

# Breakdown in the brain network subserving moral judgment in criminal psychopathy

Jesus Pujol,<sup>1</sup> Iolanda Batalla,<sup>2,3</sup> Oren Contreras-Rodríguez,<sup>1,4</sup> Ben J. Harrison,<sup>1,5</sup> Vanessa Pera,<sup>2</sup> Rosa Hernández-Ribas,<sup>1,6,7</sup> Eva Real,<sup>6,7</sup> Laura Bosa,<sup>2,3</sup> Carles Soriano-Mas,<sup>1,6,7</sup> Joan Deus,<sup>1,8</sup> Marina López-Solà,<sup>1,7</sup> Josep Pifarré,<sup>2,3</sup> José M. Menchón,<sup>6,7</sup> and Narcís Cardoner<sup>1,6,7</sup>

<sup>1</sup>MRI Research Unit, Institut d'Alta Tecnologia-PRBB, CRC Mar, Hospital de Mar, 25-29 Passeig Marítim, 08003 Barcelona, Spain,

<sup>2</sup>Psychiatry Department, Hospital de Santa Maria de Lleida, 44 Alcalde Rovira Roure, 25198 Lleida, Spain, <sup>3</sup>Institut de Recerca Biomèdica de Lleida, 80 Alcalde Rovira Roure, 25198 Lleida, Spain, <sup>4</sup>Fundació IMIM, 25-29 Passeig Marítim, 08003 Barcelona, Spain, <sup>5</sup>Department of Psychiatry, Melbourne Neuropsychiatry Centre, The University of Melbourne, 161 Barry Street, Carlton South, VIC 3053 Melbourne, Australia, <sup>6</sup>Department of Psychiatry, Bellvitge University Hospital-IDIBELL, Feixa Llarga s/n 08907 Barcelona, Spain <sup>7</sup>Instituto de Salud Carlos III, Centro de Investigación en Red de Salud Mental (CIBERSAM), Feixa Llarga s/n 08907 Barcelona, Spain, and <sup>8</sup>Department of Clinical and Health Psychology, Autonomous University of Barcelona, UAB campus, 08193 Bellaterra, Barcelona, Spain

**Neuroimaging research has demonstrated the involvement of a well-defined brain network in the mediation of moral judgment in normal population, and has suggested the inappropriate network use in criminal psychopathy. We used functional magnetic resonance imaging (fMRI) to prove that alterations in the brain network subserving moral judgment in criminal psychopaths are not limited to the inadequate network use during moral judgment, but that a primary network breakdown would exist with dysfunctional alterations outside moral dilemma situations. A total of 22 criminal psychopathic men and 22 control subjects were assessed and fMRI maps were generated to identify (i) brain response to moral dilemmas, (ii) task-induced deactivation of the network during a conventional cognitive task and (iii) the strength of functional connectivity within the network during resting-state. The obtained functional brain maps indeed confirmed that the network subserving moral judgment is underactive in psychopathic individuals during moral dilemma situations, but the data also provided evidence of a baseline network alteration outside moral contexts with a functional disconnection between emotional and cognitive elements that jointly construct moral judgment. The finding may have significant social implications if considering psychopathic behavior to be a result of a primary breakdown in basic brain systems.**

**Keywords:** functional magnetic resonance imaging (fMRI); psychopathy; amygdala; frontal lobe; brain networks; functional connectivity

## INTRODUCTION

Psychopathy is characteristically associated with abnormal moral behavior. Most criminal psychopaths know right from wrong (Raine and Yang, 2006; Cima *et al.*, 2010) but they do not appropriately assemble knowledge with action when offending people (Cleckley, 1976). The specific brain operations ultimately regulating moral behavior are not particularly well known. Nevertheless, recent neuroimaging research has provided strong evidence for the critical role of a specific brain network in moral judgment (Greene *et al.*, 2001; Moll *et al.*, 2005; Raine and Yang, 2006; Harrison *et al.*, 2008). Core areas of this network include the medial

frontal cortex, the posterior cingulate cortex and the angular gyrus bilaterally (Greene *et al.*, 2001; Harrison *et al.*, 2008). Importantly, the combination of neocortical and limbic areas that are activated together in moral dilemma situations largely coincides with the so-called 'default mode network' (Moll *et al.*, 2007; Pujol *et al.*, 2008; Harrison *et al.*, 2008).

The default mode network has taken on some relevance in human neuroimaging as being putatively related to the concept of a 'default mode of brain function' (Raichle, 2001). During wakeful rest, the components of the network show both a highly active metabolism and synchronized activity fluctuations (Raichle, 2001; Greicius *et al.*, 2003). It is assumed that activity in the default mode network concerns self-referential aspects of thinking and sensations (Gusnard and Raichle, 2001). Moreover, activity in this network generally decreases (i.e. deactivates) during tasks requiring the focusing of attention on external targets (Gusnard and Raichle, 2001; Raichle, 2001). Nonetheless, when the task involves self-relevant experiences or future personal implications, the default mode network does not show the typical task-induced deactivation but remains highly active (Buckner *et al.*, 2008). Situations involving moral dilemmas are

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Correspondence should be addressed to Dr Jesus Pujol, Department of Magnetic Resonance, CRC Mar, Hospital del Mar, 25-29 Passeig Marítim, 08003 Barcelona, Spain. Email: jpujol@crccorp.es

paradigmatic examples of such default mode network engagement. We have recently provided evidence for the striking uniformity in the basic anatomy of the default mode network across different brain states by demonstrating enhanced network activity during moral dilemmas, deactivation by an attention-demanding task and resting functional connectivity in the same individuals (Harrison *et al.*, 2008). Common areas across these three situations were the medial frontal cortex, posterior cingulate cortex and angular gyri.

Historically, researchers have been concerned with seeking data and arguments to support a neurobiological foundation of psychopathy (Blair *et al.*, 2005). Modern neuroimaging techniques have now provided cumulative evidence of subtle but significant anatomical and functional abnormalities in the brain of subjects with antisocial behavior (Crowe and Blair, 2008; Weber *et al.*, 2008; Wahlund and Kristiansson, 2009; Yang and Raine, 2009). Brain abnormalities in psychopaths have been identified in temporal lobe structures (e.g. amygdala) and orbitofrontal areas both relevant to fear conditioning (Birbaumer *et al.*, 2005; Crowe and Blair, 2008; Craig *et al.*, 2009; Blair, 2010), and in lateral and dorsal prefrontal cortex, relevant to goal-directed behavior (Yang and Raine, 2009). Previous studies have explicitly made the connection between neocortical and limbic dysfunction in murderers using PET (Raine *et al.*, 1997) and in psychopaths using functional magnetic resonance imaging (fMRI) and affective paradigms (Kiehl *et al.*, 2001; Rilling *et al.*, 2007). More specifically related to morality, fMRI studies in normal volunteers have identified increased functional integration of orbitofrontal-temporal-limbic regions during implicitly salient states (Moll *et al.*, 2002). One study has demonstrated structural alterations in these regions related to psychopathy (de Oliveira-Souza *et al.*, 2008).

Other research studies (Raine and Yang, 2006; Glenn and Raine, 2009; Glenn *et al.*, 2009a) suggest that brain alterations in psychopaths directly involves a network that is consistently activated during moral dilemmas in normal population, that coincides with the default mode network (Harrison *et al.*, 2008; Pujol *et al.*, 2008). Raine and Yang (2006) formally hypothesized that rule-breaking psychopathic behavior may be associated with a disruption to this neural network. In our view, the regulation of moral behavior involves intricate (mainly frontal-temporal) brain systems supporting emotion processing and goal-directed reasoning, in which the default mode network may act as a large-scale connection contributing to integrate the emotional and cognitive neural processes in moral dilemma situations.

In the present study, we further investigated the extent to which this brain network subserving moral judgment in the moral dilemma context (Raine and Yang, 2006) is abnormal in criminal psychopaths. Our network of interest was defined according to previous studies using similar challenges (Greene *et al.*, 2001; Harrison *et al.*, 2008; Pujol *et al.*, 2008). Our specific hypothesis was that the alteration would not be limited to the inadequate use of brain

resources for moral judgment, but that a primary network breakdown would exist with dysfunctional alterations outside moral dilemma situations. To test this notion, we examined a group of 22 criminal psychopaths and reference control subjects in three distinct fMRI contexts. First, we sought to confirm that the network responds abnormally during moral dilemmas in psychopaths. Second, to demonstrate the network alterations in situations unrelated to moral behavior, we assessed task-induced deactivation during a conventional cognitive task (i.e. Stroop color-name conflict). Finally, we tested whether the alteration is already evident during the resting-state in the form of a disruption in the functional connectivity that typically defines the network.

## MATERIALS AND METHODS

### Participants

A total of 22 psychopathic men [according to the psychopathy conception of Hare (2003)] with a documented history of severe criminal offense were assessed and compared with a nonoffender control group of 22 men, matched by age and general intelligence estimation [using the Vocabulary subscale, WAIS-III, developed by Wechsler (1997)]. The characteristics of the samples are fully described in Supplementary Table S1.).

### Selection criteria

A total of 105 convicted subjects were initially evaluated using a comprehensive clinical protocol. The sample showed a mean Psychopathy Checklist- Revised [PCL-R (Hare, 2003)] score of 27.8 and served to select individuals for fMRI evaluation according to the following criteria (i) total PCL-R score >20 or PCL-R Factor 1 >10, (ii) documented severe criminal offense, (iii) absence of DSM-IV Axis I diagnosis (First *et al.*, 1998) with the exception of past history of substance abuse, (iv) absence of DSM-IV Axis II diagnosis (First *et al.*, 1997), apart from Antisocial Personality Disorder, (v) absence of symptomatic medical and neurological illness, (vi) normal IQ according to WAIS-III-R (sample total IQ, mean  $\pm$  SD, 108  $\pm$  14) and (vii) obtaining subject-specific full administrative permissions and special police custody during the fMRI assessment day, which was limited to 23 individuals (valid cases  $n = 22$ ).

### Control group

A total of 22 healthy non-offender subjects were recruited from the community matching the psychopathy sample by age, sex and scores on the Vocabulary subscale of WAIS-III and also underwent a comprehensive medical and psychiatric assessment (Supplementary Table S1). All cases and control subjects gave written informed consent after receiving a complete description of the study, which was approved by local research and ethics committees (IMIM Hospital del Mar, Barcelona and Hospital Universitari Arnau de

Vilanova, Lleida). The investigation was carried out in accordance with the Declaration of Helsinki.

### Imaging acquisition and tasks

A 1.5 T Signa Excite system (General Electric, Milwaukee, WI, USA) equipped with an eight-channel phased-array head coil and single-shot echoplanar imaging (EPI) software was used. Functional sequences consisted of gradient recalled acquisition in the steady state [time of repetition (TR), 2000 ms; time of echo (TE), 50 ms; pulse angle, 90°] within a field of view of 24 cm, with a 64 × 64-pixel matrix and with a slice thickness of 4 mm (inter-slice gap, 1 mm). In total, 22 interleaved slices, parallel to the anterior–posterior commissure (AC–PC) line, were acquired to cover the whole-brain for all functional sequences. The first four (additional) images in each run were discarded to allow the magnetization to reach equilibrium.

Brain responses were assessed in three different situations: (i) brain activation during a moral dilemma task, (ii) brain deactivation during an attention-demanding (Stroop) task and (iii) resting-state functional connectivity. To maximally avoid interference between tasks, the resting-state sequence was acquired before, and the Stroop task after, the moral dilemma task. The tasks were identical to those described in our previous study (Harrison *et al.*, 2008) and are fully described in the Materials and Methods and Appendix sections in Supplementary Data

### Image analyses

#### Image preprocessing

Imaging data were transferred and processed on a Microsoft Windows platform running MATLAB version 7 (The MathWorks Inc, Natick, MA, USA). Image preprocessing was performed in SPM5 (<http://www.fil.ion.ucl.ac.uk/spm/>), and involved motion correction, spatial normalization and smoothing using a Gaussian filter (full-width, half-maximum, 8 mm). Motion correction was performed by aligning (within-subject) each time-series to the first image volume using a least-squares minimization and a 6-parameter (rigid body) spatial transformation. Data were normalized to the standard SPM-EPI template and resliced to 2 mm isotropic resolution in Montreal Neurological Institute (MNI) space. We excluded data from one psychopathic individual from the larger original sample of 23 subjects, because of technical problems during fMRI assessment.

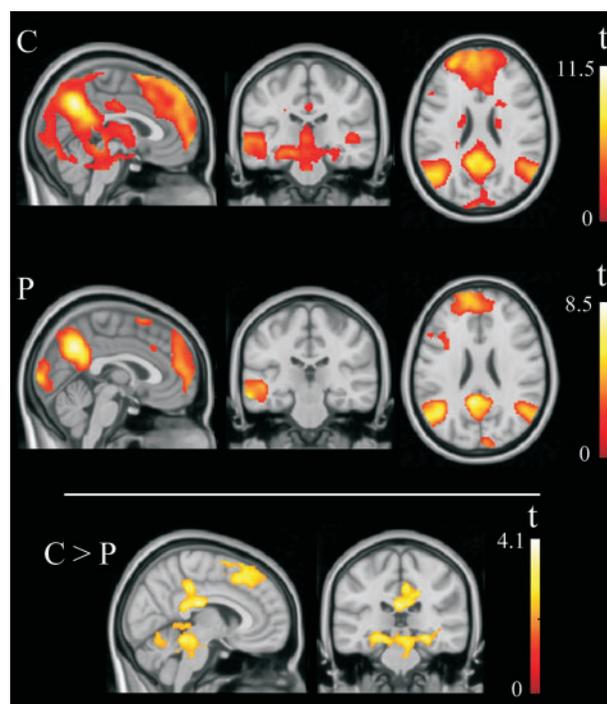
#### Task effects

Moral Dilemma and Stroop Task were analyzed using conventional SPM and Resting-State Functional Connectivity within the moral dilemma/default mode network was tested using a region of interest ('seed')-based approach as detailed at length in a previous study (Harrison *et al.*, 2009) and available as Supplementary Data.

## RESULTS

Behavioral results showed that psychopathic individuals and reference control subjects provided similar responses to most moral dilemmas (Appendix, Supplementary Data). Only in 2 out of the 24 dilemmas did both study groups differ in the proportion of positive and negative responses provided when using an arbitrary threshold of  $P < 0.01$  (moral dilemma 6: psychopaths' responses: Yes: 57.1%; No: 42.9% (Omissions = 1); controls' responses: Yes: 13.6%; No: 86.4% (Omissions = 0); Group comparison:  $\chi^2 = 9.0$ ;  $P = 0.003$ , and moral dilemma 7: psychopaths' responses: Yes: 31.8%; No: 68.2% (Omissions = 0); controls' responses: Yes: 0%; No: 100% (Omissions = 0); Group comparison:  $\chi^2 = 8.3$ ;  $P = 0.004$ ). In two additional moral dilemmas, the groups had a tendency to differ in their responses (dilemma 11:  $P = 0.018$  and dilemma 13:  $P = 0.065$ ). It is of interest, however, that in both situations (significant differences and tendencies), the responses were all in the same direction—psychopaths were more likely to endorse the harmful action.

With regard to the fMRI results, control subjects showed robust activation of the medial frontal cortex, posterior cingulate cortex-precuneus and left and right angular gyri during the moral dilemma condition. Psychopathic individuals showed significant overlapping activation in these regions, although the functional changes were notably less evident (significantly reduced) in the medial frontal cortex



**Fig. 1** fMRI patterns of brain activation during the moral dilemma task. Compared with control subjects (C), psychopathic individuals (P) showed significantly reduced activation in the medial frontal cortex and the posterior cingulate cortex and additionally in both hippocampus and posterior–inferior midbrain. Right side of the figure corresponds to the right hemisphere for both axial and coronal views.

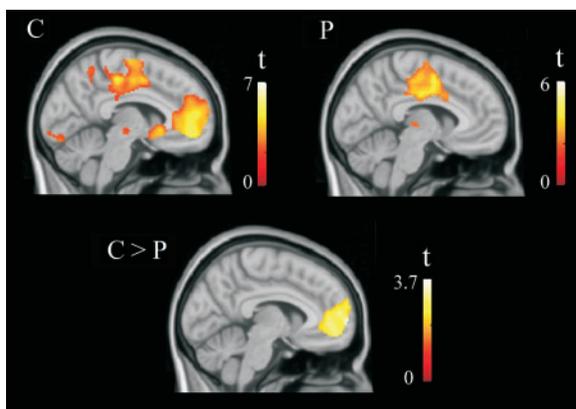
and the posterior cingulate cortex (Figure 1). Such findings are consistent with the notion of a poor moral judgment network engagement during the moral dilemma conflict.

Other areas were additionally recruited during the moral dilemma task in both study groups (Figure 1 and Supplementary Table S2). It is remarkable that psychopathic individuals showed reduced activation relative to the control group in both the right and left hippocampi (near the hippocampus–amygdala junction) and in the posterior–inferior midbrain (involving part of the periaqueductal gray, locus coeruleus region and extending to the cerebellum).

Concerning the Stroop task, the analysis of response error and reaction time confirmed subjects' attentional engagement during both task blocks in both study groups. Psychopathic individuals and control subjects did not differ in any Stroop performance variable (Supplementary Table S3). Such data are congruent with previous reports [reviewed by Zeier *et al.* (2009)] and, relevantly, they indicate that any resulting group differences in the deactivation process were not explained by task performance differences.

Typical fMRI deactivation during Stroop color-name incongruent blocks (compared with congruent blocks) involved both the medial frontal cortex and the posterior cingulate cortex in the control group. In psychopaths, however, the medial frontal cortex did not show any significant fMRI signal reduction (Figure 2 and Supplementary Table S4), which specifically reveals abnormal network functioning also in neutral situations unrelated to the moral context.

In the resting-state functional connectivity analysis, we tested whether poorly activated brain regions during the dilemma situation were abnormally connected in a non-constrained resting situation (no task), in which the elements of the moral dilemma network are typically synchronized as part of the default mode network (Greicius *et al.*, 2003). Resting-state functional connectivity of our areas of interest was tested using two 'seeds' (3.5-mm radial spheres) centered



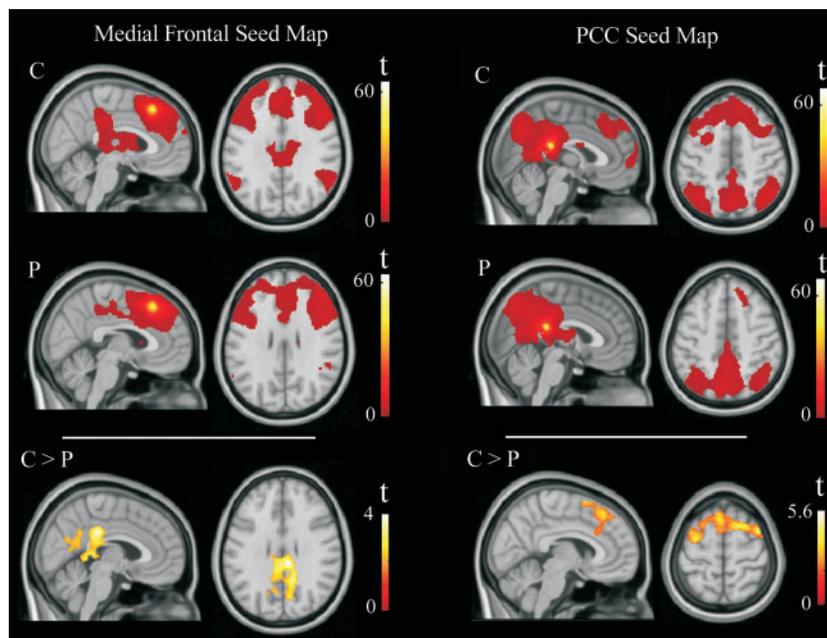
**Fig. 2** fMRI deactivation during the Stroop color-naming task. In contrast with control subjects (C), psychopathic individuals (P) showed no significant deactivation in the medial frontal cortex.

at the coordinates showing the largest dilemma task activation difference between both study groups. The results provided evidence for functional connectivity disruption between the anterior and posterior elements of the default mode network. Indeed, the medial frontal region showed significant and specific functional connectivity reduction with the posterior cingulate cortex and nearby visual areas. Reciprocally, the posterior cingulate cortex also showed an abnormally reduced functional connectivity with frontal areas (Figure 3). The alteration involved medial frontal cortex and additionally extended to dorsolateral and ventrolateral prefrontal areas (Supplementary Tables S5 and S6 and Supplementary Figure S1).

To further emphasize the association between psychopathy and the abnormal activation in the moral judgment network, a dimensional approach was performed by assessing the correlation between psychopathy scores and fMRI task-activation during moral dilemmas in the psychopathy group. We found a significant and selective negative association between psychopathy scores and moral dilemma task activation in the posterior cingulate cortex and the right angular gyrus. The correlation with the left angular gyrus showed a tendency towards significance (Figure 4). The correlation analysis was repeated controlling for total months spent in prison and results showed similar correlation strength ( $r = -0.67$  without control *vs*  $r = -0.64$  controlling for incarceration time in the region of the posterior cingulate cortex) indicating that the severity of psychopathy, as opposed to incarceration time, accounted for abnormal moral judgment network activation.

## DISCUSSION

We have functionally assessed the core regions of the network subserving moral judgment that largely overlaps with a 'default mode network' related to self-referential aspects of thinking. Psychopathic individuals showed reduced response to moral dilemmas in the medial frontal and posterior cingulate cortices. Relevantly, angular gyri activation did not differ between groups, which may well suggest some level of alteration specificity within the network, as opposed to a general response blunting. Abnormal deactivation during the Stroop task was also confined to a part of the network, as the medial frontal cortex, but not the posterior cingulate cortex, showed reduced deactivation in the psychopath group. Moreover, findings from the resting-state functional connectivity analysis again suggest qualitative variations from the normal pattern. Indeed, both medial frontal and posterior cingulate connectivity maps in psychopaths showed an equivalent pattern of preserved local connectivity and altered long-distance connectivity. All in all, results across the different fMRI assessments substantiate the predicted primary functional alteration in the brain network subserving moral judgment, with abnormal responding during tasks and disrupted long-distance functional connectivity at rest.



**Fig. 3** Functional connectivity during brain resting-state for both medial frontal and posterior cingulate cortex (PCC) ‘seed’ maps. In contrast with control subjects (C), psychopathic individuals (P) showed significantly reduced functional connectivity between the medial frontal cortex and posterior brain areas and between PCC and anterior (frontal) brain areas. Right side of the Figure corresponds to the right hemisphere for axial views.

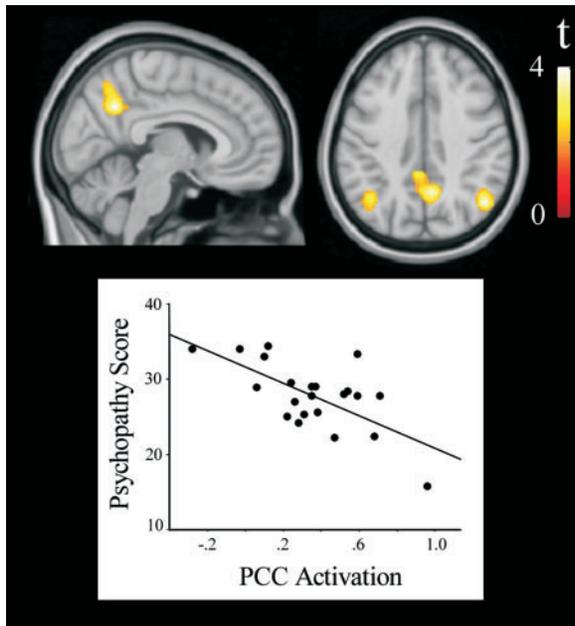
Moral judgment may also engage other brain areas and the specific anatomical patterns may depend on the specific task features (Raine and Yang, 2006; Young and Koenigs, 2007; Moll *et al.*, 2008). Our study was centered on four regions, although significant activation in control subjects was also identified in visual and auditory areas, the hippocampus and the dorsal brainstem. It is relevant to note that the abnormal hippocampus in our study involved the hippocampus–amygdala junction, which partly overlaps with the functionally altered region described in a previous study of moral judgment in psychopathy (Glenn *et al.*, 2009a).

With respect to prevailing neurobiological models of psychopathy, Blair (2009) argues that the primary phenomenon in instrumental psychopathy is a deficient processing of fear-related stimuli that prevents individuals from learning to avoid actions that will harm others. This deficit is associated with altered functioning in the amygdala–hypothalamus–periaqueductal gray basic threat response system and is probably also related to noradrenergic disturbances. We found alterations considerably overlapping with this neural system in the form of reduced activation of the hippocampus–amygdala junction, the caudal periaqueductal gray and the locus coeruleus region (noradrenergic neuron origin) during moral dilemmas. Damasio (1994) and Damasio *et al.* (1990) emphasized the role of the ventromedial frontal cortex on the basis that psychopathic behavior may result from damage to this region and suggested that its early developmental alteration may cause primary psychopathy through the inability to activate somatic states linked to

socially-related punishment and reward. We found abnormal functioning in medial frontal cortex clearly overlapping the damaged areas in the reports of this group (Anderson *et al.*, 1999; Koenigs *et al.*, 2001).

Most models of psychopathy converge in predicting functional disruption between the mutually connected anterior temporal and ventral frontal areas. Such a disruption has even been documented anatomically, as a recent diffusion tensor MRI tractography study demonstrated microstructural alterations in psychopathic individuals in the uncinate fasciculus that ventrally connects both regions (Craig *et al.*, 2009). Our data may complement this notion by suggesting that disruption between temporal and frontal structures may also be indirectly present dorsally in the brain through reduced functional connectivity between the anterior and posterior components of the default mode network, which are in turn closely related to both the hippocampal formation (and amygdala) and the orbital frontal cortex (Buckner *et al.*, 2008). Reduced binding between long-distance dorsal regions in psychopaths is coherent with the conception of Greene *et al.* (2001) proposing that moral judgment depends on the mutually competitive roles of ‘cognitive’ and ‘emotional’ elements of the moral judgment/default mode network, but may also agree with the non-competitive framework of Moll *et al.* (2005) proposing the integration of frontal, temporal and limbic elements to guide moral behavior.

Although the presented data suggest moral judgment network breakdown in the assessed psychopathic individuals, it



**Fig. 4** Correlation between brain activation during moral dilemmas and psychopathy scores. Local maximum correlation for the posterior cingulate cortex (PCC)-precuneus region showed a Student  $t = 4.0$  and  $P = 0.0004$  (cluster size 213 voxels) and for the right angular gyrus similarly  $t = 4.0$  and  $P = 0.0004$  (201 voxels). Correlation for the left angular gyrus showed a tendency to significance with local maximum  $t = 3.0$  and  $P = 0.004$  (cluster size  $< 200$  voxels). Right side of the figure corresponds to the right hemisphere for the axial view. The plot illustrates peak correlation between PCC moral dilemma activation (fMRI relative signal change) and psychopathy scores.

is important to comment on how these findings may generalize to psychopathy. Psychopathic populations are notably heterogeneous with a combination of primary (utilitarian) and secondary (reactive) types and frequent comorbidities. We specifically selected primary psychopaths with a range of secondary traits and excluded subjects with any comorbid Axis I psychiatric diagnosis, current substance abuse and symptomatic medical diseases. Nevertheless, although we aimed to recruit a 'pure' psychopathy group, the homogeneity of the sample was not wholly fulfilled. Also, all the studied psychopaths were convicted prisoners, unlike the control group participants, who were all non-offenders. Therefore, the potential effect of incarceration on brain function was not controlled for using our reference control group. Nevertheless, the results from our dimensional approach may substantially mitigate the limitation posed by the absence of an incarcerated non-psychopathic control group. Indeed, we found a negative correlation between psychopathy scores and brain activation within the psychopathic individuals (with and without controlling for the length of the incarceration period), revealing that the association between moral judgment network alteration and psychopathy was not merely an effect of the subjects' confinement.

We would also emphasize that we found no obvious behavioral differences in moral judgments between the study

groups despite significant reduction in neural function in psychopaths. This issue has previously been discussed, suggesting that psychopathic individuals may use alternative strategies to make moral judgments, mainly related to activity in the dorsolateral prefrontal cortex (Kiehl *et al.*, 2001; Rilling *et al.*, 2007; Glenn *et al.*, 2009b; Tassy *et al.*, 2009). We did not find, however, such distinct activations in the psychopath group in the context of our particular task. Our fMRI approach was probably not sensitive enough as to capture such potential 'compensatory' activations. Also, the adopted fMRI block design was not optimal to separately analyze the effect of specific dilemmas, which will be relevant in the dilemmas where psychopaths were more likely to endorse the harmful action. Future studies of psychopaths using event-related fMRI and distinct categories of moral dilemma scenarios may be useful to clarify these issues.

In conclusion, several studies have suggested the presence of a variety of alterations in the brains of psychopaths. This study has specifically focused on the brain network subserving moral judgment in the context of moral dilemma. The alterations reported herein, may directly relate to one of the main behavioral traits of psychopaths, such as the inappropriate assembling of knowledge and action when offending people. The presented data confirm the recent evidence provided by Glenn *et al.* (2009a) that psychopathy is associated with a reduced implication of brain areas subserving moral judgment and strongly suggest that network functioning is primarily abnormal showing reduced detachment in attention-demanding situations and disrupted baseline functional connectivity.

## SUPPLEMENTARY DATA

Supplementary data are available at SCAN online.

## Conflict of Interest

None declared.

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