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Evidence for Depressogenic Spontaneous Thoughts and Altered Resting-State Connectivity in Adolescents With a Maltreatment History

Ferdinand Hoffmann, PhD, Essi Viding, PhD, Vanessa B. Puetz, PhD, Mattia I. Gerin, MSc, Arjun Sethi, PhD, Georgia Rankin, BSc, Eamon J. McCrory, PhD

Objective: Childhood maltreatment has been associated with major depressive disorder (MDD). Atypical self-generated thoughts (SGT), lacking in positive and privileging negative content—a feature of ruminative thinking—might represent one vulnerability factor for developing depression. Rumination in MDD has been linked to alterations in resting-state functional connectivity (RSFC) of the subgenual anterior cingulate cortex (sgACC) to the default mode network and the fronto-parietal network (FPN). This study aimed to investigate online SGT content and its variability, as well as sgACC RSFC, as potential risk markers for depression in adolescents who experienced maltreatment.

Method: Adolescents 12 to 16 years old (29 with maltreatment history [MT] and 39 with no maltreatment history [NMT]) performed an established mind-wandering task. Participants made nondemanding number discriminations during which intermittent questions probed their SGTs that were classified as off-task, positive, negative, self-related, other-related, past-oriented, or future-oriented. Resting-state data were acquired separately for 22 of 29 MT and 27 39 NMT adolescents, and seed-based functional connectivity analyses of the sgACC were performed.

Results: MT, relative to the NMT adolescents, generated significantly fewer positively valenced thoughts, and exhibited more extreme ratings for positively valenced thoughts. MT adolescents also showed significantly reduced RSFC between the sgACC and the FPN. Group differences in depressive symptoms between the MT and NMT adolescents were partly accounted by differences in sgACC-FPN RSFC.

Conclusion: Adolescents who experienced maltreatment show a reduction in positively valenced spontaneous thoughts and reduced sgACC-FPN RSFC at the neural level. These may contribute to a ruminative thinking style, representing risk factors for developing depression later in life.

Key words: child maltreatment, depression, self-generated thoughts, rumination, resting-state functional connectivity

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Childhood maltreatment is associated with significantly increased risk of a range of psychiatric disorders.[1] A common outcome is the development of major depressive disorder (MDD).[2] Adverse early life events such as maltreatment can lead to an internalization of negative self-referential schemas that bias information processing toward negative and away from positive content, a feature of a ruminative thinking style.[3] There is some preliminary evidence that ruminative thinking partially mediates the relationship between childhood maltreatment and depressive symptoms in adults.[4,5] One way of indexing spontaneous thoughts that naturalistically captures the features of ruminative thinking is through the measurement of self-generated thoughts (SGT).[6]

SGTs arise independently of external stimulation from the environment, and comprise experiences such as mind-wandering, day-dreaming, planning, and rumination.[6] Recent evidence has shown that in line with the cognitive model of depression, there is good evidence that patients with MDD tend to engage in more ruminative SGTs.[7,8] Specifically, they appear to have less positive and more negative past and self-related thoughts than healthy controls.[7] Further studies of clinical populations are required to consolidate this evidence base. However, several studies of healthy controls complement these studies of patients who are depressed, demonstrating that past-related SGTs are associated with lower mood, depressive symptoms and an increased stress response.[9-11]

Ruminative thinking is thought to represent one vulnerability factor for developing MDD.[12] In healthy controls and patients with MDD, ruminative thinking has been strongly linked to abnormal functioning of the subgenual anterior cingulate cortex (sgACC).[13,14] The sgACC shows increased activity during sadness,[15] and has been

implicated in the behavioral withdrawal and negative self-reflective processes associated with rumination in healthy controls[14,16] and patients with MDD.[13,17] More specifically, heightened coupling between the sgACC and the default mode network has been commonly observed in MDD and associated with rumination.[17] It has been proposed that self-referential processes supported by the default mode network are integrated with affectively laden, behavioral withdrawal processes related to the sgACC.[13] Abnormal sgACC RSFC to parts of the fronto-parietal network has also been reported in adolescents with MDD.[18,19] Decreased RSFC to prefrontal brain regions was found to be associated with increased rumination.[18] This was interpreted as deficient top-down modulation of the fronto-parietal network, down-regulating negative emotional thoughts.[18] Together these findings suggest that alterations in sgACC RSFC to the default mode network and the fronto-parietal network might be critical in contributing to the emergence of depressive rumination.

According to the theory of latent vulnerability, maltreatment results in measurable alterations in a number of neurocognitive systems that reflect calibration to neglectful and/or abusive early environments.[20,21] These changes may represent (at least in part) an adaptation in response to an adverse caregiving environment during childhood. However, such alterations are also thought to incur a longer-term cost, as they may mean that an individual is poorly optimized to negotiate the demands of other, more normative environments, and as such become more vulnerable to future stressors.[20,21] For example, in a recent study we found that childhood maltreatment was associated with altered neural responses to autobiographical memories, including increased activation of the amygdala and connectivity with the salience network during negative memory recall.[22] This raises the question as to whether the valence of spontaneous thought content of adolescents who have experienced maltreatment is altered. In the current study, we aimed to investigate whether adolescents who experienced maltreatment but were without a diagnosis of MDD show depressogenic SGT patterns and altered sgACC RSFC. In light of prior clinical research, both indices potentially represent associated vulnerability markers at different levels of analysis (behavioral versus neural) for developing depression in the future.

The majority of research on rumination and thought content in the context of childhood maltreatment has relied on questionnaire methods,[4,5] which, despite certain strengths (eg, cost-efficiency, replicability), exhibit poor ecological validity in capturing online thoughts and their content.[23] A growing body of work on SGTs in healthy individuals and psychiatric populations suggests that to gain insight with regard to SGTs and their content, both in health and in illness, it is necessary to use online experience sampling measures.[7,10]

The first aim of the current study was to investigate online SGT contents and their variability in adolescents 12 to 16 years old who had experienced documented maltreatment, compared to a carefully matched control group. We therefore used an established nondemanding choice reaction time task (CRT) that allowed spontaneous SGTs in participants. During this task, participants were probed at random time points, first, about how much they were on task, and, second, about the specific content of their thoughts,[10,24] such as if their thoughts were focused on certain temporal epochs (future or past), involved different referents (self or other), or varied in valence (negative or positive). This task is particularly useful as an objective online measure of the amount and specific content of SGTs, but also of their variability over time, as participants are asked about the SGTs repeatedly throughout the task.

Our second aim was to investigate whether adolescents who experienced maltreatment compared with their peers would show alterations in sgACC RFSC, which have been strongly implicated in rumination in healthy controls and patients with MDD.[13,14] We therefore acquired resting-state data on a subset of the adolescents who had undergone behavioral testing, and seed-based functional connectivity analyses of the sgACC were performed.

Based on previous findings of altered SGTs in adults with MDD[7] and studies reporting a ruminative thinking style in adults with a history of maltreatment,[4,5] we hypothesized that adolescents who experienced maltreatment would engage in more depressogenic SGTs. We expected adolescents who had experienced maltreatment to exhibit less positive and more negative, self-related and past-oriented thoughts. At the neural level, we hypothesized that adolescents who experienced maltreatment would exhibit increased sgACC RSFC to regions within the default mode network and reduced sgACC RSFC to prefrontal brain regions, in line with studies of rumination in MDD.[13,18] Finally, we hypothesized that potential differences in SGTs and sgACC RSFC would in part explain differences in depressive symptoms between maltreated and nonmaltreated adolescents.

METHOD

Participants

A total of 29 adolescents (12−16 years old) who had experienced maltreatment (MT group) were recruited from a London Social Services (SS) Department and adoption agencies. A matched sample of 39 adolescents (12−16 years

old) with no maltreatment history (NMT group) were recruited from schools, youth clubs, and via newspaper and Internet advertisement (Table 1).[25-29] Exclusion criteria for the NMT group included previous contact with SS with regard to the quality of parental care or maltreatment. Exclusion criteria for all participants included a diagnosis of learning disability, pervasive developmental disorder, neurological abnormalities, standard magnetic resonance imaging (MRI) contraindications (eg, ferromagnetic implants, past or present neurological disorder), and IQ < 70. Resting-state functional MRI scans were available for a subset of the participants who were part of a larger study (MT group, n = 22; NMT group, n = 27). The MRI scans were obtained about 6 days after the collection of the SGT measure (NMT group: 5.79 ± 8.41 days; MT group: 6.07 ± 6.80 days; $p > .89$). Participants across groups were comparable in terms of age, IQ, verbal fluency, pubertal status, socio-economic status (SES), level of education of parents, gender, and ethnicity. The resting-state sample was representative of the larger sample (see Table S1, available online). Consent was obtained from the child's legal guardian, and assent was provided by all adolescents. All procedures in the study were approved by the University College London Ethics Committee (0895/002).

Measures

Maltreatment Experience. For adolescents referred to SS, maltreatment history, including the estimated severity, onset and duration of maltreatment was provided by the child's social worker or adoptive parent (on the basis of SS records), using an established maltreatment scale.[30] Severity of each abuse type was rated on a scale from 0 (not present) to 4 (severe). Adolescents often had experienced multiple types of maltreatment, as normally is the case and reflective of what is commonly found in community samples. Presence of maltreatment type was rated as follows: neglect, n = 21; emotional abuse, n = 28; sexual abuse, n = 3; physical abuse, n = 4; exposure to domestic violence, n = 17. Overall across subtypes, maltreatment was characterized as follows: mean onset in years = 4.12 (SD = 4.40), mean duration in years = 6.44 (SD = 4.87), and mean severity = 1.56 (SD = 0.77) (for onset, duration and severity by subtype, see Table S2, available online). In additionally, all adolescents completed the Childhood Trauma Questionnaire (CTQ). The CTQ is a 28-item, retrospective screening measure for maltreatment histories, distinguishing among five categories: emotional, physical, and sexual abuse, and emotional and physical neglect. The five subscales of the CTQ have been shown to have robust internal consistency and convergent validity with a clinician-rated interview of childhood abuse and therapists' ratings of abuse.[31] Scores on each subscale (range = 5–25) were summed to provide a total score (total score ranges = 25−125). In a large community sample, the 50th percentile of the CTQ total score has been reported to be around 28 to 29.[32]

TABLE 1 Demographic and Background Information for Adolescents With Maltreatment History (MT) and No Maltreatment History (NMT)

	MT Group (n = 29)	NMT Group (n = 39)	
Measure	**Mean (SD)**	**Mean (SD)**	***p***
Age, y	14.50 (1.71)	14.83 (1.22)	.35
WASI-IQ[a]	105.86 (13.48)	110.67 (10.56)	.10
Verbal Fluency[b]	37.67 (11.10)	35.95 (7.92)	.47
PDS[c]	2.91 (0.66)	3.07 (0.46)	.28
SES[d]	3.00 (1.61)	3.34 (1.0)	.31
	n (%)	**n (%)**	***p***
Gender (% female)	14 (48)	23 (67)	.46
Ethnicity (% white)	21 (72)	23 (59)	.31
	Mean (SD)	**Mean (SD)**	***p***
CTQ (Total)	31.63 (4.51)	27.92 (2.79)	<.01
CASI-4R, Depression Symptoms	59.76 (10.10)	53.06 (8.00)	<.01

Note: CASI-4R = Child and Adolescent Symptom Inventory–4R[25]; CTQ = Childhood Trauma Questionnaire[26]; PDS = Puberty Development Scale; SES = socioeconomic status; WASI-IQ = Wechsler Abbreviated Scales of Intelligence.

[a]*Two-subscale IQ derived from the WASI-IQ.*[27]

[b]*Verbal Fluency (phonemic + semantic).*[28]

[c]*Self-rating of PDS.*[29]

[d]*Highest level education rated on 6-point scale from 0 = no formal qualifications to 5 = postgraduate qualification.*

Cognitive Ability. Cognitive ability was assessed using two subscales (Vocabulary, Matrix reasoning) of the Wechsler Abbreviated Scales of Intelligence (WASI).[27]

Measure of Depression Symptoms. The parent version of the Child and Adolescent Symptom Inventory−4R, CASI-4R[25] was administered, including a subscale measuring depressive symptoms. No participant in the sample met the diagnostic cut-off for major depressive disorder.

Choice Reaction Time Task. We used an established mind-wandering paradigm that probes off-task thoughts during a choice reaction time task (CRT),[10] and assessed the content of the participants' thoughts on seven different dimensions: off-task, positive valence, negative valence, self-related, other-related, past-oriented, and future-oriented. During the mind-wandering paradigm, a series of black digits between 1 and 8 were presented. One-sixth of the digits were presented in red, signaling participants that they should indicate via button press whether this number was odd or even. Black digits were presented for 1,000 milliseconds and red digits for 2,000 milliseconds. Responses had to be made while the colored digits were still present on the screen. Stimuli were separated by a fixation cross of variable duration (2,200–4,400 milliseconds).

The number of thought probes and their presentation were randomly determined,[10] to avoid any expectancy biases, and thus sampling SGTs in the most unconstrained way (number of probes between four and nine). Participants were asked to rate their current thoughts using a nine-point Likert scale on the seven dimensions. In addition, they rated their current mood (ie, how positive and how negative they felt). The task lasted approximately 14 minutes. Stimuli were presented using E-prime 2.0 (Psychology Software Tools, Inc., Sharpsburg, PA).[33]

fMRI data acquisition. Participants were scanned on a 1.5 Tesla Siemens Avanto MRI scanner (Siemens Medical Systems, Erlangen, Germany) using a 32-channel head coil and whole-brain EPI sequence (parameters: voxel size: 3 × 3 × 2 mm; slices per volume, 36; slice thickness: 2mm; TR: 2880ms; TE: 45 milliseconds; field of view: 192 mm; gap between slices: 1 mm; flip angle: 90°). A magnetization-prepared rapid gradient-echo sequence (MP-Rage) was used to obtain a high-resolution structural scan (parameters: 176 slices; slice thickness: 1 mm; gap between slices: 0.5 mm; TE: 2730 milliseconds; TR: 3.57 milliseconds; field of view: 256 mm; matrix: 256 × 256 mm; voxel size: 1 × 1 × 1 mm). A fixation cross remained on the screen throughout the scan, at which the participants were instructed to look. A total of 170 volumes of resting-state data were collected (scanning time: 8 minutes 10 seconds).

CRT Data analysis. For the main analyses, we used multilevel models, as they take correlated observations within individuals into account and perform well with missing data/unequal numbers of data points within individuals.[34] Linear mixed models with a random intercept and the number of a particular sampling point within the session as covariate were calculated in SPSS v22 (SPSS Inc., Chicago, IL). Besides the rating level (eg, to what extent a certain thought was self-related), we investigated two indices of SGT variability: fluctuations and extremity. To obtain a measure of how much individuals fluctuate in their single SGT ratings from one thought probe to the next, we calculated squared successive differences, which has been established in experience sampling studies.[34,35] Fluctuation scores were calculated for each SGT dimension separately. To obtain a measure of how extreme the individual ratings were, we calculated the squared difference of each rating from the total sample mean (including both the NMT and MT groups) for that variable. In contrast to the fluctuations, this does not take into account how large successive changes are but, rather, indicates how much a certain rating differs from the "norm." In a first step, we investigated group differences in rating levels, fluctuations in ratings, and extremity of ratings. To deal more thoroughly with the challenge of multiple comparisons in this step, false discovery rate (FDR) correction was applied to reduce type 1 error ($p < .05$). In a second exploratory step, we tested for group differences in particular interrelations of the different content dimensions of SGT, on which NMT adolescents and MT adolescents were found to differ. This allowed us to investigate whether certain SGTs were more strongly correlated with one another in MT adolescents compared to NMT adolescents.

Resting-State Preprocessing and Analysis. Data were processed using the data processing assistant for the resting-state fMRI toolbox DPARSF[36] for Matlab.[37] In brief, preprocessing discarded the first three volumes, performed motion correction and realignment, and co-registered the functional time series to the T1-weighted MRI. Images underwent DARTEL-based segmentation and registration, followed by nuisance covariate regression removing effects of average white matter and CSF signal, and motion. To deal with possible differential motion artifacts, we included the scrubbing approach,[38] which models poor time points (based on the framewise displacement threshold, FD [Power], of 0.5 mm or higher, together with one time point before and one time point after each such time point) as separate regressors during the nuisance covariate correction. Time series were band-pass filtered (0.01−0.08 Hz),[39] normalized to Montreal Neurological Institute space, resampled to 3 mm voxels, and spatially smoothed (6-mm full-width-at-half-

maximum isotropic Gaussian kernel). Three of 22 adolescents who experienced maltreatment and one of 27 healthy controls showed head motion beyond 3 mm and were excluded from further analysis (final sample: MT group, n = 19; NMT group, n = 26). Functional connectivity maps were generated for 4 previously used, 3-mm, right and left inferior and superior (+ −5, −34, −4; + −5, −25, −10) sgACC seeds.[18,19,40] Time-series correlation coefficients underwent a Fisher r-to-z transformation. Group differences in RSFC were analyzed with SPM8 using two-sample t tests. Using Monte Carlo simulation[40] correcting for multiple comparison cluster size, corrected results are reported (voxelwise p value of .005 combined with an extent threshold of 161 voxels corresponded to clusterwise familywise error rate of 0.0125: Bonferroni corrected −0.05/4 seeds). Peak RSFC values were extracted from regions in which group differences were observed and correlated with depressive symptoms and SGT measures.

RESULTS

SGT Analyses

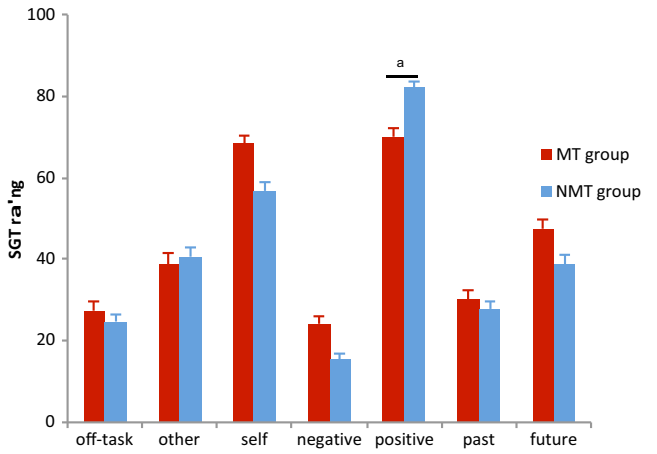
Performance. There were no group differences in accuracy (indicating whether the red digit was odd or even) (t_{66} = 1.32, p = .19; MT group: 91.5% ± 9.4%. NMT group: 88.0% ± 12.6%) or reaction times (t_{66} = −1.56, p = .12; MT group: 862.46 ± 152.15 milliseconds; NMT group: 920.57 ± 150.67 milliseconds) in the CRT.

Mood Probes. The MT group showed elevated levels of negative (b = −17.51, SE = 4.61, $p_{FDRcorr}$ < 0.05, Cohen's d = 0.46) and decreased levels of positive mood (b = 11.11, SE = 3.69, $p_{FDRcorr}$ < 0.05, Cohen's d = 0.37) (see Table S3, available online).

SGT Rating. The MT group reported significantly fewer positive thoughts compared to the NMT group (b = 11.16, SE = 3.83, $p_{FDRcorr}$ = 0.04, Cohen's d = 0.35) (Figure 1). This difference in positively valenced thoughts was independent of participants' mood ratings (see Table S4, available online), as well as age, gender, and SES (see Table S5, available online). Both groups had more positive thoughts than negative thoughts (NMT: t_{38} = −19.30, p < .001; MT: t_{28} = −7.30, p < .001), suggesting a general positive thought-bias. There were no group differences in off-task, other-, self-, past-, and future-related thoughts (see Table S3, available online).

SGT Variability: Extremity and Fluctuations. The MT group exhibited significantly greater extremity in positively valenced thought ratings (b = −299.04, SE = 78.09, $p_{FDRcorr}$ < 0.014, Cohen's d = 0.46) (Figure 2), showing reductions in positively valenced thought ratings relative to the "norm." This difference in extremity of positively valenced thought ratings was independent of participants' extremity in mood ratings (see Table S4, available online), as well as age, gender, and SES (see Table S5, available online). There were no group differences in extremity of off-task, negative, other-, self-, past-, and future-related thought ratings (see Table S3, available online). There were no group differences in SGT fluctuations.

FIGURE 1 Self-Generated Thought (SGT) Rating Levels Across the Different Dimensions for Adolescents With Maltreatment History (MT) and Adolescents With No Maltreatment History (NMT)



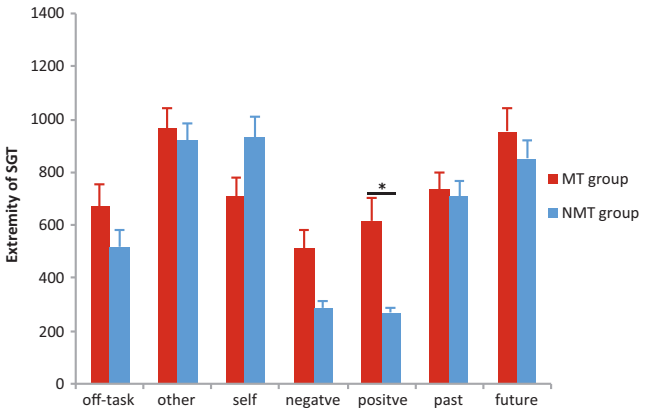
Note: *Adolescents who experienced maltreatment showed significantly fewer positively valenced thoughts. Please note color figures are available online.* [a]*Indicates a significant different in positive thoughts between maltreated and non-maltreated group.*

Interrelations Between SGTs in Adolescents With and Without a History of Maltreatment. In a further exploratory step, we investigated associations of valence and temporal relatedness of thoughts as previously reported in patients with MDD.[7] For this purpose, temporal SGT ratings (future, past) were used as covariates for the positively valenced thought ratings, and extremity of temporal thought ratings (future, past) were used as covariates for extremity of positively valenced thought ratings within the models. In terms of SGT ratings, the MT group showed less positively valenced past-related thoughts (b = 0.15, SE = 0.07, p = .033) (see Table S6, available online). There were no significant group differences in terms of associations between extremity of temporal SGT ratings (future, past) and extremity in positively valenced thought ratings.

RSFC Analysis

Whole-brain seed-based functional connectivity analyses revealed a significant difference in RSFC between the MT group and the NMT group for the right superior sgACC.

FIGURE 2 Extremity of Self-Generated Thought (SGT) Ratings Across the Different Dimensions for Adolescents With Maltreatment History (MT) and Adolescents With No Maltreatment History (NMT)



Note: *Adolescents who experienced maltreatment showed significantly greater extremity in positively valenced thought ratings, reflecting reduced positive thoughts. Please note color figures are available online.*

There were no RSFC differences for the other sgACC seeds (see Table S7, available online). The NMT group showed significantly greater positive RSFC from the right superior sgACC to the right supramarginal gyrus (rSMG) (Figure 3A), the right dorsal lateral prefrontal cortex (rDLPFC) (Figure 3B), and the cuneus (Figure 3C). These findings remained when controlling for age, gender, and SES.

Relationship Between sgACC RSFC and SGTs and Depression Symptoms

Depressive symptoms overall were negatively associated with positively valenced thoughts ($r = -0.28$, $p = .03$) as well as sgACC–cuneus RSFC ($r = -0.47$, $p < .01$). A mediation analysis was performed to investigate whether differences in sgACC–cuneus RSFC and positively valenced thoughts would mediate group differences in depressive symptoms. Analyses were conducted using bootstrapping procedures (5,000 bootstrap resamples) operationalized in an SPSS Macro.[37] Statistical significance with α at .05 is indicated by the 95% confidence intervals not crossing zero. We found a significant total mediation effect (see Figure S1, available online) with respect to the relation between maltreatment and depressive symptoms ($b = 5.23$, SE = 2.38, confidence interval [CI] = 1.64–11.33). Group differences in depressive symptoms were mediated by differences in sgACC–cuneus RSFC ($b = 4.33$, SE = 2.11, CI = 1.07–9.53) but not by differences in positively valenced thoughts ($b = 0.90$, SE = 1.16, CI = − 0.52 to 4.14).

DISCUSSION

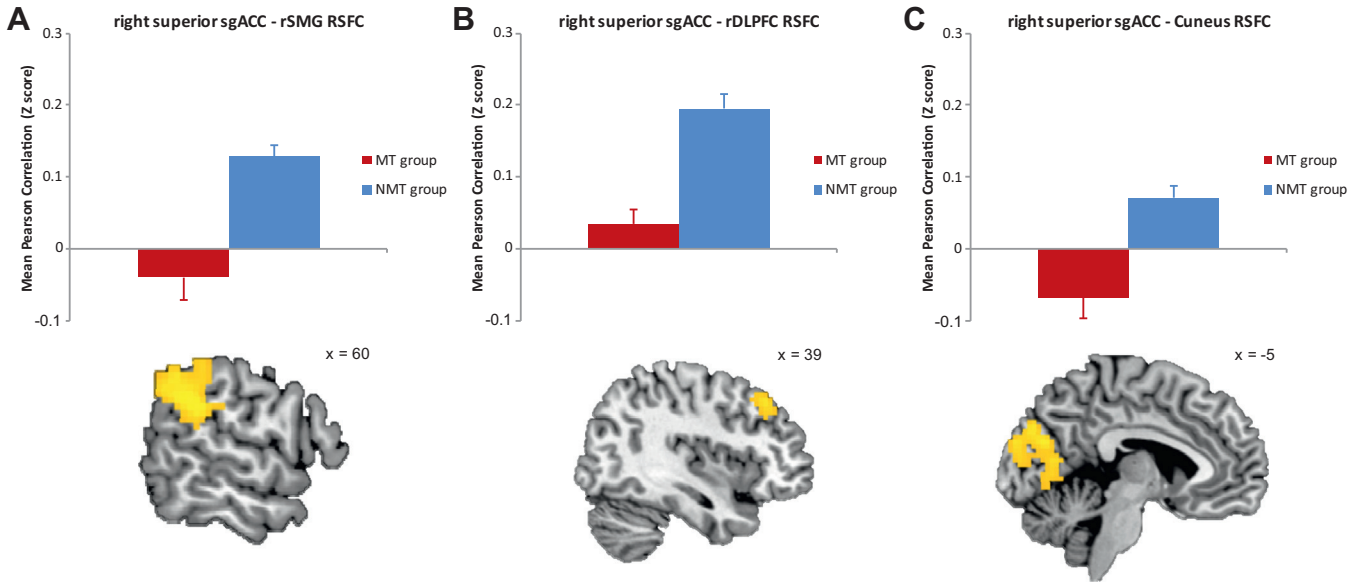
In this study, we investigated the frequency of online spontaneous thoughts and their variability in adolescents with a documented history of maltreatment relative to nonmaltreated adolescents. We used a mind-wandering laboratory task, an objective online measure that probes the amount and specific content of non–task-related thoughts in the moment in which they occur. In addition, we investigated whether adolescents who experienced maltreatment would exhibit abnormal sgACC RSFC, which has been associated with rumination in MDD.[13,18] It was found that adolescents who experienced maltreatment exhibited fewer positively valenced thoughts. Adolescents who experienced maltreatment also showed alterations in extremity of positively valenced thought ratings. At the neural level, adolescents who experienced maltreatment showed reduced RSFC to the fronto-parietal network.

As hypothesized, adolescents who had experienced maltreatment relative to their nonmaltreated peers exhibited fewer positive thoughts, in particular when they were past related—similar to what is observed in adults with MDD.[7] A trend level uncorrected effect of a greater number of negative thoughts was also observed. There were no further differences in SGTs, suggesting that, broadly speaking, similar thought patterns characterized the groups. In contrast to findings reported in adults with MDD, adolescents who had experienced maltreatment did not show a greater number of past or self-related thoughts. One possibility is that increased past and self-related SGTs are features of the MDD state and depressive rumination, whereas reduced positive SGTs represent a marker of future depression vulnerability. The observation that past or self-related thoughts did not characterize the maltreatment group (in contrast to what is observed in MDD) may also be accounted for by developmental factors. One possibility is that such a pattern may emerge following adolescence, during which there are significant changes in socio-cognitive processes.[41] Longitudinal studies are required to assess these possibilities.

SGT variability findings complemented SGT rating level findings, with adolescents with a history of maltreatment exhibiting significant differences in extremity of SGT ratings, suggesting greater deviations from normative SGT patterns. These deviations were characterized by less positive rating values in the adolescents who experienced maltreatment. There were no group differences in terms of SGT fluctuations.

Collectively, these behavioral findings suggest that early environments characterized by maltreatment lead to an atypical SGT pattern, specifically altering the positive

FIGURE 3 Subgenual Anterior Cingulate Cortex (sgACC) Resting-State Functional Connectivity Differences Between Adolescents With Maltreatment History (MT) And Adolescents With No Maltreatment history (NMT)



Note: *In contrast to adolescents with maltreatment history, adolescents with no maltreatment history showed a significantly greater positive resting-state functional connectivity (RSFC) from the right superior sgACC to (A) the right supramarginal gyrus (rSMG), (B) the right dorsal lateral prefrontal cortex (rDLPFC) and (C) the cuneus (FWE <.05). Please note color figures are available online.*

affective tone of spontaneous thoughts. In line with the cognitive model of depression, childhood abuse and neglect may lead to an internalization of negative self-referential schemas that bias information processing toward negative and away from positive content, a feature of ruminative thinking.[3] This decrease in positively valenced thoughts may represent a marker of latent vulnerability for developing clinical depression in the future.[20] Subclinical depression symptoms were associated with differences in positively valenced thoughts over the entire sample, and previous research has reported that decreased positively valenced thoughts were the strongest SGT predictor for MDD diagnosis.[7] However, longitudinal data are required to fully assess the viability of altered SGTs as a latent vulnerability marker for depression in adolescents with maltreatment histories.

The second aim of the study was to investigate whether adolescents who have experienced maltreatment would show abnormal sgACC RSFC, which has previously been linked to depressive rumination.[13,18] We hypothesized that adolescents who experienced maltreatment would exhibit altered sgACC–prefrontal RSFC, as previously reported in individuals with MDD.[18] In line with this hypothesis, adolescents who experienced maltreatment showed significantly decreased positive RSFC of the right superior sgACC to the rSMG, the rDLPFC, and the cuneus. These regions form part of a fronto-parietal network involved in cognitive and attentional control.[42,43] Group differences in subclinical depression symptoms were mediated by differences in sgACC-cuneus RSFC. This is consistent with the hypothesis that altered sgACC RSFC might underlie more depressogenic SGTs.

Collectively, these findings suggest that decreased functional integration among brain areas involved in affect processing, cognitive control, and attention in adolescents who experienced maltreatment. A stronger functional integration of these brain regions could facilitate processes such as attentional shifts from internal default mode network processes to the outside environment, making rumination less likely. Interestingly rSMG has been shown to be involved in self-other distinction in overcoming emotional egocentricity during empathy,[44,45] which is deficient in MDD.[46] Overcoming emotional egocentricity in development has also been associated with conflict processing and maturing rSMG–DLPFC functional connectivity.[47,48] The rSMG might thus serve a general function of shifting attention from internal/egocentric processes to the external environment, which is similarly critical in overcoming ruminative thinking as well as emotional egocentricity during empathy.

Based on previous findings in MDD and depressive rumination,[13,18] it was also hypothesized that adolescents who have experienced maltreatment would show increased sgACC–default mode network coupling. In this study, no significant group differences in sgACC–default mode

network coupling were detected. Increased sgACC–default mode network connectivity might thus represent a neurobiological marker of the depressed state and active depressive rumination. The observed absence of any increased sgACC–default mode network connectivity is consistent with the fact that adolescents who experienced maltreatment did not exhibit clinical depression, nor did they show any significant differences in self-referential processing in terms of the amount of self- and past-related thoughts as well as general mind-wandering as previously observed in patients with MDD.[7] As default mode network functioning has been strongly linked to self and memory processing,[49] heightened sgACC–default mode network coupling in depression might indeed relate to increased past and self-related thoughts. Future studies are needed to investigate this. Taken together, decreased functional integration between the sgACC and the fronto-parietal network in adolescents who experienced maltreatment might be associated with elevated risk of developing MDD, if such reduced integration compromises efficient regulation of negative, ruminative self-processing associated with sgACC–default mode network coupling and inhibits attentional shifts away from these egocentric processes toward the outside environment.

A number of limitations should be noted. First, the inclusion of self-report rumination measures would be useful in complementing the online mind-wandering measure. Second, the present study was cross-sectional in design, precluding any claims about causal mechanisms and thus pointing to the need for further longitudinal investigations. Such longitudinal studies could investigate whether decreased positively valenced thoughts in adolescents who experienced maltreatment might indeed predict future depression, consistent with the theory of latent vulnerability.[20] Third, the specificity of these potential behavioral and neural risk markers for depression remains unclear, and future studies should test these also alongside other psychiatric disorders associated with childhood maltreatment, including attention-deficit/hyperactivity disorder and conduct disorder.

From a preventive psychiatry perspective, abnormal SGT patterns may represent one marker of vulnerability for future depression. If atypical positive and negative SGT patterns were found to increase risk for future MDD, preventive strategies that addressed such thought patterns could help build resilience in adolescents who have experienced maltreatment, reducing the likelihood of future mental health problems. Interventions (both child and systemically focused) targeting maladaptive cognitions and increasing self-compassion may be helpful, as these approaches have been shown to be effective for patients with MDD.[50,51]

In conclusion, this study provides evidence that adolescents who have experienced maltreatment are more likely to engage in depressogenic SGTs compared to their non-maltreated peers, such that they generate fewer spontaneous positive thoughts. At the neural level, maltreatment experience was associated with decreased sgACC RSFC to the fronto-parietal network. The observed depressogenic SGT pattern and altered sgACC RSFC in adolescents who have experienced maltreatment might represent risk factors for developing depression later in life. Although adolescents with a history of maltreatment in this study were not clinically depressed, they presented with elevated levels of depressive symptoms that were partly accounted for by altered sgACC RSFC. Overall, these findings lend weight to the case for a more preventive model of help for adolescents who have experienced maltreatment. By addressing latent vulnerabilities early on, we may be able to reduce the likelihood that clinical disorders, such as depression, will emerge in the future.

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Correspondence to Ferdinand Hoffmann, PhD, Division of Psychology and Language Sciences, University College London, 26 Bedford Way, London, UK; e-mail: ferdinand.hoffmann.09@ucl.ac.uk

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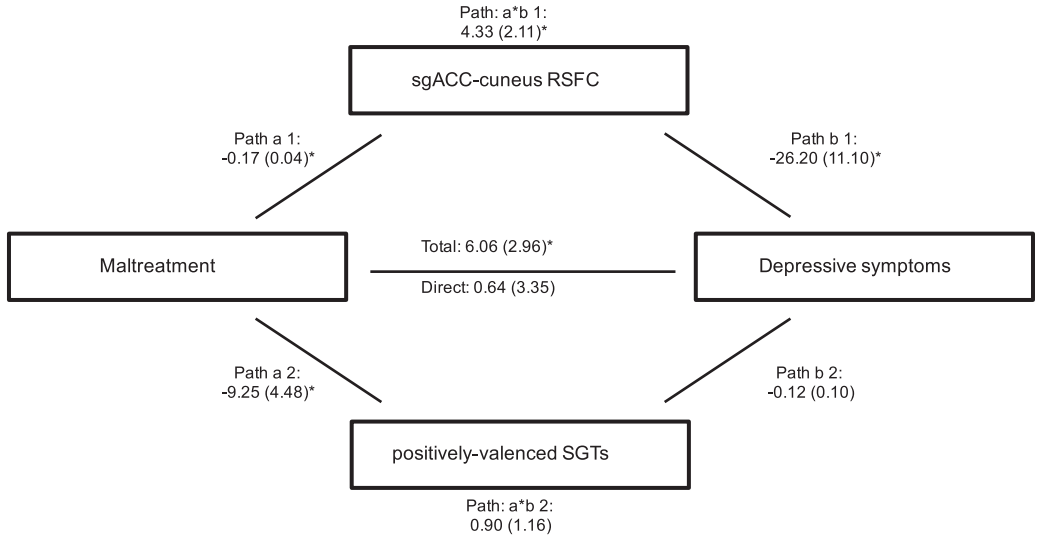
FIGURE S1 Illustration of the Mediation Model With Depressive Symptoms as the Outcome Variable, Maltreatment (Maltreatment [MT] History Versus No Maltreatment [NMT] History) as the Independent Variable, and Subgenual Anterior Cingulate Cortex–Cuneus Resting-State Functional Connectivity (sgACC–Cuneus RSFC) and Positively Valenced Self-Generated Thoughts (SGTs) as the Mediator Variables



Note: Values are nonstandardized regression coefficients. There was a significant mediation effect of sgACC–cuneus RSFC with respect to the differences in depressive symptoms between adolescents with maltreatment history and those without.

TABLE S1 Demographic and Background Information for Adolescents With Maltreatment History (MT) and No Maltreatment History (NMT) Within the Resting-State Sample

	MT Group (n = 19)	NMT Group (n = 26)	
Measure	**Mean (SD)**	**Mean (SD)**	***p***
Age, y	14.95 (1.44)	14.96 (1.14)	.98
WASI-IQ[a]	106.21 (11.50)	111.85 (9.70)	.08
Verbal Fluency[b]	35.94 (11.40)	37.42 (6.16)	.58
PDS[c]	3.08 (0.52)	3.07 (0.46)	.94
SES[d]	3.11 (1.66)	3.46 (1.0)	.38
	n (%)	**n (%)**	***p***
Gender, % female	11 (58)	16 (62)	1.00
Ethnicity, % white	13 (68)	15 (58)	.54
	Mean (SD)	**Mean (SD)**	***p***
CTQ, Total	31.35 (4.68)	28.17 (3.13)	<.05
CASI-4R, Depression Symptoms	59.94 (10.03)	53.88 (8.97)	<.05

Note: CASI-4R[1] = Child and Adolescent Symptom Inventory–4R; CTQ = Childhood Trauma Questionnaire[2]; PDS = Pubertal Development Scale; SES = socioeconomic status; WASI-IQ = Wechsler Abbreviated Scales of Intelligence.
[a]Two-subscale IQ derived from the WASI-IQ.[3]
[b]Verbal Fluency (phonemic + semantic).[4]
[c]Self rating of PDS.[5]
[d]Highest level education rated on 6-point scale from 0 = no formal qualifications to 5 = postgraduate qualification.

TABLE S2 Abuse Subtype Severity Scores and Estimated Onset Age and Duration in Years

Abuse Subtype	Mean	SD
Physical abuse (n = 4)		
Severity	1.00	0.00
Mean age at onset	4.03	4.37
Mean duration	6.89	5.10
Neglect (n = 21)		
Severity	4.95	2.56
Mean age at onset	3.30	3.83
Mean duration	5.57	4.93
Sexual abuse (n = 3)		
Severity	1.00	0.00
Mean age at onset	3.17	5.06
Mean duration	2.50	3.91
Emotional abuse (n = 28)		
Severity	3.67	0.58
Mean age at onset	3.17	5.06
Mean duration	6.53	4.74
Domestic Violence (n = 17)		
Severity	1.88	1.17
Mean age at onset	4.56	4.85
Mean duration	3.85	3.12
Overall across subtypes		
Severity	1.56	0.77
Mean age at onset	4.12	4.40
Mean duration	6.44	4.87

TABLE S3 Differences Between the No Maltreatment History (NMT) Group and the Maltreatment History (MT) Group in Rating Levels, Fluctuations in Ratings, and Extremity in Ratings as Estimated With Multilevel Modeling

Model Parameters	Rating Levels			Fluctuations in Ratings			Extremity of Ratings		
Predictors	***b***	**SE**	***p*[a]**	***b***	**SE**	***p*-[a]**	***b***	**SE**	***p*[a]**
Off task									
Intercept	81.34	3.50	<.002	488.87	154.67	.002	465.65	130.66	<.002
Group	1.81	4.04	.767	−128.52	129.30	.482	−148.82	142.37	.475
Sample	−2.97	0.60	<.027	25.36	44.75	.670	69.16	25.90	.036
Other									
Intercept	32.86	5.28	.008	859.08	233.02	<.002	995.55	119.90	<.002
Group	2.95	6.33	.767	−128.48	253.32	.754	54.21	146.82	.770
Sample	1.85	0.72	.042	−43.86	74.94	.670	−26.79	29.90	.564
Self									
Intercept	74.41	4.11	<.002	662.79	177.26	.001	759.87	141.57	<.002
Group	−9.61	5.79	.327	−185.54	155.42	.463	179.76	163.16	.475
Sample	−2.73	0.96	.036	−17.46	47.28	.739	−11.56	26.20	.739
Negative									
Intercept	22.71	3.49	<.002	590.90	113.56	<.002	492.34	117.65	<.002
Group	−8.81	3.71	.327	−148.56	94.94	.327	−247.63	112.65	.189
Sample	0.62	0.56	.564	−52.83	32.85	.282	13.33	17.51	.603
Positive									
Intercept	73.74	3.74	<.002	345.97	111.38	.002	487.11	79.03	<.002
Group	11.16	3.83	.041	−119.43	112.15	.475	−299.04	78.09	<.014
Sample	−1.06	0.54	.036	34.48	36.49	.564	30.41	19.26	.282

(continued)

TABLE S3 Continued

Model Parameters	Rating Levels			Fluctuations in Ratings			Extremity of Ratings		
Predictors	***b***	**SE**	***p*[a]**	***b***	**SE**	***p*-[a]**	***b***	**SE**	***p*[a]**
Past									
Intercept	22.71	4.37	<.002	313.20	222.28	.165	496.84	106.24	<.002
Group	−0.15	5.06	.976	−20.59	234.58	.966	93.87	114.32	.574
Sample	2.26	0.73	.027	174.46	62.72	.036	56.25	33.01	.282
Future									
Intercept	47.16	4.75	<.002	1081.83	257.94	<.002	918.24	152.24	<.002
Group	−8.11	5.71	.360	−193.44	242.39	.574	−118.81	181.77	.663
Sample	0.01	0.86	.996	−48.51	52.983	.670	26.72	22.59	.459
Negative mood									
Intercept	33.47	4.24	<.002	1060.43	298.64	.002	663.09	136.12	<.002
Group	−17.51	4.61	<.014	−494.74	308.02	.327	−181.96	143.75	.428
Sample	1.40	0.84	.282	−40.38	107.70	.739	53.99	43.89	.455
Positive mood									
Intercept	69.92	3.11	<.002	517.64	165.60	.003	549.15	103.98	<.002
Group	11.11	3.69	.027	−240.81	152.19	.327	−174.25	116.86	.346
Sample	−0.49	0.53	.564	−29.45	38.07	.603	27.36	21.22	.446

***Note**: Sample represents the covariate of the number of sampling points of the thought probes. SE = standard error.*
[a]*Corrected p – FDR < .05.*

TABLE S4 Differences Between the No Maltreatment History (NMT) Group and the Maltreatment History (MT) Group in Positive Thought Ratings and Extremity in Positive Thought Ratings Controlled for Mood

Model Parameters **Predictors**	***b***	**SE**	***p***
Positive thought rating (controlled for positive mood)			
Intercept	59.43	4.82	<.001
Group	8.80	3.63	.020
Sample	−0.93	0.55	.107
Positive mood rating	0.21	0.05	<.001
Positive thought rating (controlled for negative mood)			
Intercept	75.37	3.83	<.001
Group	10.28	3.75	.009
Sample	−0.96	0.53	.070
Negative mood rating	−0.05	0.04	.171
Extremity in positive thought rating (controlled for positive mood extremity)			
Intercept	435.98	81.75	<.001
Group	−282.54	78.57	.001
Sample	27.79	19.19	.148
Positive mood extremity	0.09	0.04	.021
Extremity in positive thought rating (controlled for negative mood extremity)			
Intercept	469.63	82.02	<.001
Group	−292.09	78.57	<.001
Sample	28.74	19.36	.138
Negative mood extremity	0.02	0.03	.430

***Note**: SE = standard error.*

TABLE S5 Differences Between the No Maltreatment History (NMT) Group and the Maltreatment History (MT) Group in Positive Thought Ratings and Extremity in Positive Thought Ratings Controlled for Age, Gender, and Socioeconomic Status (SES) (Parental Education)

Model Parameters Predictors	*b*	SE	*p*
Positive thought rating (controlled for age, gender, and SES)			
Intercept	92.69	15.53	<.001
Group	10.37	4.07	.016
Sample	−1.26	0.53	.018
Age	−1.61	1.01	.150
Gender	0.19	0.51	.718
SES	1.89	1.04	.109
Extremity in positive thought rating (controlled for age, gender, and SES)			
Intercept	325.83	425.79	.448
Group	−266.34	81.61	.002
Sample	34.70	19.41	.074
Age	16.21	28.12	.567
Gender	−13.12	18.18	.477
SES	−32.69	29.01	.267

Note: *SE = standard error.*

TABLE S6 Group Difference in Interrelations Between Positively Valenced Thought Ratings and Past-Related Thought Ratings as Estimated With Multilevel Modeling

Model Parameters Predictors	*b*	SE	*p*
Positive thought rating			
Intercept	79.18	3.05	<.001
Group	6.89	3.43	.046
Sample	−0.77	0.50	.123
Past	−0.22	0.06	<.001
Past rating × Group	0.15	0.07	.033

Note: *SE = standard error.*

TABLE S7 Subgenual Anterior Cingulate Cortex (sgACC) Resting-State Functional Connectivity Differences Between Children With and Without History of Maltreatment

Brain Region	R/L	x	y	z	*ke*	*Z*
Right Superior sgACC						
NMT > MT						
Supramarginal Gyrus	R	60	−42	30	296	4.35
	R	51	−45	33		3.94
	R	51	−30	30		3.25
Dorsal Lateral Prefrontal Cortex	R	33	30	36	206	4.26
	R	24	51	21		3.96
	R	24	42	39		3.46
Cuneus		0	−87	21	868	4.12
	L	−3	−81	21		3.96
	L	−3	−75	24		3.93
MT > NMT						NS
Left Superior sgACC						
NMT > MT						NS
MT > NMT						NS
Right Inferior sgACC						
NMT > MT						NS
MT > NMT						NS
Right Inferior sgACC						
NMT > MT						NS
MT > NMT						NS

Note: *L = left; MT = maltreatment history; NMT = no maltreatment history; NS = nonsignificant; R = right.*