RESEARCH PAPER

Acta Neurobiol Exp 2019, 79: 193–204
DOI: 10.21307/ane-2019-0017

since 1928
ACTA NEUROBIOLOGIÆ EXPERIMENTALIS

N1-P2: Neural markers of temporal expectation and response discrimination in interval timing

Halil Duzcu[1,2]*, Tolga Esat Özkurt[3], Igor Mapelli[3] and Annette Hohenberger[1,4]

[1] Department of Cognitive Science, Graduate School of Informatics, METU, Ankara, Turkey,
[2] Department of Psychology, İstanbul Arel University, Istanbul, Turkey,
[3] Department of Health Informatics, Graduate School of Informatics, METU, Ankara, Turkey,
[4] Institute of Cognitive Science, Osnabrück University, Osnabrück, Germany,
** Email: halilduzcu@arel.edu.tr*

Humans use temporal regularities in their daily life to act in accordance with future events in the most efficient way. To achieve this, humans build temporal expectations and determine a template action that is in line with those expectations. In this temporal trisection study, we aimed to study the neurophysiological counterparts of temporal expectation and response discrimination. We investigated amplitude variations of early event-related potentials (ERPs) while manipulating time intervals. We measured temporal expectation-related attenuation of neural activity and response discrimination processes in N1 and P2 ERP components. Results showed that the amplitude of the N1 component was attenuated for the predicted task-relevant temporal location of a response decision. The P2 amplitude, in contrast, was enhanced for a discriminated response in comparison to a template response. The present study supports a link between the different functional associations of the N1 and P2 components within the requirements of a timing task. N1-related amplitude modulation can determine a change in expectation level during timing. The amplitude regulation of the P2 component, in contrast, explains temporal discrimination in both expected and unexpected temporal locations. In addition to expectation-related modulation, our results suggest an additional regulation of the N1 amplitude that is linked to attention. The effect was observed in instances that included a prediction error of a task-relevant temporal location for a response decision. In conclusion, our study contributes to the growing neurocognitive literature on interval timing by capturing different aspects of a timing task; namely, N1-related expectation and P2-related response discrimination processes.

Key words: temporal expectation, interval timing, N1, P2, response discrimination, attention

INTRODUCTION

Our timing ability enables us to capture temporal regularities that produce actions that are in accordance with our expectations about future events. For example, a tennis player builds temporal expectancies regarding the arrival of the ball in a tennis match. If the opponent generally sends the ball to the service line area, the tennis player's accuracy for hitting the ball would depend on a quick selection of the most suitable motor response among many the available options. In other words, a template response would be beneficial for better performance. However, occasional slice hits of the opponent targeting the area close to the net would violate temporal expectations. In this case, the necessary motor response would be different than the template response, thus requiring an additional process for an accurate action. Although this is an oversimplification of a rather complex game such as tennis, this example captures the basic relationship between temporal expectation and behavioral response requirements.

Timing ability includes a response discrimination dimension in addition to an expectation dimension,

© 2019 by Acta Neurobiologiae Experimentalis

Received 2 October 2018, accepted 4 April 2019

exeley

and the latter is linked to the temporal detection of task-relevant issues within a given task. The relevant temporal range of these processes is called 'interval timing', which can range from seconds to minutes to hours. Important cognitive processes take place in this timeframe, such as learning and memory, decision making, and conscious time perception (Buhusi and Meck, 2005). In this respect, interval timing provides a suitable framework to study expectation and response discrimination processes together in a common context. In addition to behavioral measures, electrophysiological measures have proven useful in studying cognitive processes (Nobre et al., 2007; Ng et al., 2011; Chennu et al., 2013; Getzmann et al., 2017). In this sense, event related potentials (ERPs) allow us to investigate the neurophysiological markers of sensory and cognitive events that occur during interval timing. ERPs at the offset of an interval can provide information about expectation-related and discrimination-related processes, even prior to the execution of a behavioral response. In this study, we investigated early ERPs, namely N1 and P2 components, to study the combined effects of temporal expectation and response discrimination in an interval timing task.

Timing has also been used to study the efficiency with which our neural system processes information, particularly repeated information (Matthews, 2011; Pariyadath and Eagleman, 2008; Matthews and Gheorghiu, 2016; Miller and Desimone, 1994). The 'oddball' task is a widely used paradigm in this context that provides timing-related neural response efficiency (Eagleman and Pariyadath, 2009). Neural response efficiency is based on predictive coding such that a deviant stimulus (i.e., the 'oddball') shows greater effects than a standard stimulus (for e.g., the oddball is perceived as longer; Matthews and Gheorghiu, 2016). It is possible to combine the oddball paradigm with a timing task to predict the deviance of a perceived interval from a standard interval (i.e., the 'template'). In a temporal generalization task, a standard time interval is learned by repeated presentation, as in the oddball paradigm. After learning the standard interval, however, comparison intervals are judged and used to decide whether the perceived interval is shorter or longer than the standard interval. In an application of the oddball paradigm in a temporal generalization task, Kononowicz and Van Rijn (2014) found that the amplitude of the N1P2 component in frontocentral regions changes as a function of the difference between the target and standard interval lengths. In the predictive coding framework, an event is expected to appear after a certain interval due to the repeated experience of the standard stimulus. This expectation is accompanied by a neural response suppression that allows for more efficient processing of the stimulus (Matthews 2011; Barron et al., 2016). Moreover, the appearance of a stimulus in a certain temporal window can facilitate the detection of a deviant sensory event. Processing auditory events without an explicit need of attention has a substantial role for the prediction of deviant events (Seppänen et al., 2012). Indeed, Arnal and Giraud (2012) proposed that direct access to probabilities of sensory events is not necessary for successful task performance. Previous work shows a reduction in amplitude n of the N1 component for repeated stimuli (Zhang et al., 2011), and an enhancement for repeated stimuli that are unexpected (Matthews and Gheorghiu, 2016). In a timing task with a repeated interval offset (i.e., the auditory event that determines the offset of an interval), the temporal location of the standard offset is the most probable. High negativity in the N1 component for the unexpected events (Chennu et al., 2013; Annic et al., 2014) and a suppression of the N1 for the predictable auditory events (Paris et al., 2016) are both relevant for building expectations for an interval offset during timing tasks. An approach that combines the oddball paradigm and the predictive coding framework can allow for the prediction of changes in N1 negativity within the timing context. The temporal point predicted by the timing mechanism can serve as a reference. The interval offset that corresponds with this reference interval can serve as the standard event in the time window, from the shortest to the longest interval. Therefore, any event (i.e., interval offset) that does not match with this template interval length should be perceived as a temporal oddball.

In timing tasks (e.g., temporal generalization and bisection), there can be critical temporal locations other than those provided by the sensory events. For instance, in a bisection task, participants must decide whether a comparison interval is closer to a short or long standard. The point of subjective equality (PSE) is determined by estimating the temporal location that yields an equal proportion of the two response options (i.e., short, long). In an extension of the bisection task - the trisection task, in which participants have learned three standard intervals (short, middle, long) – there is more than one PSE. That is, the first PSE would be located between 'short' and 'middle' responses and the second PSE would be between 'middle' and 'long' responses. Although the PSE is not a sensory event like the interval offset, temporal expectation can function as a similar internal reference point (Allan, 1999; 2002; Allan and Gerhardt, 2001). Although this reference point may not be directly accessed for response decisions, it is utilized for task performance. Moreover, a reference point that is predicted by the timing mechanism can be helpful for updating future expectations. For instance, Coull (2009) proposed a hazard function model that takes into account delayed events when updating temporal expectations. In this model, updating is reflected by activity of the supplementary motor area (SMA), a brain region that is sensitive to the results of expectation-related computations. Conditional probabilities increase with elapsing time and facilitate the preparation of the required motor responses. Temporal expectations are also updated through these probabilities.

In a temporal bisection or trisection task, a standard interval or a task-relevant temporal point such as a PSE is expected by participants. However, this temporal point might not be sufficient to produce a behavioral response. A comparison between the template and the experienced duration is necessary for timing-related decisions. Therefore, the N1 component-related regulation of expectation of sensory events should be accompanied by an evaluation that takes into account task-relevant discrimination requirements. Previous studies suggest that the prediction of a temporal location of task-relevant events facilitates detection and discrimination of stimulus properties (Coull and Nobre 1998; Correa et al., 2004; Nobre et al., 2007). For example, anterior positivity (P2a) was enhanced for detection of the target in comparison to the non-target in a visual oddball task (Potts et al., 1996). Moreover, there is evidence that regulation of frontocentral P2 is not specific to only one sensory modality (Näätänen and Picton, 1987; Rif et al., 1991; Woods et al., 1993). Rather, the P2 component is a marker for distinguishing relevant information from disrupting information (Hansen and Hillyard, 1988; Garcia-Larrea et al., 1992; Oades et al., 1996), and this occurs by inhibiting stimuli that might compete with the relevant information (Senderecka et al., 2012). In this sense, a relevant response option in a timing task would compete with other response options. Higher task relevance can be associated with a higher amount of cognitive resources spent for the relevant response. Indeed, the P2 component has been related to working memory processes (Lefebvre et al., 2005, Finnigan et al., 2011). This is in line with data showing that the P2 component is related to an attentional allocation process (Crowley and Colrain 2004; Lijffijt et al., 2009; Kornilov et al., 2014). Lijfftj et al. (2009) proposed that the P2 component may serve as a gating mechanism for some of the subsequent working memory activity. In other work, Senderecka et al. (2012) observed that successful inhibition in a stop-signal task was associated with an increase in the frontocentral P2 component. These findings suggest that greater P2 amplitude in a timing task indicates a discriminated stimulus (i.e., the offset of an interval) in terms of task relevance. In other words, an augmented P2 amplitude marks a deviance from a threshold and thus requires further processing in working memory. In a previous study, an enhancement in the P2 amplitude was attributed to task-related changes (O'Donnell et al., 1994). The relation of the frontal P2 peak to task relevance was based on target detection (Potts et al., 1996, Potts and Tucker 2001). Moreover, prior data indicate that the P2 reflects a stimulus evaluation process wherein a template in working memory is compared with sensory input (Dowman 2004). In line with this evaluation process, Getzmann et al. (2017) found that relevant stimuli in working memory have higher P2 amplitudes as compared to irrelevant stimuli.

We hypothesize that the N1 amplitude reflects an overall response discrimination, i.e., a categorization of expected and unexpected events. However, the N1 component-related amplitude regulation by interval length also determines the task-relevant temporal locations, and this works by changing temporal expectation. In line with the determination of task-relevant temporal locations by an N1-related process, we expect a further response discrimination mediated by P2 amplitude regulation. Specifically, for P2 regulation, we hypothesize that the current response template would result in lower P2 amplitude with greater elapse in time. We also expect that the current template response would change from shorter to relatively longer response options, along with increasing interval length. We expect to observe greater P2 amplitudes for responses that require a task-related change, namely, from the template response to the deviant response option(s).

Together, we hypothesized that N1 and P2 components would be associated with expectation and response discrimination, respectively, in a timing task. To test these hypotheses, we applied a temporal trisection task, which provides an appropriate basis to evaluate a wide range of intervals and expectation-related, task-relevant temporal locations. Moreover, use of a trisection experiment allows us to study dynamic changes over more than one PSE. These dynamic changes allow us to evaluate a decision process between more than two response options, and more closely parallels the types of experiences that we frequently encounter in daily life. The present study tested whether the amplitude regulations of interval offset ERPs (namely, N1 and P2 components) are associated with expectation *vs.* response discrimination. Results suggest that the N1 component is a marker of temporal expectation, whereas the P2 component indicates an increased need for working memory to discriminate between responses in a timing task. This study presents a novel finding in terms of distinguishing between temporal expectation and response requirement aspects of timing. Furthermore, this study contributes to the understanding of neural markers of dynamically changing response requirements within a timing context.

METHODS

Participants

Sixteen participants volunteered for the experiment. One participant was excluded from the analysis due to technical issues during data collection, resulting in a final sample of 15 participants (11 males, age: 27.5±4.4 years). All participants gave their written informed consent prior to their inclusion in the study. Any information that might enable the disclosure of the identity of participants was omitted. The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and approved by the Ethical Committee of Middle East Technical University.

Trisection Procedure

The experiment was divided into four blocks so that participants could have short breaks in between. The first and third block were preceded by a short training session to acquaint subjects with the different interval lengths. Five trials with standard intervals (i.e., 1440, 2200, and 3220 ms) were presented in each training session. For each trial, the onset and the offset of the interval were indicated by two tone bursts (50 ms, 440 Hz). The tones were presented via headphones. In the training blocks, a feedback indicating the interval duration ('short', 'middle' or 'long') was presented immediately after the second tone. In the experimental blocks, 9 comparison intervals were used for the trisection task: interval 1: 1440 ms, 2: 1600 ms, 3: 1782 ms, 4: 1980 ms, 5: 2200 ms, 6: 2420 ms, 7: 2662 ms, 8: 2928 ms, 9: 3220 ms. During the task, participants were instructed to decide whether the presented interval was more similar to the short, middle, or long standard interval. All interval lengths were presented randomly. Participants were asked to press one of three keys (s=short, j=middle and l=long) after they saw a question mark on the screen. While the participant's left hand was used to indicate short responses, the right hand was used for the other two response options. To eliminate possible movement-related artifacts, a question mark appeared after an interval sampled from a uniform distribution ranging from 1.5 s and 2.5 s (post-interval fixation). Pre-interval and post-interval fixations were consistent across both training and experimental sessions. Comparison Intervals (CIs) were determined starting from the 'middle' CI (2200 ms), and each CI was 10% shorter or longer than the previous interval. Each block included 12 trials of each CI duration, for a total of 432 (i.e., 9 × 48) experimental trials. The pre-interval fixations were sampled from a uniform distribution ranging from 1-2 s. The fixation cross remained on the screen throughout the duration of the experiment, except when the participants were required to press a key to indicate their decision (see Fig. 1A).

EEG acquisition

Electroencephalographic (EEG) activity was recorded using a 32-channel Brain Vision Analyzer system with a sampling rate of 1 KHz. Our analyses focused on N1P2 component amplitude from the frontocentral FCz electrode, given that previous studies have found SMA activity and activity at FCz during interval timing (Macar et al., 1999; Macar and Vidal, 2002; Kononowicz and Van Rijn, 2011). Vertical and horizontal electrooculogram (EOG) activity was also measured, to identify eye movement-related artifacts. Bilateral mastoids served as the reference, and ground electrodes were placed on the earlobes. The impedances were kept below 5 kΩ during recording. Pre-processing steps were done using Brain Vision Analyzer 2.0 (Brain Products GmbH). First, the data were filtered with a Butterworth filter using 0.1 Hz-low and 100 Hz-high cutoffs, with a 12 dB/oct slope and a 50 Hz notch filter. Next, horizontal eye movements and blinks were corrected using the Gratton and Coles Method (Gratton et al., 1983). Trials with excessive ocular and movement artifacts were excluded from further analysis. 67% of all trials were included in further processing, with 32-96 artifact-free trials per condition. For the analysis, we used a single trial approach to avoid the potential impact of jittering on the grand average, given that different latencies may affect estimation of ERP components (Rossion and Jacques, 2012). In our analyses, the zero-time point corresponds to the onset of the second tone (namely, the interval offset). The time windows for the N1 and the P2 amplitude were 50-140 ms and 140-300 ms, respectively. Mean amplitudes were used instead of peak values to minimize the effects of noise in a single trial analysis (Luck et al., 2000). A baseline correction was set to be the average voltage of within the 50 ms period before and after the interval offset. This type of baseline correction was suggested by previous studies to minimize misalignments due to contingent negative variation (CNV) activity before the interval offset (e.g. Kononowicz and Van Rijn, 2014; Correa and Nobre, 2008; Griffin et al., 2002). ERP components were plotted with standard error using smooth parameters of the

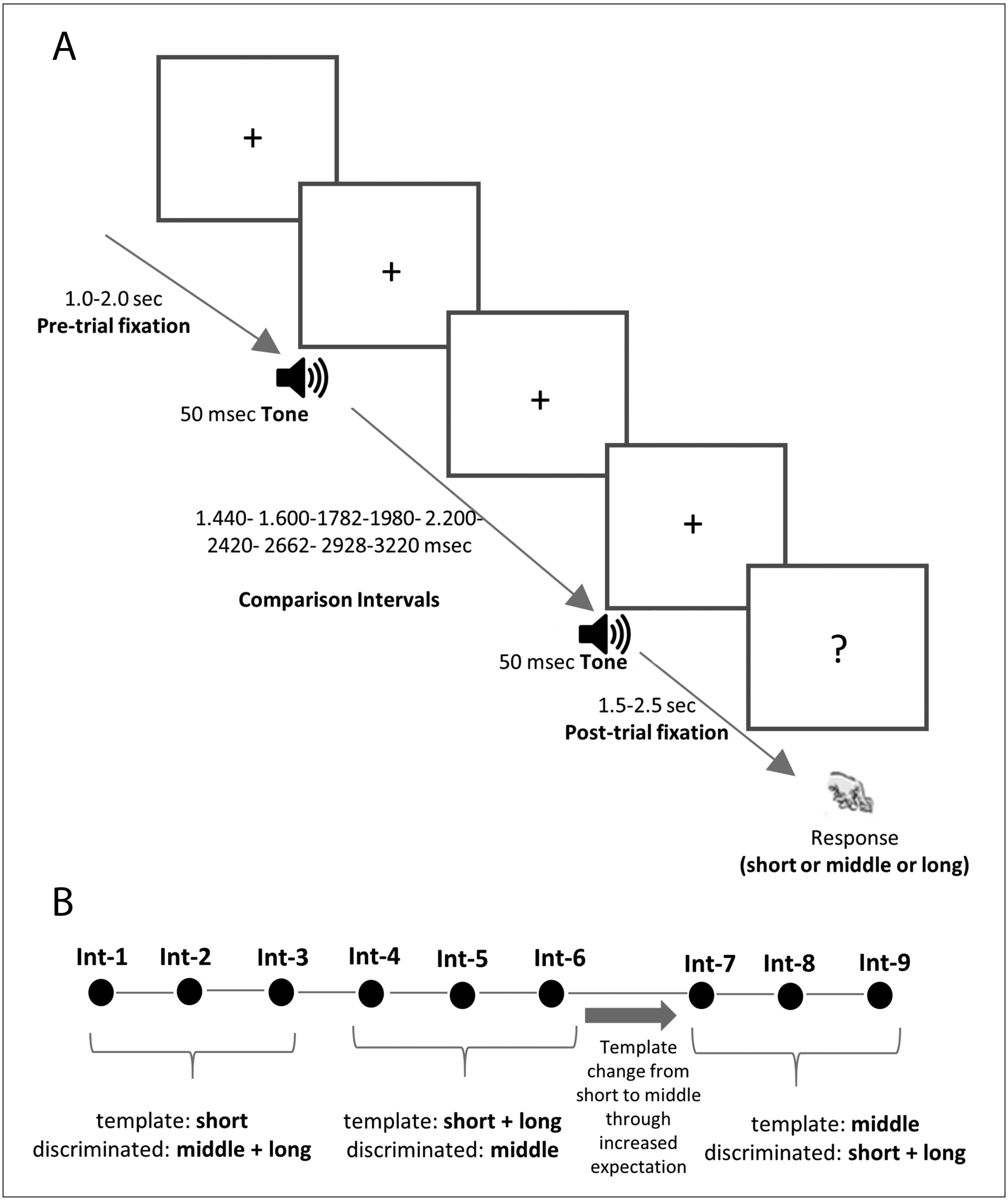

Fig. 1. (A) Experimental flow of a trial in the temporal trisection task. (B) Template responses in each interval. The template was determined to be the short response until PSE-1. In the middle range intervals, short and long responses were the two template response options, due to the ambiguity of middle responses in comparison to the other options. After the resolution of ambiguity of the middle range intervals, an increase of expectation from interval-6 to interval-7 is hypothesized. The increase of expectation changes the template response from short to middle, since the latter becomes the more appropriate template response with increasing interval length.

ggplot2 package (Wickham et al., 2018), via R numerical programming language.

Analysis method

The PSE can be defined as the point where judging a comparison interval (CI) as short or long occurs with equal probability (prob=0.5). To determine PSE, we fit our data with binomial modelling (Kingdom and Prins, 2009; Lu and Dosher, 2013; Gold and Ding, 2013) by using the response options as the binary response variables via the quickpsy package of R numerical programming language (Linares and Lopez-Moliner, 2015).

To analyze the N1 component, we performed linear mixed effect (LME) modeling. Unlike ANOVA, which considers only the group means, LME takes into account unbalanced data points for group factors. In our analyses, we used response discrimination as a factor and the number of responses was unbalanced for the same intervals. Moreover, individual trial variations in repeated measures also have valuable information that can be reflected in LME models. Model elimination was based on the Akaike information criterion (AIC) and log-likelihood-χ^2 statistics.

Determination of critical temporal locations is important for identifying discrimination-related amplitude regulation. This type of analysis requires coding of responses as discriminated or template response in different interval lengths. We hypothesize that the template response options (i.e., short, middle, long) are determined dynamically over the passage of time. Although we do not have hypotheses regarding whether or not this determination is a conscious process, there is likely a response-related efficiency process for improving performance. Increasing probability of an event with elapsing time is a part of the hazard function model (Coull, 2009) to which allow for updating of the current expectation (i.e., over the passage of time). In a traditional bisection method, determination of the template response option would be slightly more direct. In particular, the probability of the interval offset would be lower for positions closer to the interval onset. Thus, a short response is more likely to be the template response. Increasing probability of the interval offset event with elapsing time is reflected in activity in the right prefrontal cortex (PFC). Here, the interval offset corresponds to the event onset in the temporal expectation model of Coull (2009), and is reflected in SMA activity. Therefore, in the interval offset, SMA activity (i.e., activity measured at FCz) reflects the cumulative hazard function that enables participants to update their future expectations. The difference between the current expectation (i.e., increasing probability with elapsing time) and the cumulative expectation (i.e., predicted temporal location) allowed us to predict whether expectation corresponds to an actual interval offset on a single trial by evaluating activity of the SMA. Of note, evaluating the match between the predicted temporal location and the current expectation does not require an update on the future expectation. In a bisection task, in contrast, the predicted temporal location would correspond to the point where the template change occurs. In other words, the template response would be the short response until the point that is determined by the cumulative probability. However, it is still possible to experience a particular interval as longer, even if the interval length is objectively shorter than the predicted temporal location. Thus, before the predicted temporal location, any single trial experienced as long (i.e., increasing current expectation with elapsing time) can be compared to the template response option (i.e., short).

In a trisection task, the same idea of the dynamic template change is valid, even if the situation is more complicated with three response options. In this study, there are nine intervals between the shortest and longest standards. The dynamically changing template response of the timing mechanism is determined through the continuous exposure of the various interval lengths. Moreover, we should consider the fact that the learning phase of all standards was relatively brief (in terms of number of trials) in comparison to the length of the experimental session. In fact, the nature of the middle response is somewhat ambiguous, since it corresponds to a response decision that is neither the short nor the long response. Moreover, we expect a template change after the resolution of hypothesized ambiguity. This is in line with the idea that the probability of short responses decreases accordingly. Therefore, the new most probable template is the middle response option. In other words, we expect that the ambiguity of the middle response option (i.e., neither the short nor the long response) will disappear in closer proximity to the longer intervals.

Following these considerations, we determined the grouping of the template and discriminated responses as follows:

In the first three intervals (i.e., intervals 1-3), the short response is coded as the ‘template’ response. In other words, we hypothesize that the most probable response option is the short response in intervals 1-3. Thus, other responses (i.e., middle, long) are coded as ‘discriminated’ responses. In other words, any perceived length that requires processing more than the template for a relevant response is discriminated from the template. In the middle range intervals (i.e., intervals 4-6), the short and the long responses are coded as ‘template’ responses. In this interval scale, the long response becomes an available response option, given that the perceived length of an interval may correspond to a long response. Thus, the middle response is coded as ‘discriminated’, since it deviates from the two poles of the response options (i.e., short and long) in intervals 4-6. In other words, short and long responses were the two template response options due to the ambiguity of middle responses in comparison to the other options in this interval range. In the last three intervals (i.e., intervals 7-9), the middle response is coded as the ‘template’ response given that we expect the ambiguity of the middle response in the middle range intervals to disappear towards the longer intervals. In other words, the short response is not any more likely for participants to execute. Thus, it is not appropriate to use the short response option as a template after the hypothesized ambiguity of the middle response resolves. Instead, the second option in length (i.e., the middle response) suits as a template response after that point. Accordingly, the short and the long responses are coded as ‘discriminated’ responses in this interval range (Fig. 1B).

In a previous temporal generalization study, the suppressed N1P2 component was observed during the reference duration (Kononowicz and Van Rijn, 2014). In our study, this reference temporal point must emerge during the experimental session since there wasn’t only one reference but three. We hypothesize that the most likely temporal reference for decision making is interval-7. This is because interval-7 is longer than the middle range intervals, which were previously hypothesized to be ambiguous in terms of response options (Fig. 1B).

In the LME models, independent variables included interval (n=9) and response discrimination (i.e., short, middle and long responses), which was coded as either template or discriminated responses. We also examined the interaction between interval length and template term (template or discriminated) as an independent variable. We included random intercepts for participants and a random coefficient for responses. Thus, we estimated the slope of responses for each participant. We included the response discrimination term (i.e., template or discriminated response) as an independent variable in the models, despite the fact that it was a post-experimental categorical measurement. The rationale for this type of model design is to observe the difference between the categorical response options, if any, in terms of N1 or P2 amplitudes. This term is valuable to explain observed variance in N1 or P2 components that may not be explained by the objective lengths of the intervals. This is due to the fact that an interval that is objectively short can be rated as either middle or long. Moreover, we hypothesize that using a response discrimination term can distinguish the functional correlates of the N1 and P2 components[1]. For the N1 analysis, the intercept corresponded to interval-7, to compare it with other intervals. The interval length was included as a continuous variable in the P2 analysis, given our hypothesis that P2 amplitude is related to the response discrimination rather than a predicted temporal point.

RESULTS

Point of Subjective Equality (PSE)

In a trisection timing task, two bisection points were calculated for the short-to-middle and middle-to-long interval ranges (Zhang et al., 2016). We calculated the first PSE for the short and the middle response (PSE-1) using responses given in the first five intervals of the interval scale. The model estimated 1791 ms as PSE-1. The second PSE for the middle and the long response (PSE-2) was estimated using responses given in the last five intervals of the interval scale. The model estimated 2847 ms as PSE-2.

N1 analysis

For the LME model with interval and template term as factors (see Methods section), results of preliminary model-building showed that the interaction term between interval and response discrimination could be dropped from the model (ΔAIC=7; $\chi 2$=9.07, p=0.34). The absence of the interaction between the response discrimination and interval terms suggests that we can expect similar N1 amplitudes for the template and discriminated responses in interval-7. Thus, the comparison of other intervals with interval-7 can be based on an intercept that corresponds to the discriminated responses in interval-7 (i.e., the reference interval). In the final model, the effect of intercept was significant (β=-2.04, p<0.001). In particular, we found that N1 amplitude in interval-4 (β=-0.82, p=0.04), interval-5

---

[1] *Note that using response discrimination as an independent variable is a technical means to assess the relation between the N1/P2 components and subjectively perceived durations. This approach, however, does not imply a causal relationship between the two. The rationale for our design decision of including response discrimination as an independent variable and N1/P2 components as the dependent variable is twofold: First, the categorical responses given after the interval offset are linked to the subjective experience before the interval offset. Second, more practically, the categorical response variable indicates any difference regarding the N1 or P2 component more easily.*

($\beta=-1.00$, $p=0.014$), interval-8 ($\beta=-1.38$, $p<0.001$), and interval-9 ($\beta=-1.65$, $p<0.001$) was higher in comparison to the discriminated response in interval-7. Results for interval-6 did not reach significance level in terms of higher negativity than interval-7 ($\beta=-0.77$, $p=0.056$). Interval-1 ($\beta=-0.12$, $p=0.76$), interval-2 ($\beta=-0.21$, $p=0.59$), and interval-3 ($\beta=-0.11$, $p=0.78$) did not differ in their N1 amplitude from interval-7 (Fig. 3A and B). Taken together, our results did not indicate a response discrimination effect that was related to the N1 component ($\beta=-0.18$, $p=0.41$) (Fig. 2).

P2 analysis

We conducted a LME model to determine whether the discrimination-related P2 amplitude change differs in different temporal locations of the interval length scale. A LME model with interval length as a continuous variable, a second term with two levels of response discrimination (template, discriminated), and their interaction term was significantly better than the base model ($\Delta AIC=6$; $\chi 2=31.67$, $p<0.001$). Comparison of the full model with the model that did not include the interaction showed that the interaction term could be dropped ($\Delta AIC=8$; $\chi 2=0.22$, $p=0.88$). In the remaining model, the intercept corresponded to the 'discriminated' responses. Results indicated a significant main

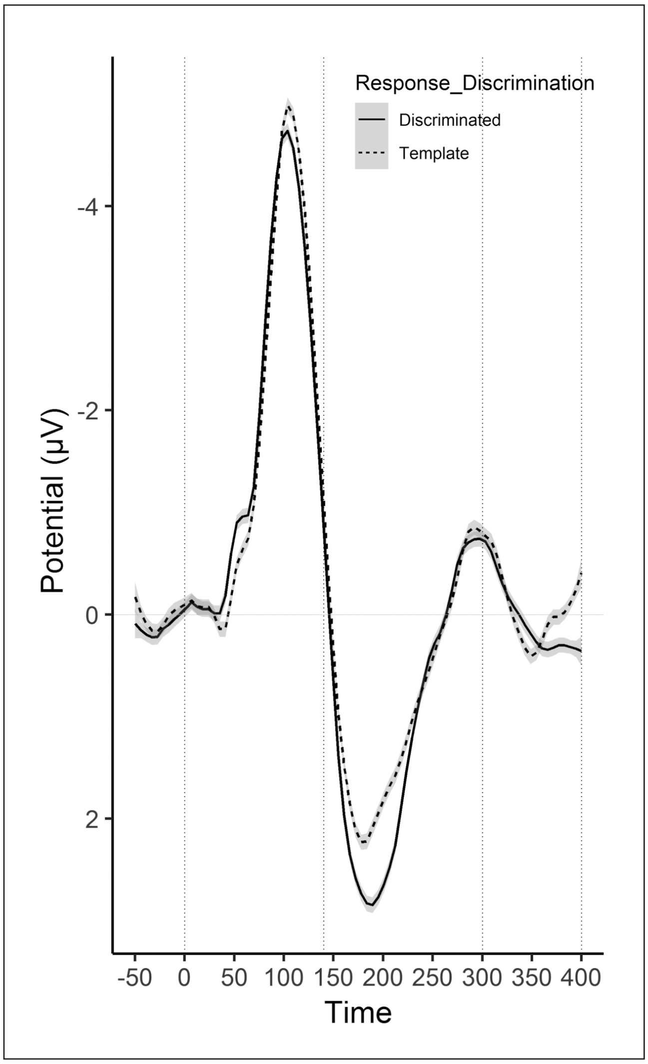

Fig. 2. Evoked potentials of the P2 component for response discrimination. P2 amplitude was higher for discriminated responses than template responses.

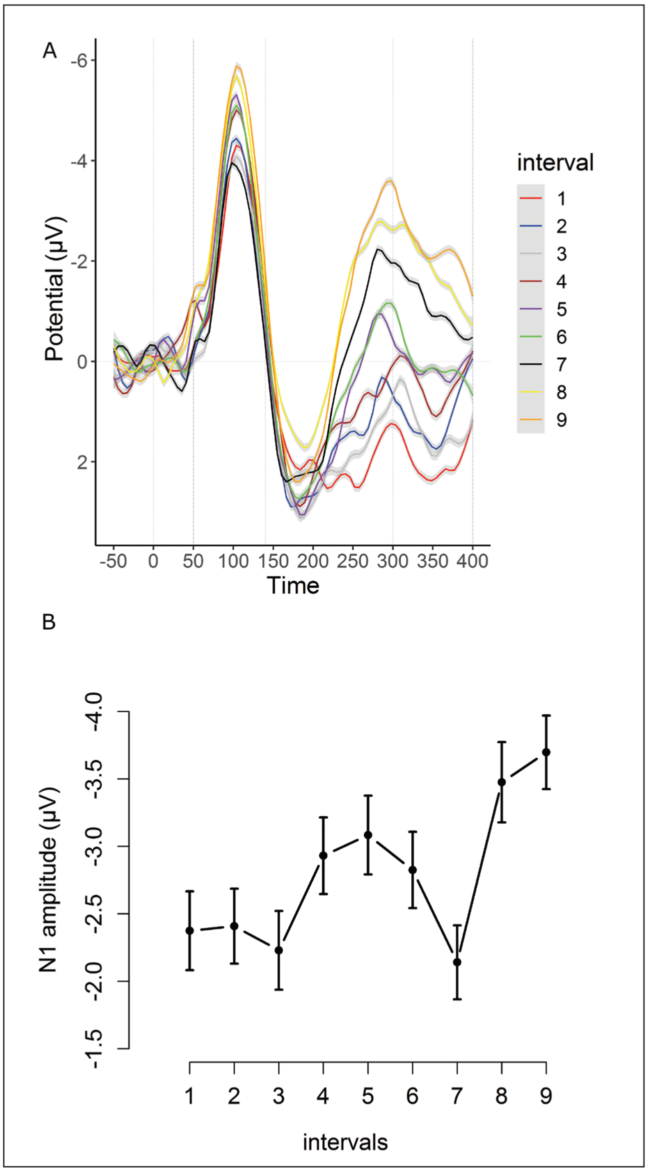

Fig. 3. (A) Interval offset auditory evoked potentials for each interval at FCz. Interval-7 showed an attenuated N1 amplitude in comparison to the intervals. (B) The average amplitude of the N1 component at the interval offset changes according to interval length. Higher temporal expectation that are associated with lower amplitudes reaches its maximum level in interval-7.

effect of intercept (β=2.70, *p*<0.01) such that P2 amplitudes were lower for 'template' responses than 'discriminated' responses (β=-0.60, *p*=0.047) (Fig. 2 and Fig. 4B). Moreover, assessment of interval length term as a continuous variable revealed that the P2 amplitude decreased as a function of increasing interval length (β=-0.33, *p*<0.001) (Fig. 4B).

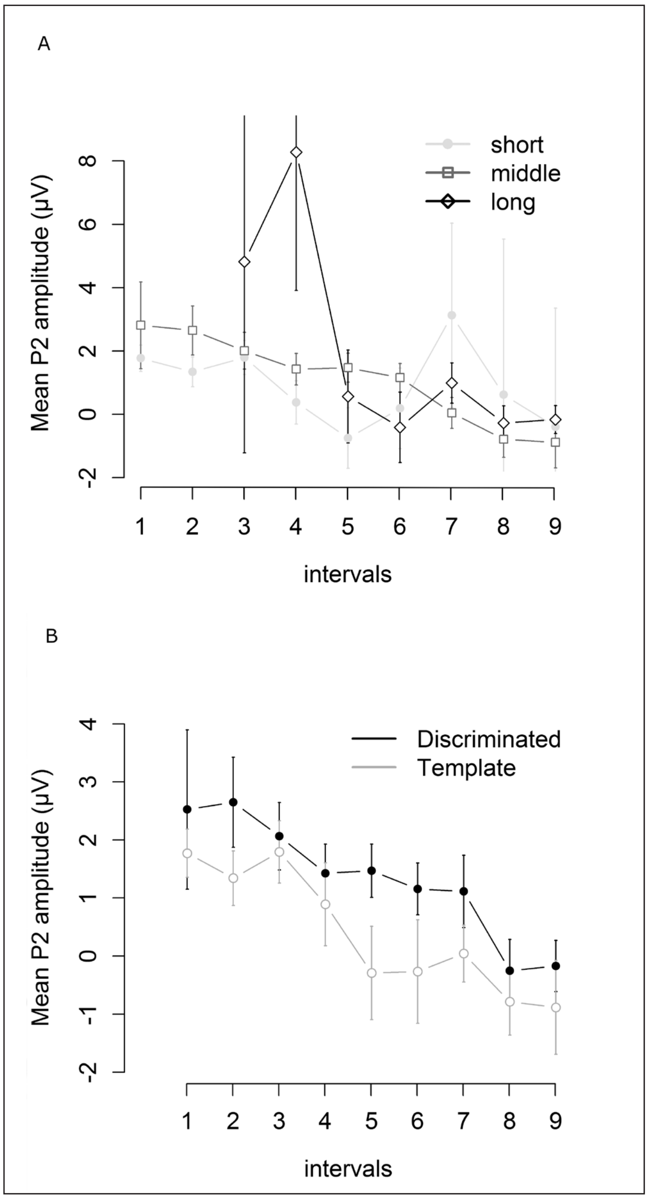

Fig. 4. (A) Average P2 amplitudes for each response in the various intervals. The short response is used as a template until the highest expectation point. The long response is used as a template after interval-3, since it becomes a potential response option in addition to the short response in intervals 4-6. The middle response is used as the template beginning with interval-7, since expectation starts to increase after interval-6 changing the template to the second response option in length (i.e., the middle response). (B) The amplitude of the P2 component at the offset of the interval shows discrimination-related regulation in each interval.

DISCUSSION

Information processing theories of interval timing (Church et al., 1984) provide a framework that distinguishes between two processes; one process keeps track of the passage of time and the second compares a currently experienced interval with a previously experienced reference interval to make a task-relevant decision/discrimination. The present study used a temporal trisection task to examine amplitude regulation in early ERPs. This approach allowed us to study two aspects of a timing task. In particular, temporal expectation and temporal discrimination are addressed by an N1-related predictive timing mechanism and a P2-related discriminative process, respectively. In N1-related amplitude regulation, expectation level determined the template change location from short to middle responses. N1 suppression indicated a decrease in the relevance of a certain response option (i.e., short) through a dynamic appropriation of the most plausible option. P2 amplitude, in contrast, reflected a comparison of the current response requirements with a pre-determined template (i.e., short, middle, long) that changed with the passage of time. Our results support the idea that the interval offset N1 component is a marker for expectation, and thus determines the threshold for temporal discrimination. In this respect, changes in the N1 amplitude at a specific point in the interval scale indicated that the participants used different expectation levels (i.e., templates) for a subsequent response discrimination. We observed an attenuation in amplitude of the N1 component after interval-6 (i.e., 2420 ms), indicating a transition point in terms of increasing probability of longer intervals. The observed N1 attenuation was largest in interval-7, and the length of interval-7 was close to the PSE of both the middle and long responses. This critical temporal location was required for deciding between the middle and long responses.

The increase in expectation level makes it possible to change the template response of the timing mechanism from one template to another. Expectation regulation enables a dynamic change of the template response over the passage of time. Thus, following the determination of a new template (i.e., the middle response) after interval-6, a P2-related discrimination process yields an enhanced amplitude for the discriminated response options (i.e., short and long responses). In this long-range interval scale, the relative contribution of the long response is expected to be higher due to the higher number of long responses. The middle intervals (i.e., interval-4-5-6), in contrast, correspond to a range that is not clearly closer to the short nor long standard. Thus, the relatively unexpected end of an interval in this range makes it possible to discriminate the middle response as the target response.

Our data support the idea that modulation of the P2 amplitude adapts to the task-relevant temporal locations. In this respect, discriminated response options had high relevance in terms of the response requirements. This finding is in line with results showing higher P2 amplitudes for relevant stimuli in working memory (Getzmann et al., 2017). Other studies have shown that working memory requirements are linked to task-relevant P2 amplitude changes (Potts et al., 1996; Potts and Tucker, 2001) and the template-sensory input evaluation (Dowman, 2004). Assuming that task relevance is high for the response requirements that differ from the template response option, a deviance from the template would correspond to different responses in different temporal locations. Our data suggest that higher P2 amplitude reflects a discrimination between a relevant response and a pre-determined template. The template change was experimentally induced by the length of the experienced duration. We found that the P2 component is lower in amplitude for relatively longer experiences of an interval (e.g. long responses in intervals 5-6) in comparison to a shorter experience of the same interval (e.g. middle responses in intervals 5-6). Thus, amplitude of the P2 component may be higher for longer subjective experiences, for e.g., long responses in intervals 7-9. The present study suggests that the P2-amplitude-related discrimination is sensitive to the N1-related prediction process for adjusting the template response option. Although we found that discrimination-related change in P2 amplitude was associated with the N1-related critical temporal locations for the template change, an increase in expectation level was not necessary for response discrimination. We observed a difference in P2 amplitude between the template and discriminated response, and this difference was not related to interval length.

Our results imply that the N1 and P2 components have different functional associations; namely, temporal expectation and response discrimination, respectively. Although N1 amplitude was not sensitive to response discrimination, the observed suppression of N1 indicated an expected temporal point that could be used to determine response requirement changes in a timing task. Indeed, this response requirement change was reflected by the P2 amplitude difference between the template and discriminated response options. Kononowicz et al. (2017) discussed a comparison mechanism of dopaminergic conditioning for the current interval and a reference duration. In this mechanism, the interval offset ERP amplitudes (e.g. N1P2) reflect the degree of temporal deviance from a reference duration. This mechanism was found to be valid for both shorter and longer comparison intervals relative to a standard interval (Kononowicz and Van Rijn, 2014; Mento et al., 2013; Van Wassenhove and Lecoutre, 2015). Our results indicated a similar pattern, but for the N1 component. While interval-7 had the lowest N1 amplitude, N1 amplitude was higher for intervals that were further away from interval-7 in both directions. In the light of these results, we propose that the N1 amplitude reflects a computational outcome of the timing process that determines whether an event occurs earlier or later than the expected temporal point. Therefore, temporal deviance provides information about the temporality of events without reference to whether the events occurs earlier (intervals 4-6) or later (intervals 8-9) than the expected temporal point. However, another process is necessary for an update of the most likely response option within an interval. This additional process is required to ensure the efficiency of an action, while keeping track of time. In other words, although the N1 and P2 components have different functional associations - namely temporal expectation and response discrimination, respectively - there must be a link these processes to allow for the updating of response options. Indeed, we demonstrated that a low P2 amplitude reflects a template response option that requires a relatively low amount of working memory processing.

CONCLUSION

In the present study, we provide support for the hypothesis that the N1 and P2 components are neurophysiological markers of distinct functions in a timing task. In particular, our results suggest that the N1 component is related to the determination of the appropriate template response. These template responses are later used in the discrimination process. In a P2 amplitude-related discrimination process, lower amplitudes for the template response options differ from discriminated responses. Greater P2 amplitudes were observed for discriminated responses, given that these responses did not correspond with the relevant template. Based on these data, we caution that treating the N1 and the P2 components as a single component can lead to some misinterpretations. In other words, the direction of the amplitude change for the same response can be different in N1 *vs.* P2. However, the functional association of the N1 amplitude to the response discrimination should be studied in greater detail, to clarify the relationship between the N1P2 complex and timing. For instance, we were not able to observe a difference in N1 amplitude between the predicted temporal location and relatively short interval lengths. This lack of observed difference can be attributed to the absence of a N1-related amplitude expectation regulation for this interval scale, due to the relatively short intervals. Although it seems plausible, this account should be tested in a further study. Findings of the present study would be further supported by evidence of N1 regulation with three states, i.e., a base N1 amplitude, an expectation-related neural suppression, and an enhancement with unexpected events.

REFERENCES

Allan LG (1999) Understanding the bisection psychometric function. In: W. Uttal and P. Killeen (Eds.), Fechner Day 99: Proceedings of the Fifteenth Annual Meeting of the International Society for Psychophysics. Tempe: Arizona State University.

Allan LG (2002) Are the referents remembered in temporal bisection? Learn Motiv 33: 10–31.

Allan LG, Gerhardt K (2001) Temporal bisection with trial referents. Percept Psychophys 63: 524–540.

Annic A, Bocquillon P, Bourriez JL, Derambure P, Dujardin K (2014) Effects of stimulus-driven and goal-directed attention on prepulse inhibition of the cortical responses to an auditory pulse. Clin Neurophysiol 125: 1576–1588.

Arnal LH, Giraud, AL (2012) Cortical oscillations and sensory predictions. Trends Cogn Sci 16: 390–398.

Barron HC, Garvert MM, Behrens TE (2016) Repetition suppression: a means to index neural representation using BOLD? Phil Trans R Soc B 371: pii: 20150355.

Chennu S, Finoia P, Kamau E, Monti MM, Allanson J, Pickard JD, Bekinschtein TA (2013) Dissociable endogenous and exogenous attention in disorders of consciousness. Neuroimage Clin 3: 450–461.

Church RM (1984) Properties of the internal clock. Ann N Y Acad Sci 423: 566–582.

Correa A, Lupiáñez J, Milliken B, Tudela P (2004) Endogenous temporal orienting of attention in detection and discrimination tasks. Percept Psychophys 66: 264–278.

Correa A, Nobre AC (2008) Neural modulation by regularity and passage of time. J Neurophysiol 100: 1649–1655.

Coull JT (2009) Neural substrates of mounting temporal expectation. PLOS Biology 7: e1000166.

Coull JT, Nobre AC (1998) Where and when to pay attention: the neural systems for directing attention to spatial locations and to time intervals as revealed by both PET and fMRI. J Neurosci 18: 7426–7435.

Crowley KE, Colrain IM (2004) A review of the evidence for P2 being an independent component process: age, sleep and modality. Clin Neurophysiol 115: 732–744.

Dowman R (2004) The pain-evoked P2 is not a P3a event-related potential. Brain Topogr 17: 3–12.

Eagleman DM, Pariyadath V (2009) Is subjective duration a signature of coding efficiency? Philos Trans R Soc Lond Biol Sci 364: 1841–1851.

Finnigan S, O'Connell RG, Cummins TD, Broughton M, Robertson IH (2011) ERP measures indicate both attention and working memory encoding decrements in aging. Psychophysiology 48: 601–611.

Garcia-Larrea L, Lukaszewicz AC, Mauguiere F (1992) Revisiting the oddball paradigm. Non-target *vs.* neutral stimuli and the evaluation of ERP attentional effects. Neuropsychologia 30: 723–741.

Getzmann S, Wascher E, Schneider D (2017) The role of inhibition for working memory processes: ERP evidence from a short-term storage task. Psychophysiology 55: e13026.

Gold JI, Ding L (2013) How mechanisms of perceptual decision-making affect the psychometric function. Prog Neurobiol 103: 98–114.

Gratton G, Coles MG, Donchin E (1983) A new method for off-line removal ocular artifact. Electroencephalogr Clin Neurophysiol 39: 526–530.

Griffin IC, Miniussi C, Nobre AC (2002) Multiple mechanisms of selective attention: differential modulation of stimulus processing by attention to space or time. Neuropsychologica 40: 2325–2340.

Hansen JC, Hillyard SA (1988) Temporal dynamics of human auditory selective attention. Psychophysiology 25: 316–329.

Kingdom FAA, Prins N (2009) Psychophysics. A Practical Introduction. San Diego, CA, US: Elsevier Academic Press.

Kononowicz, TW, Van Rijn, H (2011) Slow potentials in time estimation: the role of temporal accumulation and habituation. Front Integr Neurosci 5: 48.

Kononowicz TW, Van Rijn H (2014) Decoupling interval timing and climbing neural activity: a dissociation between CNV and N1P2 amplitudes. J Neurosci 34: 2931–2939.

Kononowicz TW, Van Rijn H, Meck WHM (2017) Timing and time perception: A critical review of neural timing signatures before, during, and after the to-be-timed interval. In: J. Wixted (Editor-in-Chief) and J. Serences (Editor, Vol. II): Stevens' Handbook of Experimental Psychology and Cognitive Neuroscience (4th ed.), Volume II: Sensation, Perception and Attention, New York: Wiley.

Kornilov SA, Landi N, Rakhlin N, Fang SY, Grigorenko EL, Magnuson JS (2014) Attentional but not pre-attentive neural measures of auditory discrimination are atypical in children with developmental language disorder. Develop Neuropsychol 39: 543–567.

Lefebvre CD, Marchand Y, Eskes GA, Connolly JF (2005) Assessment of working memory abilities using an event-related brain potential (ERP)-compatible digit span backward task. Clin Neurophysiol 116: 1665–1680.

Lijffijt M, Lane SD, Meier SL, Boutros NN, Burroughs S, Steinberg JL, Swann AC (2009) P50, N100, and P200 sensory gating: Relationships with behavioral inhibition, attention, and working memory. Psychophysiology 46: 1059–1068.

Linares D, Lopez-Moliner J (2015) quickpsy: Fits Psychometric Functions for Multiple Groups (Version 0.1.2). Retrieved from https://CRAN.R-project.org/package=quickpsy.

Luck SJ, Woodman GF, Vogel EK (2000) Event-related potential studies of attention. Trends Cogn Sci 4: 432–440.

Lu ZL, Dosher B (2013) Visual Psychophysics. From Laboratory to Theory. Cambridge MA: MIT Press.

Macar F, Vidal F, Casini L (1999) The supplementary motor area in motor and sensory timing: Evidence from slow brain potential changes. Experimental Brain Research 135: 271–280.

Macar F, Vidal F (2002) Time processing reflected by EEG surface Laplacians. Experimental Brain Research 145: 403–406.

Matthews WJ (2011) Can we use verbal estimation to dissect the internal clock? Differentiating the effects of pacemaker rate, switch latencies, and judgment processes. Behav Process 86: 68–74.

Matthews WJ, Gheorghiu AI (2016) Repetition, expectation, and the perception of time. Curr Opin Behav Sci 8: 110–116.

Mento G, Tarantino GA, Sarlo VA, Bisiacchi MA, Silvia P (2013) Automatic temporal expectancy: a high-density event-related potential study. PLOS ONE 8: e62896.

Miller EK, Desimone R (1994) Parallel neuronal mechanisms for short-term memory Science 263: 520–522.

Näätänen R, Picton T (1987) The N1 wave of the human electric and magnetic response to sound: a review and an analysis of the component structure. Psychophysiology 24: 375–425.

Ng KK, Tobin S, Penney TB (2011) Temporal accumulation and decision processes in the duration bisection task revealed by contingent negative variation. Front Integr Neurosci 5: 77.

Nobre A, Correa A, Coull J (2007) The hazards of time. Curr Opin Neurobiol 17: 465–470.

Oades RD, Dittmann-Balcar A, Schepker R, Eggers C, Zerbin D (1996) Auditory eventrelated potentials (ERPs) and mismatch negativity (MMN) in healthy children and those with attention-deficit or Tourette/tic symptoms. Biol Psychol 43: 163–185.

O'Donnell BF, Hokama H, McCarley RW, Smith RS, Salisbury DF, Mondrow E, Shenton ME (1994) Auditory ERPs to non-target stimuli in schizophrenia: relationship to probability, task-demands, and target ERPs. Int J Psychophysiol 17: 219–231.

Paris T, Kim J, Davis C (2016) The processing of attended and predicted sounds in time. J Cogn Neurosci 28: 158–165.

Pariyadath V, Eagleman DM (2008) Brief subjective durations contract with repetition. J Vis 8 : 1–9.

Potts GF, Liotti M, Tucker DM, Posner MI (1996) Frontal and inferior temporal cortical activity in visual target detection: Evidence from high spatially sampled event-related potentials. Brain Topography 9: 3–14.

Potts GF, Tucker DM (2001) Frontal evaluation and posterior representation in target detection. Brain Res Cogn Brain Res 11: 147–156.

Rif J, Hari R, Hamalainen MS, Sams M (1991) Auditory attention affects two different areas in the human supratemporal cortex. Electroencephalogr Clin Neurophysiol 79: 464–472.

Rossion B, Jacques C (2012) The N170: Understanding the time course of face perception in the human brain. In: Luck SJ, Kappenman ES, editors. The Oxford handbook of event-related potential components. Oxford: Oxford University Press; pp. 115–141.

Senderecka M, Grabowska A, Gerc K, Szewczyk J, Chmylak R (2012) Event-related potentials in children with attention deficit hyperactivity disorder: an investigation using an auditory oddball task. Int J Psychophysiol 85: 106–115.

Seppänen M, Hämäläinen J, Pesonen AK, Tervaniemi M (2012) Music training enhances rapid neural plasticity of N1 and P2 source activation for unattended sounds. Front Hum Neurosci 6: 1–13.

Van Wassenhove V, Lecoutre L (2015) Duration estimation entails predicting when. Neuroimage 106: 272–283.

Wickham H, Chang W, Henry L, Pedersen TL, Takahashi K, Wilke C and Woo K (2018) Create elegant data visualizations using the grammar of graphics. Retrieved from https://CRAN.R-project.org/package=erpR.

Woods DL, Knight RT, Scabini D (1993) Anatomical substrates of auditory selective attention: behavioral and electrophysiological effects of posterior association cortex lesions. Cogn Brain Res 1: 227–240.

Zhang F, Deshpande A, Benson C, Smith M, Eliassen J, Fu QJ (2011) The adaptive pattern of the auditory N1 peak revealed by standardized low-resolution brain electromagnetic tomography. Brain Res 1400: 42–52.

Zhang J, Nombela C, Wolpe N, Barker RA, Rowe JB (2016) Time on timing: Dissociating premature responding from interval sensitivity in Parkinson's disease. Mov Disord 31: 1163–1172.