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## RHYTHMS CAN OVERCOME TEMPORAL ORIENTING DEFICIT AFTER RIGHT FRONTAL DAMAGE

### Highlights

Controlled temporal preparation is impaired after frontal damage. > Rhythms (which induces automatic temporal preparation) can overcome this deficit. > Rhythms improve temporal preparation in right but not in left frontal patients. > Rhythms facilitate the implicit use of temporal information.

RHYTHMS CAN OVERCOME TEMPORAL ORIENTING DEFICIT AFTER  
RIGHT FRONTAL DAMAGE

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## Abstract

The main aim of this study was to test whether the use of rhythmic information to induce temporal expectations can overcome the deficit in controlled temporal preparation shown by patients with frontal damage (i.e. temporal orienting and foreperiod effects). Two tasks were administered to a group of 15 patients with a frontal brain lesion and a group of 15 matched control subjects: a Symbolic Cued task where the predictive information regarding the time of target appearance was provided by a symbolic cue (short line-early vs. long line-late interval) and a Rhythm Cued task where the predictive temporal information was provided by a rhythm (fast rhythm-early vs. slow rhythm-late interval). The results of the Symbolic Cued task replicated both the temporal orienting deficit in right frontal patients and the absence of foreperiod effects in both right and left frontal patients, reported in our previous study (Triviño, Correa, Arnedo, & Lupiañez, 2010). However, in the Rhythm Cued task, the right frontal group showed normal temporal orienting and foreperiod effects, while the left frontal group showed a significant deficit of both effects. These findings show that automatic temporal preparation, as induced by a rhythm, can help frontal patients to make effective use of implicit temporal information to respond at the optimum time. Our neuropsychological findings also provide a novel suggestion for a neural model, in which automatic temporal preparation is left-lateralized and controlled temporal preparation is right-lateralized in the frontal lobes.

## Keywords

Attention; Implicit timing; Temporal orienting; Foreperiod; Rhythms; Time perception; Neuropsychology; Frontal lobe.

## 1. Introduction

The environment provides us with regular temporal information that we use to prepare and respond at the optimal time. This kind of temporal preparation has been considered as *implicit timing* in the literature, which is defined “as a by-product of non-temporal task goals, when sensory stimuli or motor responses are temporally structured and can be used to predict the duration of future events” (Coull & Nobre, 2008). The implicit use of temporal information to respond at the appropriate moment in time may depend either on controlled or more automatic processes (Correa, 2010; Rohenkohl, Coull, & Nobre, 2011).

### 1.1. Controlled temporal preparation

Controlled temporal preparation depends on the expectation about when a stimulus will happen, which is called *Temporal Orienting* (Coull & Nobre, 1998; Nobre, 2001). When predictive information about a stimulus onset is given explicitly to subjects by temporal cues, they prepare themselves to respond at the expected time. Thus, the Temporal Orienting effect is reflected as enhanced performance (faster reaction time and/or higher accuracy) when temporal expectations are fulfilled (i.e. valid trials where the stimulus appears when subjects expect) than when they are not fulfilled (i.e. invalid trials where the stimulus appears when subjects do not expect) (Correa, Lupiáñez, Milliken, & Tudela, 2004; Correa, Lupiáñez, & Tudela, 2006; Coull, Frith, Buchel, & Nobre, 2000). In a recent neuropsychological study, we observed that this mechanism of temporal preparation, voluntary in nature, depends on the right frontal cortex (Triviño et al., 2010).

Another effect related to controlled temporal preparation is the *Foreperiod effect*, which consists of faster reactions at longer intervals after a warning cue. This effect can be

1 explained on the basis of calculation of probabilities (Karlin, 1959; Niemi & Näätänen,  
2 1981). That is, as time passes by and the stimulus has not appeared, subjects increase  
3 preparation because of the increasing likelihood of stimulus occurrence. The deficit in  
4 the Foreperiod effect has been related to right frontal lesion (Stuss et al., 2005; Vallesi  
5 et al., 2007), although in our previous study it was impaired in patients with either right  
6 or left frontal lesions (Triviño et al., 2010). The fact that both Temporal Orienting and  
7 Foreperiod effects are related to the proper functioning of frontal structures suggests  
8 these two effects rely on more evolved mechanisms, voluntary in nature, and based on  
9 top-down processing of time information (see Correa et al., 2006, for a explanation of  
10 dual-mechanism hypothesis).  
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## 26 1.2. Automatic temporal preparation

27 The finding of *Sequential effects* suggests that there are alternative ways for subjects to  
28 prepare on time that are less dependent than temporal orienting on controlled  
29 mechanisms. Sequential effects rely on the previous experiences of response  
30 preparation. As a result, subjects are faster when the foreperiod of the previous trial had  
31 the same duration or was shorter than the current foreperiod, even when the sequence of  
32 short and long preparatory intervals is completely unpredictable (Woodrow, 1914).  
33 These have been associated with automatic mechanisms of implicit timing based on  
34 trace conditioning (Los, 1996; Los & Heslenfeld, 2005; Los & Van den Heuvel, 2001).  
35 Sequential effects have been dissociated from Temporal Orienting and Foreperiod  
36 effects in behavioral and electrophysiological studies (Correa et al., 2004; Correa et al.,  
37 2006; Los & Heslenfeld, 2005; Los & Van den Heuvel, 2001), as well as in  
38 neuropsychological studies, where Sequential effects were not impaired after frontal  
39 damage (Triviño et al., 2010; Vallesi et al., 2007; Vallesi & Shallice, 2007). Sequential  
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1 effects have not been related to a specific brain structure, although classical  
2 conditioning has been associated with more ancient structures like hippocampus (Clark  
3 & Squire, 1998) or cerebellum (Kalmbach, Ohyama, Kreider, Riusech, & Mauk, 2009).  
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5 The fact that automatic mechanisms for temporal preparation are preserved after frontal  
6 damage is of special interest here, when considering the possibility of using this form of  
7 preparation to improve the performance of patients. In fact, rhythmic patterns can  
8 induce temporal preparation automatically (Jones, Moynihan, MacKenzie, & Puente,  
9 2002; Large & Jones, 1999; Rohenkohl et al., 2011; Sanabria, Capizzi, & Correa, 2011).  
10 Rhythmic contexts have been related to an enhancement in temporal discrimination  
11 tasks when the standard duration ended on predicted time compared to durations that  
12 ended earlier or later (McAuley & Jones, 2003). This pattern of improvement has been  
13 named an *expectancy profile* (Barnes & Jones, 2000), which resembles the expectation  
14 effects observed in the Temporal Orienting paradigm (Correa & Nobre, 2008; Griffin,  
15 Miniussi, & Nobre, 2001).  
16

17 Therefore, cueing time by means of rhythmic patterns seems to enhance implicit timing,  
18 which benefits performance in temporal preparation tasks. Given that automatic implicit  
19 timing mechanisms are presumably preserved after frontal damage, we should expect an  
20 improvement in temporal preparation in these patients when a rhythm is used as  
21 temporal cue. However, to our knowledge there are no studies about temporal  
22 preparation guided by rhythms in frontal patients (but see Praamstra & Pope, 2007, for a  
23 study in Parkinson Disease). Thus, the main aim of this study was to test the  
24 effectiveness of regular rhythms to induce temporal preparation in right frontal patients,  
25 who show deficit in controlled temporal orienting.  
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27 We designed a simple and short task, based on our previous studies (Correa, Miró,  
28 Martínez, Sánchez, & Lupiáñez, 2011; Correa, Triviño, Pérez-Dueñas, Acosta, &  
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Lupiañez, 2010; Triviño et al., 2010), that was administered to both control subjects and frontal patients groups. Two versions of the task were administered to each participant. In the Symbolic Cued Task, the usual symbolic cue (short vs. long static line) identical to that used in our previous studies was used as temporal cue; while in the Rhythm Cued Task a regular rhythm was used as temporal cue (fast vs. slow pace of a intermittent line). The Symbolic Cued task allowed us to replicate the results obtained in our previous study in patients. Specifically, we expected to observe that the Temporal Orienting effect was again abolished by prefrontal lesion only in the group of patients with right frontal damage; similarly, we would be able to test whether the Foreperiod effect was only associated to the right frontal cortex (Vallesi et al., 2007) or was rather not lateralized (Triviño et al., 2010). In the Rhythm Cued task, a fast rhythmic pattern was associated in 75% of trials to an early onset of the target (fast-early) and a slow rhythmic pattern was associated in 75% of trials to a delayed onset of the target (slow-late). With this new version we expected an improvement in temporal preparation in frontal groups. Finally, from a more practical point of view, the brief version of the temporal orienting task (less than 10 minutes) would approach the future design of a clinical tool to assess temporal preparation processes, whereas the rhythm task might be used with training purposes in neuropsychological rehabilitation.

### 1.3. Implicit vs. Explicit timing

Furthermore, we must take into account that there are several studies showing an impaired ability to estimate time explicitly in patients with frontal damage. This impairment has been described in temporal estimation tasks, as well as in production and reproduction tasks. Specifically, these patients show a time overestimation in the range of seconds and milliseconds (Berlin, Rolls, & Iversen, 2005; Berlin, Rolls, &



1 Kischka, 2004; Mimura, Kinsbourne, & O'Connor, 2000; Nichelli, Clark, Hollnagel, &  
2 Grafman, 1995) as well as an underproduction and an accelerated interval reproduction  
3 in the range of seconds (Berlin et al., 2005; Berlin et al., 2004; Mimura et al., 2000).  
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5 Therefore, if a patient with frontal damage tends to overestimate the passage of time and  
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7 believes that a given interval (e.g. 1000 ms) would end before (e.g. at 800 ms) it really  
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9 ends, we could expect that this patient uses that distorted information implicitly in the  
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11 task of temporal preparation. That is, time overestimation will lead to premature  
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13 preparation and responses.  
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18 Alternatively, one can expect no influence of distortions of explicit time estimation  
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20 upon the performance during implicit temporal preparation tasks, according to the  
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22 literature considering explicit and implicit timing to be independent processes (Coull &  
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24 Nobre, 2008; Lewis & Miall, 2003; Zelaznik, Spencer, & Ivry, 2002). However,  
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26 although it is generally agreed that time perception is fundamental for temporal  
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28 orienting (e.g., Coull & Nobre, 1998), there are no studies, to our knowledge, testing  
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30 directly the role of time perception accuracy in temporal orienting.  
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35 Therefore, we measured explicit timing in the range of milliseconds and minutes with a  
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37 duration discrimination task and a temporal order judgment task. We expected frontal  
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39 patients to show abnormal temporal estimation as has been described in the literature,  
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41 i.e. time overestimation. The analysis of correlations between the performances in  
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43 explicit and implicit timing tasks should inform us about the relationship between these  
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45 two processes.  
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## 51 52 53 2. Method

### 54 55 56 2. 1. Participants

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1 Fifteen subjects with a frontal brain lesion and 15 neurologically intact subjects  
2 participated in the study. All the patients had suffered an acute lesion leading to  
3 cognitive dysfunction (14 due to a traumatic brain injury and 1 due to an anterior  
4 cerebral artery stroke). Radiological reports describing the location and extension of the  
5 damage are presented briefly in Table 1 and in a greater extent in the supplementary  
6 material. In addition, we had access to PET-CT and MRI images of nine patients which  
7 have also been included in the supplementary material. Prior to the lesion, they were  
8 functionally independent, had no neurological or psychiatric disorders, and had normal  
9 intellectual level. They were divided into two different groups according to the lesion  
10 lateralization, so that there was a group of 10 patients with right frontal lesion and  
11 another group of 5 patients with left frontal lesion. Unfortunately, the Rhythm Cued  
12 task could not be administered to a right frontal subject. Each patient was matched in  
13 age, sex and years of education with a control subject. See Table 1.  
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43 Following our previous study (Triviño et al., 2010), inclusion criteria for the frontal  
44 group to be tested on the temporal tasks were the presence of acquired damage in either  
45 left or right frontal lobes according to the radiological report as well as a significant  
46 dysfunction of frontal functions observed in the neuropsychological assessment.  
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48 Exclusion criteria were the presence of bilateral frontal damage (for this reason 5  
49 patients were not included in the study) as well as the presence of aphasia, hemispatial  
50 neglect and/or dementia.  
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1 Nine patients were assessed at the Neuropsychology Unit of different hospitals in  
2 Valencia, Spain (*Valencia al Mar Nisa Hospital*, *Aguas Vivas Nisa Hospital* and  
3 *Nuestra Señora del Carmen Hospital*), whereas the 6 remaining patients and the 15  
4 controls were assessed at the Neuropsychology Unit of *San Rafael University Hospital*  
5 in Granada, Spain. The experiment was conducted in accordance with the ethical  
6 standards of the 1964 Declaration of Helsinki.  
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## 17 2.2. Neuropsychological assessment

18 The neuropsychological assessment was crucial to confirm frontal dysfunction in the  
19 frontal group (for their inclusion in the study). Therefore, all patients and controls  
20 subjects underwent a full neuropsychological evaluation. This evaluation took about 6  
21 hours for each subject distributed in about 3 to 4 sessions. A summary of the functions  
22 assessed and the tests used is shown in Table 2.  
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## 34 2.3. Behavioural tasks

### 35 2.3.1. Temporal Preparation Tasks: Symbolic and Rhythm Cued Tasks

36 We used E-prime software (Schneider, Eschman, & Zuccolotto, 2002) to program and  
37 run the experimental tasks and collect behavioural data. The tasks were administered on  
38 a 15-inch screen PC laptop computer. Participants performed two temporal-preparation  
39 tasks, one with symbolic cue and the other with a rhythm cue, administered in  
40 counterbalanced order across participants. Each task lasted about 10 to 15 minutes.  
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#### 53 2.3.1.1. Stimuli

54 We used the same stimuli and procedure as used in a recent study (Correa et al., 2010),  
55 which validated a shorter version of the task with clinical purposes. Both *Symbolic* and  
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*Rhythm* cued tasks shared the following characteristics. The stimuli were presented at the centre of the screen over a black background. Each trial included a fixation point, a temporal cue, and a target. The fixation point consisted of a dark gray square ( $0.25^\circ \times 0.25^\circ$  of visual angle at a viewing distance of 60 cm). In the *Symbolic* cued task, the temporal cue was either a short red line ( $0.38^\circ \times 0.95^\circ$ ) or a long red line ( $0.38^\circ \times 2.1^\circ$ ). The short line indicated that the target would appear early (after 400 ms), whereas the long one indicated that the target would appear late (after 1400 ms). In the *Rhythm* cued task, the temporal cue consisted of two horizontal red lines of the same length ( $1.05^\circ$ ), which appeared and disappeared 5 times at either a short (i.e. every 400 ms) or long (i.e. every 1400) pace (see figure 1). In both tasks, the target involved either go or no-go responses. The go target was either the letter ‘O’ or the letter ‘X’, whereas the no-go target was the digit ‘8’ which shares features with both go targets (all stimuli subtending  $0.38^\circ \times 0.76^\circ$ ). In the go condition, subjects had to detect any of the two letters – which appeared with identical probability ( $p=.5$ ) – by pressing the ‘B’ key. Two letters were used instead of just one in order to be able to compare the results with our previous studies and with future studies in which we will use a discrimination task. In the no-go condition, subjects should inhibit responding. Otherwise they were provided with feedback including the word “Incorrect” and a 2000-Hz auditory tone of 50 ms. The trial proportion was of .75 for the go condition (.375 for each go target) and .25 for the no-go condition.

### 2.3.1.2. Procedure

Participants seated about 60 cm from the computer screen. In both tasks the subjects were instructed to respond as quickly as possible but only to the go targets (‘X’ or ‘O’ letters), and therefore avoid responding to the no-go target (‘8’ digit). Each trial began

with the fixation point presented for a random interval ranging between 500 and 1500 ms. In the *Symbolic* cued task, the temporal cue (short or long red line) was presented for 50 ms, and then the screen remained blank for a time interval of 350 or 1350 ms, depending on the foreperiod of that trial. However, in the *Rhythm* cued task the temporal cue appeared for 50 ms and disappeared five times every 350 or 1350 ms (depending on the foreperiod condition; see figure 1). The final cue in each trial (the fifth one) turned thicker to warn about the impending target (see Sanabria et al., 2011, for a similar procedure). After the last thicker cue of these rhythm cues, the screen remained blank for 350 or 1350 ms, as in the *Symbolic* cued task, depending on the foreperiod (Figure 1). The target was displayed for 100 ms and was then replaced by a blank screen until the participant made a response or for a maximum duration of 2000 ms. A final pause of 500 ms preceded the next trial.

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Both *Symbolic* and *Rhythm* cued tasks included one practice block and 4 experimental blocks. The practice block included 32 trials with 16 early cues followed by 16 late cues (in practice trials cues were 100% valid in order to encourage participants to use their predictive value). The experimental blocks were divided into 2 ‘early’ blocks, in which the cue indicated that the target would probably appear after 400 ms, and 2 ‘late’ blocks, in which the cue indicated that the target would probably appear after 1400 ms (cue validity: 75%). Temporal expectancy was manipulated between blocks to optimise temporal orienting effects (Correa et al., 2006). Blocks of early and late cues were

presented in alternating runs, and the order of presentation was counterbalanced across participants. Each experimental block included 32 trials that were randomly presented. They were divided according to cue validity (24 valid and 8 invalid). In the valid condition, when the cue was early the target appeared after a short foreperiod of 400 ms, but when the cue was late the target appeared after a long foreperiod of 1400 ms. In the invalid condition, when the cue was early the target appeared after a long foreperiod of 1400 ms. Likewise, when the cue was late the target appeared after a short foreperiod of 350 ms. Eight of the 32 trials were nogo trials, in which the digit “8” was presented, so that the participant had to withhold responding (25% of nogo trials).

### *2.3.1.3. Design and Analyses of Behavioural Results*

Based on our previous studies, the analyses were simplified by computing an index for each temporal preparation effect<sup>1</sup> (Correa et al., 2006; Triviño et al., 2010). Specifically, the Temporal Orienting effect was indexed as the main effect of Validity in the short foreperiod experimental condition, subtracting the valid from the invalid condition (i.e., invalid minus valid). This index was calculated since the temporal orienting effect depend on the foreperiod, so that Temporal Orienting effect is only observed at the short foreperiod, unless catch trials are included (Correa et al., 2004). The Foreperiod effect was indexed as the main effect of Foreperiod in the invalid experimental condition, subtracting the long foreperiod from the short foreperiod condition (i.e., short minus long). In this case, valid trials were excluded since the literature show that the foreperiod effect is not observed when there is a strong expectancy for the target to appear at the short interval, so that when trials are valid subjects are equally fast on both short and long foreperiods (e.g., Correa et al., 2004; Correa & Nobre, 2008). However, when trials are invalid, subjects are usually slower in short vs. long foreperiods showing

1 a robust foreperiod effect. Regarding Sequential effects, they were indexed as the main  
2 effect of Previous foreperiod in the current short foreperiod, subtracting the previous  
3 short foreperiod from the previous long foreperiod condition (i.e., previous long minus  
4 previous short). The simplified analyses excluding the current long foreperiod condition  
5 was based in our previous results (Correa et al., 2006; Triviño et al., 2010) since  
6 sequential effects are typically observed at the current short foreperiod independently of  
7 validity.  
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9 These three indices were computed for RTs. In order to compare the two temporal  
10 preparation tasks, data from each index were submitted to a 3 (Group: Right frontal,  
11 Left frontal, Control) x 2 (Task: Symbolic Cue vs. Rhythm Cue) mixed analysis of  
12 covariance (ANCOVA), with the Group as a between participants factor, Task as a  
13 within participants variable and the current IQ as a covariate, since IQ has been related  
14 to timing (Wearden, Wearden, & Rabbitt, 1997). Subsequent planned comparisons were  
15 carried out to analyze the differences between tasks in each group, first comparing  
16 controls to frontal patients and second comparing the two frontal groups.  
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18 Practice trials and the first trial of each block were eliminated from the analyses. No-go  
19 trials were also eliminated from the RT analyses, as well as anticipation errors, in which  
20 participants responded before the target appeared (0.12% of trials rejected), or missing  
21 responses, in which participants did not respond when the target appeared (0.04%  
22 rejected). RT responses were filtered removing the trials with RT below 100 ms  
23 (0.04%) or above 1000 ms (0.74%). Mean RTs per experimental condition were  
24 computed with the remaining observations.  
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### 26 *2.3.2. Temporal Estimation Tasks*

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1 In order to measure processes related to fine-grained time processing in the milliseconds  
2 range, participants performed a Duration Discrimination task (providing an index of the  
3 estimation of the interval used in the temporal orienting tasks: 400 and 1400 ms) and a  
4 Temporal Order Judgment task. The tasks were administered on the same 15-inch  
5 screen PC laptop computer, using also E-prime software to run the tasks and collect de  
6 data. These tasks were performed the first and last, respectively, before and after the  
7 two temporal preparation tasks. The duration discrimination task was run first in order  
8 to familiarize participants with the interval to be used. Each task lasted 5 to 8 minutes.  
9 Finally, each of the four tasks (i.e., the two temporal preparation and the two temporal  
10 estimation tasks) included a temporal estimation task in the minutes range. For a more  
11 detailed description of the stimuli, procedure and design of these tasks, see the  
12 Appendix.

### 31 3. Results

#### 34 3.1. Demographic results

36 Each patient was matched to a control subject in age, sex and education. A single-factor  
37 ANOVA was used to analyze differences in age and education. Each frontal group was  
38 compared to the control group. No significant differences were found concerning age  
39 and years of education ( $F < 1$  in both cases). The premorbid IQ of patients was compared  
40 to the current IQ of control subjects and no significant differences were found with  
41 either the right ( $F < 1$ ) or the left frontal group ( $F(1,18)=1.55$ ,  $p=0.228$ ). However, as  
42 one would expect, the current IQ of frontal patients after brain lesions was significantly  
43 lower than that of control, both for the right frontal,  $F(1,18)=4.58$ ,  $p=0.046$ , and the left  
44 frontal group,  $F(1,8)=22.1$ ,  $p=0.002$ . However, as described below, the introduction of  
45 the current IQ as a covariate in the analysis did not change the results. See Table 2.



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PLEASE INSERT TABLE 2 ABOUT HERE  
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### 3.2. Neuropsychological assessment

Each patients group was compared to the control group using a single-factor ANOVA on the score in each neuropsychological test. The typical deficits of frontal lesions were observed, such as dysexecutive syndrome with a significant impairment of divided attention, interference control ability, abstraction, temporal sequencing, fluency and mental flexibility. We also observed memory impairment, mainly showing perseverations and poor use of encoding and recall strategies. The left frontal group showed a specific impairment on verbal learning, free recall and recognition, with differences marginally significant when compared to right frontal group. There were no differences in personality and other psychological disorders (all  $p>.10$ ). No significant differences were found between patients with right and left frontal lesion regarding any other of the neuropsychological variables ( $p>.10$ ). Further detailed analyses are provided in Table 2.

### 3.3. Behavioural results

#### *3.3.1. Temporal preparation tasks*

Detailed data are presented in Table 3. Temporal preparation indexes (described above) were computed using mean RTs. Indexes are presented in Table 4 for both the Symbolic and the Rhythm Cued Task.

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PLEASE INSERT TABLES 3 & 4 ABOUT HERE  
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A 3 (Group: Right Frontal, Left Frontal, Control) x 2 (Task: Symbolic Cued vs. Rhythm Cued) mixed ANCOVA was performed for each temporal preparation index<sup>2</sup>. The current IQ was included as a covariate to control for group differences mentioned above. Regarding the Temporal Orienting effect, the interaction between Group and Task was close to significance,  $F(2,24)=2.85$ ,  $p=0.078$ ,  $\eta^2=0.19$ . In the subsequent planned comparisons, the control group did not show differences between tasks,  $F<1$ , because the temporal orienting effect was present in both Symbolic and Rhythm Cued Tasks,  $F(1,24)=5.77$ ,  $p=0.024$  and  $F(1,24)=4.39$ ,  $p=0.047$ , respectively. On the other hand, when comparing the right and left frontal groups only (see Triviño et al., 2010 for a similar analysis), as we expected, the right frontal group showed differences between tasks that were close to significance,  $F(1,11)=3.21$ ,  $p=0.087$ , with no Temporal Orienting effect on the Symbolic Cued Task,  $F<1$ , but showing significant Temporal Orienting effect on the Rhythm Cued Task,  $F(1,11)=7.51$ ,  $p=0.019$ . The left frontal group did not show significant differences between tasks,  $F(1,11)=1.35$ ,  $p=0.270$ , although this group showed a marginally significant effect in the Symbolic Cued Task,  $F(1,11)=4.32$ ,  $p=0.062$ . However, no temporal orienting was found in the Rhythm Cued Task,  $F<1$ . See Figure 2.

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PLEASE INSERT FIGURE 2 ABOUT HERE  
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With regard to the Foreperiod effect, neither the main effect of Task nor the interaction between Group and Task were significant, both  $p > .153$ . However, in planned comparisons, the control group showed no differences between tasks,  $F(1,24)=1.45$ ,  $p=0.239$ , because the Foreperiod effect was clearly present in both Symbolic and Rhythm Cued Tasks,  $F(1,24)=10.47$ ,  $p=0.003$  and  $F(1,24)=14.19$ ,  $p=0.0009$ , respectively. When the right and left frontal groups were compared, the right frontal group showed differences between tasks,  $F(1,11)=6.00$ ,  $p=0.032$ . As we expected, they did not show the Foreperiod effect on the Symbolic Cued Task,  $F < 1$ , but did show it on the Rhythm Cued Task,  $F(1,11)=9.36$ ,  $p=0.011$ . The left frontal group did not show significant differences between tasks,  $F < 1$ , with no Foreperiod effect either in the Symbolic Cued Task,  $F < 1$ , or in the Rhythm Cued Task,  $F < 1$ . See Figure 3.

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PLEASE INSERT FIGURE 3 ABOUT HERE  
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Regarding Sequential effects, neither the main effect of Task nor the interaction between Group and Task were significant, both  $F > 1$ . In planned comparisons, none of the groups showed differences between tasks, all  $F < 1$ . Specifically, the control group showed no sequential effects on Symbolic Cued Task,  $F(1,24)=1.39$ ,  $p=0.248$ , although they showed the expected pattern (the effect was in the right direction and of almost 30 ms), but showed it on the Rhythm Cued Task,  $F(1,24)=4.50$ ,  $p=0.044$ . The right frontal group, as the control group, showed the expected pattern (almost 25 ms) although without significant effects on the Symbolic Cued Task,  $F < 1$ , but did show it close to

significance on the Rhythm Cued Task,  $F(1,11)=4.37$ ,  $p=0.060$ . Finally, the left frontal group showed no effects on any of the tasks, both  $F_s<1$ . See Figure 4.

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PLEASE INSERT FIGURE 4 ABOUT HERE  
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### 3.3.2. Temporal estimation tasks

Each patients group was compared to the control group for each score in the temporal estimation tasks. These results are presented in Table 5 (for more detailed analyses, see the Appendix).

The right frontal group showed an overestimation pattern similarly to that described after frontal lesions. Specifically, compared to controls, *right frontal* patients showed a significant larger JND (*Just Noticeable Difference*) in both the Millisecond Duration Discrimination Task and the Temporal Order Judgement Task (all  $ps<0.015$ ). However, differences in the PSE (*Point of Subjective Equality*) were only marginally significant in the short interval (400 ms) of the Millisecond Duration Discrimination Task, ( $p<0.054$ ). Regarding the Minutes Estimation task, right frontal patients showed a significant overestimation pattern in all the tasks, all  $ps<0.044$ , except for the Millisecond Duration Discrimination Task (marginally significant only at the first moment of estimation,  $p<0.055$ ). There were not significant differences in the *left frontal* group when compared to controls in any of the tasks, all  $ps>0.225$ . Only in the Minutes Estimation Task, right and left frontal groups showed significant differences,  $F(1,25)=6.85$ ;  $p=0.015$  (i.e., right overestimated whereas left underestimated). To sum up, the right frontal group showed a poor temporal discrimination and a tendency to overestimate in

short intervals (i.e., 350 ms) and in the minutes range, while the left frontal group were normal in the millisecond range and showed underestimation in the minutes range.

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PLEASE INSERT TABLE 5 ABOUT HERE  
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4. Discussion

This study has provided novel results with neuropsychological patients about the mechanisms involved in implicit timing. The main contribution of this study was the first demonstration that rhythms can compensate the Temporal Orienting deficit in right frontal patients.

Moreover, this study replicated our previous findings in patients (Triviño et al., 2010), showing a deficit in the Temporal Orienting effect (driven by symbolic cues) after right frontal damage. We have also replicated the finding that the Foreperiod effect is deficient after either right or left frontal damage. In contrast, other studies found the Foreperiod effect to be lateralized and only absent after right frontal lesions (Stuss et al., 2005; Vallesi et al., 2007). These conflicting results could be due to the different demands of the tasks, since these studies focused on the Foreperiod effect and the cue had no predictive temporal value. Nevertheless, the involvement of prefrontal structures in the controlled temporal preparation processes has been amply demonstrated in these studies, while the Sequential Effects, more automatic in nature, were preserved (Stuss et al., 2005; Triviño et al., 2010; Vallesi et al., 2007). Regarding sequential effects, the control group and the right frontal group, but not the left frontal group, showed the expected tendency (i.e., faster RT in short previous foreperiod than in long previous

foreperiod) on the symbolic task, although the trend failed to reach statistical significance. This could be related to a lack of statistical power due to the elimination from the analysis of those trials where the previous foreperiod was a nogo trial. This should be tested in future studies specifically designed to measure sequential effects without contamination of temporal cuing by extending the number of trials per block or removing the nogo trials. The left frontal group, however, did not show the typical sequential effects pattern on the symbolic task. On the contrary, they showed a negative effect which could be related to an implication of prefrontal cortex (more specifically premotor cortex and surrounding areas) on automatic temporal processing (Vallessi et al., 2007; Vallesi et al., 2007).

Therefore, based on this presumably automatic mechanism preserved after prefrontal damage, a regular rhythm was included in the present study to provide temporal information (fast rhythm-early / slow rhythm-late). A significant improvement was observed on the right frontal group so that patients showed significant Temporal Orienting and Foreperiod effects, which were absent when temporal information was provided by a symbolic cue (short line-early / long line-late). Also, Sequential effects were significant with predictive rhythms, so the rhythm seemed to facilitate the use of both automatic or controlled temporal information to respond at the optimum time. It is important to note that this improvement was almost selective to the right frontal group. In fact, the control group showed such improvement only in Sequential effects and left frontal patients showed none of the effects when rhythms were presented. This selectivity thus rules out explanations of the effectiveness of rhythms for temporal preparation in terms of unspecific arousing effects. Rather, the results may suggest a double dissociation related to prefrontal lateralization of temporal orienting and automatic vs. controlled temporal preparation.

1 A possible explanation for these results considers the importance of the left hemisphere  
2 in the implicit perception of rhythms necessary for speech processing (Geiser, Zaehle,  
3 Jancke, & Meyer, 2008). And more specifically, the left supplementary motor area  
4 (SMA) and the left premotor cortex, which have been associated not only to Sequential  
5 effects but also to musical and rhythmic beat perception (Graham & McAuley, 2009;  
6 Kornysheva, Von Anshelm-Schiffer, & Schubotz, 2011; Kornysheva, Von Cramon,  
7 Jacobsen, & Schubotz, 2010). However, the right hemisphere is involved in the  
8 controlled orientation of attention in space and time (Coull et al., 2000; Hackley et al.,  
9 2009). Therefore, a lesion in left prefrontal structures would allow participants to use  
10 the temporal information provided by a symbolic cue in order to orient attention in time,  
11 but they would be unable to process such information when provided by a rhythm. In  
12 contrast, a lesion in right prefrontal structures would prevent participants to use the  
13 information from a symbolic cue, but they could use such information when provided  
14 by a rhythm. Although these results should be interpreted cautiously due to the smaller  
15 sample of the left frontal group, they provide a novel suggestion for a neural model in  
16 which automatic temporal preparation is left-lateralized and controlled temporal  
17 preparation is right-lateralized. This proposal is in line with the finding of smaller  
18 automatic sequential effects in patients with left premotor lesions (Vallesi et al., 2007),  
19 and may be tested with TMS methodology in future research comparing the temporal  
20 orienting vs. sequential effects.

21 Focusing on the results obtained in the right frontal group, one possible explanation is  
22 that patients have a specific deficit in the controlled temporal preparation processes, so  
23 that the introduction of an automatic temporal cue allows them to use temporal  
24 information appropriately. In fact, the activation of the right fronto-parietal cortex has  
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1 been associated to the monitoring of regular and predictable spatio-temporal trajectories  
2 (Vallesi & Crescentini, 2011).  
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4 Another explanation could be that right frontal patients suffer a more basic deficit in  
5 time estimation using distorted temporal information. In fact, a recent study (Piras &  
6 Coull, 2011) has demonstrated that both explicit and implicit temporal tasks used the  
7 same type of time representation mechanism. Our right frontal patients clearly presented  
8 an overestimation in the range of milliseconds and minutes, showing that they perceived  
9 time as passing quickly. Therefore, in this case, patients might be prepared to wrong  
10 moments in time according to the overestimation they showed, leading them to respond  
11 prematurely. To test the role of time estimation in our temporal-preparation effects we  
12 performed an additional analysis by considering the PSE and the JND (in the short  
13 interval) as covariates. Since the main results remained the same, we can conclude that  
14 the deficit in temporal orienting and foreperiod effects did not depend exclusively on  
15 the ability to estimate time intervals.  
16

17 Otherwise, left frontal patients showed no significant differences compared to control  
18 group in their ability to estimate time; nevertheless they showed a significant  
19 impairment of the Temporal Orienting effect in the Rhythm Cued task, and a deficit in  
20 the Foreperiod effect in both tasks, which would support the independence between the  
21 two timing functions. However, lesions on left fronto-parietal cortex has been related to  
22 time estimation deficits in temporal order judgment tasks (Wencil, Radoeva, &  
23 Chatterjee, 2010) and therefore we should consider that the lack of time estimation  
24 deficit in our left frontal group could be due to the sample size.  
25

26 More research is needed in this area. If temporal overestimation is the core deficit in  
27 right frontal patients, we would expect these patients to prepare in time, but in an  
28 anticipatory way. Future studies with electroencephalography (EEG) could be useful as  
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1 the CNV (Contingent Negative Variation) has been associated with the anticipatory  
2 responses. Thus, if the core deficit is the overestimation but patients show the ability to  
3 prepare temporarily, the CNV should be advanced in time. While if the core deficit lies  
4 in temporal preparation processes and the implicit use of temporal information, maybe  
5 the CNV should be attenuated or altered as it has been observed in Parkinson Disease  
6 (Praamstra & Pope, 2007).  
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14 In conclusion, this study provides evidence on how the introduction of rhythms  
15 improves the ability of right frontal patients to orient themselves in time. Future  
16 research will reveal whether our proposal of a neural model of dissociated implicit  
17 timing, with automatic temporal preparation lateralized at left frontal cortex and  
18 controlled temporal preparation lateralized at right frontal cortex, is supported by new  
19 data.  
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28 Regarding the practical implications of the study, on the one hand, the replication of  
29 previous results with a brief task (less than 10 minutes) could have clinical assessment  
30 purposes. On the other hand, the improvement on temporal preparation with rhythms  
31 could have rehabilitation purposes. If right frontal lesion patients can orient in time after  
32 temporal rhythms, they could be trained to use rhythmic patterns to predict the  
33 occurrence of temporal events.  
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## Notes

1. These indices have shown to be more specific and sensitive measures of our two main effects of interest. In any case, they were validated by an analysis similar to our previous studies, in which mean RTs were submitted to a 3 (Group: Right frontal, Left frontal, Control) x 2 (Foreperiod: short vs. long) x 3 (Previous foreperiod: short, long, nogo) x 2 (Validity: valid vs. invalid) mixed analyses of variance (ANOVA). The Foreperiod x Validity interaction was close to significance,  $F(1,24)=3.99$ ,  $p=0.057$ ,  $\eta^2=0.14$ , with the effect of validity in the short foreperiod being significant,  $F(1,24)=5.52$ ,  $p=0.027$ , but not in the long foreperiod,  $F<1$ . In the same way, the effect of foreperiod was significant in the invalid condition,  $F(1,24)=5.75$ ,  $p=0.025$ , but not in the valid condition,  $F<1$ . Moreover, the Foreperiod x Previous foreperiod interaction was significant,  $F(2,48)=4.38$ ,  $p=0.018$ ,  $\eta^2=0.15$ . When sequential effects were analysed by excluding the nogo previous foreperiod, they were significant in the short current foreperiod,  $F(1,24)=12.13$ ,  $p=0.002$ , but not in the long current foreperiod,  $F<1$ . Moreover, the Foreperiod x Previous foreperiod x Validity interaction was not significant,  $F(2,24)=1.57$ ,  $p=0.219$ ,  $\eta^2=0.06$ . The proposed indices therefore focused on the clearest effects, namely, validity effects at the short foreperiod (temporal orienting effect), foreperiod effect in the invalid condition and previous foreperiod effect in the current short foreperiod (sequential effects).

2. Given that the left frontal group's sample size was smaller, a permutation test was performed comparing (10 iterations) the five left frontal subjects to five right frontal subjects and five controls randomly selected. The  $F$ 's critical value was the following:  $F(1,15)=4.49$ . The results remained the same for all the effects. Focusing on our main effect –temporal orienting–, the right frontal group never showed significant effects on

1 the symbolic task but showed significant temporal orienting in half of the permutation  
2 tests, whereas the left frontal group showed the opposite pattern. These tests also  
3  
4 showed a loss of significance for that the Temporal orienting effect decreased  
5 robustness in the Symbolic task when the control group was based on 5 participants  
6  
7 only (although in four of the permutation tests this group was close to significance,  
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9  $F_{5,4.00}$ ). This result can explain why some interactions involving group as factor did  
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11 not reach full significance.  
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## Figure legends

Figure 1. Sketch of the main experimental conditions and events in Symbolic and Rhythm Cued Tasks.

Figure 2. Mean reaction time (RT) results for the Temporal Orienting effect (RT-invalid minus RT-valid) in short foreperiod conditions for both Symbolic and Rhythm Cued Tasks. Error bars represent the standard error of the mean. Asterisks mean significant effect. The cross sign “+” means an effect close to significance ( $p < .065$ ).

Figure 3. Mean reaction time (RT) results for the Foreperiod effect (RT-short minus RT-long) in invalid conditions for both Symbolic and Rhythm Cued Tasks. Error bars represent the standard error of the mean. Asterisks mean significant effect.

Figure 4. Mean reaction time (RT) results for the Sequential effects (RT- previous long minus RT-previous short) in current short foreperiod conditions for both Symbolic and Rhythm Cued Tasks. Error bars represent the standard error of the mean. Asterisks mean significant effect. The cross means an effect close to significance ( $p < .065$ ).



Tables

Table 1. Demographic data of both frontal and control groups with the right and left division. Etiology and brief description of main lesions reported by radiologists are also included for each frontal patient. Group averaged data and standard deviation (in parenthesis) are included.

Frontal Group		Age in Years	Years of Education	Sex	Total
Right Frontal	mean (s.d)	33.7 (15.2)	10.5 (4.9)	7 M 3 F	10
Left Frontal	mean (s.d)	33.6 (10.3)	12.2 (2.7)	5 M 0 F	5
Total Frontal	mean (s.d)	33.7 (13.4)	11.1 (4.2)	12M 3F	15
Control Group		Age in Years	Years of Education	Sex	Total
Right Control	mean (s.d)	33.6 (14.8)	22 (31.8)	5 M 5 F	10
Left Control	mean (s.d)	32.8 (9.9)	13.6 (4.7)	4 M 1 F	5
Total Control	mean (s.d)	33.33 (13.0)	13.0 (4.3)	9 M 6 F	15

Etiology	Main lesions. Radiological Reports.
TBI	Right temporal and right frontobasal.
TBI	Right frontoparietal and right frontobasal.
TBI	Right frontotemporal.
TBI	DAI predominantly on right frontal.
TBI	Right frontotemporal and right frontobasal.
TBI	Right frontal.
Stroke	Right anterior cerebral artery region.
TBI	Right frontal pole and right temporal.
TBI	Right frontal.
TBI	DAI predominantly on right frontal.
TBI	Left frontoparietal.
TBI	Left frontal.
TBI	DAI predominantly on left frontal.
TBI	Left frontobasal.
TBI	Left frontal.

M: male; F: female; TBI: traumatic brain injury; DAI: diffuse axonal injury.

Table 2. Summary of cognitive functions and neuropsychological tests used in the clinical assessment, and the results comparing each frontal group to the control group as well as the comparisons between both right and left frontal groups.

FUNCTION <i>Test &amp; Subtest</i>	RESULTS					
	GROUPS			COMPARISONS		
	Right Frontal $\mu$ (sd)	Left Frontal $\mu$ (sd)	Control Group $\mu$ (sd)	Right F vs. Control	Left F vs. Control	Right F vs. Left F
Intelligence Quotient (IQ)						
Premorbid Intellectual Functioning						
Bilbao & Seisdedos (2004) formula	115 (16.7)	109 (12.2)	116 (9.3)			
Current Intelligence Quotient						
Verbal IQ of WAIS-III	103 (14.3)	95 (4.3)	115 (10.9)	**	***	
Manipulative IQ of WAIS-III	93 (23.9)	89 (16.3)	115 (11.9)	*	**	
Total IQ of WAIS-III	98 (19.4)	93 (10.2)	116 (9.3)	*	***	
Premotor Function						
Premotor Functions (Barcelona Test)						
Rhythm (errors)	0.7 (0.6)	0.0 (0.0)	0 (0.0)	***		
Bimanual coordination	2.0 (0.0)	2.0 (0.6)	2 (0.0)		*	
Motor alternances	1.3 (0.6)	2.0 (0.6)	2 (0.0)	***	*	
Graphic alternances	1.7 (0.6)	2.0 (0.0)	2 (0.0)	*		
Reciprocal inhibition (errors)	0.3 (0.6)	0.0 (0.6)	0 (0.6)			
Verbal Memory						
Test Aprendizaje Verbal España Complutense, TAVEC						
Learning	55 (8.1)	46 (11.3)	55 (8.2)		+	+
Short term free recall	10 (4.3)	7 (2.8)	13 (2.5)	+	***	
Long term free recall	10 (4.2)	8 (2.3)	13 (2.5)	+	***	
Intrusions (in both free and cued recall)	6 (5.9)	4 (2.9)	3 (4.2)			
Semantic strategies in learning (A+B list)	8 (8.4)	4 (5.2)	10 (12.1)		*	
Semantic strategies in recall (short+ long)	4 (2.2)	2 (1.1)	7 (4.1)	*	**	
Serial strategies in learning (A+B list)	4 (5.5)	5 (5.4)	4 (6.3)	*	*	
Serial strategies in recall (short+ long)	1 (2.0)	0.6 (1.1)	1 (3.0)			
Perseverations	11 (7.5)	8 (9.6)	5 (4.7)	*		
Recognition	15 (1.3)	10 (7.2)	15 (1.3)			+
Falses positives in recognition	1 (1.6)	2 (2.2)	1 (0.9)		*	
Visual Memory						
Rey Complex Figure Test						
Immediate Recall (PC)	52 (36.6)	53 (34.48)	70 (25.9)			
Working Memory						
Phonological loop						
Digit Span Subtest of WAIS-III	10 (2.4)	10 (2.1)	11 (2.8)			
Visuospatial sketchpad						
Spatial Span Subtest of WMS-III	9 (4.3)	9 (4.0)	12 (3.5)			
Central executive						
Letter-Number Subtest of WAIS-III	10 (3.2)	10 (2.9)	12 (2.1)			
Attention						
Sustained attention						
Trail Making Test, A – errors	0 (0.0)	0 (0.0)	0 (0.3)			
Selective attention						
Picture Completion Subtest of WAIS-III	10 (5.7)	11 (3.2)	14 (2.7)	*	*	
Divided attention						
Trail Making Test, B – errors	2 (2.4)	1 (1.8)	0 (1.2)	*		
Interferente						
Stroop Color and Word Test	56 (5.7)	55 (13.9)	50 (10.1)	+		
Executive Functions						
Verbal abstraction						
Similarities Subtest of WAIS-III	13 (2.9)	10 (2.4)	14 (2.2)	+	**	
Visual abstraction						
Matrix Reasoning Subtest of WAIS-III	10 (2.8)	8 (2.3)	12 (2.2)	*	**	
Temporal sequencing						
Picture Arrangement Subtest of WAIS-III	7 (2.7)	7 (2.4)	12 (3.2)	**	**	
Constructive praxia						
Block Design Subtest of WAIS-III	9 (4.9)	9 (4.2)	12 (2.8)	*	+	
Copy of the Rey Complex Figure Test	62 (32.1)	79 (13.9)	97 (3.9)	**	**	
Fluency						
FAS fluency test	31 (8.2)	28 (10.8)	42 (9.7)	*	*	
Animal fluency test	18 (3.2)	15 (2.4)	23 (5.0)	**	**	
Mental flexibility and categorization (Wisconsin Card Sorting Test, WCST)						
Errors % (PC)	43 (33.4)	63 (52.3)	50 (21.6)			
Perseverative responses % (PC)	39 (39.5)	48 (57.4)	71 (26.8)	*		
Perseverative errors % (PC)	47 (41.2)	47 (56.9)	68 (27.4)			
Non-perseverative errors % (PC)	48 (24.5)	54 (23.1)	38 (22.9)		*	
Number of categories completed (PC)	3 (1.7)	4 (2.5)	5 (1.6)	*		
Planning (Zoo Map Test of Behavior Assessment of Disexecutive Syndrome)						

<i>Execution Time (in sec) – Parte 1</i>	298 (297.8)	177 (143.2)	199 (95.9)	
<i>Execution Time (in sec) – Parte 2</i>	108 (47.8)	89 (55.3)	56 (27.4)	**
<i>Total profile</i>	2 (1.1)	2 (2.1)	3 (0.9)	
Personality and Psychological Disorders <i>Millon Clinical Multiaxial Inventory, MCMI-III</i>	No significant differences in any scale between either groups			

\*p<.10; \*p<.05 ; \*\* p<.01 ; \*\*\* p<.001

sd=standard deviation; WAIS-III=Weschler Adult Intelligence Scale 3th edition; WMS-III=Weschler Memory Scale 3th edition; TAVEC= Spanish version of California Verbal Learning Test; PC=percentile.

Table 3. Mean RTs and percentage of false alarms (in parentheses) per experimental condition from all groups (Right Frontal, Left Frontal and Control) broken down by Cue (Symbolic vs. Rhythm), Foreperiod (Short FP vs. Long FP) and Validity (Valid – val vs. Invalid – inv).

		Symbolic Cue				Rhythm Cue			
		Short FP		Long FP		Short FP		Long FP	
		Val	Inval	Val	Inval	Val	Inval	Val	Inval
Right Frontal	Mean RT (False alarms)	391 (9.4%)	402 (7.5%)	406 (13.3%)	403 (17.5%)	422 (6.7%)	467 (15.0%)	429 (15.5%)	407 (7.5%)
Left Frontal	Mean RT (False alarms)	451 (5.2%)	490 (5.0%)	463 (11.8%)	490 (10.0%)	469 (18.4%)	472 (0.0%)	450 (15.5%)	443 (18.3%)
Control	Mean RT (False alarms)	379 (16.0%)	402 (16.7%)	380 (18.9%)	362 (11.7%)	380 (13.7%)	407 (22.0%)	385 (21.4%)	355 (8.9%)

Table 4. Mean RT and standard deviation per temporal preparation index (Temporal orienting, Foreperiod and Sequential effects) from all groups (Right Frontal, Left Frontal and Control) broken down by Task (Symbolic vs. Rhythm).

		INDEX					
		Temporal Orienting Effect		Foreperiod Effect		Sequential Effects	
TASK		Symbolic	Rhythm	Symbolic	Rhythm	Symbolic	Rhythm
Right Frontal	Mean (s.d.)	3.3 (13.3)	45.3 (16.3)	2.1 (12.7)	60.6 (17.0)	23.4 (21.7)	54.9 (23.6)
Left Frontal	Mean (s.d.)	38.9 (17.8)	2.5 (21.9)	0.4 (16.9)	28.7 (22.8)	-2.0 (29.1)	39.1 (31.6)
Control	Mean (s.d.)	26.3 (10.7)	30.6 (13.1)	42.6 (10.1)	55.4 (13.6)	27.1 (17.4)	42.5 (18.9)

Table 5. Absolute (Abs.) and percentage (%) punctuations of Just Noticeable Difference (JND), Point of Subjective Equality (PSE) and Moment of Estimation for Milliseconds Temporal Discrimination, Temporal Order Judgment and Minutes Estimation Tasks, as well as the results comparing each frontal group to the control group and comparisons between both right and left frontal groups using percentage punctuations. Standard deviations (sd) are in parenthesis.

TASK <i>Score &amp; Estimation moment</i>	RESULTS							
	GROUPS						COMPARISONS USING % PUNCTUATIONS	
	Right Frontal		Left Frontal		Control Group		Right F vs. Control	Left F vs. Control
	Abs. (sd)	% (sd)	Abs. (sd)	% (sd)	Abs. (sd)	% (sd)	Right F vs. Left F	
Milliseconds Temporal Discrimination Task								
<i>JND – Short Interval (350 ms)</i>	90.8 (14.6)	25.9% (4.2)	81.9 (18.5)	23.4% (5.3)	52.4 (10.7)	15.0% (3.0)	*	
<i>JND – Long Interval (1350 ms)</i>	275.3 (40.5)	20.4% (3.0)	193.9 (51.3)	14.4% (3.8)	157.3 (29.6)	11.6% (2.2)	*	
<i>PSE – Short Interval (350 ms)</i>	375.5 (13.2)	107.3% (3.8)	341.4 (16.8)	97.5% (4.8)	342.3 (9.7)	97.8% (2.8)	*	
<i>PSE – Long Interval (1350 ms)</i>	1201.2 (3.0)	89.0% (4.2)	1320.3 (71.3)	97.8% (5.3)	1249.4 (41.1)	92.5% (3.0)		
Temporal Order Judgment Task								
<i>JND</i>	52.6 (6.9)		41.9 (9.8)		28.8 (5.1)		**	
<i>PSE</i>	45.3 (15.1)		-14.9 (21.4)		0.3 (11.1)		*	
Minutes Estimation Task								
<i>Milliseconds Discrimination Task</i>								
<i>First Moment</i>	90.2 (88.1)	16.7% (15.2)	-229.8 (124.6)	-37.5% (21.6)	-122.2 (71.9)	-22.6% (12.4)	*	
<i>Second Moment</i>	-77.3 (142.4)	-5.7% (12.5)	-505.6 (201.4)	-41.4% (17.8)	-292.1 (116.3)	-28.3% (10.3)		
<i>Temporal Order Judgement Task</i>								
<i>First Moment</i>	397.1 (119.5)	144.0% (40.1)	18.6 (169.0)	11.2% (56.6)	-5.1 (97.6)	-2.1% (32.7)	**	
<i>Second Moment</i>	445.8 (140.3)	85.1% (26.5)	-33.0 (198.4)	-3.3% (37.5)	-29.5 (114.5)	-5.9% (21.6)	*	
<i>Symbolic Cued Task</i>								
<i>First Moment</i>	290.6 (79.0)	86.3% (23.2)	-107.8 (111.8)	-28.3% (32.8)	32.1 (64.5)	10.3% (18.9)	*	*
<i>Second Moment</i>	388.3 (114.9)	64.3% (19.4)	-51.0 (162.4)	-6.6% (27.4)	47.2 (93.8)	9.0% (15.8)	*	
<i>Rhythm Cued Task</i>								
<i>First Moment</i>	97.1 (135.2)	28.2% (16.6)	-173.2 (181.4)	-28.7% (22.3)	-122.6 (108.4)	-20.2% (13.3)	*	
<i>Second Moment</i>	157.1 (194.8)	19.9% (14.5)	-469.8 (261.4)	-43.5% (19.5)	-213.0 (156.2)	-19.5% (11.6)	*	+

\*p<.10; \*p<.055 ; \*\* p<.01 ; \*\*\* p<.001

## Appendix A. Temporal estimation tasks

### 1. Method

#### 1.1. Milliseconds Duration Discrimination Task

##### *1.1.1. Stimuli and Procedure*

Participants were seated about 60 cm from the computer screen. They were to estimate whether a comparison interval was longer or shorter than a standard interval. Therefore, each trial included a fixation point, a standard interval and a comparison interval. The stimuli were presented at the centre of the screen over a black background. The fixation point consisted of a dark gray square ( $0.03^\circ \times 0.03^\circ$  of visual angle at a viewing distance of 60 cm). The duration of a red '@' symbol ( $2.20^\circ \times 2.20^\circ$ ) was used as the standard interval, while the duration of a white '@' symbol was used as the comparison interval. The up- and down-arrow keys on the keyboard were used to indicate whether the comparison interval was longer or shorter than the standard interval, respectively. All participants were instructed to keep their gaze on the centre of the screen, just where the fixation point appeared, as well as to respond as accurately as possible without time limit. Each trial began with the fixation point presented for a random interval ranging between 500 and 1000 ms. Next, the standard interval (red '@') was presented for a short (350 ms) or a long (1350 ms) duration, followed by the fixation point (again shown between 500 and 1000 ms). After this, the comparison interval appeared for a duration that could be either 5%, 15%, 25% or 50% above or below the duration of the standard interval. Thus, for the short-standard interval (350 ms) condition, the comparison interval on each trial could be either 175, 263, 298, 333, 368, 403, 438 or 525 ms. In the long-standard interval (1350 ms) condition, the comparison interval were 675, 1013, 1148, 1283, 1418, 1553, 1688 and 2025 ms. Finally, the screen remained

1 blank until the participant made a response without time limit. The next trial only began  
2 when the participant responded.  
3

4 The task included 4 experimental blocks, 2 with the short-standard interval and 2 with  
5 the long-standard interval. Blocks of short and long intervals were presented in  
6 alternating runs, and the order of presentation was counterbalanced across participants.  
7 Each experimental block included 6 trials for each comparison interval, leading to 48  
8 trials in total. The different durations were presented randomly within the block.  
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### 20 *1.1.2. Design and Analyses of Behavioural Results*

21 Data from this task were plotted as the proportion of 'long' responses as a function of  
22 target durations (see Figure A.1). In order to compute the just noticeable difference  
23 (JND) and the point of subjective equality (PSE), data from each participant were  
24 transformed to Z scores, and the Z score distributions were fitted to linear regressions  
25 (Finney, 1964). The slopes and intercept point of such linear trends were used to  
26 compute the JNDs and PSEs for each participant for both short and long standard  
27 durations. Large values of JND means poor temporal discrimination. In the case of PSE,  
28 positive values meant overstimulation of the comparison interval and negative values  
29 meant understimulation of the comparison interval. Four participants showed negative  
30 JNDs. Two of them showed a correct JND but in a reversed pattern (i.e., they were  
31 confounding the response keys using them in the opposite way), so the scores were  
32 corrected and included in the analyses. The other two participants (from the right frontal  
33 group) were excluded from the subsequent analyses because they showed a poor  
34 temporal resolution (i.e., their JNDs fell outside the range of foreperiods tested in the  
35 study). Therefore, the sample for this task consisted of 8 right frontal patients, 5 left  
36 frontal patients and 15 control subjects.  
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PLEASE INSERT FIGURE A.1 ABOUT HERE  
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In order to perform the full analysis combining short and long standard durations, absolute JND and PSE scores were transformed to percentages relative to the duration of each standard. With percentages scores, PSE means overstimulation of the comparison interval when the score is higher than 100% and understimulation of the comparison interval when it is lower than 100%. JNDs and PSEs scores were submitted to a 3 (Group: Right frontal, Left frontal, Control) x 2 (Standard duration: short vs. long) mixed analyses of variance (ANOVA) with the first variable as a between participants factor and the other as a within participants variable.

## 1.2. Temporal Order Judgment Task

### *1.2.1. Stimuli and Procedure*

In this task, the participants were to indicate at which side, left or right, a stimulus appeared first. The fixation point consisted of a dark gray cross ( $0.04^\circ \times 0.04^\circ$  of visual angle at a viewing distance of 60 cm) presented at the centre of the screen, as well as two empty dark gray squares ( $2.10^\circ \times 2.10^\circ$ ) placed on the left and right of the fixation point ( $6.58^\circ$  from fixation point to the internal border of each square). Two red rings ('O') appeared on the screen ( $1.05^\circ \times 1.05^\circ$ ), one in the middle of the left square and the other in the middle of the right square. The 'Z' and 'M' keys on the keyboard were used to indicate that the left or right ring appeared first, respectively. All the participants were instructed to keep their gaze on the centre of the screen, as well as to respond



1 accurately and without time limit. Each trial began with the fixation point presented for  
2 a random interval ranging between 500 and 1000 ms. Next, one of the rings appeared  
3  
4 either at left or right side of the fixation point, and after a variable interval of 17, 34, 50  
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6 or 100 ms, the other ring appeared on the other side. The two rings remained on the  
7  
8 screen until the participant made a response. The next trial started after the participant's  
9  
10 response.  
11  
12

13 The task included 4 experimental blocks with 48 trials each. Each block was divided  
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15 into 24 trials (6 for each interstimuli interval) where the ring on the left appeared first  
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17 and 24 trials where the ring on the right was first, presented in random order.  
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### 25 *1.2.2. Design and Analyses of Behavioural Results*

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27 Data from this task are also plotted as S-shaped curve, in which the proportion of 'right  
28  
29 first' responses is plotted as a function of target durations. A conversion to Z scores  
30  
31 were performed in order to obtain a linear regression. The JND and PSE were calculated  
32  
33 for each participant. In this task, three participants (two from the right frontal group and  
34  
35 one from the left frontal group) were excluded due to a poor temporal resolution (i.e.,  
36  
37 their JNDs fell outside the range of foreperiods tested in the study). Therefore, the  
38  
39 sample consisted of 8 right frontal patients, 4 left frontal patients and 15 control  
40  
41 subjects. Positive PSE values meant a right side bias (i.e., a tendency to respond "right  
42  
43 first") and negative PSE values meant a left side bias. The groups were compared using  
44  
45 a single-factor ANOVA for JND scores (PSE scores were not analyzed because they  
46  
47 were not informative about the participants' timing performance), with the Group  
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49 (Right frontal, Left frontal, Control) as between participants factor.  
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### 59 **1.3. Minutes Estimation Task**

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### *1.3.1. Procedure*

At the beginning of each task, participants were informed that at certain times of the experiment they would be asked to estimate the time elapsed since the exact moment they were reading the instructions. They were instructed to keep track of time just with their “internal clock”, and therefore they took off watches and mobile phones. Subjects had to estimate the passage of time twice (at the middle and at the end of the task) since the estimation was performed every two blocks of trials. A message appeared on the screen which asked participants to estimate the minutes since the beginning of the task and to type the number using the number keypad. After confirming their answers, participants could make a break before continuing with the task.

### *1.3.2. Design and Analyses of Behavioural Results*

Each response made in the range of minutes was transformed to the range of seconds. That score was subtracted from the actual time elapsed since the beginning to the two estimation moments (at the middle and at the end of the task), thereby obtaining a temporal estimation bias for each moment in each task. A positive temporal bias meant overestimation of time and negative temporal bias meant underestimation of time. Since the duration of each task was different, the absolute scores were converted to percentages. A 3 (Group: Right frontal, Left frontal, Control) x 2 (Estimation moment: first vs. second) mixed analyses of variance (ANOVA) for each temporal task was performed, with the first variable as a between participants factor and the other as a within participants variable.

## **2. Results**

### **2.1. Milliseconds Duration Discrimination Task**

Percentages punctuations were analyzed for both the Just Noticeable Difference (JND) and the Point of Subjective Equality (PSE) scores. These data are shown in Table A.1 (as well as in Table 5 of the main text).

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PLEASE INSERT TABLE A.1 ABOUT HERE  
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In the JND analysis, a main effect of group was observed,  $F(2,25)=3.48$ ,  $p=0.046$ ,  $\eta p^2=0.21$ , with a highest JND in the right frontal group (23.2%) followed by the left frontal group (18.9%) and controls (13.3%). Planned comparisons revealed significant differences between right frontal and control groups ( $F(1,25)=6.72$ ,  $p=.015$ ), but not between left frontal and controls ( $F(1,25)=1.54$ ,  $p=.225$ ). There was a main effect of the Standard duration,  $F(1,25)=6.70$ ,  $p=0.015$ ,  $\eta p^2=0.21$ , showing a worse temporal judgment in the short duration (21.4%) than in the long duration (15.5%). The interaction between Group and Standard duration was not significant,  $F<1$ .

In the PSE analysis, there was no main effect of Group,  $F<1$ . A main effect of Standard duration was observed,  $F(1,25)=8.18$ ,  $p=0.008$ ,  $\eta p^2=0.25$ , showing overestimation temporal bias in the short duration (100.9%), while subestimation in the long duration (93.1%). The interaction between Group and Standard duration was significant,  $F(2,25)=3.84$ ,  $p=0.035$ ,  $\eta p^2=0.23$ . In planned comparisons, marginally significant differences were observed between right frontal and control groups only in the short standard duration,  $F(1,25)=4.08$ ,  $p=0.054$ , but not in the long duration,  $F<1$ . There were no differences between left frontal and controls in none of the durations, both  $F_s<1$ . See Figure A.2.

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PLEASE INSERT FIGURE A.2 ABOUT HERE  
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## 2.2. Temporal Order Judgment Task

Absolute JND scores were analyzed. These data are presented in Tabla A.1 (and Table 5 of the main text). A main effect of group was observed,  $F(2,24)=3.92$ ,  $p=0.033$ ,  $\eta^2=0.24$ , with the highest JND in right frontal group (52 ms) followed by the left frontal group (42 ms) and controls (29 ms). Planned comparisons showed significant differences only between right frontal and control groups,  $F(1,24)=7.64$ ,  $p=0.010$ , but not between left frontal group and controls,  $F(1,24)=1.41$ ,  $p=0.247$ . See Figure A.3.

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PLEASE INSERT FIGURE A.3 ABOUT HERE  
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## 2.3. Minutes Retrospective Estimation Task

Percentage punctuations of temporal estimation bias are represented in Table A.2 (and Table 5 of main text) and were analyzed for each task.

Regarding the Milliseconds Discrimination Task, a main effect of Estimation moment was observed,  $F(1,27)=7.97$ ,  $p=0.008$ ,  $\eta^2=0.23$ , showing a larger temporal bias in the second moment (-25.2%) than in the first moment (-14.5%). The interaction between Group and Estimation moment almost approached significance,  $F(2,27)=2.80$ ,  $p=0.078$ ,  $\eta^2=0.17$ . When the right frontal group was compared to controls, there were

marginally significant differences at First moment of estimation,  $F(1,27)=3.97$ ,  $p=0.055$  (i.e., overestimation). There were not differences between left frontal and control groups in none of the moments, both  $F<1$ . See Figure A.4.

In the Temporal Order Task a main effect of Group was observed,  $F(2,27)=4.14$ ,  $p=0.027$ ,  $\eta^2=0.23$ , with a larger temporal bias in the Right frontal group (114.6%) compared to both left frontal (3.9%) and control (-3.9%) groups. There was a main effect of Estimation moment,  $F(1,27)=7.12$ ,  $p=0.012$ ,  $\eta^2=0.21$ , with larger overestimation at the First moment (51.1%) compared to the Second (25.3%). Finally, in this task there was a significant interaction between Group and Estimation moment,  $F(2,27)=4.11$ ,  $p=0.027$ ,  $\eta^2=0.23$ . Planned comparisons showed the right frontal group showed significant differences with controls in both the first and second estimation moment,  $F(1,27)=7.98$ ,  $p=0.008$  and  $F(1,27)=7.06$ ,  $p=0.013$ , respectively. Specifically, right frontal patients overestimated at both the first (144%) and the second (85.1%) moment, while the control group showed a negligible underestimation at both the first (-2.1%) and second (-5.9%) moments. Left frontal group did not show any difference with controls, both  $F<1$ . See Figure A.4.

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Regarding the Symbolic Cued Task, there was a main effect of Group,  $F(2,27)=4.37$ ,  $p=0.022$ ,  $\eta^2=0.24$ , with an overestimation bias in the Right frontal group (75.3%) followed by control (9.7%) and left frontal (-17.5%) groups. The main effect of Estimation moment was not significant,  $F<1$ , although tended to depend of Group,

1  $F(2,27)=3.25$ ,  $p=0.054$ ,  $\eta^2=0.19$ . Planned comparisons showed that differences  
2 between the right frontal group and controls were significant in both the first and second  
3 estimation moment,  $F(1,27)=6.45$ ,  $p=0.017$  and  $F(1,27)=4.88$ ,  $p=0.035$ , respectively;  
4 however left frontal group did not differ with respect to controls, both  $ps>0.300$ . See  
5 Figure A.5.  
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11 Finally, in the Rhythm Cued Task, there was a main effect of Group,  $F(2,25)=3.63$ ,  
12  $p=0.041$ ,  $\eta^2=0.22$ . Again the right frontal group showed an overestimation bias  
13 (24.0%) compared to the underestimation bias in both left frontal (-36.1%) and control  
14 (-19.9%) groups. Neither the main effect of Estimation moment nor the interaction  
15 between Group and Estimation moment were significant,  $F(1,25)=3.00$ ,  $p=0.095$ ,  $\eta^2$   
16  $=0.10$  and  $F(2,25)=1.16$ ,  $p=0.327$ ,  $\eta^2=0.085$ . Planned comparisons showed significant  
17 differences between right frontal and control groups in both estimation moments,  
18  $F(1,25)=5.15$ ,  $p=0.032$  and  $F(1,25)=4.49$ ,  $p=0.044$ , respectively; left frontal group did  
19 not show any difference compared to controls in any estimation moments,  $ps>0.300$ .  
20 See Figure A.5.  
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## Appendix A

### Figure legends

Figure A.1 Mean proportion of 'longer' responses as a function of duration intervals for right frontal (diamonds), left frontal (squares) and control (triangles) groups. Top. Short duration interval (350 ms). Bottom. Long duration interval (1350 ms). Note that the psychometric function showed a softer slope for the right frontal group, which means poorer temporal discrimination.

Figure A.2 Millisecond Duration Discrimination task. Percentage of JND (*top*) and PSE (*bottom*) scores as a function of group (right frontal, left frontal and control groups) for the short standard duration (grey bars) and the long standard duration (white bars). Error bars represent the standard error of the mean. Asterisks mean significant effect.

Figure A.3 Temporal Order Judgement task. Absolute JND score as a function of group (right frontal, left frontal and control groups) for the short standard duration (grey bars) and the long standard duration (white bars). Error bars represent the standard error of the mean. Asterisks mean significant effect.

Figure A.4 Minutes Retrospective Estimation Task for explicit timing tasks, i.e. Milliseconds Duration Discrimination Task (*top*) and Order Temporal Judgement Task (*bottom*). Percentage of estimation bias as a function of group (right frontal, left frontal and control groups) for the first moment (grey bars) and the second moment of estimation (white bars). Error bars represent the standard error of the mean. Asterisks mean significant effect.

Figure A.5. Minutes Retrospective Estimation Task for implicit timing tasks, i.e. Symbolic (*top*) and Rhythm Cued Tasks (*bottom*). Percentage of estimation bias as a function of group (right frontal, left frontal and control groups) for the first moment (grey bars) and the second moment of estimation (white bars). Error bars represent the standard error of the mean. Asterisks mean significant effect.



APPENDIX A

Table A.1 Absolute (Abs.) and percentage (%) punctuations of Just Noticeable Difference (JND) and Point of Subjective Equality (PSE) for both Milliseconds Temporal Discrimination Task (left) and Temporal Order Judgment Task (right). In milliseconds discrimination task, the punctuations are broken down by Interval (short vs. long).

	Milliseconds Temporal Discrimination Task								Temporal Order Task	
	Short Interval-350				Long Interval-1350					
	JND Abs.	JND %	PSE Abs.	PSE %	JND Abs.	JND %	PSE Abs.	PSE %	JND Abs.	PSE Abs.
Right Frontal	90.8	25.9%	375.5	107.3%	275.3	20.4%	1201.2	89.0%	52.6	45.3
Left Frontal	81.9	23.4%	341.4	97.5%	193.9	14.4%	1320.3	97.8%	41.9	-14.9
Control	52.4	15.0%	342.3	97.8%	157.3	11.6%	1249.4	92.5%	28.8	0.3

Table A.2 Absolute and percentage (%) punctuations of Retrospective Estimation in Minutes per each Time Estimation and Temporal Preparation tasks, broken down by Moment of estimation (first vs. second).

		Minutes Retrospective Estimation Task							
		Time Estimation Tasks				Temporal Preparation Tasks			
		Millisecond Temporal Discrimination		Temporal Order Judgement Task		Symbolic Cue Task		Rhythm Cue Task	
		First moment	Second moment	First moment	Second moment	First moment	Second moment	First moment	Second moment
Right Frontal	Absolute (%)	90.2 (16.7%)	-77.3 (-5.7%)	397.1 (144.0%)	445.8 (85.1%)	290.6 (86.3%)	388.3 (64.3%)	97.1 (28.2%)	157.1 (19.9%)
Left Frontal	Absolute (%)	-229.8 (-37.5%)	-505.6 (-41.4%)	18.6 (11.2%)	-33.0 (-3.3%)	-107.8 (-28.3%)	-51.0 (-6.6%)	-173.2 (-28.7%)	-469.8 (-43.5%)
Control	Absolute (%)	-122.2 (-22.6%)	-292.1 (-28.3%)	-5.1 (-2.1%)	-29.5 (-5.9%)	32.1 (10.3%)	47.2 (9.0%)	-122.6 (-20.2%)	-213.0 (-19.5%)

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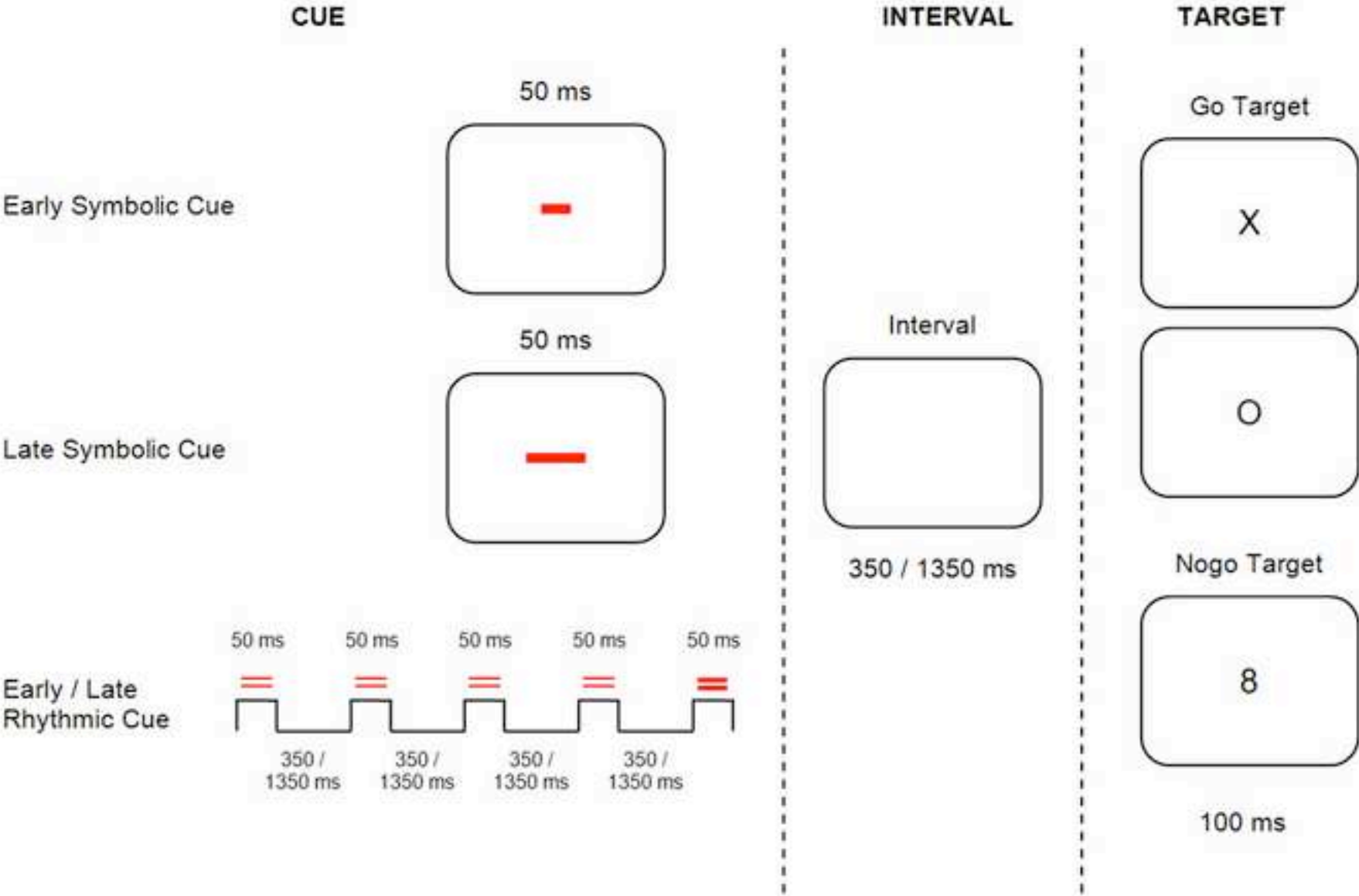


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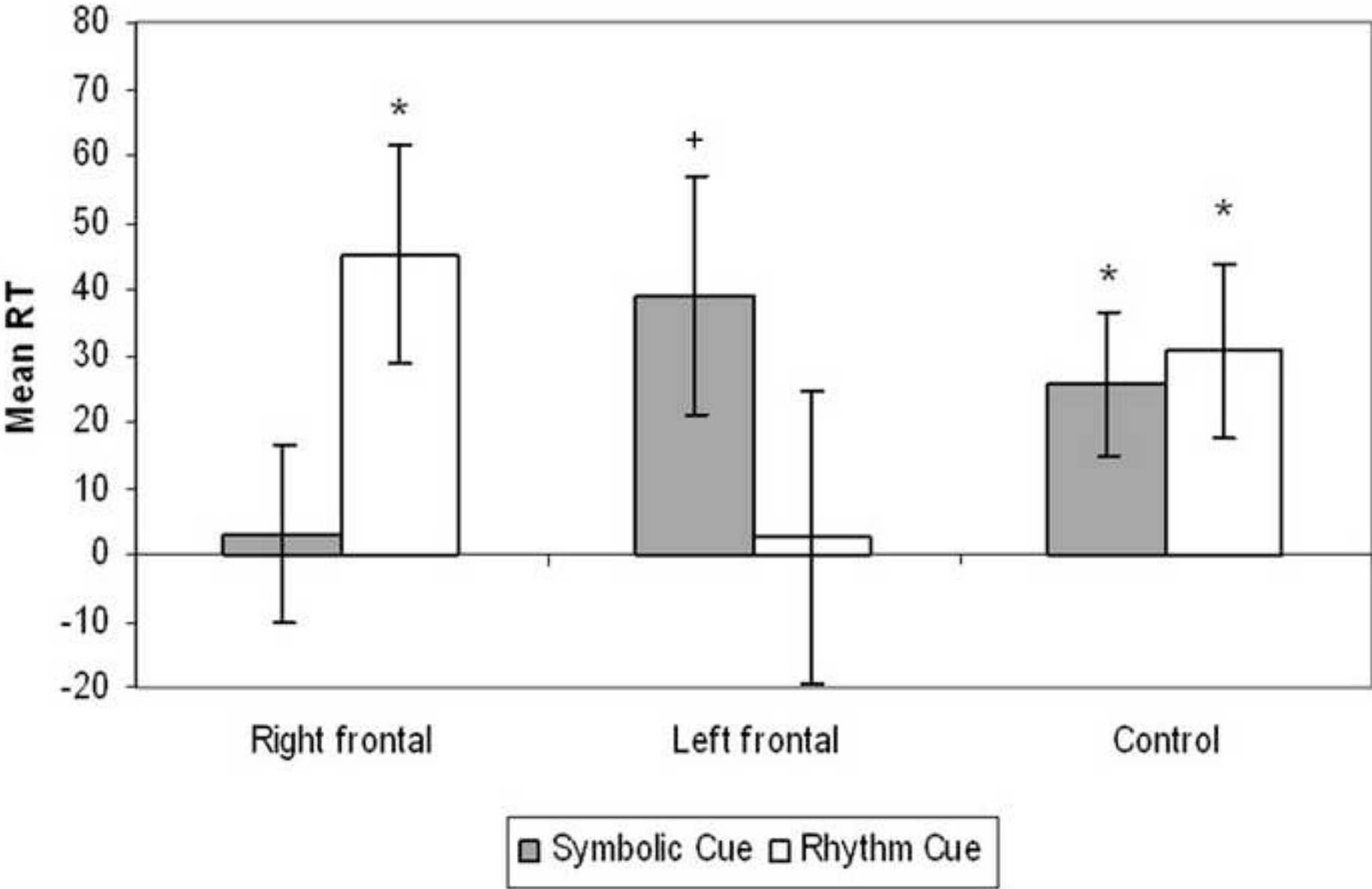


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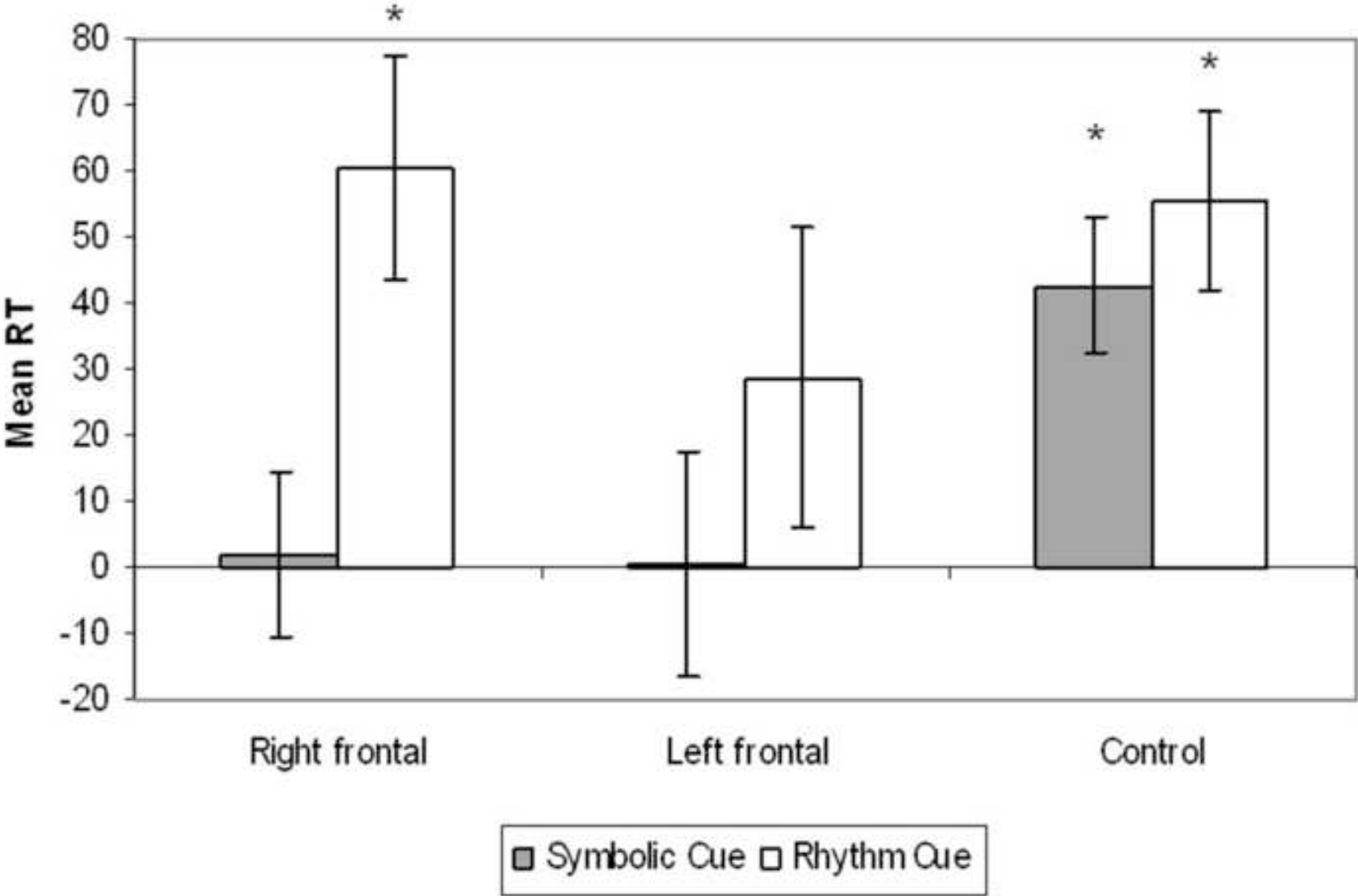


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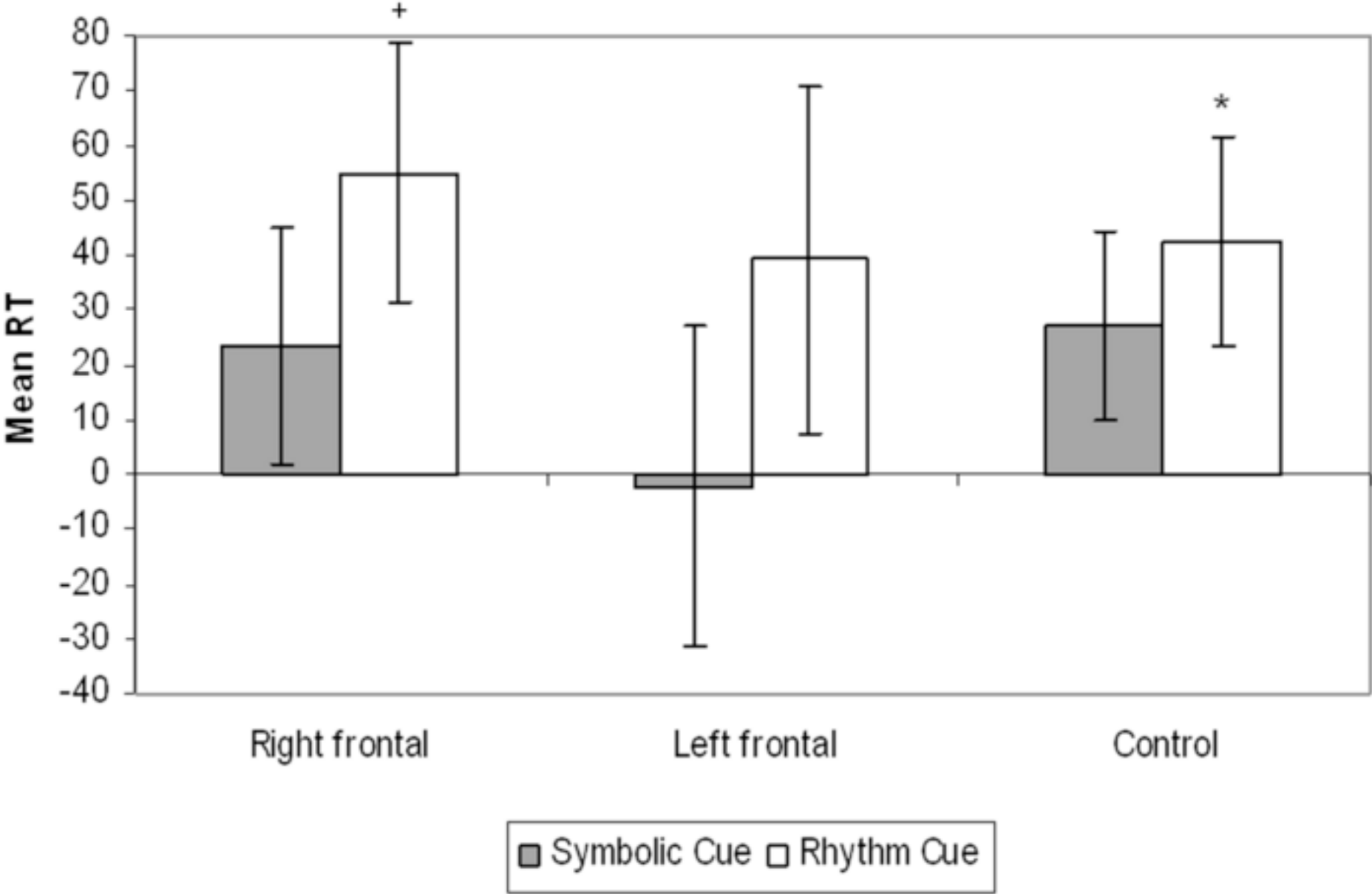
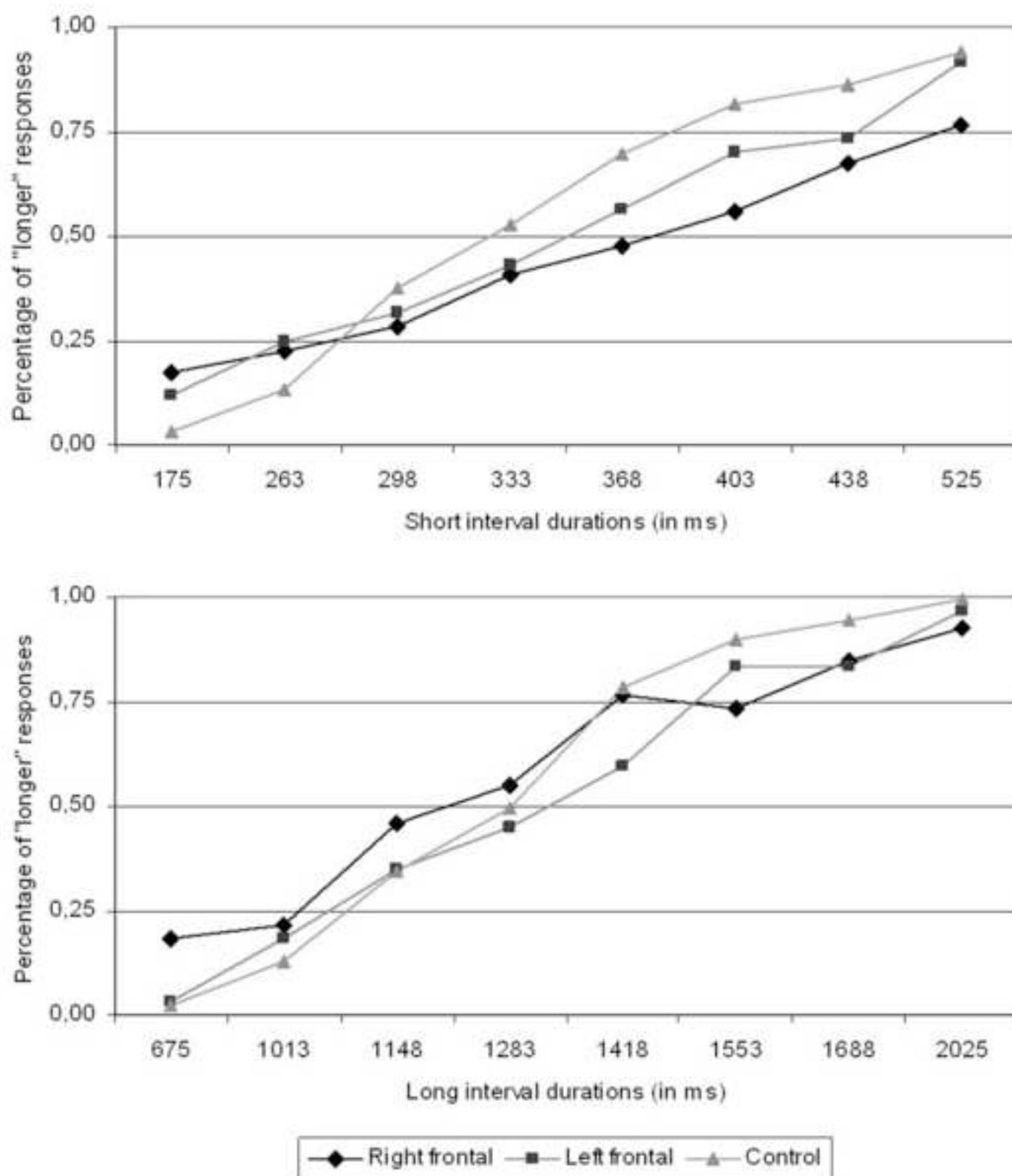
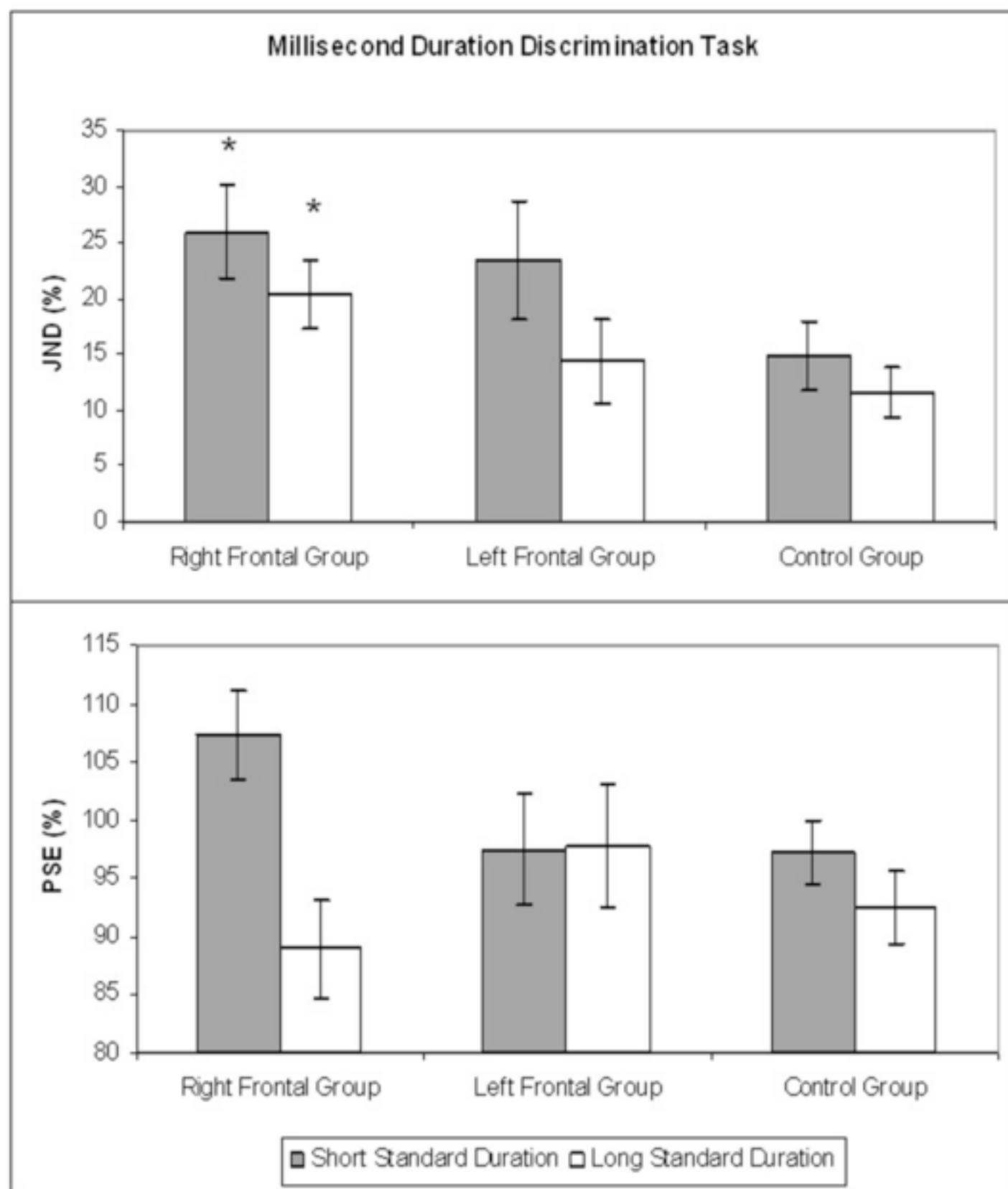


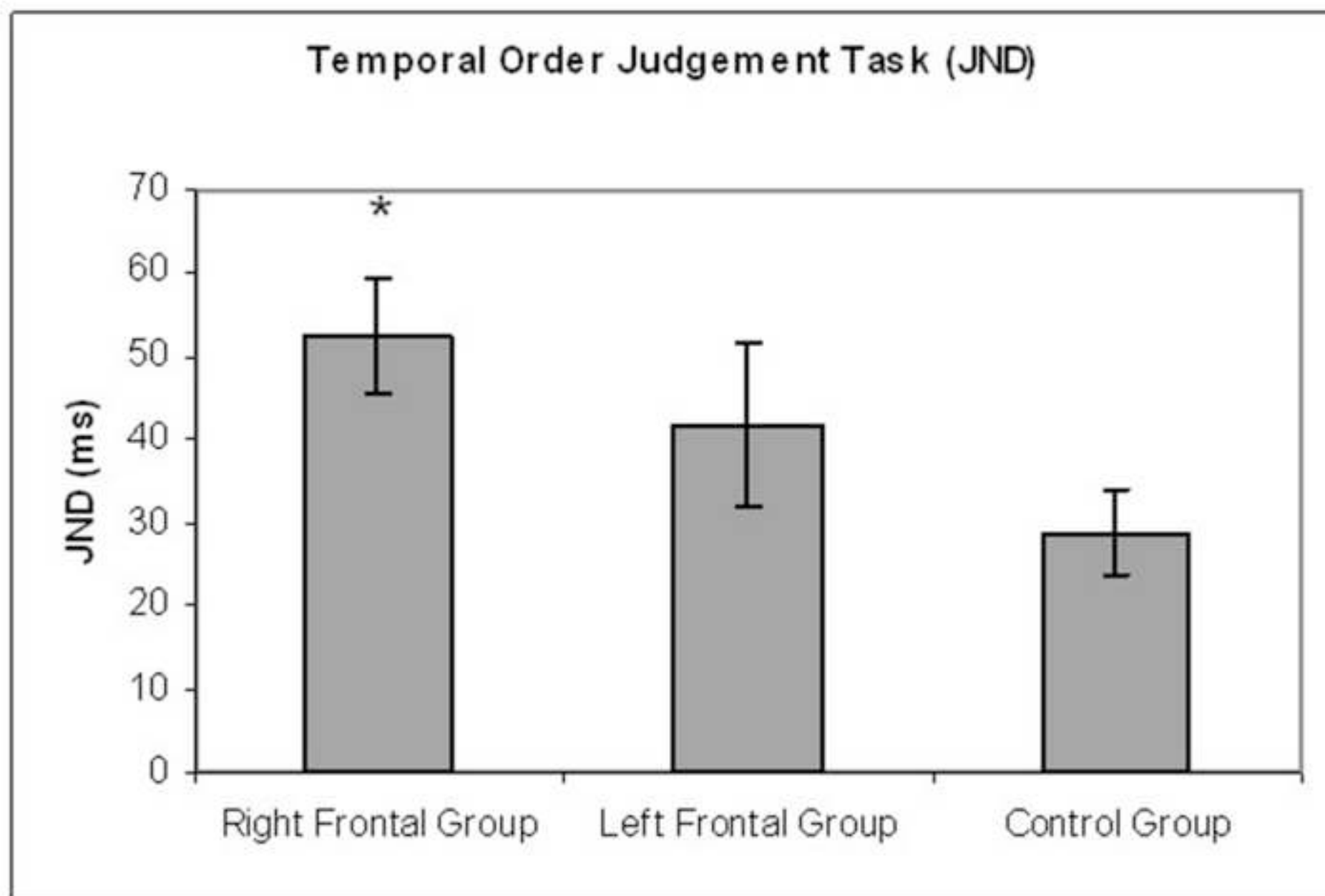
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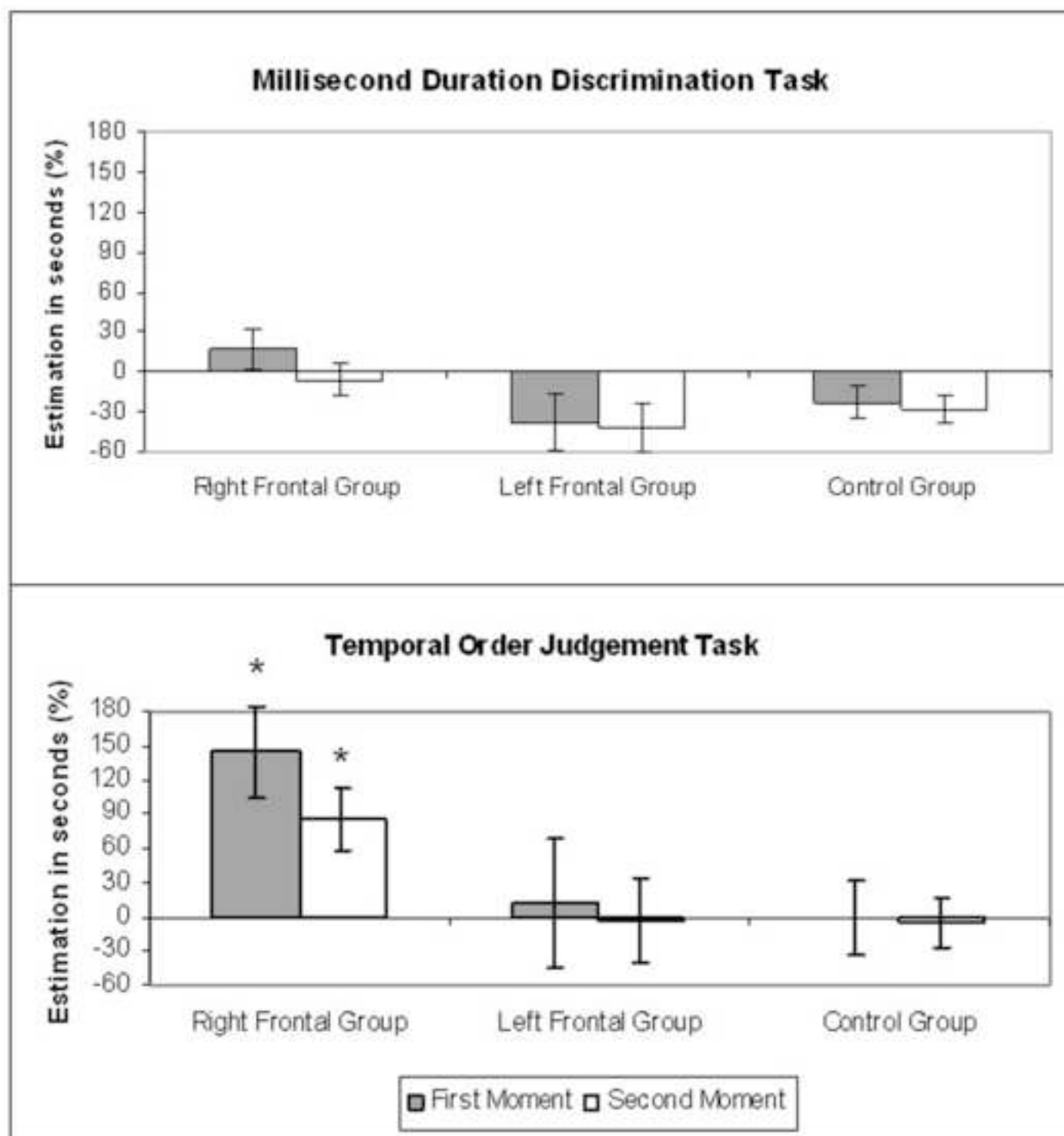


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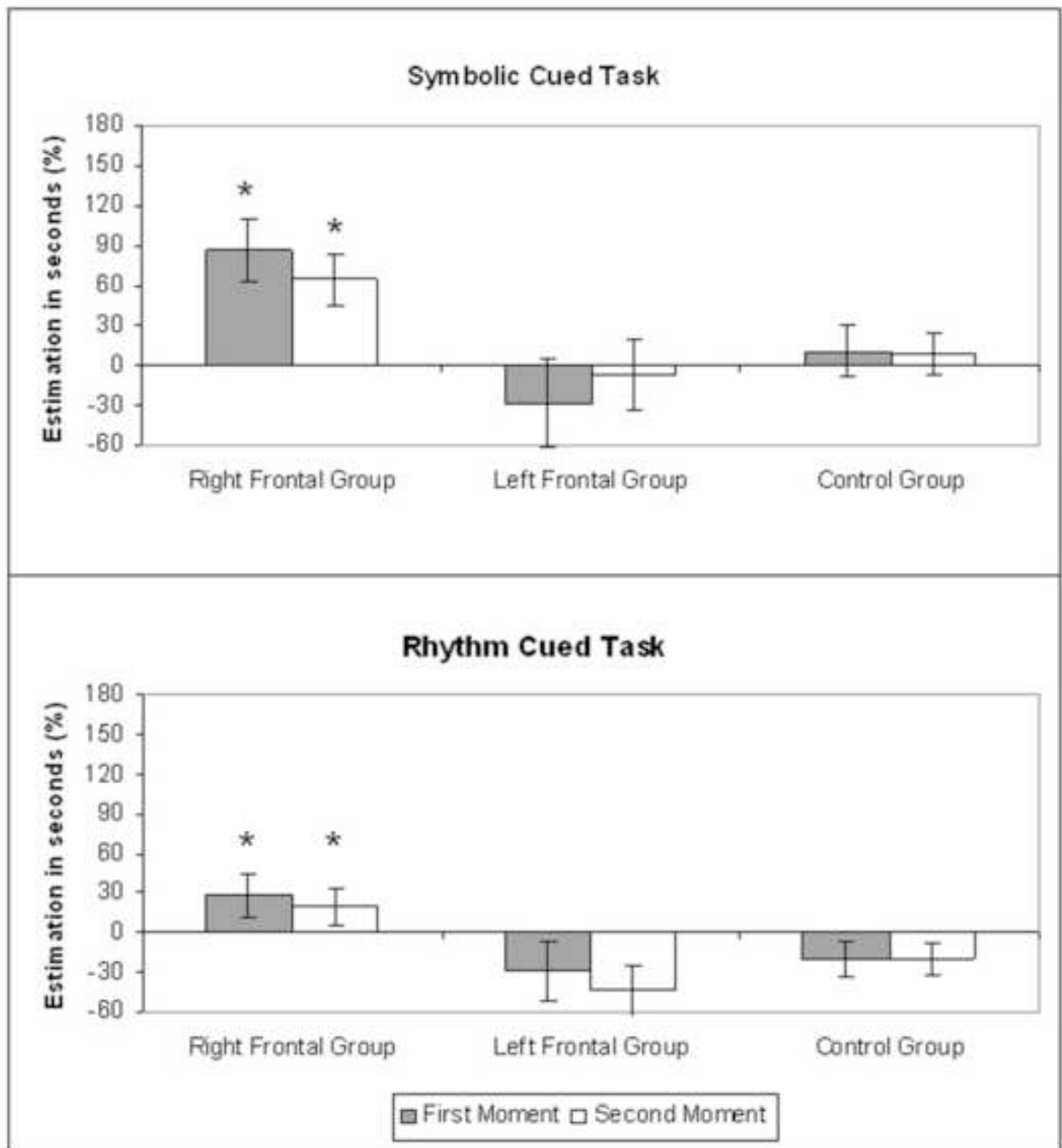




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**Figure A5**  
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