performed using the log transformed trial numbers ($\log_{10}(\text{trial number})$)

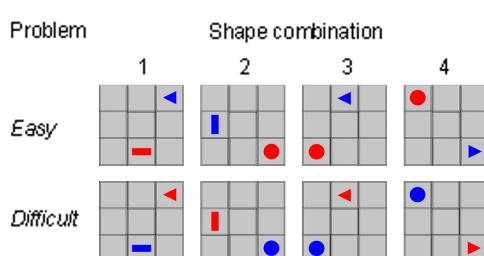


Figure 4. The goal configurations belonging to the different problems and the corresponding shape combinations. The tokens of the players are switched for the problems, but each combination is matched in shape for the easy and the difficult problem.

as independent variable, considering the change over trials as a logarithmic change.

The similarities between the Senders' and the Receivers' mean values of the different psychometric tests were investigated by one-way ANOVA analyses. Bivariate correlation analyses showed the correlations between the four tests.

To investigate the differences in performance between the pairs, the separate psychometric test scores of the Senders and of the Receivers were linked with the mean accuracy scores and with the change over trials of the accuracy values of each pair. By means of linear regression analyses with as dependent variable the moving average of accuracy for each problem and as independent variable the log transformed trial numbers, it was possible to extract the beta values for each pair that indicate the slope of the change over trials. The test scores were compared to those beta values. The mean accuracy scores of each pair were compared to the psychometric test scores by means of linear regression analyses, in which the mean accuracy scores of each problem were the dependent variables and the test scores the independent variables. The independent variables were entered into the linear regression model following a stepwise fashion. This analysis enabled the detection of independent variables that explained a significant (and unique) part of the variance of the dependent variable. If none of the independent variables had an explanatory influence on the variance, no model could be created.

We created absolute "mismatch values" ($\text{Abs}(\text{Sender score} - \text{Receiver score})$) to look at the effect of the combination of the psychometric scores of a pair. These mismatch values were indicators of the similarity of the two individuals that constitute a pair, because the lower the mismatch the more a

pair was alike on that particular psychometric test. These mismatch values were entered as independent variable into a linear regression model. The dependent variables were the mean accuracy and the beta values of the accuracy values over log transformed trial numbers of each pair.

2.5 fMRI data analyses

We focused our fMRI related analyses on the actions of the Receiver, as the activity of the Receiver observed in a previous study using the TCG and investigating similar mechanisms, was much stronger than that of the Sender (Noordzij et al., 2007).

2.5.1 Image acquisition

BOLD sensitive functional images were acquired by means of a single shot gradient EPI sequence using the 1.5T Sonata MRI scanner (TE/TR = 40ms/2.70s, 34 transversal slices, ascending acquisition, voxel size 2.0 x 2.0 x 2.0 mm).

2.5.2 Image analysis

Preprocessing and statistical analysis of the functional data were done using SPM5 (Statistical Parametric Mapping, www.fil.ion.ucl.ac.uk/spm). The image time series were spatially realigned using a sinc interpolation algorithm (Friston, 2003). The time series for each voxel were realigned temporally to acquisition of the first slice. Subsequently, the images were normalized onto a custom Sonata MNI-aligned EPI template (based on 39 brains acquired on the Siemens Sonata at the F.C. Donders Centre). Finally, the normalized images were spatially smoothed using an isotropic 8 mm full-width-at-

Table 1. The seven event types, the corresponding actions that the Receiver observed and performed, and the details for the fMRI model.

Event #	Action	Problem	Duration
1.	Observation planning	All	Variable (from presentation of goal configuration until Sender pressed the start button)
2.	Observation (execution Sender)	Easy	Fixed – 5 seconds (from Sender pressing the start button)
3.	Observation (execution Sender)	Difficult	Fixed – 5 seconds (from Sender pressing the start button)
4.	Planning	All	Variable (from presentation of the yellow bar until the Receiver pressed the start button)
5.	Execution	Easy	Variable (5 seconds, unless the Receiver pressed the start button to end the trial)
6.	Execution	Difficult	Variable (5 seconds, unless the Receiver pressed the start button to end the trial)
7.	Feedback	All	Fixed – 1.5 seconds (from presentation of Feedback stimulus)

half-maximum Gaussian kernel.

The pre-processed fMRI time series were analyzed using an event-related approach in the context of the General Linear Model. Seven event types (see Table 1), based on the behavioural actions as shown in Figure 3, were used to create single subject models. In the model, each event's time series was convolved with a canonical hemodynamic response function and used as a regressor in the analyses. All the event types were modeled as stationary over time, but we modeled event 2, 3, 5 and 6 also as being first order time modulated, meaning that the effect could change linearly over trials. We considered six other regressors, namely the separate covariates describing the head-related movements. Data was high-pass filtered (cut-off 128 s) to remove low frequency confounds, such as scanner drifts. Serial correlations due to biorhythms and unmodelled neuronal activity were accounted for using the autoregressive AR(1) process.

Our main interest was the difference in activity of the Receiver for the Observation (execution) of the easy and the difficult problems, because the Receiver had to try to recognize and understand the intentions of the Sender during the observation period. It was possible to look at this difference by testing for an Observation/Execution x Problem interaction using a full-factorial model treating subjects as a random variable. The degrees of freedom were corrected for nonsphericity at each voxel. From the model, two t-contrasts were created looking at the activity during the observation period with the execution period as baseline, resulting in the easy contrast (event #2 versus event #5) and the difficult contrast (event #3 versus event #6). The difficult contrast was masked exclusively by the easy contrast (Diff(masked by easy) contrast), to retrieve the effects relating to the establishment of a new communication. To make sure that the possible differences were related to positive activations and not to deactivations, the easy contrast was masked exclusively by the difficult contrast (Easy(masked by diff) contrast). Another method to investigate our main interest was based on the differences between the activations of the first order time modulated observation periods of the easy and of the difficult problem using a Paired t-test. For this model, a contrast reflecting the difficult activity was created taking event #3 over time versus event #2 over time (Diff_vs_easy(time) contrast) and another contrast reflecting the Easy activity taking event #2 over time versus event #3 over time (Easy_vs_diff(time) contrast).

Furthermore, to improve the statistical sensitivity of the test, we have evaluated the results of the

contrasts using anatomical information based on published stereotactical coordinates of areas related to the ToM and to the MNS (Friston, 1997). Using this procedure, we created sets of volumes of interests (VOI) with a radius of 10mm. The ToM network was defined according to (Saxe & Wexler, 2005; Saxe et al., 2004), resulting in six VOIs positioned at the left and right TPJ (-48, -69, 21; 54, -54, 24), the left and right pSTS (-54, -42, 9; 54, -42, 9), the mPFC (0, 60, 12), and the posterior cingulate (3, -60, 24). The areas of the MNS were defined on the basis of (Iacoboni et al., 1999), resulting in six VOIs positioned at the left and right inferior frontal gyrus (-51, 12, 14; 51, 12, 14), the left and right superior parietal lobule (-59, -26, 22; 59, -26, 33) and the left and right intraparietal sulcus (-37, -44, 60; 37, -44, 60). We report the results of the contrasts with the application of the VOI's using family-wise error correction ($p < .05$).

The beta value of each voxel was extracted from each significant cluster by means of a VOI time-series extraction. These beta values were imported into SPSS to further analyze them.

To investigate the relation between the BOLD and behavioural data of the TCG, the beta values of the clusters resulting from the analysis using the Diff(masked by easy) and the Diff_vs_easy(time) contrasts were compared to the pair's accuracy measures and the Receiver's planning times using linear regression analyses. When the beta values from the Diff(masked by easy) contrast were the independent variables, the mean values of accuracy and planning time were the dependent variables. When the beta values from the Diff_vs_easy(time) contrast were the independent variables, the beta values resulting from the accuracy and planning time values over time were the dependent variables.

The beta values of the clusters from the Diff(masked by easy) and the Diff_vs_easy(time) contrasts were compared with the psychometric test results. The beta values of the significant variables were compared with the psychometric test scores of the Receivers using linear regression analyses. For the comparisons with a hypothesized directional outcome, a one-way correlation was performed separately to look for an interaction between the beta values and that particular psychometric test without the other tests.

Table 2. Means and SEs of mean Accuracy for the problems.

Problem	Easy	Difficult
Mean (SE)	95 (0.9)	49 (3.5)

3 Results

3.1 Behavioural results

One pair was excluded from analyses because of their poor performance on both easy and difficult trials (79%, 0% correct, respectively), indicating an inability in establishing and maintaining a communicative system.

To investigate performance during the game, the mean accuracy scores from the pairs were analyzed using repeated-measures ANOVA with the factor problem. The change in performance of the pairs during the game was investigated using linear regression analyses with as dependent variable mean accuracy and as independent variable trial number. The ANOVA showed a significant effect of problem, $F(1,25) = 184.4$, $p < .001$, indicating that pairs made more errors for the difficult than the easy problem (see Table 2).

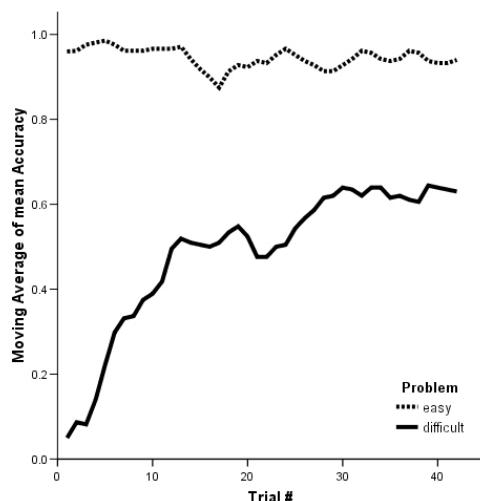


Figure 5. The average learning curves for the different problems.

Figure 5 visualizes the changes in performance during the game. Linear regression analyses investigating the learning effect over time, showed a significant effect for the difficult problem, $F(1,40) = 35.2$, $p < .001$. This seemed to resemble a logarithmic curve. We therefore performed linear regression analyses using the log transformed trial numbers as independent variable. The difficult problem now showed a higher significant change over trials,

Table 3. the Pearson correlations between the different psychometric tests and the extra values.

	NCS		Raven's		EQ		SQ	
	r	p	r	p	r	p	r	p
NCS			.363	.008	-.194	.168	.390	.004
Raven's	.363	.008			-.255	.068	.224	.111
EQ	-.194	.168	-.255	.068			.067	.638
SQ	.390	.004	.224	.111	.067	.638		

$F(1,40) = 51.6$, $p < .001$. This indicated that the logarithmic transformation resulted in a better match of the difficult trials. There was no significant effect for the easy problem.

The ANOVA's investigating the similarity between the psychometric test scores of the Senders and Receivers only showed a significant difference on the NCS, $F(1, 50) = 4.8$, $p = .034$, indicating that the average scores of Senders were higher than those of Receivers. The correlations between the four tests are shown in Table 3.

The pairs had disparate performance during the game. Seven pairs solved all the problems and had a high percent of trials correct for the difficult problem compared to the other pairs. To investigate which psychometric abilities could influences the difference in behaviour, linear regression analyses were performed with as dependent variables the mean and the beta value of accuracy and as independent variables the test scores of each pair. Combinations of the psychometric test scores (mismatch scores) of each pair were also used as independent variables to investigate whether the pair's similarity influenced performance.

The results from the analyses of the mean accuracy with the test scores can be found in Table 4. For the difficult problem, the higher the NCS scores of the Sender and the Raven scores of the Receiver, the higher the mean accuracy score. No model could be created with as independent variables the mismatch values ($\text{Abs}(\text{Sender score} - \text{Receiver score})$). This indicates that there was no influence of the pair's (dis)similarity on their performance.

The improvement of performance during the game based on the beta values of accuracy compared to the psychometric scores showed that the higher the SQ-R scores (systemizing abilities) of the Receiver,

Table 4. Linear regression analyses (stepwise method) with as dependent variable mean accuracy scores of each pair for the problems and as independent variables test scores of the sender and the receiver of each pair.

Dependent variable	Model			
Problem	F	R ²	p	Tests included in model
Easy	No model could be created including the psychometric test scores.			
Difficult	(2,23)= 6.0	.343	.008	NCS (Sender) Raven's (Receiver)
				2.1 .367 .042 3.0 .516 .006

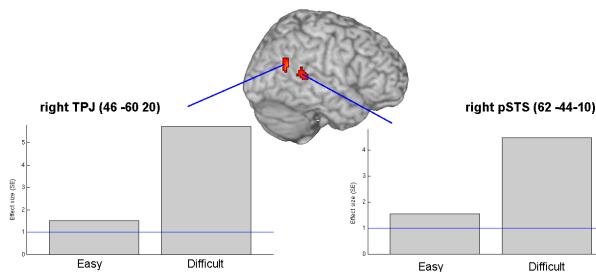


Figure 6. The areas activated by main contrast 1 and their effect sizes.

the more that pair improved their performance on the easy problem, $t(25)= 2.4$, $p= .027$. The higher the Receiver's score on the Raven's test, the greater the performance increase on the difficult problem, $t(25)= 2.1$, $p= .045$. No model could be created for the other analyses. The mismatch psychometric test scores were also used to investigate the change in performance, no significant effects were found.

3.2 fMRI results

One receiver was excluded from the analyses because this subject did not show any activity in the motor-related areas for the execution contrasts.

The resulting activations for the Diff(masked by easy) contrast with the application of the ROI based on the ToM, are one region at the right TPJ, MNI coordinates [46 -60 20], $z= 5.3$, and one region at the right posterior STS, MNI coordinates [62 -44 10], $z= 4.3$ (see Figure 6). No significant activation was found for this contrast using the ROI based on the MNS. No significant activation was found for the Easy(masked by diff) contrast ($p<.05$).

The influence of the Receiver's psychometric scores and the mean values of accuracy and Receiver's planning time on the beta values extracted from the brain areas was investigated. The beta values were extracted separately from the whole cluster at the right TPJ and from a 7mm sphere around the main voxel of the right pSTS by means of a VOI time-series extraction. The amount of voxels used to collect the beta values correspond to the voxels significantly explaining the contrast. There was no linear relation between the activated brain areas and the mean values of accuracy and those of the planning times. No models could be created when comparing the beta values of the Diff(masked by easy) contrast to the psychometric test scores. We performed one-way correlations on the beta values of the right TPJ and the right pSTS for the significant easy and difficult variables with the EQ and the SQ-R. We did not find a significant correlation between the easy variables with the psychometric values. We found a

significant correlation between difficult contrast and EQ, $r= .364$, $p= .037$, at the right TPJ. This meant that the higher the empathizing abilities of a person, the greater the activity of the right TPJ will be when establishing a communicative action.

The resulting activations for the Diff_vs_easy(time) contrast with the application of the ROI based on the ToM, were one cluster at the Posterior Cingulate (PC), MNI coordinates [-8 -68 28], $z= 4.5$, and one cluster at the right TPJ, MNI coordinates [52 -74 28], $z= 4.3$. For this contrast with the application of the ROI based on the MNS two clusters were found, one cluster at the right intraparietal sulcus, MNI coordinates [36 -36 68], $z= 4.4$ and one at the left intraparietal sulcus, MNI coordinates [-44 -36 66], $z= 4.3$ (see Figure 7). No significant activation was found for the Easy_vs_diff(time) contrast.

To investigate whether the psychometric abilities of the Receivers and the beta values based on the moving average of accuracy and Receiver's planning time influenced the significant clusters at those four areas, the same procedures as before were applied. There was no linear relation between the activated brain areas and the beta values based on the moving average of accuracy and those based on the planning times. No models could be created when comparing the beta values of the PC, the right TPJ and the right intraparietal sulcus corresponding to the Diff_vs_easy(time) contrast with the psychometric test scores. For the beta values of the cluster at the left intraparietal sulcus representing the Diff_vs_easy(time) contrast a model could be created with the EQ scores, $t= 2.5$, $p= .018$. They indicate that the higher the Receiver's empathizing abilities the greater the increase of activation at the left intraparietal sulcus over time for the Diff_vs_Easy(time) contrast. Further, we did not find interesting new information when performing one-way correlations on the beta values of the clusters with the EQ, the SQ-R and the d-values.

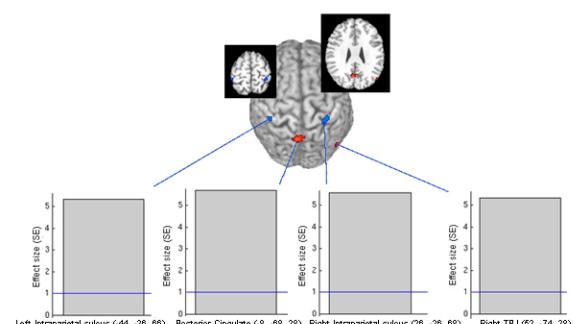


Figure 7. The areas activated by main contrast 3 and their effect sizes. The red areas represent the ToM related activations and the blue areas the MNS related activations.

4. Discussion

The aim of this study was to investigate the personal differences and pair (dis)similarities that lead to the large inter-subject variation found during the emergence of a successful communicative action. We tested two hypotheses proposing that either the individual abilities or the alikeness of the participants have the greatest influence on the success of the novel communication. These hypotheses were investigated with the use of the behavioural performance of pairs on the TCG, the fMRI data of the Receiver collected while the pair was playing, and four psychometric tests. The TCG enabled us to differentiate the establishment of human-to-human communication from the superstructure of conventional signs that normally accompanies it. We could measure the neurophysiological correlates responsible for the recognition of the intentions when establishing a novel communication using the fMRI data. The psychometric test scores, the performance on the game and the related brain activities were compared with each other.

Our main findings are that most pairs can successfully establish novel communicative actions and that this ability is enhanced when the Sender has a high need for cognition and the Receiver has a high fluid intelligence. Furthermore, the right TPJ and the right pSTS are the structures that seem specifically involved in understanding novel communicative actions. When intentional models are starting to form, the posterior cingulate and the right and left intraparietal sulcus get involved in the process. Finally, the empathizing abilities of the Receiver are positively correlated with the activation of the right TPJ during the whole game and of the left intraparietal sulcus over time. In the following parts, we discuss these results and their significance for current models of the human intention recognition faculty.

4.1 The behavioural performance

The behavioural results show that we succeeded in creating a situation in which a pair had to apply an already established communication versus the situation in which a pair had to establish a novel communication system. For the easy problem the pairs had almost all the trials correct. For the difficult trials, the pairs were in the beginning of the experiment not capable of constructing communicative actions that effectively conveyed their intentions. This indicates that they had to establish new communicative actions for these trials. During

the game they showed that they were capable to construct new ways to communicate their intentions and recognize the intentions of the other.

The ability of a pair to establish novel communicative actions seems to be influenced by the Sender's need for cognition and by the Receiver's capacity to deal with complex problems. Research on danger control showed that people high in need for cognition respond with more efficient and useful actions when confronted with information holding secluded consequences. People low in need for cognition require information that is easy to understand and contains a straight forward indication of the best action (Ruiter et al., 2004). This indicates that when the Sender enjoys effortful cognitive activities and has the affinity to engage in those (Cacioppo et al., 1984), he will put more effort into finding a good solution to the problem. Combined with our results this indicates that when the Sender is high in need for cognition, he will be better in translating his intentions into understandable actions. Our results further indicate that when a Receiver has an excellent fluid intelligence (Carpenter et al., 1990), he is good at developing an understanding of the intentions behind the Sender's actions. The primary processes that entail fluid intelligence are being able to find meaning in confusion and to handle information that was communicated by another person (Raven, 2000). To have a high score on the Raven's progressive matrices test, the subject needs to successfully find the missing element belonging to a visual spatial pattern (Raven, 2000). To be successful at the TCG, the Receiver has to discover the Sender's intention underlying a sequence of visual spatial movements. This study suggests that a subject is better able to do this when he is good at seeking patterns and through that unraveling the underlying messages.

For the learning behaviour over trials in relation to the psychometric tests, it is important to remember that this concerns the changes in behaviour and especially for the easy problem, not how well a pair performed during the game. The easy trials showed a positive effect of the Receiver's systemizing abilities on the improvement during the game. This indicates that when the Receiver kept consistently following rules, possibly the ones they established during the training, the better the pair performed on these trials as the game prolonged. For the difficult problem, the Raven's test score of the Receiver had a positive influence on the learning behaviour and therefore on the efficiency when establishing a new communication system. This is in correspondence to the results based on mean accuracy.

4.2 The fMRI data

The two areas involved during the establishment of novel communicative actions (Diff(masked by easy) contrast) over the whole game were the right TPJ and the right pSTS, two ToM areas. This indicates their involvement when learning the intentions behind actions. The areas with increasing activity over time were the ToM related areas, the right TPJ and the PC, and the MNS related areas, the right and left intraparietal sulcus. During the game the participants learned a system to transfer their intentions using novel communicative actions. It has been found that when learning a skill, motor activity related to that skill can increase (Poldrack et al., 1998). Because the participants were learning a skill during the study, this could explain the finding that the observed activity increased over time.

The right pSTS has been associated with the understanding and the production of intentional actions (Noordzij et al., 2007; Saxe et al., 2004). During this study the right pSTS was especially activated in the situations when establishing novel communicative actions. This indicates that this area was actively involved in the representation and understanding of the intentional actions. Because the right pSTS was already involved when the Receiver did not understand the messages, it seems that this area is also involved in the initial consideration of intentions behind actions and the formation of a coherent model about these intentions.

The TPJ combines input from different areas and has connections with the prefrontal cortex and the temporal lobes (Blanke & Arzy, 2005). The right TPJ is involved when reasoning about the thoughts and beliefs of others and in the establishment of a coherent model about another's mind (Saxe & Powell, 2006). In this study the right TPJ was involved when establishing a novel communication and this activation increased when the intention understanding improved. This could also indicate that the right TPJ is the key player in the process of understanding novel actions with certain intentions and in the formation of a coherent model about the intentions behind the actions of the other.

The posterior cingulate cortex is part of the ToM network. This area is believed to be involved in the attribution of thoughts and beliefs to another person, similar to the TPJ, only less strong (Saxe & Powell, 2006). The right and left intraparietal sulcus are part of the mirror neuron network involved in the observation and imitation of actions (Iacoboni et al., 1999). These areas show a larger activation

when actions are learned compared to when they are novel (Calvo-Merino et al., 2005). From this observation it has been suggested that the 'mirror system' incorporates others' actions with the person's own individual motor actions (Calvo-Merino et al., 2005). Combined with the result from this study, these three areas seem to reflect an involvement in the construction of a coherent model of the other's mind, but not until the recognition of the other's intentions has started.

The TPJ seems to be involved in ToM and in empathy related tasks, while the right superior temporal lobe has been found to be more activated in ToM tasks than in empathy related tasks (Vollm et al., 2006). It seems that the STS is not influenced by empathy, what is supported by the results from this study. The right TPJ and the left intraparietal sulcus did show a higher activation when the Receiver had higher empathizing abilities, indicating that persons with higher empathizing abilities more actively use these areas to learn to understand the intentions behind the Sender's actions. This also means that persons with higher empathizing abilities were more actively involved using the right TPJ in establishing a coherent model about the other's intentions.

4.3 The behavioural data, the fMRI data and the hypotheses

The results of this study indicate that the first hypothesis in which the individual abilities of the participants have the greatest influence on the establishment of novel communicative actions is the most applicable. The behavioural data do not supply any evidence for the hypothesis based on the alikeness of the participants within a pair. This hypothesis was based on the shared manifold hypothesis that is supposed to enable us to ascribe intentions to and communicate with others through shared cognition and consensus. To do this we need to perceive similar sensations, actions and emotions (Gallese, 2003). There was no situation in which the same abilities for the Sender and the Receiver led to a better performance. The first hypothesis was supported by the behavioural data. The individual abilities of the participants influenced the pairs' performance on the TCG. We predicted that a pair both high on the EQ, low on the SQ-R, high on the NCS and high on the Raven's test, had the best performance when establishing a novel communication. This was not the case, but there seemed to be a trend into that direction, with measures such as the need for cognition and the Raven's tests dominating their influence.

Furthermore, the first hypothesis emphasizes the involvement of certain ToM areas, because of its association with making inferences about the context of another's mental state. We showed that right TPJ and the right pSTS are the two structures involved in the formation and the updating of ideas about the intentions of the other. The right TPJ seems to be an important player within this process, because its activity increased when the pair learned constructive communicative actions. Because this area is believed to reflect the attribution of thought to another person and the establishment of a coherent model about that persons mind (Saxe & Powell, 2006), its increased activation supports the first hypothesis.

The right and left intraparietal sulcus, areas part of the MNS, became involved over time and are proposed to be related to the processing of recognized actions. These findings therefore do not support our second hypothesis and show that the shared manifold hypothesis of intersubjectivity (Gallese, 2003) is not involved in the establishment of novel communicative actions. First the new communicational messages need to be established and experienced, before people are able to match it to their own thought and beliefs (Proust, 2003). The shared manifold hypothesis can still apply to the understanding of each others intentions behind conventional systems or by a sufficiently transparent action (Decety & Grezes, 2006). This is supported by the increase in activation at the intraparietal sulci when they were improving their understanding of the Senders intentions and the correlation with the empathizing abilities of the Receiver at the left sulcus. Within this study it could be that when a person starts to recognize the actions of the other person and his intentions behind them, the actions get mirrored onto the knowledge about the relationship of those actions.

4.4 Interpretational limitations

The activated brain areas did not correspond with the performance of the pairs or with the planning times of the Receivers when establishing novel communicative actions. The right TPJ and the left intraparietal sulcus correlated with the Receivers' empathizing abilities, while a pairs' performance on the game correlated with the Receiver's capacity to deal with complex problems. This indicates that there must still be another process occurring that was not captured within these analyses. It has been shown that one person is able to disturb the establishment of the communication, but an individual can also lead to a

more sufficient exchange. For these analyses only the Receiver's BOLD data was considered, but it would be interesting to also take the Sender's activation into account and to have a better comparison between the pairs performance and the neural activity.

It is important to remember that the psychometric tests used in this study were chosen because they were believed to match the possible influences on the establishment of novel communicative actions. Part of the communicative success was explained by those measures, but a large portion remained unexplained. Herrmann and colleagues (2007) recently suggested that humans have evolved special social-cognitive abilities in order to perform complex collaborative activities. According to their hypothesis, it is because of those communicative and social learning skills that knowledge within a group can be exchanged and complicated underlying intentions can be understood (Herrmann et al., 2007). This specific faculty could be the foundation for the use and development of effective communications such as language (Levinson, 2006). Our task provides the opportunity to explore these assumptions, because within this study it was possible to rigorously investigate and manipulate the development of such communication systems. Therefore it is interesting to look at the possible influence of other measures, such as a verbal intelligence task, on the establishment of novel communicative actions within the TCG.

4.5 Implications

Sebanz, Bekkering and Knoblich (2006) proposed that the success of joint actions depends on the capacities to share representations, to predict actions, and to combine the expected outcomes of own and others' actions. To be able to establish novel communicative actions a pair had to use all of these features. One of the mechanisms involved in joint action is the incorporation of the 'what' and 'when' behind others' actions into one's personal action planning (Sebanz et al., 2006). Intention recognition is an important aspect of this mechanism, because this is needed to understand the 'what' and 'when'. The behavioural data showed that the individuals' abilities, but not the similarities, influence this process. The Receiver's fMRI data indicates that the ToM area the right TPJ is the key player behind the process of understanding the actions. Further, we showed that the ToM area the right pSTS is involved in the development of novel communication understanding about the 'what' and 'when'. The ToM area PC and the MNS areas left and right

intraparietal cortex get involved when there is some understanding about the ‘what’ and ‘when’.

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Spatial strategies have an impact on the SNARC Effect

Juan Abolafia

Supervisors: Oliver Lindemann & Harold Bekkering

The tendency to respond faster in a parity judgment task with the left hand to relatively small numbers and faster with the right hand to large numbers has been interpreted as an automatic association of spatial and numerical codes (SNARC). The presented study investigates the impact of task demands on spatial numerical processing and the role of cognitive strategies for the SNARC effect. Participants were required to memorize three simultaneously presented digits. The digits ranged from 3 to 7 and described a left-to-right ascending number sequence (e.g., 3-4-5), a descending sequence (e.g., 5-4-3) or disordered sequence (e.g., 5-3-4). After the sequence disappeared, participants indicated the parity status (odd vs. even) of a centrally presented single digit (i.e., 1, 2, 8, or 9) with a left/right keypress response. Each trial ended with a recall of the location of one digit of the sequence. The analysis of response latencies in the parity judgment task showed that SNARC effects were present when participants memorized an ascending or disordered number sequence. Interestingly, however, when representing a descending sequence the SNARC effect disappeared. Our data suggests that spatial biases in number processing can be influenced by task demands indicating that are not deeply rooted in automatic processes.

State and trait markers in depression: an fMRI study on memory encoding and recognition of happy and neutral faces

Henk Cremers

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Major depressive disorder is accompanied by an enhancement of memory recall congruent with a sad mood. A potentially equally important aspect of depression forms a memory bias away from positive information. The current study therefore tested the neural basis of this process. We aimed to detect state and trait markers of mnemonic operations for faces, stimuli that are highly relevant in the pathology of depression. An event-related fMRI design was applied to test memory encoding and recognition memory of happy and neutral faces. Three groups of participants were included: patients with a first episode major depressive disorder (before treatment onset), patients in remission from depression, and matched healthy control participants. To detect state markers, we compared the currently depressed individuals to the patients in remission and control participants. To detect trait markers, we compared the both patient groups to the control participants. The behavioural results showed that there were no differences in memory accuracy and memory bias across the different groups. The fMRI results, however, showed a distinctive pattern of state related activity during memory encoding. The depressed patients showed activity in the bilateral amygdala for memory encoding of happy faces, while the patients in remission and controls showed activity in the dorsolateral prefrontal cortex (DLPFC) for this process. Trait related activity was found in the bilateral orbitofrontal cortex (OFC) during successful recognition memory. That is, the two patient groups showed activity for happy faces, while the controls showed activity for neutral faces in these regions. These results indicate that to maintain a normal behavioural performance, depressed individuals apply different neural pathways during memory encoding and recognition, then healthy controls. Activity in some of the brain regions devoted to these memory processes (amygdala and DLPFC) normalize after successful treatment, while others (OFC) remain active.

Brain-Computer Interface using imagined time-locked handtapping

Jeroen Geuze

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Imagining movement is a commonly used mental task in current Brain-Computer Interface (BCI) research. Most BCI systems based on imagined movement need much calibration and training. Much may be won by defining a movement more clearly and adding rhythmicity, thus introducing a tighter time-lock. In this way, the time-dimension can also be exploited. This study aims to develop a BCI system that uses imagined movement while requiring little or no training for subjects to use it. This has been done by doing a BCI experiment that aims to introduce this timelock to the mental task of imagining movement, and the EEG pattern that arises when rest and movement are alternated. This was done by inducing a tapping tempo that was guided by an auditory stimulus. The goal was to distinguish between imagined left and right hand tapping. Three classification methods were used. The first method, based on Root Mean Square Error (RMSE), had a classification rate between 57% ($p < 0.01$) and 58% ($p < 0.01$) for actual movement, for imagery the results were non-significant. The second classification method was based on a normal distribution and did not give significant classification results in general. The third method was based on Sparse Logistic Regression and had a classification rate between 61.67% ($p < 0.001$) and 67.50% ($p < 0.001$) for actual and between 54.03% ($p < 0.05$) and 65.21% ($p < 0.001$) for imagined movements. Although classification rates are still modest, the short latencies and absence of a training period show this paradigm to deserve further investigation.

Investigating the relationship between the phase of neuronal gamma-band oscillations and reaction times

Iris Grothe

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Previous studies have emphasized the role of neuronal phase relationships in sensory processing by showing that oscillatory synchronization influences synaptic events. Fries et al. (2001) showed that variability in neuronal response onset latencies could be explained by the phase of the transmembrane oscillation preceding response onset *in vivo*. We hypothesized that having to detect a stimulus change at a preference phase of the neuronal oscillation would optimize neuronal processing and would thereby shorten reaction times. Recently, Hoogenboom et al. (2006) were able to design a task in which it was possible to induce strong and reliable visual gamma-band synchronization in human subjects and measure it with MEG. Here, we use the same change detection task to correlate the phase of visually induced gamma-band oscillations to reaction times. This study confirms the findings of Hoogenboom et al. (2006). However, we found no influence of the phase of oscillatory activity on reaction times. As far as we know, we were the first to investigate oscillatory phase by encompassing the entire neuronal processing chain from the stimulus change event to the behavioural response. It is likely that the statistical tests lost sensitivity because we had considerable variability in the data due to the multiple neuronal processing levels and because we had to perform a broad-band phase analysis. However, we should also consider the possibility that the hypothesis is not correct. Since this study is not conclusive about the hypothesis yet, we would recommend additional investigations.

A Bayesian approach to modelling spatial orientation during roll rotation

Maarten van der Heijden

Supervisors: Rens Vingerhoets, Jan van Gisbergen & Pieter Medendorp

Spatial orientation in darkness relies mostly on information from the semicircular canals and the otoliths. The canals sense angular orientation and the otoliths can detect both tilt and linear acceleration caused by translation. One hypothesis on how the inherently ambiguous otolith signal can be interpreted is the canal-otolith interaction model. This model has recently been reformulated in a Bayesian framework by Laurens and Droulez (2007). We have explored whether an extended version of this model can account for body tilt and for visual-verticality perception during roll rotation. In separate experiments, we tested five subjects on their ability to estimate subjective body tilt (SBT) and the subjective visual vertical (SVV) during constant velocity roll rotation. In addition we measured the SVV under static conditions. Subjects performed relatively well in the SBT task, showing random errors but no systematic bias. In the SVV tasks all subjects made large systematic errors that could be classified in two response modes consistent with A-effects and E-effects

reported in the literature. Model simulations showed that the SBT data could be reproduced quite well with the original Bayesian model. After extension with a tilt prior, the model could account for the static SVV data as well. When the same model was applied to the dynamic SVV data, it could partially fit the A-effects but not the E-effects. In conclusion, the model can explain certain aspects of spatial orientation. However, with regard to the dynamic SVV, refinement of the model is necessary, whether this can be achieved by adjusting the set of model parameters remains a subject for further investigation.

Action co-representation: Your action is my command

Birgit Knudsen

Supervisor: Harold Bekkering

In two experiments we examined the action co-representation preconditions of jointly acting partners. The question addressed here is, if a slowing in reaction times of jointly acting partners is due to the fact that participants perform different actions (action conflict) or if it is due to the fact that participants respond according to different task rules (task rule conflict). In experiment 1 the dyads had the same task rules but different action alternatives. In experiment 2 the dyads had different task rules but the same action alternative. In experiment 1 we found impaired reaction times which we attributed to a conflict at the action level. Therefore, in Experiment 2 we investigated if a slowing in reaction times would still remain, when for both the participants only one action alternative would be available. The reduction in possible actions indeed diminished the slowing in response times, indicating a co-representation on the action level to be the underlying mechanism of slow response times in jointly acting partners.

Syntactic modulation of beta and theta rhythm in online sentence processing

Lilla Magyari

Supervisor: Marcel Bastiaansen

The aim of the present study was to explore the oscillatory brain dynamics related to syntactic processing during language comprehension. A time-frequency (TF) analysis of power changes was performed on magneto-encephalographic (MEG) data. Subjects had to read Dutch sentences in three experimental conditions: correct sentences, sentences containing moderate syntactic violations (word-category violations, where a noun was replaced by the corresponding verb, e.g. hunter → hunt) and series of words without syntactic structure (the same words as in the correct sentences, but now in random order). A statistical evaluation of the TF data (based on random permutation testing (Maris, Oostenveld, 200&)), revealed power differences between correct sentences and violated sentences in the theta (here roughly 3-9 Hz), in the lower beta (13-18 Hz) and in higher (above 20 Hz) frequency ranges. The theta power differences were concentrated over right centro-parietal areas, whereas the beta power differences were present over midfrontal, right parietal and left parietal areas. For the beta frequency range, the condition differences were produced by a linear increase in power over the correct sentences, which increase was not present in the word-category violation and in the random word order conditions. The beta power changes modulated by the syntactic structure distortion suggests that beta oscillations are involved in normal syntactic processing. Based on the present results and on previous studies, theta power changes can be related to the building up of a working memory trace of the language input.

Monitoring in sentence perception: Mild and strong conflicts elicit different ERP patterns

Nan van de Meerendonk

Supervisors: Herman Kolk, Constance Vissers & Dorothee Chwilla

The N400 effect is commonly thought to reflect semantic integration difficulties. No common view exists among researchers about what the P600 effect reflects. Several researchers have proposed the P600 effect reflects syntactic (re)processing, since P600 effects have been found after various syntactic violations, garden-path sentences and sentences with a relatively complex structure. However, recent studies found a P600 effect to semantic and orthographic anomalies. According to the monitoring theory the P600 reflects

a more general process of reprocessing: a monitoring process to check for possible processing errors. This monitoring process is triggered when the brain encounters a highly unexpected linguistic event that is in conflict with a highly expected linguistic event. An important question then is why typical N400 sentences like "He spread the warm bread with socks" elicit an N400 effect and not a P600 effect? We propose that there are two 'levels' of unexpectedness, which, influenced by plausibility, can give rise to two different reactions. When a critical noun is of medium plausibility in the given context, a mild conflict arises between the expected and unexpected linguistic event; the language system can still interpret the unexpected event and a monophasic N400 effect is elicited due to integration difficulties. When a critical noun is of low plausibility however, a strong conflict arises; the language system starts integrating the unexpected event but fails and a monitoring process is triggered, eliciting a biphasic N400-P600 pattern. In the present ERP study this was investigated by presenting subjects with sentences of which the critical noun could be of low, medium or high plausibility. The medium plausibility condition (e.g., "Herbs like chive, basil and mustard ...") indeed elicited a monophasic N400 effect, while the low plausibility condition (e.g., "Herbs like chive, basil and report ...") elicited a biphasic N400-P600 pattern. In support of the monitoring theory, these results show the P600 reflects a more general process of reprocessing. However, only when the conflict between the expected and unexpected linguistic event is strong enough, a monitoring process is triggered.

The influence of dietary lipids on cognition, cerebral blood volume and amyloid pathology in the APP/PS1 mouse model of Alzheimer's Disease

Yael Reijmer

Supervisors: AJ Kilian & CR Hooijmans

High serum cholesterol and low DHA intake are risk factors for Alzheimer's disease (AD). However, how these parameters influence the pathology is still a topic of debate. The present study assessed the influence of a cholesterol (typical western diet: TWD) and a DHA containing diet on spatial memory, amyloid beta ($A\beta$) deposition and relative cerebral blood volume (rCBV) in a 15-month-old APP/PS1 mouse model of Alzheimer's disease and wildtype littermates. rCBV was determined by contrast enhanced MRI and $A\beta$ deposition by using immunohistochemistry.

APP/PS1 mice showed impaired spatial learning and memory in the Morris Water Maze test. Furthermore, transgenic mice showed a decrease in cortical rCBV. The cholesterol enriched TWD diet decreased the rCBV in the cortex compared to a standard diet in both APP/PS1 and control mice without affecting $A\beta$ deposition. APP/PS1 mice on a DHA diet showed a decrease in vascular $A\beta$ deposition and improved memory performance. In conclusion, these results show disease relevant behavioural and cognitive changes in an APP/PS1 mouse model accompanied by a decrease in rCBV. This study further indicates an important role for dietary lipids in the development of Alzheimer's disease by influencing the rCBV and vascular $A\beta$.

The cognitive capacities of the dopamine D1 mutant rat

Ji un Youn

Supervisors: Gerard Martens & Bart Ellenbroek

The importance of dopamine as a neurotransmitter has been studied extensively. However, the selective role of dopamine D1 receptor (D1) in cognition is yet to be clarified. The rat model with a D1 mutation offers an intriguing possibility which the pharmacological model can not provide due to the lack of selective D1 (ant)agonists.

In the present study, the mutant rats were tested with a battery of cognitive tests. Despite the absence of any gross impairment in locomotor activity, the animals showed deficits in most of the spatial memory tasks replicating the previous studies with D1/D5 antagonists. This impairment was most pronounced in cognitively more demanding tasks such as the response based (egocentric) Morris Water Maze test.

However, the results from non spatial memory tasks (object recognition, passive avoidance) revealed no major deficit in the D1 mutant rats. The mutant animals could discriminate novel object as well as the controls did. Moreover, they showed superior performance in passive avoidance test. It can be speculated that either the tests involve memory functions which are not D1 dependent or they failed to challenge the D1 related cognitive function strongly enough. This question can only be answered when more tests which require a higher level of cognitive capacities (such as set shifting) are performed along with molecular work, which will elucidate the possible compensatory mechanism underlying the D1 mutation in the current study.

**Syntactic priming in German-English bilinguals during sentence comprehension:
RT and fMRI studies**

Kirsten Weber
Supervisor: Peter Indefrey

During reading we have to process the syntactic structure of the sentences in front of us. Thus, if we process sentences in two different languages, for example German and English, do we access and use the same syntactic information for both languages if the structures are similar? In this study we show that on the neural level sentences in the first and in the second language (L1 and L2) are processed in the same neural areas in left inferior frontal and left temporal regions indicating a shared sentence processing system. Moreover, we used a syntactic priming paradigm in comprehension to establish interaction between the L1 and L2. We find behavioural evidence of syntactic priming in comprehension within the L2 as well as a possible word-order effect from L2 into L1. At the neural level we were not able to demonstrate syntactic priming. Possible implications of this negative finding are discussed.

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