Research Report

Cognitive reappraisal and expressive suppression relate differentially to longitudinal structural brain development across adolescence

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ABSTRACT

Emotional disorders commonly emerge in adolescence, a period characterized by changes in emotion-related processes. Thus, the ability to regulate emotions is crucial for well-being and adaptive social functioning during this period. Concurrently, the brain undergoes large structural and functional changes. We investigated relations between tendencies to use two emotion regulation strategies, cognitive reappraisal and expressive suppression, and structural development of the cerebral cortex and subcortical structures (specifically amygdala and nucleus accumbens given these structures are frequently associated with emotion regulation). A total of 112 participants (59 females) aged 8–26 were followed for up to 3 times over a 7-year period, providing 272 observations. Participants completed the Emotion Regulation Questionnaire (ERQ), yielding a measure of tendencies to use cognitive reappraisal and expressive suppression at the final time point. Linear mixed model analyses were performed to account for the longitudinal nature of the data. Contrary to expectations, volumetric growth of the amygdala and nucleus accumbens was not associated with either emotion regulation strategy. However, frequent use of expressive suppression was linked to greater regionally-specific apparent cortical thinning in both sexes, while tendency to use cognitive reappraisal was associated with greater regionally-specific apparent thinning in females and less thinning in males. Although cognitive reappraisal is traditionally associated with cognitive control regions of the brain,

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our results suggest it is also associated with regions involved in social cognition and semantics. The continued changes in cortical morphology and their associations with habitual use of different emotion regulation strategies indicate continued plasticity during this period, and represent an opportunity for interventions targeting emotion regulation for adolescents at risk.

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1. Introduction

Adolescence is characterized by affective experiences that are distinct from those experienced in childhood and adulthood, for reviews see Guyer, Silk, and Nelson (2016), Nook and Somerville (2019) and Sims and Carstensen (2014). Adolescents experience emotions that are more complex than children, and more intense than adults (Nook & Somerville, 2019). They also experience more negative emotions in comparison to other life stages (McLaughlin, Garrad, & Somerville, 2015). These affective changes make the regulation of emotions a principal developmental task of adolescence. Emotion regulation refers to processes that influence which emotions one has, as well as when and how they are experienced and expressed (Gross, 1998). As children grow older, emotion regulation becomes more self-initiated (Sims & Carstensen, 2014). Acquiring skills to successfully regulate emotions is critical because poor emotion regulation relates to adolescent psychopathology (McLaughlin, Hatzenbuehler, Mennin, & Nolen-Hoeksema, 2011). Since the adolescent brain undergoes substantial structural and functional changes (Blakemore, 2012; Sturman & Moghaddam, 2011; Walhovd, Tamnes, & Fjell, 2014), the insights into the neurodevelopmental basis of emotion regulation in adolescence may provide novel insight into the biological risk factors for psychopathology, and ultimately inform prevention and early intervention programs.

Several theoretical models propose a link between emotion regulation and patterns of brain development across adolescence. A model proposed by Somerville, Jones, and Casey (2010) suggests that adolescent behavior can be accounted for by relative imbalance of the (structural and functional) maturity between brain regions implicated in behaviors related to emotion and incentives (amygdala and ventral striatum) and regions implicated in cognitive and impulse control (prefrontal cortex, PFC). Other models (Casey, 2015; Casey, Heller, Gee, & Cohen, 2019; Ernst, 2014) propose more complex interactions between cortical and subcortical circuits. Despite some differences, the basic idea common to these models is that i) subcortical structures mature earlier than frontal cortical regions and ii) this maturational mismatch may result in an overreliance on subcortical systems, which may account for emotional- or incentive-driven behavior in adolescence. So far, attempts to test these models have faced numerous statistical and conceptual challenges (Meisel, Fosco, Hawk, & Colder, 2019). By illuminating the relations between emotion regulation and longitudinal development across the whole cortex, as well as

development of nucleus accumbens (a part of ventral striatum; Squire et al., 2012) and amygdala, this study hopes to inform (although not directly test) these theoretical models of adolescence.

Regulating emotions entails influencing which emotions an individual has, when emotions are experienced, and how they are expressed (Gross, 1998). Two commonly used emotion regulation strategies are cognitive reappraisal and expressive suppression (Gross, 2002). Cognitive reappraisal is defined as changing the way one thinks about a situation in order to change its emotional impact, and expressive suppression is conceptualized as inhibiting behavioral expressions of an emotion (Gross, 2002). Habitual use of cognitive reappraisal has been positively associated with better interpersonal functioning, positive affect and several indicators of mental health; the opposite holds for habitual use of expressive suppression (Gross & John, 2003; Hu et al., 2014; John & Gross, 2004). There is agreement that successful emotion regulation likely depends on cognitive control (Schweizer, Gotlib, & Blakemore, 2019). Emotion regulation strategies may each relate differentially to sub-components of cognitive control, which in turn may have different neural substrates (Lemire-Rodger et al., 2019). Expressive suppression involves the inhibition of affective expressions, while cognitive reappraisal involves updating and shifting one's interpretation of emotional experiences, thoughts and events. Improvements in both cognitive control and emotion regulation occur across adolescence (Crone & Steinbeis, 2017; Guyer et al., 2016). However, these processes are not mutually exclusive; decreases in cognitive control later in life are not always accompanied by deterioration of emotion regulation (Paxton, Barch, Racine, & Braver, 2008; Tuck, Mauss, & Consedine, 2014). Thus successful emotion regulation is also dependent on additional mental processes (McRae et al., 2012; Messina, Bianco, Sambin, & Viviani, 2015). Functional magnetic resonance imaging (fMRI) studies suggest that cognitive reappraisal engages regions putatively involved in i) cognitive control, spreading across frontal and parietal cortices and ii) affective processing, amygdala and ventral striatum in particular (Ahmed, Bittencourt-Hewitt, & Sebastian, 2015; Buhle et al., 2014; Casey et al., 2019; Kohn et al., 2014; Messina et al., 2015; Morawetz, Bode, Baudewig, & Heekeren, 2017; Ochsner & Gross, 2005; Ochsner, Silvers, & Buhle, 2012). Additional fMRI findings suggest that cognitive reappraisal also recruits regions associated with social cognition [medial prefrontal cortex (mPFC), temporoparietal junction (TPJ), posterior superior temporal sulcus (pSTS), anterior temporal cortex (ATC), see Mills, Lalonde, Clasen, Giedd, and Blakemore

(2012)] and the semantic network [inferior parietal, temporal and mPFC, see Binder, Desai, Graves, and Conant (2009)]. fMRI studies of expressive suppression suggest engagement of fronto-parietal cortical regions and amygdala (Cutuli, 2014). Some of these fronto-parietal regions are distinct from regions associated with cognitive reappraisal (Dörfel et al., 2014), others are overlapping, but their engagement may differ temporally during the emotion-generation process (Vanderhasselt, Kühn, & De Raedt, 2012).

MRI derived developmental changes in brain structure have been linked to cognitive and emotion-related processes (Ahmed et al., 2015; Walhovd et al., 2014), and are assumed to reflect biological processes related to neurocognitive optimization, specialization and increased efficiency, including myelination and synaptic pruning, see e.g., Natu et al. (2019). Brain structural studies of cognitive reappraisal and expressive suppression use are relatively scarce. Existing studies have identified positive associations between the tendency to use cognitive reappraisal and regional volumes, including the ventromedial prefrontal cortex (vmPFC, Welborn et al., 2009), amygdala (Hermann, Bieker, Keck, Vaitl, & Stark, 2013) and dorsal anterior cingulate cortex (dACC, Giuliani, Drabant & Gross, 2011). Others have shown that tendency to use cognitive reappraisal is associated with greater cortical thinning in the dlPFC and ventrolateral PFC (vlPFC), albeit only in females (Vijayakumar et al., 2014). For expressive suppression tendencies, positive relations were found with volumes of frontal regions (particularly vmPFC) in several studies (Hermann et al., 2013; Kühn, Gallinat, & Brass, 2011; Li et al., 2017), except for one study where the relation was negative (Welborn et al., 2009). Positive relations with expressive suppression were also identified for the dorsal anterior cingulate/paracingulate cortex (Hermann et al., 2013), dlPFC (Li et al., 2017) and anterior insula (Giuliani, Drabant, Bhatnagar, & Gross, 2011). Studies assessing relations between expressive suppression and cortical thickness (Vijayakumar et al., 2014; Wang et al., 2017) revealed both positive and negative relations depending on sex (see next paragraph). Aside from two notable exceptions that used whole brain approaches (Kühn et al., 2011; Wang et al., 2017), the majority of these studies examined regions of interests primarily located in frontal regions [e.g., Vijayakumar et al. (2014)], hence not considering other regions that potentially play a central role in regulating emotions.

For both emotion regulation strategies, behavioral studies have reported sex differences, with males reporting less cognitive reappraisal and more expressive suppression than females (Gross & John, 2003; Gullone, Hughes, King, & Tonge, 2010). Given gender differences in emotional display rules (Safdar et al., 2009), the degree to which these observed differences are biologically or socially driven is unknown. Moreover, fMRI studies (Burr et al., 2019; Whittle, Yücel, Yap, & Allen, 2011) and structural MRI studies of emotion regulation have indicated group-level sex differences; e.g., greater cortical thinning in predominantly prefrontal cortices in adolescent females related to higher cognitive reappraisal and lower expressive suppression (Vijayakumar et al., 2014). Expressive suppression was also linked to thinner cortices of the superior frontal gyrus and less gray matter volume of the right dorsolateral PFC in males, and more gray matter volume

in mPFC in females (Li et al., 2017; Wang et al., 2017). Since existing studies suggest sex differences both in use of emotion regulation strategies, and in associations between brain indices and emotion regulation strategies and there are sex-specific incidence rates of psychological disorders related to poor emotion regulation (Dalsgaard et al., 2019), examining the role of sex in brain – emotion regulation relations may be informative.

To summarize, theoretical accounts of emotion regulation across adolescence and empirical studies (mostly cross-sectional with predominantly adult samples) suggest involvement of distinct cortical and subcortical structures in emotion regulation. Structural neuroimaging studies of emotion regulation strategies are scarce and none have examined longitudinal structural correlates of how children and adolescents tend to regulate their emotions, with the exception of Vijayakumar et al. (2014). This study assessed whether cortical maturation [at time point (TP) 1 and 2] would predict later emotion regulation (at TP3) and found that greater cortical thinning in adolescent females related to higher cognitive reappraisal and lower expressive suppression in selected regions of interests. Longitudinal datasets are considered crucial in the study of individual differences in brain and cognition (Foulkes & Blakemore, 2018), because they can extend and aid interpretation of cross-sectional studies, and provide stronger inferences about developmental processes (Brown, 2017). Thus, to inform our understanding of the brain structural correlates of emotion regulation tendencies, which are for the most part currently based on cross-sectional studies, longitudinal studies are essential.

The current study examined the temporal dynamics of cortical and subcortical development across adolescence and into young adulthood and assessed how these changes in brain structure relate to habitual use of cognitive reappraisal and expressive suppression. By doing so, we aim to inform current theoretical models of the neuroanatomical basis of emotion regulation development. Specifically, this study intended to extend on the work by Vijayakumar et al. (2014) by i) testing for regional associations across the whole cortical mantle and selected subcortical structures, ii) studying a sample with wider age range, and iii) addressing prior limitations by using a larger dataset from a single scanner. Given the extensive literature on cortical and subcortical brain regions and circuits involved in different aspects of emotion regulation, several hypotheses were made. First, we hypothesized that this developmental period would be characterized by increases in cognitive reappraisal and decreases in expressive suppression, and that males would score higher than females on expressive suppression (Gross & John, 2003; John & Gross, 2004). We then explored whether relations between each emotion regulation strategy and brain structure (previously identified in adults) were already present in younger populations, or if they emerge over development. Given the protracted cortical and subcortical development, see Supplementary Material (S1.1) for overview, and the theoretical assumption of maturation characterized by increased cognitive reappraisal and decreased expressive suppression (John & Gross, 2004), we hypothesized that greater volumetric growth of amygdala and nucleus accumbens volumes would be associated with

less expressive suppression and more cognitive reappraisal tendencies. Since cognitive reappraisal has previously been linked to regions involved in cognitive control, semantics and social cognition, and cortical thinning has been linked to more emotional stability (Ferschmann et al., 2018), we also expected that more pronounced cortical thinning in mPFC, TPJ, pSTS, ATC, and inferior parietal cortices would relate to greater use of cognitive reappraisal. Conversely, we speculated that expressive suppression, being a less adaptive emotion regulation strategy when used habitually across situations (Gross & John, 2003), would be associated with reduced cortical thinning in mPFC. Finally, based on existing literature (Vijayakumar et al., 2014), we hypothesized that these relations between brain structural development and cognitive reappraisal/expressive suppression tendencies may interact with sex.

2. Methods

2.1. Participants

The sample was drawn from *NeuroCognitive Development*, an accelerated longitudinal study with three waves (Ferschmann et al., 2019; Tamnes et al., 2010, 2013), and approved by the Regional Committee for Medical and Health Research Ethics of South Norway. A total of 112 participants (59 females) aged 8–26 years (mean = 17.0, SD = 4.2, across all observations) provided 272 observations for the analyses. Each participant was required to have at least one MRI scan of satisfactory quality (see 2.7) and a measure of emotion regulation from wave 3. Three participants had MRI data available only from one TP, 58 had two TPs, and 51 had MRI data collected 3 TPs. Details on the recruitment strategies, consent procedures and the sociodemographic and intellectual characteristics of the samples are provided in S2.1 and in Fig. 1.

2.2. Emotion regulation strategies

Emotion Regulation Questionnaire (ERQ; Gross & John, 2003), a ten-item self-report, was used to measure dispositional emotional regulation tendencies at wave 3. This measure has shown sound psychometric qualities in adolescents and young adults (Gómez-Ortiz, Romera, Ortega-Ruiz, Cabello, & Fernández-Berrocal, 2016; Melka, Lancaster, Bryant, & Rodriguez, 2011). To rate items such as “I control my emotions by changing the way I think about the situation I’m in” or “I control my emotions by not expressing them”, the questionnaire uses a 7-point Likert scale ranging from 1 (strongly disagree) to 7 (strongly agree). Table 1 provides details regarding the subscales. Of note, subsequent referral to “cognitive reappraisal” and “expressive suppression” refers to the tendency to use each of these strategies.

2.3. General cognitive ability

We used the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) to assess general cognitive ability. At wave 1 and 2, we used all four subtests (Vocabulary, Similarities, Block Design and Matrix Reasoning) to estimate IQ. At

Overview of the participants’ age

Fig. 1 – Spaghetti plot, representing the study’s longitudinal sample, provides an overview of the participants’ age and number of available time points. Males depicted in blue, females in purple.

wave 3 we only used two subtests (Vocabulary and Matrix Reasoning), see S2.1.

2.4. Psychosocial functioning

Data from the self-report version of the Strength and Difficulties Questionnaire (SDQ; Goodman, 1997) from wave 3 was used to measure four areas of psychosocial adjustment: emotional symptoms, hyperactivity/inattention, peer relationships problems and conduct problems (see Table 1).

2.5. MRI acquisition

Data were collected using the same 12-channel head coil on the same 1.5 T S Avanto scanner (Siemens Medical Solutions, Erlangen, Germany) at Rikshospitalet, Oslo University Hospital. The MPRAGE sequence used for morphological analyses

Table 1 – Overview of subscales of the emotion regulation questionnaire (Gross & John, 2003) and the strength and difficulties questionnaire (Goodman, 1997).

Scale	Cronbach’s alpha	Median (SD)	Min-Max
ERQ			
Cognitive reappraisal	.80	24.0 (6.1)	6–36
Expressive suppression	.75	10.0 (5.3)	1–24
SDQ			
Emotional symptoms	.74	2.0 (2.3)	0–9
Hyperactivity/inattention	.72	2.0 (2.1)	0–7
Peer relationships problems	.46	1.0 (1.3)	0–6
Conduct problems	.16	1.0 (.9)	0–5

Note. SD refers to standard deviation, ERQ refers to Emotion Regulation Questionnaire and SDQ to Strength and Difficulties Questionnaire.

had following parameters: repetition time/echo time/time to inversion/flip angle = 2400 msec/3.61 msec/1000 msec/8°, matrix = $192 \times 192 \times 160$, sagittally acquired, field of view = 240 mm, bandwidth = 180 Hz/pixel, voxel size $1.25 \times 1.25 \times 1.2$ mm. Acquisition time was 7 min, 42 sec.

2.6. MRI processing

The longitudinal stream in FreeSurfer 6.0 (<http://surfer.nmr.mgh.harvard.edu/>) was utilized to perform whole brain segmentation and cortical surface reconstruction (Dale, Fischl, & Sereno, 1999; Fischl, 2012; Fischl et al., 2002; Fischl, Sereno, & Dale, 1999; Reuter, Schmansky, Rosas, & Fischl, 2012). Data from each TP was initially processed independently. Then, using all available TPs, a within-subject template was created for each participant by means of robust inverse registration (Reuter, Rosas, & Fischl, 2010). The aim of this step was to create an estimate of an average individual anatomy. The final step utilized information gathered in the initial two steps and each TP was processed longitudinally through a series of algorithms. The longitudinal stream uses each participant as their control and thus reduces the confounding effects of inter-individual morphological variability.

Based on reviews of the neurocognitive basis of emotion regulation (Ahmed et al., 2015; Casey et al., 2019; Messina et al., 2015; Ochsner et al., 2012), we chose to examine development of cortical thickness across the surface (vertex-wise), and amygdala and nucleus accumbens volumes. Estimates of cortical thickness were acquired by reconstructing representations of the gray matter/white matter boundary and the cortical surface and calculating distance between these surfaces at each vertex across the cortical mantle. Cortical thickness was down-sampled to the 81,924 vertices of *fsaverage6*, and surface maps were smoothed with a 10 mm FWHM Gaussian kernel. Note that the anatomical and underlying biological processes causing apparent cortical thickness and thinning as measured with MRI are not known in detail (Mills & Tamnes, 2014; Walhovd, Fjell, et al., 2016). Amygdala and nucleus accumbens volumes were segmented and extracted from each hemisphere and then summed across hemispheres. We chose not to control for global indices of brain size as prior work has shown that it can differentially impact observed sex differences, as well as developmental trajectories of regional brain volumes, in longitudinal studies (Mills et al., 2016). However, we do present supplemental analyses that control for intracranial volume (ICV), to illustrate the effects of “normalization”.

2.7. MRI quality control

Detailed and rigorous quality control of the MRI data was performed since head motion is known to introduce bias in morphological and developmental analyses (Alexander-Bloch et al., 2016; Reuter et al., 2015). Images were carefully inspected during the scan session and sequences were re-run if needed and possible. More specifically, a trained individual at a graduate level monitored the MRI images as they were acquired during the scanning session and requested re-scans within the same session if the quality

was insufficient. Judgements of whether or not scans were of satisfactory quality were based on visual inspections, as detailed (with example images) in Walhovd, Krogstad, et al. (2016). Next, all raw and processed images were manually inspected following a stringent standardized quality control rating procedure (Backhausen et al., 2016), adapted for longitudinal data. Images not meeting the required criteria were excluded from the analyses. The remaining scans from participants with one or more excluded scans were re-processed through the longitudinal pipeline, so as to recreate within-subject templates that were independent of excluded data.

Several studies (Pardoe, Hiess, & Kuzniecky, 2016; Savalia et al., 2017) suggest that visual quality assurance should be supplemented by more objective measures of data quality, particularly when studying effects of age on cortical thickness. For this purpose, we used the Euler number which informs about the topological complexity of the reconstructed cortical surface (Dale et al., 1999). Euler number is considered an index of image quality derived from the T1-weighted scans and has demonstrated regionally heterogeneous relations with cortical thickness (Rosen et al., 2018). FreeSurfer produces one Euler number per hemisphere. Here, we used an average value across hemispheres, and used it as a covariate in models testing for relations between cortical thickness and emotion regulation strategies.

2.8. Statistical analyses

Statistical analyses were performed using R (R Core Team, 2018) in RStudio (www.rstudio.com), unless otherwise specified. There are several suitable statistical approaches available to deal with longitudinally acquired data. Linear mixed models (LMM) represent one such powerful approach for analyses of data with repeated measurements from the same individuals (Gibbons, Hedeker, & DuToit, 2010; Matuschek, Kliegl, Vasishth, Baayen, & Bates, 2017). While other approaches, such as generalized additive mixed models (GAMM, Zuur, Ieno, Walker, Saveliev, & Smith, 2009; Coupé, 2018), are more flexible than LMMs, the application of these modelling strategies to vertex-wise analyses of neuroimaging data is limited. As such, we employed LMMs to analyze the associations between emotion regulation strategies and cortical and subcortical development. Here, data had two levels, with the first level representing the repeated measures on the same individuals (with participant ID entered as a random effect), and the second level representing all the individuals that participated in the study. Responses from the same individual are likely to be correlated, and LMM can efficiently account for this type of dependency in the data (West, Welch, & Galecki, 2014). For models where significant relations between emotion regulation strategies and brain structure were identified, we plotted data both using i) linear function in the nlme package in R (Pinheiro, Bates, DebRoy, Sarkar, & R Core Team, 2020) to facilitate comparison with other longitudinal studies of brain development, and ii) GAMM in R (Wood, 2006) with a cubic spline basis to estimate the developmental trajectories. The latter approach is recommended for interpretation of visual data, i.e., shapes of developmental trajectories (Fjell et al., 2010).

2.8.1. Associations between emotion regulation strategies and cortical thickness development

Before examining associations with emotion regulation tendencies, we first explored the effects of age on cortical thickness across the mantle was assessed using Surfstat (<http://www.math.mcgill.ca/keith/surfstat/>), a toolbox created for MATLAB. Age at each point of measurement was entered as the independent variable, along with a random effect for participant ID to account for the repeated-measures component. Studies using multiple independent samples have identified regionally specific non-linear effects of age on cortical thickness (Tamnes et al., 2017). Therefore, cubic, quadratic and linear age models were compared to identify developmental trajectories of cortical thickness using an approach where the most complex model is chosen based on the significance of the polynomial parameter (S2.2.1). This approach may be prone to overfitting which constitutes a limitation (Vijayakumar, Mills, Alexander-Bloch, Tamnes, & Whittle, 2017). However, the aim of these analyses was not characterizing the shape of development for brain regions, but rather identifying a good enough (i.e., significant) model of brain development and then seeing if the developmental model would be impacted by inclusion of emotion regulation strategies. Note that analyses examining the effects of age on cortical thickness identified both decreasing linear and inverted U-shaped (negative quadratic) patterns of change as significant across widespread regions of the cortex (see S2.2.1), and therefore analyses including emotion regulation strategies were repeated with both linear and quadratic age terms (see S2.2.2). Additionally, since there is not a general consensus as to whether or not there are subtle sex differences in cortical thickness development in this age range (e.g., Amlen et al., 2014; Mutlu et al., 2013) we also tested for age by sex interaction on cortical thickness (again using Surfstat and RFT, S2.2.1).

After exploring effects of age (and sex) on cortical thickness, we further tested whether there were any associations between emotion regulation strategies and longitudinal cortical thickness development. Initially, we tested main effects of emotion regulation strategies on cortical thickness. This was followed by testing two sets of models that examined the effects of emotion regulation strategies on cortical development: i) interaction between emotion regulation and age and ii) interactions between emotion regulation strategy, age and sex on cortical thickness development, given previously identified sex differences in the relations between cortical maturation and emotion regulation strategies (Vijayakumar et al., 2014). On the basis of the identified developmental trajectories of cortical thickness across the surface, the analyses were repeated using both linear and quadratic age, see details in S2.2.2. Finally, all models that identified significant associations between emotion regulation strategies and brain structure were repeated while controlling for Euler number and estimated IQ (both covariates assessed at each time point), in addition to parental income and parental education which reflect the family's socioeconomic status (SES; Farah, 2017; Noble & Gieddler, 2020). Parental variables were only collected at TP1 and TP2 (see S2.1) and were entered into the analyses as mean values across time

points based on both parents if available. The additional covariates including SES and IQ were selected because of their reported associations with both cortical and subcortical development (for review see Noble & Gieddler, 2020, Schnack et al., 2015), in neural networks underlying emotion regulation from childhood to adulthood (McDermott et al., 2019).

In all models (developmental age models and emotion regulation models), multiple comparisons were accounted for by means of Random field theory corrections (RFT; Worsley, Taylor, Tomaiuolo, & Lerch, 2004). Results were noted as significant if they passed $p < .05$, cluster-defining threshold .005.

Post hoc analyses were performed to unpack interactions if they were significant. Where significant 3-way interactions between emotion regulation strategy, age and sex were identified, analyses were repeated for each sex separately to test whether the effects were driven by significant interactions between age and emotion regulation strategy in a particular sex. Significant 2-way interactions between emotion regulation strategy and age were further probed by means of simple slope analyses, using Reghelper in R (Hughes, 2017), details regarding the simple slope analyses can be found in the Supplementary Material, S2.2.5 and S3.3.4.

2.8.2. Associations between emotion regulation strategies and subcortical volume development

The nlme package in R (Pinheiro et al., 2020) was used to run LMM to assess longitudinal changes in amygdala and nucleus accumbens volumes, and their relations to cognitive reappraisal and expressive suppression tendencies. First, we assessed the effect of age on subcortical structural development by comparing null, linear, quadratic and cubic age terms. The null model was compared to the linear model, linear model was compared to the quadratic model and quadratic model was compared to the cubic one. The likelihood ratio test (LRT) was used for significance testing where models were fit by maximum likelihood estimation (details in S2.2.3). Both p-values and AIC values were considered. We then compared the best fitting model with all the other models, again using LTR, to examine if it is still the best fit. After identifying the best fitting age model, we further tested whether the inclusion of i) sex as main effect and ii) sex by age interaction improved the model fit. When the best fitting developmental model was identified, we also tested whether inclusion of i) main effect of emotion regulation strategy, or ii) interaction with emotion regulation strategy, improved the model fit (see S2.2.4). Models where emotion regulation strategy – brain structure relations were identified as significant were repeated with IQ and SES as covariates.

3. Results

3.1. Emotion regulation strategies

Table 2 shows means and standard deviations (SD) of cognitive reappraisal and expressive suppression subscales of the ERQ. The tendency to use each of these strategies was not significantly related to each other [$r(109) = -.13$, $p = .187$].

Table 2 – Emotion regulation strategies for females, males and the total sample at time point 3.

Emotion regulation strategy	Females	Males	Total
Cognitive reappraisal	23.9 (6.1)	22.3 (6.0)	23.1 (6.1)
Expressive suppression	9.3 (5.1)	11.2 (5.3)	10.2 (5.3)

Note. Values are Means (Standard Deviations).

There were no significant sex differences in the tendency to use emotion regulation strategies, for either cognitive reappraisal ($t = 1.46$, $df = 109$, $p = .147$) or expressive suppression ($t = -1.85$, $df = 110$, $p = .967$). Violin plots (supplementary figure 4) show the distribution of cognitive reappraisal and expressive suppression scores for each sex.

There was no association between cognitive reappraisal and age [Pearson's $r(105) = .03$, $p = .758$], but expressive suppression showed signs of reductions with increasing age [Pearson's $r(106) = -.20$, $p = .035$], see supplementary figure 5. Table 3 shows correlations among the two emotion regulation strategies, estimated IQ and four subscales of the SDQ. Please note that the peer relationship and conduct problem subscales of the SDQ had a low reliability in this sample.

3.2. Emotion regulation strategies and cortical development

3.2.1. Cognitive reappraisal and cortical thickness development

Analyses testing the main effect of cognitive reappraisal, as well as the interaction between cognitive reappraisal and (linear/quadratic) age, in predicting cortical thickness did not reach statistical significance after correction for multiple comparisons. However, the interaction between cognitive reappraisal, (linear) age and sex significantly predicted cortical thickness following correction for multiple comparisons. This analysis yielded significant effects in three clusters: i) right middle temporal gyrus and temporo-parietal junction, ii) dorsal parts of the right superior parietal cortex and parts of precuneus, and iii) parts of right inferior parietal lobule, while controlling for several covariates (Euler number, estimated IQ, parental education and parental income), see Fig. 2 and Supplementary table 2). The interaction between cognitive reappraisal, sex and the quadratic age term did not identify any significant clusters.

Associations between Cognitive Reappraisal and cortical thickness across the whole brain.

To facilitate interpretation of the results, the 3-way interactions between cognitive reappraisal, (linear) age and sex on cortical thickness were plotted. More specifically, the

Fig. 2 – Cortical regions where 3-way interactions between cognitive reappraisal, age and sex on cortical thickness were significant. Yellow-pink regions represent cluster level p-value map $\leq .05$, Random Field Theory corrected.

relations between cognitive reappraisal and cortical thickness were plotted separately for males and females, and median split was created to visualize individuals low or high on the tendency to use cognitive reappraisal. The resulting Fig. 3 suggests that females who rated themselves as high on cognitive reappraisal showed greater cortical thinning, while the opposite pattern was found for males. Supplementary figure 6 using the linear function to visualize the data suggests similar patterns. Note that the statistical analyses were performed with cognitive reappraisal as a continuous variable and the median split only was performed to facilitate plotting and interpretation.

Visualization of the 3-Way Interaction between Cognitive Reappraisal, linear age and sex.

Post hoc analyses were conducted to test whether the effects were driven by significant interactions between age and cognitive reappraisal in one sex, but not the other. Cortical thickness data from each identified significant cluster was used to test which model: i) linear age model, ii) main effect of cognitive reappraisal and iii) linear age by cognitive reappraisal model was the best fit, assessed separately in males and females (for details see S3.3.4). Results of these analyses suggest that effects of cognitive reappraisal in the cluster spreading across the right middle temporal gyrus and temporo-parietal junction was statistically significant in both males and females. Findings in the two remaining clusters

Table 3 – Correlates of cognitive reappraisal and expressive suppression.

Emotion regulation strategy	IQ	Emotional symptoms	Hyperactivity/inattention	Peer relationships problems	Conduct problems
Cognitive reappraisal	-.01 (.934)	-.19 (.042)	-.11 (.240)	-.07 (.461)	-.06 (.525)
Expressive suppression	-.02 (.807)	.23 (.017)	.08 (.381)	.28 (.003)	-.16 (.099)

Note. Values refer to Pearson's correlation r (p-value).

Fig. 3 – Associations between cortical development and cognitive reappraisal in (A) females and (B) males. The plots show mean cortical thickness from the clusters where 3-way interactions between cognitive reappraisal, age and sex were significant: i) right middle temporal gyrus and temporo-parietal junction, ii) dorsal parts of the right superior parietal cortex and part of precuneus, and iii) parts of right inferior parietal lobule. The fits were produced using the following model: $\text{thickness} \sim s(\text{age}, \text{bs} = 'cr')$ by means of GAMM in R (plotted separately for each sex), $\text{bs} = 'cr'$ refers to splines with cubic spline basis (Wood, 2006). Median split was used to split the sample into high use (orange) and low use (blue) of cognitive reappraisal. Note that the low/high division was made for illustrative purposes only, while the statistical analyses were run with cognitive reappraisal as a continuous measure.

were driven by females and did not reach statistical significance in males.

3.2.2. Expressive suppression and cortical thickness development

Analyses testing main effects of expressive suppression on cortical thickness development did not reach statistical significance. However, the analyses revealed a significant 2-way interaction between expressive suppression and (linear) age on cortical thickness development. This model yielded six clusters spread over several regions while Euler number, estimated IQ, parental education and income were controlled for: i) left ventromedial prefrontal cortex and orbitofrontal cortex, ii) left precuneus and superior parietal cortex, iii) right posterior middle temporal gyrus iv) right lateral occipital cortex, v) right supramarginal gyrus and vi) right inferior parietal lobule, see Fig. 4 and Supplementary Table 4.

Associations between Expressive Suppression and cortical thickness across the whole brain.

The interaction between expressive suppression and the quadratic age term did not identify any significant clusters.

To aid interpretation of the data, the 2-way interactions between expressive suppression and (linear) age on cortical thickness were plotted and median split was used to visualize

Fig. 4 – Regions where interactions between expressive suppression and age on cortical thickness were significant. Yellow-pink regions represent cluster level p-value map, $p \leq .05$, Random Field Theory (RTF) corrected.

Fig. 5 – Associations between cortical development and expressive suppression. The plots show mean cortical thickness from the clusters where interactions between expressive suppression and age were significant: i) left ventromedial prefrontal cortex, ii) left precuneus and superior parietal cortex, iii) right posterior middle temporal gyrus, iv) right lateral occipital cortex, v) right supramarginal gyrus and vi) right inferior parietal lobule. The fits were produced using the following model: $\text{thickness} \sim s(\text{age}, \text{bs} = 'cr') + \text{sex}$ by means of GAMM in R, $\text{bs} = 'cr'$ refers to splines with cubic spline basis (Wood, 2006). Median split was used to split the sample into high use (blue) and low use (purple) of expressive suppression. Note that the low/high division was made for illustration purposes only, while the statistical analyses were run with expressive suppression as a continuous measure.

data for individuals with low and high tendency to use expressive suppression. The resulting Fig. 5 and supplementary figure 7 suggest that individuals who report more frequent use of expressive suppression showed greater regional cortical thinning.

Visualization of the 2-Way Interaction between Expressive Suppression and linear age.

3.3. Emotion regulation strategies and development of amygdala and nucleus accumbens volumes

3.3.1. Development of amygdala volume

A cubic age by sex model was identified as the best fit for amygdala volume growth. The model fit was not further improved by inclusion of either cognitive reappraisal or expressive suppression (Table 4). S3.3.3 shows how controlling for ICV impacted model selection.

3.3.2. Development of nucleus accumbens volume

Linear age model with sex as main effect was identified as the best model fit. The model was not further improved by inclusion of either cognitive reappraisal or expressive suppression (Table 5). S3.3.3 shows how controlling for ICV impacted model selection.

4. Discussion

The present study examined relations between tendencies to use of specific emotion regulation strategies and longitudinal development of the amygdala, nucleus accumbens, and cortex. Cognitive reappraisal tendency was related to greater cortical thinning in females and less cortical thinning in males, both in clusters spreading across right temporal and parietal cortices. Expressive suppression use was associated with more pronounced thinning in both sexes in PFC, as well as in occipital, parietal and temporal cortices in both hemispheres. Contrary to expectations, volumetric growth of amygdala and nucleus accumbens was not related to either of the two assessed emotion regulation tendencies. Intellectual abilities and SES were controlled because of their reported associations with the development of the cerebral cortex and subcortical structures (McDermott et al., 2019; Noble & Giebler, 2020; Schnack et al., 2015).

4.1. Emotion regulation strategies

In line with existing literature, expressive suppression tendency was negatively associated with age in this study

Table 4 – Comparison of models predicting volumetric growth of amygdala.

Model	Model	df	AIC	BIC	Loglik	Test	L ratio	p
Developmental models								
null	1	3	3628.66	3639.48	–1811.32			
linear	2	4	3620.51	3634.93	–1806.25	1 vs 2	10.15	.001
quadratic	3	5	3605.63	3623.66	–1797.81	2 vs 3	16.88	<.0001
cubic	4	6	3597.58	3619.21	–1792.79	3 vs 4	10.05	.002
cubic	4	6	3597.576	3619.21	–1792.79	2 vs 4	26.93	<.0001
cubic	4	6	3597.57	3619.21	–1792.79	1 vs 4	37.08	<.0001
Sex	5	7	3555.15	3580.39	–1770.57	4 vs 5	44.43	<.0001
Sex*age ³	6	10	3532.05	3568.11	–1756.03	5 vs 6	29.10	<.0001
Sex*age ³	6	10	3532.05	3568.11	–1756.03	4 vs 6	73.52	<.0001
Models including cognitive reappraisal								
CR	7	11	3532.21	3571.87	–1755.11	6 vs 7	1.84	.175
CR*sex*age ³	8	18	3539.83	3604.74	–1751.92	7 vs 8	6.38	.496
Models including expressive suppression								
ES	9	11	3532.60	3572.26	–1755.30	6 vs 9	1.46	.227
ES*sex*age ³	10	18	3539.89	3604.80	–1751.95	6 vs 10	6.70	.460

Note: Table shows comparisons of different models that predict amygdala volume development; age models (null, linear, quadratic and cubic models), models including main effect of sex and interaction between sex and age³, and finally models that include cognitive reappraisal (CR) and expressive suppression (ES). Significance testing was performed by means of the likelihood ratio test, using maximum likelihood estimation method.

Table 5 – Comparison of models predicting volumetric growth of nucleus accumbens.

Model	Model	df	AIC	BIC	Loglik	Test	L ratio	p
Developmental models								
null	1	3	3258.13	3268.95	–1626.07			
linear	2	4	3247.76	3262.18	–1619.88	1 vs 2	12.37	<.0001
quadratic	3	5	3248.52	3266.55	–1619.26	2 vs 3	1.24	.266
cubic	4	6	3250.37	3272.01	–1619.19	3 vs 4	.14	.704
sex	5	5	3223.80	3241.83	–1606.90	2 vs 5	25.96	<.0001
Sex*age	6	6	3225.741	3247.376	–1606.871	2 vs 6	.06	.813
Models including cognitive reappraisal								
CR	7	6	3225.78	3247.42	–1606.89	5 vs 7	.02	.897
CR*age	8	7	3227.77	3253.02	–1606.89	5 vs 8	.01	.925
Model including expressive suppression								
ES	9	6	3225.79	3247.42	–1606.89	5 vs 9	.01	.922
ES*age	10	7	3227.64	3252.89	–1606.82	5 vs 10	.14	.704

Note: Table shows comparisons of different models that predict nucleus accumbens volume development; age models (null, linear, quadratic and cubic models), models including main effect of sex and interaction between age and sex and finally models that include cognitive reappraisal (CR) and expressive suppression (ES). Significance testing was performed by means of the likelihood ratio test, using maximum likelihood estimation method.

(Gullone et al., 2010). Tendency to use cognitive reappraisal was not associated with age, which was unexpected given that it is thought to increase with maturation and experience (John & Gross, 2004). Our finding is, however, in agreement with existing studies (Gullone et al., 2010). Contrary to existing literature (Gross & John, 2003; Gullone et al., 2010), no sex differences were found for cognitive reappraisal or expressive suppression. In line with these studies, however, plots suggested slightly more frequent use of cognitive reappraisal in females and more frequent use of expressive suppression in males, but group differences did not reach statistical significance. Moreover, others have shown that there are no sex differences in the capacity to generate reappraisals, albeit women may rate themselves lower on self-efficacy to regulate emotion (Perchtold et al., 2019). Large longitudinal multi-method studies are needed to further probe potential sex

differences and sex-specific developmental differences in emotion regulation.

4.2. Cognitive reappraisal and cortical thickness development

Tendency to use cognitive reappraisal was related to greater cortical thinning in females and less thinning in males. This finding is somewhat difficult to integrate with existing knowledge of brain development. Even though stronger effects in one of the sexes could be conceivable, the opposite relation for males and females is difficult to explain. Nevertheless, this finding is interesting as it replicates findings from a different longitudinal study of adolescents (Vijayakumar et al., 2014). We speculate that these sex differences may potentially be attributable to puberty (Juraska & Willing, 2017),

and further research incorporating pubertal stage and sex hormones may provide more clarity into these complex relations.

Greater cortical thinning was linked to greater use of cognitive reappraisal in females, while the opposite pattern was identified in males. This is an interesting finding as epidemiological data suggest that females are substantially more likely to suffer from mental disorders rooted in emotional dysregulation (WHO, 2017). It has been proposed that cognitive reappraisal can be more protective for males, yielding gender differences in the prevalence of these mental disorders (Masumoto, Taishi, & Shiozaki, 2016; Perchtold et al., 2019). For example, males and females do not differ in the ability to generate cognitive reappraisals, but improved ability to reappraise is linked to reduced depressive experiences only in males (Perchtold et al., 2019). It is possible that women need additional traits, such as higher self-efficacy beliefs in regard to emotion regulation, to reap the benefits of cognitive reappraisal.

In contrast to our hypotheses and the study by Vijayakumar et al., (2014), we did not find any associations between tendency to use cognitive reappraisal and development in frontal control regions. Our findings were located predominantly in parietal and temporal regions. Even though these regions are involved in executive functions (Esterman, Chiu, Tamber-Rosenau, & Yantis, 2009; Lemire-Rodger et al., 2019), they are also known for their roles in e.g., perspective taking and semantics (Binder et al., 2009; Mills et al., 2012). Successful reappraisal may require perspective taking (McRae et al., 2012) and a wealth of semantic representations may facilitate generation of alternative representations of the emotion-eliciting event (Messina et al., 2015). Thus, social cognition and semantics may possibly play a larger role in cognitive reappraisal than previously assumed.

4.3. Expressive suppression and cortical thickness development

Different patterns of steeper cortical thinning in clusters spreading across frontal, temporal, parietal and occipital cortices were related to more frequent use of expressive suppression, contrary to our initial hypothesis. Even though both emotional regulation tendencies were related to cortical development, there were some notable differences. First, in addition to regional differences of the identified significant clusters, relations between habitual use of cognitive reappraisal and cortical thinning were limited to the right hemisphere, as opposed to expressive suppression use where associations were found in both hemispheres. Second, although expressive suppression and cognitive reappraisal are generally considered as maladaptive and adaptive emotion regulation strategies respectively (confirmed by relating each strategy to emotional problems in our sample), they were not negatively related to each other. This may imply that some individuals frequently use both strategies. Additionally, expressive suppression can be adaptive in particular situations (Bonanno, Papa, Lalande, Westphal, & Coifman, 2004). Although highly speculative, it is possible that an adaptive pattern of emotion regulation does not entail exclusive use of cognitive reappraisal but an ability to flexibility

switch between emotion regulation strategies depending on situational needs. Similarly, Larsen and English (2014) propose that the most adaptive emotion regulation strategy is the one chosen in accord with one's own attributes that provides feelings of authenticity. In adolescents, expressive suppression seems to be less related to feelings of inauthenticity and less harmful to youth than to adults (Larsen & English, 2014). Finally, and most importantly, closer examination of the interaction between expressive suppression and age on cortical thickness suggested that different maturational patterns may be related to this emotion regulation tendency. In some clusters, frequent use of suppression appeared to be linked to steeper trajectory of apparent cortical thinning in younger ages, but the differences may possibly disappear in young adulthood. In other clusters, on the other hand, habitual use of suppression was linked to steeper pattern of cortical thinning throughout the studied age span, i.e., individuals who often engage in expressive suppression may start off with thicker cortex but may end up with thinner cortex in these regions as they approach the third decade of life.

A positive relation between expressive suppression and cortical thinning use was shown before, albeit only in males (Vijayakumar et al., 2014). Contrary to our findings, sex differences have been demonstrated in relations between indices of brain function and structure and expressive suppression in several studies (Burr et al., 2019; Li et al., 2017; Vijayakumar et al., 2014; Welborn et al., 2009). Still, there is a considerable overlap in regions implicated in expressive suppression in this study and other structural imaging studies of expressive suppression (Li et al., 2017; Welborn et al., 2009). These regions (particularly the ones in frontal and parietal cortices) also correspond to key structures of the default mode and fronto-parietal networks. Functional connectivity in these networks, which are involved in reflecting over emotions and controlling them, has previously been positively related to expressive suppression (Burr et al., 2019; Pan et al., 2018).

4.4. Emotion regulation strategies and subcortical development

Since amygdala and ventral striatum are at the core of models of adolescent emotional behavior (Casey, 2015; Ernst, 2014; Somerville et al., 2010), the lack of associations between emotion regulation strategies and volumetric growth of amygdala and nucleus accumbens volumes was surprising. Future studies should repeat these analyses in larger samples. Additionally, it is possible that studying microstructural changes in these regions rather than volumes, or the maturational coupling between them may be more informative (Bos et al., 2018; Lebel, Walker, Leemans, Phillips, & Beaulieu, 2008; Vijayakumar, Allen, et al., 2017; Westlye et al., 2010).

4.5. Limitations

Results of this study should be interpreted in the light of the study's limitations. First, emotion regulation strategies were assessed using a self-report questionnaire on the tendency of use. Future studies would benefit from using a multi-informant approach to capture the unique and different

aspects of emotion regulation tendencies in youth (Achenbach, 2006), as well as behavioral measures of emotion regulation. Second, emotion regulation tendencies were measured only at wave 3, which limits which relations between brain structural development and emotional regulation strategies can be assessed. The design of the current study cannot clarify whether brain structure is responsible for preference of a specific emotion regulation strategy, whether frequent use of a specific emotion regulation strategy influences brain structure and its development over time, or whether both constantly interact and modify each other. For example, it is unclear whether cortical thinning, which may reflect myelination and thus increased efficiency of information processing (Natu et al., 2019), facilitates more frequent use of cognitive reappraisal; or whether frequent use of reappraisal drives these cortical changes by increased neural activity (Metzler-Baddeley, Caeyenberghs, Foley, & Jones, 2016). The relations are likely dynamic and complex. Such questions may possibly be resolved by future studies that measure both brain and emotion regulation on multiple occasions and use structural equation models designed to disentangle level and change effects at a latent level (Becht et al., 2018; Kievit et al., 2018). Finally, the current study used only chronological age as a measure of maturation. Future studies may disentangle the complex sex differences identified in this study by employing measures of puberty.

5. Conclusion

The present study demonstrates links between longitudinal structural cortical development across adolescence and habitual use of specific emotion regulation strategies; cognitive reappraisal and expressive suppression. Habitual use of cognitive reappraisal was linked to a pattern of regionally greater cortical thinning in females and less thinning in males. The results imply that regions associated with social cognition and semantics should be the target of future studies, in addition to the traditionally studied frontal control regions. Even though habitual use of expressive suppression was also related to greater cortical thinning, the developmental trajectories of more pronounced thinning appeared to have temporally specific features, were found for both sexes and also in different regions than found for cognitive reappraisal. Failure to find association between volumetric growth of amygdala and nucleus accumbens was surprising, and the relations should be probed by future studies. Taken together, the results of the current study imply neurodevelopmental origins of expressive suppression and relate both emotion regulation strategies to aspects of cortical development.

Author statement

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Others

- no part of the study analyses was pre-registered.
- The conditions of the ethics approval do not permit public archiving of study data. Readers seeking access to the data should contact the first or last author. Access will be granted depending on completion of a formal data sharing agreement, proper measures taken for protection of privacy and approval by the relevant ethical committee.
- We report how we determined our sample size, all data exclusions, all inclusion/exclusion criteria, whether inclusion/exclusion criteria were established prior to data analysis, all manipulations, and all measures in the study.
- Legal copyright restrictions prevent public archiving of the various instruments used in the current study, which can be obtained from the copyright holders in the cited references
- Code for analyses can be found here <https://osf.io/6y3d4>

Declaration of Competing Interest

None.

Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.cortex.2020.11.022>.

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