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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.

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, Correa, Arnedo, & Lupiañez, 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 explained on the basis of calculation of probabilities (Karlin, 1959; Niemi & Näätänen, 1981). That is, as time passes by and the stimulus has not appeared, subjects increase preparation because of the increasing likelihood of stimulus occurrence. The deficit in the Foreperiod effect has been related to right frontal lesion (Stuss et al., 2005; Vallesi et al., 2007), although in our previous study it was impaired in patients with either right or left frontal lesions (Triviño et al., 2010). The fact that both Temporal Orienting and Foreperiod effects are related to the proper functioning of frontal structures suggests these two effects

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rely on more evolved mechanisms, voluntary in nature, and based on top-down processing of time information (see Correa et al., 2006, for a explanation of dual-mechanism hypothesis).

1.2. Automatic temporal preparation

The finding of *Sequential effects* suggests that there are alternative ways for subjects to prepare on time that are less dependent than temporal orienting on controlled mechanisms. Sequential effects rely on the previous experiences of response preparation. As a result, subjects are faster when the foreperiod of the previous trial had the same duration or was shorter than the current foreperiod, even when the sequence of short and long preparatory intervals is completely unpredictable (Woodrow, 1914). These have been associated with automatic mechanisms of implicit timing based on trace conditioning (Los, 1996; Los & Heslenfeld, 2005; Los & Van den Heuvel, 2001).

Sequential effects have been dissociated from Temporal Orienting and Foreperiod effects in behavioural and electrophysiological studies (Correa et al., 2004, 2006; Los & Heslenfeld, 2005; Los & Van den Heuvel, 2001), as well as in neuropsychological studies, where Sequential effects were not impaired after frontal damage (Triviño et al., 2010; Vallesi et al., 2007; Vallesi & Shallice, 2007). Sequential effects have not been related to a specific brain structure, although classical conditioning has been associated with more ancient structures like hippocampus (Clark & Squire, 1998) or cerebellum (Kalmbach, Ohyama, Kreider, Riusech, & Mauk, 2009).

The fact that automatic mechanisms for temporal preparation are preserved after frontal damage is of special interest here, when considering the possibility of using this form of preparation to improve the performance of patients. In fact, rhythmic patterns can induce temporal preparation automatically (Jones, Moynihan, MacKenzie, & Puente, 2002; Large & Jones, 1999; Rohenkohl et al., 2011; Sanabria, Capizzi, & Correa, 2011). Rhythmic contexts have been related to an enhancement in temporal discrimination tasks when the standard duration ended on predicted time compared to durations that ended earlier or later (McAuley & Jones, 2003). This pattern of improvement has been named an *expectancy profile* (Barnes & Jones, 2000), which resembles the expectation effects observed in the Temporal Orienting paradigm (Correa & Nobre, 2008; Griffin, Miniussi, & Nobre, 2001).

Therefore, cueing time by means of rhythmic patterns seems to enhance implicit timing, which benefits performance in temporal preparation tasks. Given that automatic implicit timing mechanisms are presumably preserved after frontal damage, we should expect an improvement in temporal preparation in these patients when a rhythm is used as temporal cue. However, to our knowledge there are no studies about temporal preparation guided by rhythms in frontal patients (but see Praamstra & Pope, 2007, for a study in Parkinson Disease). Thus, the main aim of this study was to test the effectiveness of regular rhythms to induce temporal preparation in right frontal patients, who show deficit in controlled temporal orienting.

We designed a simple and short task, based on our previous studies (Correa, Miró, Martínez, Sánchez, & Lupiáñez, 2011; Correa, Triviño, Pérez-Dueñas, Acosta, & 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 min) 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, & Kischka, 2004; Mimura, Kinsbourne, & O'Connor, 2000; Nichelli, Clark, Hollnagel, & Grafman, 1995) as well as an underproduction and an accelerated interval reproduction in the range of seconds (Berlin et al., 2004, 2005; Mimura et al., 2000). Therefore, if a patient with frontal damage tends to overestimate the passage of time and believes that a given interval (e.g. 1000 ms) would end before (e.g. at 800 ms) it really ends, we could expect that this patient uses that distorted information implicitly in the task of temporal preparation. That is, time overestimation will lead to premature preparation and responses.

Alternatively, one can expect no influence of distortions of explicit time estimation upon the performance during implicit temporal preparation tasks, according to the literature considering explicit and implicit timing to be independent processes (Coull & Nobre, 2008; Lewis & Miall, 2003; Zelaznik, Spencer, & Ivry, 2002). However, although it is generally agreed that time perception is fundamental for temporal orienting (e.g., Coull & Nobre, 1998), there are no studies, to our knowledge, testing directly the role of time perception accuracy in temporal orienting.

Therefore, we measured explicit timing in the range of milliseconds and minutes with a Duration Discrimination Task and a Temporal Order Judgment Task. We expected frontal patients to show abnormal temporal estimation as has been described in the literature, i.e. time overestimation. The analysis of correlations between the performances in explicit and implicit timing tasks should inform us about the relationship between these two processes.

2. Method

2.1. Participants

Fifteen subjects with a frontal brain lesion and 15 neurologically intact subjects participated in the study. All the patients had suffered an acute lesion leading to cognitive dysfunction (14 due to a traumatic brain injury and 1 due to an anterior cerebral artery stroke). Radiological reports describing the location and extension of the damage are presented briefly in Table 1 and in a greater extent in the supplementary material. In addition, we had access to PET-CT and MRI images of nine patients which have also been included in the supplementary material. Prior to the lesion, they were functionally independent, had no neurological or psychiatric disorders, and had normal intellectual level. They were divided into two different groups according to the lesion lateralization, so that there was a group of 10 patients with right frontal lesion and another group of 5 patients with left frontal lesion. Unfortunately, the Rhythm Cued Task could not be administered to a right frontal subject. Each patient was matched in age, sex and years of education with a control subject, see Table 1.