Cross-frequency Phase–Amplitude Coupling as a Mechanism for Temporal Orienting of Attention in Childhood

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Abstract

■ Temporal orienting of attention operates by biasing the allocation of cognitive and motor resources in specific moments in time, resulting in the improved processing of information from expected compared with unexpected targets. Recent findings have shown that temporal orienting operates relatively early across development, suggesting that this attentional mechanism plays a core role for human cognition. However, the exact neurophysiological mechanisms allowing children to attune their attention over time are not well understood. In this study, we presented 8- to 12-year-old children with a temporal cueing task designed to test (1) whether anticipatory oscillatory dynamics predict children's behavioral performance on a trial-by-trial basis and (2) whether anticipatory oscillatory neural activity may be supported by cross-frequency phase–amplitude coupling as previously shown in adults. Crucially, we found that, similar to what has been reported in adults, children's ongoing beta rhythm was strongly coupled with their theta rhythm and that the strength of this coupling distinguished validly cued temporal intervals, relative to neutral cued trials. In addition, in long trials, there was an inverse correlation between oscillatory beta power and children's trial-by-trial reaction, consistent with oscillatory beta power reflecting better response preparation. These findings provide the first experimental evidence that temporal attention in children operates by exploiting oscillatory mechanism. ■

INTRODUCTION

The Neural Underpinnings of Temporal Orienting in Adults

The ability to selectively allocate attention in time (i.e., temporal orienting [TO]) plays an essential role in the proactive regulation of human behavior (Nobre, 2001). Specifically, using external environmental cues to establish temporal expectancy toward upcoming events represents an important gating mechanism that enables us to prioritize relevant stimuli (Correa, 2010; Nobre, 2001). This results in the improved processing of information from expected compared with unexpected targets. This is evidenced by faster RTs and increased perceptual accuracy for expected versus neutrally or invalidly cued targets (Correa, 2010). High temporal resolution neuroimaging techniques, like ERPs, have elucidated the brain dynamics, which unfold during the anticipatory allocation of cognitive and motor resources. Generally, these studies show that anticipatory brain activity varies as a function of subjective temporal expectation (Kononowicz & Penney, 2016). In particular, the contingent negative variation (CNV) is a reliable anticipatory ERP signature reflecting temporal expectancy (Mento, 2013, 2017; Mento,

Tarantino, Sarlo, & Bisiacchi, 2013; Capizzi, Sanabria, & Correa, 2012; Kononowicz & van Rijn, 2011; van Rijn, Kononowicz, Meck, Ng, & Penney, 2011; Trillenberg, Verleger, Wascher, Wauschkuhn, & Wessel, 2000; Miniussi, Wilding, Coull, & Nobre, 1999) and correlates with both temporal predictability of events and with behavioral performance in terms of RT speed (Mento, Tarantino, Vallesi, & Bisiacchi, 2015).

More recently, there has been an increasing interest in understanding the role of neural oscillations in temporal processing (Kononowicz & van Wassenhove, 2016). The advantage of using oscillatory EEG to investigate TO is that it captures ongoing neural processes that are missed by the averaging across trials and collapsing across frequencies bands, as is usually the case in event-related analyses. When anticipating lateralized visual stimuli, both the alpha-band activity in visual areas and beta-band activity in motor areas is increased ipsilaterally and decreased controlaterally to the expected side of stimulus presentation (Cravo, Rohenkohl, Wyart, & Nobre, 2011; Thut, Nietzel, Brandt, & Pascual-Leone, 2006; Sauseng, Klimesch, Schabus, & Doppelmayr, 2005). These effects correspond to specific outcomes in participant's performance, being inversely related to perceptual detectability (Romei, Gross, & Thut, 2010; Ergenoglu et al., 2004), discriminability (van Dijk, Schoffelen, Oostenveld, & Jensen, 2008), and speed of visual and motor processing (Zhang, Wang, Bressler, Chen, & Ding, 2008). Remarkably, this

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effect seems to be cross-modal, given that similar oscillatory patterns have been reported also when anticipating tactile (van Ede, de Lange, Jensen, & Maris, 2011) and auditory (Todorovic, Schoffelen, van Ede, Maris, & de Lange, 2015) expected stimuli. One possibility is that the modulation of oscillatory activity preceding expected events reflects a general rather than a modality-specific anticipatory allocation of attentional resources.

Different frequency oscillations should not be considered as distinct, unrelated signals, but rather as different hierarchical levels of neuronal coupling, that can be integrated to organize and coordinate neural activity across different spatial and temporal scales. It has been proposed that the nested activity of different frequency bands may represent a reliable neurophysiological mechanism underpinning complex behaviors such as those implying the hierarchical coordination of different computational processes, such as executive control and visual memory (Sauseng et al., 2006). Phase–amplitude coupling (PAC) provides a mechanistic framework by which different rhythms can become hierarchically nested. PAC refers to a phenomenon whereby the amplitude of higher-frequency activity is significantly associated with the phase of lower-frequency oscillation (Onslow, Jones, & Bogacz, 2014). Low-frequency oscillations may mediate large-scale functional connectivity among distal, large neuronal populations, whereas high-frequency activity mostly reflects local oscillatory patterns of activity involving small populations of neurons (Buzsaki, 2009). PAC has been observed in different cortical regions, including both primary, secondary, and associative areas both in humans adults (Axmacher et al., 2010), children (Barnes, Nobre, Woolrich, Baker, & Astle, 2016), and nonhuman models (Whittingstall & Logothetis, 2009). This has implicated PAC in many cognitive functions, including perceptual processes (Esghaei & Xue, 2016), working memory (Barnes et al., 2016; Lisman & Jensen, 2013), executive control (Engel, Fries, & Singer, 2001), and motor responses (Yanagisawa et al., 2012).

Few studies have investigated the oscillatory dynamics underlying anticipatory TO. But those few studies provide converging evidence that various oscillatory patterns play a role in the allocation of cognitive and motor resources over time. Both alpha (8–12 Hz) and beta (13–30 Hz) bands may play an important role in TO as a possible mediating mechanism for tuning cortical excitability at the expected timing of upcoming stimuli (Rohenkohl & Nobre, 2011; Tzagarakis, Ince, Leuthold, & Pellizzer, 2010; Sauseng, Klimesch, Gerloff, & Hummel, 2009; Schroeder & Lakatos, 2009; Alegre et al., 2006). A crucial role has also been hypothesized for lower-frequency bands, including both delta (1–4 Hz) and theta (5–7 Hz), whose power is highest in anticipation of critical targets (Cravo et al., 2011). The theta band may provide a central mechanism for encoding anticipation rate and that this may support higher-frequency activity, which may reflect more specific and local processes that reflect the nature of the sensory or motor computations that need to be readied before the stimulus appears.

TO: A Developmental Perspective

Investigating the TO of attention in childhood may shed light on the temporal dynamics that enable the adult end state of attentive functions (Mento & Vallesi, 2016), as it has been suggested for the study of attentional control more generally (Amso & Scerif, 2015). Moreover, from a clinical perspective, temporal attention seems to be impaired in several developmental disabilities, including dyslexia (Visser, 2014), language disorders (Dispaldro & Corradi, 2015; Dispaldro et al., 2013), attention deficit/hyperactivity disorder (Carelli & Wiberg, 2012), and autism spectrum disorder (Ronconi et al., 2013). It has been difficult to understand the specific mechanisms impaired across these disorders, however, because little is currently known about the mechanisms underpinning TO in typical development. TO has been demonstrated in children as young as 6 years old, using a child-friendly temporal cueing paradigm (Mento & Tarantino, 2015). However, the absence of significant age-related changes in the TO delta effect (i.e., RTs in temporally cued minus RTs in neutrally cued targets) from 6 years of age onward suggests that TO benefits are not substantially influenced by developmental changes in other functions such as memory, language, executive function, and motor processing. Rather, it is possible that TO may represents a fundamental attentional mechanism for biasing our attention in time, analogous to that reported for spatial attention in children (Amso & Scerif, 2015).

More recently, Mento and Vallesi (2016) combined the investigation of ERP effects with source reconstruction in children. In line with adult findings (Mento et al., 2013, 2015; Capizzi, Correa, & Sanabria, 2013; Miniussi et al., 1999), in children the CNV reflects the implementation of a priori target expectancy over time. Moreover, the need to update a posteriori temporal expectancy over time as a function of elapsing time (i.e., hazard function) resulted in the modulation of a prefrontal ERP signature defined as anterior anticipatory index or ANTANI. A CNV-like anticipatory effect has also been reported in 9-month-old infants (Mento & Valenza, 2016). In this study, we wanted to explore the presence of specific oscillatory EEG mechanisms, akin to those implicated in adults (Cravo et al., 2011; Rohenkohl & Nobre, 2011) and nonhuman models, as a framework by which children proactively regulate their attention in time. We hypothesized that 8- to 12-year-old children who already demonstrate TO behavioral benefits (Mento & Tarantino, 2015) and anticipatory slow potentials (CNV and ANTANI; Mento & Vallesi, 2016) modulate oscillatory activity when endogenously orienting attention in time. In addition, we further addressed (1) whether the anticipatory oscillatory dynamics predict children's behavioral performance on a trial-by-trial basis and (2) whether anticipatory oscillatory

neural activity may be supported by cross-frequency coupling (PAC) as previously shown in adults (Cravo, Rohenkohl, Wyart, & Nobre, 2013). In short, we wanted to identify a neurophysiological framework by which children regulate their attention over time and understand how it supports this fundamental attentional process in childhood.

METHODS

An orthogonal ERP analysis of this data set has already been reported by Mento and Vallesi (2016).

Participants

As described in Mento and Vallesi (2016), data were collected from 18 typically developing children (mean age = 9.3 years, $SD = 2.05$, range = 8–12 years; eight male; 16 right-handed). Visual acuity was normal or corrected to normal. For each child involved in this study, a signed parental form was submitted. All experimental methods were approved by the Research Ethics Committee of the School of Psychology, University of Padua (Prot. No. 1179).

Stimuli and Task

On all trials, participants were instructed to respond to the onset of a target stimulus. On half of these trials, this stimulus was predictable, because it was preceded by a valid cue. On the remaining trials, the onset of this target item was unpredictable, being preceded by an uninformative neutral trial. This paradigm has already been shown to reliably elicit both behavioral (Mento & Tarantino, 2015) and ERP (Mento & Vallesi, 2016) TO effects in children as well as adults (Mento, 2017). Importantly, both kinds of trials were matched for sensorimotor requirements, because the sequence of stimuli and the required responses were always the same, with the only difference between conditions being the level of target predictability. Each trial began with the central presentation of a visual cue, followed by the presentation of a target stimulus. The visual cue remained on screen until target onset and consisted of the image of a black camera lens surrounded by a circle (total size of the stimulus: 840 × 840 pixels, 144 dpi, 10.62° × 10.54° of visual angle). The target stimulus consisted of the picture of a gray-scale animal, which was displayed centrally within the camera lens (840 × 840 pixels, 144 dpi, 10.62° × 10.54° of visual angle) until response and in any case up to a maximum of 3000 msec. The cue–target SOA was manipulated (either 600 or 1400 msec). The intertrial interval was randomly and continuously manipulated between 600 and 1500 msec. Participants were required to press the spacebar with the index finger of the dominant hand as soon as possible at target onset. To encourage good performance, children were given the following

instructions: "Imagine that you are at the zoo and you have a camera. Your task is to take a picture of the animals appearing within the camera lens as soon as possible. To do that, you have to press the spacebar with your index finger. Please, be careful to click as quickly as possible once you see the animals, otherwise they will disappear. Please, be also careful not to click before the animals appear!" Children were also instructed that, depending on trial type, they may or may not be able to predict the onset of the animal.

On temporal cueing trials (Figure 1A), the visual cue provided valid temporal information concerning the SOA duration. In particular, the outer circle of the camera lens was colored, either in blue or orange. Each color was associated with a specific SOA duration (i.e., 600 or 1400 msec): a temporal short (T-Short) and a temporal long (T-Long) SOA condition. Children were explicitly told about the cue–SOA association. In line with Mento and Tarantino (2015) and Mento and Vallesi (2016), the association between colors and SOA was fixed (100% validity) and counterbalanced across participants. No catch trials were included, that is, the target stimulus always appeared at the expected SOA. This was done to increase the likelihood of TO effect and avoid the so-called
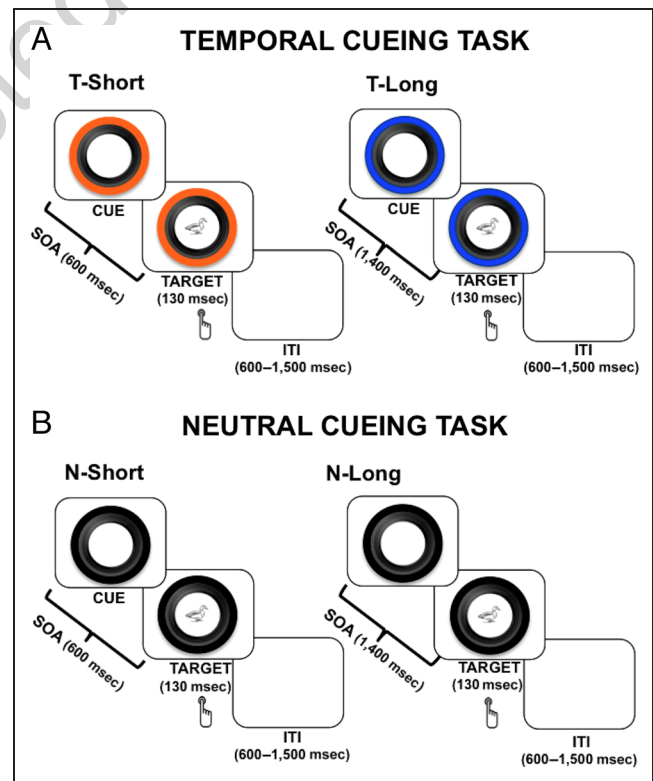

Figure 1. Experimental paradigm. In the temporal cueing block (A), the visual cue provided fixed temporal information concerning the SOA duration, which could be short (left) or long (right), according to the color of the cue. By contrast, in the neutral cueing block (B), participants never knew in advance the duration of the SOA, which could nevertheless have the same short or long duration as in the temporal cueing block.

"dispreparation effects," as defined by Correa, Lupiáñez, Milliken, and Tudela (2004).

On neutral cueing trials (Figure 1B), the outer circle surrounding the camera lens was always black, providing no information about SOA duration. In this case, the cue simply acted as a warning signal, which nonspecifically prepared for the forthcoming target without furnishing temporal information about it. Nevertheless, as for the temporal cueing conditions, the SOA was manipulated to create a neutral short (N-Short) and a neutral long (N-Long) SOA condition (600 and 1400 msec, respectively). To maximize the hazard ratio-related effects inducing TO updating over time, an "aging" probability distribution (Trillenberg et al., 2000; Niemi & Näätänen, 1981) was used, with an equal a priori odd ratio (50%) for each SOA duration. Stimuli were presented on a 17-in. monitor at a resolution of 1,280 × 1,024 pixels. Participants were seated comfortably in a chair at a viewing distance of ~60 cm from the monitor.

Experimental Design

Both the type of cue (temporal vs. neutral) and the SOA length (short vs. long) were manipulated and orthogonally contrasted, leading to a 2 × 2 factorial design. This allowed us to test for the presence of TO (i.e., cue effect) for different SOA durations. More specifically, the TO in short SOA trials was calculated by comparing N-Short and T-Short trials; the TO effect in long SOA trials was calculated by comparing N-Long and T-Long trials. The experimental task included temporal and neutral cueing blocks, which were administered block-wise rather than trial-by-trial to reduce top–down control required to switch continuously from a predictive to a nonpredictive setting (Capizzi et al., 2013), as continuous switching may have particularly affected children. In the temporal cueing blocks, a total of 120 trials (60 for the T-Short condition and 60 for the T-Long condition) were randomly delivered. In the remaining neutral cueing blocks, participants were given a total of 120 trials (60 for N-Short condition and 60 for N-Long condition), randomly delivered. The order of the blocks was counterbalanced across participants. The whole experiment lasted about 16 min.

EEG Recordings

During the session, EEG data were continuously recorded and amplified using a geodesic EEG system (Electric Geodesic Instruments GES-300), through a precabled high-density 128-channel HydroCel Geodesic Sensor Net (HC GSN-128) and referenced to the vertex. The acquisition band-pass filtering was between 0.01 and 100 Hz. The sampling rate was 500 Hz. The impedance was maintained below 30 KΩ for each sensor. To reduce the presence of EOG artifacts, children were instructed to limit both eye blinks and eye movements as much as possible.

Data Analysis

Behavioral Analysis

RTs to target stimuli in all experimental conditions were recorded. RTs below 150 msec or above 1500 msec were discarded. A 2 × 2 repeated-measures ANOVA was performed, with cue (temporal vs. neutral) and SOA (short vs. long) as within-subject factors. Bonferroni corrections were employed to deal with for multiple comparisons. Effect size was calculated by using partial eta square (η_p^2).

EEG Analysis

All the EEG recordings were preliminary processed offline by using the MATLAB toolbox EEGLAB (Delorme & Makeig, 2004). The data were first band-pass filtered between 0.1 and 45 Hz and segmented into epochs starting 200 msec before cue onset and ending 1500 msec after it. Epochs were then visually inspected to interpolate bad channels and remove artifacts. Artifact-reduced data were then subjected to independent component analysis (Stone, 2002). All independent components were visually inspected, and those related to eye blinks or eye movements according to their morphology and scalp distribution were discarded. The remaining components were then projected back into electrode space to obtain cleaner EEG epochs. The remaining epochs containing excessive noise or drift (±100 μV at any electrode) were further rejected. Data were then re-referenced to the average of all electrodes. A mean of 51.7 ± 6 (SD) epochs per condition were accepted. A four-way ANOVA with all conditions as repeated measures yielded no significant differences in epochs retained across conditions, $F(3, 51) = 2.49, p > .7$.

Trial-wise Time–Frequency Analysis

In our initial analysis, we explored the oscillatory correlates of children's anticipation of the target. We examined this separately for the two SOAs (600 and 1400 msec). These two SOAs had to be considered separately because this analysis is repeated across time, meaning that the timing of events has to be consistent across all trial types included in the analysis. This first analysis collapsed across trial types (valid vs. neutral trials) and instead used RT as a continuous measure of children's preparedness. We adopted this approach because this trial-wise RT measure is the most sensitive metric of children's anticipation of the onset of the target and using it as continuous factor in our analysis allowed us to capture the trial-to-trial variability in children's TO. To be clear, the purpose of this initial analysis is to identify the most sensitive EEG marker of children's preparedness for the target. This would then be used in our subsequent PAC analysis that compared the different conditions.

We used a continuous Morlet wavelet transform to decompose the raw EEG data into distinct frequencies,

from 3 to 40 Hz. This was performed across the entire epoch, from −200 to 1500 msec, relative to the onset of the target. Within each child, for each frequency and each time point, we applied a trial-wise general linear model (GLM). This contained the child's normalized RT values and a constant term. For ease of interpretation, the output of this GLM was expressed as a standard *T* value. This value expresses the trial-to-trial association between amplitude at that time point, frequency, and the child's RT. This process was repeated over all combinations of frequency and time. The result was that for each individual child we had a new data set, in which we had established the trial-to-trial association between amplitude and how prepared children were at the end of the trial (as indexed by their RT on that trial).

Once this process was repeated across all children, we combined their data with a second-level analysis. This was done using a one-sample *t* test: At each frequency and time point, the subject specific *t* values were compared with 0. This process was repeated over all combinations of frequency and time to produce a group-level data set, in which the effect of trial-to-trial EEG variability on preparation is established at each time point and frequency. This process results in a substantial multiple comparisons problem that needs to be controlled for. This was done using a nonparametric sign-flipping permutation approach (Maris & Oostenveld, 2007). We identified any clusters of consecutive values of $t > 2.3$ (this is arbitrary but approximates an uncorrected threshold of $p = .05$), across frequencies, time points, and sensors. We calculated the size of these and then used a permutation testing approach to test whether any of these clusters were significant. For each permutation, the first steps of the analysis were identical, but at the final step, the sign of each child was randomly assigned. We then identified the largest cluster, using the same threshold as in the original analysis. This process was repeated 1000 times, building up a null distribution of cluster sizes that would be expected by chance. Against this distribution, we could then compare the actual effects and derive *p* values. This randomization procedure is an extremely powerful way of testing for significance in an analysis such as this. Any nonlinearities in the data or biases occurring as a result of the various necessary steps are corrected for, because they are recreated perfectly in each permutation. Furthermore, it makes no a priori assumptions about when or where effects are likely to be apparent, correcting for multiple comparisons over time, frequency, and electrodes.

PAC Analysis

We used the initial trial-wise time–frequency analysis to guide a subsequent PAC analysis that explored differences between the two trial types. To foreshadow the result of the above analysis, we identified activity in the beta band over central areas during the long SOA trials,

as these best indexed the degree of preparation (see Results section). We used the sensors and frequencies from this significant cluster and explored the extent to which this rhythmic component became coupled with ongoing theta band cycle as measured at Cz (following the methodology developed for adults data by Cravo et al., 2013). To do this, we calculated circular–linear correlations (Barnes et al., 2016; Berens, 2009) to test the strength of association between the phase of activity within the theta band and the amplitude of the beta activity established in our first analysis. For each child, taking 400 msec windows at a time, we calculated the strength of association between the phase of the theta cycle and the amplitude of the beta rhythm. This was expressed as a circular–linear correlation, which was then converted to a *z* score using a standard Fisher *r*-to-*z* transform. This was repeated over all frequencies within the theta band (3–8 Hz) in 0.5-Hz steps and over all time points by sliding the window along the epoch in 4-msec increments. The result was a data set in which we had estimated the strength of PAC, at each frequency of theta, for each child, expressed as a *z* score. We performed this process separately for valid and neutral trials so that we could compare these two conditions. To do this, we used a paired-sample *t* test, which was applied over each frequency and time point. A multiple comparisons correction was then performed using the same nonparametric sign-flipping permutation approach described above.

RESULTS

Behavioral Results

As described in Mento and Vallesi (2016), behavioral performance in this task reached a high-accuracy level (93.75 ± 0.87% correct) and was not differentiated between conditions ($p > .5$). The behavioral benefits conferred by TO were observed in RTs. These consisted of overall faster responses for temporally than neutrally cued targets, $F(1, 17) = 5.66, p < .03, \eta_p^2 = 0.25$. We also found a main effect of the SOA, because RTs were overall shorter in the long than in the short SOA conditions, $F(1, 17) = 18.83, p < .0001, \eta_p^2 = .53$. In addition, a significant Cue × SOA interaction, $F(1, 17) = 6.03, p < .03, \eta_p^2 = .26$, revealed that TO produced an asymmetrical effect, as the speeding up of RTs induced by the temporal cue was present for short ($p < .01$) but not long ($p > .4$) SOAs (Figure 2).

Trial-wise Time–Frequency Results

Our trial-by-trial time–frequency analysis revealed a significant cluster on long SOA trials in the beta band (22–40 Hz), between 1240 and 1296 msec postcue ($p_{\text{corrected}} = .041$). The relationship between this and RT was positive—the stronger the beta suppression effect, the faster children tended to be. In short, beta suppression
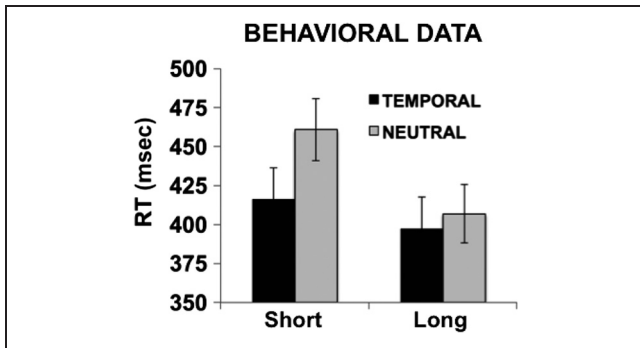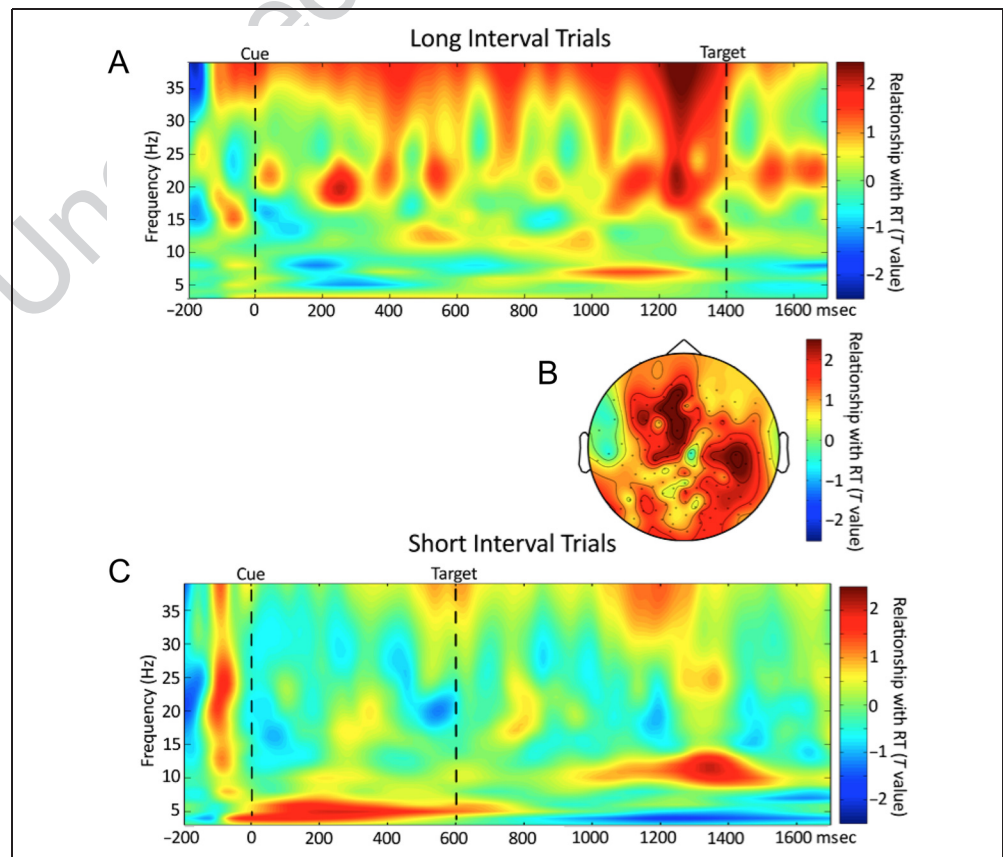
BEHAVIORAL DATA

Figure 2. Behavioral performance (RTs) of children.

leading up the onset of the target was significantly associated with children's degree of preparation. This result can be seen in Figure 3A. A topographical display of this effect can be seen in Figure 3B. By contrast, there were no significant associations at the short SOA, as can be seen in Figure 3C. The significant beta oscillatory modulation was then used to guide a phase–amplitude analysis that explored the coupling mechanisms that might underpin TO.

Phase–Amplitude Coupling

The purpose of the PAC analysis was to explore whether the beta effect associated with preparedness tracked the cycle of the theta rhythm during the cueing interval (Cravo et al., 2013). The beta effect was more strongly coupled to the theta rhythm on temporally cued versus neutral trials. This was apparent just before the onset of the target, just as the original main effect reported by Mento and Vallesi (2016). However, we also observed substantial differences in coupling earlier in the trial, with a significant cluster centered on 390 msec and the phase of the 6 Hz theta rhythm ($p_{corrected} = .011$). This effect can be seen in Figure 4A. We also plotted the time course of the coupling between the beta effect and the phase of the 6-Hz theta cycle. This can be seen in Figure 4B. In short, when children knew the gap between the cue and the target, the beta rhythm became strongly coupled to the cycle of the slow theta rhythm.

DISCUSSION

Although the neurocognitive mechanisms underlying TO in adults have been relatively well elucidated (Coull, 2010), little is known about the developmental aspects of this important attentional function. In the present article, we show that neural oscillations in healthy children mirror the deployment of preparatory resources over time (Cravo et al., 2013; Rohenkol et al., 2011).

Our primary finding is that children's beta rhythm becomes strongly coupled with their ongoing theta rhythm and that the strength of this coupling is altered as

Figure 3. The result of our trial-wise GLM analysis, showing the significant relationship between beta-band activity and RT in long trials. The top (A) shows the strength of this relationship (as *T* values) across time at those sensors forming part of our significant cluster. The middle topographical plot (B) shows the distribution of those sensors. The bottom plot (C) shows the absence of relationship between beta band activity and RT in short trials.

Figure 4. The top shows the impact of cueing (cued vs. neutral trials) on PAC across different phase frequencies within the theta band. The bottom shows the time course of that coupling effect for the two conditions: validly cued and neutral trials.
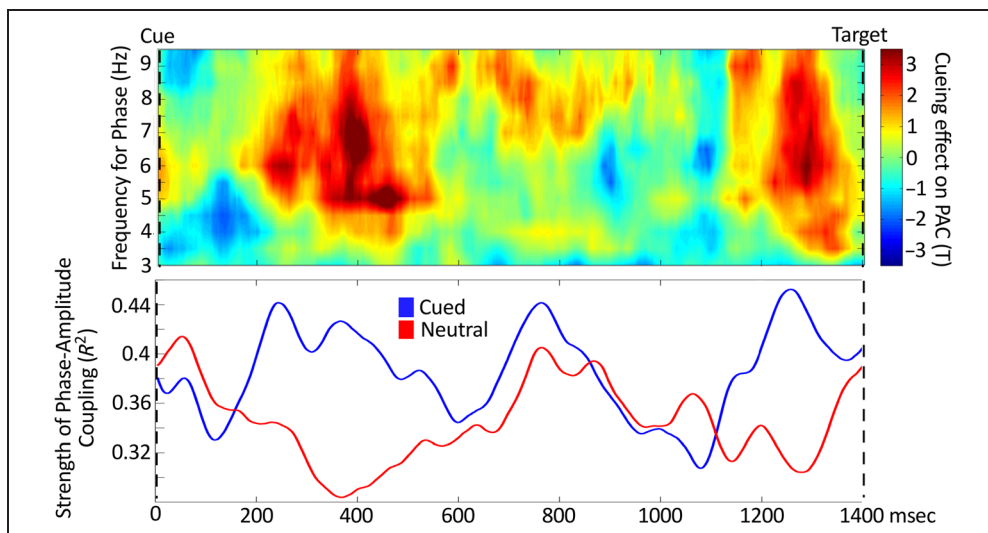
children update their temporal expectancy; it increases periodically for validly cued trials, relative to neutral trials. This is in keeping with a framework in which higher-frequency local activity, reflecting specific sensory or motor processes, becomes nested within a slower rhythm and that this provides a means of organizing the local activity according to higher-level expectations (Onslow et al., 2014). This effect can be clearly identified as a marker of TO. First, it distinguishes the trial types, so is sensitive to children's advance knowledge of the upcoming interval. Second, it occurs relatively early in the trial, well in advance of any hazard function or specific motor preparation per se. And third, the PAC analysis is purposefully insensitive to the overall amplitude of the beta effect but is instead sensitive to the degree of coupling. Specifically, in line with neuroimaging and ERP evidence in adults (Mento, 2017; Coull, Cotti, & Vidal, 2016; Mento et al., 2015; Coull, 2011) and children (Mento & Vallesi, 2016), we propose that theta–beta coupling may represent an oscillatory mechanism mediating the ability to generate, implement, and update temporal expectancy.

A secondary finding, established in preparation for our PAC analysis, is an inverse correlation between the oscillatory power in the beta range (22–40 Hz) and the behavioral performance collected on a trial-by-trial basis. Specifically, our data show that the more the anticipatory beta activity was desynchronized, the faster the children were in detecting and responding to targets. This effect was present in a narrow temporal window extending about a hundred milliseconds before targets and only in the long SOA trials. This result may be interpreted as an oscillatory neural signature reflecting action preparatory mechanisms induced by the simple temporal structure of trials. Indeed, in the context of the current paradigm, long trials are characterized by the automatic boost of temporal expectancy as a function of the very passage of time. This phenomenon, well-known as the cumulative hazard function (Coull, 2009; Nobre, Correa,

& Coull, 2007; Luce, 1986; Niemi & Näätänen, 1981), is instantiated by the conditional probability of stimulus occurrence over time as a function of the evidence that it has not occurred yet. Thus, in line with previous evidence (van Ede et al., 2011), we might assume that overall beta desynchronization in long but not short trials could reflect the presence of the hazard function rather than the effect of endogenous TO itself. Importantly, whatever this beta suppression process indexes, it varies systematically across trials in line with children's degree of preparedness, as indexed by their RT. This makes it a particularly useful effect for our subsequent PAC analysis. These trial-by-trial oscillatory findings suggest that the intertrial variability in behavioral performance in children may be accounted for by anticipatory mechanisms rather than or simply by a greater or faster posttarget processing per se. This suggests a possible avenue for investigating the relationship between anticipatory neural activity and behavioral performance in atypical developmental population characterized by a high intra- and intersubject variability in RTs, such as children with attention-deficit/hyperactivity disorder.

As a possible interpretation of this finding in neurophysiological terms, the slower rhythm may modulate local spike timing, thereby modulating neuronal excitability. The scalp distribution of beta suppression shows that this effect mainly spreads over frontocentral areas, suggesting a possible neural origin around premotor or motor cortices. Concerning the nested oscillations revealed by the PAC analysis, this effect may represent a mechanism that allows different cortical regions to become functionally attuned (Fries, 2005). This coordination may support an efficient exchange of information, in this case providing a candidate neurophysiological mechanism for temporal expectation. Importantly, this putative oscillatory mechanism is already established and functionally operative from 8 years of age onward, corroborating previous experimental evidence of TO as a fundamental, relatively

early attentional mechanism for biasing our attention in time.

In conclusion, our findings show that TO behavioral effects previously reported in children (Mento & Vallesi, 2016; Mento & Tarantino, 2015) may be supported by patterns of oscillatory neural activity taking place during the anticipation of expected events.

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