Neuropsychologia xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

Neural functional correlates of the impact of socio-emotional stimuli on performances on a flanker task in children aged 9–11 years☆

Morgane Réveillon[a,*], François Lazeyras[b], Laurens Van Calster[a], Yann Cojan[c], David Sander[d], Petra S. Hüppi[e,1], Koviljka Barisnikov[a,1]

[a] Child Clinical Neuropsychology Unit, University of Geneva, Bld. Du Pont-d'Arve 40, CH-1211 Geneva 4, Switzerland
[b] Radiology Department, University Hospital of Geneva, Switzerland
[c] Department of Neuroscience, University Medical School of Geneva, Switzerland
[d] Laboratory for the study of Emotion Elicitation and Expression, University of Geneva, Switzerland
[e] Division of Development and Growth, Department of Pediatrics, University Hospital of Geneva, Switzerland

ARTICLE INFO

Keywords:
Children
Interference
Emotion
Amygdala
ACC
Faces

ABSTRACT

Immature cognition is susceptible to interference from competing information, and particularly in affectively charged situations. Several studies have reported activation in the anterior cingulate cortex, prefrontal cortex and amygdala associated with emotional conflict processing in adults but literature is lacking regarding children. Moreover, studies in children and adolescents still disagree regarding the functional activation of amygdala related to facial stimuli. In the purpose of investigating both the effect of socio-emotional stimuli and its interaction with interference control, we designed a flanker task associated with an event-related fMRI paradigm in 30 healthy children ages 9–11. In addition to happy, angry and neutral faces, we presented scrambled stimuli to examine a potential effect of faces. Regarding both brain and behavior results, no effect of emotional valence was observed. However, both results evidenced an emotional effect of faces compared with scrambled stimuli. This was expressed by faster RTs associated with increased amygdala activity and activation of the ventral ACC, in congruent trials only. When scrambled were inversely compared to faces, increased activity was observed within the lateral prefrontal cortex. Regarding the amygdala, the results suggest that in late school age children, activity in the amygdala seemed to underlie the socio-emotional effect induced by faces but not the emotional conflict. Studying brain regions involved in emotion regulation is important to further understand neurodevelopmental disorders and psychopathologies, particularly in late childhood and adolescence.

1. Introduction

Conceiving the relation between cognitive and affective brain networks is thought to be crucial for self-regulation and decision making, and thus for understanding psychopathologies, particularly in late childhood and adolescence (Arnsten and Rubia, 2012; Kar et al., 2013; Nigg et al., 2010). It has been well established that immature cognition is susceptible to interference from competing information and actions (Bunge and Crone, 2009; Durston et al., 2002; Kar et al., 2013), and particularly in affectively charged situations. Interference control, also referred to as conflict monitoring, is a core aspect of cognitive control which is crucial to higher functioning. It is defined as the ability to selectively attend to task-relevant information while inhibiting distracting information and covers both selective attention and inhibition abilities. Most fMRI studies measuring interference control in children used Flanker or Stroop tasks (Adleman et al., 2002; Bunge et al., 2002; Huyser et al., 2011; Konrad et al., 2005), which have been found well suited to study neural correlates associated with developmental changes (Casey et al., 2005; Kerns et al., 2005; Menon, 2013; Schulz et al., 2005). None one of these studies explored the impact of an emotional context on interference control abilities. However, in everyday life, we are often confronted with affectively charged situations.

The presence of affect or emotion can have an impact on our ability to inhibit the interference of distracting information to focus on our

☆ Note: The funding sources had no involvement in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

* Corresponding author.
E-mail addresses: Morgane.Reveillon@unige.ch (M. Réveillon), Francois.Lazeyras@unige.ch (F. Lazeyras), Laurens.VanCalster@unige.ch (L. Van Calster), y.cojan@gmail.com (Y. Cojan), David.Sander@unige.ch (D. Sander), Petra.Huppi@hcuge.ch (P.S. Hüppi), Koviljka.Barisnikov@unige.ch (K. Barisnikov).
[1] These two authors contributed equally to this work.

https://doi.org/10.1016/j.neuropsychologia.2018.04.004
Received 29 May 2017; Received in revised form 17 March 2018; Accepted 4 April 2018

main goal. Adult studies using fMRI to examine the impact of emotional stimuli on interference control or inhibition (Etkin et al., 2006; Goldstein et al., 2007; Hare et al., 2005; Kanske and Kotz, 2011b; Ochsner et al., 2008; Shafritz et al., 2006) have reported activity in the anterior cingulate cortex (ACC), amygdala, and prefrontal regions including orbitofrontal cortex (OFC), posterior medial frontal cortex and lateral prefrontal cortex (PFC). Interference control in general has been primarily associated with activation in regions from the PFC and the ACC. Moreover, the PFC is critically involved in top-down regulation of attention, inhibition, and emotion through connections with posterior cortical and subcortical structures (Arnsten and Rubia, 2012). These fronto-striato-cerebellar or fronto-limbic circuits develop late and progressively between childhood and adulthood and are thus sensitive to neurodevelopmental disorders (Arnsten and Rubia, 2012; Blair and Dennis, 2010; Kar et al., 2013; Nigg et al., 2010). The ACC, which maturation has been related to age improvements in conflict resolution (Posner and Rothbart, 2007), seems to be divided in two major parts. The dorsal part has connections with the PFC and is related to conflict monitoring (Botvinick et al., 2004; Ridderinkhof et al., 2004), irrespective of the cognitive or emotional status of the task (Kanske and Kotz, 2011a; Ochsner et al., 2008). The second part, more ventral and rostral, has connections with the limbic system and is associated with emotional processes (Bush et al., 2000). The amygdala and OFC are both part of the socio-emotional processing network, which also includes the fusiform and inferior occipital gyri, and the superior temporal sulcus (Leppanen and Nelson, 2009; Monk et al., 2003; Vuilleumier, 2005). These regions are involved in the recognition of facial emotional expressions and cues from social relations that are important for social interactions and peer relationships (Healy et al., 2013; Leppanen and Nelson, 2009). Activation of the OFC, ACC and amygdala have also been evidenced in an fMRI study comparing 8–17 year olds and adults on selective attention during the viewing of emotional face stimuli (Monk et al., 2003). More precisely, compared with adults, adolescents showed greater activation of the OFC, ACC and right amygdala related to fearful vs neutral faces, when attention was unconstrained (passive viewing condition) but less activation of the OFC in goal-directed attention situation. Activation of the amygdala has been predominantly associated with explicit recognition, passive viewing, and implicit processing of emotional faces in studies including children and adolescents (see Wu et al., 2016). Compared with adults, children and adolescents exhibit greater activation in paralimbic regions and the amygdala and less activation of prefrontal regions, including ventromedial PFC (Guyer et al., 2008; Hare et al., 2008; Passarotti et al., 2009) to emotional faces. Nevertheless, results differ depending of the emotional valence. For example, Thomas et al. (2001a), (2001b) have reported that adults demonstrate greater amygdala activation to fearful faces compared to neutral ones whereas 11-year-old children demonstrate the opposite pattern (Thomas et al., 2001a, 2001b). In a recent study, children and adolescents aged 8–16 exhibited greater activation of amygdala to angry, fearful and neutral faces as compared to happy faces (Marusak et al., 2013). Functional investigation of amygdala in children is still needed as it is important for understanding the maturation of emotional processing in the typically developing brain in order to further help understanding selective vulnerability to affective disorders (Menon, 2013).

The main aim of the current study was to explore the effect of facial expressions of emotions and its impact on interference control in late school-age children, using a flanker-type of task. Considering that children's cognition is particularly susceptible to interference from competing information and actions (Bunge and Crone, 2009; Durston et al., 2002; Kar et al., 2013), we hypothesized a negative impact of emotional stimuli on interference control at both brain and behavior level. The flanker task with faces stimuli (happy, angry and neutral) was designed in a way that allowed us to manipulate the socio-emotional effect (implicit emotional perception) independently of interference control (Kanske and Kotz, 2011b). Given that neutral faces were reported to activate emotion-related areas such as the amygdala in late school-age children and adolescents (Marusak et al., 2013; Thomas et al., 2001a, 2001b), the current study included a fully neutral, non-social and non-semantic stimulus ("scrambled"). This enabled investigating both brain regions related to a main effect of faces stimuli and those related to a more specific effect of emotional valence. Despite the fact that Stroop and flanker tasks seem well suited to study neural correlates associated with developmental changes, whereas flanker tasks are known to be sensitive tools, Stroop tasks have been questioned (Huizinga et al., 2006; Mullane et al., 2009; Nigg, 2000). Angry faces were preferred to fearful ones given the divergent literature regarding fearful faces in children and adults. Moreover, angry is the opposite emotion to happy and we wanted comparable emotions.

We expected the socio-emotional effect of faces and its impact on interference control to be related to activation in regions such as the ACC, OFC and amygdala (emotional conflict and emotional network). Finally, we aimed to explore whether these regions, in particular amygdala, and other regions from the PFC are associated with task performances.

2. Methods

2.1. Sample

Thirty-five children aged 9–11 years recruited though local mainstream primary schools took part to the study. Five children were excluded due to poor fMRI scan quality (n = 1), poor behavioral data due to a lack of motivation (n = 2), or motion greater than 1 mm exceeding a rate of 20% of the scans (n = 2), leaving 30 subjects (15 girls and 15 boys) available for analyses. Age at assessment ranged between 9.01 and 11.97 (M = 10.47; SD = 0.8) and the family's socioeconomic status (SES) based on parental occupation and maternal education (Largo et al., 1989) ranged between 2 (highest score) and 10 (12 being the lowest score - M = 5.94; SD = 1.88). Children were assessed with the Coloured Progressive Matrices (Raven et al., 1998) to estimate their basic non-verbal intelligence (raw score: M = 30.97; SD = 2.99; all participants' percentile scores ≥ 50).

This study was approved by the ethical review board of Geneva University. Written informed consent to take part in the study was obtained from parents and oral consent from participants. They were acknowledged of being free to withdraw from the procedure at any time.

2.2. Testing procedure

Participants were individually assessed with a modified version of a flanker task (Eriksen and Eriksen, 1974) using an event-related fMRI paradigm. On each trial, they were presented an array of three pictures consisting of a central picture (target stimulus) surrounded by two pictures on either side of it (flankers). The three stimuli composing one array were always of the identical identity and type: happy, angry, neutral or scrambled. They were presented in black and white or in color. The task contained two flanker conditions. In congruent conditions (50%), the flankers appeared in the same color as the central stimulus, while in incongruent conditions (50%), the flankers were in the opposite color (i.e. if the central stimulus was in color, the flankers were in black and white and inversely). Participants responded by using the index and middle finger of their right hand to press either of two buttons on a button box which rested in their lap, maintained by their left hand. They were instructed to respond as quickly and accurately as possible by pressing the left button if the central stimulus was in color and the right button if it was in black and white, while ignoring the flanking stimuli. The stimulus-response assignments were reversed for half of the participants.

Faces stimuli consisted in photographs of happy, angry and neutral facial expressions from 16 individuals (8 females and 8 males) selected

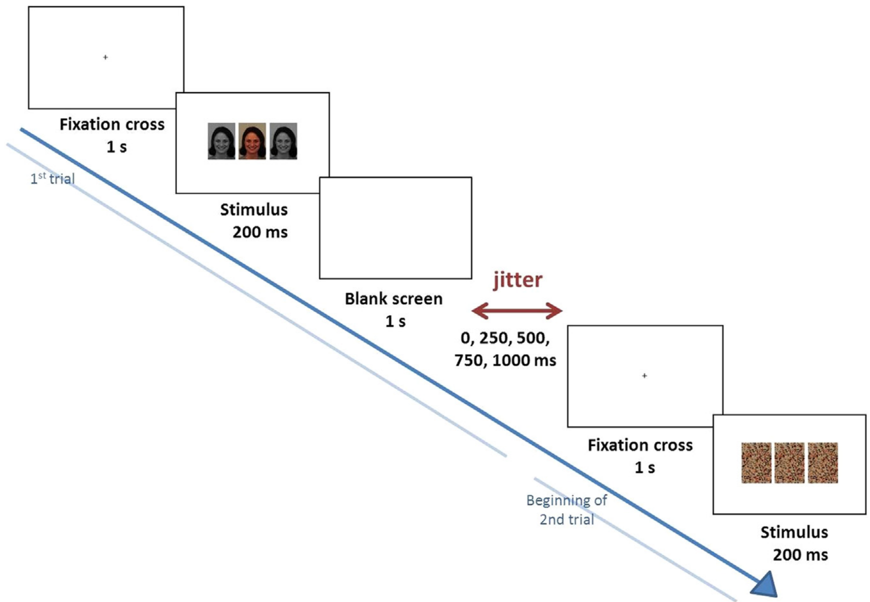

Fig. 1. Time course of a trial.

from the NimStim Set of Facial Expressions available at www.macbrain.org (Tottenham et al., 2009). Scrambled stimuli were made from the same photographs by scrambling them such that faces were impossible to recognize (see Fig. 1). The task consisted of 512 trials and was divided in two identical runs composed of 256 trials each. Following Fenske and Eastwood (2003), each run contained 32 repetitions of the eight different types of trials (i.e. task conditions), defined by the factorial combination of flankers (i.e. congruent or incongruent) and stimuli (i.e. happy, angry, neutral, or scrambled). Each photograph of one individual was only presented once for each possible combination (flanker condition x stimuli type x color vs black and white). Each run lasted approximately 12 min and was divided into four blocks, separated by 10 s rest periods during which the word "pause" appeared on the screen. Each trial started with a central cross (1000 ms), followed by the brief appearance of the array of three stimuli (200 ms), and ended with a blank response screen (1000 ms). The appearance of the array of stimuli was intentionally brief to ensure its processing is implicit. The next trial was preceded by a jittered between-trials interval of 0, 250, 500, 750, or 1000 ms (Goghari and MacDonald, 2008; Huyser et al., 2011) (Fig. 1).

All children viewed the stimuli displayed on a white background on the screen at the head of the scanner via a 45° angled mirror fixed to the MRI head coil. Each stimulus measured 2.3 cm horizontally and 3.2 cm vertically, subtended visual angles of 1.32° and 1.83° respectively. The stimuli array measured 7.9 cm, subtending a visual angle of 4.5°. Prior to scanning, a practice session of 12 trials was performed to ensure familiarity with the task and was repeated if necessary. The Paradigm programming, stimuli display and responses logging were done using E-prime (Psychology Software Tools, Pittsburgh, PA, USA). The anatomical images were collected in the middle of the two identical runs of the flanker task. This structural 6 min long scan allowed the participants to rest, watching a cartoon of their choice.

2.3. Data acquisition

Scanning was performed using a 3 T system with a 12-channel receiver head coil (Magnetom Tim-Trio, Siemens Medical Solutions, Erlangen, Germany). For the functional scans, echo-planar imaging (EPI) blood oxygenated level-dependent (BOLD) images were acquired with the following parameters: time repetition [TR] = 2500 ms; echo time [TE] = 30 ms; 42 axial slices; slice thickness = 3 mm, no gap between slices, flip angle = 90°, matrix size = 74 × 100, field of view [FOV] = 220 mm. High resolution 3D anatomical images were also collected for each participant using isotropic T1-weighted MPRAGE sequence, with the following parameters: TR = 2500 ms; TE = 2.91 ms; TI = 900 ms; flip angle = 8°; voxel size = 1 × 1 × 1 mm^3 ; matrix size = 256 × 96, FOV = 256 mm, 224 slices. Subject's head was immobilized using foam pads inside the coil to minimize motion.

2.4. Data analyses

Behavioral data from the two identical runs were averaged for each condition and analyzed using SPSS (version 19.0; SPSS Inc., USA) and Statistica (version 12; StatSoft Inc., USA) softwares. Error rate and mean reaction time (RT) related to correct responses were measured for each participant and further correlated Pearson correlations were ran between those measures and age, gender, SES, basic non-verbal intelligence and speed of processing. Repeated-measures ANOVAs were then conducted in order to investigate the influence of the type of flanker condition (interference effect) on performances, as well as the influence of the type of stimulus (effect of faces and effect of emotion) and the possible interaction between flanker condition and stimulus.

Imaging data were processed and analyzed using Matlab (Mathworks, Natick, MA, USA Version 7.13) and SPM8 (Wellcome Trust Center for Neuroimaging, London, UK: http://www.fil.ion.ucl.ac.uk/spm/). Images were motion corrected using rigid-body realignment. Regarding motion parameters, scans with motion greater than 1 mm (total displacement) were considered as corrupted scans. Estimated motion parameters were examined on a subject-by-subject basis, and subjects demonstrating a rate of motion-corrupted scans (> 1 mm) exceeding 20% were excluded. Image slices were acquired in descending order and slice time correction was conducted with the use of the middle slice as reference. T1-weighted anatomical images of each individual were coregistered to the mean realigned functional image and then segmented using diffeomorphic anatomical registration through exponentiated lie algebra (Dartel) algorithm (Ashburner, 2007) to generate a custom template from all the subjects included in the present study. This template was subsequently used to normalize the realigned fMRI images to the MNI standard space. The normalized images were then spatially smoothed using an 8 mm Gaussian filter.

A general linear model (Friston et al., 1994) was built using SPM8 to analyze the data. Activity of interest comprised brain activity from the

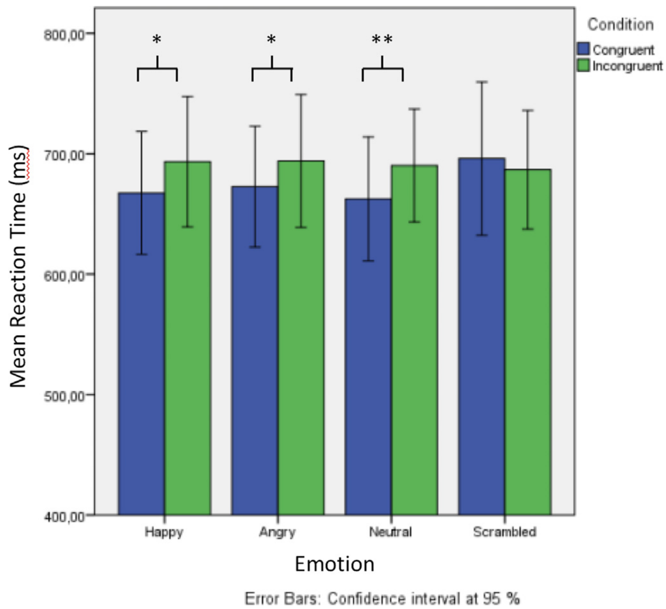

Fig. 2. Flanker condition by stimulus interaction. The difference of mean reaction times (ms) between congruent and incongruent conditions was significant in all faces (happy, angry, and neutral, showing an interference effect, but was not significant in scrambled stimuli. * significant at p < .05; ** significant at p < .01.

end of the stimuli presentation till the beginning of the response. The event-related regressors related to the two runs were entered as two sessions in one model. This design matrix consisted of the event onsets of each condition (8) in each run, separated for correct responses and errors, their time and dispersion derivatives, and head movement parameters from realignment. For each subject, contrasts images related to correct responses were computed for each condition pooled across the two runs. Second-level random effects were analyzed using repeated measures analysis of variance (ANOVA). This model was similar to the behavioral ANOVA model and tested the interaction between the socio-emotional effect of stimuli and the interference control effect. We investigated a specific effect of emotional valence by contrasting happy and angry faces with each other and neutral faces. Further contrasts were then performed in line with behavioral results. First, to further investigate the socio-emotional effect, we contrasted faces (happy + angry + neutral) with scrambled stimuli. Second, the incongruent > congruent contrast was performed in general to investigate brain activity associated with interference. Third, we investigated the interference effect specific to faces by contrasting incongruent and congruent faces. Finally, the faces > scrambled contrast was performed separately for congruent and incongruent trials to investigate the face effect in congruent or incongruent conditions. The scrambled > faces contrast was performed separately for congruent and incongruent trials as a simple matter of verification that our patterns of activation were actually following behavioral results. Whole brain analysis contrasts employed a statistical threshold of p < .05, corrected for multiple comparisons (FWE-corrected), with a minimum extent threshold of 5 contiguous voxels. Because the aim of the study was to identify activity in a priori defined regions of interest, coordinates reported for each region of interest were selected from the literature on cerebral activity associated with the processing of facial expressions of emotions and its interaction with interference control (Etkin et al., 2006; Goldstein et al., 2007; Hare et al., 2005; Kanske and Kotz, 2011b; Ochsner et al., 2008; Shafritz et al., 2006). In case of multiple coordinates for a small region, a mean was calculated for the same functional region (this was the case for the amygdala). Each coordinate of interest was used as a center for a 10-mm radius sphere. The selected coordinates included the left amygdala (−20, −2, −20), the right amygdala (22, −8, −15), the ventral ACC (−10, 42, 1), dorsal ACC (9, −3, 36), the posterior Medial Frontal Cortex (−9, 27, −18; 6, 22, −21), and the lateral PFC (−44, 18, 24; 45, 10, 32; −42, 40, 8). In order to control for the effect of age on brain activation during the task (unexpected given the narrow age range), we computed a second model with age entered as a covariate. Per convention, we named "activations" all statistically significant differences in BOLD signal response (Goldstein et al., 2007). Finally, to identify regions for which level of activation across subjects was correlated with in-scanner behavioral performance or age (as a second verification), Pearson linear correlations were calculated using SPSS Version 19. Correlation analyses with behavioral performances were restricted to several regions of interest (PFC, ACC, and amygdala). In order to perform correlation analyses, we extracted mean first eigenvariates from the significantly activated regions of interest, using a 10 mm diameter sphere at the peak statistical value. All results are displayed in MNI space.

3. Results

3.1. Behavioral data

Overall, mean error rate was 11.5% ($M = 11.5\%$, $SD = 7.4$) and mean RT was 682.3 ms ($M = 682.3$ ms, $SD = 136.2$). Most errors consisted of incorrect responses rather than non-responses. Pearson correlations between errors (number of errors) and RTs did not reveal any speed-accuracy tradeoff ($r = .095$, $p > .050$). RTs did not correlate with age, gender, SES, or basic non-verbal intelligence. Errors were negatively associated to age ($r = -.370$; $p = .042$) only. A repeated measures ANOVA performed on RT with a Greenhouse-Geisser correction showed an interference effect (RT incongruent (690.8 ms) > RTs congruent (674.1 ms); $F(1,29) = 6.39$, $p = .017$, $\eta^2 = .181$) and a significant flanker by stimulus interaction ($F(2,66) = 3.79$, $p = .023$, $\eta^2 = .116$; see Fig. 2). Average RT did not differ significantly between stimuli, $F(3,71) = 1.31$, $p = .279$, $\eta^2 = .043$. Planned contrasts revealed an interference effect for happy (693.3 vs. 667.4 ms; $F(1,29) = 7.24$, $p = .012$), angry (694.0 vs. 672.6 ms; $F(1,29) = 4.61$, $p = .040$), and neutral (690.3 vs. 662.5 ms; $F(1,29) = 9.5$, $p = .005$) stimuli. Mean RT for faces differed from RT for scrambled stimuli in congruent flanker condition (667.5 vs. 696.0 ms; $F(1,29) = 5.62$, $p = .025$) only. We did not observe significant differences in other conditions. Another repeated measures ANOVA performed on errors with a Greenhouse-Geisser correction did not reveal a main effect of interference ($F(1,29) = 1.19$, $p = .285$, $\eta^2 = .039$. However, the number of errors varied across stimuli (happy: 6.8; angry: 7.1; neutral: 6.9; scrambled: 8.6; $F(3,80) = 5.64$, $p = .002$, $\eta^2 = .163$) and a stimulus by flanker interaction ($F(3,83) = 4.09$, $p = .010$, $\eta^2 = .124$) was found. Planned contrasts indicated a higher mean number of errors for scrambled (8.6) compared to face stimuli (6.9; $F(1,29) = 12.21$, $p = .002$) and this effect was driven by congruent conditions only (4.6 vs. 3.2; $F(1,29) = 32.27$, $p = .000004$). However, given that errors were shown to correlate with age, when controlling for age, the main effect of stimuli on errors and the interaction between flanker and stimuli were not maintained. We did not observe significant differences in other conditions.

3.2. Brain imaging data

3.2.1. Socio-emotional effect

Brain activity associated with emotional valence showed no significant activations in the ROI analysis or whole-brain analysis. Based on behavioral results, happy, angry and neutral stimuli were averaged together as "faces" in order to be compared to scrambled stimuli. When investigating the effect of faces in general, ROI analysis has shown significant activation of the left and right amygdala as well as the ventral ACC (see Table 1). Additional regions, more specifically the left fusiform gyrus and the right inferior occipital gyrus, were observed in

Table 1
Activations revealed by the ROI analysis.

Brain region	Hem	Peak MNI coord. (*x, y, z*)			*t*(peak voxel)	Cluster size
Faces > Scrambled						
Amygdala**	R	18	−15	−15	4.81	14
	L	−18	−6	−15	4.17	19
ventral Anterior Cingulate Cortex *		−6	42	−9	3.82	5
Scrambled > Faces						
Lateral Prefrontal Cortex*	L	−39	39	15	3.77	6
Faces congruent > Scrambled congruent						
Amygdala**	R	18	−15	−15	4.58	19
	L	−18	−6	−15	4.67	24
ventral Anterior Cingulate Cortex *		−3	42	−6	3.63	7

Note. Activation related to correct responses. *ROIs are significant at $p < .05$, corrected for multiple comparisons at peak and cluster level (FWE-corrected) over small VOI. **ROIs are significant at $p < .01$, corrected for multiple comparisons at peak and cluster level (FWE-corrected) over small VOI. Hem = hemisphere. Faces = happy + angry + neutral stimuli averaged together.

Table 2
Activations revealed by the whole-brain analysis.

Brain region	Hem	Peak MNI coord. (*x, y, z*)			*t*(peak voxel)	Cluster level	BA
Faces > Scrambled							
Inferior Occipital Gyrus***	R	45	−81	−9	9.78	175	19
Fusiform Gyrus**	L	−39	−48	−24	5.52	8	37
Scrambled > Faces							
Fusiform Gyrus**	L	−27	−54	−15	6.67	19	37
Faces congruent > Scrambled congruent							
Inferior Occipital Gyrus***	L	45	−81	−9	6.65	80	19
Faces incongruent > Scrambled incongruent							
Inferior Occipital Gyrus***	R	45	−81	−6	7.04	31	19
Fusiform Gyrus***	R	39	−51	−18	6.46	34	37
Scrambled incongruent > Faces incongruent							
Fusiform Gyrus***	L	−27	−54	−15	5.64	13	37

Note. Activation related to correct responses. **ROIs are significant at $p < .01$, corrected for multiple comparisons at peak and cluster level (FWE-corrected) over small VOI. ***ROIs are significant at $p < .001$, corrected for multiple comparisons at peak and cluster level (FWE-corrected) over small VOI. Hem = hemisphere. BA = (nearest) Broadmann Area. Faces = happy + angry + neutral stimuli averaged together.

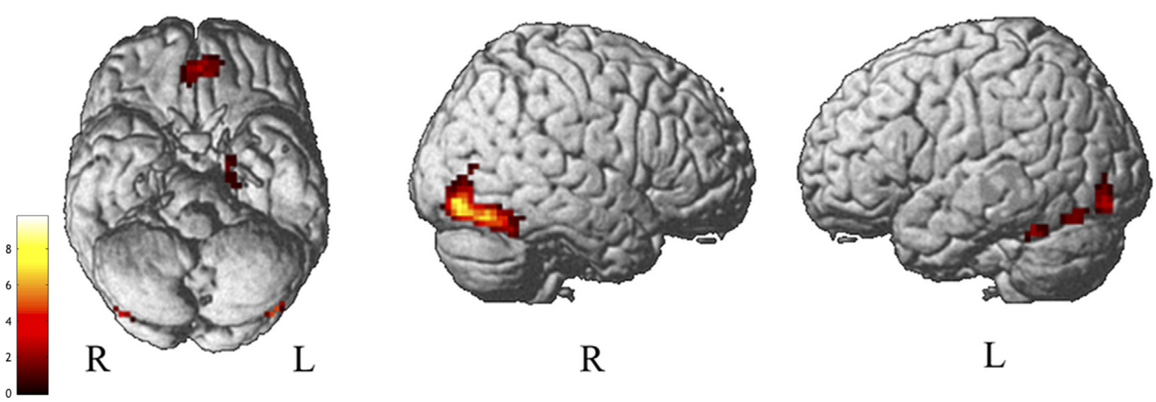

Fig. 3. Brain activity associated with socio-emotional effect of face perception. Activation related to faces vs. scrambled trials, displayed on 3-dimensional reconstructed brain images displayed at $p < .001$, uncorrected with a minimum cluster size of 30 voxels. The color bar represents the T score. Faces = happy + angry + neutral stimuli averaged together.

the whole-brain analysis (see Table 2 and Fig. 3). For the opposite effect, contrasting scrambled versus faces, we observed activation of the lateral PFC in the ROI analysis and an additional activation of the left fusiform gyrus in the whole-brain analysis.

3.2.2. Interference x face interaction

We observed no significant activations associated with the interaction of interference and faces (incongruent versus congruent x faces versus scrambled) in both the ROI and whole-brain analysis. Additional contrasts were performed based on the main behavioral results revealed by planned contrasts. First, the effect of interference was investigated by contrasting incongruent to congruent conditions. No significant activations were observed in the 'incongruent versus congruent' contrast for both the ROI and whole-brain analysis. Similarly, there were no significant activations for the 'incongruent faces versus congruent faces' contrast. Second, the face effect in congruent conditions, contrasting faces congruent to scrambled congruent, was associated with activation of the ventral ACC, and right and left amygdalae (Table 1) in the ROI analysis and showed additional activation of the right inferior occipital gyrus in the whole-brain analysis (Fig. 4). The face effect in incongruent conditions, contrasting faces incongruent to scrambled incongruent, did not show activation in our regions of interest, but was associated with activation in the right inferior occipital and fusiform gyri in the whole-brain analysis. No significant activations related to

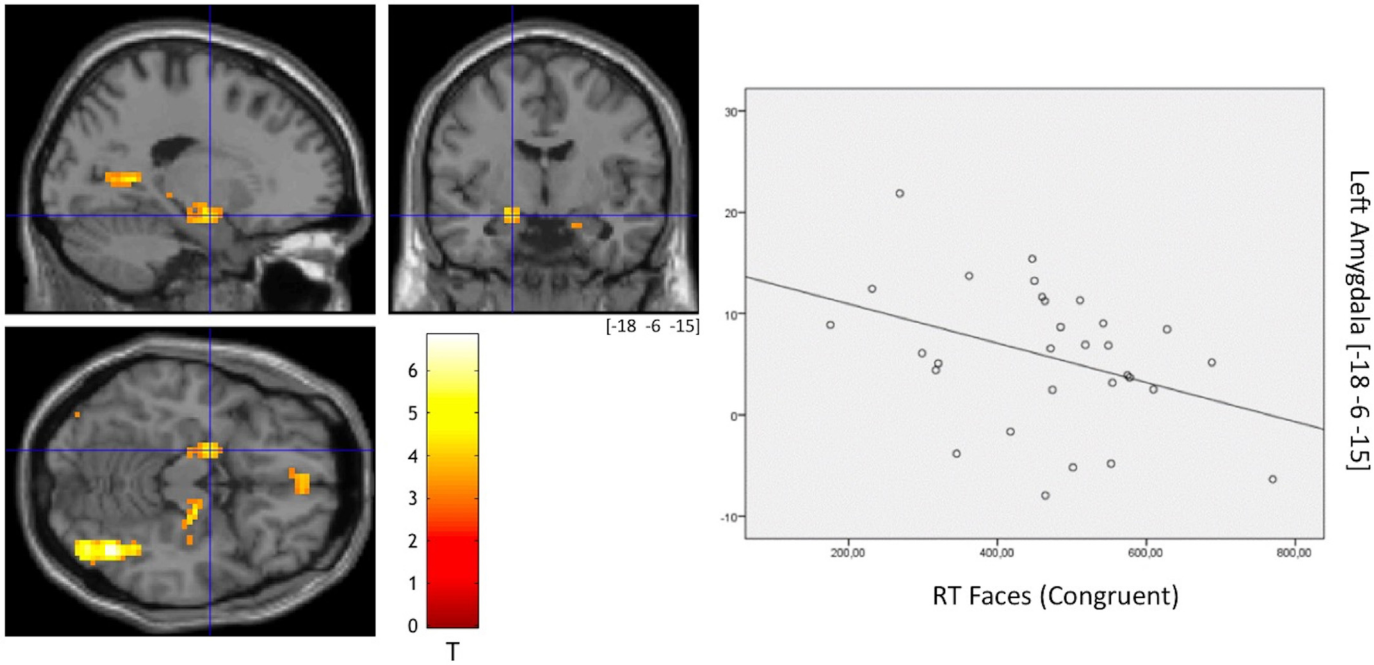

Fig. 4. Correlations between regions of interest and behavioral performances. Activation related to faces vs. scrambled trials in congruent conditions. Regression slopes are displayed. Left amygdala was negatively associated with reaction time (RT) for faces in correct responses for congruent conditions. The color bar represents the T score.

the 'scrambled congruent > faces congruent' contrast were observed. Whole-brain analysis showed activation related to the 'scrambled incongruent > faces incongruent' contrast in the left fusiform gyrus (Table 2), but no regions of interest were observed in the ROI analysis for this contrast.

Given previous developmental and functional inconsistency regarding amygdala activation (e.g. Guyer et al., 2008; Hare et al., 2008; Thomas et al., 2001a, 2001b; Yurgelun-Todd and Killgore, 2006), relations between activation in amygdala and behavioral performances were further explored. Activation in the left amygdala (MNI coordinates: −18, −6, −15) was negatively correlated with RT for correct responses for congruent faces ($r = -.380, p < .05$; see Fig. 4). We observed no other significant correlations.

3.2.3. Age effect

Based on behavioral results, the exact same statistical model was repeated with age entered as a covariate. No change was observed; activation associated with each contrast remained exactly as previously described. In order to confirm this result and verify that age was not related to brain activation during the task, correlation analyses between age and brain regions that were mainly activated for each contrast were performed. None of these regions correlated significantly or even marginally significantly with age.

4. Discussion

The aim of the present study was to examine neural mechanisms underlying the perception of facial expressions of emotions and its interaction with interference control in school age children. We designed a flanker-type of task associated with an event-related fMRI paradigm which allowed us to manipulate the socio-emotional effect independently of interference control.

4.1. Socio-emotional effect of face perception

Results related to the stimuli converged towards a main effect of faces, but unlike previous studies (Marusak et al., 2013; Thomas et al., 2001a), no specific effects of emotional valence were observed. Behavioral results showed that children made fewer errors in faces compared to scrambled trials. Brain results revealed activation in the socio-emotional brain network (Leppanen and Nelson, 2009; Vuilleumier, 2005), including both activation in (1) the lateral fusiform and inferior occipital gyri, regions of the main face network (Stiles et al., 2013) and (2) the ventral ACC, left and right amygdala, regions typically activated in the perception of emotions in children and adolescents (Guyer et al., 2008; Hare et al., 2008; Monk et al., 2003; Passarotti et al., 2009). Moreover, when scrambled were compared to faces, activation was observed only in the left fusiform gyrus and in the dorsolateral PFC. Altogether, these activation are in agreement with previous research showing that compared with adults, children and adolescents exhibit greater activation in paralimbic regions and the amygdala and less activation of prefrontal regions, (Guyer et al., 2008; Hare et al., 2008; Passarotti et al., 2009) to emotional faces. Additionally, when faces were compared to scrambled stimuli, this activation of ACC and amygdala was observed for all faces stimuli and was not stronger for angry or happy compared to one another or to neutral stimuli, suggesting no difference between the different emotional contents of faces. In a study by Vrticka et al. (2012), similar amygdala activation was observed for social positive and negative images, such as two people fighting or a mother interacting with her baby, and a difference in valence was only reported for non-social images including animals, landscapes or objects. Accordingly, Fitzgerald et al. (2006) tested a group of 20 adults and found activation of the left amygdala across six different emotional expressions, including happy, angry and neutral faces. Thomas et al. (2001a, 2001b) have reported that both late school age children and adults activated amygdala in front of fearful and neutral faces but, whereas adults showed stronger activation for fearful compared to neutral faces, the opposite pattern was observed in children. They proposed that a neutral facial expression does not yet represent a signal of neutrality in children, and instead produces activation consistent with continued attempts to decode or interpret emotional signals. Altogether, regarding our present results, we could suggest that faces by themselves, as socio-emotional stimuli, are affectively relevant to children (Fig. 3)

4.2. Interaction between socio-emotional stimuli and interference control

Regarding the interaction between faces perception and interference control, firstly, in line with behavioral results, imaging results showed that activation related to the socio-emotional effect of faces compared with scrambled stimuli was more pronounced in congruent trials. Activity was observed in similar regions than the general faces > scrambled contrast (socio-emotional brain network), including emotion-related regions such as amygdala and ventral ACC whereas in incongruent trials, activation was observed in the right fusiform & inferior occipital gyri only. Moreover, greater activation of the left amygdala correlated respectively with faster RTs in faces congruent trials but not in faces incongruent trials (Fig. 4). Secondly, behavioral results showed that the interference effect was larger for faces compared with scrambled stimuli and this was due to facilitated RTs for faces compared to scrambled stimuli in congruent trials but not to longer RTs in incongruent trials. This scenario has been observed in previous studies which compared negative and neutral stimuli (e.g. Cohen et al., 2012; Dennis et al., 2008; Kar et al., 2013) but has led to different interpretations regarding the improvement or impairment of interference control (for an opinion, see Cohen and Henik, 2012). Cohen and Henik interpreted this as an attenuation of the emotional effect during conflict situations; they proposed that findings of a null emotional effect in incongruent targets may result from top-down regulatory mechanisms that inhibit the effect of emotion. It has been suggested that this top-down modulation of emotional information is related to the connections from the PFC to subcortical regions, such as a negative correlation between activation in the amygdala and in the PFC (Hare et al., 2008; Nigg et al., 2010). Moreover, a developmental shift from positive to negative correlation has been recently described in the functional connectivity between amygdala and ACC/medial PFC, independently of the emotional expression of the faces processed (Wu et al., 2016). Etkin et al. (2006) reported that activity in the amygdala reflects the degree of emotional conflict, regardless of the emotional positive or negative valence. They suggested that the resolution of emotional conflict is associated with activity in the rostral ACC which leads to a simultaneous correlated reduction of activity in the amygdala, in incongruent trials. Following the idea of an attenuation of the emotional effect in conflicting conditions, results of the current study did not show amygdala activation during the face effect in incongruent conditions and during the interference effect in an emotional context. This idea should be more specifically investigated in further research, with an emphasis on the top-down connections between the ventral PFC and amygdala. Hare et al. (2008) have reported that as high emotional reactivity might increase the need for top-down control, individuals with less control could be at greater risk for poor outcomes. These findings could therefore be of interest for further clinical studies with children and adolescents susceptible to emotional and/or cognitive control difficulties, such as for example those born preterm (Anderson and Doyle, 2008; Johnson and Wolke, 2013), with attention deficit and hyperactivity or conduct disorders (Cadesky et al., 2000; Da Fonseca et al., 2009), and with depression or anxiety disorders (Dalgleish et al., 2003; Thomas et al., 2001a).

4.3. Strengths and limitations

The design of the task used in the present study, with the implicit impact of emotion, allowed to evaluate the impact of emotion and interference control separately. Indeed, in some previous studies with adults, emotions were part of the interference conflict (Etkin et al., 2006; Ochsner et al., 2008), which prevented from differentiating activation related to emotional conflict from activation related to a main emotional effect. However, the present study lacks functional connectivity analyses to support inferences such as the relation between the ventral PFC and amygdala. Furthermore, based on the study by Etkin and colleagues (2006) who found greater amygdala activation in low compared to high conflict resolution, a perspective of research could be to separate between the types of conflict trials. A strength of this study is that in addition to a face with neutral expression, our task comprised a real neutral condition (scrambled face) which could not be semantically interpreted. However scrambled stimuli were only 25% of all stimuli and the rest of them were all faces, which could have introduced a “rarity effect” and therefore impacted RT. Further research could compare children and adults with a similar task to verify that activation observed in the present study is children- and not task-related.

4.4. Conclusions

The present study aimed to explore neural functional correlates of the effect of facial expressions of emotions and its impact on interference control in late school-age children. Altogether, our results showed an emotional effect of faces compared with scrambled stimuli, no specific impact of emotional valence. Behavioral results evidenced an interference effect in face stimuli, expressed by faster RTs in congruent conditions. Brain results showed increased activity in the ventral ACC and the right and left amygdala in congruent trials only. Moreover, the faster RTs were associated with increased amygdala activity. It seems that in children ages 9–11, activity in the amygdala underlies the socio-emotional effect that faces induce but not emotional conflict. Studying brain regions involved in emotion regulation and its interaction with cognitive control in late childhood is important to further help with understanding neurodevelopmental disorders.

Acknowledgments

This work was supported by the Swiss Confederation Grant (PI K. Barisnikov, No UN7528); and the Swiss National Science Foundation (PI PS Hüppi No 32000B0-113632). The authors would like to acknowledge Bruno Bonnet from the Brain and Behaviour Laboratory for data acquisition. We also thank Pascal Vrticka and Sébastien Urben for their great help in designing the task and all the children and their parents for participation.

References

Adleman, N.E., Menon, V., Blasey, C.M., White, C.D., Warsofsky, I.S., Glover, G.H., Reiss, A.L., 2002. A developmental fMRI study of the Stroop color-word task. NeuroImage 16 (1), 61–75. http://dx.doi.org/10.1006/nimg.2001.1046.

Anderson, P.J., Doyle, L.W., 2008. Cognitive and educational deficits in children born extremely preterm. Semin. Perinatol. 32 (1), 51–58. http://dx.doi.org/10.1053/j.semperi.2007.12.009.

Arnsten, A.F.T., Rubia, K., 2012. Neurobiological circuits regulating attention, cognitive control, motivation, and emotion: disruptions in neurodevelopmental psychiatric disorders. J. Am. Acad. Child Adolesc. Psychiatry 51 (4), 356–367. http://dx.doi.org/10.1016/j.jaac.2012.01.008.

Ashburner, J., 2007. A fast diffeomorphic image registration algorithm. NeuroImage 38 (1), 95–113. http://dx.doi.org/10.1016/j.neuroimage.2007.07.007.

Blair, C., Dennis, T., 2010. An optimal balance: the integration of emotion and cognition in context. In: Calkins, S.D., Bell, M.A. (Eds.), Child Development at the Intersection of Emotion and Cognition. American Psychological Association, Washington, DC, US, pp. 17–35.

Botvinick, M.M., Cohen, J.D., Carter, C.S., 2004. Conflict monitoring and anterior cingulate cortex: an update. Trends Cogn. Sci. 8 (12), 539–546. http://dx.doi.org/10.1016/j.tics.2004.10.003.

Bunge, S.A., Crone, E.A., 2009. Neural correlates of the development of cognitive control. In: Rumsey, J.M., Ernst, M. (Eds.), Neuroimaging in Developmental Clinical Neuroscience. Cambridge University Press, Cambridge (UK), pp. 22–37.

Bunge, S.A., Dudukovic, N.M., Thomason, M.E., Vaidya, C.J., Gabrieli, J.D.E., 2002. Immature frontal lobe contributions to cognitive control in children: evidence from fMRI. Neuron 33 (2), 301–311. http://dx.doi.org/10.1016/S0896-6273(01)00583-9.

Bush, G., Luu, P., Posner, M.I., 2000. Cognitive and emotional influences in anterior cingulate cortex. Trends Cogn. Sci. 4 (6), 215–222. http://dx.doi.org/10.1016/S1364-6613(00)01483-2.

Cadesky, E.B., Mota, V.L., Schachar, R.J., 2000. Beyond words: how do children with ADHD and/or conduct problems process nonverbal information about affect? J. Am. Acad. Child Adolesc. Psychiatry 39 (9), 1160–1167. http://dx.doi.org/10.1097/00004583-200009000-00016.

Casey, B.J., Tottenham, N., Liston, C., Durston, S., 2005. Imaging the developing brain:

what have we learned about cognitive development? Trends Cogn. Sci. 9 (3), 104–110. http://dx.doi.org/10.1016/j.tics.2005.01.011.

Cohen, N., Henik, A., 2012. Do irrelevant emotional stimuli impair or improve executive control? (Article33). Front. Integr. Neurosci. 6. http://dx.doi.org/10.3389/fnint.2012.00033.

Cohen, N., Henik, A., Moyal, N., 2012. Executive control attenuates emotional effects-For high reappraisers only? Emotion 12 (5), 970–979. http://dx.doi.org/10.1037/a0026890.

Da Fonseca, D., Seguier, V., Santos, A., Poinso, F., Deruelle, C., 2009. Emotion understanding in children with ADHD. Child Psychiatry Hum. Dev. 40 (1), 111–121. http://dx.doi.org/10.1007/s10578-008-0114-9.

Dalgleish, T., Taghavi, R., Neshat-Doost, H., Moradi, A., Canterbury, R., Yule, W., 2003. Patterns of processing bias for emotional information across clinical disorders: a comparison of attention, memory, and prospective cognition in children and adolescents with depression, generalized anxiety, and posttraumatic stress disorder. J. Clin. Child Adolesc. Psychol. 32 (1), 10–21. http://dx.doi.org/10.1207/S15374424JCCP3201_02.

Dennis, T.A., Chen, C.C., McCandliss, B.D., 2008. Threat-related attentional biases: an analysis of three attention systems. Depress. Anxiety 25 (6), E1–E10. http://dx.doi.org/10.1002/da.20308.

Durston, S., Thomas, K.M., Yang, Y., Uluğ, A.M., Zimmerman, R.D., Casey, B.J., 2002. A neural basis for the development of inhibitory control. Dev. Sci. 5 (4), F9–F16. http://dx.doi.org/10.1111/1467-7687.00235.

Eriksen, B.A., Eriksen, C.W., 1974. Effects of noise letters upon the identification of a target letter in a nonsearch task. Percept. Psychophys. 16 (1), 143–149. http://dx.doi.org/10.3758/bf03203267.

Etkin, A., Egner, T., Peraza, D.M., Kandel, E.R., Hirsch, J., 2006. Resolving emotional conflict: a role for the rostral anterior cingulate cortex in modulating activity in the amygdala. Neuron 51 (6), 871–882. http://dx.doi.org/10.1016/j.neuron.2006.07.029.

Fenske, M.J., Eastwood, J.D., 2003. Modulation of focused attention by faces expressing emotion: evidence from flanker tasks. Emotion 3 (4), 327–343. http://dx.doi.org/10.1037/1528-3542.3.4.327.

Fitzgerald, D.A., Angstadt, M., Jelsone, L.M., Nathan, P.J., Phan, K.L., 2006. Beyond threat: amygdala reactivity across multiple expressions of facial affect. NeuroImage 30 (4), 1441–1448. http://dx.doi.org/10.1016/j.neuroimage.2005.11.003.

Friston, K.J., Holmes, A.P., Worsley, K.J., Poline, J.P., Frith, C.D., Frackowiak, R.S.J., 1994. Statistical parametric maps in functional imaging: a general linear approach. Human Brain Mapping. 2 (4), 189–210. http://dx.doi.org/10.1002/hbm.460020402.

Goghari, V.M., MacDonald III, A.W., 2008. Effects of varying the experimental design of a cognitive control paradigm on behavioral and functional imaging outcome measures. J. Cogn. Neurosci. 20 (1), 20–35. http://dx.doi.org/10.1162/jocn.2008.20007.

Goldstein, M., Brendel, G., Tuescher, O., Pan, H., Epstein, J., Beutel, M., Silbersweig, D., 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. http://dx.doi.org/10.1016/j.neuroimage.2007.01.056.

Guyer, A.E., Monk, C.S., McClure-Tone, E.B., Nelson, E.E., Roberson-Nay, R., Adler, A.D., Ernst, M., 2008. A developmental examination of amygdala response to facial expressions. J. Cogn. Neurosci. 20 (9), 1565–1582. http://dx.doi.org/10.1162/jocn.2008.20114.

Hare, T.A., Tottenham, N., Davidson, M.C., Glover, G.H., Casey, B.J., 2005. Contributions of amygdala and striatal activity in emotion regulation. Biol. Psychiatry 57 (6), 624–632. http://dx.doi.org/10.1016/j.biopsych.2004.12.038.

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. http://dx.doi.org/10.1016/j.biopsych.2008.03.015.

Healy, E., Reichenberg, A., Nam, K.W., Allin, M.P., Walshe, M., Rifkin, L., Nosarti, C., 2013. Preterm birth and adolescent social functioning-alterations in emotion-processing brain areas. J. Pediatr. 163 (6), 1596–1604. http://dx.doi.org/10.1016/j.jpeds.2013.08.011.

Huizinga, M., Dolan, C.V., van der Molen, M.W., 2006. Age-related change in executive function: developmental trends and a latent variable analysis. Neuropsychologia 44 (11), 2017–2036. http://dx.doi.org/10.1016/j.neuropsychologia.2006.01.010.

Huyser, C., Veltman, D.J., Wolters, L.H., de Haan, E., Boer, F., 2011. Developmental aspects of error and high-conflict-related brain activity in pediatric obsessive-compulsive disorder: a fMRI study with a Flanker task before and after CBT. J. Child Psychol. Psychiatry 52 (12), 1251–1260. http://dx.doi.org/10.1111/j.1469-7610.2011.02439.x.

Johnson, S., Wolke, D., 2013. Behavioural outcomes and psychopathology during adolescence. Early Hum. Dev. 89 (4), 199–207. http://dx.doi.org/10.1016/j.earlhumdev.2013.01.014.

Kanske, P., Kotz, S.A., 2011a. Emotion speeds up conflict resolution: a new role for the ventral anterior cingulate cortex? Cereb. Cortex 21 (4), 911–919. http://dx.doi.org/10.1093/cercor/bhq157.

Kanske, P., Kotz, S.A., 2011b. Emotion triggers executive attention: anterior cingulate cortex and amygdala responses to emotional words in a conflict task. Hum. Brain Mapp. 32 (2), 198–208. http://dx.doi.org/10.1002/hbm.21012.

Kar, B.R., Vijay, N., Mishra, S., 2013. Development of cognitive and affective control networks and decision making. Prog. Brain Res. 202, 347–368. http://dx.doi.org/10.1016/B978-0-444-62604-2.00018-6.

Kerns, J.G., Cohen, J.D., MacDonald 3rd, A.W., Johnson, M.K., Stenger, V.A., Aizenstein, H., Carter, C.S., 2005. Decreased conflict- and error-related activity in the anterior cingulate cortex in subjects with schizophrenia. Am. J. Psychiatry 162 (10), 1833–1839. http://dx.doi.org/10.1176/appi.ajp.162.10.1833.

Konrad, K., Neufang, S., Thiel, C.M., Specht, K., Hanisch, C., Fan, J., Fink, G.R., 2005. Development of attentional networks: an fMRI study with children and adults. NeuroImage 28 (2), 429–439. http://dx.doi.org/10.1016/j.neuroimage.2005.06.065.

Largo, R.H., Pfister, D., Molinari, L., Kundu, S., Lipp, A., Due, G., 1989. Significance of prenatal, perinatal and postnatal factors in the development of AGA preterm infants at five to seven years. Dev. Med. Child Neurol. 31 (4), 440–456. http://dx.doi.org/10.1111/j.1469-8749.1989.tb04022.x.

Leppanen, J.M., Nelson, C.A., 2009. Tuning the developing brain to social signals of emotions. Nat. Rev. Neurosci. 10 (1), 37–47. http://dx.doi.org/10.1038/nrn2554.

Marusak, H.A., Carré, J.M., Thomason, M.E., 2013. The stimuli drive the response: an fMRI study of youth processing adult or child emotional face stimuli. NeuroImage 83 (0), 679–689. http://dx.doi.org/10.1016/j.neuroimage.2013.07.002.

Menon, V., 2013. Developmental pathways to functional brain networks: emerging principles. Trends Cogn. Sci. 17 (12), 627–640. http://dx.doi.org/10.1016/j.tics.2013.09.015.

Monk, C.S., McClure, E.B., Nelson, E.E., Zarahn, E., Bilder, R.M., Leibenluft, E., Pine, D.S., 2003. Adolescent immaturity in attention-related brain engagement to emotional facial expressions. NeuroImage 20 (1), 420–428. http://dx.doi.org/10.1016/S1053-8119(03)00355-0.

Mullane, J.C., Corkum, P.V., Klein, R.M., McLaughlin, E., 2009. Interference control in children with and without ADHD: a systematic review of Flanker and Simon task performance. Child Neuropsychol. 15 (4), 321–342. http://dx.doi.org/10.1080/09297040802348028.

Nigg, J.T., 2000. On inhibition/disinhibition in developmental psychopathology: views from cognitive and personality psychology and a working inhibition taxonomy. Psychol. Bull. 126 (2), 220–246. http://dx.doi.org/10.1037/0033-2909.126.2.220.

Nigg, J.T., Martel, M.M., Nikolas, M., Casey, B.J., 2010. Intersection of emotion and cognition in developmental psychopathology. In: Calkins, S.D., Bell, M.A. (Eds.), Child Development at the Intersection of Emotion and Cognition. American Psychological Association, Wahington (DC), pp. 225–245.

Ochsner, K.N., Hughes, B., Robertson, E.R., Cooper, J.C., Gabrieli, J.D.E., 2008. Neural systems supporting the control of affective and cognitive conflicts. J. Cogn. Neurosci. 21 (9), 1841–1854. http://dx.doi.org/10.1162/jocn.2009.21129.

Passarotti, A.M., Sweeney, J.A., Pavuluri, M.N., 2009. Neural correlates of incidental and directed facial emotion processing in adolescents and adults. Soc. Cogn. Affect. Neurosci. 4 (4), 387–398. http://dx.doi.org/10.1093/scan/nsp029.

Posner, M.I., Rothbart, M.K., 2007. Research on attention networks as a model for the integration of psychological science. Annu. Rev. Psychol. 58, 1–23. http://dx.doi.org/10.1146/annurev.psych.58.110405.085516.

Raven, J.C., Court, J.H., Raven, J., 1998. Progressive Matrices Couleur. Oxford Psychologists Press, Oxford (UK).

Ridderinkhof, K.R., Ullsperger, M., Crone, E.A., Nieuwenhuis, S., 2004. The role of the medial frontal cortex in cognitive control. Science 306 (5695), 443–447. http://dx.doi.org/10.1126/science.1100301.

Schulz, K.P., Tang, C.Y., Fan, J., Marks, D.J., Cheung, A.M., Newcorn, J.H., Halperin, J.M., 2005. Differential prefrontal cortex activation during inhibitory control in adolescents with and without childhood attention-deficit/hyperactivity disorder. Neuropsychology 19 (3), 390–402. http://dx.doi.org/10.1037/0894-4105.19.3.390.

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. http://dx.doi.org/10.1016/j.neuroimage.2005.11.053.

Stiles, J., Akshoomoff, N., Haist, F., 2013. The development of visuospatial processing. In: Rubenstein, J.L.R., Rakic, P. (Eds.), Comprehensive Developmental Neuroscience: Neural Circuit Development and Function in the Healthy and Diseased Brain 3. Academic Press, San Diego (CA), pp. 271–296.

Thomas, K.M., Drevets, W.C., Dahl, R.E., Ryan, N.D., Birmaher, B., Eccard, C.H., Casey, B.J., 2001a. Amygdala response to fearful faces in anxious and depressed children. Arch. Gen. Psychiatry 58 (11), 1057–1063. http://dx.doi.org/10.1001/archpsyc.58.11.1057.

Thomas, K.M., Drevets, W.C., Whalen, P.J., Eccard, C.H., Dahl, R.E., Ryan, N.D., Casey, B.J., 2001b. Amygdala response to facial expressions in children and adults. Biol. Psychiatry 49 (4), 309–316. http://dx.doi.org/10.1016/S0006-3223(00)01066-0.

Tottenham, N., Tanaka, J.W., Leon, A.C., McCarry, T., Nurse, M., Hare, T.A., Nelson, C., 2009. The NimStim set of facial expressions: judgments from untrained research participants. Psychiatry Res. 168 (3), 242–249. http://dx.doi.org/10.1016/j.psychres.2008.05.006.

Vrticka, P., Sander, D., Vuilleumier, P., 2012. Lateralized interactive social content and valence processing within the human amygdala (Article358). Front. Hum. Neurosci. 6. http://dx.doi.org/10.3389/fnhum.2012.00358.

Vuilleumier, P., 2005. How brains beware: neural mechanisms of emotional attention. Trends Cogn. Sci. 9 (12), 585–594. http://dx.doi.org/10.1016/j.tics.2005.10.011.

Wu, M., Kujawa, A., Lu, L.H., Fitzgerald, D.A., Klumpp, H., Fitzgerald, K.D., Phan, K.L., 2016. Age-related changes in amygdala–frontal connectivity during emotional face processing from childhood into young adulthood. Hum. Brain Mapp. 37 (5), 1684–1695. http://dx.doi.org/10.1002/hbm.23129.

Yurgelun-Todd, D.A., Killgore, W.D.S., 2006. Fear-related activity in the prefrontal cortex increases with age during adolescence: a preliminary fMRI study. Neurosci. Lett. 406 (3), 194–199. http://dx.doi.org/10.1016/j.neulet.2006.07.046.