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Neural correlates of self- and other-referential processing in young adolescents and the effects of testosterone and peer similarity

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ABSTRACT

During adolescence, self-concept develops profoundly, accompanied by major changes in hormone levels. Self-evaluations become more complex, and peers and their opinions increasingly salient. Neuroimaging studies have investigated self- and other-related processing in adolescents, however, the influence of similarity of peers on these processes is still unclear, as well as functional connectivity underlying such processes. We investigated the effect of peer similarity on neural activity and connectivity underlying self- and other-referential processing, by distinguishing between a similar and dissimilar peer when making other-evaluations. Moreover, we explored the association between testosterone and brain activity during self-evaluations. Sixty-six young adolescents underwent functional MRI while performing a trait judgement task in which they indicated whether an adjective described themselves, a similar or a dissimilar classmate. The ventral medial prefrontal cortex (MPFC) showed increased engagement in self-referential processing, and the posterior cingulate cortex and right temporal parietal junction during other-evaluations. However, activity did not differ between the similar and dissimilar other conditions. Functional connectivity of the ventral MPFC included the striatum when evaluating the similar peer and frontoparietal regions when evaluating the dissimilar peer. Furthermore, inter-individual differences in testosterone levels were positively associated with dorsal MPFC activity in males. This study provides insight into the influence of peer similarity on activity and connectivity underlying other-referential processing in young adolescents, and suggests that testosterone affects neural correlates of self-referential processing.

1. Introduction

During adolescence, representation of the self changes profoundly. Adolescents develop a more differentiated self-concept, and self-evaluations become increasingly complex (Labouvie-Vief et al., 1995). At the same time, they experience heightened sensitivity to social surroundings, in particular to peers, possibly triggered by changes in hormone levels, social cognitive processes and their underlying brain mechanisms (Crone and Dahl, 2012; Kilford et al., 2016; Pfeifer and Peake, 2012). Adolescents not only become more interested in the opinions of others (Vartanian, 2000), also peer evaluations become increasingly salient and self-relevant (Jankowski et al., 2014; Sebastian et al., 2008). Moreover, adolescents' beliefs, attitudes and behavior are often similar to that of their friends, and adolescents preferentially affiliate with peers who they perceive as similar (Brechwald and Prinstein, 2011; Steinberg and Morris, 2001). Prior studies have started to investigate self- and other-related processing and their neural correlates in adolescents (Jankowski et al., 2014; Pfeifer et al., 2013, 2009; Romund et al., 2017; Schneider et al., 2012; van der Cruijsen et al., 2018), however, the influence of perceived similarity of peers on these processes and their neural mechanisms is unclear. Also, functional connectivity between regions underlying self- and other-evaluations in young adolescents remains as of yet unexplored.

In adults, numerous studies have investigated self- and other-referential processing (see for meta-analysis (Denny et al., 2012; Murray et al., 2012; Northoff et al., 2006)). Core regions involved in self- and other-referential processing include the ventral medial prefrontal cortex (vMPFC), the dorsal MPFC (dMPFC), midline posterior regions, including

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the posterior cingulate cortex (PCC) and precuneus, and the temporal parietal junction (TPJ), extending into the angular gyri. When comparing self-to other-referential processing, the vMPFC is preferentially engaged in self-referential processing, whereas the dMPFC and TPJ are more strongly associated with other-referential processing. Moreover, the MPFC showed differential activity depending on the similarity, perceived closeness or familiarity of the other, as evidenced by studies that included multiple other characters (De Brigard et al., 2015; Krienen et al., 2010; Mitchell et al., 2006). More specifically, the vMPFC has been related to processing of the self and of a close other, while the dMPFC appears to be more involved in processing of unknown, or more socially distant others (Denny et al., 2012; Murray et al., 2012).

The core regions implicated in self- and other-referential processing in adults are also involved in these processes in adolescents. For example, in a recent study in mid-adolescents, Romund and colleagues (Romund et al., 2017) investigated differences between the neural mechanisms of reflective processing about oneself and about multiple others (friend, teacher and politician). In line with studies in adults (Benoit et al., 2010; Krienen et al., 2010), they showed a linear pattern of decreasing activity within the vMPFC with decreasing closeness of the other. However, despite large overlap, developmental changes in activity have also been observed. For example, studies have reported reduced recruitment of the dMPFC (Pfeifer et al., 2009, 2007) and left TPJ (Pfeifer et al., 2009) during self-evaluations in adults, compared to adolescents and children. Additionally, a positive association between activity within the vMPFC during self-evaluations and age was revealed from late childhood to early adolescence (Pfeifer et al., 2013) as well as between MPFC activity and age across adolescence (van der Cruijsen et al., 2018). Together, these studies tentatively suggest developmental changes in recruitment of the vMPFC and dMPFC, and to a lesser extent of the TPJ, during self- and other-referential processing.

Developmental differences may be driven by pubertal-related changes in hormone levels that affect cognitive and neural processes (Goddings et al., 2019). Testosterone shows strong puberty-related increases during adolescence in males (Khairullah et al., 2014) and is related to the organization of the neural circuitry in rodents (Schulz and Sisk, 2016) and structural brain changes in humans (Herting and Sowell, 2017). Moreover, pubertal testosterone levels have been associated with brain activity during affective (Tyborowska et al., 2016) and reward processes (Braams et al., 2015), and administration studies in adults related testosterone to social cognitive processes and underlying brain mechanisms (Bos et al., 2016; Kopsida et al., 2016; Van Honk et al., 2011). Although activity within the vMPFC during self-referential processing has been positively associated with self-reported pubertal development (Pfeifer et al., 2013), it is as yet unclear whether testosterone affects the neural correlates of self-referential processing.

Not only brain activity patterns, but also functional connectivity between brain regions show developmental changes across adolescence (Grayson and Fair, 2017; Stevens, 2016). A limited number of studies has investigated functional connectivity during self-referential processing in adults, and showed a diverse pattern of connectivity, with increased functional connectivity of the vMPFC with sensorimotor regions and lateral frontal regions in two studies (Lombardo et al., 2010; Van Buuren et al., 2010) and with the insula, amygdala, and striatum in another study (Schmitz and Johnson, 2006). Also, decreased interactions of the vMPFC with the PCC and angular gyri were reported (Van Buuren et al., 2010). Furthermore, in a combined group of adolescents and adults, Davey et al. (2016) showed a negative influence of vMPFC activity on the PCC, and a positive influence of PCC activity on the TPJ and vMPFC during self-referential processing. Although these studies provide initial evidence of the possible functional connectivity patterns underlying self-referential processing, it remains to be explored how functional interactions underlie such processing in young adolescents and how these interactions are influenced by the perceived similarity of others.

Here, we probe self- and other-referential processing and underlying neural activity and connectivity in young adolescents, and examine the effects of peer similarity on other-referential processing. Moreover, we explore for the first time the effects of testosterone levels on brain activity underlying self-referential processing. We are particularly interested in this association in males, given their high puberty-related increases in testosterone levels starting in their early adolescence. Using functional MRI, brain activity was measured during a trait judgement task in which participants had to indicate whether a trait adjective described their personality, that of a classmate regarded as similar, that of a classmate regarded as dissimilar, or whether the trait contains the letter A (control condition). We opted for classmates to better match the (social) context of the two peers, and because young adolescents experience daily interactions with classmates that may shape their self-concept and representations about others. To increase sensitivity in detecting neural activity differences related to peer similarity as well as to self-referential processing, we employ a region-of-interest approach to test our hypotheses. Based on both studies in adults (Denny et al., 2012; Murray et al., 2012; Northoff et al., 2006; Schurz et al., 2014; Van Buuren et al., 2010) as well as studies in adolescents (Pfeifer et al., 2013, 2009; Romund et al., 2017) on self- and other-referential processing, we focus on the vMPFC, dMPFC, TPJ and PCC as *a priori* defined regions-of-interest. We hypothesize that the vMPFC, PCC and TPJ will show an effect of reference, and in addition expect the vMPFC to show a decrease in activity from evaluating the similar to the dissimilar other (Benoit et al., 2010; Krienen et al., 2010; Romund et al., 2017). Additionally, we investigate functional connectivity by examining interactions of the vMPFC during self- and other-referential processing, however we do not have specific hypotheses regarding the emerging connectivity patterns due to the novelty of this study aim. Last, given findings of developmental-related differences in activity within the vMPFC and dMPFC during self-referential processing (Pfeifer et al., 2013, 2009; 2007; van der Cruijsen et al., 2018), we tentatively expect activity within the vMPFC to be positively associated, and activity within the dMPFC to be negatively associated with inter-individual differences in testosterone.

2. Material and methods

2.1. Participants

The current study is part of a longitudinal study, the #SO CONNeCT project, investigating the development of social cognition, behavior and social networks during adolescence. Six hundred ninety-two young adolescents were included in October 2017 in the first year of their secondary education and are tested twice a year for 3 years at school in a classroom setting. Informed consent was obtained from both parents and adolescents, and participants could indicate if they were interested in receiving information about additional participation opportunities within the #SO CONNeCT study, including the fMRI study. We then contacted all participants that showed initial interest and fulfilled the inclusion criteria of the full MRI study (370 adolescents). Of these potential participants, 284 were excluded from participation (44% had dental braces, a contraindication for MRI, 37% did not want to participate, 19% failed to reply), and 86 agreed to participate and did not have any contraindications for MRI or a self-reported current or past neurological disorder. All participants and their parents gave additional written informed consent for the fMRI study part before participation. Two participants were anxious either before scanning started or at the beginning of the scan session, therefore fMRI data was acquired of 84 young adolescents. In total, 18 participants (mean 12.9 $\pm$ 0.3 years; 8 females, 10 males; 5 left-handed) were excluded from data analyses; 9 were excluded because of excessive motion (total displacement of more than 3 mm), 3 because of incorrect task execution (wrong buttons were used), and 6 because of failure to measure testosterone accurately (in 5 participants testosterone could not be detected and in 1 participant testosterone level was more than thirty times as high as the average measured male testosterone level). This resulted in 66 participants (aged 11–14 years, mean 12.9 $\pm$ 0.4 years; 28 females, 38 males; 10 left-

handed) for data analyses. The included and excluded participants did not differ in age ($p = .500$), gender ($p = .878$), or handedness ($p = .296$). After participation, participants received a picture of their brain and €20 as monetary compensation. The experimental protocol was reviewed and ethical approval was provided by the institutional review board (VCWE, Faculty of Behavioral and Movement Sciences, VU Amsterdam, The Netherlands).

2.2. General procedure

When arriving at the research center, participants and their parents signed the informed consent and filled in a questionnaire to check for MRI contraindications. Furthermore, participants were instructed to fill in a brief questionnaire about two of their classmates. In the questionnaire, participants were first asked to give the name of a classmate who was perceived as being similar (similar beliefs, interests, sports) and the name of a classmate who was regarded as dissimilar. The names of these classmates were subsequently used in the trait judgement task as cues for the similar and dissimilar other condition. Both classmates had to be well known and liked by the participant. This was done to ensure that the participants would be able to make trait judgements about both of the classmates, and to limit the effects of liking and familiarity instead of perceived similarity on other-referential processing. The names of the two classmates were noted down and participants were asked to rate, on a scale of 1–10, how similar the classmates were (i.e. similarity), how familiar they were to them (i.e. familiarity), and how much they liked them (i.e. liking). When the two classmates differed on similarity ratings with less than 4 points, the participants were asked if they could think of a classmate they regarded as more similar or more dissimilar. After the questionnaire, participants received instructions about the MRI scanner procedure and the trait judgement task was explained. Participants were then asked to rinse their mouth with water and were placed in a mock MRI scanner where MRI sounds were played and the participant practiced another task that was performed during scanning (not part of the current study). Next, saliva was obtained by passive drool (see section ***2.4 Testosterone and pubertal development measurements***). Participants were then placed in the MRI scanner and button boxes for the left and the right hand were placed on the lower abdomen. Participants could view the task presented on a screen through a mirror mounted on the head coil.

2.3. Experimental task

In the trait judgement task (Craik et al., 1999; Kelley et al., 2002; Van Buuren et al., 2010) (see Fig. 1), participants were asked to indicate whether a trait adjective described themselves (self condition), the classmate regarded as similar (similar other condition), the classmate regarded as dissimilar (dissimilar other condition), or whether the trait contained the letter "a" (control condition), by pressing the left "yes" or the right "no" button with their index fingers (see Fig. 1). In total, 160 adjectives were presented, 80 of negative and 80 of positive valence. The positive and negative adjectives were equally, but randomly, distributed to each condition and presented in blocks of five per condition. The order of the adjectives was randomized per subject and per condition in a pseudorandom fashion, with no more than three adjectives of the same valence in a block. The blocks were presented in a pseudorandom order, with one block of each condition presented randomly after each other, followed by a rest period of 17 s. Each block started with a cue of 1 s indicating the condition, which contained the name of the classmate regarded as similar to indicate the similar condition and the name of the dissimilar classmate to indicate the dissimilar condition (see Fig. 1). The cue was followed by five adjectives that were each presented for 3 s or until the participant pressed a button. After responding, a fixation cross was presented for the remaining trial duration. The task was programmed in and presented with Presentation (version 19.0, Neurobehavioral Systems). Endorsement of negative and positive traits in the three experimental conditions (self, similar other and dissimilar other), as well as reaction time in these conditions were used for behavioral analyses.

2.4. Testosterone and pubertal development measurements

To measure testosterone levels, saliva was obtained approximately 1 h after arriving at the research center using passive drool. Time of sampling differed from approximately 10:30 in the morning until 3:30 in the afternoon, with 1 h intervals between participants. Participants were provided with a cryovial locked in a Saliva Sampling Aid kit (Salimetrics) and were instructed to passively drool into the kit, until between 1 and 2 ml of saliva was collected. To avoid distress of the participants, collection was stopped after 10 min if an insufficient amount had been collected. Saliva was stored at -20° and sent to the Dresden Lab Service, TU Dresden, on dry ice after all participants were tested. Testosterone was measured using liquid chromatography with coupled tandem mass spectrometry (LC-MS/MS).

As part of the behavioral data acquisition at schools that took place approximately zero to three months after the end of the fMRI data acquisition, pubertal development was measured using the Pubertal Development Scale (PDS (Petersen et al., 1988)) administered on Ipads. Participants indicated on a four-point scale whether and how a physical characteristic of puberty was developed. The questionnaire contained three characteristics applicable for boys and girls (body growth, pubic hair, skin changes), two applicable only for boys (voice changes, facial hair) and two only for girls (breast development and menarche). The average score was calculated and used for analysis (Op de Macks et al., 2016). PDS data of 4 participants were missing, limiting this analysis to 62 participants (26 female, 36 male).

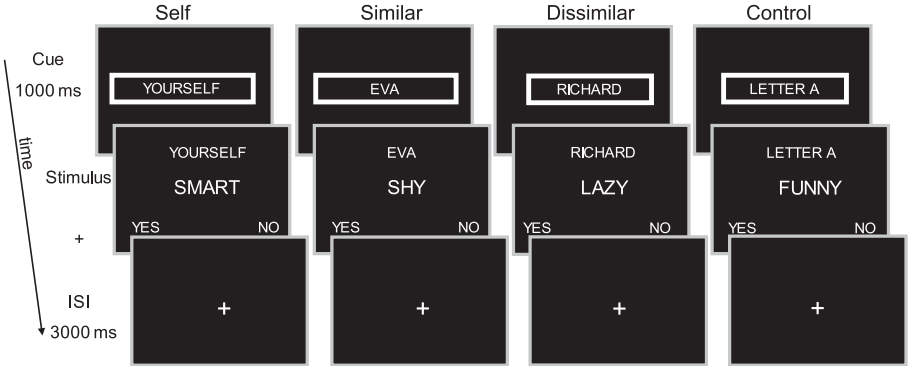

Fig. 1. Trait judgement task. The task comprised four conditions presented in blocks of five adjectives. A cue was presented at the start of each block for 1 s, followed by the first adjective, with a reminder of the condition at the top of the screen and the response options at the bottom. The interstimulus interval (ISI) depended on the reaction time, when a participant responded within 3 s, a fixation cross appeared for the remaining trial duration.

2.5. Peer ratings and behavioral analyses

Ratings of similarity, familiarity and liking of the similar and dissimilar classmate used in the trait judgement task were compared using paired-sample t-tests. Effect sizes were calculated using Cohen's d.

Next, to examine behavioral responses during the three reference conditions of the trait judgement task, endorsement of positive and negative traits (i.e. yes responses to positive and negative traits respectively) and reaction time were analyzed as dependent variables in two separate ANOVAs. Repeated-measures ANOVAs were carried out for endorsement and reaction time with reference condition (self, similar, dissimilar) and valence (positive, negative) as factors, and were each followed by one-way ANOVAs per valence and per condition, as well as pairwise comparisons between the conditions and between negative and positive traits when indicated by significant interactions and main effects. To control for possible effects of age, motion or gender on reaction time and endorsement, mean-centered values of age and motion (calculated as framewise displacement in mm (Power et al., 2012)) were included as covariates and gender as between-subject factor in the behavioral analyses. Greenhouse-Geisser correction was applied when the assumption of sphericity was violated and all post-hoc pairwise comparisons following significant one-way ANOVAs were corrected for multiple comparisons using a Bonferroni-corrected threshold of $p = .016$ ($p = .05/3$ reference conditions).

2.6. MRI data acquisition

MRI data were acquired on a 3.0 T Philips Ingenia CX MRI scanner equipped with a 32-channel-phased array head coil (Spinoza Centre for Neuroimaging; Philips Medical Systems, Best, The Netherlands). During the trait judgement task, 326 functional images were obtained using a two-dimensional echo planar imaging-sensitivity encoding (EPI-SENSE) sequence, with the following parameters: voxel size 3 mm isotropic; repetition time (TR): 2000 ms; echo time (TE): 27.63 ms; flip angle = 76.1°; matrix 80 x 80; field of view 240 x 240 x 121.8; 37-slice volume with a 0.3 mm gap. Next, a T1-weighted structural image was acquired using a three-dimensional fast field echo sequence (parameters: voxel size 1 mm isotropic, TR = 8.2 ms; TE = 3.7 ms; flip angle = 8°; matrix 240 x 188; field of view 240 x 188 x 220; 220 slices in total).

2.7. MRI data preprocessing

The functional and anatomical images were spatially preprocessed using SPM12 (http://www.fil.ion.ucl.ac.uk/spm). Functional images were realigned to the reference image, followed by co-registration of the structural image to the mean functional image obtained after realignment using mutual information optimization. Next, unified segmentation was applied. To segment the co-registered structural image and to estimate the normalization parameters, tissue probability maps matched for the age and gender of our subject sample were generated using the CerebroMatic toolbox (Wilke et al., 2017) and implemented in SPM12 to perform segmentation. Subsequently, estimated normalization parameters were used to transform the functional images as well as the structural image into Montreal Neurological Institute (MNI) space. Voxel size of the functional images remained 3 mm isotropic after normalization. As a final step, a 3D Gaussian filter (6-mm full width at half maximum) was applied to smooth the normalized functional images.

2.8. Definition of regions-of-interest

Regions-of-interest (ROIs) were based on the meta-analysis of Denny et al. (2012) of studies on self and other-referential processing. ROIs were created by 10-mm radius spheres centered on the peak coordinates of activation within the vMPFC (coordinates x, y, z = −6, 56, 10), dMPFC (x, y, z = −6, 54, 32), PCC (x, y, z = −4, −56, 30) and left TPJ (x, y, z = −50, −62, 22) in a conjunction analysis of activity during self and other-referential processing conditions. For the right TPJ, mirrored coordinates of the left TPJ were taken as the center of the 10 mm sphere.

2.9. MRI data analyses

Normalized and smoothed functional images were submitted to a general linear model regression analysis. This analysis contained four regressors of interest, modeling the four conditions (self, similar, dissimilar and control). These regressors were time-locked to the onset of the first trial of each block and modeled with a box-car function of 15 s. The cue periods were modeled as a regressor of no-interest (duration 1 s). All regressors were convolved with a canonical hemodynamic response function (Friston et al., 1995). Additionally, the six realignment parameters were included as regressors of no-interest to remove head motion and a high-pass filter was applied to remove low-frequency fluctuations (cut-off 128 s). Next, contrast images were created by contrasting each reference condition to the control condition and to each other.

To examine activity during self- and other-referential processing, ROI-analyses were performed by extracting contrast estimates for each subject and each ROI using the MarsBar toolbox (version 0.44, http://marsbar.sourceforge.net/). These average signal changes (all relative to the control condition) were submitted to a repeated-measures ANOVA with reference condition (self, similar and dissimilar) and ROI (vMPFC, dMPFC, PCC, left and right TPJ) as factors. To control for effects of age, motion and gender, these variables were again included in the model. When indicated, this analysis was followed by a one-way ANOVA for each ROI and post-hoc pairwise-comparisons. Greenhouse-Geisser correction was applied when the assumption of sphericity was violated and all post-hoc pairwise comparisons were corrected for multiple comparisons using a Bonferroni-corrected threshold of $p = .016$. Moreover, to explore the activity pattern outside our ROIs, we performed exploratory whole-brain analyses. Again, to test the effect of reference on brain activity, a one-way repeated-measures ANOVA was conducted with reference condition (self, similar, dissimilar, all relative to the control condition) as factor, and age, motion and gender as control variables. Follow-up t-tests were performed to elucidate a main effect of reference. A normalized average grey matter mask of all subjects was used as an explicit mask during model specification of the second-level analyses.

Last, we investigated functional connectivity of the vMPFC during self- and other-referential processing using the generalized form of context-dependent psycho-physiological interaction analyses (gPPI, (McLaren et al., 2012). Generalized PPI shows changes in functional connectivity between a seed region (vMPFC) and the rest of the brain in interaction with a psychological variable, or a task condition. Using the gPPI toolbox (version 13.1, https://www.nitrc.org/projects/gppi), we extracted for each subject the timecourse of the vMPFC and adjusted it for average activation during the task. Next, for each subject, we created a first-level gPPI model comprising the task conditions, the timecourse of the vMPFC, interactions between the task conditions and this timecourse, as well as the motion regressors. As we were interested in changes in connectivity during the self condition relative to the control condition, and during the two other conditions relative to the control condition and to the self condition, we created contrast images for these respective condition-dependent interactions. These contrast images were then submitted to second-level one-sample t-tests and tested for significance using cluster-inference with a cluster-defining threshold of $p < .001$, and a cluster-probability of $p < .05$ family-wise error corrected (FWE). Age, motion and gender were again included in the analyses and a normalized average grey matter mask of all subjects was used as an explicit mask during model specification of the second-level analyses.

To test if the results remain consistent when excluding the 10 left-handed participants, we repeated the behavioral, ROI and connectivity analyses on the 56 right-handed participants. Results were largely consistent with the findings of the analyses on the whole group and main findings remained significant (see supplementary materials and Supplementary Table 3).

2.10. Testosterone analyses

To test the assumption that testosterone levels are more pronounced in boys compared to girls, testosterone levels of boys and girls were compared using a two-sample *t*-test. Furthermore, we correlated scores on the PDS with testosterone measures in the whole group, and in boys and girls separately, to test the assumption that testosterone is especially related to male pubertal development. Additionally, we examined whether testosterone levels correlated with time of day of sampling. To this aim, we divided time of day into two groups, before and after 1:00 in the afternoon, resulting in two groups of 17 and 21 males (36 and 30 participants in the whole group), respectively, and subsequently calculated the association between time of day and testosterone levels using a non-parametric correlation analysis.

Next, to test our hypotheses regarding the association between testosterone levels and activity within the vMPFC and dMPFC during self-referential processing, we calculated the correlation (Pearson's *r*) between activity within these ROIs and testosterone levels in boys. In case of significant findings, we investigated the specificity of the result for males by repeating the analysis in female participants. Moreover, to control for possible effects of time of day of saliva sampling, we ran a linear regression analysis with time of day as independent variable and testosterone as dependent variable and saved the unstandardized residuals. Using these testosterone levels adjusted for time of day of sampling, we again analyzed the association with activity within the vMPFC and dMPFC during the self condition (relative to the control condition). Additionally, we explored the association between testosterone levels and whole-brain activity during the self condition relative to the control condition, by adding testosterone levels as a covariate in a whole-brain group analysis. Results of this exploratory analysis are presented in the supplementary material, see Supplementary Table 2.

2.11. Data and code availability

The participants and their parents did not provide explicit consent for public archiving of the research data, therefore the data is not stored in a public repository. However, anonymized data will be made available to individual researchers upon request, when compatible with the General Data Protection Regulation. Additionally, researchers that request the data will be required to have obtained ethics approval from their host institution and are not allowed to share the data. Matlab code that was written to preprocess and analyze the fMRI data has been made publicly available on Github.

(https://github.com/marietvbuuren/self_other_2020).

3. Results

3.1. Peer ratings

Ratings of similarity, familiarity and liking all differed significantly between the similar and dissimilar classmate (see Table 1). Effect sizes were large for all three effects, however, effect size for the difference in similarity was more than three times as large as the effect sizes of familiarity and liking (see Table 1).

Table 1
Average ratings on a 10-point scale of similarity, familiarity and liking of the classmate regarded as similar and of the classmate regarded as dissimilar. Differences in ratings between the classmates were tested with paired-sample t-tests. SD = standard deviation, between brackets.

	Similar classmate mean (SD)	Dissimilar classmate mean (SD)	statistic	p	Cohen's d
Similarity	8.11 (0.70)	3.79 (1.30)	$t(65) = 29.12$	<.0005	3.58
Familiarity	8.44 (1.36)	6.79 (1.97)	$t(65) = 5.74$	<.0005	0.71
Liking	9.00 (0.93)	7.52 (1.47)	$t(65) = 8.04$	<.0005	0.99

3.2. Behavioral findings

First, differences in the endorsement of negative and positive traits between the self, similar and dissimilar other were examined (see Table 2). We observed an interaction effect of reference by valence ($F(1.71, 105.86) = 11.18$, $p < .0005$) as well as main effects of reference ($F(1.80, 111.37) = 5.31$, $p = .008$) and valence ($F(1,62) = 401.90$, $p < .0005$). No main effects were observed for age ($p = .936$), motion ($p = .257$) or gender ($p = .698$). Follow-up one-way ANOVAs were conducted to test the effect of reference condition for positive and negative traits separately, as well as to test the effect of valence per reference condition. These analyses showed a main effect for reference for both positive ($F(1.70, 105.50) = 11.66$, $p < .0005$) and negative traits ($F(1.78, 110.31) = 5.69$, $p = .004$), and a main effect of valence for the self ($F(1,62) = 283.03$, $p < .0005$), similar ($F(1,62) = 267.15$, $p < .0005$) and dissimilar condition ($F(1,62) = 91.82$, $p < .0005$). Pairwise comparisons of endorsement between the three reference characters revealed that participants endorsed fewer negative traits in the similar other condition compared to the self condition ($t(65) = 3.04$, $p = .003$) and compared to the dissimilar condition ($t(65) = 2.70$, $p = .009$), and fewer positive traits in the dissimilar compared either to the self condition ($t(65) = 3.59$, $p = .001$), or to the similar condition ($t(65) = 3.94$, $p < .0005$). Pairwise comparisons between negative and positive traits showed that participants endorsed more positive traits compared to negative traits in all three conditions (self: $t(65) = 17.40$, $p < .0005$; similar: $t(65) = 16.93$, $p < .0005$; dissimilar: $t(65) = 9.65$, $p < .0005$).

Next, reaction time differences between the reference conditions and positive and negative traits were analyzed (see Table 2). A repeated measures ANOVA revealed an interaction effect of reference by valence ($F(2,124) = 4.14$, $p = .018$) and a main effect of reference on reaction time ($F(2,124) = 4.61$, $p = .012$), no main effect of valence was observed ($p = .086$). No main effects were observed for age ($p = .936$), motion ($p = .929$) or gender ($p = .567$). Follow-up one-way ANOVAs showed a main effect of reference on reaction time for both the positive and negative traits ($F(2, 124) = 4.18$, $p=.017$, and $F(2, 124) = 4.83$, $p=.010$), respectively). A main effect of valence was observed within the self condition only ($F(1, 62) = 11.43$, $p=.001$) (similar condition: $p = .616$; dissimilar condition: $p = .781$), with faster responses to the positive traits compared to the negative traits ($t(65) = 3.21$, $p = .002$). Post-hoc pairwise comparisons of reaction time of the reference conditions revealed that the participants responded faster to positive traits in the similar condition compared to the dissimilar condition ($t(65) = 2.48$, $p = .016$), and to negative traits in the similar condition compared to the self condition ($t(65) = 3.17$, $p = .002$).

3.3. Brain activity

A repeated-measures ANOVA was conducted to test for the effect of

Table 2
Average endorsement in number of adjectives and reaction time in ms of responses to the positive and negative adjectives in the three reference conditions. SD = standard deviation, between brackets.

	Self mean (SD)	Similar mean (SD)	Dissimilar mean (SD)
Endorsement positive traits	14.27 (2.92)	14.70 (3.25)	12.23 (4.05)
Endorsement negative traits	4.74 (2.85)	3.67 (3.06)	4.95 (3.20)
Reaction time positive traits	1222 (188)	1216 (219)	1267 (217)
Reaction time negative traits	1272 (205)	1222 (194)	1260 (193)

reference (self, similar, dissimilar, all against control condition) in the five ROIs (vMPFC, dMPFC, PCC, lTPJ, rTPJ; see Fig. 2A). A main effect was observed of ROI (F (3.22, 199.57) = 83.46, p < .0005) and an interaction effect of reference by ROI was revealed (F (6.25, 387.75) = 19.58, p < .0005), indicating that the effect of reference on activity differed between the five ROIs (see Fig. 2B). No main effect of condition was observed (p = .205) and no main effects were observed for age (p = .239), motion (p = .691), or gender (p = .090). Follow-up one-way ANOVAs were conducted to test for the effect of reference for each ROI separately. The vMPFC (F (2,124) = 4.79, p = . 010), PCC (F (2,124) = 14.32, p < .0005) and rTPJ (F (1.79, 110.79) = 11.10, p < .0005) showed a significant effect of reference, which was not observed within the lTPJ (p = .525) or within the dMPFC (p = .103). Post-hoc pairwise comparisons of activity between the conditions within the vMPFC, PCC and rlTPJ, revealed increased activity within the vMPFC during self compared to the similar (t (65) = 2.67, p = .009) and compared to the dissimilar condition (t (65) = 2.64, p = .010), however, the predicted decrease from similar to dissimilar was not observed (p = .917). Within the PCC, reduced activity was observed during the self condition compared to both the similar (t (65) = −4.47, p < .0005), and dissimilar condition (t (65) = −5.01, p < .0005), but no differential activity was revealed when comparing the similar and dissimilar other condition (p = .985). Activity within the rTPJ showed a similar pattern, with reduced activity during the self compared to the similar (t (65) = −3.62, p = .001) and dissimilar condition (t (65) = −4.36, p < .0005), but no activity differences were found when comparing the two other reference conditions (p = .835). In sum, ROI analyses showed differential activity within the vMPFC, PCC and rTPJ for self-referential processing relative to other-related processing. However, no activity differences were observed when comparing the similar and dissimilar other conditions.

Additional whole-brain analyses were conducted to test for activity outside the ROIs and reported in the supplementary material, see Supplementary Figure 1 and Supplementary Table 1. These findings are consistent with the ROI findings. In brief, a main effect of reference condition was observed predominantly in medial and right lateral posterior regions. When contrasting the self, similar and dissimilar condition to the control condition, activity increases were largely comparable over the conditions and apparent within the vMPFC, dMPFC, striatum, posterior cingulate cortex, precuneus, as well as left lateral posterior regions, including the temporal parietal junction, temporal gyri and angular gyri. When comparing the similar and dissimilar other conditions to the self condition, we observed increased activity within the posterior midline regions and right angular gyrus, extending into the rTPJ, with additional activity increases in dorsal lateral prefrontal cortices and left angular gyrus during the dissimilar condition. The reverse contrasts revealed increased activity within a left dorsal prefrontal region when comparing the self to the similar other condition, and increased activity within the anterior cingulate cortex during the self condition relative to the dissimilar other condition.

3.4. Brain connectivity

We examined connectivity of the vMPFC with the rest of the brain during self- and other-referential processing (see Fig. 3 and Table 3). No regions showed increased or reduced interactions with the vMPFC during self-referential processing compared to the control condition. During other-referential processing in the similar condition, increased interactions were revealed with the right striatum, extending into the insula, right superior parietal lobule, extending into the post- and precentral gyrus, left middle frontal gyrus, and cerebellum. During the dissimilar condition, the vMPFC showed increased connectivity with the bilateral middle frontal gyri, extending into the precentral gyri, left ventral lateral prefrontal cortex, bilateral superior parietal lobule, overlapping with the angular gyri, right inferior temporal gyrus, and left middle occipital gyrus (Fig. 3A). Again, no reduced connectivity was observed. When comparing the similar condition to the self condition, no differential connectivity was observed with the vMPFC. However, increased interactions between the vMPFC and the bilateral angular gyri

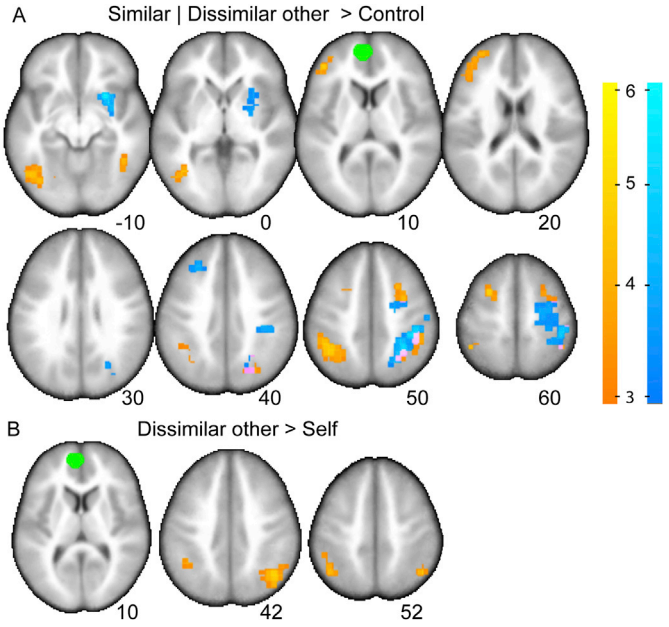

Fig. 3. Connectivity of the vMPFC. Connectivity changes between the vMPFC (seed region in green) and the rest of the brain during **(A)** the similar (cold colors) and dissimilar (warm colors) other condition relative to the control condition. Overlap in connectivity between the similar and dissimilar condition is depicted in purple. **(B)** Connectivity of the vMPFC during the dissimilar other condition relative to the self condition. Results are shown at a cluster-defining threshold of p < .001 and a p < .05 FWE-corrected cluster threshold. Connectivity changes are overlaid on an average anatomical brain obtained with Cerebromatic toolbox, matched for the age and gender of our subject sample. Numbers represent the z coordinates, left = left. Color bars represent t-values.

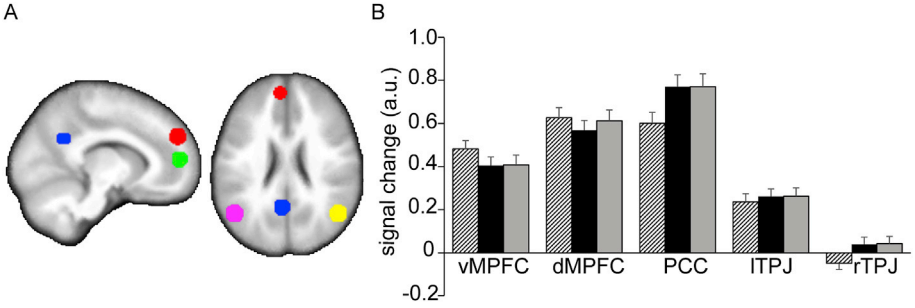

Fig. 2. Activity in the regions-of-interest. A) Colored representation of the five spherical regions-of-interest overlaid on an average anatomical brain obtained with Cerebromatic toolbox, matched for the age and gender of our subject sample; vMPFC (green), dMPFC (red), PCC (blue), left TPJ (pink), and right TPJ (yellow). **B)** Signal changes in all five ROIs (in arbitrary units) during the self condition (striped bars), the similar other condition (black bars) and the dissimilar other condition (grey bars), relative to the non-reference control condition. Error bars depict standard error of the mean.

Table 3
Connectivity changes between the vMPFC (seed region) and the rest of the brain during other-referential processing. MNI coordinates represent the location of the peak voxels of the first local maximum within each cluster. The specific task contrasts are presented in bold. Cluster-defining threshold of $p < .001$ and a $p < .05$ FWE-corrected critical cluster size of 52 voxels. L = left, R = right.

	MNI Coordinates			Z score	voxels
Brain region and contrast	x	y	z		
Similar other > Control					
R putamen	30	9	−6	5.15	129
R superior parietal gyrus	42	−36	51	5.03	714
L middle frontal gyrus	−30	36	45	4.59	59
L cerebellum	−36	−57	−39	4.21	174
R cerebellum	36	−66	−33	3.88	100
Dissimilar other > Control					
L superior parietal gyrus	−42	−54	57	5.27	227
L middle occipital gyrus	−42	−66	−3	4.93	177
R superior parietal gyrus	27	−54	45	4.71	167
L middle frontal gyrus	−27	9	60	4.53	60
L inferior frontal gyrus	−45	42	9	4.39	173
R inferior temporal gyrus	45	−51	−9	4.19	62
R middle frontal gyrus	33	0	54	4.17	83
Dissimilar other > Self					
R angular gyrus	48	−60	48	5.01	162
L angular gyrus	−45	−54	54	4.10	83

were revealed when comparing the dissimilar condition to the self condition (Fig. 3B). No connectivity changes were observed when formally testing the dissimilar condition to the similar condition.

3.5. Association with testosterone

Testosterone levels were significantly higher in male participants (mean ± SD = 14.07 ± 15.93 pg/ml) compared to female participants (mean ± SD = 6.71 ± 2.36 pg/ml; t (39.2) = 2.80, $p = .008$). Moreover, testosterone levels correlated with pubertal development, as measured on the PDS, in the whole group (Pearson's $r = 0.269$, $p = .035$). When testing the correlation between PDS score and testosterone levels separately for males and females, correlation was significant in males only (males: Pearson's $r = 0.508$, $p = .002$, mean ± SD score PDS = 2.02 ± 0.63; females: $p = .273$, mean ± SD score PDS = 2.38 ± 0.76). Time of day of sampling did not correlate with testosterone levels in either the boys, ($p = .498$) or the whole group ($p = .642$). When time of day of sampling was taken as a continuous measure, also no correlation with testosterone levels was observed in the boys ($p = .383$) or in the whole group ($p = .225$).

Next, we examined the association between activity within the vMPFC and dMPFC during the self condition, and individual differences in testosterone levels in the male group. We did not find the predicted association between vMPFC activity and testosterone ($p = .113$), however, dMPFC activity was positively correlated to testosterone levels (Pearson's $r = 0.341$, $p = .036$, see Fig. 4). To test the specificity of this finding, we explored this association in the female group and did not obtain a significant correlation between dMPFC activity and individual variation in testosterone levels ($p = .867$).

To further examine the specificity and robustness of these findings, we ran multiple control analyses. First, because we did not find an effect for reference in the dMPFC in the whole group (see section ***3.3 Brain activity***) or when repeating the ANOVA in the male group ($p = .599$), we examined whether the association with testosterone and dMPFC activity was specific for the self condition. The observed correlation was not specific, and was also observed when correlating testosterone levels with dMPFC activity during the similar condition (Pearson's $r = 0.332$, $p = .041$) and the dissimilar condition (Pearson's $r = 0.349$, $p = .032$). Second, to account for possible effects of time of day of sampling on testosterone levels, we reran the analyses with testosterone levels after controlling for time of day of saliva sampling. These analyses again showed a significant association of testosterone with activity within the dMPFC ($r = 0.326$, $p = .046$) but not the vMPFC ($r = 0.254$, $p = .123$) during the self condition. Third, we tested whether the association between testosterone and dMPFC activity during the self condition remained significant after winsorizing two testosterone values that could be termed statistical outliers to the mean + 3* SD (= 61.86) of the male testosterone levels (Carré et al., 2013). The observed association remained significant, both before and after adjusting for time of day (Pearson's $r = 0.340$, $p = .037$ and Pearson's $r = 0.326$, $p = .046$, respectively).

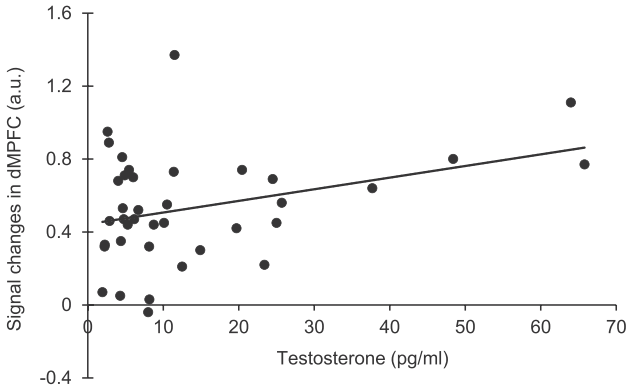

Fig. 4. Association dMPFC activity and testosterone levels. Correlation between testosterone levels and signal changes (in arbitrary units) in the dMPFC during self-referential processing relative to the control condition in the male participants.

4. Discussion

The aim of this study was twofold. First, we examined self- and other-referential processing and underlying neural activity and connectivity in young adolescents, distinguishing between similar and dissimilar peers with other-referential processing. We specifically focused on peers in a school context, as many peer interactions occur in this social environment. An effect of reference was observed for behavioral performance on the task as well as for brain activity in the vMPFC, PCC and right TPJ. Behaviorally, participants endorsed fewer negative adjectives for the similar peer compared to themselves or the dissimilar peer, and fewer positive adjectives for the dissimilar peer compared to themselves and the similar peer. Additionally, participants responded faster to positive traits when evaluating the similar peer compared to the dissimilar peer, and to negative traits when evaluating the similar peer compared to when making self-evaluations. Neurally, we found stronger activity within the vMPFC, and reduced activity within the PCC and right TPJ during self-referential processing compared to other-referential processing, both when evaluating a similar classmate and when evaluating a dissimilar classmate. We did not find an effect of similarity on brain activity during other-referential processing. When probing functional connectivity of the vMPFC, we did not observe changes in connectivity when comparing self-referential processing to the control condition. During other-referential processing, increased connectivity was observed with the right striatum, insula, left dorsolateral frontal region, right superior parietal lobe, right post- and precentral gyrus and cerebellum during the similar condition, as well as increased interactions with bilateral frontoparietal regions, right inferior temporal gyrus and left visual cortex during the dissimilar other condition. When comparing other-referential to self-referential processing, increased interactions with the bilateral angular gyri were revealed in the dissimilar condition only. Second, we explored for the first time the association between inter-individual differences in testosterone levels and activity within the MPFC during self-referential processing. We expected, but did not find, an association between vMPFC activity during self-referential processing and testosterone. We did observe an association of testosterone levels with

dMPFC activity, albeit in the positive instead of in the predicted negative direction. This association was specific to male participants and not present in the female participants.

Our region-of-interest analyses showed differential activity for self- and other-referential processing in the vMPFC, PCC and right TPJ. While the vMPFC was more engaged in self-referential compared to other-referential processing, the PCC and right TPJ showed the reverse pattern. This is in line with most prior studies in adolescents showing increased engagement of the vMPFC in self-, and of the TPJ and PCC (or medial posterior parietal cortex) in other-referential processing (Pfeifer et al., 2013, 2007; Schneider et al., 2012). Interestingly, in our study, the dMPFC and left TPJ did not show an effect of reference and were active during all reference conditions. This absence of a reference effect may be due to increased involvement of both regions in self-referential processing during adolescence. In line with this notion, prior research showed enhanced recruitment of the dMPFC and left, but not the right, TPJ during self-referential processing in young adolescents and children when compared to adults (Pfeifer et al., 2009, 2007). Moreover, increased activity within the dMPFC and TPJ was reported in mid-adolescents during self compared to other-referential processing (Romund et al., 2017). The PCC and lateral posterior regions, including the TPJ, have been related to self-referential processing (Northoff et al., 2006) through their role in episodic and autobiographical memory processes (Rugg and Vilberg, 2013) as well as in detecting and assessing salient stimuli (Cabeza et al., 2008), while the dMPFC has been implicated in evaluating self-relevant stimuli (Schmitz and Johnson, 2006). On the other hand, these regions have also been implicated in social cognitive processes, such as mentalizing (Blakemore, 2008; Mars et al., 2012). It is possible that adolescents may rely more on the opinions of peers when making trait judgements about themselves and are engaged in such mentalizing processes when developing their own self-concept, resulting in more involvement of the dMPFC and left TPJ during self-referential processing (Pfeifer et al., 2009; Romund et al., 2017). However, although appealing, this notion has to be tested by future studies incorporating both adolescents and adults.

We did not observe any effects of similarity on brain activity within our regions-of-interest. Based on prior research, we did not expect such an effect within the PCC or TPJ (Denny et al., 2012; Krienen et al., 2010). However, we did predict an effect of similarity of the reference person on vMPFC activity. Such an effect was recently observed in mid-adolescents in response to various other-reference characters (Romund et al., 2017), and, similarly, increased vMPFC activity with increasing similarity ratings was reported in adults (Benoit et al., 2010). The lack of such a finding here might be due to the use of only peers in our study. Even though the participants did rate the selected peers differently on the dimension of similarity, both peers were classmates of the participant, and were both familiar to and liked by the participants. This might have resulted in feelings of closeness to or personal relevance of both classmates, which in turn, might have resulted in comparable engagement of the vMPFC. That is, the vMPFC is involved in identifying stimuli as personally relevant or significant through integrating affective and cognitive processes (D'Argembeau, 2013). This idea is supported by studies showing activity in the vMPFC in relation to perceived closeness or relevance and not just to similarity of others (Krienen et al., 2010; Moore et al., 2014).

Next, we examined functional connectivity of the vMPFC during self- and other-referential processing. Although no connectivity changes were observed during self-referential processing relative to the control condition, connectivity patterns were widespread during other-referential processing and seemed to depend on the similarity of the other, with increased vMPFC connectivity with the right striatum, insula, left dorsolateral frontal cortex, the right superior parietal lobe and cerebellum during the similar other condition, and increased connectivity with bilateral dorsal and left ventral prefrontal regions, bilateral superior parietal and angular gyri, as well as right inferior temporal gyrus and left visual cortex during the dissimilar other condition. Overlap was limited and mostly apparent in the right superior parietal lobe. However, no differential connectivity was revealed when directly comparing the two other-reference conditions. Interestingly, evaluating the similar peer resulted in increased connectivity with the right striatum, while evaluating the dissimilar peer was accompanied by increased connectivity with more widespread fronto-parietal regions, and, when compared to self-referential processing, with the angular gyri. The striatum, as well as the vMPFC (D'Argembeau, 2013), is involved in reward-related processing, but also implicated in self-related processing possibly by assessing personal relevance or value (Northoff and Hayes, 2011). Striatal activity was observed in young adolescents when they reflected on social self-evaluations made from the perspective of their best friend (Jankowski et al., 2014), and when anticipating social evaluations of peers of high compared to low interest (Guyer et al., 2009). Increased interplay between the vMPFC and striatum may possibly reflect integration of reward or value-based, and self-related processing when evaluating a personal close and relevant peer. Also, this interplay might not only be related to the perceived similarity of the peer, but also to feelings of liking that could heighten the personal relevance and value of peer. In line with this, striatal and vMPFC involvement were previously reported in response to being liked (Davey et al., 2010). Evaluating a peer perceived as being dissimilar on the other hand, is supported by interactions of the vMPFC and frontoparietal regions as well as the angular gyri, which might reflect more effortful, memory-related processing (Cole et al., 2013; Sestieri et al., 2017). This interpretation is, however, speculative and further investigation is warranted, especially when considering the limited number of studies that have investigated functional interactions of the vMPFC during self- and other-referential processing.

Last, we explored the role of inter-individual differences in testosterone on neural activity within the MPFC during self-referential processing. We did not find the hypothesized association with vMPFC activity, but did observe a positive association of individual differences in testosterone levels and dMPFC activity in male participants. Testosterone levels increase especially in males during puberty, and we were therefore particularly interested in the relation to activity levels in males. Indeed, self-reported pubertal status was correlated to testosterone only in males, in line with previous studies (Herting et al., 2012; Op de Macks et al., 2016). Based on prior research showing developmental decreases in dMPFC activity during self-referential processing (Pfeifer et al., 2009, 2007), we expected a negative, instead of a positive association with testosterone. However, these studies compared brain activity of adolescents or children with brain activity of adults, instead of across adolescence. One study did probe changes across adolescence and showed developmental-related increases in activity during self-referential processing in a combined dorsal and ventral MPFC region (van der Cruijsen et al., 2018). It might therefore be possible that dMPFC activity during self-referential thought first increases during adolescence, before decreasing towards adulthood. Although our finding may suggest that individual differences in testosterone may affect neural correlates of self-referential processing, it should be interpreted with caution. First, the association between testosterone levels and dMPFC activity was not specific to self-referential processing, but was also present during other-referential processing. This lack of specificity might be due to the absence of differential activity of the dMPFC related to the reference character (i.e. self, similar or dissimilar other). Alternatively, we tentatively suggest that with increasing levels of testosterone and advancing puberty, adolescents may rely more strongly on the perspective of others, resulting in involvement of the dMPFC in both self- as well as other-evaluations. However, longitudinal investigation is necessary to probe if and when this association between dMPFC activity and testosterone levels weakens, and when adolescents engage the dMPFC less during self-referential processing and reach the level of adult dMPFC recruitment. Second, testosterone levels varied widely between participants resulting in high levels in some participants. During adolescence, testosterone levels show up to 7-fold increases in boys (Khairullah et al.,

2014), making these high testosterone levels not only biologically plausible but even the most interesting cases, rather than mere outliers. However, the observed association with dMPFC activity during self-referential processing was strongly affected by these participants although the findings remained significant after applying winsorizing.

Of note, we were interested in the relation between neural activity during self-referential processing and inter-individual differences in testosterone levels. These inter-individual differences in testosterone levels may not only be related to inter-individual differences in pubertal status, but instead may also be present between individuals of the same pubertal status (Dorn, 2006). Moreover, testosterone has been reported to affect social cognitive processing and underlying neural correlates in adults (Bos et al., 2016; Kopsida et al., 2016; Van Honk et al., 2011), indicating that differences in hormone levels affect such processing beyond puberty. Our finding of increased dMPFC activity with higher individual levels of testosterone might therefore not be specifically related to puberty, but may instead be related to testosterone levels in general. A related possible caveat of our study is that by analyzing boys and girls separately, our sample size was relatively small to probe individual differences in activity levels in relation to hormone levels. Also, it would have been interesting to investigate the association between brain activity and other hormones, for example estrogen, that change profoundly during puberty in addition to testosterone. However, our study is an initial investigation of the effects of testosterone on neural activity underlying self-referential processing, and provide a basis for future studies to build upon. Another possible limitation of our study concerns our operationalization of the two other-reference characters. To be able to test the influence of peers of the highly salient social context of school on the developing self-concept, we chose to use two classmates. Although these classmates did differ on the dimensions of similarity, familiarity and liking, instead of only similarity, the two peers may have been too much alike given the shared context of the class. That is, while endorsement of the traits and reaction times on the task did differ between the two peers, neural activity underlying other-referential processing did not differ between the two peers. It would be interesting to probe differences in neural activity by including a third, more distant peer or reference character in follow-up studies. Additionally, to investigate the effects of similarity, liking and familiarity, future studies might consider using a paradigm that incorporates other-reference characters with a broader range of ratings on these dimensions. Last, studies have recently shown that both type and valence may affect activity underlying self-referential processing (Pfeifer et al., 2013; van der Cruijsen et al., 2018, 2017). Here, we used a block-design with different types of both negative and positive traits within one block. Although this design provided robust activity levels and enabled connectivity analyses, event-related study designs may be better suited to investigate interactions of valence, type and peer influences in one experiment.

This study investigated the influence of similarity of peers on self- and other-referential processing and underlying neural mechanisms in young adolescents. We did not find an effect of similarity on brain activity during other-referential processing, instead we showed more engagement of the vMPFC in self-referential processing, and of the PCC and right TPJ in other-referential processing. Functional connectivity of the vMPFC underlying other-referential processing were wide-spread and included the striatum when evaluating the classmate perceived as similar and more frontoparietal regions when evaluating the dissimilar peer. Furthermore, we examined the effects of testosterone levels on brain activity underlying self-referential processing and showed for the first time a positive association between inter-individual differences in testosterone levels in males and activity of the dMPFC. In sum, this study provides insight into self-referential processing and the influence of peer similarity on both activity and connectivity underlying other-referential processing in young adolescents, and suggests that testosterone levels, which change profoundly during adolescence, may affect neural correlates of self-referential processing.

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Declaration of competing interest

None.

CRediT authorship contribution statement

Mariët van Buuren: Conceptualization, Methodology, Software, Formal analysis, Writing - original draft, Project administration, Supervision. **Reubs J. Walsh:** Conceptualization, Investigation. **Hester Sijtsma:** Investigation, Project administration, Resources. **Miriam Hollarek:** Investigation, Project administration, Resources. **Nikki C. Lee:** Project administration, Supervision, Resources. **Peter A. Bos:** Writing - review & editing. **Lydia Krabbendam:** Conceptualization, Writing - review & editing, Supervision, Funding acquisition.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neuroimage.2020.117060.

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