

Why are friends special? Implementing a social interaction simulation task to probe the neural correlates of friendship

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Friendships form one of the most proximal contexts with a critical role in mental health and social and psychological development. Yet, the neurobiological basis of this crucial developmental factor is largely uninvestigated. In this study, we tested the hypothesis that the interaction with friends is associated with specific activity increases in brain areas known to be involved in interpersonal phenomena, such as empathy, and in reward expectancy. Using functional magnetic resonance imaging (fMRI), we assessed neural activity in a social interaction simulation task implementing the factors ‘type of relationship’ (peers vs. familiar celebrities) and ‘emotional valence’ (positive (liked), negative (disliked), and neutral (neither liked nor disliked)). In this design, all stimuli were selected individually for each of the 28 participants and positive peers constituted the friends. Participants were asked to approach a stimulus, to avoid it, or remain neutral. Behavioral results confirmed the expectations in the sense that the participants approached positive stimuli more often than they approached neutral, which were also more often approached than negative stimuli. Moreover, peers were more often approached than celebrities were. Imaging results revealed, among others, three regions of particular interest as selectively more strongly activated when subjects interacted with their friends than with other peers and celebrities: the amygdala and hippocampus, the nucleus accumbens, and the ventro-medial prefrontal cortex. These results might highlight the role of empathy and reward-related processes in friendship. Thus, we may have identified a potential mechanism by which friendships exert such a critical role in development and mental health.

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The engagement in interpersonal relationships is a fundamental human motivation and a pivotal developmental domain across the life span with far-reaching effects on (mental) health (Baumeister

and Leary, 1995; Cacioppo et al., 2000; Reis et al., 2000). Particularly friendships form one of the most crucial and immediate contexts of social and psychological development (Rubin et al., 2006). There are positive associations between having friends and, for instance, psychosocial adjustment (Hartup, 1996), cancer survival (Waxler-Morrison et al., 1991), well-being in old age (Street et al., 2007), decreased cortisol under stress (Heinrichs et al., 2003), and protection against mortality (Giles et al., 2005), as well as negative associations between lack of friends and, for instance, cancer mortality (Kroenke et al., 2006) and depressive symptoms (Rockhill et al., 2007; Rudolph et al., 1994). However, the mechanisms by which friendships are related to mental health and the neurobiological basis of this critical developmental factor are largely unknown (Leon, 2005).

The present study uses functional magnetic resonance imaging (fMRI) to explore brain processes involved in the interactions with friends. Extending previous research (Gobbini et al., 2004; Lane et al., 1997; Leibenluft et al., 2004; Paradiso et al., 1999) and disentangling specifically the role of friendship, we implemented a full-factorial design with the factors *type of relationship* (peers vs. familiar celebrities) and *emotional valence* (positive vs. neutral vs. negative). To capture the personal character of relationships, each participant was investigated with an individually acquired set of stimuli while involved in a social interaction simulation task.

The interaction with friends is signified by the bidirectional link between social cognitions, emotions, behaviors, and goal orientations of two friends as epitomized by empathy and typically involves positive feelings of pleasure, making it a rewarding experience (Bigelow, 1977; Bigelow and La Gaipa, 1975). Empathy is related to social competence and positive development (Eisenberg and Fabes, 2006) and functional imaging studies have revealed that the ventro-medial prefrontal cortex (ventro-medial PFC) plays an important role in empathy-related brain processes (Jackson et al., 2005; Shamay-Tsoory et al., 2003). The ability to experience rewards is crucial for mental health due to its survival value (Elliot et al., 2000) and reward-related processes, such as perceptions of pleasant stimuli (Berridge, 2003; Elliot et al., 2000;

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O'Doherty et al., 2003), winning (Bjork et al., 2004), and interactions with cooperative others (Rilling et al., 2002; Singer et al., 2004), are found to involve a circuit of brain regions centered around the nucleus accumbens. Diminished functioning of the ventro-medial prefrontal cortex (Mirza et al., 2004) and the reward/motivational circuit have been found to be linked to mood disorders like major depression (Epstein et al., 2006; Nestler and Carlezon, 2006). Thus, we hypothesized that the interaction with friends evokes stronger activations in the ventro-medial prefrontal cortex and the nucleus accumbens than interactions with peers who are not friends or with celebrities independent of their emotional valence. Such a result would help to develop a mechanistic account on a neurobiological fundament explaining how friends or the lack of friends affect mental health and development.

Method

Subjects and procedure

A complete student wind orchestra with 58 members formed the participant pool for this study. The participants were told that the study was about 'musicality and social relationships' in order not to attract too much attention to the social relationship aspect of the study, which could eventually influence their reactions to the social interaction simulation task they performed during scanning (see below). There were three assessment points. The first assessment was a group assessment where 56 orchestra members (36 females) participated and filled out self-report questionnaires. The participants were gathered in one room and placed on individual desks to insure privacy during data collection. Participants provided information on their involvement with the orchestra activities, nominated (ex-)friends, enemies, and (ex-)romantic partners within the orchestra, provided sociometric nominations of antisocial, prosocial, and withdrawn behavior displayed by their peers, and rated each individual peer on a 5-point scale, ranging from (1) do not like at all, to (3) neutral, and to (5) like very much. The questionnaire included also bogus questions related to musical abilities and music education. At the end of this session, a picture of each orchestra member was taken. The camera was placed behind a poster with a small opening for the camera lens. The poster presented a complicated painting. The participants were told to examine the poster and fixate on the camera lens as soon as they could detect it. This procedure enabled neutral facial expressions without explicit instructions.

A total of 31 participants were further selected for participation in the second and third assessment points, which were conducted with individual appointments. Selection was based on eligibility to take part in fMRI scanning, orchestra membership duration, and (high) involvement with the orchestra activities. The second assessment point involved nominations of at least six (and at most 10) most and least liked peers, rating of the further stimuli (see below), and questions on personality and internalizing and externalizing problem behaviors. The final assessment consisted of fMRI scanning where the participants were asked to perform a 'social interaction simulation task' (see below). Data from one left-handed participant, one participant who switched hands during scanning, and one participant where technical problems occurred during data acquisition were excluded. Finally, neuroimaging data from 28 right-handed participants (20 females) could be used in the analyses. Mean age of these participants was 22.6 (SD=2.04, range 19–27). Written consent was obtained from all participants. The orchestra

received a collective monetary fee for its participation in the study. The orchestra members were debriefed after the data collection.

Stimuli

A personalized set of stimuli was used for each participant. The stimuli were based on nine conditions emerging from a 3×3 research design. The first factor, *type of relationship*, had three levels of stimuli: peers, celebrities, and objects. Object stimuli were included in the design as a control condition. The second factor, *emotional valence*, referred to the valence of the stimuli: positive, neutral, and negative. During the second assessment point, each participant was asked to rate a total of 53 objects and 74 celebrities on a 5-point scale ranging from (1) do not like at all, to (3) neutral, and to (5) like very much. For each participant, the most characteristic six stimuli per condition were selected. Positive stimuli (i.e., objects and celebrities) were rated with 4 or 5, negative stimuli were rated with 1 or 2, and neutral stimuli were rated with 3. The positive and negative peer stimuli were based, respectively, on the most and least liked six peer nominations obtained from the participant during the second assessment session. The positive peers were considered to be the 'friends'. These stimuli excluded current or former romantic relationships. On average, four out of the six most liked peers had been nominated as a friend during the first assessment. Neutral peer stimuli were selected among the peers rated by the participant as neutral (3) during the first assessment. All face stimuli were colored front-facing photographs with direct gaze.

Stimuli were presented using a blocked design; the above named nine conditions formed the blocks. Each stimulus was presented for 4 s with a 1-s interstimulus interval. Each block contained three stimuli, yielding a block length of 15 s. Nine conditions and three fixation blocks of 15 s each were randomized within each cycle, resulting in a cycle length of 180 s. There were 12 cycles; each stimulus was presented six times in total.

Social interaction simulation task

During the functional image acquisition, participants were instructed to imagine that they are in the middle of a room, indicated by a person figure in the middle of the screen (see Fig. 1). Using a joystick, they were asked to move the person figure either toward (simulating *approach*) or away (simulating *avoidance*) from the stimulus appearing at the top of the screen (i.e., ahead of them in the room). They could also choose to *remain neutral* (neither approach nor avoid), which they indicated by moving the joystick to the left.

MRI data acquisition

Participants were scanned using a 1.5 T Siemens Sonata scanner (Erlangen, Germany). For functional magnetic resonance imaging (fMRI), 35 axial slices with ascending slice acquisition were obtained with a T2*-weighted echo-planar imaging (EPI) sequence that measures the blood-oxygen-level-dependent (BOLD) signal (volume-repetition time (TR)=2.75 s, echo time (TE)=40 ms, 90° flip-angle, slice-matrix=64×64, slice thickness: 3.0 mm, slice gap: 0.5 mm, field of view (FOV): 224 mm). After the functional scanning, a T1-weighted MP-RAGE sequence was acquired for structural scanning (176 sagittal slices, volume-TR=2250 ms, TE=3.68 ms, 15° flip-angle, slice-matrix=256×256, slice thickness: 1.0 mm, no gap, field of view: 256 mm).

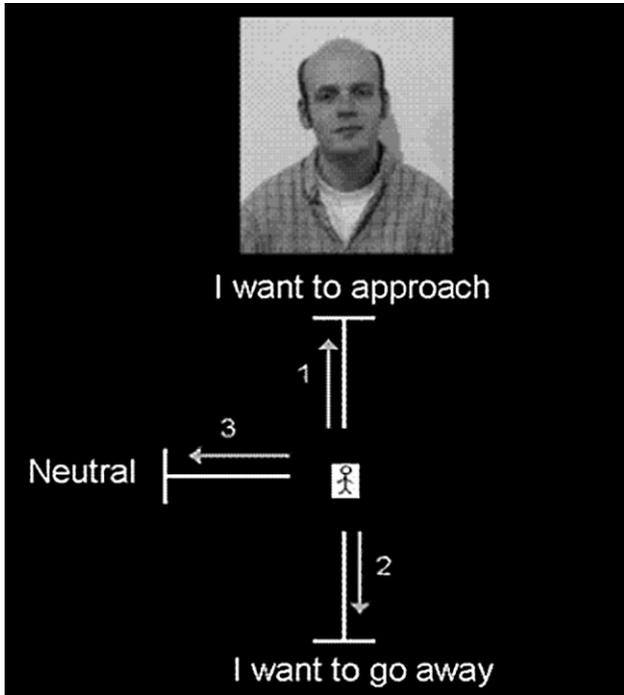


Fig. 1. Example of stimuli. Social interaction simulation task. The figure shows an example of the stimuli used during scanning. The participants were instructed to move the stick-figure in the center with a joystick in one of the three indicated directions. Direction 1 indicates approach, direction 2 indicates avoidance, and direction 3 indicates neutral. The numbered arrows were not presented to the participants; they are included here for the purposes of explanation only.

MRI data analysis

Image pre-processing and data analyses were performed using SPM5 software (www.fil.ion.ucl.ac.uk). Acquired functional images were (1) realigned, (2) co-registered with the corresponding structural MRI scan (using the subject mean of realigned images), (3) slice-time corrected, (4) spatially normalized and transformed into a common space defined by the SPM5 MNI T1 template, and (5) spatially smoothed using an 8-mm full width at half maximum 3D Gaussian filter. The data were analyzed using a general linear model that included regressors for each condition and additional regressors based on the six head-movement realignment (translation and rotation) parameters. First, contrast parameter images were generated per participant, which were consequently used in the second-level group analysis of variance using the random effects model. All analyses are conducted at a threshold of $p < 0.05$ with familywise error correction and a voxel threshold of 20 functional voxels, unless it is otherwise indicated.

Results

Behavioral results

Behavioral responses of participants during the task performance in the scanner were recorded; each approach reaction was coded as 1, neutral reaction as 0, and avoidance reaction as -1. The reliabilities of the behavioral responses to the stimuli were high (all Cronbach's α 's > 0.84). In order to investigate the differences between behavioral responses to the nine conditions, a 3 × 3 repeated measures

analysis of variance with the two factors, type of relationship and emotional valence, was conducted (see Fig. 2). There were main effects of type of relationship, $F(2,54) = 613.17$, $p < 0.001$, and emotional valence, $F(2,54) = 70.11$, $p < 0.001$. *Post hoc* tests indicated that participants approached peers more often than they approached objects, which were also more often approached than celebrities. Positive stimuli were approached more often than neutral stimuli, which were also approached more often than negative stimuli.

Neuroimaging results

The factor level of 'objects' was included as an additional control condition in the experimental design and is not further relevant for the purposes of this report. Therefore, the analyses reported here will focus on the remaining two types of relationship factor levels, namely peers and celebrities. The 2 × 3 full factorial design was tested using analysis of variance to assess the association between the BOLD signal and the six categories in our design. There were significant main effects of both factors: type of relationship, $F(1,135) = 26.07$, and emotional valence, $F(2,135) = 15.38$, at the threshold of $p < 0.05$ with familywise error correction. There was also a significant interaction effect between the factors type of relationship and emotional valence, $T(1,135) = 3.15$.

Main effect of type of relationship

Compared to celebrities, peers evoked a significantly higher level of activation in the posterior midline region (precuneus, calcarine gyrus), anterior midline region (anterior cingulate cortex, mid orbital gyrus, superior medial gyrus), lateral temporal regions (right and left angular gyrus, right and left middle temporal gyrus), medial temporal lobe (hippocampus, amygdala, insula), prefrontal cortex (superior and middle frontal gyrus), and subcortical regions (nucleus accumbens, thalamus, hypothalamus) (see Fig. 3). These results are in line with other findings on brain activation related to retrieval of person knowledge during face perception (Maddock et al., 2001; Sugiura et al., 2006; Todorov et al., 2007), theory of mind (Adolphs, 2003; Castelli et al., 2000; Frith and Frith, 1999; Gallagher et al., 2000; Gallagher and Frith, 2003; Gobbini and Haxby, 2007; McCabe et al., 2001; Walter et al., 2004), social

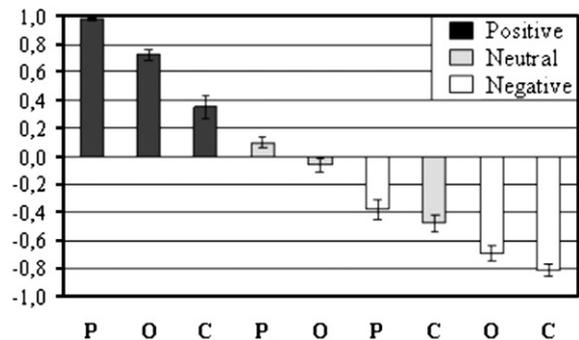


Fig. 2. Behavioral results. The scale on the y-axis indicates the mean of the behavioral reactions given to peers (P), objects (O), and celebrities (C) separately for the three levels of emotional valence (i.e., positive, neutral, and negative). A score of 1 indicates approach, 0 indicates neutral, and -1 indicates avoidance.

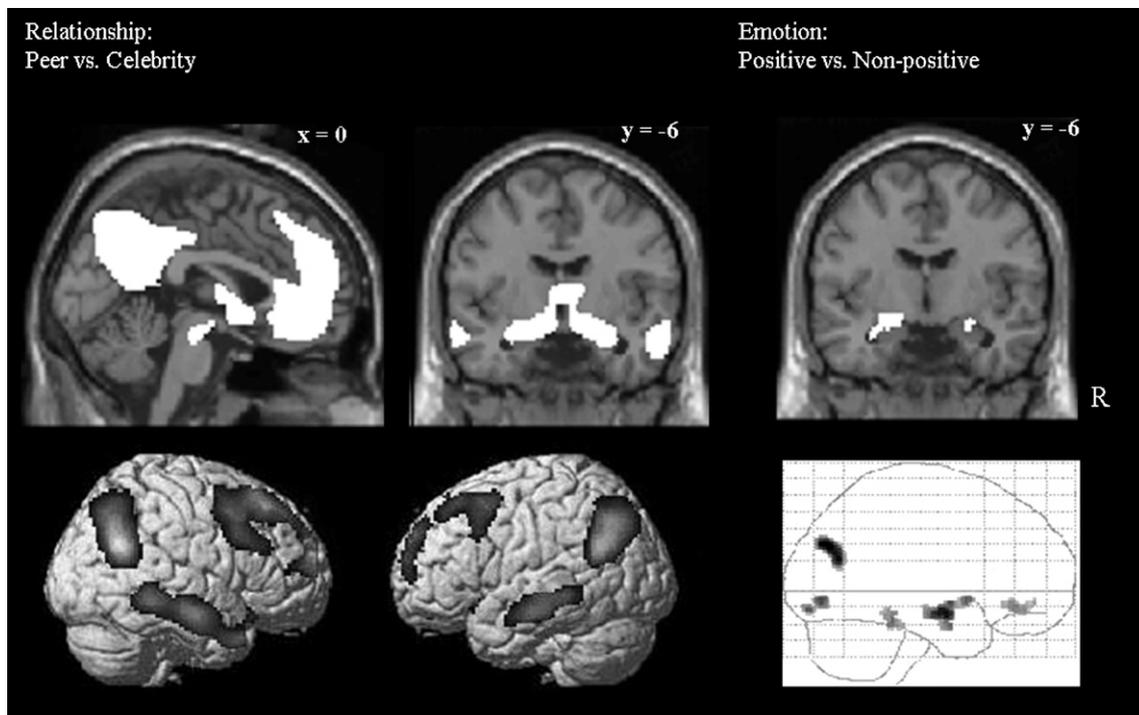


Fig. 3. Main effects. Main effects of the factors type of relationship and emotional valence ($p < 0.05$, familywise error-corrected) are depicted on selected slices of a high-resolution T1 image, 3D renderings, or as an intensity projection provided by SPM5.

cognition and self-related processing (Northoff and Bermpohl, 2004; Schilbach et al., 2006), and social and emotional attachment evoked by personally familiar faces (Gobbini et al., 2004). Interacting with celebrities evoked higher levels of activity than interactions with peers only in the right and left lingual gyrus, possibly due to higher visual processing required by less familiar stimuli (Gobbini and Haxby, 2006; Leibenluft et al., 2004).

Main effect of emotional valence

In order to investigate the main effect of emotional valence, three *post hoc t*-comparisons were conducted. Results indicated that positive stimuli evoked a higher level of response than both the neutral and the negative stimuli, whereas the brain activity during perception of neutral and negative stimuli did not significantly differ from one another. Therefore, we combined the neutral and negative conditions and report here the emotional valence effect for the positive vs. non-positive stimuli. Positive stimuli evoked a stronger response in the right and left amygdala, the caudate nucleus, lateral and inferior temporal regions extending into the inferior occipital gyrus, and midline structures like the mid-orbital gyrus and the calcarine gyrus (see Fig. 3). Although amygdala activation is strongly associated with threat- and fear-related negative stimuli, our results support the view that amygdala is involved in emotional arousal due to higher levels of stimulation evoked by positive than negative stimuli in this study (Adolphs, 1999; Lewis et al., 2007; McClure et al., 2004; Zalla et al., 2000).

Type of relationship and emotional valence interaction effect

We further investigated the interaction between the factors type of relationship (peer vs. celebrity) and emotional valence (positive

vs. non-positive). There was a significant interaction in the ventro-medial prefrontal cortex, the nucleus accumbens, the medial temporal lobe, the superior temporal lobe, and the occipito-temporal junction (see Fig. 4). A detailed list of brain areas involved in this interaction at a cluster-corrected threshold of $p < 0.05$ is depicted in Table 1. Investigation of the effect sizes of activity revealed that the positive peer (i.e., friend) condition evoked a stronger response in each of these regions than the remaining three conditions.

Discussion

In this study, we investigated the neural correlates of social interaction with friends based on a design implementing the factors ‘type of relationship’ (i.e., peers vs. familiar celebrities) and ‘emotional valence’ (i.e., positive vs. neutral vs. negative). Behavioral results showed that subjects in the social interaction simulation task approached positive stimuli more often than neutral and negative ones and peers more often than celebrities. In line with our predictions, the imaging results revealed that interacting with friends involves specifically the ventro-medial prefrontal cortex and nucleus accumbens. This pattern of results suggests that encountering a friend is associated with operations linked to interpersonal phenomena such as empathy and reward (expectancy).

In addition to our predictions, we found friend-specific activations in the amygdala, the hippocampus, the left lateral occipital-temporal junction, and a superior temporal region including the Heschl’s gyrus. The activation of the occipital-temporal junction in interactions with friends might be related to its role in visual spatial representation involved in autobiographic memory retrieval (Chaminade et al., 2005; Gobbini et al., 2004; Maddock et al., 2001). Furthermore, the activation in the occipital-temporal junction together with the medial temporal lobe including

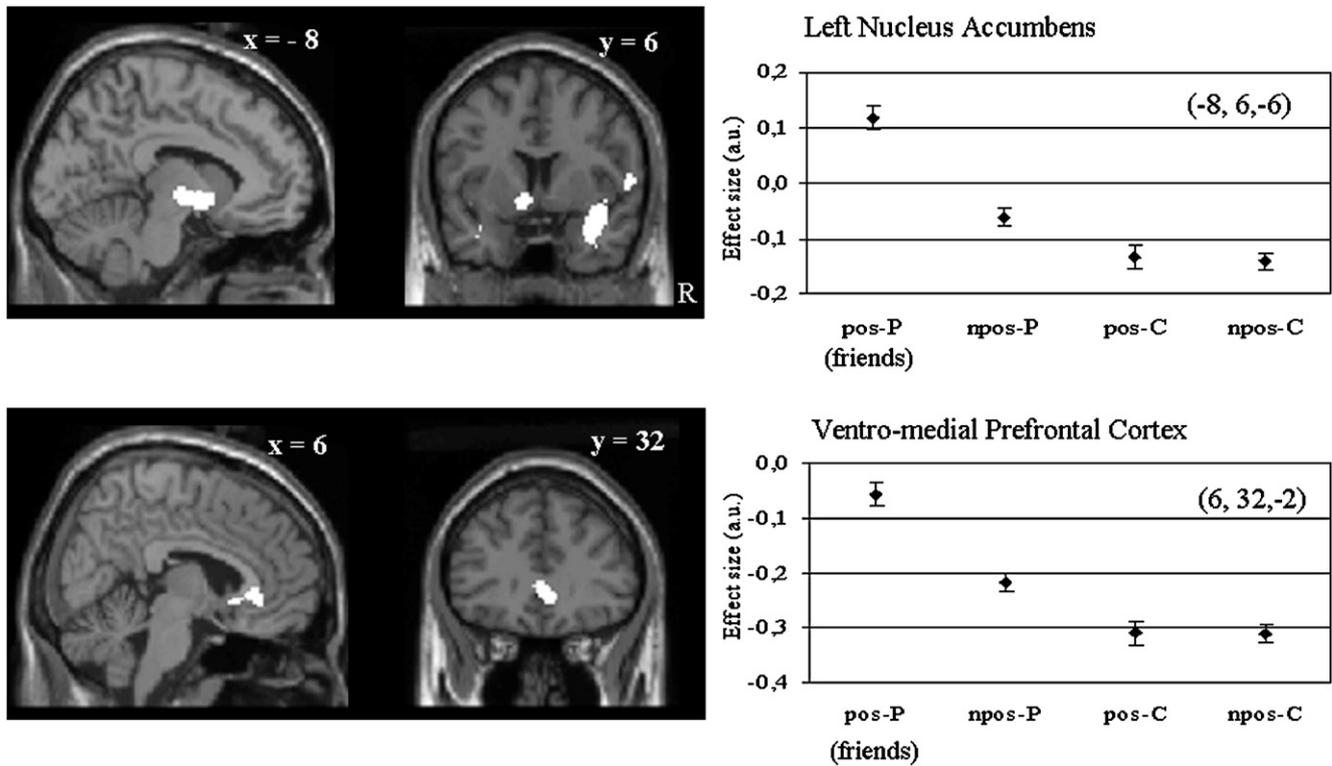


Fig. 4. Interaction effect. Interaction effects between the factors type of relationship and emotional valence ($p < 0.05$, familywise error corrected at the cluster level) are shown on selected slices of a high-resolution T1 image provided by SPM5 and two plots depicting the mean and the standard error of the effect size (a.u.) for the local maxima in the nucleus accumbens and the ventro-medial prefrontal cortex (pos-P: positive peer, npos-P: non-positive peer, pos-C: positive celebrity, npos-C: non-positive celebrity).

both hippocampus and amygdala may indicate that the interaction with friends induces spontaneously more retrieval of emotionally salient memories (Berntsen and Hall, 2004; Dolcos et al., 2004, 2005; Fink et al., 1996; Greenberg et al., 2005; Sugiura et al., 2006). This difference in emotional memory retrieval might be

simply based on the fact that friends share more joint-experiences, which are also more emotionally charged, than they do with other peers or celebrities. Certainly, one may have had strong emotionally charged interactions with disliked individuals (e.g., enemies) as well, and thus one could have expected a similar effect for

Table 1

Areas of significant interaction between the factors type of relationship (peer vs. celebrity) and emotional valence (positive vs. non-positive), $p < 0.05$ cluster corrected

Brain region		Cluster size	Cluster p	Left/right	x	y	z	Z
Midline structures	Ventro-medial PFC	174	0.003	R	6	32	-2	4.16
				R	4	20	-4	
				L	-2	32	4	
Subcortical structures	Nucleus accumbens	211	0.018	L	-8	6	-6	4.51
					-6	-10	0	
Medial temporal lobe	Amygdala	393	0.001	R	34	2	-34	5.03
	Hippocampus			R	30	-4	-22	
	Temporal pole	R	38	8	-22			
	Hippocampus	490	<0.001	L	-28	-4	-26	
	Amygdala			L	-28	-12	-8	
Superior temporal lobe	Heschl's gyrus	500	<0.001	R	52	-8	8	4.55
	Rolandic operculum			R	58	2	6	
	Superior temporal gyrus	R	32	-22	-4			
	Superior temporal gyrus	185	0.003	L	-44	-26	2	
Occipito-temporal junction	Middle occipital gyrus	231	0.012	L	-44	-76	28	3.84
	Middle temporal gyrus			L	-40	-62	20	
				L	-50	-64	18	

Note. All interactions are based on increased activity for friends as opposed to all other conditions (see Results and Fig. 4 for details).

negative peers. However, the group of disliked peers used here might have been not negative enough in their valence for inducing this effect, as indicated by the small behavioral and missing imaging difference in the responses toward neutral vs. negative peers.

The role that the superior temporal region including the Heschl's gyrus plays in the interaction with friends is less readily explained. One might speculate that this effect is related to the type of peer group investigated. The interaction with friends within an orchestra might lead to memories with a strong auditory component that were also automatically retrieved while performing the social simulation task. This auditory component of autobiographical memories could have been enhanced by the association between music and the emotional salience of friends (Schulkind et al., 1999).

The overall pattern of our neuroimaging results may provide us with a mechanistic account for the critical role that friendships seem to have for development and mental health. We showed a link between friendship and activity in a set of brain regions including the amygdala, hippocampus, ventro-medial prefrontal cortex, and the nucleus accumbens. Each of these brain structures has been linked to both empathy and emotion regulation and reward processing.

Empathy is part of the interpersonal processes that are crucial for healthy social and moral development (Eisenberg and Fabes, 2006). For instance, empathy is negatively related to displays of antisocial and aggressive behavior (Kaukiainen et al., 1999; Robinson et al., 2007). In turn, aggression and antisocial behavior are negatively related to having friends and friendship quality (Berndt, 1996; Parker and Seal, 1996), whereas prosocial behavior and empathy are related to having more friends and higher quality friendships (Berndt, 2002; Sebanc, 2000). Activations of the neural circuitry revealed here have been related to empathy and emotion regulation and its damage or dysfunction has been linked with an increased inclination to failure of emotion regulation, impulsive aggression and violence (Davidson et al., 2000; Völlm et al., 2006). Particularly amygdala dysfunction has been found in individuals with psychopathy, which is characterized by impulsive and sensation seeking behaviors, low frustration tolerance, and lack of empathy and moral socialization (Blair, 2001). Similarly, Müller et al. (2003) found reduced emotional responses in the ventro-medial prefrontal cortex of psychopaths. Furthermore, patients with ventro-medial prefrontal cortex lesions were found to show deficits in personal moral judgments, possibly due to reduced social reasoning abilities such as empathy (Ciarra et al., 2007). Also, as a genetically defined trait marker, activity linked to emotional arousal is reduced in the same area of individuals carrying the low expression allele of the monoamine oxidase A gene, a variant associated with increased risk of violent behavior (Meyer-Lindenberg et al., 2006). Therefore, this neural circuit might form the link between positive prosocial development and friendships experienced throughout childhood and adolescence.

Reward processing is crucial for mood regulation through maintenance of behaviors that elicit pleasure and positive feelings (Elliot et al., 2000). Both acute stress and depression are related to altered reward responsiveness (Bogdan and Pizzagalli, 2006; Forbes et al., 2007). In rats, lack of dopamine responsiveness to serotonin in the nucleus accumbens has been shown to be related to depressive behavior (Zangen et al., 2001). Neuroimaging studies in humans have shown that impairment of the brain reward system is related to mood disorders like major depression (Drevets, 2001; Nestler et al., 2002; Pizzagalli et al., 2004; Tremblay et al., 2005). In a postmortem study of depressed patients, abnormalities in the dopamine system of the amygdala were found, suggesting a role of the amygdala in

altered reward responsiveness in mood disorders (Klimek et al., 2002). Furthermore, reductions of the overall volume (Coryell et al., 2005), the grey matter volume (Drevets et al., 1996), the glial cell density and neuronal size (Cotter et al., 2001), as well as the cerebral blood flow (Skaf et al., 2002) of the ventro-medial prefrontal cortex have been found in various mood disorders such as major depressive and bipolar mood disorders (Drevets et al., 1996). In turn, activity increases in this brain structure due to antidepressant treatment are associated with treatment success in patients with major depression (Pizzagalli et al., 2001). Thus, one may speculate that friendships constitute a protective epigenetic factor by a longer-lasting effect on the tonic activity in this set of brain regions. Such a model might show some analogy to the tonic activation model proposed by Canli et al. (2006) for the amygdala. In such a model, friends might provide a tonic activity increase protecting against depressed mood and in turn lack of friends may induce a decrease of the tonic activity constituting a neural mechanism for epigenetic vulnerability toward depression.

In summary, by revealing the neural correlates of social interactions with friends, we might have offered initial insight in the mechanism accounting for the fundamental role that friends play in positive social development and avoidance of mental disorders like depression. It remains difficult to pinpoint the exact role of the brain regions forming the neural circuit involved in interactions with friends. However, our results provide the neural link between friendship on the one hand and social development and mental health on the other, suggesting that reward and interpersonal processes like empathy are particularly relevant for interactions with friends. This study may provide a base for future investigations probing the development of individual differences of friendship patterns (Güroğlu et al., 2007) and their links with psychosocial adjustment and mental health.

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