



## Mid-adolescent neurocognitive development of ignoring and attending emotional stimuli



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### ABSTRACT

Appropriate reactions toward emotional stimuli depend on the distribution of prefrontal attentional resources. In mid-adolescence, prefrontal top-down control systems are less engaged, while subcortical bottom-up emotional systems are more engaged. We used functional magnetic resonance imaging to follow the neural development of attentional distribution, i.e. attending versus ignoring emotional stimuli, in adolescence. 144 healthy adolescents were studied longitudinally at age 14 and 16 while performing a perceptual discrimination task. Participants viewed two pairs of stimuli – one emotional, one abstract – and reported on one pair whether the items were the same or different, while ignoring the other pair. Hence, two experimental conditions were created: “attending emotion/ignoring abstract” and “ignoring emotion/attending abstract”. Emotional valence varied between negative, positive, and neutral. Across conditions, reaction times and error rates decreased and activation in the anterior cingulate and inferior frontal gyrus increased from age 14 to 16. In contrast, subcortical regions showed no developmental effect. Activation of the anterior insula increased across ages for attending positive and ignoring negative emotions. Results suggest an ongoing development of prefrontal top-down resources elicited by emotional attention from age 14 to 16 while activity of subcortical regions representing bottom-up processing remains stable.

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### 1. Introduction

Neuroimaging studies have focused on the exploration of emotional attention – that is attention toward or away from emotional stimuli (Corbetta and Shulman, 2002; Corbetta et al., 2008; Posner and Petersen, 1990; Vuilleumier and Huang, 2009). Emotional attention can be impaired in affective disorders and given that mid-adolescence is a core incidence phase for affective disorders (Paus et al., 2008), characterizing the development of emotional attention in adolescence is of high clinical relevance.

Emotional attention can be divided into (1) the automatic impulse to attend toward emotionally salient stimuli, bottom-up emotional attention, and (2) the goal-directed, controlled attention

toward emotional stimuli, top-down emotional attention (Corbetta and Shulman, 2002; Vuilleumier and Huang, 2009). Bottom-up and top-down systems are in line in tasks in which participants have to focus on the emotion. However, in tasks, in which the emotion is irrelevant, bottom-up and top-down-systems interfere. Here, the individual either gets distracted and turns her attention toward the emotional distractor (bottom-up attention) or successfully keeps it on the primary task (top-down attention) ignoring the distractor (Vuilleumier and Huang, 2009).

In adults, the two types of emotional attention are represented by different neural networks: For top-down emotional attention a dorsal frontoparietal network is activated including the dorsolateral prefrontal cortex, the dorsal parietal cortex, and the anterior cingulate cortex (ACC). Bottom-up emotional attention is modulated by a ventral frontoparietal network including the occipitotemporal cortex, orbitofrontal cortex, and the amygdala (Corbetta et al., 2008; Jordan et al., 2013; Vuilleumier and Huang, 2009).

In adolescence, more engaged bottom-up regions and less engaged top-down resources may result in an imbalance of both attention systems with prepotent bottom-up processing (Casey

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et al., 2008). Therefore, the inhibition of distracting emotional stimuli required in top-down emotional attention is challenging for adolescents. For example, in a classroom context the impulse to direct attention toward emotional stimuli, e.g. the attractive classmate passing by, has to be inhibited to direct attention in a top-down fashion on the primary task, e.g. on the current essay. If these challenging developmental tasks are not successfully managed, the risk of affective disorders might increase (Steinberg, 2005).

Few behavioral studies have investigated adolescent development of emotional attention. Most studies assessed inhibition of the motor impulse toward distractor stimuli in emotional go-no-go tasks. Overall, greater age-related improvements from adolescence to adulthood were found for negative and positive compared to neutral no-go-stimuli (Tottenham et al., 2011). When investigated separately, both negative (Cohen-Gilbert and Thomas, 2013) and positive (Somerville et al., 2011) no-go stimuli led to an increased false alarm rate for adolescents in comparison to adults. Thus, adolescents seem to be specifically sensitive toward distracting emotional stimuli. This pattern is also evident in a task that assesses the attentional inhibition of a distracting emotional incongruent flanking stimulus presented together with the task-relevant stimulus: Adolescents had larger interference effects for negative distractors and overall lower accuracy than adults (Grose-Fifer et al., 2013). Taken together, ignoring task-irrelevant emotional distractor stimuli undergoes developmental changes during adolescence.

Adolescent neural development of emotional attention has been initially investigated by a handful of cross-sectional studies. For negative distractors two studies suggest ongoing development of prefrontal regions: Monk et al. (2003) reported lower ACC activation in adults compared to adolescents for evaluating the nose width of emotional faces and Deeley et al. (2008) found decreasing prefrontal activation from childhood over adolescence across adulthood for evaluating the gender of emotional faces. In contrast, Lindstrom et al. (2009) did not find development for negative, but for positive distractors: cuneus and caudate activation decreased with increasing age from 9 to 40 years in a dot-probe task (Lindstrom et al., 2009). Positive distractors also led to stronger orbitofrontal cortex activation in adolescents compared to adults (Monk et al., 2003).

However, longitudinal approaches are mandatory to investigate developmental trajectories precisely. Amongst the sparse number of such studies one found increasing activity from age 10 to 13 in the temporal pole for attending emotional versus neutral faces unconstrained (i.e. passive viewing; Pfeifer et al., 2011).

Paulsen et al. (2015) studied how incentives, age, and performance modulate brain activity during inhibitory control in a longitudinal design including 10- to 22-year-olds. In an incentivized antisaccade task, amygdala-mediated bottom-up processing elicited by loss trials decreased through adolescence. In contrast, activity of prefrontal control regions – which was also associated with better behavioral performance – increased linearly with age.

Change in regions involved in social cognition (including the inferior frontal gyrus, IFG, and superior temporal sulcus) was investigated in 12- to 19-year-olds with a two-year interval using pictures of eye regions (Overgaauw et al., 2014). Activity elicited by evaluating the mental state versus evaluating age/gender was stable in the superior temporal sulcus. While the right IFG showed relative stability, age comparisons revealed a decrease in activation. The medial prefrontal cortex showed a dip of activation in mid-adolescence. Taken together, previous longitudinal studies suggest subtle developmental changes in activation patterns of brain regions crucial for emotion regulation.

The current study sought to systematically investigate the extended neural development of emotional attention (a) with a

longitudinal approach beyond early adolescence from age 14 to 16, (b) in a large community-based sample of 144 typically developing adolescents, (c) disentangling bottom-up and top-down processes, and (d) differentiating between positive and negative emotions.

We expected a greater neural development for the ignoring emotion condition compared to the attending emotion condition, given previous studies on mid-adolescent behavioral development. Based on previous neuroimaging studies (Monk et al., 2003; Deeley et al., 2008; Paulsen et al., 2015) we expected this development in prefrontal brain regions. Since the systematic contrast with regard to a baseline was missing in most previous studies, we contrasted negative and positive with neutral pictures. Regarding emotional valence, negative versus neutral in contrast to positive versus neutral distractors might elicit stronger distraction (Öhman et al., 2001) and might require a stronger top-down regulation of the prefrontal cortex (PFC), when being ignored. Therefore, and since in general PFC increases were found on both the functional and structural level throughout adolescence (Crone and Dahl, 2012; Gogtay et al., 2004), we expected an increase of prefrontal activity for negative in contrast to positive distractors from age 14 to 16. Additionally, amygdala activation was tested given previous findings of elevated amygdala activation in adolescence compared to children and adults toward negative stimuli in a go-no-go paradigm (Hare et al., 2008).

## 2. Method

### 2.1. Participants

Data acquisition was part of the project “The adolescent brain” (for more details see Ripke et al., 2012). Data of the first wave (age 14) of this project was recently published comparing participants with and without a family history of depression (Pilhatsch et al., 2014a). The local ethics committee approved the study. 260 adolescents were recruited via school visits in the local school district. Monetary compensation was provided for participation and informed consent was obtained from participants and from one of their legal guardians. Participants had no record of medical, neurological or psychiatric disorders and those with current mental disorders were excluded according to the Development and Well-Being Assessment (DAWBA; Goodman et al., 2000). Of the initial sample 187 participants were successfully assessed at both time points of which 144 (73 girls) are included in the present analyses. The others were excluded because of 1) excessive head movements ( $N=23$ ), (2) low behavioral performance during the fMRI task, i.e. more than 25% incorrect answers ( $N=14$ ), or mean reaction times higher than 3 standard deviations (SD) from the mean of their age samples at age 14 or 16 ( $N=6$ ). The resulting sample consisted of 144 participants (for participant characteristics see Table 1) with normal or corrected to normal vision, which completed data collection at two visits (separated by  $24.12 \pm 1.97$  months, range 22–37 months). A urine test assured no use of illicit drugs (e.g. cannabis, heroin, cocaine) at the day of assessment.

### 2.2. Stimuli, design and procedure

Based on previous work (Vuilleumier et al., 2001) we developed a perceptual discrimination task, in which participants decided whether a pair of visual target stimuli was equal while another pair was presented as distractor. In each trial a pair of non-emotional pictures and a pair of pictures from one of three emotional categories (negative, positive, neutral) taken from the International Affective Picture System (IAPS; Lang et al., 2005) was shown. The selection of IAPS stimuli was balanced with respect to normed emotional valence and arousal ratings (Table S1, available online). Non-emotional control pictures were created by shredding the

**Table 1**  
Subject characteristics and comparisons between time points ( $n = 144$ ).

Parameter	Age 14	Age 16	Comparison between time points		
	<i>M</i> (SD)	<i>M</i> (SD)	<i>t</i>	df	<i>p</i>
Age in years	14.78 (0.35), range 13.38–15.22	16.59 (0.36), range 15.66–17.54			
No. of females	73				
No. of right handers	133 (1 bimanual, 10 left)				
Maternal education <sup>a</sup>	3.64 (1.60)				
Paternal education <sup>a</sup>	3.38 (1.70)				
School type	102 higher grammar school (German “Gymnasium”) <sup>b</sup> ; 42 lower grammar school (German “Realschule” or “Hauptschule”) <sup>b</sup>				
IQ <sup>c</sup>	114 (10), range = 86–142	115 (12), range 81–145	–.59	143	.555
Pubertal status <sup>d</sup>	3.65 (0.65), i.e. mid- to late pubertal status	4.17 (0.55), i.e. late pubertal status	10.5	143	<.001
State anxiety <sup>e</sup>	36.72 (6.33)	37.10 (6.52)	–.59	110	.558
Trait anxiety <sup>e</sup>	36.25 (7.24)	36.85 (7.662)	–.864	110	.389
Probability of having a depression <sup>f</sup>	2.21 (7.0)	1.29 (6.49)	1.22	143	.224

<sup>a</sup> Parental education ranges from 1 = “Professional qualification, e.g. PhD” to 7 = “Did not attend school or completed primary school education only”.

<sup>b</sup> The “Gymnasium” is a German school type preparing for university until grade 12 and the “Realschule” or “Hauptschule” until grades 9 or 10 prepares for jobs with practical training.

<sup>c</sup> To estimate general cognitive ability the subtests Similarities, Block Design, Vocabulary, and Matrices from the Wechsler Intelligence Scale For Children (WISC-IV, German adaptation; [Petermann and Petermann, 2007](#)) were used for age 14. For age 16 the Wechsler Adult Intelligence Scale (WAIS, German adaptation; [von Aster et al., 2007](#)) was used with the same subtests and additionally with Letter–Number Sequencing, Symbol Search, Digit Span, and Coding.

<sup>d</sup> Pubertal status ranges from 1 for prepubertal to 5 for postpubertal status, measured with the Pubertal Development Scale (PDS; [Petersen et al., 1988](#)).

<sup>e</sup> State and Trait anxiety were measured with the State Trait anxiety Inventory (STAI, [Spielberger, 1983](#)). Due to technical problems the STAI was only assessed in 111 participants at both time points.

<sup>f</sup> Probability of having a depression was measured with the DAWBA ([Goodman et al., 2000](#)).

chosen IAPS pictures beyond recognition using picture manipulation software ([www.gimp.org](http://www.gimp.org)). Because the development of emotion recognition in facial stimuli ([Vetter et al., 2013, 2014](#)) might interfere with the development of emotional attention targeted here, we used emotional scenes rather than faces.

One pair was arranged horizontally and the other vertically around a fixation cross ([Fig. 1](#)). Participants had to attend to the horizontal or vertical pair for a given trial as indicated by a task cue (double-arrow) and report whether the two items of the pair were the same (which was the case in 50%). In half of trials participants had to compare IAPS pictures (attending emotion) and in the other half shredded pictures (ignoring emotion). Positioning of IAPS or shredded pairs was random. Altogether, there were six different trial types: Attending emotion (negative, positive, neutral) while ignoring abstract (shredded control stimuli) and ignoring emotion (negative, positive, neutral) while attending abstract (shredded control stimuli). The attending emotion and ignoring-emotion-conditions were presented counterbalanced. In total, there were twenty trials per condition, pseudo-randomly interleaved by jittered inter-stimulus intervals.

One trial consisted of the following phases: After a task cue (1 s), two picture pairs were shown for 1 s on the next screen. During the presentation of the picture screen and the following 1.5 s, the participant responded via button press (maximum time to answer 2.5 s). After the picture screen jittered inter-stimulus intervals were employed (mean: 5000 ms, range: 3000–7000 ms) presenting a fixation cross. Dependent on the reaction time the jitter was flexibly adapted resulting in a mean trial length of seven seconds. There was a total of 120 trials and the whole functional run lasted about 14 min.

Behavioral data were collected by ResponseGrips (©NordicNeuroLab) with a button on a grip in each hand. Task presentation and recording of the behavioral responses was performed using Presentation<sup>®</sup> software (version 11.1, Neurobehavioral Systems, Inc., Albany, CA). The scanning session was preceded by a practice session inside the scanner using stimuli not included in the experiment.

### 2.3. Analysis of behavioral data

Statistical analyses were performed using SPSS for Windows (Version 18) on the mean reaction times (RTs) and mean error rates.

Repeated measures ANOVAs with a  $2 \times 2 \times 3$  factorial design were calculated using a threshold of  $p < .05$  with age (14 years, 16 years), attention (attending emotion, ignoring emotion), and emotional valence (negative, positive, neutral) as within-subject-factors.

## 2.4. Functional imaging

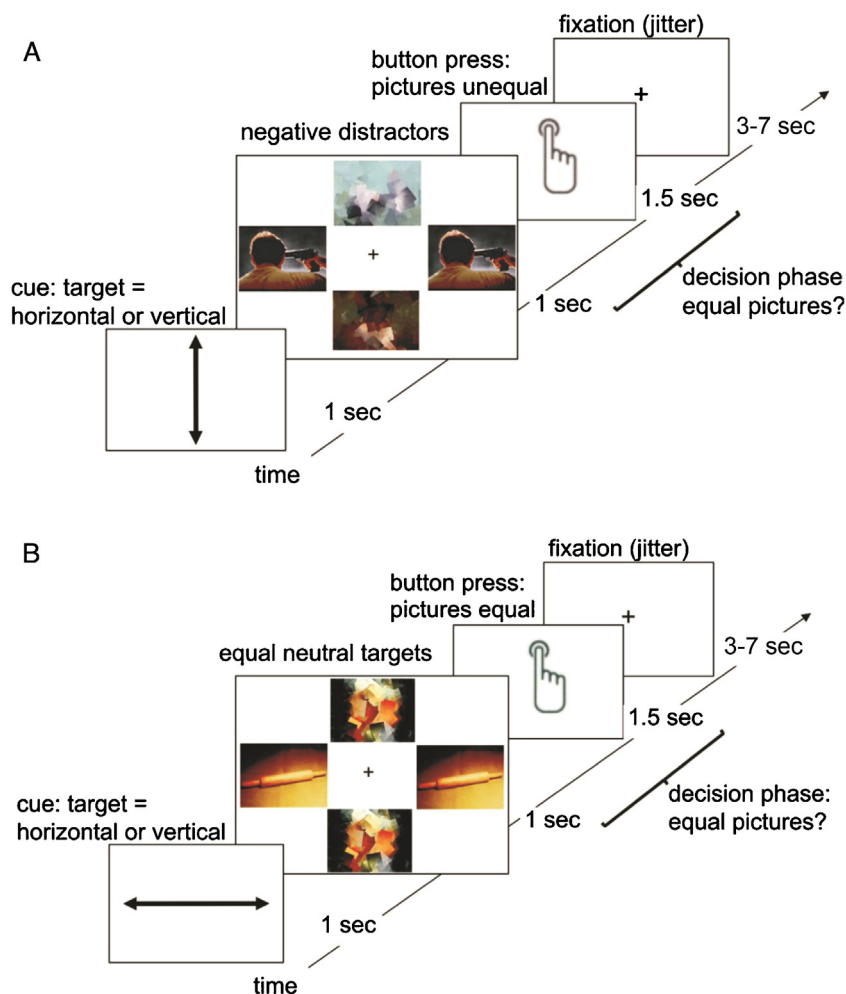
### 2.4.1. Image acquisition

Scanning was performed with a 3T whole-body MR tomograph (Magnetom TRIO, Siemens, Erlangen, Germany) equipped with a 12-channel head coil. For functional imaging, a standard Echo Planar Imaging (EPI) Sequence was used (repetition time, TR: 2410 ms; echo time, TE: 25 ms; flip angle: 80°). fMRI scans were obtained from 42 transversal slices, tilted up 30° clockwise from the anterior commissure–posterior commissure line to improve signal in the orbitofrontal cortex and minimize susceptibility artifacts. A thickness of 2 mm (1 mm gap), a field of view (FOV) of 192 mm  $\times$  192 mm and an in-plane resolution of 64  $\times$  64 pixels resulted in a voxel size of 3 mm  $\times$  3 mm  $\times$  3 mm. Only marginal sections of the most superior part of the parietal cortex and the most inferior part of the cerebellum were omitted. Moreover, a 3D T1-weighted magnetization-prepared rapid gradient echo (MPRAGE) image data set was acquired (TR = 1900 ms, TE = 2.26 ms, FOV = 256 mm  $\times$  256 mm, 176 slices, 1 mm  $\times$  1 mm  $\times$  1 mm voxel size, flip angle = 9°). Images were presented via a head-coil-mounted display system based on LCD technology (NordicNeuroLab AS, Bergen, Norway). Scanning settings and timing were identical at age 14 and 16 for both the functional and structural measurements.

## 2.5. Analysis of fMRI data

### 2.5.1. Preprocessing

Functional images were preprocessed and statistically analyzed using SPM5 (Wellcome Department of Imaging Neuroscience, London, UK). For each participant, functional images were first slice-time corrected by using the middle slice as reference, then realigned to the first image by 6° rigid spatial transformation, spatially normalized to the standard space defined by the Montreal Neurological Institute (MNI) EPI template and smoothed with a Gaussian kernel of 8 mm at full-width half maximum. Maximum



**Fig. 1.** (a) Example trial for the Ignoring emotion condition. (b) Example trial for the Attending emotion condition.

participant movement at each time point in any direction did not exceed 3 mm or degrees.

### 2.5.2. Statistical analysis

In the first-level analysis, a fixed effects analysis was computed for each participant on the basis of the general linear model within each voxel of the whole brain by modeling the different conditions (emotional valence and attention) as regressors of interest. Six regressors of interest, attending (1) negative, (2) positive, and (3) neutral emotion, as well as ignoring (4) negative, (5) positive, and (6) neutral emotion, were modeled at the point of presentation as stick functions convolved with a canonical hemodynamic response function. Additionally, trials with missing or wrong responses were modeled as a separate regressor, i.e. only correct answers were analyzed. The six subject-specific movement regressors, which were derived from the rigid-body realignment, were included as covariates of no interest. Each component of the model served as a regressor in a multiple regression analysis. A high-pass filter with cut-off 128 s was applied to remove the low frequency physiological noise (Henson, 2006). Also an AR(1) model was employed for the residual temporal autocorrelation (Henson, 2006). We always used the neutral condition as the reference category to eliminate neural processes not related to emotional valence. Four contrasts of interest were thus computed within each subject: attending negative minus attending neutral (contrast 1), ignoring negative minus ignoring neutral (contrast 2), attending positive minus attending neutral (contrast 3) and ignoring positive minus

ignoring neutral (contrast 4). The first-level contrast images from the weighted beta-images were introduced into a second-level whole brain random-effects analysis to allow for population inference.

The present study explored age-related differences in functional activity in brain regions related to ignoring negative contrasted with positive emotion and attending negative and positive targets, that is, brain regions that would show a significant age by attention by emotional valence interaction effect. Therefore, at the group level an ANOVA was computed using a  $2 \times 2 \times 2$  full factorial model with the within-subject factors age (14 years, 16 years), attention (attending emotion, ignoring emotion) and emotional valence (negative versus neutral, positive versus neutral) using contrasts 1–4. Aiming at an overall picture of cortical development, we analyzed developmental differences on a whole brain level. The resulting set of significant voxel values constituted an SPM map. Only those regions are reported in all tables and figures that survive a statistical threshold of  $p \leq .05$  (corrected for multiple tests on the cluster threshold criterion). This was equivalent to a minimum cluster size of 32 voxels. For significant activation clusters we created masks and applied them to extract percent signal change with rfxplot (Glaescher, 2009). All brain coordinates are reported in MNI atlas space.

### 2.5.3. Exploratory region of interest analysis of the amygdala

Both amygdalae were used as one anatomical region of interest (ROI) generated with the WFU-pickatlas using the Talairach



Daemon (TD) Brodmann atlas. Percent signal change of these ROIs was extracted with rfxplot. An ANOVA was computed using a  $2 \times 2 \times 2$  full factorial model with the within-subject-factors age (14 years, 16 years), attention (attending emotion, ignoring emotion) and emotional valence (negative versus neutral, positive versus neutral).

### 3. Results

#### 3.1. Behavioral results

##### 3.1.1. Reaction times

For RTs as the dependent variable the ANOVA revealed a main effect of age,  $F(1,143) = 8.16$ ,  $p < .01$ , with 16-year-olds being faster than 14-year-olds (see Fig. S1). There was also a main effect of attention,  $F(1,143) = 64.74$ ,  $p < .001$ , driven by faster RTs for attending than ignoring emotion. The main effect of valence was also significant,  $F(2,142) = 19.38$ ,  $p < .001$ , i.e. lowest RTs for neutral followed by negative and positive emotion. The only significant two-way-interaction emerged for attention  $\times$  valence,  $F(1,142) = 23.17$ ,  $p < .001$ , driven by lower RTs toward attending but not ignoring neutral,  $t(143) = -8.17$ ,  $p < .001$ , and positive,  $t(143) = -7.19$ ,  $p < .001$ , emotions while RTs for attending and ignoring negative emotions were similar,  $t(143) = -.23$ ,  $p = .82$ , see Fig. S1. In contrast no significant differences between the three valences emerged in the ignoring emotion condition (see Fig. S1).

##### 3.1.2. Error rates

A missing or an incorrect response was considered as an error trial. For error rates as the dependent variable the ANOVA revealed a main effect of age,  $F(1,143) = 7.03$ ,  $p < .01$ , arising from lower error rates at age 16 than at age 14 (see Table S2). The ANOVA revealed also a main effect of attention,  $F(1,143) = 210.33$ ,  $p < .001$ , driven by lower error rates for attending compared to ignoring emotion. The main effect of valence was also significant,  $F(2,286) = 3.18$ ,  $p < .05$ , i.e. error rates were lowest in the neutral followed by the positive and the negative condition. There were no significant interactions.

There was no relation for neither RTs nor error rates of the main effect of age and the variables gender, pubertal change from age 14 to 16, or mean IQ from age 14 and 16 (see supplementary material).

#### 3.2. fMRI results

##### 3.2.1. Main effects of attention and emotional valence as a proof of concept

A  $2 \times 2 \times 2$  ANOVA with the within-subject factors age (14 years, 16 years), attention (attending emotion, ignoring emotion) and emotional valence (negative versus neutral, positive versus neutral) was analyzed. First, to reassure that the paradigm elicited activations in the regions previously found for emotional attention (Corbetta and Shulman, 2002; Corbetta et al., 2008; Vuilleumier and Huang, 2009), the main effects of attention and emotional valence were analyzed. Results showed higher activity in the inferior occipital lobe, the middle temporal and the fusiform gyrus as well as the inferior orbitofrontal lobe when participants attended emotion in comparison to when they ignored emotion (Table 2 and Fig. 2). Higher activity was found in the middle frontal gyrus, the posterior cingulate cortex, the precuneus and the inferior parietal lobe when participants ignored emotion in comparison to when they attended emotion (Table 2 and Fig. 2). For trials containing negative stimuli in contrast to trials containing positive stimuli the activity was higher in the fusiform gyrus, cuneus, inferior frontal gyrus, amygdala extending to the hippocampus, and middle occipital gyrus. Activity was higher in the middle and inferior frontal gyrus, nucleus caudatus, precentral gyrus, anterior cingulate, inferior and superior parietal lobe in trials containing positive stimuli in

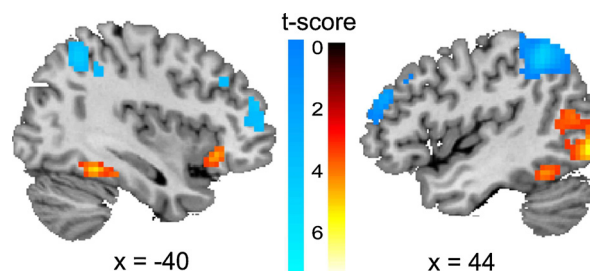


Fig. 2. Functional activity associated with the main effect of condition thresholded at  $p < .05$  corrected cluster level. Blue scale: Ignoring emotion > Attending emotion and red scale: Attending emotion > Ignoring emotion.

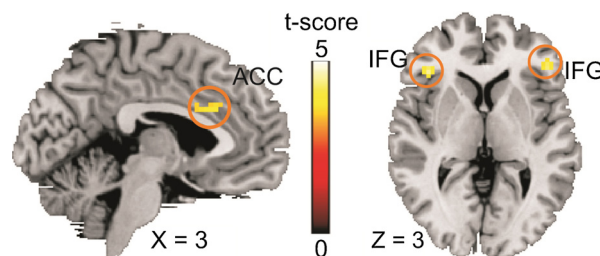


Fig. 3. Result of the main effect of age (age 16 > 14) in the ACC and left and right IFG thresholded at  $p < .05$  corrected cluster level.

contrast to trials containing negative stimuli (supplementary Table S3).

##### 3.2.2. Developmental effects

Following our hypotheses, the main effect of age, and the three way interaction of attention  $\times$  emotional valence  $\times$  age were analyzed. Furthermore, to capture all possible developmental effects the two-way interactions age  $\times$  emotional valence and age  $\times$  attention were analyzed. Regarding the *main effect of age*, activation during presentation of emotional target and distractor stimuli was higher for participants at age 16 versus 14 (Fig. 3) in the right ( $x, y, z = 45, 33, 0$ ;  $k = 46, z = 4.52$ ), and left inferior frontal gyrus (IFG;  $x, y, z = -42, 30, 3$ ;  $k = 34, z = 4.52$ ), and the ACC ( $x, y, z = 3, 21, 27$ ;  $k = 42, z = 3.95$ ). All three clusters survived  $p < .05$  correction on the cluster level. No significant activation emerged for participants at age 14 versus 16. There were no effects of gender, mean IQ from age 14 and 16, change of pubertal stage, or change of reaction times on the main effect of age. Following up on Pilhatsch et al. (2014a) we explored the influence of the change of clinical variables, specifically symptoms of depression measured with the DAWBA and trait anxiety measured with the State Trait anxiety Inventory (STAI, Spielberger, 1983). The change of these variables did not correlate with the developmental activation change. However, controlling for change of trait anxiety in the main effect of age revealed an additional cluster in the left cuneus/precuneus ( $x, y, z = -15, -60, 21$ ;  $k = 72, z = 3.72$ ). See supplementary material and table S4 for details.

The *two-way interactions* of age  $\times$  attention, and age  $\times$  emotional valence yielded no significant results.

Regarding the hypothesis of ongoing development for ignoring negative versus positive emotion in contrast to attending negative versus positive emotion, we analyzed the *three-way interaction* of age by attention by emotional valence. There was a significant three-way-interaction in one cluster: the left anterior insula ( $x, y, z = -51, 12, 0$ ;  $k = 45, z = 3.77$ ,  $p < .05$  corrected cluster level, Fig. 4). Extracting percent signal change values from this cluster and conducting post hoc *t*-tests revealed the following: a higher activity

**Table 2**  
Functional activity associated with the main effect of condition (ignoring > attending emotion and attending > ignoring emotion).

Brain region	L/R	BA	Peak voxel (mm)			t-Value	Cluster corrected p-value	Cluster size
			x	y	z			
<b>Ignoring &gt; attending emotion</b>								
Middle frontal gyrus	R	10	42	42	27	4.48	.001	114
	L	10	-36	54	18	4.18	<.001	106
Posterior cingulate cortex	R	31	12	-36	42	4.17	.025	43
Precuneus	R	7	12	-72	51	4.93	<.001	433
Inferior parietal lobe	R	40	45	-51	51	5.63	<.001	421
	L	40	-45	-54	51	4.32	<.001	142
<b>Attending &gt; ignoring emotion</b>								
Inferior orbitofrontal lobe	L	47	-36	27	-9	4.76	.021	46
Middle temporal gyrus	L	39	-54	-60	21	3.45	.007	67
Fusiform gyrus	L	37	-39	-45	-18	4.96	.048	32
Middle occipital gyrus	R	37	42	-51	-18	4.43	.020	47
	R	19	48	-81	-3	6.73	<.001	291

Note: Brodmann areas (BAs) are approximate.  $p < 0.05$ , corrected cluster level.

at age 16 versus 14 for attending positive emotion,  $t(143) = -2.64$ ,  $p < .01$ , and ignoring negative emotion,  $t(143) = -2.55$ ,  $p < .05$ . The pattern of increasing activation from age 14 to 16 occurred not in the ignoring positive emotion condition,  $t(143) = 0.88$ , nor the attending negative emotion condition,  $t(143) = -0.46$ ,  $p$ 's > 4 (Fig. 4).

The three-way interaction was driven by a different activation pattern for ignoring positive emotion and attending negative emotion versus other conditions at age 14 in contrast to 16. At age 14 activation for ignoring positive emotion was higher than both attending positive emotion,  $t(143) = -2.75$ ,  $p < .01$ , and ignoring negative emotion,  $t(143) = 3.72$ ,  $p < .001$ , but did not differ from attending negative emotion,  $t(143) = -1.0$ ,  $p = .321$ . In contrast, for age 16 activation for ignoring positive emotion did not differ from attending negative or positive emotion, or ignoring negative emotion,  $p$ 's > .1. Taken together, at age 14 ignoring positive emotion was processed similarly in the anterior insula as attending negative emotion but elicited higher activation in comparison to the two other conditions while at age 16 ignoring positive emotion was processed similarly as all other conditions.

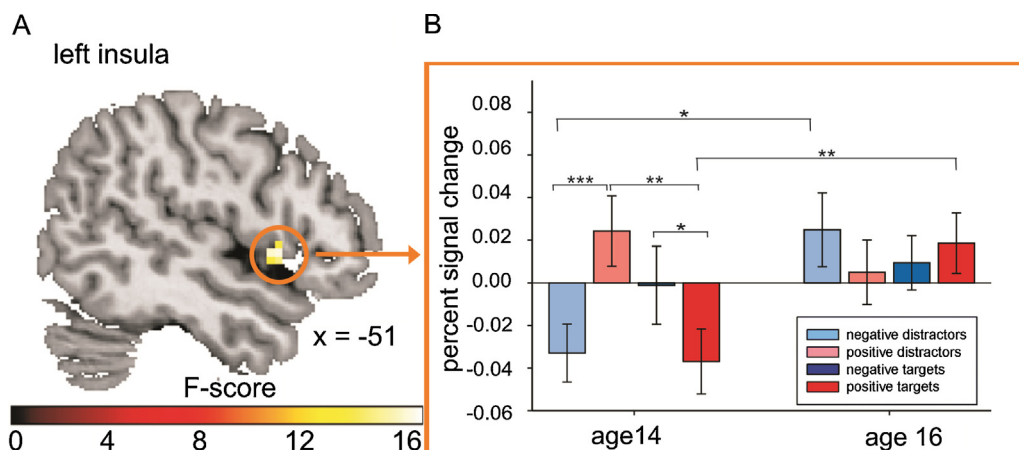
### 3.2.3. Exploratory amygdala analysis

For percent-signal-change in a bilateral anatomical amygdala ROI no main effect of age,  $F(1,143) = 75$ , or attention was found  $F(1,143) = 12$ ,  $p$ 's > .3. But – expectedly – we found a main effect for emotional valence,  $F(1,143) = 8.90$ ,  $p = .003$ , i.e. the amygdala was activated more strongly for negative in contrast to positive stimuli. The only significant two-way interaction

emerged for attention  $\times$  emotional valence,  $F(1,143) = 5.43$ ,  $p = .021$ , which was driven by a higher amygdala activation for attending negative versus positive emotion but a similar activation for ignoring negative and positive emotion. The three-way interaction age  $\times$  attention  $\times$  emotional valence was not significant. Similar results emerged when testing the left and right amygdalae separately.

In addition, we conducted a post hoc psycho-physiological interaction (PPI) analysis using the signal from the left or right amygdala as the physiological variable (see Supplement 1, for methods and detailed results). Only the statistic for the right amygdala showed two significant clusters for the 3-way interaction in the posterior cingulate cortex and the precuneus bordering the cuneus (Fig. S2). These two clusters showed a similar connectivity pattern: These regions increase in connectivity to the right amygdala from age 14 to 16 for attending negative and ignoring positive but not for attending positive and ignoring negative stimuli. All other investigated main effects or interactions were not significant.

Moreover, in order to investigate stability, we explored the fMRI reliability using the intraclass correlation (ICC) and the overlap of second-level group activation (Bennett and Miller, 2010) both for “high-level” contrasts (condition of interest versus the matching neutral condition) and for the contrast versus implicit baseline (condition of interest versus baseline). Conditions of interest were “attending negative”, “ignoring negative”, “attending positive” and “ignoring positive”.



**Fig. 4.** (A) Result of the interaction age  $\times$  attention  $\times$  emotional valence in the left anterior insula thresholded at  $p < .05$  corrected cluster level. (B) The shape of the interaction using the mask of the resulting cluster from (A) was further explored extracting percent signal change. Error bars denote SEM. \*\*\* $p < .001$ ; \*\* $p < .01$ ; \* $p < .05$ .

As a result, group-level activation from age 14 and 16 overlapped in several, mostly temporo-occipital regions. According to the classification of [Cicchetti \(2001\)](#) reliability was poor ( $<.40$ ) for all of the ROIs in the high-level contrasts. In the contrasts vs. baseline, reliability was poor for frontal and good to excellent ( $>.75$ ) for temporal and occipital regions.

#### 4. Discussion

This longitudinal study investigated the adolescent development from age 14 to 16 of neural bottom-up and top-down processes underlying two aspects of emotional attention, i.e. attending versus ignoring emotion. For this aim a paradigm enabled systematic variation of attention (attending emotion, ignoring emotion) and emotional valence (negative, positive, neutral). Behavioral results indicated an expected longitudinal improvement in reaction times and accuracy from age 14 to 16 in both attending and ignoring emotion and across emotional valence.

Overall, patterns of brain activity elicited by the task were consistent with previous studies ([Dolcos and McCarthy, 2006](#); for a review see also [Jordan et al., 2013](#), [Vuilleumier and Huang, 2009](#)). Developmental effects between age 14 and 16 were most present in regions related to cognitive top-down control while in contrast activity in regions mediating bottom-up processing was stable. However, by employing a neutral baseline and always contrasting emotional versus neutral conditions, the current results extend previous findings since they demonstrate emotion-specific development. The main novel developmental finding is twofold and partly confirms the a priori hypothesis: First, there was a main effect of age in the bilateral IFG and the ACC indicating an overall increasing activation for emotional attention. Expectedly, this increase in PFC activation was found for ignoring negative emotions. However, this increase in PFC activation was additionally found for ignoring positive emotions and attending negative and positive emotions. Second, rather unexpected, there was a three-way interaction in the left anterior insula indicating higher activation elicited by ignoring negative emotions, as well as attending positive emotions, but a stable neural activity for ignoring positive and attending negative emotions. As expected we did not find amygdala development. A PPI analysis of both amygdalae revealed a 3-way interaction in the posterior cingulate cortex and the precuneus with an increase in connectivity to the right amygdala from age 14 to 16 for attending negative and ignoring positive but not for attending positive and ignoring negative.

##### 4.1. Longitudinal neural development

###### 4.1.1. Developmental effects in the bilateral IFG and the ACC

Across conditions activation in the IFG and ACC increased from age 14 to 16. Thus, for ignoring and attending emotion in general adolescent top-down control seems to develop corroborating findings from [Paulsen et al. \(2015\)](#). Regarding the specific condition of ignoring negative emotions current results add to previous findings of lower prefrontal activation in adolescents compared to adults ([Monk et al., 2003](#); [Deeley et al., 2008](#)). While these previous findings might point to a linear decrease of prefrontal activation, current results suggest a longitudinal increase of prefrontal activation in mid-adolescence. This mid-adolescent increase of ignoring negative emotion in prefrontal regions might be followed by a later decrease, e.g. an inverted U-shaped trajectory until adulthood. However, integration of current and previous developmental findings of emotional attention in adolescence remains speculative, since different processes were investigated, i.e. the distracting emotion as a part ([Monk et al., 2003](#); [Deeley et al., 2008](#)) or no

part (current study) of the task-related stimulus. Thus, further longitudinal research discriminating between different processes of emotional attention is needed.

The two regions IFG and ACC have been suggested to be core regions for the cognitive control of emotions enabling emotion regulation strategies ([Ochsner and Gross, 2005](#)).

More specific, fMRI and lesion have characterized the IFG as a core region for inhibition, exerting its effects on subcortical and posterior-cortical regions ([Aron, 2007](#)). [Hampshire et al. \(2010\)](#) suggested the right IFG supports top-down processing allowing it to win the competition for execution in presence of visual distractors. In line with this [Jordan et al. \(2013\)](#) concluded that the IFG plays a role in coping mechanisms for distracting emotions and thus exerts top-down control, mainly shown for ignoring negative emotion. Corroborating our findings, the IFG seems to be critically involved in the effortful maintenance and execution of a planned behavior.

The region of the ACC that shows the age effect is the anterior midcingulate cortex (aMCC). Metabolic disturbances of this region are considered risk and state markers of affective disorders ([Pilhatsch et al., 2014b](#)). In a meta-analysis it has been shown to be relevant for negative affect, and cognitive control ([Shackman et al., 2011](#)). With regard to cognitive control, it is involved in action selection when confronted with conflicting sensory information ([Shackman et al., 2011](#)). Other authors ([Lindquist et al., 2012](#)) have suggested that this region is relevant for core affect and therefore motivational salience of external events, i.e. indicating if something is approachable or avoidable. Both interpretations of core affect and motivational salience as well as cognitive control for competing responses may fit to current task demands. The ACC may function as a top-down region to minimize emotional interference in order to focus on the main task, here comparing stimuli ([Shafer et al., 2012](#)).

Task-irrelevant emotional interference might exist in both the ignoring and attending emotion condition in a different form: while in the attending-emotion-condition the task-irrelevant emotion is part of the task-relevant stimulus; in the ignoring-emotion-condition the emotion is part of a different task-irrelevant stimulus. This is corroborated by both neural (similar activation for ignoring and attending emotion) and behavioral findings (e.g. heightened RTs for attending negative in comparison to neutral targets). Taken together, current findings demonstrate a significant neural developmental step between 14 and 16 years in cognitive control of emotions by an increased activation of top-down control regions when faced with positive or negative emotional distractors.

###### 4.1.2. Developmental effects in the left anterior insula

Activation in the anterior insula increased for attending positive and ignoring negative emotion from age 14 to 16. For ignoring positive and attending negative emotion, however, there was no activation change. Additionally, our results show that the pattern of activation of ignoring positive emotion versus other conditions differs between time points: At age 14, ignoring positive emotion elicited higher activation in the left anterior insula compared to other conditions. In contrast, at age 16 no activation differences between conditions were observed. Thus, at age 14 specifically positive distractors such as a rewarding scene involving happy people might be relevant. This finding is in line with [Somerville et al.'s \(2011\)](#) finding of more impulsive errors toward positive distractors in adolescents relative to both children and adults. The authors discussed this referring to adolescent sensation seeking and risky behavior in order to receive potential rewards ([Steinberg, 2005](#)). Nevertheless it is unclear why the current results only showed higher activation at age 14 for ignoring but not for attending positive emotion.



Dolcos and McCarthy (2006) found heightened anterior insula activation for negative versus neutral distractors – using similar IAPS pictures as in the current study – for young adults. Comparing the insula activation from age 14 to 16 for negative vs. neutral distractors it seems as if the 16-year-olds are showing the “mature” pattern, i.e. an increase of activation for negative vs. neutral distractors vs. the opposite (decrease) at age 14.

The finding of the anterior insula is unexpected and has to be treated with caution. This region has been suggested to be important for emotional attention processing, especially for awareness and evaluation of interoceptive information (Craig, 2009). The anterior insula might be involved in emotion regulation as the suppression of emotional expression was found to increase left anterior insula activation (Goldin et al., 2008).

Current results are consistent with meta-analytic findings that suggest a particular role of the anterior insula in processing the salience of emotional stimuli and recruiting top-down resources such as the ACC if necessary (Cromheeke and Mueller, 2014; Menon and Uddin, 2010).

The anterior insula has been described as a cognitive–emotional hub with an increased activation in adulthood for response inhibition (for a review see Smith et al., 2014). In a recent model, these authors suggest that the relative immaturity of the anterior insula might lead to an adolescent bias toward affectively driven decisions and therefore toward risk taking (Smith et al., 2014).

All three regions with developmental effects have recently been shown to be important for cognitive control of emotion in a recent meta-analysis in adults (Cromheeke and Mueller, 2014). Thus, the function of these regions seems to be already present but continues to develop across adolescence.

Extending previous studies (Cromheeke and Mueller, 2014) the current study investigated both ignoring positive and negative emotion. A specific longitudinal development for ignoring positive emotion has been shown for the anterior insula but not for ACC/IFG regarding emotional valence. However, future studies are needed to disentangle cognitive control of positive and negative emotions.

#### 4.1.3. Exploratory analysis of amygdala activation

Here, we explored whether the amygdala, a region critical for emotional detection and monitoring, would show changes across adolescence. Our finding of stable amygdala activity elicited by emotional attention between age 14 and 16 extends findings of Hare et al. (2008) showing a heightened amygdala activation in adolescents compared to both children and adults. This was expected since Hare et al. found the amygdala activation peak in mid-adolescents. A further longitudinal assessment of the current participants might show a decrease of amygdala activation until adulthood.

Other findings suggest no increase of amygdala activation in adolescence but a steady decrease in amygdala activation across adolescence in a wider age-range: Decety et al. (2012) found such decrease for viewing of negative emotions, i.e. intentionally harmed people and at the same time an increase in ventromedial PFC activation across adolescence. The current results suggest stability of amygdala activation within two years in mid-adolescence and also an increase of PFC activation. Future studies are needed to follow up on amygdala activation across adolescence. This is related to one limitation of the current findings: only a small-age range in mid-adolescence was studied naturally not covering the whole developmental span of adolescence. The current longitudinal study is going to a third data acquisition phase when the adolescent participants turn 18 and hence, we will be able to look at the late adolescent phase soon. Future studies should also include early adolescents (i.e. age 12–14) or older children to be able to cover the full spectrum of development in- and out-of adolescence.

Second, the current study shares a drawback with most emotion studies: stimuli have been classified according to ratings of adults. Adolescent ratings might differ. Moreover current results are in line with previous studies (Koolschijn et al., 2011; van den Bulk et al., 2013) that show poor to fair reliability in adolescent fMRI. Thus, it seems to be difficult to disentangle between “true” development and changes due to unreliable measurement in developmental fMRI. Albeit the variability across measurements we could detect developmental changes. We are currently working on a study including a thorough analysis and discussion of implications for future developmental studies.

We further explored developmental effects of functional connectivity with the amygdala. Here, the PPI analysis suggests an increased functional connectivity from age 14 to 16 of the right amygdala with the right precuneus and the posterior cingulate cortex for attending negative and ignoring positive but not for attending positive and ignoring negative stimuli.

The posterior cingulate cortex has been suggested to function in regulating attention (Leech and Sharp, 2014). The cuneus has been found to show a developmental effect by Lindstrom et al. (2009): with increasing age cuneus activation decreased until adulthood, which was investigated cross-sectionally. Together with the finding of an increasing cuneus/precuneus activation across age when controlling for state anxiety in the current longitudinal study, the finding of an enhanced cuneus/precuneus connectivity with the amygdala suggests that this region might play a particularly important role in mid-adolescent development for emotional attention. This region has been shown to be important in attention-orienting (Corbetta and Shulman, 2002) and cognitive control (Dosenbach et al., 2008). This might suggest that mid-adolescents develop a stronger connectivity in those networks supporting the regulation of attention in order to keep their focus on the main task.

## 5. Conclusions

The current study indicates some significant neurodevelopmental steps for the effortful maintenance of a planned behavior in adolescents. PFC networks for top-down control of emotional attention continue to develop within a narrow age-range of two years in mid-adolescence in a longitudinal course. Additionally, the anterior insula seems to continue to develop longitudinally. These observations might help to better characterize healthy in contrast to dysfunctional development since several clinical studies demonstrated the critical role of these networks in the manifestation of affective disorders. An increase of top-down attentional control while activity of neural networks representing bottom-up processing remains stable might indicate the continuing development of basic emotion regulation strategies. The development of such strategies might be important to solve the wealth of socio-affective developmental tasks in adolescence.

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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.2015.05.001>

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