



Developmental changes within the extended face processing network: A cross-sectional functional magnetic resonance imaging study

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Abstract

In the field of face processing, the so-called “core network” has been intensively researched. Its neural activity can be reliably detected in children and adults using functional magnetic resonance imaging (fMRI). However, the core network’s counterpart, the so-called “extended network,” has been less researched. In the present study, we compared children’s and adults’ brain activity in the extended system, in particular in the amygdala, the insula, and the inferior frontal gyrus (IFG). Using fMRI, we compared the brain activation pattern between children aged 7–9 years and adults during an emotional face processing task. On the one hand, children showed increased activity in the extended face processing system in relation to adults, particularly in the left amygdala, the right insula, and the left IFG. On the other hand, lateralization indices revealed a “leftward bias” in children’s IFG compared to adults. These results suggest that brain activity associated with face processing is characterized by a developmental decrease in activity. They further show that the development is associated with a rightward migration of face-related IFG activation, possibly due to the competition for neural space between several developing brain functions (“developmental competition hypothesis”).

KEYWORDS

amygdala, children, extended face processing network, inferior frontal gyrus, insula, lateralization

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1 | INTRODUCTION

Face processing is mediated by a distributed neural system, often divided into a *core system* and an *extended system* (Gobbini & Haxby, 2007; Haxby et al., 2000). The *core system* comprises several bilateral brain regions in the occipitotemporal cortex, including the fusiform face area (FFA), the occipital face area (OFA), and a face-selective region in the posterior superior temporal sulcus (pSTS). The *extended system* comprises regions from neural systems for other cognitive functions (Haxby et al., 2000). These areas are not specifically dedicated to the basic processing of face information. They are rather recruited for additional operations, such as the interpretation of facial expressions and/or inferring a person's mood (Duchaine & Yovel, 2015; Haxby et al., 2000).

The extended system and its ontogenetic development have been studied scarcely compared to the core system of face processing in children (e.g., Gathers et al., 2004; Haist et al., 2013; Hildesheim et al., 2020; Joseph et al., 2011). Therefore, in the present functional magnetic resonance imaging (fMRI) study, we compared the brain activation pattern between children aged 7–9 years and adults during a face processing task. We particularly focused on the amygdala, the insula, and the inferior frontal gyrus (IFG). The amygdala and the insula have been associated with the perception of emotional expressions from faces (Gobbini & Haxby, 2007; Haxby et al., 2000; Tippett et al., 2018). The *amygdala* is particularly associated with fear (Breiter et al., 1996; Morris et al., 1996, 1998; Whalen, 1998). It also plays a role for the familiarity of a face (Gobbini & Haxby, 2007). The *insula* is known as a part of a salience network integrating sensory information into cognitive and affective processes (Cole & Schneider, 2007; Menon & Uddin, 2010; Naqvi & Bechara, 2009; Smith et al., 2014). During face processing, the insula shows an increased response for faces of high emotional valence in the context of intense relationships (Gobbini & Haxby, 2007). In addition to the amygdala and insula, the IFG is also part of the extended network and plays a role in processing emotional faces. The IFG is particularly associated with the judgement of emotional content of facial expressions (Dal Monte et al., 2014; Haxby et al., 2002; Kitada et al., 2013). In more recent neuroanatomical models of face processing, a specific sub-region of the IFG has been postulated to show face selectivity comparable to that of the core system (Duchaine & Yovel, 2015).

In children's face processing network, both increased (progressive) as well as decreased (regressive) brain activity changes were observed across age. Although progressive developments were shown in regions within the core system and right prefrontal areas of the extended system (IFG, opercular part), regressive changes occurred in parietal and lateral temporal cortices (Joseph et al., 2011). Previous research points to an hyperactivation of the extended face process-

ing system in primary school age (Haist et al., 2013) and a posterior–anterior shift of face-related activity as a consequence of increasing specialization for faces (Gathers et al., 2004).

In primary school age, important skills develop simultaneously: Cognitive control (Gee et al., 2013) and empathy are shaped (Hoffman, 2008), both suggested to influence face processing (Dapretto et al., 2006; Enzi et al., 2016; Ishai et al., 2005). The acquisition of writing and reading skills further affects the brain's functionality (Dehaene et al., 2010; Li et al., 2006; Petersson et al., 1999, 2000, 2007). Because cognitive control increases with growing age (Giedd et al., 1999; Halperin et al., 1994; Ridderinkhof & van der Stelt, 2000), the prefrontal cortex likewise exhibits increased activity in response to faces when children grow older (Wu et al., 2016). Cognitive control, a top-down regulation of emotional responses, is typically associated with the prefrontal cortex. It is for example supposed to exert an increasing inhibitory influence on the amygdala with age (Vink et al., 2014). Cognitive control is also required for emotion categorization (Kawasaki et al., 2001) and empathy (Hinnant & O'Brien, 2007). At the age of 9–10, functional interactions between the insula, the amygdala, and the IFG can be detected as reported by Pfeifer et al. (2008). The authors suggested that the insula and the amygdala would be dedicated to emotional responses, whereas the IFG subserved empathy-related processes. The IFG likely fulfills a double role, being indispensable for cognitive control, but also important for empathy.

The IFG also plays an important role in the language network (Hickok & Poeppel, 2007), which substantially develops in primary school age. In particular, the IFG is associated with verb generation (Sreedharan et al., 2015) and the storage of phonological representations (Suárez-Pellicioni et al., 2019). Both language and face processing systems show an increased specialization with age. Their neural activation develops from a diffuse pattern in children to an increasingly focal pattern in adults. Although for the language system this specialization predominantly occurs in the left hemisphere (Brown, 2005; Holland et al., 2001; Kadis et al., 2011, 2016; Ressel et al., 2008), the face system typically specializes in the right hemisphere (Aljuhanay et al., 2010; Joseph et al., 2011; Young & Ellis, 1976). This concurrent development is thus suggested to be accompanied by lateralization processes due to the competition for functional space, as by the interaction of the core system and the *Visual Word Form Area* (Behrmann & Plaut, 2015; Canário et al., 2020; Hildesheim et al., 2020). However, to our knowledge, lateralization of the extended face processing system has never been compared between children and adults.

In summary, the present study investigated differences in brain activity of the extended system of face processing between children and adults. Applying a cross-sectional approach, we compared the fMRI brain activation pattern

elicited by a face localizer task between 7- to 9-year-old children and adults. We used faces with different emotion categories (neutral, sad, fearful), rendering it possible to assess both general face-sensitive brain activity in the extended system as well as its modulation by different emotions. First, we investigated general face-related brain activation differences between children and adults. Based on previous reports on a more widely distributed activation pattern in the extended face processing network in children compared to adults (e.g., Haist et al., 2013), we hypothesized that face-sensitive brain activity in the amygdala, insula, and IFG would be stronger in the children compared to the adult group. We additionally explored lateralization differences of brain activity patterns in the extended system, which has to our knowledge never been researched so far.

2 | MATERIALS AND METHODS

2.1 | Participants

Ten adults (three females, seven males; 24–45 years; mean age 32.1 ± 6.1 years) and 12 children were recruited for the study. Four children were excluded from the final analysis. One child aborted the measurements prematurely due to anxiety. Two children were excluded due to high motion during the scanning session (see Section 2.4). Another child was excluded because he was suspected to suffer from epilepsy. Epilepsy was an exclusion criterion for the present study. During the time of measurement, however, it was not known that the child suffered from epilepsy, because the first epileptic seizure occurred a few weeks after the measurement.

The final children sample therefore comprised eight children (two females, six males), aged 7–9 years (9.0 ± 0.7 years). All participants had normal or corrected-to-normal vision and had no history of psychiatric or neurological disorders. Handedness was assessed by the Edinburgh Handedness Inventory Questionnaire (mean laterality quotient [LQ] children $+89.8$; mean LQ adults $+88.3$; Oldfield, 1971). Children's overall cognitive abilities were assessed using the short form of the Wechsler Nonverbal Scale of Ability (WNV) (Wechsler & Naglieri, 2006). The ability of self-reflection and empathy was estimated by the self-report measurement Empathy Quotient (EQ; child version: Empathy–Systemizing Quotient Questionnaire/EQ–SQ–Child; Baron-Cohen & Wheelwright, 2004). Additionally, the forced-choice questionnaire Autism Quotient (AQ) (Cambridge Autism Research Center, Baron-Cohen et al., 2001) was used to assess characteristics associated with autism spectrum disorder. The results showed that all children scored in normal range.

All participants provided written informed consent after they were apprised in detail about the experimental setup and the study procedure. In case of minor participants, their par-

ents provided informed consent. The study was approved by the local ethics committee of the Department of Psychology of the Justus-Liebig University Giessen, Germany (reference number 2018-0024).

The data were originally collected in a study that primarily aimed to investigate the ontogenetic development of the core system of face processing, in particular regarding changes in hemispheric lateralization of the FFA. The results of this analysis are published elsewhere (Hildesheim et al., 2020). For the present study, we reanalyzed the data to additionally assess the development of specific regions of the extended system of face processing.

2.2 | Experimental paradigm

The study was set in a child-oriented procedure, embedding the data acquisition into a narrative frame with the child flying as an astronaut in its rocket (i.e., the MR scanner). A cuddly mascot was brought into the story to motivate the child. In order to awake curiosity, a “mocking” date was agreed with a few days’ distance from the actual measurement date, where subjects and their parents were introduced to the magnetic resonance imaging (MRI) method and the frame story. At this date, the child was invited to inspect the “narrow interior” and the “noisy background” of the rocket to prevent discomfort and anxiety. An extensive description of the procedure can be found in Hildesheim et al. (2020).

The face processing network was assessed using a face localizer paradigm. Participants viewed grayscale photographs of faces with neutral, sad, or fearful expressions in the activation condition and houses in the control condition in a blocked design. Face stimuli were taken from the Karolinska Directed Emotional Faces (KDEF) dataset (<http://www.emotionlab.se/resources/kdef>). House stimuli were selected from the internet. The paradigm was split into two sessions, including 16 blocks each (four blocks with neutral, sad, and fearful faces, respectively; four house blocks). The sessions were divided by a short break of 20 s. The blocks contained 11 stimuli, of which each was displayed for 900 ms in pseudorandomized order, separated by a 425-ms inter stimulus interval, which resulted in a fixed block length of 14.15 s. The blocks were separated by a 6-s interblock interval, during which the participants were instructed to fixate a cross in the center of the screen. The total duration of the fMRI paradigm was ~11 min. The order of blocks remained the same across all subjects, whereas the order of images in each block was pseudorandomized. To ensure attention, subjects were asked to indicate via button press with the right index finger when a stimulus was shown twice consecutively. Within one block, either two or three stimulus-pairs arose, which sum up to 40 target events in the whole fMRI paradigm. Our result showed that the one-back matching task successfully kept the

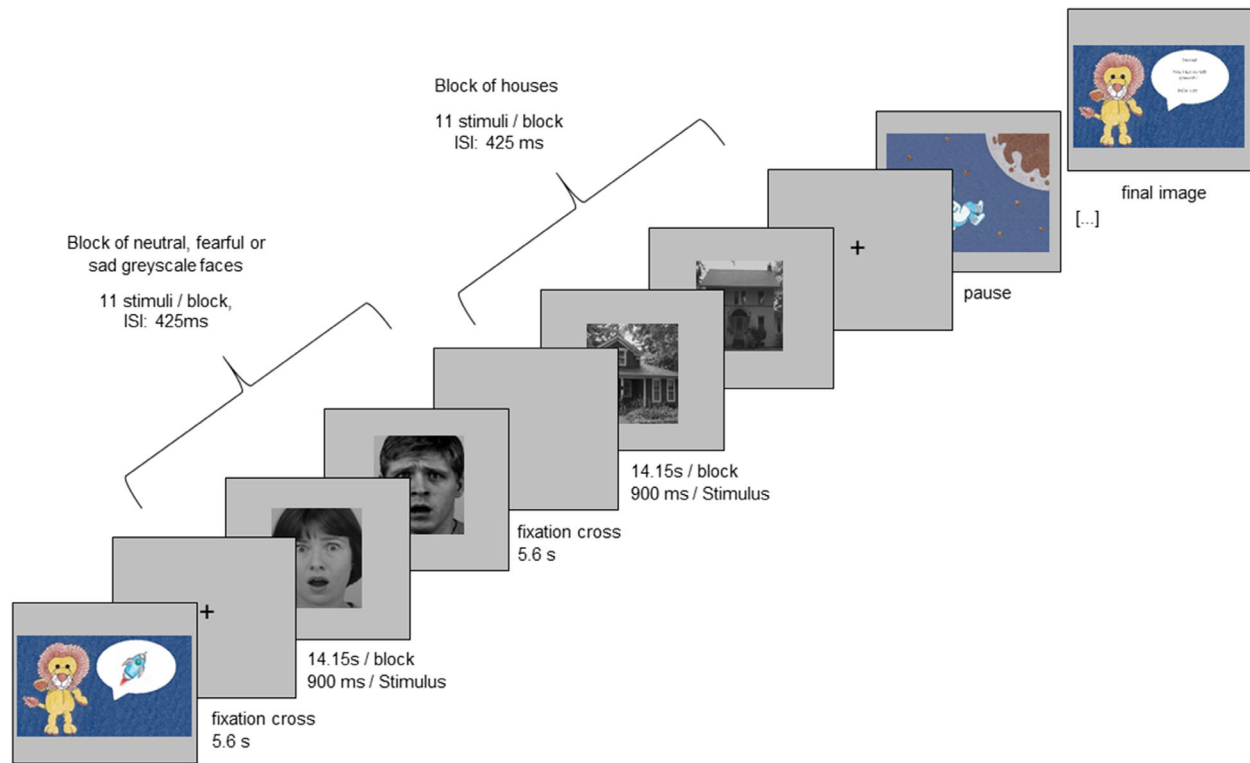


FIGURE 1 Schematic overview of the experimental design

attention of both groups, which showed a mean performance of $>90\%$ accuracy (adults: $97.90\% \pm 2.82\%$, children: $94.27\% \pm 10.65\%$). Figure 1 shows a schematic overview of the block design.

2.3 | MRI data acquisition

Imaging was performed on a 3-T MR-scanner (Siemens Magnetom Prisma; Siemens AG, Erlangen, Deutschland) at the Bender Institute of Neuroimaging (BION), Department of Psychology, Justus-Liebig-University Gießen. All images were acquired using a 64-channel head matrix receive coil. First, a high-resolution anatomical image was acquired using a T1-weighted magnetization-prepared rapid gradient-echo (MPRAGE) sequence. The following parameters were applied: acquisition time (TA) 4:29 min, repetition time (TR) 1580 ms, echo time (TE) 2.30 ms, field of view (FOV) 240 mm, 176 slices, slice thickness (ST) 0.94 mm, resolution $0.9 \times 0.9 \times 0.9$ mm, phase encoding direction (PE) anterior \gg posterior, distance factor (DF) 50%, flip angle 8° , bandwidth 200 Hz/Px, sagittal ascending acquisition. Second, functional images were collected using a T2*-weighted gradient echo-planar imaging (EPI) sequence sensitive to Blood Oxygen Level Dependent (BOLD) contrast. The following parameters were used: TA 11:14 min, TR 1780 ms, TE 36 ms, FOV 256 mm, 20 slices per slab, ST 2.4 mm, resolution $2.0 \times 2.0 \times 2.4$ mm, PE anterior \gg posterior, DF 20%, flip

angle 70° , bandwidth 1396 Hz/Px, ascending acquisition. We did not measure the whole brain, but only a slab. Reducing the coverage allowed reduction of the voxel size, in particular the slice thickness, and therefore an increased spatial resolution. Sequence parameters were especially chosen to capture the activity of subcortical regions prone to susceptibility artifacts, in particular the amygdala (Morawetz et al., 2008). The slab was manually oriented, using the T1-weighted image. It covered parts of the frontal and temporal lobe as well as limbic structures and ranged up to the occipital lobe. It was chosen to cover on the one hand all regions of the core system of face processing, and on the other hand in particular the amygdala, insula, and IFG (for an illustration of the orientation of the slab, see Hildesheim et al., 2020).

2.4 | MRI data analysis

Image preprocessing and statistical analyses were carried out using Statistical Parametric Mapping (SPM 12, Version 7219, Wellcome Trust Centre for Neuroimaging, London, UK; <http://www.fil.ion.ucl.ac.uk>) and Matlab (Version R2016b).

2.4.1 | Preprocessing

First, functional images from both sessions were realigned to the mean image of each subject to correct for head

movements. Second, realigned images were coregistered with the high-resolution anatomical image. Third, the anatomical images were normalized to an age-specific template using the unified segmentation–normalization approach implemented in SPM. We used separate templates for adults and children. For adults, images were normalized to the canonical MNI template provided by SPM. For children, images were normalized to a synthetic template that was specially created for our sample of children by entering detailed age information accurate to the month using the CerebroMatic Toolbox in SPM12 (Wilke et al., 2017) (see Section 2.5 for an extensive description of different procedures of how to compare brain activity between children and adults). Fourth, the transformation parameters obtained from the normalization of the anatomical images were applied to the functional images. Last, normalized functional images were spatially smoothed with an isotropic 6-mm full-width at half-maximum (FWHM) Gaussian kernel.

2.4.2 | Statistical analysis

Statistical analysis was carried out in a two-level, mixed-effects procedure. At the individual subject level, voxel-wise BOLD activity was modeled using a General Linear Model (GLM) approach. Block regressors for each of the conditions in the face localizer paradigm were created (i.e., neutral, sad, and fearful faces; houses) and convolved with the hemodynamic response function in SPM12. Both sessions were separately modeled within one design matrix. To account for movement-related artifacts, the six realignment parameters of each session were included in the GLM design matrix as nuisance regressors. A high-pass filter (cutoff frequency: 1/128 Hz) was used to account for low-frequency noise. Face-sensitive brain activity was assessed by a *t*-contrast comparing faces (regardless of emotional content) against houses, averaged across sessions (i.e., setting for both sessions the contrast weight “1” on each face condition and “–3” on the house condition). In the following, this contrast will be referred to as “faces > houses.” At the group level, the “face > houses” contrast images were entered separately for children and adults into one-sample *t*-tests. Anatomical localization of the activated brain regions was assessed using the WFU-Pickatlas (Maldjian et al., 2003).

2.4.3 | Quality control

We additionally performed an extensive quality control of the fMRI data. General quality control was conducted by the software package MRIQC (<https://mriqc.readthedocs.io/en/stable/>). A specific motion analysis was performed by a self-developed software (“motion estimator,” see [https://](https://github.com/kessler/motionEstimator)

github.com/kessler/motionEstimator for details). An extensive description of the quality control procedure can be found in Hildesheim et al. (2020).

2.5 | Aim 1: Assessment of activation differences between groups

First aim of the study was to assess whether face-sensitive brain activity differs between children and adults in the extended system of face processing. There are (at least) two possibilities to compare fMRI brain activity between groups. The first approach is to normalize all fMRI data to the same template and assess activation differences for each voxel. Because the brains of children and adults largely differ in size and form, one has to take care that the template is not biased toward one of the groups. When, for example, the canonical MNI template (which is based on adult brains) is used, fMRI data of children will undergo stronger transformations in comparison to adults. This might bias voxel-wise statistical comparisons. A possible solution would be to create a study-specific template from all brains of children and adults included in the study. We refrained, however, from this approach because the number of participants in our study was relatively small. This might have led to the creation of a nonrepresentative template. A second, more conservative approach is to assess brain activity for each subject in specific, predefined Regions-of-interest (ROIs) at the single subject level. One can, for example, determine for each subject the location of strongest brain activity in a specific anatomical mask (e.g., left IFG), calculate the activation strength in a small sphere centered on this location, and compare subsequently brain activity strength between groups using appropriate statistical tests. This approach avoids a potentially biased voxel-wise comparison, albeit at the cost of being restricted to the assessment of group differences in predefined ROIs. In the present study, we decided to use the second approach.

Because we determined brain activity at the single subject level, we could have completely omitted the normalization process. We nevertheless introduced a normalization step (using, however, different templates for children and adults, as described above) and assessed the individual brain activity in the normalized images. The additional normalization step helped us to assign activations with more certainty to specific regions. To give an example: if there are for one subject two activated clusters in the (anatomically relatively large) IFG mask, it could be difficult to decide which cluster to choose to calculate brain activity. If the data is normalized, however, it is possible to use the group activation data to select the cluster nearest to the group maximum (“jump to nearest local maximum” algorithm).

In summary, we compared brain activity between children and adults as follows: First, we normalized data from

children and adults to different templates (for adults: the canonical MNI template; for children: an age-matched synthetic template). Second, we calculated the group activation pattern for the contrast “faces > houses” for each group separately using one-sample *t*-tests. Third, we determined the group activation maxima within our predefined ROIs (left and right amygdala, left and right insula, left and right IFG; see Section 1). The ROI masks were anatomically defined using the WFU-Pickatlas (version 3.0.5, Maldjian et al., 2003). These masks were based on the IBASPM 116 atlas (Tzourio-Mazoyer et al., 2002). For all masks, we applied a dilation factor of 1. For adults, the masks could be used directly because they conformed to the canonical MNI template. For children, we transformed the masks into the space of the CerebroMatic children template using the inverse transformation parameters resulting from a normalization to the MNI space. Fourth, to account for individual differences in the localization of activated clusters, we determined for each ROI the individual activation maximum closest to the group maximum using the “jump to the next local maximum” algorithm. Here, we thresholded the *t*-map for the contrast faces > houses at $p = .01$, uncorrected, and located the nearest maximum within the ROI. Fifth, we calculated the activation strength for each ROI by averaging the weighted beta values (for the contrast faces > houses) for all voxels within a 6-mm sphere centered at the individual maximum. Sixth, we compared brain activity between children and adults using a $2 \times 2 \times 3$ factorial design with the between-subject factor GROUP (children, adults) and the within-subject factors HEMISPHERE (left, right) and REGION (IFG, insula, amygdala). We were specifically interested in the main effect GROUP and the interactions GROUP \times HEMISPHERE \times REGION, GROUP \times HEMISPHERE, and GROUP \times REGION. These effects were assessed with the appropriate F-contrast in the statistics software JASP (version 0.9.2.0), using a statistical threshold of $p < .05$.

2.6 | Aim 2: Assessment of lateralization differences between groups

Second aim of the study was to compare children and adults with regard to the hemispheric lateralization of brain activity in the in the amygdala, the insula, and the IFG. The degree of regional face-sensitive hemispheric lateralization was assessed by a lateralization index (LI). The LI is given by the following expression:

$$LI = (A_L - A_R) / (A_L + A_R),$$

where A_L and A_R refer to values of fMRI-measured activity for homologous ROIs within the left (L) and right (R) hemisphere (Jansen et al., 2006). The LI yields values between 1 and -1 . In the present study, an $LI > 0.20$ was considered

to represent left-hemispheric dominance and an $LI < -0.20$ right-hemispheric dominance. An LI between -0.20 and 0.20 was denoted as bilateral (Springer et al., 1999). There are different ways to calculate activity measures and to define ROIs (for an overview, see Jansen et al., 2006; Seghier, ; Wilke & Lidzba, 2007). In the present study, we decided to calculate A_L and A_R as the averaged weighted beta-value (describing the contrast faces > houses) in a 6-mm sphere centered at the individual activation maximum in each ROI (as described in Section 2.5). To derive the LI, the magnitude of activation strength (mean beta) for each ROI (i.e., amygdala, insula, and IFG) and within each hemisphere was calculated. We accounted for intersubject variability of activation strength by calculating individual beta-value thresholds comparable to the procedure described by Fernández et al. (2001). Contrast images (“faces > houses”) were masked with a 6-mm sphere around individually determined coordinates in both hemispheres. For the determination, we used the “jump to the nearest local maximum.” Separately for each hemisphere, all beta-values within this sphere were then sorted by their activation strength. The mean of the most activated 5% of all voxels was calculated, divided by two, and subsequently used as a threshold. All beta-values surpassing this threshold were averaged for each hemisphere and entered as A_L and A_R into the LI formula. Using this implementation, the LI describes the hemispheric lateralization of the brain activity measure analyzed before. We compared brain activity between children and adults using a 2×3 factorial design with the between-subject factor GROUP (children, adults) and the within-subject factor REGION (amygdala, insula, IFG). We were specifically interested in the main effect GROUP and the interaction GROUP \times REGION. These effects were assessed with the appropriate F-contrast, using a statistical threshold of $p < .05$.

We also examined whether the LI values of the amygdala, insula, and IFG were correlated with each other and with the LI values of the OFA, FFA, and pSTS that we calculated in the first part of our study (Hildesheim et al., 2020). For the core system regions, brain activation strength A_L and A_R was determined in the same way as for the extended system (see Section 2.5). Here, we used the following anatomical masks: For OFA, we chose the inferior occipital gyrus in the brain atlas IBASPM116 (as implemented in the WFU Pickatlas, Maldjian et al., 2003). FFA-ROI masks were built choosing the fusiform gyrus. For pSTS, we chose the superior and middle temporal gyrus. Activation clusters that appeared inside one of the ROI masks were considered as potential candidates of core system brain activity. To verify the correct anatomical localization, both the anatomical localization on the individual single-subject T1-image and the positions of the activated brain regions in the occipitotemporal lobe relative to each other were used. For adults, this identification procedure was performed by four and for children by two individual raters separately to maximize accuracy and minimize

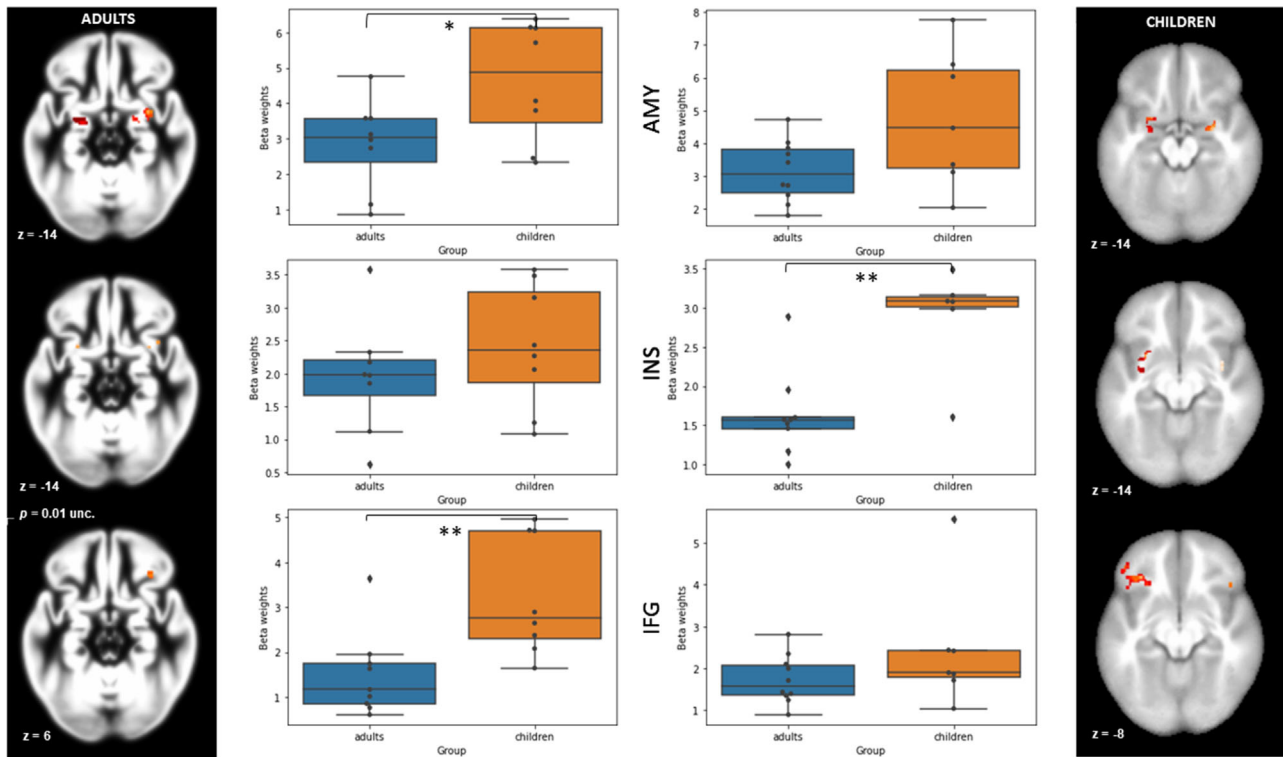


FIGURE 2 Brain activation differences between children and adults. Middle: The boxplots describe the group-averaged brain activation strength in the predefined ROIs amygdala (AMY), insula (INS), and inferior frontal gyrus (IFG) (adults = blue, children = orange). The left boxplot depicts brain activity for the left hemisphere, the right boxplot for the right hemisphere. Brain activity strength is assessed by the weighted beta weights of the contrast “faces > houses.” Significant differences between groups are marked with asterisks. They were found in the left amygdala, the right insula, and the left IFG. Left/right: On the left and the right side, we show the brain activation pattern separately for each group (left: adults, right: children; second-level contrast “faces > houses”)

error-proneness due to interrater differences (adults: authors F.E.H., I.D., R.K., and K.M.Z. of Hildesheim et al., 2020; children: authors I.S. and I.T.).

3 | RESULTS

3.1 | Assessment of activation differences between children and adults

The face processing task activated in both children and adults a large-scale neural network. This network encompassed, as expected, the core system of face perception (i.e., bilateral OFA, FFA, pSTS) and regions in the extended system, in particular our predefined ROIs bilaterally in the amygdala, the insula, and the IFG.

Our first aim was to assess whether face-sensitive brain activity differs between children and adults in the extended system of face processing, in particular in the bilateral amygdala, insula, and the IFG. For a group comparison, individual beta weights of each subject’s ROI activation were extracted and transferred into a $2 \times 2 \times 3$ factorial design as described in Section 2.5 (see Supporting Information A for

two detailed lists of ROI coordinates: Table A1 lists the group maxima of adults and children for each ROI; Table A2 lists the individual local ROI maxima of each subject). The ANOVA revealed significant activation differences between children and adults in several brain regions. More specifically, children showed compared to adults significantly stronger activity in the left amygdala (post hoc Mann–Whitney test, $U = 14.00$, $p = .032$), the right insula ($U = 2.00$, $p < .001$), and the left IFG ($U = 7.00$, $p = .002$) (Figure 2).

We used the t -contrast “faces > houses” as the main metric to compare brain activity between groups. To provide more detailed insights in the activation pattern, we performed two additional post hoc analyses for those regions in which we found activation differences between both groups (i.e., left amygdala, right insula, left IFG). First, we also assessed the brain activation strength for both conditions separately (i.e., for the contrasts “faces > baseline,” “houses > baseline”). This analysis assessed whether the activation difference described above can be specifically attributed to a decrease in face activity in adults or an increase in nonface object activity in adults. We calculated for each of the three regions an additional 2×2 factorial ANOVA. As dependent variable, we used the beta weights for the contrasts

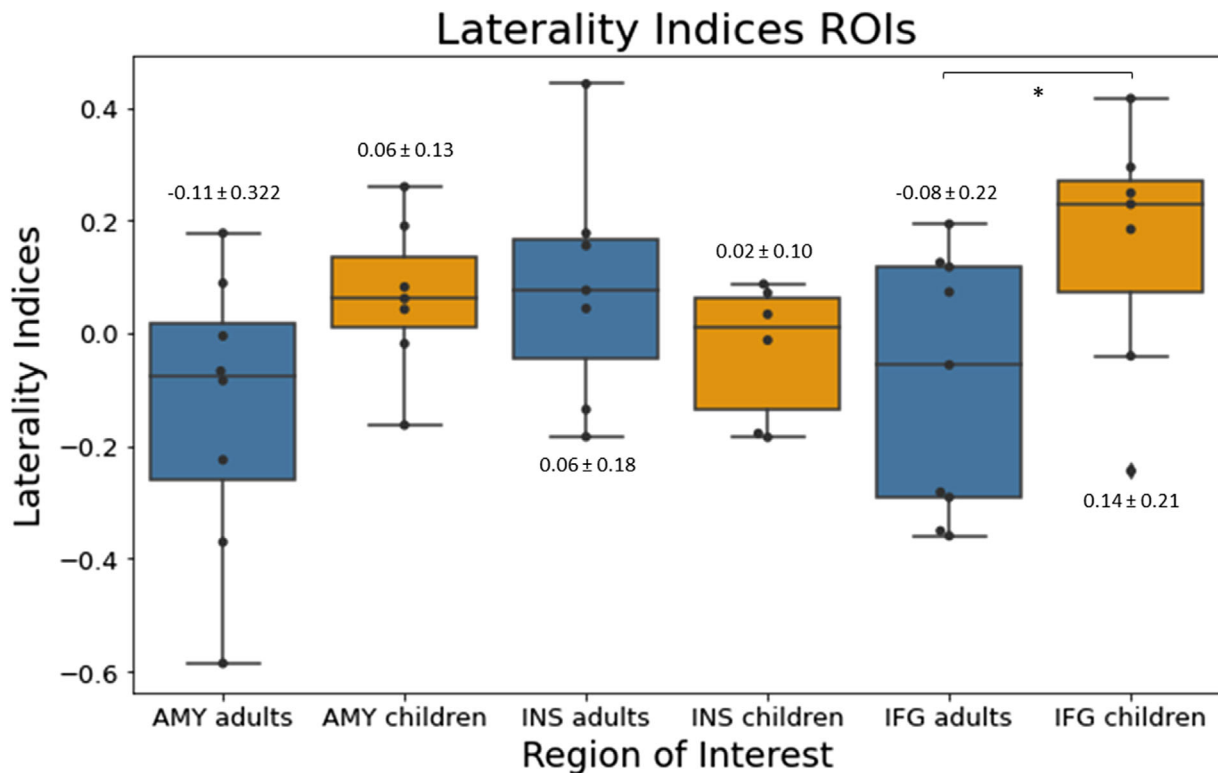


FIGURE 3 Hemispheric lateralization (expressed by a lateralization index) of face-sensitive brain activity in the amygdala (AMY), the insula (INS), and the inferior frontal gyrus (IFG) in children (orange) and adults (blue). Children show a significantly higher left-lateralized activation pattern compared to adults in the IFG. Values of mean lateralization \pm SD are specified above/below error bars

“faces > baseline” and “houses > baseline.” As independent variables, we used the factors CONDITION (faces, houses) and GROUP (children, adults). These ANOVAs, however, did not show for any region a significant GROUP \times CONDITION interaction (all $ps > .05$). This suggests that the group activation differences for the “faces > houses” contrast were not specifically driven by changes within one single condition (for more details, see Supporting Information B). Second, we assessed the brain activation strength separately for each emotion category (i.e., for neutral, sad, and fearful faces). We calculated for each of the three regions an additional 3×2 factorial ANOVA. As dependent variable, we used the beta weights for the contrasts “neutral faces > houses,” “sad faces > houses,” and “fearful faces > houses.” As independent variables, we used the factors EMOTION (neutral, sad, fearful) and GROUP (children, adults). Again, these ANOVAs did not show for any region a significant GROUP \times CONDITION interaction (all $ps > .05$). This suggests that the group activation differences for the “faces > houses” contrast were not driven by a specific emotion category (for more details, see Supporting Information C).

3.2 | Hemispheric lateralization of extended network regions in children and adults

Our second aim was to compare hemispheric lateralization within the extended system of face processing between adults and children, in particular for the amygdala, insula, and IFG. The data distribution and mean lateralization is described in Figure 3. The activation pattern showed an overall trend toward increased left-lateralized activity in children in all regions. Lateralization differences between groups were formally assessed by a two-factorial ANOVA. This analysis revealed a GROUP \times REGION interaction, explained by a significantly stronger left-lateralized brain activity in the IFG for children compared to adults (post hoc Mann–Whitney test, $U = 10.00$, $p = .023$). We additionally investigated whether the lateralization of amygdala, insula, and/or IFG was correlated with lateralization of the core network regions OFA, FFA, and/or pSTS. No significant correlations, however, were found at $p = .05$, corrected for multiple comparisons.

4 | DISCUSSION

In the present study, we compared the fMRI brain activation pattern elicited by a face processing task between 7- to 9-year-old children and adults using a cross-sectional design. Our analysis focused on the extended face processing network, in particular on the amygdala, the insula, and the IFG. Our main findings can be summarized as follows: First, children showed increased activity in the left amygdala, the right insula, and the left IFG. Second, children showed a leftward shift in IFG activity. These results suggest a hyperactivation of the examined areas in children compared to adults. They are in line with previous studies that have found less activity in children's core face processing network, but a stronger recruitment of the extended network (e.g., Gathers et al., 2004; Haist et al., 2013; Joseph et al., 2011). However, none of these studies investigated lateralization differences of corresponding regions between children and adults. As far as we know, our study is the first to specifically examine the developmental lateralization of emotion-associated areas in the extended face processing network and to address possible origins for differences in lateralization.

In primary school age, an important developmental milestone in cognition is reached and three further maturing processes additionally influence the specialization and lateralization of face-sensitive areas: First, children learn to read and write. Second, cognitive control over emotional affects continues in maturation. Third, the ability to empathize progresses in development as well. In the following, our results are discussed regarding the ROI's role in these developmental processes and their impact on face processing.

4.1 | The role of the amygdala

In children, the left amygdala was stronger activated during emotional face perception than in adults. The amygdala is known for emotion processing and, in the context of face perception, particularly associated with the processing of fearful expressions in adults (Breiter et al., 1996; Morris et al., 1996, 1998; Whalen, 1998). One explanation for the higher amygdala activity in children might be a different evaluation of the stimulus material. If children would conceive all—or at least some—of the face stimuli as emotionally more arousing, amygdala activity might be increased. We therefore conducted post hoc another purely behavioral study in which another sample of children (in an equivalent age range) and adults assessed valence and arousal of the face stimuli (see Supporting Information D). However, ratings for both valence and arousal for all three face stimulus categories (neutral, fearful, sad) were comparable between children and adults. From this point of view, it is therefore unlikely that a higher emotional classification of faces led to the hyperactivity. Another expla-

nation might lie in an underdeveloped specialization of the extended network. Since the ability to categorize emotions is still developing, enhanced amygdala activity might be related to a recruitment of additional neural resources due to their still maturing face specialization and emotion categorization ability.

4.2 | The role of the insula

Our findings revealed a stronger recruitment of the right insula in children compared to adults. Our result is partly in line with a finding by Haist and colleagues (2013) who found a bilateral insula activation in 6- to 12-year-olds and a negative relationship of insula activity and age. However, the examined age range is broader compared to our study, which post limits the comparability of both datasets. In adults, the insula represents a kind of “hub” in which salient sensory information is transferred into cognitive and affective circuits (Cole & Schneider, 2007; Menon & Uddin, 2010; Naqvi & Bechara, 2009; Smith et al., 2014). Based on the hypothesis that the facial specialization of the ROIs and the ability to categorize emotional expressions is not yet fully developed in the examined children, the insula may also undergo strong developments in this age range with regard to the “hub” function. Here, again, the hyperactivation of the right insula in children in relation to adults may be explained by the fact that additional neural resources are needed. If the insula is at least partially performing the “hub” function, it seems plausible that the insula may also show more neural activity than in adults, as amygdala and insula may already exchange emotional information. However, future studies are necessary to investigate the role of the insula during the ontogenetic development of face processing abilities.

4.3 | The role of the IFG

Children's IFG showed a significant heightened response to faces in the left hemisphere compared to adults. In the same vein, our LI calculation hints at a rightward shift from a more left-lateralized IFG activation in 7- to 9-year-old children to a more right-lateralized activation in adults. This raises the question of the underlying mechanisms leading to this lateralization process. One possibility would be that the IFG is subject to a competition between the two developing cognitive domains language and face processing, resulting in a left dominant language processing (e.g., Gaillard et al., 2004; Hund-Georgiadi et al., 2001; Knecht et al., 2000) and right-dominant face processing in adults (De Renzi, 1986; Kanwisher et al., 1997; Puce et al., 1996; Wada & Yamamoto, 2001). This so-called developmental competition hypothesis (Li et al., 2013) is still a matter of intensive debate. We speculate that a

potential migration process of face-sensitive IFG activity from a more left-dominant to a bilateral or right-hemispheric distribution may be related to the progressive acquisition of language abilities in primary school children, in particular due to the acquisition of reading skills. To test this hypothesis, connectivity and correlation measures related to the inter- and intrahemispheric networks and LIs in larger samples of equivalent age ranges or in a longitudinal design are required.

A recent study has shown that in adults the Visual Word Form Area (VWFA) receives top-down modulation from the Broca's area in the IFG (Canário et al., 2020). This indicates a developmental process regarding the IFG's role within the language network and may explain why the region may also be affected by lateralization mechanisms occurring in posterior network parts (i.e., FFA and OFA; see also Hildesheim et al., 2020 for a discussion on the competition between FFA and visual word form area). The findings of left-dominance in IFG activity are also in line with another study, which found a left-dominant face activation pattern in 5- to 9-year-old children that gradually migrates to the right hemisphere with age (Joseph et al., 2011). Progressive changes in the occipital-fusiform area and right inferior frontal cortex and regressive changes in parietal and lateral-temporal cortices across age were assumed. More in-depth investigations and connectivity analyses are now necessary to elucidate the underlying top-down and bottom-up mechanisms and affective neural activation cycles, especially with regard to lateralization.

4.4 | Emotion-specific development within the extended face perception network

In post hoc analyses, we assessed whether brain activation differences between children and adults were driven by specific emotion categories. A successful processing of emotional expressions requires the coordination of visual working processes with early evolving emotional processes and later developing high-order cognitive functions. At the age of five, children can label basic emotions, such as happiness, anger, sadness, surprise, and fear (Widen & Russell, 2003). Furthermore, evidence suggests a developmental leap between the ages of six and eight and a second improvement approaching adult performance in the discrimination of facial expressions at the age of 14 (Kolb et al., 1992; Lobaugh et al., 2006). Thus, our children sample, aged 7–9, should already have passed the first developmental leap, that is, they should be able to discriminate fearful expressions from other categories on a neural level. Our results, however, did not show a significant different ROI activation in children depending on the presented emotion category. For adults, an atlas of emotion-specific neural patterns for face processing is available (Fusar-Poli et al., 2009), but so far, it is still unclear at which developmental stage these patterns are mature. Our results demonstrate

that the regions amygdala, insula, and IFG are important for the processing of neutral, sad, and fearful faces in the age range 7–9, but may rather be involved in more general neural emotion circuits than in emotion-specific processing.

In summary, the current study demonstrated during a face processing task increased brain activity in 7- to 9-year-old children compared to adults in the extended system of face perception, in particular in the amygdala, the insula, and the IFG. The study further showed increased left-lateralization of face-sensitive brain activity in the IFG. This shift in brain activity might be associated with migration processes from a left-dominant to a bilateral face-sensitive IFG activation that might be influenced by a competition of the language and face processing system for functional space.

At last, we would also like to mention a limitation of the study. The final sample finally comprised only eight children and 10 adults. Twelve children were originally recruited for the study. Four children, however, had to be excluded from the final analysis (one child aborted the study, one child was post hoc diagnosed with a potential epilepsy, two children showed excessive motion artifacts; see Section 2.1). The small sample size limits the generalizability of our results. To disentangle the driving forces for the discovered processes, further studies with larger samples are indispensable. These should ideally be planned in a longitudinal design to reflect the ROI's trajectory in the context of face processing.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Isabell Sahraei and Franziska E. Hildesheim conceptualized the experiment, collected the data, performed MR image processing, analyzed and interpreted the data, and wrote and revised the manuscript. Ina Thome and Roman Kessler analyzed and interpreted the data and revised the manuscript. Kristin M. Rusch designed the fMRI protocol and analyzed and interpreted the data. Jens Sommer designed the fMRI protocol and analyzed the data. Inge Kamp-Becker and Rudolf Stark financially enabled the study and revised the manuscript. Andreas Jansen was the leader of the group, financially enabled the study, conceptualized the experiment, analyzed and interpreted the data, and drafted and revised the manuscript.

DATA AVAILABILITY STATEMENT

Due to the young age of the participants, parents and children were assured raw data would remain confidential and would not be shared.

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