

Subgenual cingulate activity reflects individual differences in empathic concern

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Abstract

Recent fMRI studies linked subgenual cingulate cortex (SCC) activity with feelings of guilt for acting counter to social values and altruistic donations towards societal causes. We hypothesized that SCC activity across those different tasks was driven by feelings of attachment. In order to investigate this further, we used fMRI to probe the association of empathic concern and strength of SCC activation in response to guilt- and compassion-evoking verbal descriptions of social behaviour. We were able to confirm our prediction that participants with higher empathic concern had increased activity in the SCC in the guilt condition, whereas there was no association for compassion. These results shed new light on the role of the SCC which shows abnormalities in clinical depression.

Introduction

Recently, functional MRI (fMRI) studies found selectively increased activity in the subgenual cingulate cortex (SCC) associated with feelings of guilt when participants imagined acting counter to social and moral values [26] or made altruistic decisions to donate money to societal causes subjects felt attached to [17]. Further, this region was part of a network of regions activated when participants viewed pictures of romantic partners or their own infants [1]. One hypothesis for activation of the SCC across those different tasks is its involvement in the representation of affiliation to other people as well as affiliation to abstract social and moral values. Guilt requires compassion for the victim of one's actions [8] and guilt-proneness is associated with empathic concern [24]. Empathic moral sentiments such as guilt and compassion both require feelings of attachment towards another person. Further, guilt is often tied to violation of social and moral values one feels attached to [26] .

The cingulate gyrus, lateral septal nuclei, medial preoptic area, mediobasal hypothalamus and ventral tegmental area form a neural system implicated in pair bonding and affiliative rewards across a broad range of species [6, 12]. Whereas parts of this mesolimbic system are well known for their role in basic self-serving rewards (e.g. ventral tegmental area), human fMRI suggests that when altruistic and self-serving choices are directly compared, the SCC and adjacent septal region are specific for anonymous altruistic decisions [17], presumably driven by affiliative feelings. Further, it has been demonstrated that the septal region is associated with unconditional trust in economic cooperation, whereas the ventral tegmental area is activated when calculating the benefits for oneself [14].

Studies that did not use personally relevant materials or did not assess individual differences in responding to guilt- or compassion-evoking scenarios have, however, failed to demonstrate SCC activity [13, 16, 22, 23]. Another factor contributing to negative findings for SCC activity in previous studies may be the difficulty in obtaining fMRI signal in this region without specific sequence optimisation and its activation even during emotionally neutral social interactions [16].

Empathic moral sentiments such as guilt and compassion consistently entail the feeling of attachment towards another person or abstract social value. Here, we tested the hypothesis that guilt- and compassion-related activity in the SCC during fMRI is stronger in individuals with higher empathic concern, which would support a role of this region in attachment-related experiences. Empathic concern (i.e. emotional empathy) was measured by a well validated psychometric scale which is sensitive to individual differences [3].

Materials and Methods

The group analysis on a subset of participants has been reported previously [16]. Out of 22 right-handed, healthy participants with no history of psychiatric or neurological disorders originally included in the study, only 12 were included in the previous report, because 7 had signal loss in regions other than the ventral frontal lobes or had scores above 9 on the Beck Depression Inventory. Here, we included 9 female and 7 male participants (age: mean [m] = 27, standard deviation [sd] = 6.2, years of education: m=14.4, sd=2.2) who were not taking psychotropic medications. This included all 12 participants of the previous report and 4 additional participants who had no signal loss in the ventral frontal lobes. Two of these participants scored at 10 on the Beck Depression Inventory (BDI)

which is considered the threshold for mild depression [2]. However, it has been demonstrated that in non-clinical populations, scores on the BDI are more likely to be related to general distress than clinical depression [11]. Since the focus of this study was on individual variability rather than on consistency across the group of healthy participants, we did not exclude the 2 participants with borderline scores on the BDI.

Empathic concern was measured by the respective subscale of the Brazilian version of the Interpersonal Reactivity Index (IRI, [3]). BDI and IRI empathic concern subscale scores showed a non-significant inverse relationship which therefore rules out that our results can be explained by subclinical depression (Pearson's $r[15]=-0.31$, $P=0.27$).

Informed consent was obtained according to procedures approved by the LABS-*Or* ethics committee, Rio de Janeiro, Brazil.

The fMRI paradigm and details of the MRI acquisition have been described previously [16]. In brief, MRI data were collected with a sequence optimised for investigating the ventral frontal lobe on a 1.5 Tesla MRI scanner (Vision, Siemens, Erlangen, Germany). T2*-echo-planar imaging used the following parameters: TR=3000ms, TE=66ms, 25 angulated slices at 30 degrees from the anterior-posterior commissure line, slice thickness=2.6 mm with 1 mm gap, matrix 64x64, FOV=240 mm, flip angle 90 degrees.

Stimuli presented during fMRI consisted of short written statements in Portuguese describing scenarios ("scripts") in 8 conditions classified according to feelings associated with the scripts when rated in a normative study (around 80% agreement in 48 participants): guilt (e.g. "Your mom called you and said she didn't feel well. You ignored her, and the next day she died"), embarrassment, compassion, disgust, indignation-with

another person as victim, indignation-with oneself as victim, emotionally neutral but describing social interaction (e.g. “Your mom asked you for an address, but you didn’t have it. You left for work and she used the phonebook.”), no social agents involved. Participants had to press a button after reading each script presented through goggles in the scanner. Each script was shown for 6 sec, followed by a 6 sec fixation star. Participants had to press a button when finished with reading the script. Fifteen scripts (events) for each condition were pseudorandomly spread across the experiment. After the scan, each participant chose the moral feeling most strongly associated with each script: guilt, contempt, embarrassment, compassion, pride, indignation, gratitude, neutral. The ratings indicated very good agreement with the normative data with all conditions evoking the respective moral sentiment or neutral feelings in more than 80% of the scripts. Only the indignation conditions resulted in lower overall agreement: 60% when oneself was the victim and 74% when another person was the victim [16].

Event-related imaging data were analyzed using SPM2 (<http://www.fil.ion.ucl.ac.uk/spm/software/spm2>) and a random-effects analysis with individual empathic concern as a predictor variable at the second level. Supporting peak-voxel-based and behavioural data analyses were carried out with SPSS15 (<http://www.spss.com>) reporting 2-tailed significance. Parameter estimates for guilt vs. neutral and compassion vs. neutral as well as empathic concern subscale scores were normally distributed as judged by skewness and kurtosis ratios between -2 and +2 and there were no outliers (<-2 or > 2 standard deviations around the mean). We considered effects as significant when they survived an uncorrected voxel-level significance threshold of $P=.005$ and in addition a family-wise error (FWE) corrected threshold of $P=.05$ over either

the whole brain or a 12 mm sphere around the original left or the right hemispheric homologue of the mean peak (Montreal Neurological Institute (MNI) coordinates (x, y, z): -8.5, 25.5, -5.5) of two previous studies reporting SCC activity in relation to empathic moral sentiments (Talarach coordinates: -2, 14,-5 transformed using Matthew Brett's formula [<http://www.mrc-cbu.cam.ac.uk/Imaging/Common/mnispac.html>] => MNI: -2, 15, -5 [17] and MNI: -15, 36, -6 [26]).

Results

Figure 1 shows the significant association of empathic concern differences with the Blood-Oxygenation-Level-Dependent (BOLD) signal within the right SCC for guilt-inducing scripts compared with emotionally neutral scripts (details see Figure 1 legend).

(Figure 1 here please)

On the standard analysis, there was no significant correlation of empathic concern with SCC BOLD on any of the other conditions (compassion, embarrassment, indignation when oneself is the victim, indignation when another person is the victim, disgust) compared with the emotionally neutral condition. Also when using peak voxel correlations, guilt was the only condition for which there was a significant correlation with empathic concern (Pearson's $r[16]=.65$, $P=.006$), whereas correlation coefficients for all other conditions were non-significant ($R[16]<.38$, $P>.15$). Figure 2 shows correlations of empathic concern scores with SCC BOLD during guilt and compassion conditions.

(Figure 2 here please)

Discussion

We confirmed the hypothesis that individuals with higher empathic concern show increased activation within the SCC in response to guilt-evoking stimuli. This result could not be explained by effects of subclinical depression as BDI scores did not correlate with empathic concern in our sample. Contrary to our predictions, however, we failed to see the same correlation of empathic concern with SCC BOLD during compassion. Because the size of our sample may not have been large enough, our negative findings regarding compassion could be due to a lack of statistical power or, alternatively, due to a more specific role of the SCC in empathic moral sentiments when one is the agent rather than the observer of a social action.

We speculate that the SCC response found during guilt may have been associated with translating feelings of attachment into action rather than mere experiences of passive attachment. This could explain why SCC signal evoked by compassion scripts in which one observes fates of others but is not the agent did not correlate with individual differences of empathic concern. Guilt-evoking scenarios, in contrast, described self-agency and guilt is known to induce reparative action [24]. In contrast to the compassion condition of the current study, our previous experiment showing activity in the subgenual region [17] required to act upon compassionate feelings by donating rather than to merely observe.

These effects of individual differences on guilt-related responses within the SCC are of particular interest since resting state activity in this region is abnormally high in patients with major depression [7, 20], a disorder associated with overgeneralized sentiments of interpersonal guilt and self-blame [18]. The SCC has also been activated in sadness induction imaging studies in healthy participants, particularly during recall of personally relevant memories [10]. Sad emotions usually occur in response to loss of a

person or of a personal value one feels attached to [10]. It is therefore possible that SCC activation in response to sad autobiographical events was due to the attachment towards the lost person or value contained in feelings of sadness.

Our findings concur with studies investigating patients with lesions of the ventral (orbitofrontal) part of the frontal cortex which was suggested to play a central role for enabling emotional empathy [9]. Both cognitive and emotional empathy were found to be compromised in patients with combined medial prefrontal and orbitofrontal lesions [21]. A recent study on patients with frontotemporal lobar degeneration, in whom a lack of empathy is consistently observed, has demonstrated atrophy of right anterior temporal, dorsomedial and ventromedial prefrontal cortex including the SCC as well as caudate and septal region to be associated with empathic concern and perspective taking which could not be dissociated [19].

A further clinical implication of our findings could be for the understanding of delusional misidentification syndromes, such as the Capgras syndrome, in which a person believes a familiar other, usually a relative, to be an impostor. These syndromes have been linked to dysfunction of the ventral frontal cortex in some reports [15]. Characteristically, it has been described that these patients perceive a dissonance between clearly recognizing the familiar person, but having lost the feeling of emotional significance of that person to the self [15]. We speculate, that loss of feelings of interpersonal attachment in patients with ventral frontal lobe lesions involving the SCC may contribute to this dissonance of familiarity and personal significance which has been hypothesized to predispose to a delusional resolution of this dissonance in some patients.

Functional imaging studies of emotional empathy in healthy participants have studied the ability to simulate or infer other people's feelings. It has been pointed out that feeling empathic moral sentiments such as compassion (i.e. sympathy, pity), investigated here, is not equal to simulation-based emotional empathy, because feeling compassionate with someone implies a different quality of feeling in the observer than in the observed person rather than an isomorphic simulation of the feelings of the other person [4]. Functional imaging studies investigating the cognitive and emotional aspects of empathic simulation or inference of other people's feelings have not reported consistent SCC activation [4, 5, 25]. These negative findings with regard to the SCC in functional imaging studies of empathy is in keeping with its hypothesized role in attachment-related feelings, because empathic simulation of other people's feelings as investigated in those studies, and in contrast to the present one, did not necessarily and consistently entail feelings of interpersonal or social value-related attachment.

Conclusion

Taken together, we have demonstrated that guilt-evoked activity in the SCC is stronger in individuals with high empathic concern. We failed to show the same effect for compassion-evoked activity. As compassion differs from guilt mainly by being felt in response to observing social outcomes rather than acting oneself, one could hypothesize that self-agency is an important additional factor in driving SCC activation. Our data suggest that individual differences in brain activity within the SCC could in part be driven by individual differences in the proneness to experience strong affiliation with other people and moral values, however this needs to be confirmed by more direct measures of these

different forms of affiliation. Furthermore, it will be important to investigate whether different sectors of the SCC represent different qualities of affiliative reward and punishment associations with different contexts of social actions.

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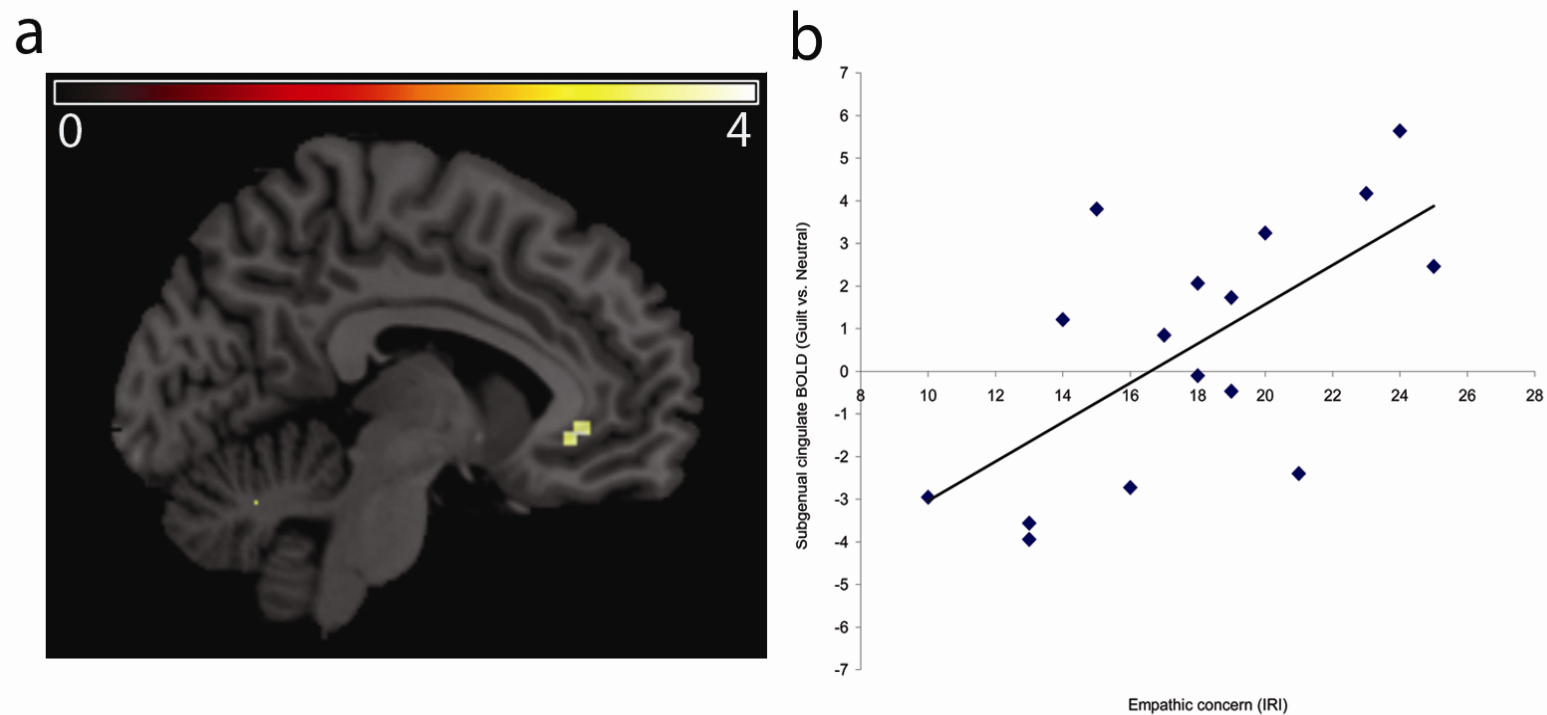


Fig 1. Correlation of individual empathic concern subscale scores (IRI) with BOLD signal during the guilt condition compared with the emotionally neutral condition within right SCC (MNI: 6, 36, -4, BA 32, $P < .001$, $t = 4.71$, Small Volume FWE-corrected $P = .04$). Panel a) depicts a whole brain statistical mask at uncorrected $P = .005$ projected onto a standard brain template using MRIcron (<http://www.sph.sc.edu/comd/rorden/mricron/>; [21]). Panel b) shows peak voxel parameter estimates and empathic concern scores for each subject (Pearson's $r[16] = .65$, $P = .006$).

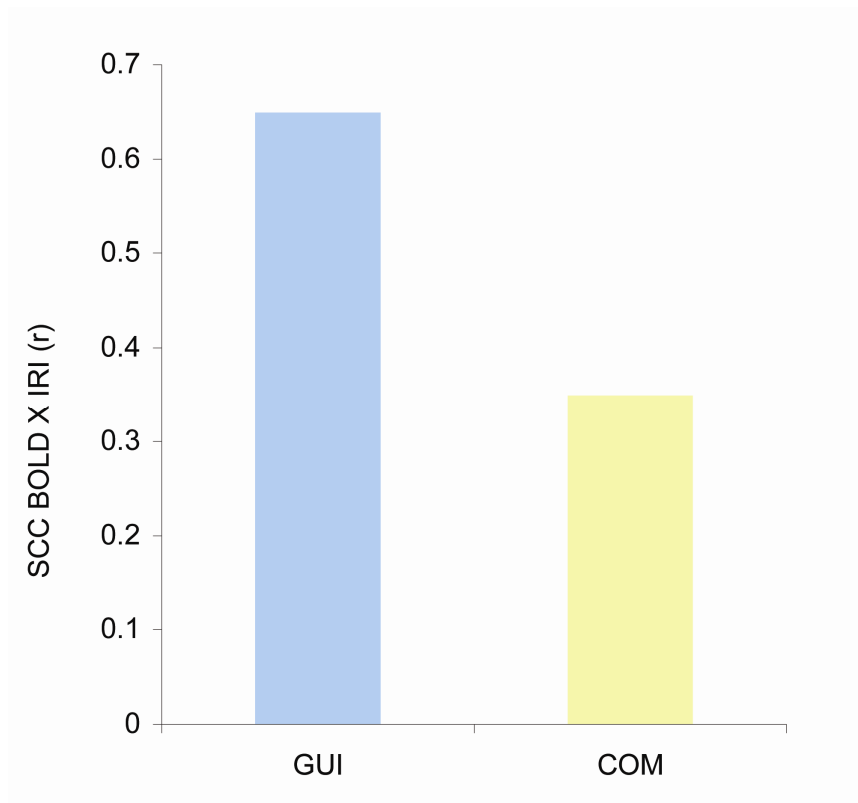


Fig 2. Correlation of individual empathic concern subscale scores (IRI) with BOLD signal during the guilt condition compared with the emotionally neutral condition (Pearson's $r[16]=.65$, $P=.006$) and during the compassion condition compared with the emotionally neutral condition ($r[16]=.35$, $P=.19$) within right SCC. Please note that mean BOLD effects across the group were not significantly different from zero [16].

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