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Special Issue Article

Emotional maltreatment and neglect impact neural activation upon exclusion in early and mid-adolescence: An event-related fMRI study

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Abstract

Child maltreatment gives rise to atypical patterns of social functioning with peers which might be particularly pronounced in early adolescence when peer influence typically peaks. Yet, few neuroimaging studies in adolescents use peer interaction paradigms to parse neural correlates of distinct maltreatment exposures. This fMRI study examines effects of abuse, neglect, and emotional maltreatment (EM) among 98 youth (n = 58 maltreated; n = 40 matched controls) using an event-related Cyberball paradigm affording assessment of both social exclusion and inclusion across early and mid-adolescence (≤13.5 years, n = 50; >13.5 years, n = 48). Younger adolescents showed increased activation to social exclusion versus inclusion in regions implicated in mentalizing (e.g., superior temporal gyrus). Individual exposure-specific analyses suggested that neglect and EM coincided with less reduction of activation to social exclusion relative to inclusion in the dorsal anterior cingulate cortex/pre-supplementary motor area (dACC/pre-SMA) among younger versus older adolescents. Integrative follow-up analyses showed that EM accounted for this dACC/pre-SMA activation pattern over and above other exposures. Moreover, age-independent results within respective exposure groups revealed that greater magnitude of neglect predicted blunted exclusion-related activity in the parahippocampal gyrus, while EM predicted increased activation to social exclusion in the precuneus/posterior cingulate cortex.

Keywords: adolescence; emotional maltreatment; neglect; fMRI; social exclusion

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Early adversity and child maltreatment, in particular, confer risk for poor mental and physical health as well as relationship difficulties across the lifespan (Jaffee, 2017; Gunnar & Reid, 2019). Yet, the neurobiological mechanisms underpinning this link remain contentious. On the one hand – inspired by the "cumulative risk approach" that quantifies exposure without an eye to qualitative differences in adversity (Evans et al., 2013) – most neuroimaging research primarily focuses on global (vis-à-vis exposure-specific) effects of maltreatment. On the other hand, recent theory and research support a "dimensional model of adversity", suggesting that neurodevelopmental effects of early adversity may vary as a function of threat and deprivation exposure (McLaughlin et al., 2014; Sheridan & McLaughlin, 2014). While deprivation (i.e., reduction of expected cognitive and social input) is thought to engender neurodevelopmental adaptations within fronto-parietal networks subserving cognitive control and executive functioning, threat exposure (i.e., increased threat to one's physical integrity), in particular, is thought to incur adaptations in neural circuits involved in emotional learning. Neuroimaging data from a systematic large-scale review indeed corroborate that deprivation coincides with volume reductions and altered function in fronto-parietal regions, whereas threat-exposure entails heightened amygdala and anterior insula (AI) activation as well as decreased volume of the amygdala, hippocampus, and medial prefrontal cortex (mPFC; McLaughlin et al., 2019).

Although past neuroimaging work establishes partly distinct neural correlates of deprivation and threat related to learning and reward processing (e.g., McLaughlin & Sheridan, 2016), maltreatment also putatively exerts a considerable part of its pathogenic influence indirectly, via its deleterious effects on interpersonal processes (McCrory et al., 2019). Maltreated children and adolescents not only experience more rejection by caregivers, but evidence indicates decrements in social networks and support over time ("social thinning"), as well as elevated peer rejection,

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victimization, and isolation during youth and adulthood (Benedini et al., 2016; Sheikh, 2018; McCrory et al., 2019; McCrory, 2020). However, maltreatment studies examining neural activation during social encounters remain low in number, thus, arguably raising the concern that hitherto identified neural correlates of deprivation and threat may not generalize to the social domain (McCrory et al., 2019). Therefore, to our knowledge, few social neuroscience studies to date attempt to disentangle effects as a function of differential types of maltreatment exposures. Besides abuse (~threat) and neglect (~deprivation), a subtype which may figure especially prominently in this case is emotional maltreatment (EM), inasmuch as it involves disruption of the species-expected caregiving relationship that carries forward to new social encounters (e.g., Tottenham, 2012; White et al., 2020). Aiming to fill this crucial gap, our study set out to examine neural activation during social inclusion and exclusion among youth exposed to abuse, neglect, and EM as compared to carefully matched unexposed controls.

Neuroimaging studies on social exclusion in adult samples

Examining neural responses to social exclusion has garnered widespread interest over the last two decades. In a seminal study, Eisenberger et al. (2003) initially provided evidence for elevated brain activity in the dorsal anterior cingulate cortex (dACC), the AI, as well as right ventral PFC to social exclusion (compared to inclusion) in the Cyberball paradigm (i.e., a virtual ball-tossing game involving the participant and two computer-generated avatars). Stressing the overlap with neural correlates of physical pain, early work viewed exclusion-related activation in terms of "social pain", while recent work conceptualizes brain activation during social exclusion more broadly in terms of detection of aversion, expectancy violation and/or increased saliency (see Eisenberger, 2015). Moreover, recent meta-analyses of neural activation during social exclusion implicate regions thought to subserve mentalizing/emotion regulation including the mPFC, posterior cingulate cortex (PCC), and precuneus (PRC; Cacioppo et al., 2013; Vijayakumar et al., 2017). The most recently published meta-analysis applying activation likelihood estimation reported consistent activation to social exclusion in the ventral ACC (vACC), PCC, inferior frontal gyrus extending to ventrolateral PFC (vlPFC), superior frontal gyrus (SFG) extending to mPFC, posterior insula, as well as the occipital pole (Mwilambwe-Tshilobo & Spreng, 2021). In keeping with previous meta-analyses, Mwilambwe-Tshilobo and Spreng (2021) also failed to replicate reliable dACC activation upon social exclusion. Instead, based on results from connectivity mapping, the authors suggest a functional overlap with the default-mode network. That said, one meta-analysis found that dACC activation varied as a function of exclusion dose, with dACC activation increasing as the length of the exclusion interval grew longer (Rotge et al., 2015). To surmise, social exclusion not only appears to elicit neural activation in regions associated with aversion and saliency, but also, and perhaps primarily, in regions subserving emotion processing and regulation, mentalizing, as well as self-referential processing.

Adult work assessing perceived maltreatment via self-reports offers preliminary evidence for exposure-specific effects of EM and neglect on neural reactivity to social exclusion in regions implicated in saliency and self-referential processing. In a study by van Harmelen et al. (2014), a positive association emerged between dorsomedial PFC (dmPFC) responsivity to social exclusion and EM severity. Though other maltreatment exposures were unassociated, the specificity of this effect to EM remains uncertain, as the study did not adjust for potentially confounding effects of abuse and neglect, despite multicollinearity between EM and these exposures, as reported by the authors. Nevertheless, these findings align with structural alterations in brain areas supporting emotion regulation including dmPFC, PCC, and PRC for adults with a history of EM (Heim et al., 2013; van Harmelen et al., 2010). Furthermore, an intergenerational study assessing neural activation of parents and offspring during social exclusion reported positive associations between exposure to neglect (a combined physical and emotional neglect score) and activation in the left insula and the dmPFC as well as an inverse association between global maltreatment and dACC activation (van den Berg et al., 2018).

Neuroimaging studies on social exclusion in developmental samples

As compared to adults, reviews and meta-analyses have indicated that adolescents activate the vACC as opposed to the dACC during social exclusion (Eisenberger, 2012; Rotge et al., 2015). Alternately, Vijayakumar et al. (2017) reported increased activation in vlPFC and ventral striatum (and not the vACC vs. dACC) for youth samples compared to increased mPFC activation in young adult samples. Importantly, to date, no neuroimaging studies using Cyberball have attempted to decompose adolescence into its sub-stages. Yet, much developmental and recent neuroimaging research can be taken to imply that the subjective meaning of exclusion by unfamiliar peers should vary markedly for younger versus older adolescents (e.g., Blakemore, 2018; Brown & Anistranski, 2019). Thus, fitting into peer groups is thought to carry particular significance for younger adolescents as they potentially adopt a provisional sense of group identity (Brown, 1990, 1999). Only with time can they increasingly resist peer pressure, standing up for themselves and putatively develop an autonomous sense of identity (Steinberg & Monahan, 2007). Given that social exclusion is a widespread tool to sanction norm violations (Tomasello & Vaish, 2013) and induce cooperation and conformity (Molden & Maner, 2013), exclusion by unfamiliar peers might pose a markedly higher threat to younger versus older adolescents. Accordingly, behavioral Cyberball data specifically support hypersensitivity to social exclusion during early versus mid-adolescence and adulthood (Sebastian et al., 2010).

Moreover, despite preliminary adult work, no developmental studies to date contrast the contributions of differential adversity or maltreatment exposures (i.e., abuse, neglect, and EM) on neural activation to social exclusion. One study on social exclusion (compared to a technical exclusion condition) demonstrated that the related phenomenon of early caregiver separation coincided with reduced activation in dACC, AI, dorsolateral PFC (dlPFC), and inferior parietal lobule (IPL), as well as increased activation of the left middle temporal gyrus – compared to non-separated controls (Puetz et al., 2014). Additionally, the number of separation experiences significantly predicted reduced neural activation to social exclusion in the dACC and dlPFC. As more than half of the participants experienced neglect, it could be speculated that these findings support the notion of hypo-reactivity to social exclusion in association with neglect. However, the specific contribution of neglect, much less of different maltreatment subtypes, was not probed in this study.

The present study

Given the crucial developmental role attributed to aberrant social functioning in the wake of maltreatment (McCrory et al., 2019), we set out to examine the effects of differential maltreatment exposures on the neural correlates of social exclusion during adolescence. As peers pose a prominent source of influence at this stage, and especially so during early adolescence (Steinberg & Monahan, 2007; Blakemore, 2018), we aimed to recruit an adolescent sample spanning early and mid-adolescence with a history of maltreatment experiences as well as a matched control group. To sample the full spectrum of maltreatment and affording dimensional within-group analyses of neglect, abuse, and EM, we recruited participants with a varying degree of exposure to maltreatment from child protection services (CPS), child and adolescent psychiatric services (CAPS), as well as the community. Unlike most classic neuroimaging work on Cyberball, but akin to a growing number of studies in the field (e.g., van Harmelen et al., 2014), we exploited the advantages of an event-related version of Cyberball. On the one hand, we compared rejection-related events (i.e., not receiving the ball during the exclusion phase) to a less stringent, but more commonly used control condition in neuroimaging research (i.e., receiving the ball during the inclusion condition; Gunther Moor et al., 2012; van Harmelen et al., 2014; Will et al., 2016) that maximizes the difference in meaning by contrasting rejection with acceptance. On the other hand, our version also afforded a more stringent, visuospatially identical, but less common control condition in neuroimaging research (i.e., not receiving the ball during the inclusion condition; van den Berg et al., 2018) that may, however, underestimate social exclusion effects owing to its own potential for inducing (weaker) feelings of "micro-rejection" (Crowley et al., 2009; Will et al., 2016).

In line with the considerations above, we expected predominant neural activity during social exclusion in regions supporting emotion regulation and mentalizing (e.g., mPFC, PCC, and PRC) across our full sample (Vijayakumar et al., 2017; Mwilambwe-Tshilobo & Spreng, 2021). In addition, given the prolonged interval of social exclusion in our event-related Cyberball task, we also expected increased activation in the dACC (Rotge et al., 2015). Beyond this overall activation pattern, we predicted differential brain activation according to participant age and/or maltreatment exposures (i.e., neglect, abuse, and EM).[1] First, we anticipated exclusion-related brain activity to be stronger in the aforementioned areas during early compared to mid-adolescence (Blakemore, 2018). Second, we posited exposure-specific effects of neglect, abuse, and EM on neural reactivity to social exclusion both at the between- as well as within-group level. Concerning neglect, based on previous empirical work (Puetz et al., 2014), we hypothesized a reduced exclusion-related activation in fronto-parietal regions (e.g., IPL, dlPFC, and vlPFC), also broadly corresponding to theoretical predictions (McLaughlin et al., 2014). As a tentative proposition due to currently lacking empirical evidence in the field of social neuroscience, we expected an exclusion-related hyper-reactivity in association with abuse exposure in saliency processing regions (e.g., AI; McLaughlin et al., 2019). We further predicted that EM would coincide with an increased activation in brain areas implicated in emotion regulation and mentalizing (e.g., dmPFC, PCC, and PRC; van Harmelen et al., 2014). Finally, based on the theoretically proposed salience of social threat for early adolescents, we additionally tested the possibility of age by maltreatment interactions.

[1]In contrast to exposure-specific maltreatment effects, the adult literature reports both elevated and diminished exclusion-related activation in association with global maltreatment (e.g., van Harmelen et al., 2014; van den Berg et al., 2018). In light of these inconsistencies, we considered the possibility of both increased and decreased exclusion-related activation regarding global maltreatment, as well as potential maltreatment by age interactions. Refer to Appendix A and Appendix B for information on methods and results of these global maltreatment analyses.

Methods

Sample

For this study, 110 12-to-17-year-olds with (n = 63) and without (n = 47) maltreatment histories were selected from a pre-existing large-scale sample of maltreated and nonmaltreated youth at the Department of Child and Adolescent Psychiatry of Leipzig University. Participants were recruited via CPS, CAPS, and the community (AMIS Project, N = 851; see study protocol by White et al., 2015). For the present subsample of maltreated youth, n = 30 (47.6%) reported previous CPS contact. Adolescents with MRI contraindications (e.g., metal implants), a history of neurological disorders or significant head injury, severe physical disorders, severe prenatal and perinatal complications, pervasive developmental disorders, an IQ below 70, current medication, current or lifetime substance use disorders, or who were pregnant or currently breastfeeding were excluded.

Of the 110 recruited participants, 107 completed both study appointments. Three participants could not take part at the second appointment due to MRI contraindications (i.e., tattoos, piercings, as well as high anxiety levels during a mock scan). A total of nine participants were excluded due to incidental findings in the structural MRI scans (n = 4), substance abuse (n = 1), technical difficulties (n = 2), or excessive movement during scanning (baseline translation > voxel-size, i.e., 2.5 mm in any of the three directions; n = 2). Thus, the final sample consisted of 98 adolescents (52% girls; age 14.6 ± 1.90 years) with (n = 58) and without (n = 40) maltreatment experiences matched for age, gender, socioeconomic status (SES), IQ, and handedness (see Table B1 in Appendix B).

The recruitment strategy initially targeted younger and then older adolescents, yielding a bimodal age distribution with peaks at age 13 and 17, respectively. Based on Steinberg's (2002) distinction between early (~10–13 years) and mid-adolescence (~14–18 years) and a median split at age 13.5, we divided the sample into two subgroups consisting of 50 early adolescent (≤13.5 years; 50% females; n = 28 maltreated) and 48 mid-adolescent participants (>13.5 years; 50% females; n = 30 maltreated), with matching between maltreated and nonmaltreated youth preserved (see section Sample Characteristics in Appendix B). Within the maltreated group, maltreatment exposure did also not differ between early and mid-adolescents (see Table B2 in Appendix B).

The present study and the former AMIS Project (see White et al., 2015, for a detailed description) received ethical approval by the Institutional Review Board of the University of Leipzig. After thorough description of the study, we obtained informed written and oral consent (caregivers) as well as oral assent (adolescents) of the participating families. Families received monetary compensation for their participation.

Maltreatment characteristics

The Maltreatment Classification System (MCS; Barnett et al., 1993) – a widely used, well-validated, and highly reliable coding scheme (English et al., 2005; Manly et al., 2013; Sierau et al., 2017) – provided the manual for scoring participants' maltreatment histories on the basis of the semi-structured Maternal

Maltreatment Classification Interview (MMCI; Cicchetti et al., 2003) and CPS records, if accessible (n = 9). The MCS distinguishes six maltreatment subtypes (i.e., physical neglect including failure to provide and lack of supervision as well as moral-legal/educational neglect, sexual abuse, physical abuse, and EM). For the latter dimension, we added a distinction between emotional abuse and emotional neglect as well as a code for witnessing domestic violence. Subtype, severity, and perpetrator were assessed for each event per developmental period (birth–17 months, 18 months–2 years, 3–5 years, 6–7 years, 8–12 years, 13+ years). Based on these assessments, we computed maximum severity (1–5), chronicity (percentage of affected developmental periods), and subtype number for abuse (1–2; i.e., physical and sexual abuse), neglect (i.e., physical and moral-legal/educational neglect), as well as EM (i.e., emotional neglect and abuse), yielding three scores per exposure dimension.

Interviewers received extensive training in the MCS coding system and in conducting caregiver interviews. One of the authors of the MCS provided on-site training and ongoing supervision to the research team during the project to resolve coding issues. All interview sessions were recorded for subsequent coding and to provide regular feedback to interviewers on their interview and coding performance, thus facilitating reliability and standardization. Given that collection of neuroimaging data and the first maltreatment assessment were spaced up to 4 years apart, a second MMCI was conducted with caregivers to acquire information on potential events occurring in the intervening period. Information from interviews and files was integrated using all available information per developmental period. Based on the presence or absence of any coded maltreatment incidences, we assigned participants to the maltreated and nonmaltreated group, respectively. For further differentiation of maltreatment types, three additional dichotomous variables were created representing the presence or absence of any coded abuse (n = 19), neglect (n = 34), as well as EM (n = 49) incidences for each participant. Due to co-occurrence of maltreatment exposures, maltreated participants could be assigned to up to three groups.

Furthermore, confirmatory factor analyses were employed in the full AMIS sample to extract aggregate factor scores for the extent of abuse, neglect, and EM exposure using MPLUS, version 7.4 (Muthén & Muthén, 1998-2015). To this end, measurement models for each exposure type were computed by estimating latent factors for abuse, neglect, and EM from their respective number of subtypes, chronicity, and severity. Covariation between error variances of respective dimensional indicators of each exposure (chronicity, subtype number, and severity) was accounted for by the model.

Covariates

To characterize our sample and control for potential confounders in our models, we administered the following scales: adolescents' self-reported pubertal status using the Tanner Scales (Marshall & Tanner, 1969, 1970), maternal school education, and self-reported psychopathological symptoms on the Youth Self Report (YSR; Achenbach & Edelbrock, 1989). We further computed a composite score based on select subscales of the Wechsler Intelligence Scale for Children – Fourth Edition (Wechsler, 2003) or the Wechsler Adult Intelligence Scale – Fourth Edition (Wechsler, 2008) to assess the IQ of participants aged 12–15 and of participants aged 16–17, respectively. Additionally, participants were screened for features of fetal alcohol syndrome (FAS) applying the FAS Facial Photographic Analysis Software, Version 2.1.0 (Astley, 2016).

Cyberball

During collection of functional brain images, participants performed an adapted version of the Cyberball paradigm (Williams et al., 2000; Eisenberger et al., 2003; see Figure 1) (~18 min). Here, participants were led to believe that they were playing a ball-tossing game with two other adolescents via an internet platform, while in fact the co-players were computer-generated confederates programmed to include and exclude the participant during the game. Cyberball was used to compare neural responses during two main and consecutive experimental conditions: (i) social inclusion (i.e., the participant received the ball as often as the confederates, in ~1/3 of cases and ~30 times each); and (ii) social exclusion (i.e., the confederates tossed the ball to each other most of the time, ~40 times each, and participants received the ball only very rarely to maintain attention, ~4 times). Classically, the Cyberball paradigm is analyzed by averaging neural responses across the entire duration of the two experimental conditions using a block-design. Here, however, we used an event-related design (see Crowley et al., 2010; Gunther Moor et al., 2012) allowing us to further differentiate the two main experimental conditions into their three specific subcomponents: (a) participant "catches" the ball (events of interest are called "acceptance events" during inclusion); (b) participant observes another player "catching" the ball (events of interest are called "not-my-turn events" during inclusion and "rejection events" during exclusion); and (c) participant throws the ball to another player after having "caught" it (N.B. to further standardize the event-related version an algorithm ensured that co-players received the ball a minimum number of times, irrespective of any preferences a participant might have had for throwing the ball to one co-player over another). Accordingly, of the total six event types that were modeled, only three were of interest for this study (acceptance, not-my-turn, and rejection). Our adaptation of the Cyberball paradigm also comprised a third experimental condition termed social re-inclusion during which the participant again received the ball as often as the other players after having experienced social exclusion (i.e., in ~1/3 of cases and ~30 times each). However, for the current analysis, this social re-inclusion phase was not considered. The paradigm was programmed in Presentation® (Version 18.0, Neurobehavioral Systems, Inc., Berkeley, CA).

fMRI data acquisition

Neuroimaging data were acquired on a 3T Siemens Skyra scanner with a 32-channel head coil. Structural brain scans were obtained using a T1-weighted Magnetization Prepared Rapid Gradient Echo (MPRAGE) sequence (TR = 2300 ms, TE = 2.98 ms, flip angle = 9°, FoV = 256 mm, voxel size: 1 × 1 × 1 mm, 176 slices). T2*-weighted gradient-echo planar imaging (GE-EPI) with multiband acceleration (acceleration factor 3) was employed to acquire functional images (TR = 2000 ms, TE = 22 ms, flip angle = 80°, FoV = 204 mm, voxel size: 2.5 × 2.5 × 2.5 mm, interslice gap: 0.25 mm, 60 slices (interleaved); Feinberg et al., 2010; Moeller et al., 2010). For comfort and to reduce head motion, foam cushions were fitted between participants' head and the coil. Please refer to the section Procedure in Appendix A for a detailed description of the two study appointments.

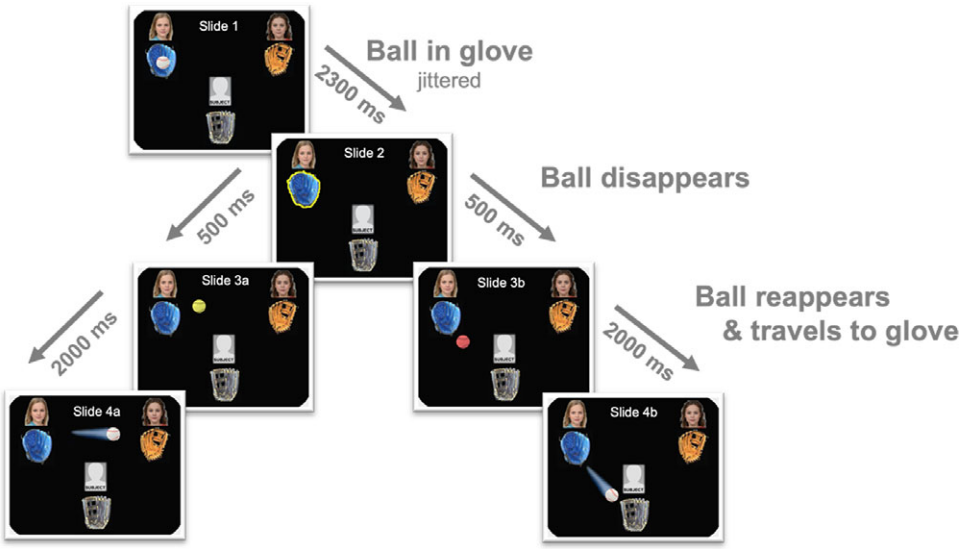

Figure 1. Event-related Cyberball paradigm. The figure illustrates two possible sequences of the event-related Cyberball task which imposes static events on a dynamic paradigm. First, the ball is in the glove of the computerized confederate (Slide 1; jittered 500–4000 ms; average 2300 ms). Next, the ball disappears and the glove outline yellows (Slide 2; 500 ms) when the confederate has apparently decided where to throw the ball. Measurements are locked to the event when the ball reappears, briefly remains stationary (1000 ms), and travels to the other player. In not-my-turn/rejection trials (i.e., not receiving the ball in the inclusion versus exclusion phase, respectively), the ball is thrown to the other confederate (Slide 3a-4a; yellow ball; left pathway) whereas in acceptance trials, the ball is thrown to the participant (Slide 3b-4b; right pathway; red ball).

fMRI data analysis

Whole-brain analyses

Statistical Parametric Mapping 12 (SPM12, version 7487; Wellcome Department of Imaging Neuroscience Group, London, UK) was used for all event-related Cyberball whole-brain analyses. Imaging data were pre-processed applying standard procedures, including slice time correction, realignment with a rigid-body transformation to correct for head motion, as well as co-registration to individual structural scans. Subsequently, pre-processed volumes were normalized to the Montreal Neurological Institute (MNI) template with a 12-parameter affine and non-linear transformation (after having manually set the origin of each structural image), and resampled to 2 mm^3. Finally, spatial smoothing was applied using an 8 mm Full Width at Half Maximum (FWHM) Gaussian kernel. Onsets of all six event-types with a duration of 0 convolved with the canonical hemodynamic response function (HRF) served as the basis for the single-subject design matrix (i.e., first level analysis). A high-pass frequency filter (cutoff 128s) and corrections for autocorrelation between scans were applied to fMRI time-series data during model estimation. The six motion parameters derived from realignment were subsequently included as regressors of no interest to account for movement-related covariance.

Based on the three event-types of interest, the following two main contrasts were computed on the first level: (i) rejection events versus not-my-turn events; and (ii) rejection events versus acceptance events. These single-subject contrasts were subsequently used to generate a random-effects group-level whole-brain analysis (one-sample t-tests) across all participants to examine task-induced brain activation. All group-level analyses were corrected for multiple comparisons according to most recent recommendations using a stringent family-wise error (FWE) correction procedure (Eklund et al., 2016; Roiser et al., 2016; i.e., $p < 0.05$ FWE corrected at the voxel level, with a cluster extent of $k > 20$).

Analyses of age, maltreatment, and maltreatment X age effects

Using the SPM Volume toolbox, we extracted and averaged raw activation values (betas) from theoretically relevant clusters identified by computing the aforementioned whole-brain contrasts across all participants. Significant clusters from whole-brain contrasts were screened on whether the brain regions had been previously reported to be activated by Cyberball paradigms. First, we entered the peak coordinates of each cluster in the Neurosynth platform (www.neurosynth.org) and searched for studies reporting activation within a 6 mm radius using the key words "exclusion", "rejection", "Cyberball", and "ostracism". Secondly, we verified for each study that Cyberball was used as an fMRI paradigm. In a third step, we compared our results to the results from the most recent meta-analyses in the field (Mwilambwe-Tshilobo & Spreng, 2021; Rotge et al., 2015; Vijayakumar et al., 2017), two Cyberball studies on adversity (Puetz et al., 2014; van den Berg et al., 2018), and two event-related Cyberball studies (Will et al., 2016; Will et al., 2015) which are all not included in the Neurosynth database. Clusters were chosen for further maltreatment and age analyses which had previously been reported in at least two original studies (or one Cyberball study on adversity) or one meta-analysis. This selection procedure yielded 21 clusters of interest: three clusters for the contrast rejection > not-my-turn, one cluster for the contrast not-my-turn > rejection, eleven clusters for the contrast rejection > acceptance, as well as six clusters for the contrast acceptance > rejection. For the latter contrast, one very large cluster was further subdivided into five theoretically important subpeaks based on the same selection procedure to increase specificity. Activation differences for these clusters were computed based on the averaged beta values for each event type. All further analyses were conducted with IBM SPSS Statistics for Windows, version 25.0.

We first probed main effects of age and maltreatment exposure (i.e., abuse, neglect, and EM) as well as age by maltreatment exposure interactions for our contrasts of interest. Because we identified maltreatment exposure by age effects, we compared adolescents with and without the respective exposure separately within young and mid-adolescent groups and vice versa. In this first step, the uncontrolled between-group effects of the neglected, abused, and emotionally maltreated versus nonmaltreated participants were tested. Next, within the two age groups, we modelled all three types of maltreatment exposure, while controlling for one another. Finally, within individuals with the respective maltreatment exposure, we regressed activation differences on aggregate factor scores for abuse, neglect and EM to examine the dose-dependent effects of

each type of exposure. All analyses were controlled for multiple comparisons (number of clusters used for extraction per contrast; $q < .0045$ for rejection > acceptance contrast; $q < .0083$ for acceptance > rejection contrast; $q < .0167$ for rejection > not-my-turn contrast; $p < .05$ for not-my-turn > rejection contrast). Refer to section Analyses of Age, Maltreatment, and Maltreatment × Age Effects in Appendix A for a more detailed description of the conducted analyses.

Results

Whole-brain analyses

Rejection versus not-my-turn

Whole-brain analyses showed heightened neural activity for rejection relative to not-my-turn trials in the superior temporal gyrus (STG) as well as two clusters within the PRC/PCC. Significant clusters are displayed in Figure B1 and summarized in Table B3 in Appendix B. For the inverse contrast, please also refer to Table B3 in Appendix B.

Rejection versus acceptance

For the rejection > acceptance contrast, we observed increased neural activity in primary and secondary visual cortex, lingual gyrus, PRC/PCC, IPL, precentral gyrus, dlPFC, STG, SFG, inferior frontal gyrus, parahippocampal gyrus (PHG), and AI. Conversely, for the acceptance > rejection contrast we observed increased neural activity in the dACC/pre-supplementary motor area (pre-SMA), primary somatosensory cortex, middle frontal gyrus (MFG)/dlPFC, insula/putamen, and the thalamus/hypothalamus (see Figure B2 and Table B4 in Appendix B).

Effects of age, maltreatment subtypes, and maltreatment subtypes × age

Main effects of age and maltreatment subtypes

A significant main effect of age only emerged within clusters derived from the contrast rejection > acceptance, namely in the left STG (peak voxel at [−48, −34, 6]; $F(1, 87.76) = 8.94$, $p = .004$, $\eta_p^2 = .084$), IPL (peak voxel at [−44, −72, 38]; $F(1, 96) = 11.53$, $p < .001$, $\eta_p^2 = .107$), and SFG (peak voxel at [−24, 24, 52]; $F(1, 96) = 9.40$, $p = .003$, $\eta_p^2 = .089$), as well as right dlPFC (peak voxel at [48, 30, 20]; $F(1, 96) = 8.82$, $p = .004$, $\eta_p^2 = .084$), always indicating a greater activation difference for younger adolescents (see Figure 2 as well as Table B5 in Appendix B). These results remained unchanged when controlling for psychopathological symptoms (all ps < .05). No main effects of maltreatment exposure which were robust to controlling for multiple comparisons emerged for any cluster.

Interaction effect of age × maltreatment subtypes

Within two clusters derived from the contrast acceptance > rejection, we found significant interaction effects of age by maltreatment subtype, namely in a cluster with its main peak in the left dACC/pre-SMA (peak voxel at [−6, 4, 50]) and another cluster encompassing the left MFG/dlPFC (peak voxel at [−32, 38, 32]; ps ≤ .008). For the dACC/pre-SMA cluster, abuse ($F(1, 55) = 7.52$, $p = .008$, $\eta_p^2 = .120$), neglect ($F(1, 70) = 10.82$, $p = .002$, $\eta_p^2 = .134$), and EM ($F(1, 85) = 13.00$, $p < .001$, $\eta_p^2 = .133$) each showed a significant interaction with age. For the MFG/dlPFC cluster, a significant interaction effect emerged between abuse and age ($F(1, 55) = 9.16$, $p = .004$, $\eta_p^2 = .143$). Notably, while EM also interacted with age in predicting activation differences in the same cluster ($F(1, 85) = 7.25$, $p = .009$, $\eta_p^2 = .079$), this effect was abolished after correction for multiple comparisons ($q < .0083$ for acceptance > rejection contrast). Likewise, another EM x age interaction emerged in a cluster derived from the contrast rejection > acceptance with its peak in the right primary visual cortex (peak voxel at [12, −90, −2]; $F(1, 85) = 7.86$, $p = .006$, $\eta_p^2 = .085$) which was also abolished after correction for multiple comparisons ($q < .0045$ for rejection > acceptance contrast).

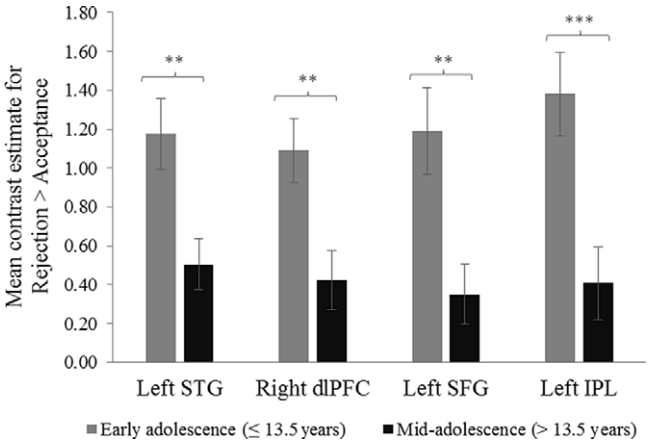

Figure 2. Main effects of age for the Rejection > Acceptance contrast. The bar graphs display mean beta values and their standard errors for the activation difference rejection > acceptance in the superior temporal and frontal gyrus (STG, peak voxel at [−48, −34, 6]; SFG, peak voxel at [−24, 24, 52]), dorsolateral prefrontal cortex (dlPFC; peak voxel at [48, 30, 20]) and inferior parietal lobule (IPL; peak voxel at [−44, −72, 38]) separately for early and mid-adolescent participants. ** $p < .01$. *** $p < .001$.

Next, in light of the size of the dACC/pre-SMA cluster (>7000 voxels) we conducted further specification analyses within a 5 mm-sphere around the main peak in the left dACC/pre-SMA at [−6, 4, 50].[2] Interaction effects for neglect x age and EM x age were also significant ($q < .01$) for the main peak sphere (neglect: $F(1, 70) = 7.08$, $p = .0096$, $\eta_p^2 = .092$; EM: $F(1, 85) = 9.86$, $p = .002$, $\eta_p^2 = .104$)[3], whereas abuse did not show a significant interaction with age for the left dACC/pre-SMA sphere. All significant interaction effects survived controlling for SES and psychopathological symptoms (ps < .05).

[2]Additionally, interaction effects between maltreatment subtypes and age were tested for four theoretically important subpeaks of the dACC/pre-SMA cluster (defined by the selection criteria described in the methods section Analyses of age, maltreatment, and maltreatment X age effects): (a) the primary somatosensory cortex (peak voxel at [−38, −26, 54]), (b) premotor cortex/supplementary motor area (PMC/SMA; peak voxel at [−30, −10, 60]), (c) right dACC (peak voxel at [10, 22, 32]), and (d) paracentral lobule (peak voxel at [−10, −22, 46]). Significant interaction effects with age emerged in the right dACC sphere for all three maltreatment subtypes (abuse: $F(1, 55) = 8.67$, $p = .005$, $\eta_p^2 = .136$; neglect: $F(1, 70) = 9.18$, $p = .003$, $\eta_p^2 = .116$; EM: $F(1, 85) = 9.83$, $p = .002$, $\eta_p^2 = .104$). Further, neglect and EM interacted with age in the prediction of acceptance > rejection activation differences in the primary somatosensory cortex (neglect: $F(1, 70) = 7.28$, $p = .009$, $\eta_p^2 = .094$; EM: $F(1, 85) = 7.55$, $p = .007$, $\eta_p^2 = .082$). For the left PMC/SMA, only the interaction between EM x age proved significant ($F(1, 85) = 7.17$, $p = .009$, $\eta_p^2 = .078$), whereas for the paracentral lobule sphere no significant interaction effects emerged. All interaction effects for dACC/pre-SMA subpeaks remained significant when controlling for SES and psychopathological symptoms (ps < .05). However, separate follow-up analyses for early and mid-adolescents including all three maltreatment subtypes to predict acceptance > rejection activation differences within the three subpeaks did not reveal any significant main effects (ps > .05), indicating no exposure-specific effects.

[3]The EM x age interaction for the dACC/pre-SMA sphere remained significant even after removing all cases with exposure to witnessing domestic violence from the EM group (remaining $n = 34$; $F(1, 70) = 10.35$, $p = .002$, $\eta_p^2 = .129$).

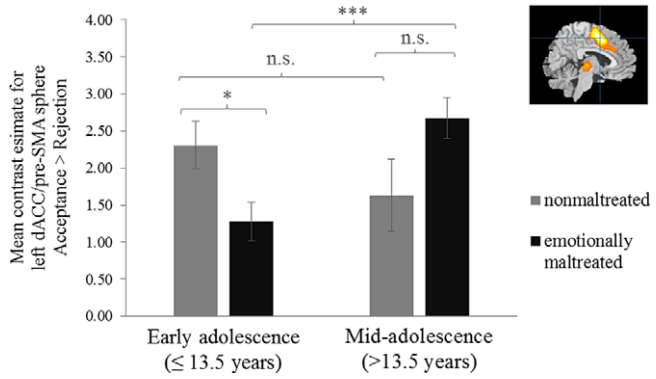

Figure 3. Age × emotional maltreatment interaction within left dACC/pre-SMA sphere (Acceptance > Rejection contrast). The bar graphs display the mean beta values and their standard errors for the activation difference acceptance > rejection in the left dorsal anterior cingulate cortex/pre-supplementary motor area (dACC/pre-SMA; 5 mm sphere at peak voxel [−6, 4, 50]) separately for emotionally maltreated and nonmaltreated participants within the early and mid-adolescent groups. n.s. = non-significant. * $p < .05$. *** $p < .001$.

Descriptively, reported effects for the acceptance > rejection contrast in the dACC/pre-SMA sphere (neglect × age, EM × age) and MFG/dlPFC cluster (abuse × age) emerged due to a decrease in the activation difference with increasing age for nonmaltreated adolescents, but an increase in this activation difference with increasing age for maltreated adolescents (refer to Figure 3 for an illustration of this pattern). Yet, between-group differences for early versus mid-adolescents only reached significance within the maltreated groups ($ps \leq .009$). Compared to their nonmaltreated counterparts, within early adolescence only the emotionally maltreated and abused groups (but not the neglected group) showed a significantly lower acceptance > rejection activation difference in the dACC/pre-SMA sphere and the MFG/dlPFC cluster, respectively ($ps \leq .016$). Between-group differences for abuse, neglect and EM-exposed versus nonmaltreated participants within the mid-adolescent group as well as for the comparison of early versus mid-adolescents within the nonmaltreated group were not significant ($ps > .05$).

To further specify age by exposure interactions, we tested between-group effects of the three types of exposure within early and mid-adolescence separately while controlling for one another. When including all three exposure types within a single model, only one significant main effect emerged for the early adolescent group. Younger emotionally maltreated adolescents showed significantly decreased brain activation to acceptance versus rejection in the dACC/pre-SMA sphere when compared to younger adolescents without a history of EM ($F(1, 46) = 4.27, p = .045, \eta_p^2 = .085$). In the same model, neglect and abuse did not explain brain activation within this region. The above effect remained significant after controlling for SES and psychopathological symptoms ($ps < .05$). Refer to Figure 3 for an illustration of the interaction effect between age and EM in dACC/pre-SMA sphere.

Effects of continuous maltreatment dimensions

To examine the effects of continuous maltreatment dimensions, associations between each maltreatment dimension and extracted betas from clusters showing significant rejection versus acceptance as well as rejection versus not-my-turn activation differences were computed including only those participants having experienced the specific maltreatment subtype (i.e., $n = 34$ neglected, $n = 19$ abused, and $n = 49$ emotionally maltreated adolescents). After correction for multiple comparisons, we found a significant negative association between the neglect dimension scores and the rejection > acceptance activation difference in the left PHG (peak voxel at [−28, −28, -20]; $\beta = -.51, p = .002, R^2 = .261$). Thus, higher neglect dimension scores were associated with decreasing activation for rejection versus acceptance in the left PHG (see Figure 4a). In contrast, the EM dimension correlated positively with the rejection > not-my-turn activation difference in the left PRC/PCC (peak voxel at [−8, −38, 40]; $\beta = .41$, $p = .003$, $R^2 = .169$).[4] Therefore, higher EM dimension scores were associated with increasing activation for rejection versus not-my-turn in the left PRC/PCC (see Figure 4b). In addition, analyses revealed an association of the EM dimension scores with the rejection > acceptance activation difference in the left IPL (peak voxel at [−44, −72, 38]; $\beta = .39, p = .005, R^2 = .153$). However, the latter association did not survive correction for multiple comparisons ($q < .0045$ for rejection > acceptance contrast). All effects remained significant when controlling for the respective other maltreatment dimensions as well as for age and psychopathological symptoms ($ps < .05$). In addition, analyses yielded no significant associations between activation differences in the left PHG and PRC/PCC and the respective other maltreatment dimensions ($ps > .05$).

Supplementary analyses

In addition to the above analyses focusing on the effects of maltreatment subtypes and dimensions, we also assessed the main and interaction effects of global maltreatment experiences and age (see section Analyses of categorical age and maltreatment variables in Appendix A for the methods, and section Effects of Age, Maltreatment, and Maltreatment × Age in Appendix B for the results).

Discussion

This study examined age- and maltreatment-related alterations in neural reactivity to social exclusion during early and mid-adolescence. A striking pattern of age-dependent effects emerged in between-group analyses of emotionally maltreated versus nonmaltreated youth. Regions implicated in saliency processing (dACC/pre-SMA) and regulatory functions (MFG/dlPFC) thus exhibited activation patterns consistent with maltreatment-related hypersensitivity to peer cues during early versus mid-adolescence. At the within-group level, exposure-specific analyses underscored the pertinence of EM (for activation in PRC/PCC) and neglect (for activation in PHG) for altered neural responses to social exclusion versus inclusion among adolescents. In what follows, we briefly embed our whole-brain analyses of the social exclusion task as well as our age-dependent effects in the literature before turning to our maltreatment-related findings.

Our whole-brain findings relating to social exclusion across the full adolescent sample mesh well with data from recent meta-analyses (Vijayakumar et al., 2017; Mwilambwe-Tshilobo & Spreng, 2021). We found social exclusion-related brain activation (contrasted to acceptance events) predominantly in a network of brain regions supporting social cognition (i.e., mentalizing, cognitive control, and emotion regulation). In contrast, acceptance elicited greater activation in the salience and motor preparation networks. Aligning with previous Cyberball findings (Puetz

[4]The positive association of the EM dimension with the rejection > not-my-turn activation difference in the left PRC/PCC remained significant even after removing all cases with exposure to witnessing domestic violence from the EM group (remaining $n = 34$; $\beta = .58, p < .001, R^2 = .332$).

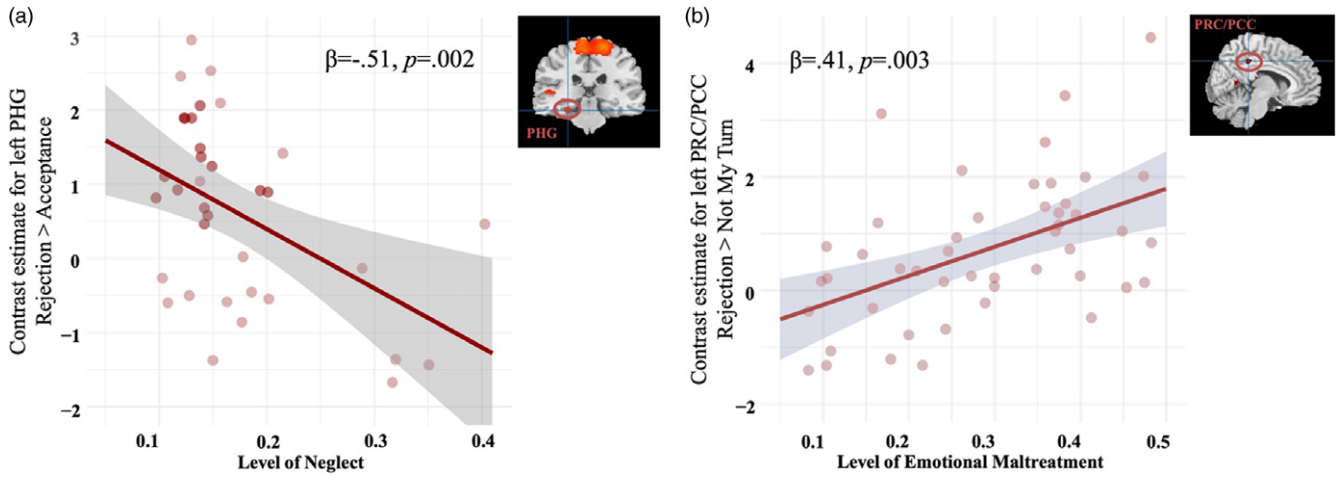

Figure 4. Dose-dependent within-group effects of maltreatment exposures on activation differences in left PHG (Rejection > Acceptance contrast) and PRC/PCC (Rejection > Not-my-turn contrast). Scatterplot (a) displays the association between the factor values for the neglect dimension and the extracted raw activation values (betas) for the rejection > acceptance contrast in left parahippocampal gyrus (PHG; peak voxel at [−28, −28, −20]; β = −.51, p = .002, R^2 = .261) within the neglected group (n = 34). Scatterplot (b) displays the association between the factor values for the emotional maltreatment dimension and the extracted betas for the rejection > not-my-turn contrast in left precuneus/posterior cingulate cortex (PRC/PCC; peak voxel at [−8, −38, 40]; β = .41, p = .003, R^2 = .169) within the emotionally maltreated group (n = 49).

et al., 2014; van der Meulen et al., 2017; Will et al., 2015), these brain regions also subserve social decision-making and may reflect various computations before passing the ball to one of the other players.

Within some of the regions above, we additionally found a prominent age-related decrease for activation during rejection versus acceptance-related events from early to mid-adolescence. Specifically, such associations with age emerged for the left STG, IPL, and SFG, as well as right dlPFC, indicating increased activation to social exclusion among early adolescents. The respective brain regions are thought to play an important role in mentalizing (STG, IPL; Mars et al., 2012), self-awareness (SFG; Goldberg et al., 2006), as well as cognitive control (SFG; Li et al., 2013), particularly during social decision-making or emotion regulation (dlPFC; Crone et al., 2014; Golkar et al., 2012). Elevated activation in these regions might signal increased self-awareness, internally-oriented thoughts, and perspective-taking as well as elevated cognitive effort to regulate exclusion-related emotions in young adolescents. For younger (as compared to older) adolescents, social inclusion might represent a particularly desirable, whereas social exclusion may reflect a particularly aversive state of affairs. While broadly mapping onto proposals of early adolescence being a phase with high susceptibility to peer influence (e.g., Brown, 1990; Steinberg & Monahan, 2007; Blakemore, 2018), these data could also suggest an adaptive hyper-activation due to the ongoing developmental process in these late-developing cortical regions (Giedd & Denker, 2015).

Turning to maltreatment, no main effect emerged either for maltreatment subtype or for global maltreatment (see Appendix B for results on between-group analyses of global maltreatment and its interaction with age). Instead, age-related effects implied that early adolescent neglected and emotionally maltreated individuals showed less decrease in (or continuingly elevated) dACC/pre-SMA activation during rejection (relative to acceptance and compared to nonmaltreated controls), while their mid-adolescent counterparts showed the reverse pattern. Follow-up analyses indicated that the interaction effect in the dACC/pre-SMA was mainly driven by early adolescents and EM. Specifically, in early adolescence, only EM exposure accounted for unique variance in dACC/pre-SMA activation differences over and above other exposures (abuse, neglect). Conversely, there were no exposure-specific effects of maltreatment within the mid-adolescent group (though global maltreatment indicated a reversal of the effects in early adolescence; see Appendix B).

EM has also been linked to an increased responsivity to social exclusion in another Cyberball study (van Harmelen et al., 2014). In adult participants, this study reported an association of EM with exclusion-related activation in the dmPFC, a brain region adjacent to the dACC, forming part of a network thought to be involved in appraisal and expression of negative emotions (Etkin et al., 2011). Likewise, van den Berg et al. (2018) reported a positive relationship between a combined physical and emotional neglect score and dmPFC as well as insula activation in an intergenerational sample of children and adults. Given that our study found an effect of EM after controlling for physical neglect, our results suggest that the effect may be primarily attributable to EM. Potentially EM – owing to its roots in disruptions of the species-expected caregiver-child relationship – may specifically predispose to vulnerability to analogous situations involving peer exclusion. For youth exposed to exceedingly rejecting caregivers (as in the case of EM), even the slightest cues of peer rejection may be highly salient, conveying a sense of feeling doubly rejected (by peers and caregivers, alike), especially in early adolescence when acceptance by the peer group may matter most (cf. Brown, 1990; Steinberg & Monahan, 2007; Blakemore, 2018).

It might be noteworthy that, unlike previous reports, the increased activation in the dACC/pre-SMA cluster did not emerge for the rejection > acceptance but for the acceptance > rejection contrast. However, follow-up analyses of this cluster suggested that activation differences between maltreated versus nonmaltreated youth were at least partly attributable to continuing activation to rejection following diminished activation to acceptance (see section Effects of Age, Maltreatment, and Maltreatment × Age in Appendix B). Moreover, other studies examining youth and early adult samples with the Cyberball paradigm similarly report acceptance > rejection (or inclusion > exclusion in a block design) activation in the salience network including the dACC, pre-SMA, insula, and putamen as well as in regions supporting social

decision-making and emotion regulation like the MFG/dlPFC (Puetz et al., 2014; van der Meulen et al., 2017; Will et al., 2015). Thus, one important contributing factor might be participants' developmental stage. Early adolescents are particularly receptive for (social) rewards (Galvan, 2010). Likewise, fitting into a peer group is a key motivational goal during early adolescence (Brown, 1990). Therefore, inclusion/acceptance might constitute the cue with the highest salience during (early) adolescence, which would, in turn, increase the probability to find an effect for the acceptance > rejection contrast. Incidentally, this developmental perspective could also shed light on previous failures to find effects of social exclusion versus inclusion in the dACC for adolescent samples (Eisenberger, 2012; Rotge et al., 2015).

A further age-dependent effect of abuse emerged in the MFG/dlPFC. Here, the same activation pattern as for the dACC/pre-SMA emerged: a decrease in the activation difference for acceptance > rejection with increasing age for nonmaltreated adolescents, contrasted by an increase in this activation difference with increasing age for maltreated adolescents. However, when controlling for the respective other maltreatment subtypes in follow-up analyses, we did not find a significant effect of abuse, neglect or EM within the early or mid-adolescent group. On the one hand, these non-significant findings could be due to the lower sample size in the age-specific follow-up analyses. On the other hand, it might point to similar effects of different maltreatment exposures in line with our detected global maltreatment effect as a function of age (see section Effects of Age, Maltreatment, and Maltreatment × Age in Appendix B for the results). Thus, besides maltreatment-related hypersensitivity to social exclusion in early adolescence, global maltreatment effects supported a reversal of effects in mid-adolescence. This potentially points to a neurobiologically-based age- or time-dependent adaptation to persistent adversity, as often reported using stress-hormone measures (G. E. Miller et al., 2007; Trickett et al., 2010; White et al., 2017).

Our dimensional analyses within the subgroups of neglected, abused or emotionally maltreated adolescents also lend further support to exposure-specific effects for social exclusion. Thus, we detected a dose-dependent effect of EM for the highly stringent rejection > not-my-turn contrast in the left PRC/PCC, even after adjusting for the level of neglect and abuse exposure as well as psychopathological symptoms and age. A similar positive association between EM and the contrast rejection > acceptance emerged in the left IPL (trend-level after correcting for multiple comparisons). Notably, Puetz and colleagues (2014) reported reduced IPL activation to social exclusion for children with a history of early caregiver separation (a majority exposed to neglect) compared to non-separated controls. Together with Puetz et al.'s (2014) finding of separation-related dACC blunting to exclusion, these findings contrast markedly with the patterns we found for EM. Potentially, this may imply exposure-specific activation patterns for EM versus neglect-exposed youth during social exclusion, involving hyper-activation versus hypo-activation of the default-mode and salience networks mediating internally-oriented thoughts (e.g., mentalizing) as well as detection of salient stimuli, respectively (Spreng et al., 2009; Menon, 2011).

A second notable finding from our within-group analysis revealed an association of neglect with blunted activation during social exclusion in the left PHG. This correlation was specific for neglect, as it survived controlling for the extent of co-occurring EM and abuse as well as psychopathological symptoms and age. Alterations in structure and function of the hippocampus and the adjacent PHG have been reported in other studies with maltreated samples (McLaughlin et al., 2019). In turn, given the proximity to the HPA axis, links may exist to neglect-related hypocortisolism detected using neuroendocrine measures (e.g., Doom et al., 2020). Conversely, threat/abuse experiences coincide with increased activation in this region using other fMRI tasks (especially during memory encoding; e.g., Lambert et al., 2019).

Meta-analytic evidence suggests that the PHG is involved in theory-of-mind and navigation processes as well as autobiographical memory and default-mode network activity (Spreng et al., 2009). It is assumed that all these processes reflect some kind of self-projection (i.e., envisioning yourself in the past, in the future, as well as in another person's perspective; Buckner & Carroll, 2007). As a consequence, adolescents having experienced physical neglect might detach from self-projection during social exclusion in an attempt to suppress the occurrence of negative emotions. These findings support our hypothesis of hypo-reactivity to social exclusion in relation to neglect.

Notably, however, caregiver deprivation/emotional neglect has equally been associated with increased activation to threat cues in overlapping areas (Maheu et al., 2010). Yet, unlike this work, our study employed a more ambiguous social threat (social exclusion) requiring cognitive-emotional appraisal that may afford participants more latitude for avoidant construals. Indeed, for Cyberball, psychophysiological work has recently demonstrated blunted physiological responses as a corollary of less positive internal representations of parents (White et al., 2021), in line with such an avoidant interpretive bias.

A number of limitations of this study deserve attention. First, similar to previous fMRI research, but unlike much of the aforementioned psychophysiological research (e.g., Crowley et al., 2010; White et al., 2021), our study primarily yielded effects for the less stringent acceptance versus rejection contrast that compares two visually distinct events. For the more stringent rejection versus not-my-turn contrast that compares two visuo-spatially identical events in different experimental contexts, we merely found a dose-dependent within-group effect of EM on elevated PRC/PCC activation. Potentially, given their similarity with not-my-turn events, which themselves potentially resemble "micro-rejections" within the inclusion period (see Crowley et al., 2009; Will et al., 2016), this contrast may underestimate exclusion-related brain activation, making detection of effects less likely. This notion was supported by the small set of clusters identified in whole-brain analyses for this contrast. From such a vantage point, the dose-dependent within-group association of EM with exclusion-related PRC/PCC activation actually seems quite striking.

Furthermore, matching maltreated and nonmaltreated groups could have led to an increased number of unreported maltreatment cases within the nonmaltreated group (Scott et al., 2010). To counter this issue, nonmaltreated participants were thoroughly checked for any maltreatment incidences with caregiver interviews conducted at two time-points. Notably, in the event of unreported maltreatment incidences as well as other adversities and disruptions of attachment within the nonmaltreated group, this would have presumably led to an underestimation, not overestimation of the actual effects. Potentially, this provides one reason why regions exhibiting dose-dependent exposure-related within-group effects (i.e., PRC/PCC, PHG) failed to show between-group effects, pointing to the future research avenue of distinguishing more and less burdened nonmaltreated subgroups.

Moreover, abuse was under-represented in our maltreated sample potentially contributing to an underestimation of its effects. While 84.5% ($n = 49$) of our maltreated participants experienced some form of EM, only 32.8% ($n = 19$) of our maltreated group had a history of physical and/or sexual abuse. Thus, it is incumbent on future studies to oversample for abuse experiences to test the specific associations of abuse with neural correlates of social exclusion.

Conclusion

Our findings provide important new insights for the ongoing debate whether EM is best subsumed under the umbrella of threat/deprivation exposures or whether it is a qualitatively distinct experience, calling for an additional adversity dimension in its own right. To be sure, some aspects of EM appear to map onto the existing deprivation or threat dimensions (e.g., witnessing domestic violence).[5] Moreover, recent behavioral work also invokes the "dimensional model of adversity and psychopathology" (DMAP; Miller et al., 2018) to account for distinct longitudinal pathways linking emotional abuse (via peer relations) and emotional neglect (via school engagement and peer relations) to depressive outcomes (McNeil et al., 2020). However, some aspects of EM (e.g., role reversal of child and caregiver, restricting the child's age-expected need for autonomy, caregiver threats of abandonment or suicide) do not neatly map onto the deprivation/threat distinction. More crucially, irrespective of the utility of distinguishing emotional abuse and neglect, behavioral data are inherently limited in shedding light onto whether EM exerts its effects on development via unique neuro-cognitive mechanisms or whether it co-opts overlapping neural circuits implicated in abuse/threat and neglect/deprivation.

Our data offer some first indications that EM at least partly impinges on development via a unique set of neural mechanisms which may be particularly relevant for processing social information (i.e., saliency processing, mentalizing). Thus, inasmuch as EM is first and foremost a relational phenomenon, our data offer tentative support for a somewhat domain-specific mechanism whereby EM impacts future social interactions. Acting as threatening or insufficient sources of co-regulation, emotionally maltreating caregivers may engender disruptions in the species-expected child–caregiver attachment relationship, which, in turn, is thought to facilitate crucial capacities for forming and maintaining relationships (White et al., 2020). To clarify, effects of maltreatment on attachment security and disorganization (Cyr, Euser, Bakermans-Kranenburg, & van IJzendoorn, 2010) as well as of attachment on social functioning (Groh et al., 2014) are now both well-established meta-analytically. Therefore, it seems plausible that the effects of maltreatment on social functioning (McCrory et al., 2019) are at least partly propagated via neural pathways proposed to underlie individual differences in attachment security (Long et al., 2020) and disorganization (White et al., 2020). In the present study, we therefore relied on a paradigm that has proven effective in eliciting EM- and attachment-related differences in neural and psychophysiological activation across different developmental stages (e.g., DeWall et al., 2012; van den Berg et al., 2018; van Harmelen et al., 2014; White et al., 2012; White et al., 2021). To the extent that the neural circuitry implicated by us corresponds with results from some of this work (e.g., elevated dACC activation for anxious attachment; DeWall et al., 2012) and aforementioned theoretical models (e.g., PRC, PCC; Long et al., 2020; White et al., 2020), we contend that EM and attachment insecurity/disorganization may partly share a common neural basis.

Another important aspect is that our study focused on the effects of maltreatment-related adversities (i.e., abuse, neglect, and EM). Due to this focus on neural correlates of maltreatment, we controlled or matched groups for other adversities or environmental influences (e.g., SES) which could have confounded our maltreatment effects. In the case of SES, however, associated adversities like cognitive deprivation (i.e., less cognitive stimulation by caregivers) or neighborhood violence might have consequently been controlled for. It follows that underestimation of the influence of deprivation and threat for neural activation to social exclusion is conceivable in our study. Therefore, future research needs to extend the present study to other adversities beyond child maltreatment to test the effects of various aspects of deprivation and threat for neural activation to social exclusion.

In sum, ours is the first study to examine the relationship between differential maltreatment exposures and neural activity in a social interaction task within a sample of early and mid-adolescents. We extended previous research by applying an event-related Cyberball paradigm in a well-characterized maltreated sample and a carefully matched nonmaltreated control group. By recruiting a sizable sample of maltreated adolescents from the community, CAPS, well as CPS, we were able to include participants with a broad spectrum of different maltreatment exposures. Our design thus afforded the possibility of considering both between and within-group effects of differential maltreatment exposures.

In conclusion, the present study highlights effects of differential maltreatment exposures on neural mechanisms underlying atypical social functioning. It lends support to the hypothesis of a hypo-reactive response to social exclusion following deprivation exposure (e.g., neglect). Moreover, disruptions in the species-expected child-caregiver attachment relationship (i.e., EM) appear to represent a crucial further aspect of maltreatment, accounting for independent variance in neural reactivity to social exclusion. These alterations in a brain network contributing to social cognition might provide part of the neuro-cognitive mechanism underlying the well-documented social deficits in the wake of maltreatment. Yet, further research is required to replicate and extend our findings in longitudinal designs in order to warrant causal conclusions on distinct neural mechanisms underpinning the pathways from severe childhood adversities including maltreatment to behavioral outcomes such as psychopathology and social functioning.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/S0954579421001681

Author contributions. Pascal Vrtička and Lars O. White contributed equally/share last authorship.

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[5]Please note that witnessing domestic violence is unlikely to account for our effects of EM, as these persisted even after excluding children exposed to this subform of EM (see Footnotes 3 and 4).

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Conflicts of interest. The authors declare that there is no conflict of interest.

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