

The temporal and spatial brain dynamics of automatic emotion regulation in children

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ABSTRACT

Mechanisms for automatic emotion regulation (AER) are essential during childhood as they offset the impact of unwanted or negative emotional responses without drawing on limited attentional resources. Despite the importance of AER in improving the efficiency and flexibility of self-regulation, few research studies have investigated the underlying neurophysiological mechanisms. To fill this gap, we used magnetoencephalography (MEG) to investigate AER-related brain processes in 25 children (~10 years old) who performed a go/no-go task that included an incidental exposure to faces containing socio-emotional cues. Whole brain results revealed that the inhibition of angry faces (compared with happy faces) was associated with a stronger recruitment of several brain regions from 100 to 425 ms. These activations involved the right angular and occipital gyri from 100 to 175 ms, the right orbito-frontal gyrus (OFG) from 250 to 325 ms ($p^{corr} < 0.05$), and finally, the left anterior temporal lobe (ATL) from 325 to 425 ms. Our results suggest a specific involvement of these regions in the automatic regulation of negative emotional stimuli in children. In the future, this knowledge may help understand developmental conditions where inhibition impairments are exacerbated by an emotional context.

1. Introduction

During development, children learn how to adapt, or inhibit, their behaviour in accordance with exposure to various types of emotions (Cole et al., 2004). Particularly in the context of peer interactions and social activities, children rapidly detect implicit socio-emotional cues (e.g., facial expressions) and use appropriate strategies to regulate their emotions accordingly (Gross, 2002; Cole et al., 2004). For instance, whereas smiling faces will encourage answers and approach, a negative countenance will trigger behavioural regulation (e.g., inhibition) to avoid a potentially disturbing situation. This suggests that the impact of emotion on cognition depends on the arousal and valence of the stimulus (Pessoa, 2009).

Although the development of emotion regulation strategies has important affective, cognitive and social consequences in children, behavioural and neuroimaging studies investigating this process are few and their results are discrepant. For instance, at the behavioural level, whereas Cohen Kadosh et al. (2014) reported that children (11–12 years old) encounter more attentional control difficulties in

the context of fearful compared to happy faces (Cohen Kadosh et al., 2014), others have shown that emotional context alters response inhibition ability in children; however, this inhibition is equal to both happy and sad faces (Urban et al., 2012).

Knowledge about the inhibitory brain mechanisms, in children, that trigger emotion regulation, particularly those that allow adaptive functioning in the presence of socio-emotional cues (face expressions), is also limited. Thus far, a few ERP studies in children have highlighted the functional role of the N2, an inhibitory-related frontal component occurring 200–400 ms after stimulus onset, in the regulation of socio-emotional cues (Lewis et al., 2007; Todd et al., 2008; Hum et al., 2013a,b). These studies used an *emotional go/no-go task* where participants responded to 'go' stimuli and withheld responses to 'no-go' stimuli in the context of happy, angry or fearful faces. Although the results are of interest, the protocols could be improved in several ways. Firstly, these studies compared go trials (containing a motor response) with no-go trials (containing no motor response), thus integrating a motor confound into the analysis (see discussion in Vidal et al., 2012). Secondly, previous ERP studies have used explicit socio-emotional cues

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during the emotional go/no-go task which required participants to directly respond to emotion (i.e., Happy/Angry/Fearful; (Hare et al., 2008)) or gender (Lewis et al., 2007; Hum et al., 2013a,b) of the stimulus. However, although emotion regulation is usually portrayed as a deliberate and explicit process (Gross, 2014), a growing body of research has shown that emotion regulation often operates on more implicit or automatic levels (Gyurak et al., 2011; Koole and Rothermund, 2011; see Koole et al., 2015, for a review). According to these models, automatic emotion regulation (AER) processes operate almost constantly in daily life and represent a powerful aid in keeping emotional context from interfering with one's ongoing activities. Hence, investigating the impact of an incidental exposure to emotional stimuli on controlled behaviour provides a more realistic measure of socio-behavioural interactions, where emotional cues are often incidental (Goldstein et al., 2007; Todd et al., 2008, 2012). The AER assists children in developing adaptive emotion regulation strategies by facilitating an implicit and rapid monitoring of whether an emotional response is appropriate or not (Hopp et al., 2011 and see Koole et al., 2015 for a recent review). For instance, by efficiently offsetting the impact of unwanted or negative emotional responses without drawing on limited attentional resources, the AER crucially contributes to resilience to stressful life events and to personal growth (Bonanno, 2004; Gross and Muñoz, 1995; Moore et al., 2008). Moreover, implicit emotion regulation has been associated with improved well being or social adjustment and reduced depressive symptoms (Bonanno, 2004; Hopp et al., 2011).

Despite the importance of the AER in improving self-regulation in children, a clear understanding of AER-related neurophysiological mechanisms is still missing. To our knowledge, only one functional magnetic resonance imaging (fMRI) study has characterized the brain regions involved in AER regulation (i.e., incidental exposure to happy or angry faces during a go/no-go task) in children (Todd et al., 2012). Results showed that inhibition-related activity in the orbito-frontal cortex (OFC) was modulated by the emotional valence of the faces. In particular, whereas Happy faces triggered more activity in the left OFC, compared to Angry faces, in younger children (4.4–6.5 years), the emotion-related modulation of the OFC shifted to greater activation for Angry faces in older children (6.5–9.0 years; Todd et al., 2012). Although Todd et al. (2012)'s fMRI study showed the specific contribution of the OFC in socio-emotional regulation processes in children, and possibly its crucial importance during development, the poor temporal resolution of fMRI precludes an understanding of the brain dynamics that regulate inhibition and emotion interaction.

The goal of the present study was to characterise precisely the spatio-temporal brain dynamics of AER in children. To do so, we used magnetoencephalography (MEG) which offers a unique opportunity to investigate both the spatial and temporal brain patterns that underlie inhibitory brain mechanisms. We determined how these brain processes were modulated by an incidental exposure to negative (angry faces) vs. positive (happy faces) emotions, thus, allowing adaptive functioning in children. As MEG provides excellent time resolution and better spatial localisation than ERPs, it represents a remarkable tool for studying such complex cognitive processes (e.g., see Hari et al., 2010 for a review). The MEG analyses compared the timing and localisation of inhibition-related brain activity which occurred with incidental exposure to positive vs. negative emotional faces. Moreover, to prevent the usual confound of movement-related activity (when go and no-go trials are contrasted), we compared no-go trials associated with stimuli in an *inhibitory* condition to no-go trials occurring within a *vigilance* condition (same no-go stimuli in a non-inhibitory context) to ensure the specificity of the inhibition task effect. We hypothesised that the emotional context, particularly the presence of angry faces, would

affect inhibitory brain processes and this would be expressed by greater activation in brain areas classically linked to inhibition.

2. Material and methods

2.1. Participants

Participants were selected from a larger series of 40 children [age range: 7–13 yrs]. All children had normal vision and no history or existing diagnosis of psychiatric, neurological disorders or learning disability. One child was excluded due to high IQ (> 140), three were excluded due to excessive movement in the MRI and MEG scanners and 11 were excluded due to poor performance on the task (high false alarm (FAs) rate of no-go trials, < 10% difference between HITS and FAs).

Thus, the final sample of this study included 25 children (17 males: 8 females, mean \pm SD: 10.23 \pm 1.79yrs), 21 were right handed and 4 left-handed. All children provided informed assent and parents gave informed written consent. The study was approved by the Research Ethics Board at the Hospital for Sick Children and is in accordance with the declaration of Helsinki. All children were in the appropriate grade level in school and were recruited through fliers, advertisements and word of mouth. Prior to MEG testing, all participants received instructions and completed practice trials to ensure full understanding of the task.

2.2. Experimental MEG task and procedure

The children completed an emotional go/no-go task (see Fig. 1a) in the MEG scanner. During this task, children were instructed to respond as fast as possible to 'go' stimuli by pressing a button, and to withhold a response to 'no-go' stimuli. The go and no-go trials were identified by a coloured frame around either an Angry or a Happy face. Participants were instructed to ignore the faces and only attend to the colour of the frame (e.g., go trials were identified by a blue frame and no-go stimuli by a purple frame). Children were thus incidentally exposed to two different emotional valences of faces which allowed us to investigate how emotional context (Happy vs. Angry) affects inhibition processing.

Inhibition performance and the associated brain activity were compared to a go/no-go vigilance (control) task. In the *Inhibition* (I) condition, the majority of stimuli were go trials (75%) so the prepotent tendency to respond was established, and thus it was difficult to inhibit to no-go trials (25%). In contrast, the *Vigilance* (V) condition included 75% no-go trials, with only 25% go trials, and can thus be seen as a classic vigilance task. The two MEG tasks were presented in randomized order across participants.

The go or no-go stimuli were randomized to be either a blue or purple frame, within which emotional distracter faces were presented. There were 52 emotional faces (26 females: 26 males) that were selected from the NimStim Set of Facial Expressions (Tottenham et al., 2009). Only images that were correctly classified as Happy or Angry with $\geq 80\%$ accuracy were used.

All stimuli appeared on a projection screen located 80 cm from the children's eyes; the visual angle of the stimuli subtended approximately 4° of visual field. Trials began with a stimulus duration of 700 ms, which was adjusted between 300 and 700 ms, followed by a fixation cross in the inter-stimulus interval (ISI), which varied between 650 and 1300 ms, based on response accuracy. The paradigm was designed to maintain a steady error rate ($\geq 95\%$ accuracy for go trials, $\geq 80\%$ accuracy for no-go trials). Therefore, the stimulus duration and ISI were adjusted in real time based on global go and no-go accuracies (calculated from the start of the run) as well as recent accuracy rates (calculated from the last 5 trials of each stimulus type). ISI duration

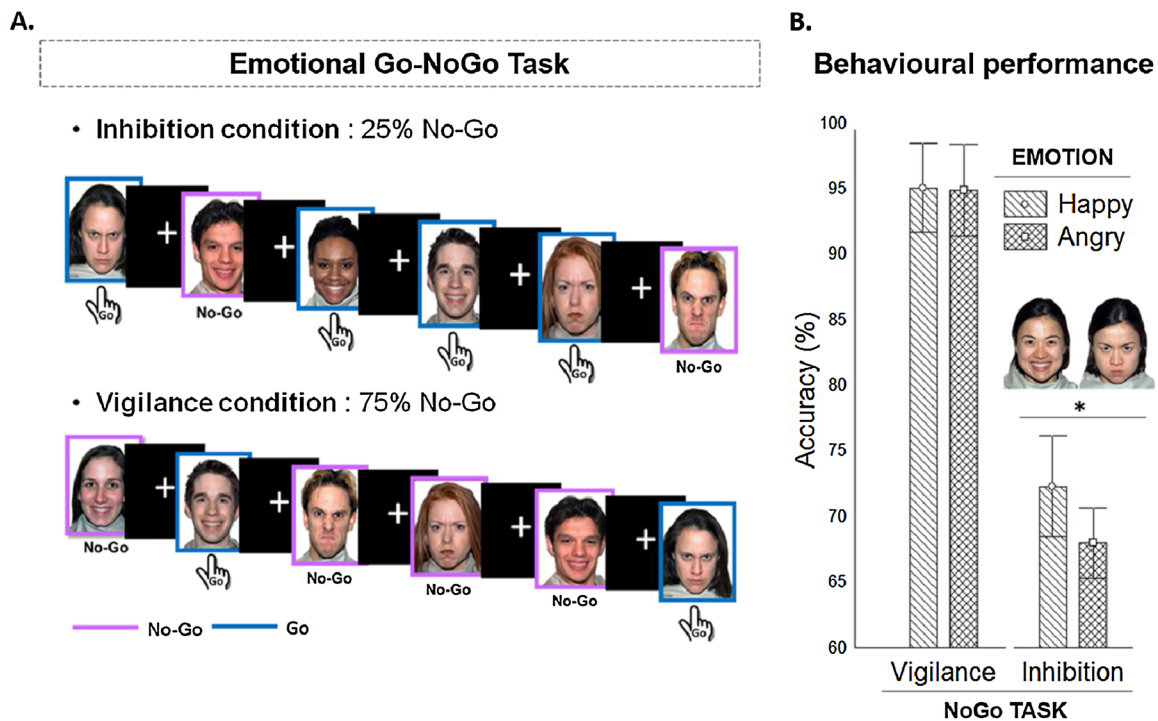


Fig. 1. (A) Task Design: Two conditions were used, an inhibition (with 25% no-go trials) and vigilance (with 75% no-go trials) condition. This was done to ensure that the no-go trials from both conditions could be compared without a motor confound associated with go trials. Participants were required to respond (button press) to 'go' stimuli as fast as possible and to withhold a response (no button press) to 'no-go' stimuli (randomized target: either blue or purple frame). Happy or Angry faces were incidentally presented within the frames as emotional distractors. (B) Inhibition-related behavioural results revealed a main effect of Task ($p = .00001$; Inhibition < Vigilance) and Emotion ($p = 0.03$; Angry < Happy) as well as a main interaction between emotional valence and task condition ($p = 0.023$). LSD Fisher post-hoc analyses showed that children had greater no-go accuracy in the presence of Happy faces compared to Angry faces within the inhibition condition ($p < 0.002$) but no differences between emotions were found in the vigilance condition ($p > 0.88$).

always contained a random jitter of ± 200 ms from the adjusted value. For all the details of the titration of the timing in the task, please see Supplemental materials.

2.3. MEG data acquisition

MEG data were recorded continuously (600 Hz sampling rate, 0–150 Hz band pass, third-order spatial gradient noise cancellation) using a 151 channel CTF system (Coquitlam, BC, Canada). Before testing, three localization coils were placed at the nasion and the left and right pre-auricular points to ascertain head position, and allow continuous head motion correction. MEG data were co-registered with anatomical magnetic resonance images (MRI) for each participant to estimate activation at each location in the brain.

2.4. MRI data acquisition

Each child had a T1-weighted MRI (3D SAG MPRAGE: PAT, GRAPPA = 2, TR/TE/FA = 2300 ms/2.96 ms/90°, FOV = 28.8 × 19.2 cm, 240 × 256 matrix, 192 slices, slice thickness = 1.0 mm isotropic voxels) from a 3T MR scanner (MAGNETOM Tim Trio, Siemens AG, Erlangen, Germany) with a 12-channel head coil.

2.5. Behavioural analyses

At the behavioural level, accuracy scores (percentage of correct responses) [Acc] were calculated both for the go (Button press) and the no-go trials (no button press).

To ensure adequate quality of behavioural results for the no-go

trials prior to source analysis, children's data were excluded if they did not perform above chance, meaning that the percentage of HITS (accuracy) was always higher (> 10%) than the percentage of false alarms (FAs; the opposite of the intended action, e.g., a button press to no-go stimuli) across tasks (I and V) and the emotional context (Happy and Angry faces). Mean reaction times [RT], and RT coefficient of variation [CV] (calculated for each subject as the standard deviation of the mean RT divided by mean RT) associated with the go trials were also recorded. Performance on the go and the no-go trials were submitted to repeated measures ANOVA (performed using Statistica version 7.0; Statsoft Inc., Tulsa, OK, USA) with Task type (Inhibition vs. Vigilance) and Emotional context (Happy vs. Angry) as the within-subject factors.

2.6. MEG analyses

With MEG we investigated how the incidental exposure to Happy or Angry faces impacted inhibition-related brain processes involved in the processing of no-go trials in children. To ensure the specificity of the inhibition task effect, functional brain activity associated with the processing of no-go trials in the Vigilance (control) condition (75% no-go) was also included in the factorial analysis (see below) and directly compared to the functional brain activity associated with the processing of no-go trials in the Inhibition condition (25% no-go). Worth noting, the vigilance condition (no-go 75%) may still involve some subtle inhibitory processes that may be generated by the absence of a response required to the visual stimuli. Hence, the contrast (Inhibition > Vigilance) allows the identification of brain regions that are specifically associated with processes generated by the inhibition of

the prepotent response, while also excluding common brain activity shared between the Inhibition and Vigilance conditions (e.g., visual processing, etc.), as well as the motor confound which would be seen in the more conventional go vs. no-go comparison. Preprocessing and brain functional analyses described below were performed using SPM12 (Wellcome Trust Centre of Neuroimaging, London) implemented in MATLAB 2014b (The MathWorks, 2014).

2.6.1. Preprocessing steps

MEG data were band-pass filtered at 1–40 Hz and time-locked to each go/no-go trial onset using a photodiode. Baseline-corrected epochs associated with correct go/no-go trials were then extracted from –200 ms pre-stimulus to 500 ms post-stimulus. Data were then corrected for head motion, removing any epochs with motion greater than 5 mm. Ocular and muscle artefacts were detected and subtracted from the trials on a subject-by-subject basis using ICA (Independent Component Analysis) as implemented by FieldTrip (Oostenveld et al., 2011). ICA decomposition was performed simultaneously across all conditions and all subjects as recommended in the literature (Kovacevic and McIntosh, 2007). For each participant, 30 components were examined for artefacts and a minimum of two and a maximum of four components were removed per participant based on visual analysis of the component performed by an ICA expert. Epochs during which an MEG sensor signal exceeded the level of 2500fT/cm were also rejected.

2.6.2. Source reconstruction

Functional images of whole-head activity were generated for Happy and Angry no-go trials in both task conditions (Inhibition and Vigilance) by applying vector beamformer weights on 50 ms sliding time windows, overlapping 25 ms each over the task epoch of interest (0–500 ms).

Weights were derived using both a forward field (a model of the fields measured in response to a unit current with known location/orientation) and an estimated channel-level covariance matrix. Beamforming is a spatial filtering approach to MEG inverse source modeling that relies on a minimization of total brain power while constraining the gain in the voxel of interest, resulting in the suppression of background noise (Brookes et al., 2011). Head modeling was computed using a single shell head model (Nolte, 2003) fitted to the inner skull surface derived from each child's MRI. Resulting individual contrast images (for Happy and Angry conditions in the Inhibition and Vigilance tasks) were spatially smoothed using a Gaussian kernel of 12 mm full-width at half maximum, then entered in a factorial design (Penny and Holmes, 2003).

Emotion-dependent changes in inhibition-related brain processes were then tested as changes in event-related magnetic fields (ERFs) between Happy and Angry contexts using a factorial design model including two within-subject factors: Tasks (Inhibition vs. Vigilance) and Emotion (Happy vs. Angry). The resulting set of voxel values constituted a map of t -statistics [SPM(T)], reported significant at $p^{\text{uncorr}} < 0.005$. A family-wise error correction ($p^{\text{corr}} < 0.05$) was also applied to the results. The family-wise error was controlled using a Bonferroni correction (Wens et al., 2015) which adjusted the p -value for the number of spatial degrees of freedom involved in beamformer reconstructions. This technique is somewhat analogous to the random field theory approach considered in SPM (Kilner et al., 2005; Litvak et al., 2011), and adapted to MEG (Barnes et al., 2011), wherein the number of independent voxels is estimated from the smoothness of the images. The smoothness of source activity is essentially controlled by the forward model and the number of spatial degrees of freedom can be estimated as the rank of the lead field matrix (Wens et al., 2015). The correction corresponded effectively to a significance level of $P < 0.002$ (see Table 1 in bold).

Table 1

Interaction effect between the emotion (angry vs. happy) and task condition (inhibition vs. valence) factors on whole brain processes associated with the processing of no-go stimuli (0–500 ms post-stimulus onset).

INHIBITION Angry > Happy								
Brain regions	Time window (ms)	z-value	p-value	MNI coordinates				
				x	y	z		
R Middle OG	100–175	2.82	0.004	26	–94	6		
R Angular G	125–175	2.76	0.003	54	–56	20		
R Posterior OFG	225–275	2.73	0.003	32	22	–14		
R Anterior OFG	225–275	2.54	0.005	28	52	–4		
R Posterior OFG	250–300	3.17	0.001	26	20	–16		
R Anterior OFG	250–300	2.93	0.002	32	50	–8		
R Posterior OFG	275–325	3.04	0.001	26	20	–18		
R Anterior OFG	275–325	2.63	0.004	34	50	–10		
L Anterior ITG	325–375	2.73	0.003	–46	–18	–32		
L Occipital G	325–375	2.67	0.004	–8	–94	–18		
L Anterior ITG	350–400	2.72	0.003	–44	–18	–32		
L Occipital G	350–400	2.63	0.003	–8	–94	–18		
L Anterior ITG	375–425	2.64	0.004	–44	–20	–34		
L Hippocampus	375–425	2.64	0.005	–34	–4	–32		

Note: Statistical significance was set for the significant voxels of activations at $p^{\text{uncorr}} < 0.005$. Activations highlighted in bold are corrected for multiple comparisons at $p^{\text{corr}} < 0.05$.

3. Results

3.1. Behavioural results

Behavioural analysis performed on no-go trials showed a main effect of task [$F(1, 24) = 185.68, p = 0.000001$ (Inhibition < Vigilance)] and Emotion [$F(1, 24) = 4.79, p = 0.03$ (Angry < Happy)]. We also identified an interaction between emotional valence and task condition [$F(1, 24) = 5.89, p = 0.023$]. LSD Fisher post-hoc analyses showed that children had greater accuracy at withholding responses to no-go stimuli in the context of Happy faces compared to Angry faces during the inhibition task (25% No-Go; Angry < Happy, $p < 0.002$) whereas emotional context did not impact performance during the vigilance task (75% no-go, Happy = Angry, $p > 0.88$).

3.2. MEG results

Analyses performed at the source space level on no-go trials showed a main interaction between our two factors of interest Task and Emotion (see Table 1 and Fig. 2) where Inhibition-related brain processes significantly differed when no-go trials occurred in the context of Happy or Angry faces whereas similar effects were not present in the Vigilance condition. Inhibition processes occurring in the context of Angry faces elicited stronger brain activations than similar inhibition processes in the context of Happy faces. Angry-related inhibition processes encompassed a distributed parieto-fronto-temporal network from 125 ms to 425 ms. This sequence of activation involved the right angular and occipital gyri (100–175 ms), then the right orbito-frontal gyrus (OFG, 225–325 ms) and, finally, the left occipital and ventral aspect of the anterior temporal lobe (ATL, 325–425 ms).

These brain regions were more active in the inhibition condition in the Angry trials, whereas no activations were found to be stronger in the Happy condition regardless of task condition (see Fig. 3 for an example of these results in the right OFG).

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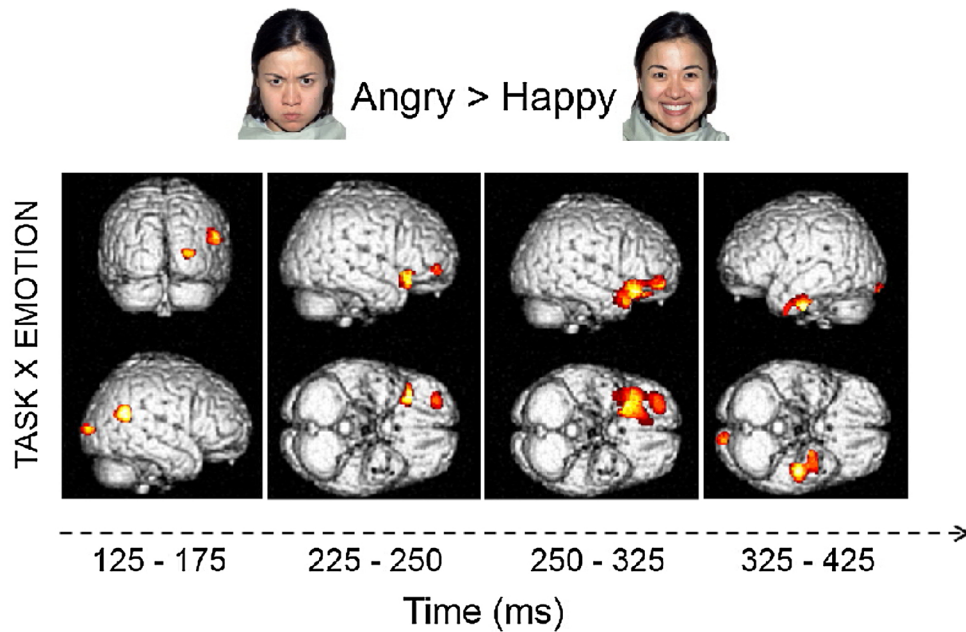


Fig. 2. 3D brain representations of the significant sources associated with the main interaction of Task and Emotion for no-go (Inhibition > Vigilance condition: Angry > Happy) from 125 to 425 ms. This sequence of activation involved progressively the right angular and occipital gyri (100–175 ms), the right orbito-frontal gyrus (OFG, 225–325 ms) and finally the left occipital and ventral part of the anterior temporal lobe (ATL, 325–425 ms).

Emotional regulation processes related to the right OFG

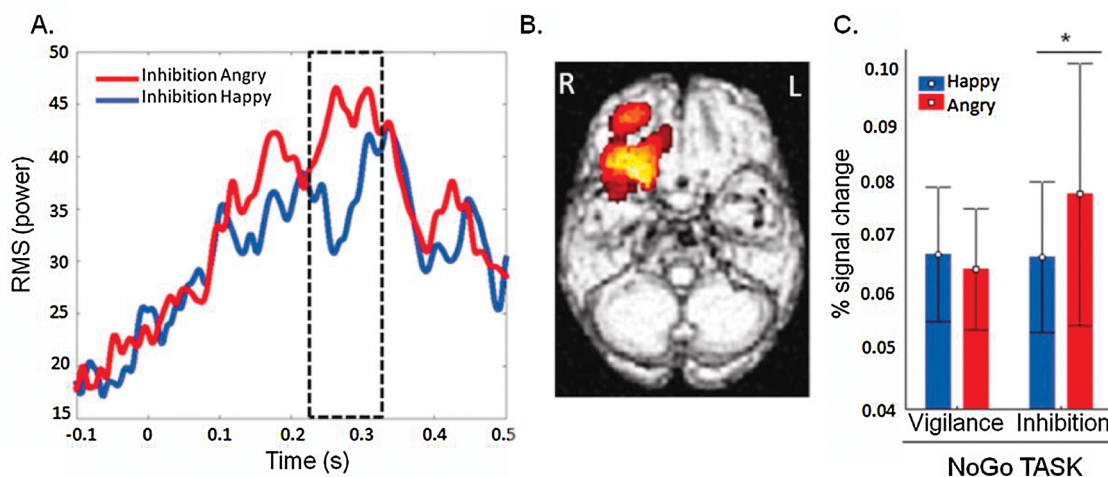


Fig. 3. Right orbitofrontal gyrus (OFG) activation during the time window 275–325 ms. (A) Grand-averaged amplitude of right frontal sensors for no-go trials associated with Inhibition Angry (in red) vs. Inhibition Happy (in blue). The dotted rectangle represents the time window of interest, 275–325 ms, where the Inhibition Angry trials had greater magnitude compared to the Inhibition Happy condition. (B) Analyses performed in source space on no-go trials revealed a significant main interaction between Task × Emotion (Inhibition: Angry > Happy) in the right anterior OFG. (C) A repeated measures ANOVA was performed on the mean activation (% signal change) for the right anterior OFG (x: 26, y: 20, z: -18), with Emotion (Happy/Angry) and Task (Vigilance/Inhibition) as the within-subject variables. Results revealed a main interaction of Task × Emotion ($p = 0.023$) with the Inhibition Angry condition driving the interaction.

4. Discussion

In this study, we used MEG to characterize the precise timing and localisation of brain activity involved in automatic emotional regulation (AER) processes in children. To eliminate the motor confound present in earlier studies which compared go with no-go trials, we compared brain activity associated with two no-go experimental

conditions (Inhibition vs. Vigilance) both containing incidental exposures to a positive vs. negative socio-emotional context (Happy vs. Angry faces).

Behavioural results showed that children had more difficulty inhibiting their responses in the context of Angry than Happy faces, suggesting greater attentional regulation in the presence of aversive socio-emotional cues (Lamm and Lewis, 2010), consistent with adoles-

cent and adult studies (Albert et al., 2010; Cohen Kadosh et al., 2014).

At the neurophysiological level, we hypothesised that the emotional context, particularly the presence of angry faces, would affect inhibitory brain processes and this would be expressed by greater activation in brain areas classically linked to inhibition.

Whole brain analyses revealed a significant interaction between task conditions (no-go Inhibition vs. no-go Vigilance) and socio-emotional cues (Angry vs. Happy): specific brain regions were more active in the inhibition condition (Inhibition no-go trials) with the incidental exposure to Angry but not Happy faces.

The early sensitivity of the angular gyrus and occipital cortex to emotion regulation mechanisms (Inhibition: Angry > Happy) was unanticipated. While previous ERP studies reported a crucial role of the P100, located over posterior occipito-parietal sites, for inhibition processes or face processing (Batty and Taylor, 2006), the sensitivity of this early component to emotion regulation was not systematically reported in other EEG studies (Hum et al., 2013a,b). However, adult fMRI studies found stronger activity in the right angular gyrus when inhibition processes occurred with the incidental exposure to aversive compared to neutral pictures (Brown et al., 2012) but fMRI cannot provide information on the timing of activation. Both the P1 and the angular gyrus have been related to processes of visual attention and conflict monitoring during go/no-go tasks (Corbetta, 1998; Hillyard et al., 1998; Corbetta and Shulman, 2002; Singh-Curry and Husain, 2009; Seghier, 2013). Thus, our results suggest that the early activity in the right angular gyrus may reflect neural recruitment to meet the higher visual attention demands required to mediate impulse control due to the emotional context.

The combination of high temporal and spatial resolution provided by our MEG study, also helped clarify the N2 generators, reported as a key component of inhibition and emotion regulation processes by several ERP studies (e.g., Lewis et al., 2007; Todd et al., 2008). In particular, our results showed that the incidental exposure to Angry compared to Happy faces was associated with stronger, longer-lasting brain inhibition-related activations in the right OFG from 225 to 325 ms. Worth noticing, activations reported in the orbito-frontal gyrus were the only ones surviving the correction for multiple comparisons threshold ($p < 0.05$ corrected), other activations discussed here were significant at $p < 0.005$ uncorrected (see Table 1 in bold).

The OFG is known to be modulated by interactions between response inhibition (go/no-go task) and stimulus valence, both in children (Todd et al., 2012) and adults (Shafritz et al., 2006; Goldstein et al., 2007). Moreover, convergent research studies indicate that the orbitofrontal region evaluates and regulates how emotion influences control mechanisms which guide ongoing actions (Pessoa, 2009) and, thus plays an important role in flexible social behaviour [for reviews see, Schoenbaum et al., 2009; Nelson and Geyer, 2011]. For instance, it has been shown that the OFG is implicated in evaluating the degree of control required to modify or inhibit actions elicited by the facial expression (e.g., unpleasant or discouraging) in children (Blair et al., 1999; Todd et al., 2012). Our results suggest that OFG-related changes in amplitude associated with inhibition processes occurring from 225 to 325 ms after no-go (inhibitory) trials would help guide further behaviour in response to facial expressions (i.e., towards action vs. inaction). In addition, our results showed that automatic emotion regulation processes related to the OFG were *right* lateralized. This is consistent with adult studies showing that negative affect (see Davidson, 2004) or avoidance behaviour (Harmon-Jones, 2004) will trigger greater right-lateralized frontal responses. As well, earlier studies of facial affect in children which also showed right-lateralised OFG activity (Todd et al., 2008, 2012).

Immediately after the recruitment of the right OFG, inhibitory-related brain processes to Angry faces activated the ventral part of the left anterior temporal pole (ATL) from 325 to 425 ms, although this did not survive correction for multiple comparisons. However, this region of the ATL is known to be involved in the encoding and retrieval of

individual faces, and also in the rapid binding of faces with other pieces of information including affective tone (Eifuku et al., 2010; Olson et al., 2013). Prior studies have shown that the non-conscious perception of facial expressions can activate learned associations and/or modulate cognitive processes (Ohman, 2002; Tottenham et al., 2011). Therefore, it may be that the recruitment of the right OFG, which analyzes the control required for decision making regarding an aversive stimulus, may trigger the retrieval of learned associations stored in the ventral left ATL. This hypothesis is supported by a recent meta-analysis suggesting that socially and emotionally tagged knowledge stored in the ATL would guide orbitofrontal-based decision processes (Olson et al., 2013 and see Olson et al., 2007 for a review of temporal pole functions).

In conclusion, this study is the first to characterize the precise spatiotemporal brain dynamics underlying automatic emotion regulation in children using MEG. Our results showed that inhibition processes which occurred with the incidental exposure to aversive socio-emotional stimuli (Angry compared to Happy faces) which produced brain activity which helped children regulate their responses in an emotional context. Our results suggest that 125 ms after the no-go stimulus, the angular gyrus may participate in the recruitment of extra visual attention needed to mediate impulse control, after which, the right OFG and the ventral section of the left ATL would work in concert, from 225 to 425 ms, to analyze the degree of control required to guide appropriate decision drawing upon learned associations related to the aversive situation. These findings align with previous studies which have shown that these regions, and in particular connectivity patterns including the OFG and the ATL, are critical in high-level social behaviours and should be further investigated in various psycho-affective or neurodevelopmental disorders known to have difficulties with emotion regulation. Finally, future investigations such as connectivity analyses involving causality measures, could clarify the functional contribution of the spatio-temporal dynamics observed between the fronto-temporo-parietal regions and the relation between behavioural processes and automatic emotion regulation in children.

Conflict of Interest:

None.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.dcn.2017.05.004>.

References

- Albert, J., Lopez-Martin, S., Carretie, L., 2010. Emotional context modulates response inhibition: neural and behavioral data. *Neuroimage* 49 (1), 914–921.
- Barnes, G.R., Litvak, V., Brookes, M.J., Friston, K.J., 2011. Controlling false positive rates in mass-multivariate tests for electromagnetic responses. *Neuroimage* 56 (3), 1072–1081.
- Batty, M., Taylor, M.J., 2006. The development of emotional face processing during childhood. *Dev. Sci.* 9 (2), 207–220.
- Blair, R.J., Morris, J.S., Frith, C.D., Perrett, D.I., Dolan, R.J., 1999. Dissociable neural responses to facial expressions of sadness and anger. *Brain* 122 (Pt 5), 883–893.
- Bonanno, G.A., 2004. Loss, trauma, and human resilience: have we underestimated the human capacity to thrive after extremely aversive events? *Am. Psychol.* 59 (1), 20–28.
- Brookes, M.J., Wood, J.R., Stevenson, C.M., Zumer, J.M., White, T.P., Liddle, P.F., et al., 2011. Changes in brain network activity during working memory tasks: a

- magnetoencephalography study. *Neuroimage* 55 (4), 1804–1815.
- Brown, M.R., Lebel, R.M., Dolcos, F., Wilman, A.H., Silverstone, P.H., Pazderka, H., et al., 2012. Effects of emotional context on impulse control. *Neuroimage* 63 (1), 434–446.
- Cohen Kadosh, K., Heathcote, L.C., Lau, J.Y., 2014. Age-related changes in attentional control across adolescence: how does this impact emotion regulation capacities? *Front. Psychol.* 5, 111.
- Cole, P.M., Martin, S.E., Dennis, T.A., 2004. Emotion regulation as a scientific construct: methodological challenges and directions for child development research. *Child Dev.* 75 (2), 317–333.
- Corbetta, M., Shulman, G.L., 2002. Control of goal-directed and stimulus-driven attention in the brain. *Nat. Rev. Neurosci.* 3 (3), 201–215.
- Corbetta, M., 1998. Frontoparietal cortical networks for directing attention and the eye to visual locations: identical, independent, or overlapping neural systems? *Proc. Natl. Acad. Sci. U. S. A.* 95 (3), 831–838.
- Davidson, R.J., 2004. What does the prefrontal cortex “do” in affect: perspectives on frontal EEG asymmetry research. *Biol. Psychol.* 67 (1–2), 219–233.
- Eifuku, S., Nakata, R., Sugimori, M., Ono, T., Tamura, R., 2010. Neural correlates of associative face memory in the anterior inferior temporal cortex of monkeys. *J. Neurosci.* 30 (45), 15085–15096.
- Goldstein, M., Brendel, G., Tuescher, O., Pan, H., Epstein, J., Beutel, M., et al., 2007. Neural substrates of the interaction of emotional stimulus processing and motor inhibitory control: an emotional linguistic go/no-go fMRI study. *Neuroimage* 36 (3), 1026–1040.
- Gross, J.J., Muñoz, R.F., 1995. Emotion regulation and mental health. *Clin. Psychol.: Sci. Pract.* 2, 151–164.
- Gross, J.J., 2002. Emotion regulation: affective, cognitive, and social consequences. *Psychophysiology* 39 (3), 281–291.
- Gross, J.J., 2014. *Handbook of Emotion Regulation*, 2 ed. Guilford Press, New York, NY.
- Gyurak, A., Gross, J.J., Etkin, A., 2011. Explicit and implicit emotion regulation: a dual = process framework. *Cogn. Emot.* 25, 400–412.
- Hare, T.A., Tottenham, N., Galvan, A., Voss, H.U., Glover, G.H., Casey, B.J., 2008. Biological substrates of emotional reactivity and regulation in adolescence during an emotional go-nogo task. *Biol. Psychiatry* 63 (10), 927–934.
- Hari, R., Parkkonen, L., Nangini, C., 2010. The brain in time: insights from neuromagnetic recordings. *Ann. N. Y. Acad. Sci.* 1191, 89–109.
- Harmon-Jones, E., 2004. Contributions from research on anger and cognitive dissonance to understanding the motivational functions of asymmetrical frontal brain activity. *Biol. Psychol.* 67 (1–2), 51–76.
- Hillyard, S.A., Vogel, E.K., Luck, S.J., 1998. Sensory gain control (amplification) as a mechanism of selective attention: electrophysiological and neuroimaging evidence. *Philos. Trans. R. Soc. Lond. B: Biol. Sci.* 353 (1373), 1257–1270.
- Hopp, H., Troy, A.S., Mauss, I.B., 2011. The unconscious pursuit of emotion regulation: implications for psychological health. *Cogn. Emot.* 25 (3), 532–545.
- Hum, K.M., Manassis, K., Lewis, M.D., 2013a. Neural mechanisms of emotion regulation in childhood anxiety. *J. Child Psychol. Psychiatry* 54 (5), 552–564.
- Hum, K.M., Manassis, K., Lewis, M.D., 2013b. Neurophysiological markers that predict and track treatment outcomes in childhood anxiety. *J. Abnorm. Child Psychol.* 41 (8), 1243–1255.
- Kilner, J.M., Kiebel, S.J., Friston, K.J., 2005. Applications of random field theory to electrophysiology. *Neurosci. Lett.* 374 (3), 174–178.
- Koole, K.L., Rothermund, K., 2011. “I feel better but I don’t know why”: the psychology of implicit emotion regulation. *Cogn. Emot.* 25, 389–399.
- Koole, S.L., Webb, T.L., Sheeran, P.L., 2015. Implicit emotion regulation: feeling better without knowing why. *Curr. Opin. Psychol.* 3, 6–10.
- Kovacevic, N., McIntosh, A.R., 2007. Groupwise independent component decomposition of EEG data and partial least square analysis. *Neuroimage* 35 (3), 1103–1112.
- Lamm, C., Lewis, M.D., 2010. Developmental change in the neurophysiological correlates of self-regulation in high- and low-emotion conditions. *Dev. Neuropsychol.* 35 (2), 156–176.
- Lewis, M.D., Todd, R.M., Honsberger, M.J., 2007. Event-related potential measures of emotion regulation in early childhood. *Neuroreport* 18 (1), 61–65.
- Litvak, V., Mattout, J., Kiebel, S., Phillips, C., Henson, R., Kilner, J., et al., 2011. EEG and MEG data analysis in SPM8. *Comput. Intell. Neurosci.* 2011, 852961.
- Moore, S.A., Zoellner, L.A., Mollenholt, N., 2008. Are expressive suppression and cognitive reappraisal associated with stress-related symptoms? *Behav. Res. Ther.* 46 (9), 993–1000.
- Nelson, E.E., Guyer, A.E., 2011. The development of the ventral prefrontal cortex and social flexibility. *Dev. Cogn. Neurosci.* 1 (3), 233–245.
- Nolte, G., 2003. The magnetic lead field theorem in the quasi-static approximation and its use for magnetoencephalography forward calculation in realistic volume conductors. *Phys. Med. Biol.* 48 (22), 3637–3652.
- Ohman, A., 2002. Automaticity and the amygdala: nonconscious responses to emotional faces. *Curr. Dir. Psychol. Sci.* 11, 62–66.
- Olson, I.R., Plotzker, A., Ezzyat, Y., 2007. The Enigmatic temporal pole: a review of findings on social and emotional processing. *Brain* 130 (Pt 7), 1718–1731.
- Olson, I.R., McCoy, D., Klobusicky, E., Ross, L.A., 2013. Social cognition and the anterior temporal lobes: a review and theoretical framework. *Soc. Cogn. Affect. Neurosci.* 8 (2), 123–133.
- Oostenveld, R., Fries, P., Maris, E., Schoffelen, J.M., 2011. FieldTrip: open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. *Comput. Intell. Neurosci.* 2011, 156869.
- Penny, W., Holmes, A., et al., 2003. Random-effect analysis. In: Frackowiak, R., Friston, K., Frith, C., Dolan, R., Price, C. (Eds.), *Human Brain Function*, 2nd ed. Academic Press, London.
- Pessoa, L., 2009. How do emotion and motivation direct executive control? *Trends Cogn. Sci.* 13 (4), 160–166.
- Schoenbaum, G., Roesch, M.R., Stalnaker, T.A., Takahashi, Y.K., 2009. A new perspective on the role of the orbitofrontal cortex in adaptive behaviour. *Nat. Rev. Neurosci.* 10 (12), 885–892.
- Seghier, M.L., 2013. The angular gyrus: multiple functions and multiple subdivisions. *Neuroscientist* 19 (1), 43–61.
- Shafritz, K.M., Collins, S.H., Blumberg, H.P., 2006. The interaction of emotional and cognitive neural systems in emotionally guided response inhibition. *Neuroimage* 31 (1), 468–475.
- Singh-Curry, V., Husain, M., 2009. The functional role of the inferior parietal lobe in the dorsal and ventral stream dichotomy. *Neuropsychologia* 47 (6), 1434–1448.
- Todd, R.M., Lewis, M.D., Meusel, L.A., Zelazo, P.D., 2008. The time course of social-emotional processing in early childhood: ERP responses to facial affect and personal familiarity in a Go-Nogo task. *Neuropsychologia* 46 (2), 595–613.
- Todd, R.M., Lee, W., Evans, J.W., Lewis, M.D., Taylor, M.J., 2012. Withholding response in the face of a smile: age-related differences in prefrontal sensitivity to Nogo cues following happy and angry faces. *Dev. Cogn. Neurosci.* 2 (3), 340–350.
- Tottenham, N., Tanaka, J.W., Leon, A.C., McCarry, T., Nurse, M., Hare, T.A., 2009. The NimStim set of facial expressions: judgments from untrained research participants. *Psychiatry Res.* 168 (3), 242–249.
- Tottenham, N., Hare, T.A., Casey, B.J., 2011. Behavioral assessment of emotion discrimination, emotion regulation, and cognitive control in childhood, adolescence, and adulthood. *Front. Psychol.* 2, 39.
- Urban, S., Van der Linden, M., Barisnikov, K., 2012. Emotional modulation of the ability to inhibit a prepotent response during childhood. *Dev. Neuropsychol.* 37 (8), 668–681.
- Vidal, J., Mills, T., Pang, E.W., Taylor, M.J., 2012. Response inhibition in adults and teenagers: spatiotemporal differences in the prefrontal cortex. *Brain Cogn.* 79 (1), 49–59.
- Wens, V., Marty, B., Mary, A., Bourguignon, M., Op de Beeck, M., Goldman, S., 2015. A geometric correction scheme for spatial leakage effects in MEG/EEG seed-based functional connectivity mapping. *Hum. Brain Mapp.* 36 (11), 4604–4621.