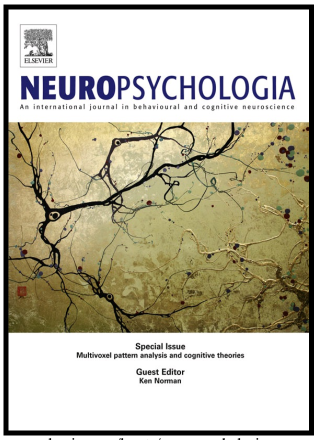

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Difference in neural response to social exclusion observation and subsequent altruism between adolescents and adults

Original Article

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Abstract

Empathy and prosocial behaviors toward peers promote successful social development and creation of significant long-term relationships, but surprisingly little is known about the maturation of these skills during the period of adolescence. As the majority of studies have used questionnaires or pain observation paradigms, it remains unknown whether the empathic response of adolescents differs from that of adults in a paradigm that is closer to everyday life. In the current study, fMRI was used to examine the neural correlates of social exclusion observation and subsequent prosocial behavior in 20 adolescents (aged 12-17 years) and 20 adults (aged 22-30 years) while playing a ball-tossing game with what they believed to be real individuals. Observing someone being excluded compared to observing equal inclusion of all players elicited a significantly higher activation of the IFG (pars triangularis) in adults compared to adolescents. When given the opportunity to directly help the excluded player during the game, adolescents showed significantly less prosocial behavior than adults, which was underpinned by a significantly lower activity in the right temporoparietal junction, medial/dorsomedial prefrontal cortex and fusiform face area. These findings might indicate that adolescents have a lower propensity to take the victim's perspective and share his or her distress when witnessing social exclusion, which leads to a lower altruistic motivation to help. The factors that could generate what can be interpreted as a downward modulation of empathy during adolescence are discussed.

Keywords: Empathy; altruism; prosocial; adolescence; development; social exclusion

1. Introduction

Social interactions, whether they are real or virtual, are central to our lives. One of the interpersonal faculties that support and harmonize these exchanges is empathy, the ability to share and understand other's affective states. Although empathy is a quite complex phenomenon, it is generally conceptualized as comprising two main aspects that work together to generate an empathic response: i) affective sharing, which refers to a bottom-up process leading to the vicarious experience of other's emotional state, and ii) perspective-taking, which consists in a deliberate projection into the other's perspective in order to understand his/her feelings, and is often considered to be closely related to mentalizing (Bird & Viding, 2014; Decety & Jackson, 2004; Engen & Singer, 2013; Shamay-Tsoory, 2011). The neural correlates of affective sharing have typically been studied by looking at the shared representations of directly experienced pain and pain observation, mainly involving activation of bilateral anterior insula (AI) and adjacent inferior frontal gyrus (IFG), as well as the dorsal anterior cingulate cortex/anterior midcingulate cortex (dACC/aMCC; Lamm, Decety, & Singer, 2011). Another meta-analysis has revealed activation of these same regions during observation of various emotional states, including studies that explicitly asked to share other's emotional state (Fan et al., 2011). The neural correlates of perspective-taking can be highlighted in paradigms where participants have to imagine how others might feel, but in which there is no direct evidence of distress (Lamm et al., 2011; Masten, Morelli, & Eisenberger, 2011), mainly revealing activation of the medial prefrontal cortex (mPFC), posterior cingulate cortex (PCC), superior temporal cortex, temporal poles and temporoparietal junction (TPJ; Frith & Frith, 2006; Van Overwalle & Baetens, 2009).

The experience of empathy can lead to different reactions, such as a personal distress accompanied by a desire to withdraw from the situation, or a feeling of empathic concern that typically produces a desire to help (Singer & Klimecki, 2014). In the last few years, increasing attention has been given to what is called altruistic motivation or prosocial drive (Decety, Bartal, Uzefovsky, & Knafo-noam, 2015; Zaki & Ochsner, 2012). According to Batson's empathy-altruism hypothesis (Batson, 2011), empathic concern towards another automatically produces a desire to enhance his/her welfare, and this altruistic motivation may lead to prosocial behavior depending on other motivational forces present at the time. This relationship between empathy and prosocial behavior has also been supported in other behavioral studies (Eisenberg & Fabes, 1990; Lockwood, Seara-Cardoso, & Viding, 2014). The neural correlates of prosocial behavior still remain unclear as this complex process likely comprises a number of cognitive sub-processes, but a few studies have pointed out the role of regions implicated in reward-processing, including the orbitofrontal cortex (OFC), the ventral striatum, the nucleus accumbens, the caudate nucleus and the subgenual ACC (FeldmanHall, Dalgleish, Evans, & Mobbs, 2015; Harbaugh, Mayr, & Burghart, 2007; Lockwood, Apps, Valton, Viding, & Roiser, 2016; Zaki & Mitchell, 2011).

Empathy and prosociality are key processes for successful social development, especially during the stage of adolescence when peer relationships are central (Beauchamp & Anderson, 2010). Adolescents are facing a great deal of psychological and social challenges, such as peer rejection experiences, which are particularly prevalent at this age and may lead to severe and long-lasting mental health problems (Arseneault, Bowes, & Shakoor, 2010; Nishina & Juvonen, 2005). A lack of empathy during this period might play a role in these negative social behaviors and, more generally, could threaten the creation of long-lasting relationships (Allemand, Steiger, & Fend, 2014; van Noorden, Haselager, Cillessen, & Bukowski, 2014).

Behavioral studies have shown that affective sharing develops well before adolescence, whereas perspective-taking shows a more protracted course of development (for reviews see Decety, 2010; Tousignant, Eugène, & Jackson, 2015). The few neuroimaging studies on empathy development generally support these conclusions. For instance, using an fMRI pain observation paradigm in children, adolescents and adults, Decety and Michalska (2010) showed a gradual shift with age from a visceral response to the emotional representation of pain, as suggested by activation in the posterior insula, medial OFC and amygdala, to a more detached and regulated appraisal of the stimulus, associated with activation in the left IFG, right dorsolateral PFC, lateral OFC and AI. Similarly, observing intentional harm towards another has been shown to elicit a gradual decrease in amygdala activity and an increase in mPFC in participants from 4 to 37 years old (Decety, Michalska, & Kinzler, 2012). The development of perspective-taking abilities with age might provide a greater top-down modulation that favors a more adapted empathic response, an hypothesis also raised in other neuroimaging studies of pain observation using EEG (Cheng, Chen, & Decety, 2014; Mella, Studer, Gilet, & Labouvie-Vief, 2012).

While these results provide a global perspective on empathy development, studies that specifically focus on the period of adolescence are clearly lacking, and the majority of studies have used self-reported questionnaires (Allemand et al., 2014; Nancy Eisenberg, Cumberland, Guthrie, Murphy, & Shepard, 2005) or pain observation paradigms. During adolescence, the context of social interactions and its motivational salience is thought to influence the engagement of cognitive abilities (Crone & Dahl, 2012). The presence of peers, as well as their admiration, acceptance or rejection, represent extremely salient rewards and threats (Chein, Albert, Brien, Uckert, & Steinberg, 2011; Masten et al., 2009; Somerville, 2013).Therefore, the investigation of empathy during this period would certainly benefits from using more realistic tasks and paradigms that represent more common and salient experiences. In this regard, Masten, Eisenberger, Pfeifer, and Dapretto (2010) have investigated the neural correlates of social exclusion observation in 20 early adolescents aged from 12 to 13 years, using a computerized ball-tossing game. In this paradigm, called the Cyberball game, participants are led to believe that they are playing with real individuals. Their results showed that observing a peer being excluded compared to observing this peer being included in the game activated the mPFC, the dorsomedial PFC (dmPFC), the precuneus and the posterior superior temporal sulcus (pSTS). Given that the Cyberball paradigm does not provide any visual cue of the victim's distress, one possible interpretation of these findings was that they reflected a cognitive perspective-taking process to understand the victim's feeling. Interestingly, activity in the AI correlated with subsequent prosocial behavior, as measured qualitatively by emails written to the victim after the fMRI session.

Measuring empathy for social exclusion in both adolescents and adults could reveal interesting developmental differences, but no study has made this comparison so far. This type of interactive paradigm is expected to elicit reactions that are closer to everyday life. Furthermore, the neural correlates of prosocial behavior in adolescents have been very little studied and would certainly add interesting information on the decisional processing that underlies it. The goal of the study was thus to investigate the development of empathy for social exclusion and subsequent altruism in adolescents (12-17 years) and adults (22-30 years). More precisely, we aimed to 1) examine the difference between adolescents and adults on the neural correlates of social exclusion observation, to 2) compare both groups on subsequent prosocial behavior towards the excluded individual (the victim), as well as on the neural correlates underlying this behavior. To accomplish this, each participant underwent fMRI scanning while playing a modified Cyberball game that alternated between blocks of observation and participation to the game. After observing exclusion, the participants had the possibility to directly help the victim of the exclusion by including him/her in the game. This new version of the task differs from existing studies, which have mainly used qualitative measures of prosocial behavior such as emails to the victim, or questionnaires and tasks of allocation distribution. Considering that the decision to act in a prosocial way greatly depends on the form of assistance (e.g. volunteering, donating, comforting, sharing, physically helping) and its context (Eisenberg, Eggum-Wilkens, & Spinrad, 2015), we believed that the most relevant measure should be quantifiable and directly related to the context of distress.

For the first objective, based on previous neuroimaging studies showing that perspective-taking has a protracted course of development throughout adolescence (e.g., Decety et al., 2012; Mella et al., 2012), we hypothesized that adults would display higher activation in regions that have been associated with this process during social exclusion observation (e.g., mPFC, TPJ). Also, while some studies of first-hand social exclusion have shown activation of dACC and AI, regions often activated in paradigms soliciting affective-sharing of other's emotions (see Eisenberger, 2012), observing exclusion does not seem to consistently elicit such activation, except in highly empathic individuals (Masten et al., 2011). However, compared to the original Cyberball task, our modified version included additional features designed to increase the realism, such as pictures and names for each player, which could increase the salience of the task and therefore, the empathic reaction. According to studies of empathy development and considering that adolescents have a particularly heightened sensitivity to rejection, observing exclusion should elicit greater distress in adolescents compared to adults, thus resulting in higher activity in affective regions. Considering the protracted development of perspective-taking during adolescence, this higher affective resonance could result in an unregulated personal distress reaction that would be associated with a less adapted empathic response compared to adults and thus less empathic concern toward the victim. Therefore, for the second objective, it was hypothesized that adolescents would display less prosocial behavior – which was measured by the proportion of throws to the victim – than adults. According to many behavioral studies, helping someone in need depends at least partially on altruistic motivation, which is directly related to the level of empathic concern (Batson, 2011; Decety et al., 2015; Pavey, Greitemeyer, & Sparks, 2012). Here, because it was thought that adolescents would present a less adapted empathic reaction, we expected a weaker altruistic motivation and thus fewer throws to the victim from this group.

2. Method

2.1 Participants

Twenty (20) adolescents (*M* age = 14.3, *SD* = 1.3, 10 females), and 20 adults (*M* age = 24.3, *SD* = 2, 10 females) were included in the study. All participants spoke French as their first language. Both groups were recruited using email lists to Laval University's students and employees, according to the following inclusion criteria: (i) aged 12-17 years for the adolescent group and 22-30 years for the adult group; (ii) Caucasian (considering that Quebec is 87,2% Caucasian, this criterion was included in order to avoid introducing documented ethnicity bias; e.g., Hein, Silani, Preuschoff, Batson, & Singer, 2010); (iii) right-handed. The age range 18-21 years was not included in the study as some authors associate it with the period of "late adolescence", during which there is an overlap between adolescence and adulthood (Zarrett & Eccles, 2006). Exclusion criteria were: (i) documented pre-existing neurological, psychiatric or developmental disorder; (ii) being a Laval University's graduate Psychology student (for the adult group only), as pictures of fictitious players were Psychology graduates; (iii) presenting a contraindication for magnetic resonance imaging (e.g. metallic implants, claustrophobia, pregnancy, etc.) as measured by a screening questionnaire; and (iv) presenting an uncorrected vision disorder. The local Ethics Committee approved the study (#2013-346).

All participants completed two subscales of the Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999), Vocabulary and Matrices, in order to estimate intellectual functioning and to verify the equivalence of the two groups on this aspect. There was no significant estimated IQ difference between the groups, $t(39) = 1.53$, $p = 0.13$ (see Table 1 for descriptive data).

2.2 Functional MRI task

The social exclusion paradigm used to assess empathy is Cyberball, a computerized ball-tossing game that simulates an interactive experience of social exclusion (Williams, Kippling, Cheung, & Choi, 2000; Williams & Jarvis, 2006). This instrument presented a strong ecological validity in several studies, including a decreased sense of belonging and self-esteem in excluded participants (Eisenberger, Lieberman, & Williams, 2003; Zadro, Williams, & Richardson, 2004), as well as an empathic concern towards the socially excluded subject (Masten et al., 2011). In the present study, participants were told that they would take part in an online ball game with previous participants of the same age who volunteered to play online during the experiment. In order to increase ecological validity and realism of the study, the real purpose of the experiment was not revealed to the participants until the end. They were initially told that the objective was to examine their brain activity during a computerized social interaction with real players.

A new version of Cyberball, modified and implemented in E-prime software (Psychology Software Tools, Inc., Sharpsburg, PA) was used (see Figure 1 for an illustration of the experimental paradigm). A pilot study was carried out prior to the present study in order to evaluate the validity of this modified Cyberball game, and the results confirmed its ability to generate an empathic response (i.e., a mean of 32/50 on a self-reported scale of situational empathy) and subsequent prosocial behavior. Most previous studies have used two rounds of one minute each, one of inclusion and one of exclusion, in order for the exclusion to occur only once (e.g., Masten et al., 2010). However, with such long blocks, the signal of interest is most likely to fall under the low frequency noise band, and thus to be removed during the conventional high-pass filtering. To counter this and increase design efficiency, we programmed more rounds of shorter duration. Moreover, this novel adaptation of the task involved two main conditions: An Observation condition, during which participants had to observe other players throw the ball, and a Participation condition, in which participant took part in the game and were free to throw the ball to whoever they wanted. Each game involved three players and 20 ball throws. A total of five fictitious players were involved in the task, each represented by a picture and a name, counterbalanced between subjects. Gender and approximate age of the fictitious players were matched to that of the participant. For the observation condition, subjects were instructed to "Watch the game attentively and think about what the other players might think or feel, as well as the possible strategies other players use to determine to whom they send the ball." For the Participation condition, they were told to throw the ball to one of the other players each time they received the ball. They had to use 3 keys of a response glove to select the player they wanted to throw the ball to. In order to increase the credibility of the scenario, a screen showing what looked like a successful internet connection with each fictitious player appeared before starting the game. The picture and name of each player as well as an "online" indication under each name was displayed. A screen stating "interrupted connection" also appeared at one point during the set-up to increase the realism of the task.

fMRI scans were acquired during two separate runs, each comprising 12 games (or blocks). Six of the 12 games corresponded to the Observation condition, among which three consisted of Observation of Inclusion (i.e., all players received the ball an equal number of times), and three were Observation of Exclusion (i.e., one of the player did not receive any of the 20 throws). The six other games corresponded to the Participation condition, among which three were Post-inclusion, and three were Post-exclusion. The number of throws and the players to which the ball was sent was automatically recorded by the E-Prime software. Post-exclusion blocks were designed to observe the behavior of the participants after observing a player being rejected; prosocial behavior was represented by the proportion of throws sent to the victim (i.e., the excluded player) during these blocks. A Participation block always followed each Observation block. The Exclusion and Inclusion conditions were presented in a pseudorandom order, in which two rules were applied: i) the first block of the first run was always in the Inclusion condition; and ii) the same condition could not be repeated consecutively more than twice. In order to increase the realism of the task, the excluded player was always the same and was included only once during the first block. One of the five players was also present at each exclusion block in order to increase the probability that this player would be identified as the main “excluder” by the subjects.

Each block lasted approximately 19 seconds for a total of 5.8 minutes per session. A period of rest lasting between 2500-6500 milliseconds was inserted between each block and indicated the instructions for the next block (i.e., whether the participant was going to be observing or playing). Jitters of 250 to 600 milliseconds were also introduced between each ball throw.

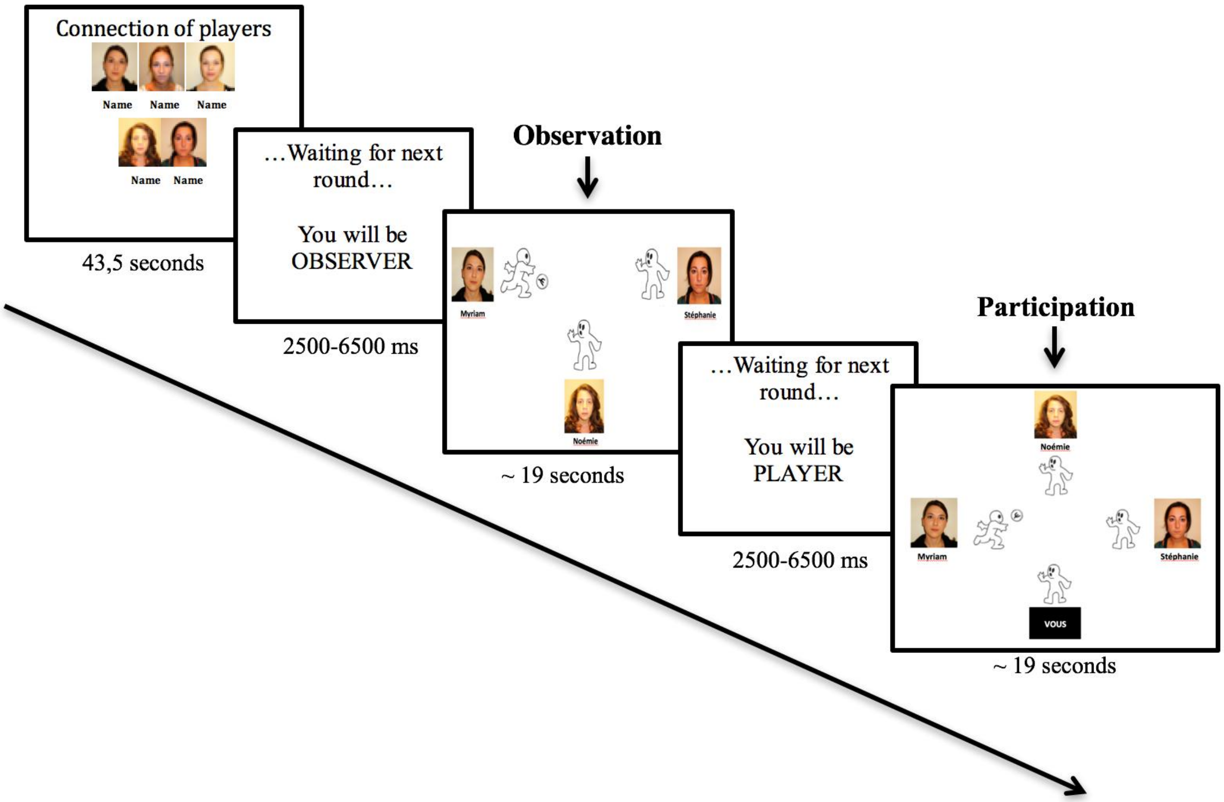

Figure 1. Schematic representation of the experimental task. Participants first observed a screen illustrating the connection of each player, showed only once at the beginning of the task. Then, a rest period of a variable duration between 2500-6500 ms was presented and indicated the condition of the following block. This was followed by an Observation block lasting approximately 19 seconds (jitters of 250-600 ms introduced between each throw) for a total of 20 ball throws. Each Observation block was followed by another rest period and a Participation block of similar durations. A single run contained a total of 12 blocks, including six Observation blocks and six Participation blocks.

2.3 Behavioral measures

2.3.1 Post-experiment questionnaires. After the fMRI session, participants were administered a short questionnaire about their observations during the Cyberball game in order to verify whether everyone had noticed the social exclusion. Results confirmed that each participant of the study noticed the exclusion. The amount of situational empathy felt when observing social exclusion was also measured by a short questionnaire consisting of 10 items, scored on a Likert scale from 1 ("not at all "), to 5 (" very much"), containing questions such as “I felt bad for him/her", "it hurt to watch him/her play", or "I felt sad for him/her". The manipulation check and the empathy questionnaire were inspired from the study of Masten et al. (2011).

2.3.2 Mentalizing. The Combined Stories test of the Integrated Social Cognition Battery (BICS; Achim, Ouellet, Roy, & Jackson, 2012) was administered in order to measure the mentalizing capacities of the participants. This test includes several mentalizing stories translated and adapted from tasks that have been validated and used in experimental and developmental psychology. Participants were asked to read a total of twenty-nine stories, including 20 second-order mentalizing stories (i.e., attribution of a mental state about another character's mental state), 3 first-order inference stories (i.e., attribution of a mental state about the physical world) and 6 non-social reasoning stories (i.e., making an inference about physical causalities). The text remained in front of the participant during questioning and participants were told that they could go back to the text if they felt the need. The responses were written verbatim and then scored 2, 1 or 0 point by the experimenter, according to a validated correction grid. The task took approximately 30 minutes to complete. The total raw score of the 20 second-order mentalizing stories serves as the dependent variable. Since six of these 20 stories included two questions, the maximum score was 52.

2.3.3 Dispositional empathy. Dispositional empathy was measured using the Interpersonal Reactivity Index (IRI; Davis, 1983), a self-reported questionnaire that includes affective and cognitive dimensions of empathy. For the affective aspect, the Empathic Concern subscale measures respondents' tendency to experience feelings of concern or compassion for others, and the Personal Distress subscale assesses the tendency to experience distress or discomfort in response to others' distress. For the cognitive aspects, the Fantasy subscale measures people's propensity to get involved in fictional situations and to identify with fictional characters, and the Perspective-Taking subscale assesses the propensity to adopt another's perspective or point of view. Each subscale includes 7 items, assessed on a 5-point scale ranging from 1 ("does not describe me well") to 5 ("describes me very well"). The validity of the IRI has been well documented and its subscales constitute valid measures of four facets of empathy that can be analyzed separately (Davis, 1983). The total raw score of each subscales thus served as four separate dependent variables. A French translation of the IRI was used in this study, as in previous work (Achim, Ouellet, Roy, & Jackson, 2011).

2.3.4 Rejection sensitivity. Rejection sensitivity was assessed by the Rejection Sensitivity Questionnaire (RSQ; Downey & Feldman, 1996), using the adult version (Berenson et al., 2009) or the children version (also validated with adolescents; Downey, Lebolt, Rincon, & Freitas, 1998), depending on the participant's group. This measure was used in order to test whether the expected developmental differences in empathy and prosocial behavior between groups could be partly explained by this aspect. The adult version contains 9 items whereas the children version has 12 items, each describing situations in which a character has to ask something to someone. The participant is asked to imagine himself in this situation and to rate, on scales from 1 to 6, the probability that the other person would help him and how much he/she is preoccupied about the answer. A high score is thus associated with low rejection sensitivity, and total scores could range from 1 to 6. Measures of reliability (internal consistency and test-retest) and construct validity have proved to be satisfactory for both questionnaires (Berenson et al., 2009; Berenson, Downey, Rafaeli, Coifman, & Paquin, 2011; Downey et al., 1998).

2.3.5 Social desirability. The Balanced Inventory of Desirable Responding (BIDR) developed by Paulhus (1984) measures the tendency to respond in a social desirable manner. This questionnaire was used to make sure that prosocial behavior was not partly explained by a high level of social desirability in participants. The BIDR measures two main constructs: self-deceptive positivity (i.e., one's tendency to give self-reports that are a positively biased, but that the subject believes to be true) and impression management (i.e., one's tendency to deliberately present a positive self-image to an audience). This self-reported questionnaire consists of 40 items, 20 for each construct, assessed on a 7-point scale ranging from "false" to "completely true". One point is given for each extreme score (6 or 7), so that total score can range from 0 to 40. This inventory has been associated with good internal consistency with Cronbach's alpha from 0.68 to 0.86 and good test-retest reliability (Paulhus, 1988).

2.3.6 Pubertal development. A French version of the Pubertal Development Scale (Petersen & Crockett, 1988; Verlaan, Cantin, & Boivin, 2001) was administered to the adolescent group. Pubertal development is rated by the participant on a scale from 1 to 4 for each of the five items. The dependent variable for this construct is composed of a score from 1 to 4; a score of 1 indicates that puberty has not yet started, while a score of 4 suggests that puberty is complete.

2.4 Procedure

Written informed consent was obtained from each participant (plus the parental consent for participants under 18). Following completion of the fMRI scan, participants completed the manipulation check questionnaire to verify if they had noticed the exclusion, and reported the level of empathy they felt for the victim during the Cyberball game. They were also questioned about the strategies they adopted for throwing the ball. Then, participants were administered two subscales of the Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999), Vocabulary and Matrices, and completed the Combined stories test as well as the Interpersonal Reactivity Index, the RSQ, the BIDR and the Pubertal Development Scale for the adolescent group. At the end of the testing session, participants were asked about their level of belief in the study paradigm (i.e.

if they really believed that they played with real online players) and were then fully debriefed about the deception involved in the study. Testing sessions lasted approximately 2.5 hours.

2.5 fMRI data acquisition

Magnetic resonance imaging was acquired on a 3T Philips Achieva TX scanner, equipped with 8-channel head coil. A sagittal high-resolution T1 weighted structural scan was first acquired using a magnetization-prepared rapid acquisition gradient echo (MPRAGE) sequence (TR = 8.2 ms; TE = 3.7ms, flip angle = 8°, FOV=250mm, 256 X 256 matrix, 180 slices/volume, slice thickness = 1mm, no gap) lasting approximately 8 minutes. Then, functional images were acquired during two separate runs of 116 volumes each. Changes in blood oxygenation level-dependent (BOLD) T2* weighted MR signal was measured using a gradient echo-planar imaging (EPI) sequence (TR=3000 ms, TE=35 ms, FoV=230x230mm, flip angle=90 °, 96x96 matrix, 45 slices/slab covering the whole brain including the cerebellum, slice thickness 3mm, no gap, voxel size = 1.8mmx1.8mmx3mm).

2.6 fMRI data analysis

Functional images were preprocessed and analyzed with SPM8 (Statistical Parametric Mapping, Wellcome Department of Imaging Neuroscience, London, UK) implemented in Matlab 2011 (Mathworks Inc., Sherborn, MA, USA). All functional images were first realigned to an average image using a two-pass procedure, in order to correct for head motion. The structural T1 image was then co-registered to the mean EPI image for each subject and segmented into different tissue types. Subsequently, all volumes were spatially normalized into a standard stereotactic space defined by the Montreal Neurological Institute (MNI305) with a resampled voxel size of 2 mm^3 for functional images and 1 mm^3 for structural image, and a spatial smoothing using an 8 mm full-width at half-maximum (FWHM) isotropic Gaussian kernel was applied. The preprocessed functional images and the realignment parameters were then entered in the Artifact Rejection Toolbox (ART tool; web.mit.edu/swg/software.htm) to identify signal intensity and movement outliers. Volumes in which average signal intensity was 3 standard deviations above or below the global mean intensity were considered as outliers, as well as volumes in which movement (translation and/or rotational movement parameters) exceeded 1 mm, corresponding to half the size of a voxel.

First-level statistical analyses were performed using the general linear model (GLM). The Cyberball game was modeled as a block-design. The design matrix included two regressors for each conditions: the Observation condition included observed Inclusion and observed Exclusion, whereas the Participation condition included Post-inclusion participation and Post-exclusion participation, for a total of four conditions of interest. Six head-motion parameters defined by the realignment were added to the model as regressors of no interest, as well as the signal intensity and movement outliers identified by the ART toolbox. Low frequency noise was removed using a high-pass filter of 280 seconds, based on twice the longest time possible between the start of one block of a specific type and the start of the next block of the same type (e.g., time between two exclusion observation blocks). The following linear contrasts were calculated for each participant: i) Observed exclusion > Observed inclusion, to isolate the effect of observing the victim being excluded, and ii) Post-exclusion participation > Post-inclusion participation, to isolate the effect of playing with the victim after the exclusion.

The resulting first-level contrast images were then entered into a second-level group analysis using a random-effect model to allow for inferences at the population level. One-sample *t*-tests were first performed across groups to examine main effects of the two contrast of interest described earlier. Between-group differences were then examined using two-sample t-tests for each contrast of interest. In order to correct for multiple comparisons and limit false-positive (Type I) errors in whole-brain group-level analyses, a Monte Carlo simulation implemented in AFNI 3dClustSim program (Cox, 1996), based on an estimation of spatial autocorrelation function parameters, was used (see Cox, Reynolds, & Taylor, 2016 for an explanation of the 3dClustSim update). According to this simulation, a p value of < 0.001 with a cluster threshold of 59 voxels, or a p value of < 0.005 with a cluster threshold of 170 voxels, were equivalent to a family-wise error (FWE) rate threshold of $p < 0.05$. For visualization of results, group contrasts were overlaid on a surface representation of the MNI canonical brain using MRIcroGL software (http://www.mccauslandcenter.sc.edu/mricrogl/home). The SPM Anatomy toolbox (Eickhoff et al., 2005) as well as the online database Neurosynth (http://neurosynth.org) were used to define anatomical and cytoarchitectonic localization. In order to examine relationships between neural activity and behavioral measures, ROI were created (sphere radius = 8mm) with MarsBaR (http://marsbar.sourceforge.net) based on the peak activation coordinates of each significant cluster of the group-level analyses (both one and two-sample *t*-tests). The β-values of each of these spheres were then extracted and included in bivariate correlations using SPSS, which were examined with a false discovery rate at $q < 0.05$ as a control for Type I errors.

3. Results

3.1 Behavioral results

3.1.1 Questionnaires. We first investigated whether there were some group differences on mentalizing capacities, dispositional empathy, rejection sensitivity and social desirability (means and standard deviations for each group are presented in Table 1). Independent *t*-tests were performed with a $p < .05$ threshold corrected for multiple comparisons using the Bonferroni correction, thus producing a $p < .007$ threshold (0.05/7). The adolescent group reported a significantly lower score than adults on the Perspective-Taking subscale of the IRI, [t (39) = 3.40, p = 0.002, d = 1.12]. No significant difference was found between groups for the Fantasy subscale [t (39) = 1.21, p = .24, d = 0.38], the Empathic Concern subscale [t (39) = 0.31, p = 0.76, d = 0.10], and the Personal Distress subscale [t (39) = 0.96, p = 0.34, d = 0.30]. For the mentalizing capacities, no significant difference was found between groups on the Combined stories test [t (39) = 0.25, p = 0.80, d = 0.07]. The two groups did not significantly differ in their social desirability tendencies [t (39) = 0.55, p = 0.58, d = 0.17], nor on their rejection sensitivity scores [t (39) = 1.94, p = 0.06, d = 0.62], although this difference was associated with a moderate effect size.

Table 1

Means and standard deviations of descriptive data for each group

Measures	Adolescents (n = 20)	Adults (n = 20)
	M (SD)	*M (SD)*
Age**	14.25 (1.33)	24.25 (1.97)
IQ (WASI)	113.1 (8.82)	117.2 (8.04)
Pubertal development	2.8 (0.7)	-----
Mentalizing	47.5 (2.48)	47.3 (2.81)
Rejection sensitivity	4.31 (0.71)	4.73 (0.63)
Social desirability	14.31 (4.07)	13.50 (4.99)
IRI – Perspective-taking**	24.3 (3.02)	27.7 (3.06)
IRI – Fantasy	25.8 (6.38)	23.5 (5.72)
IRI – Personal distress	16.31 (5.23)	14.75 (4.91)
IRI – Empathic concern	24.95 (4.74)	25.4 (4.26)

**p < .01.

3.1.2 Cyberball game. For the Observation condition, both groups reported a certain amount of situational empathy for the excluded player (M adults = 35, SD = 7.9, M adolescents = 32.7, SD = 8.13, range = 10-50), suggesting that the task effectively elicited an empathic reaction in all participants. These situational empathy scores did not significantly differ between groups [t

(39) = 0.89, $p = 0.37$, $d = 0.29$]. See details of Cyberball behavioral data in Table 2. For the Participation condition, the mean proportion of throws made to the excluded player was significantly higher in adults than adolescents [t (39) = 3.33, $p < 0.01$, $d = 1.12$]. Moreover, in the adult group, the proportion of throws to the victim was significantly higher than the proportion of throws to the excluders [t (19) = 9.06, $p < 0.001$], suggesting an altruistic behavior, whereas this difference was not significant in the adolescent group [t (19) = 1.63, $p = 0.12$]. Bivariate correlations across groups revealed that the proportion of throws to the victim was significantly correlated to the situational empathy score ($r = 0.42$, $p < .01$). Concerning the level of belief in the study paradigm, measured on a scale from 1 (i.e., I did not believe at all that I was playing with real individuals) to 100 (i.e., I really thought I was playing with real individuals), the results showed that the groups did not differ on this aspect [t (19) = -0.79, $p = 0.43$]. Moreover, this variable did not correlate with any other measure.

Table 2

Behavioral results of the Cyberball game for each group

Measures	Adolescents (n = 20)	Adults (n = 20)
	M (SD)	*M (SD)*
Situational empathy	32.7 (8.13)	35.0 (7.88)
Proportion of throws to the victim**	0.40 (0.18)	0.57 (0.11)
Proportion of throws to the excluders**	0.29 (0.10)	0.22 (0.06)
Level of belief (%)	56 (31)	50 (28)

**$p < .01$.

3.2 Imaging results

3.2.1 Neural activity during exclusion observation. One sample t-test was first performed across age groups in order to test the main effect of Observation of exclusion. All significant clusters are reported in Table 3 and shown in Figure 2. Observing a player being excluded (*t*-contrast: Observation of exclusion > Observation of inclusion) yielded activation in the left mPFC (extending into the dmPFC), the inferior temporal cortex (bilateral, extending into the IFG, amygdala and AI), the left TPJ, the PCC, the dACC and the thalamus (mediodorsal nucleus). Correlation between parameter estimates of significant clusters and behavioral measures further revealed that prosocial behavior of adults during the Participation condition of the Cyberball game was positively related to neural activity within the amygdala ($r = .47$, $p < .05$, FDR corrected) and the AI ($r = .46$, $p < .05$, FDR corrected) during observation. These relationships were not significant in the adolescent group.

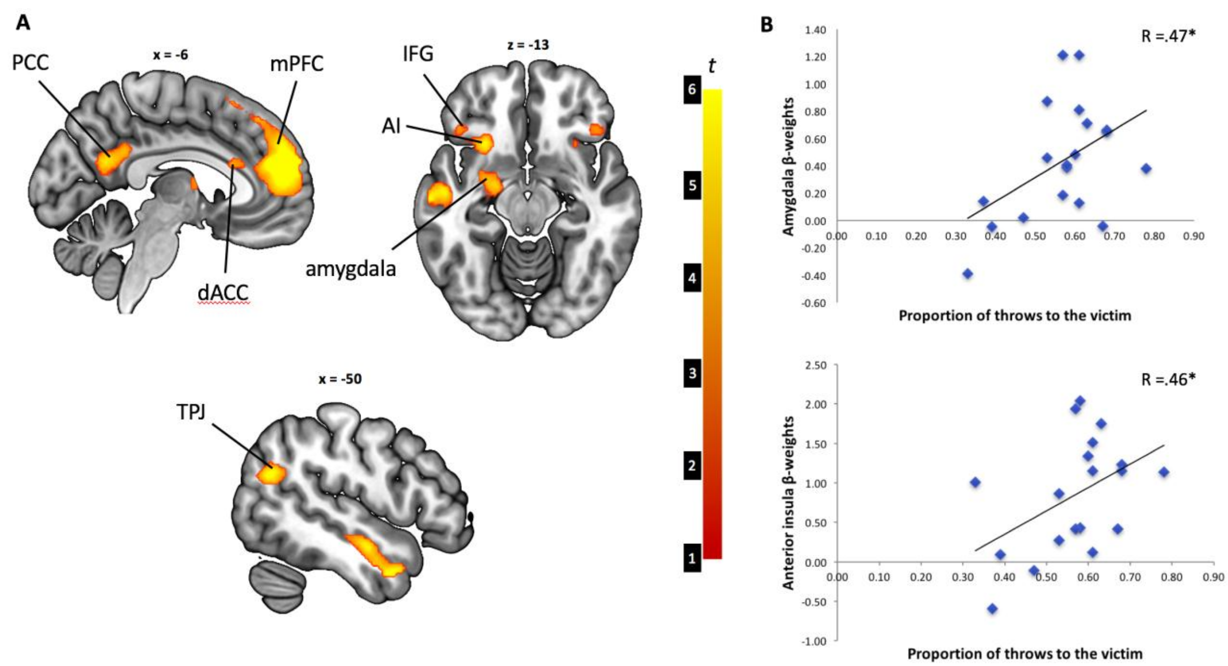

Figure 2. Activation maps resulting from the contrast Observation of exclusion > Observation of inclusion. (A) Significant clusters across groups. (B) The scatterplots illustrate the correlation between amygdala (top) and anterior insula (bottom) activity and prosocial behavior toward the victim in the adult group only. All clusters and coordinates are presented in Table 3.

Table 3

Regions showing significant activation while observing an exclusion vs. observing an inclusion

Region	BA	Hemisphere	*k*	*Z*	Peak MNI coordinates		
					x	*y*	*z*
Medial prefrontal cortex* (extending into dmPFC)	10	L	3960	5.90	-6	56	20
Inferior temporal cortex (extending into IFG, AI and amygdala)	20	L	1356	5.44	-42	-2	-36
				4.79	-34	20	-20
		R	365	4.23	44	4	-36
				3.97	30	22	-16
Temporoparietal junction	39	L	239	4.58	-48	-66	24
Posterior cingulate cortex	31	L	345	4.28	-6	-58	22
Anterior cingulate cortex	24	L	94	3.89	-4	20	20
Thalamus	—	R	121	3.68	2	-4	8

Note. Statistical *T*-maps were obtained using a p value of $< .001$ combined with a cluster threshold of $k = 60$ voxels. BA, Brodmann's Area; dmPFC, dorsomedial prefrontal cortex; IFG, inferior frontal gyrus; AI, anterior insula. *Regions where activation remains significant at FWE $p < .05$.

3.2.2 Neural activity during post-exclusion participation. The main effect of Participation after witnessing exclusion was then explored by performing a one sample *t*-test across groups. All significant clusters are listed in Table 4 and shown in Figure 3. Playing the game right after observing a social exclusion compared to playing after a normal interaction (*t*-contrast: Participation post-exclusion>Participation post-inclusion) significantly activated the PCC, the TPJ (bilaterally), the medial/dorsomedial PFC (extending into DLPFC), the temporal poles (extending into the AI and the OFC), the right lateral temporal cortex, as well as the right caudate nucleus (head). This whole-brain analysis also revealed activation in the occipital lobe and the right fusiform gyrus, involved in facial recognition, as well as in the left posterior lobe of the cerebellum (Lobule VIIa/Crus I).

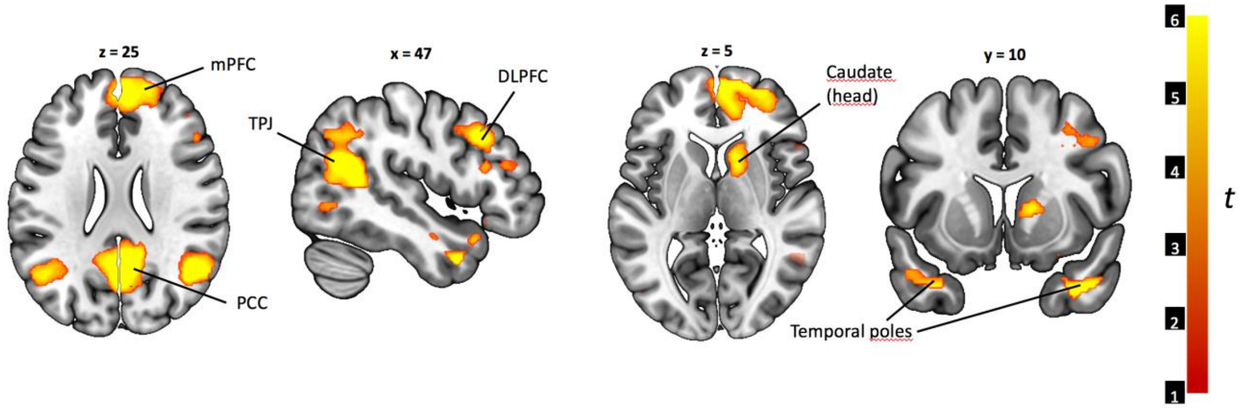

Figure 3. Activation maps resulting from the contrast Participation post-exclusion > Participation post-inclusion. All clusters and coordinates are presented in Table 4.

Table 4

Regions showing significant activation while participating to the game after an exclusion vs. participating after an inclusion

Region	BA	Hemisphere	*k*	*Z*	Peak MNI coordinates		
					x	*y*	*z*
Posterior cingulate cortex*	23	R	1495	6.35	4	-58	26
Temporoparietal junction*	39	R	1883	6.03	50	-56	18
		L	473	4.59	-46	-62	26
Medial prefrontal cortex/dorsomedial prefrontal (extending into DLPFC)*	10	R	5660	6.01	6	52	20
Temporal pole (extending into AI/OFC)*	38	R	772	5.86	42	6	-36
				5.26	30	20	-16
		L	428	4.61	-36	12	-34
				4.33	-24	20	-14
Lateral temporal cortex	21	R	147	5.07	58	-6	-18
Caudate nucleus	—	R	218	4.61	16	14	6
Occipital lobe	19	L	123	3.98	-50	-72	0
Fusiform gyrus	37	R	103	3.89	52	-62	-2
Cerebellum	—	L	86	3.86	-16	-78	-26

Note. Statistical *T*-maps were obtained using a p value of $< .001$ combined with a cluster threshold of $k = 60$ voxels. BA, Brodmann's Area; DLPFC, dorsolateral prefrontal cortex; AI, anterior insula; OFC, orbitofrontal cortex.
*Regions where activation remains significant at FWE $p < .05$.

3.2.3 Age group differences. Two-sample *t*-tests were performed in order to test age group differences in brain activity during Observation and Participation to the Cyberball game. Details of significant clusters are presented in Table 5 and shown in Figure 4. When observing a player being excluded [*t*-contrast: Adults (Observation of exclusion>Observation of inclusion) > Adolescents (Observation of exclusion>Observation of inclusion)], the analysis revealed a significantly greater activation of the left IFG (pars triangularis) in adults compared to adolescents. The reverse comparison (Adolescents>Adults) for the same contrast did not yield any significant activation.

When playing the game after observing exclusion [*t*-contrast: Adults (Participation post-exclusion>Participation post-inclusion) > Adolescents (Participation post-exclusion > Participation post-inclusion)], adults had significantly more activity in the TPJ, the mPFC, the dmPFC and the fusiform face area (FFA) than adolescents, all clusters being right-lateralized. Interestingly, in adolescents, activation within the right TPJ cluster was significantly correlated to the amount of situational empathy felt while observing exclusion ($r = .56$, $p < .05$, FDR corrected). Similarly, the mPFC cluster was positively correlated with adolescents' situational empathy ($r = .51$, $p < .05$, FDR corrected) and related to their prosocial behavior in the Cyberball game, although this correlation did not reach significance ($r = .40$, $p = .08$).

Table 5

Regions that were more active in Adults compared with Adolescents for both contrasts of interest

Region	BA	Hemisphere	*k*	*Z*	Peak MNI coordinates		
					x	*y*	*z*
Observation of exclusion > Observation of inclusion							
Inferior frontal gyrus*	45	L	180	4.30	-40	38	12
Participation post exclusion > Participation post-inclusion							
Temporoparietal junction*	39	R	288	3.64	54	-50	36
Dorsomedial prefrontal cortex	9	R	254	3.57	10	26	56
Medial prefrontal cortex	10	R	242	3.32	26	56	16
Fusiform face area	—	R	309	3.29	22	-52	-14

Note. Statistical *T*-maps showed here were obtained with a p value of <.005 and a cluster threshold of $k = 147$ voxels, effectively producing a FWE corrected $p < .05$. BA = Brodmann's Area.
*Regions that also reached significance with a p value of <.001 combined with a threshold of $k = 60$ voxels.

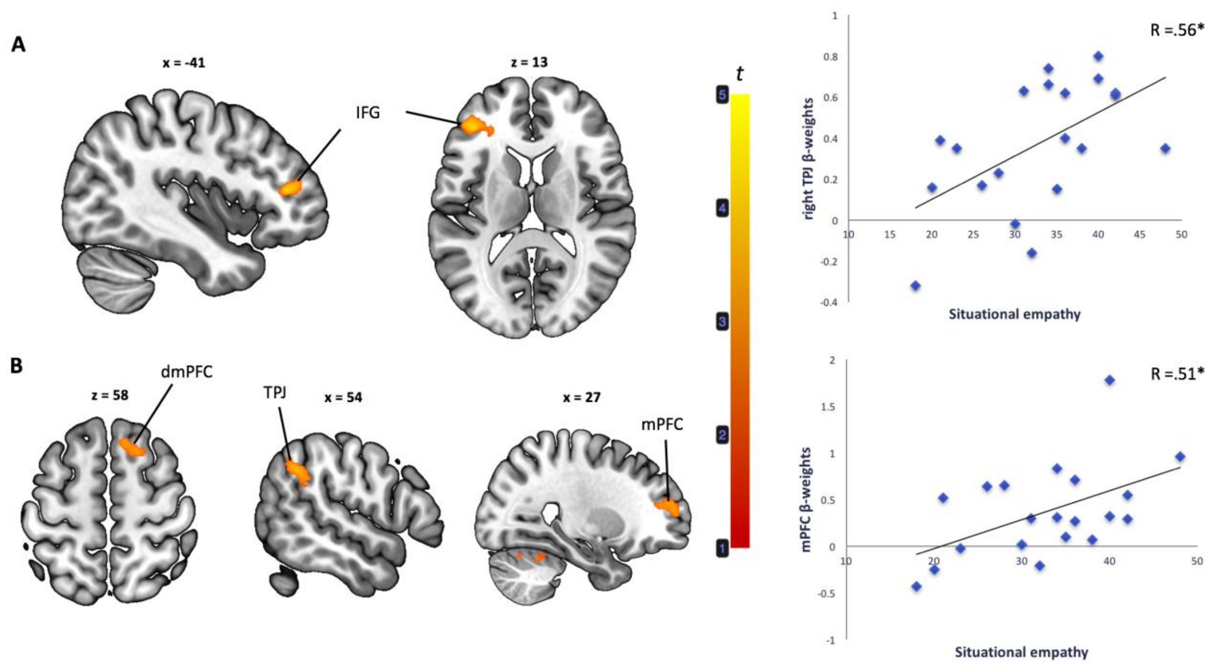

Figure 4. Activation maps resulting from two-sample *t*-tests, thus showing age group differences in brain activity. (A) Significant cluster in the IFG resulting from the contrast [Adults (Observation of exclusion > Observation of inclusion) > Adolescents (Observation of exclusion > Observation of inclusion)]. (B) Significant cluster in the right dmPFC, mPFC, TPJ and FFA (not shown) resulting from the contrast [Adults (Participation post-exclusion > Participation post-inclusion) > Adolescents (Participation post-exclusion > Participation post-inclusion)]. The scatterplots on the right illustrate the correlation between right TPJ (top) and mPFC (bottom) activity in the adolescent group and situational empathy felt while witnessing social exclusion.

4. Discussion

The goal of this study was to investigate the developmental differences between adolescents and adults on the neural processing of social exclusion observation and subsequent prosocial behavior. Using a computerized game that simulates real social interactions with same-age peers, compared to adults, adolescents showed a reduced activation of the left IFG while observing a player being excluded. Moreover, according to a quantifiable and ecological measure of helping, adolescents engaged in significantly less prosocial behavior toward the excluded player, which was paralleled by less activity in the right mPFC, TPJ and FFA while participating to the game. We believe that this is the first study to directly compare adolescents and adults on the neural correlates of social exclusion observation and subsequent altruism.

4.1 Neural correlates of social exclusion observation

Across groups, observing a peer being excluded compared to observing a normal social interaction yielded activation of the medial and dorsomedial PFC, the inferior temporal cortex, the TPJ and the PCC, which is consistent with the study of Masten et al. (2011) who observed PFC and PCC activations. Considering that the task did not provide any visual cue of the victim's distress, these findings might indicate an effort to take the perspective of the victim and to predict how she may feel, as well as a general attempt to understand the situation. This interpretation is further supported by the fact that both groups reported a certain amount of empathy for the victim during exclusion and that the task instructions were explicit in this regard. Moreover, as expected, our modified Cyberball game effectively elicited activity in affective-processing regions, including the dACC, the AI, the IFG (pars orbitalis) and the amygdala. Activation of the dACC and AI could be interpreted as an affective sharing of the victim's distress, as these results were also obtained in studies of first-hand rejection across different paradigms (Cacioppo et al., 2013; Premkumar, 2012). These regions have also been associated with observation of physical pain and other emotions (Fan et al., 2011; Shamay-Tsoory, Aharon-Peretz, & Perry, 2009) and, more generally, to the processing of salient sensory events (Iannetti & Mouraux, 2010). The involvement of amygdala in empathy has been less consistent, but many lesion studies in humans have pointed toward a general role in processing salient and relevant social stimuli, especially in threatening situations (Adolphs, 2010), which is coherent with social rejection observation. A recent study further showed a specific role of amygdala when reading about other's emotional pain compared to physical pain, especially in the deliberate modulation of an empathic response (Bruneau, Jacoby, & Saxe, 2015).

Regarding age group differences, greater activation in regions associated with perspective-taking was expected in adults while observing exclusion, which would have been consistent with a more detached appraisal and a greater top-down modulation of affective-processing with age. Surprisingly, our findings did not reveal any significant difference on these regions. One possibility is that these developmental differences would have been more prominent if adults were compared to younger adolescents; previous studies of empathy development included younger samples (Decety & Michalska, 2010; Decety et al., 2012) and some studies of emotion attribution have revealed differences only in early adolescents, aged 10 to 12 years (Gunther Moor et al., 2012). Rather, our age group comparison revealed a unique activation of the left IFG (pars triangularis) in adults, which is consistent with previous studies of empathy development (Greimel et al., 2010). Although the left IFG has often been associated with action observation and understanding (Mar, 2011; Van Overwalle & Baetens, 2009), it was also identified as a core structure of affective empathy in meta-analyses of pain observation studies (e.g., Lamm et al., 2011) and lesion studies (Shamay-Tsoory et al., 2009). One possible interpretation of this result could thus be that adults felt greater affective-sharing of the victim's distress. While it was expected that adolescents would exhibit greater personal distress, our findings might rather indicate that they were less touched by the exclusion. A lower affective reaction toward the victim in adolescents could be explained by a desensitization to social exclusion, given that peer rejection is a common experience at this period compared to physical pain (Nishina et al., 2005). It could also be explained by the fact that the players were strangers, and adolescents could be more "selective" in their empathic reaction than adults. In fact, studies have shown that affective-sharing is much higher when the victim is a friend (Beeney, Franklin, Levy, & Adams, 2011; Meyer et al., 2013), and relationship with the victim has been shown to be the most important factor in the decision to act prosocially in adolescents (Bellmore, Ma, You, & Hughes, 2012).

4.2 Subsequent prosocial behavior

As expected, when given the opportunity to include the victim in the game after observing his/her being excluded, adolescents showed significantly less prosocial behavior than adults. Not only did they send a smaller proportion of throws to the victim compared to adults, but their behavior toward the victim and the excluders was undifferentiated. Across groups, prosocial behavior was positively correlated to the level of empathy felt during the observation. These results further support the hypothesis that adolescents felt less empathic concern toward the victim than adults, which could have generated a lower altruistic motivation to help. Interestingly, in adults only, those who showed more activation in the amygdala and AI were those who acted more prosocially. It has been proposed that these regions are part of a brain "valuation system" that assigns motivational properties of all situations, and guides subsequent decision-making (Ruff & Fehr, 2014). Observing exclusion was possibly processed by the amygdala and AI as sufficiently distressing to foster an approach behavior toward the victim (Decety et al., 2015).

Helping someone in need depends on altruistic motivation, but also on a cost-benefit analysis, in which a high cost for the benefactor reduces the motivation to help (Batson, 2011; Bode, Miller, O'Gorman, & Codling, 2015). Another factor that may have contributed to lower prosocial behavior in adolescents could be that helping the victim, and thus taking the side of the excluded, involved a too high "social cost" and thus decreased their motivation to help. Developmental psychology studies have shown that what prevents bystanders to help an ostracized victim is the fear of being excluded themselves (Polanin, Espelage, & Pigott, 2012; Unnever & Cornell, 2003). Considering that the task simulates a real social interaction with same-age peers, and that being accepted by peers has a great motivational value at this age (Somerville, 2013), some participants may have been afraid to experience the same exclusion as the victim.

4.3 Neural correlates of participation after observing an exclusion

Examining the neural correlates of participating to the game after observing exclusion, compared to playing after observing a normal interaction, has helped clarify what processes may underlie altruistic behavior in this context. Across groups, the analyses revealed activation of the PCC, bilateral TPJ, right mPFC and dmPFC, as well as the temporal poles. Considering that the victim was also being excluded during those rounds, it is possible that participants were still trying to understand the victim's feelings, but also trying to infer the excluders' intentions and strategies toward them. Interestingly, activation was also observed in the right dorsolateral PFC (included in the mPFC cluster), the OFC, the AI, as well as in the caudate nucleus. While these regions have been associated with many different cognitive functions, including cognitive and affective perspective-taking (e.g., Abu-Akel & Shamay-Tsoory, 2011), their activation could also represent a general process of decision-making in the context of altruism (Decety et al., 2015). The dorsolateral PFC is known to be involved in "cold" processes such as goal maintenance, response selection and cognitive control more generally, but it has also been associated with various emotional tasks including social decision-making (Buhle et al., 2013; Kohn et al., 2014; Rilling & Sanfey, 2011). Via its connections with the lateral OFC, it has been proposed that activation of the dorsolateral PFC might be involved in the selection between different approach or avoidance behaviors based on their reward value (Haber & Knutson, 2009), such as throwing the ball to the victim. The actual helping might then have generated activity in the AI and the caudate nucleus, which have been related to receiving and anticipating reward or value signals (Ruff & Fehr, 2014), as well as to different forms of altruism (Harbaugh et al., 2007).

When comparing groups, the analysis revealed a unique activation of right-lateralized regions in adults compared to adolescents, including the TPJ and the medial/dorsomedial PFC. As these regions are frequently activated in paradigms soliciting mental state attributions and perspective-taking (Abu-Akel & Shamay-Tsoory, 2011; Saxe & Kanwisher, 2003; Valk et al., 2016), another explanation of the difference in prosocial behavior between groups could be that adolescents had a lower propensity to take the victim's perspective during participation and, more generally, to infer other players' intentions. This hypothesis is further supported by the significantly lower IRI's perspective-taking score in adolescents compared to adults. Interestingly, adolescents who presented more activation in the right TPJ are those who reported feeling more empathy toward the victim during observation. The mPFC cluster was also significantly correlated with self-reported situational empathy, and related to prosocial behavior, although this relationship did not reach significance. During social interaction, it has been proposed that the TPJ gives unique information about agents whose behavior is relevant for guiding one's future decisions, such as rewarding decisions, by inferring their strategies and motivations (Carter, Bowling, Reeck, & Huettel, 2012). The medial PFC is known to support meta-cognitive abilities allowing people to think about mental states and about the values linked to actions (Amodio & Frith, 2006). It is thus likely that adolescents who reported being more touched by the victim's exclusion were those who engaged in more mental state attributions while playing the game, and possibly those who subsequently showed more prosocial behavior toward the victim.

The results of the current study should be interpreted in light of certain additional considerations. While this study aimed at providing a global perspective on empathy development from adolescence to adulthood, the use of a relatively large age-range (12-17) in the adolescent group might have limited the probability of finding differences between groups. Adolescence is a period of ongoing physical, social, and neurological changes, so that early adolescents might behave differently than older ones, and even more differently than adults. In our study, helping behavior toward the victim was significantly correlated with age within the adolescent group, thus confirming an ongoing development on this aspect. Similarly, although 18-21 years old (i.e., late adolescents) have been deliberately excluded from this study in order to avoid an overlap between adolescence and adulthood, starting our adult group at 22 years could still have blurred some developmental differences considering that there is evidence of protracted brain development up to 30 years (Petanjek et al., 2011). Future studies should explore empathy development while using more fine-grained age-ranges. Finally, it should be reminded that our sample included both men and women, and considering that gender differences in empathy have been widely documented (Christov-moore et al., 2016; Van der Graaff et al., 2014), it is possible that some results have been influenced by gender. However, the fact that the number of women and men was equal in both groups ensure that the developmental differences could not be explained by gender effects.

5. Conclusion

This study brings novel findings on adolescent's empathy and altruism by showing a lower altruistic behavior toward an excluded peer in adolescents compared to adults, that could be underlined by a reduced sharing of the victim's distress and a lower propensity to take his or her perspective. These results may provide enlightenment on intimidation and rejection experiences that are frequently reported among schools, but also on adolescents' social behavior more generally. More particularly, a range of factors specific to adolescents might create a downward modulation of the empathic response. Future studies should explore this hypothesis with different empathy paradigms, as it certainly provides interesting clues as to how to promote empathy and sensitivity toward others among this developing population.

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Highlights

- A modified version of Cyberball was used to study empathy and altruism development
- Adolescents showed lower activation of the IFG while witnessing exclusion
- Adolescents showed significantly less prosocial behavior toward the victim
- Adolescents had lower activity in the rTPJ and mPFC while playing with the victim
- Adolescents who were more empathic and prosocial had more activation in these regions