

**LETTERS TO THE EDITOR****Do psychopathic patients use their DLPFC when making decisions in moral dilemmas?**

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We found the letter recently published by Glenn *et al.*<sup>1</sup> in *Molecular Psychiatry* very interesting as it sheds new light not only on the understanding of the neural correlates of psychopathic behavior but more generally on the growing field of moral cognition. The authors report that when psychopathic patients face moral dilemmas—and are asked to make decisions—they exhibit a deficit of activation in the amygdala and some other so-called ‘emotional’ cerebral structures. However, it seems that, in their study, the dorsolateral prefrontal cortex (DLPFC) was not part of the regions of interest, in spite of several studies reporting an important function of this structure in moral decisions.<sup>2,3</sup> In the experiment by Glenn *et al.*, if the DLPFC was less activated than in healthy individuals, this could suggest that its activity in such a context might only be a by-product of a process of ‘cognitive control’. It would therefore not support the hypothesis that the DLPFC is specifically involved in a subsystem of moral decision making as generally reported in the literature on decision neuroscience, be it in the context of moral or economic decisions.<sup>3–6</sup>

Recently, Koenigs *et al.*<sup>7</sup> investigated the decisions made by patients with emotion-related brain damage in the ventromedial prefrontal cortex (VMPFC; BAs, Brodman areas 10, 11, 25 and 32) when facing moral dilemmas. These patients made unusual utilitarian judgments as they endorsed harmful actions to peers promoting greater social good (quantitatively speaking), when healthy individuals did not. They used dilemmas previously introduced by Greene *et al.*<sup>2</sup> who had proposed a dual-process theory of brain functioning in moral judgement:

- an ‘emotional’ subsystem eliciting a prepotent, negative emotional response of healthy individuals (associated with a higher activity in the amygdala, medial prefrontal cortex, superior temporal and posterior cingulate gyri) when facing personal dilemmas involving harming someone directly to save other persons;
- a more ‘cognitive’ subsystem eliciting a utilitarian reasoning (aggregate cost–benefit analysis) and a conflict with prepotent emotions. In such a case, overriding prepotent emotional responses would require additional cognitive control and, therefore, an increased activity in the anterior DLPFC as people make difficult (non personal) utilitarian moral judgments.

Thus, according to Greene’s theory, when the VMPFC is damaged, the ‘cognitive’ system remains efficient and patients make utilitarian judgments.<sup>3</sup>

In addition, Jorge Moll, another very influential author in moral cognition, argues that the VMPFC—in conjunction with temporal and limbic-basal forebrain systems—has an important function in the experience of pro-social sentiments (that is, guilt, compassion and interpersonal attachment), whereas the DLPFC is more relevant for socially aversive ones (anger or indignation).<sup>8</sup> Conflicting decisions would not entail a competition between emotion and cognition *per se*, but between two (or more) moral sentiments. Lesions of the VMPFC would therefore induce a dissociation in moral sentiments, a reduced compassion leading to increased ‘cold-blooded’ (that is, strictly rational) utilitarian choices in personal dilemmas and a preserved (or increased) punishment of others (anger) when facing, for example, unfairness in the ultimatum game under certain circumstances.<sup>9</sup>

As psychopathic patients have a lower activation in the amygdala, medial prefrontal, posterior cingulate and superior temporal gyri during moral dilemmas, there should no longer be a competition between those two subsystems according to the dual-process theory. Hence, cognitive control would be primarily at stake. This would result in an underactivation of the DLPFC of psychopathic patients and be in line with recent findings by Rilling *et al.*<sup>10</sup> They reveal that healthy individuals have an emotional bias toward cooperation when playing economic games in which the behavior of each player (defect or not) depends on how (un)fair he considers the decisions made by his peer to be.<sup>6</sup> Hence, defecting would require higher cognitive control, sustained by an increase in DLPFC activity. Conversely, highly psychopathic individuals exhibit less activity in the DLPFC to defect as they do not have the emotional bias toward cooperation that requires cognitive control.<sup>11</sup>

Following these results, many questions still remain to be answered and new ones arise:

- Are psychopaths ‘cool-blooded’ utilitarian, as one could expect?
- How do they cope with different types of dilemmas (personal, impersonal and nonmoral)? And, by extension, which neural structures/networks are primarily at stake when they make decisions in moral dilemmas as activity in areas related to emotional response seem lower compared with those in healthy patients?

- In such context, what is the dynamics of the insula, an area known to encode disgust and exhibit higher activity when healthy individuals make decisions in difficult personal moral dilemmas that they consider as repugnant acts.<sup>11,12</sup>

Considering the variations of activity in the DLPFC and the insula and their connectivity to the areas of interest reported by Glenn *et al.* might provide answers to these questions.<sup>6</sup>

### Conflict of interest

The authors declare no conflict of interest.

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## Increased DLPFC activity during moral decision-making in psychopathy

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Tassy *et al.*<sup>1</sup> inquire as to whether psychopathy was associated with differential activity in the dorsolateral

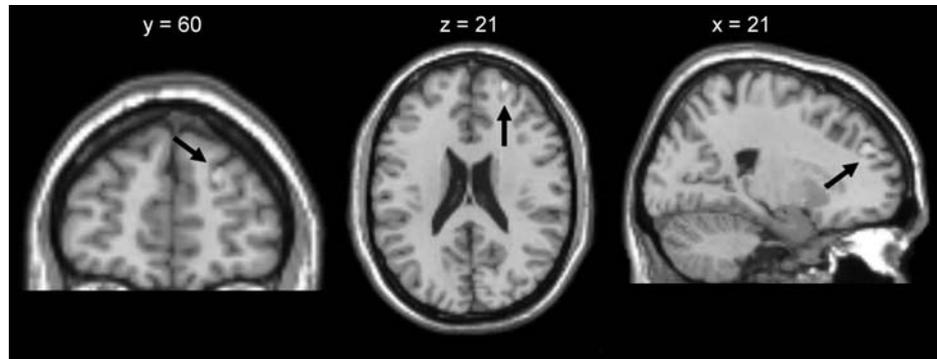
prefrontal cortex (DLPFC) in our study of moral decision-making in psychopathy.<sup>2</sup> This is an important question that we had not considered previously. Tassy *et al.*<sup>1</sup> also ask about behavioral responding and activity in another relevant brain region, the insula. Here we provide additional analyses of our data. We find that psychopathy is associated with *increased* activity in the dorsolateral prefrontal cortex during emotional moral decision-making. No significant relationship was observed between psychopathy and behavioral responses to the dilemmas. These findings, in conjunction with the reduced activity in emotion-related regions reported previously,<sup>2</sup> suggest that psychopathic individuals may use alternative strategies to make moral judgments; alternative interpretations are also discussed.

Tassy *et al.*<sup>1</sup> highlight the important role of the DLPFC in recent theories regarding brain functioning in moral judgment. In particular, the DLPFC has been hypothesized to have at least three distinctive roles: (1) to provide cognitive control to override prepotent social-emotional responses elicited by the dilemmas,<sup>3</sup> (2) to facilitate abstract reasoning (e.g., cost-benefit analyses),<sup>3,4</sup> and (3) to generate self-centered and other-aversive emotions (e.g., anger, frustration or moral disgust).<sup>5</sup> Tassy *et al.*<sup>1</sup> suggest that the examination of this region in our sample of individuals with varying degrees of psychopathic traits may help to clarify the role of DLPFC in moral judgment.

We defined a new region of interest in the DLPFC (see Supplementary Methods) and carried out the same correlational analysis as previously reported.<sup>2</sup> Participants with higher psychopathy scores showed increased activity in the right DLPFC (Figure 1). Analyses of the four factors of psychopathy showed that DLPFC activity was positively associated with Factor 3 (Impulsive lifestyle) and Factor 4 (Antisocial) of psychopathy (F3: 21, 60, 18; 46 voxels,  $T=2.59$ ,  $P=0.048$ , corrected; F4: 21, 60, 21; 117 voxels,  $T=3.03$ ,  $P=0.024$ , corrected); a trend-level relationship was observed for Factor 2 (Affective) (21, 60, 21; 26 voxels,  $T=1.98$ ,  $P=0.114$ , corrected). No relationship was observed with Factor 1 (Interpersonal).

Tassy *et al.*<sup>1</sup> also inquired about activity in the insula, given its role in encoding disgust. No significant relationship was found between total or factor psychopathy scores and activity in the insula. Associations between insula activity and Factors 1 and 2 were in the negative direction, but did not survive correction for multiple comparisons ( $P>0.251$ ).

Finally, Tassy *et al.*<sup>1</sup> asked whether psychopathic individuals give more utilitarian responses, as might be predicted based on the findings reported for patients with bilateral, adult onset damage to the ventral medial prefrontal cortex (VMPC).<sup>6</sup> Results from our sample, as well as from additional subjects from the same population, indicated that there was not a significant relationship between psychopathy scores and the proportion of ‘yes’ (e.g., utilitarian) responses to the personal moral dilemmas.<sup>7</sup> This lack



**Figure 1** Positive association between psychopathy total scores and activity in the right dorsolateral prefrontal cortex (DLPFC) during emotional moral decision-making (MNI coordinates: 21, 60, 18; 36 voxels,  $T = 2.15$ ,  $P = 0.024$ , corrected).

of behavioral differences in moral judgment appears to be consistent with forthcoming data from other groups (e.g., M Hauser, personal communication).

Taken together, these findings suggest that more psychopathic individuals are able to provide relatively similar moral judgments to less psychopathic individuals, despite differences in activation in the amygdala and the DLPFC. Such findings may lend support for a hypothesis that has been previously set forth—that in the absence of appropriate input from emotion-related regions, psychopathic individuals may make use of alternative cognitive strategies to process emotional information.<sup>8</sup> More psychopathic individuals, who show reduced amygdala activity when processing the emotionally salient moral dilemmas,<sup>2</sup> may use abstract reasoning processes to a greater extent than less psychopathic individuals. Thus, these findings may provide support for the role of the DLPFC in abstract reasoning processes (hypothesis 2 mentioned above), though not to the exclusion of the other two hypotheses.

This finding of increased DLPFC activity in psychopathy is consistent with previous studies. Rilling *et al.*<sup>9</sup> found increased activity in the DLPFC in more psychopathic individuals when choosing to cooperate with another individual, suggesting that psychopathic individuals may require more DLPFC activation to choose a morally appropriate option (see Supplementary Discussion). Similarly, increased activity in the DLPFC has been observed during emotional processing in both criminal psychopaths<sup>8</sup> and undergraduates scoring higher in psychopathy.<sup>10</sup> In the moral dilemmas used in the present study, participants were asked whether a particular action was appropriate or not;<sup>4</sup> with less input from emotion-related regions, it is possible that psychopathic individuals rely more on abstract reasoning processes to determine whether specific actions are appropriate according to societal standards. Thus, although they may cognitively *know* the difference between right and wrong (i.e., the moral judgment), they may not have the *feeling* of what is right and wrong,<sup>11</sup> and thus may lack the motivation to

translate their moral judgments into appropriate moral behavior.

Alternatively, our findings of no differences in moral judgments of the more psychopathic individuals despite reduced activity in the amygdala may suggest that the emotional processes impaired in psychopathy may not be *necessary* for moral judgment, or more specifically, that the amygdala may not have a significant role in moral judgment despite its importance for emotional processing in other domains. Emotional processes that are impaired in psychopathy may have their most critical role in motivating morally relevant behavior once a judgment has been made.<sup>12</sup> On this view, the deficit observed among psychopaths results from a failure to link moral judgment to behavior with appropriately motivating emotions.

We thank Tassy *et al.*<sup>1</sup> for their inquiry and hope to have answered some of the questions posed; however, many questions still remain. Our study is limited by a small sample size, so findings should be considered preliminary. Future studies will be necessary to further elucidate the role of the DLPFC and other regions both in moral decision-making and psychopathy.

### Conflict of interest

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Supplementary Information accompanies the paper on the Molecular Psychiatry website (<http://www.nature.com/mp>)

## **SUPPLEMENTARY MATERIAL**

Reply to Tassy et al.: Increased DLPFC activity during moral decision-making in psychopathy

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### **Supplementary Methods**

The DLPFC region of interest was defined as in previous studies<sup>S1</sup> using the software WFU\_PickAtlas ([www.ansir.wfumc.edu](http://www.ansir.wfumc.edu)) and intersecting the following parts: the middle frontal gyrus in the TD AAL (Automated anatomical labeling) atlas and the gray matter in the TD Type atlas. The insula region of interest for this area was defined by intersecting the insula in the TD AAL atlas, and the gray matter in the TD Type atlas.

Analyses of the DLPFC and insula regions of interest were performed using the same statistical analyses as previously reported<sup>S2</sup>, using psychopathy scores as a covariate of interest in the second-level multiple regression model. Both positive and negative relationships were examined for all regions of interest.

The four factors of psychopathy<sup>S3</sup> are as follows: Factor 1 (Interpersonal) involves manipulation, conning, superficial charm, and egocentricity. Factor 2 (Affective) involves lack of guilt, remorse, and empathy. Factor 3 (Lifestyle) involves impulsivity and stimulation-seeking. Factor 4 (Antisocial) involves criminal versatility and antisocial behavior at an early age.

### **Supplementary Discussion**

Tassy et al. are correct that in the study by Rilling et al.<sup>S4</sup>, subjects scoring higher in psychopathy had reduced DLPFC activation when deciding to defect during a socially interactive game. In that study, subjects scoring higher in psychopathy appeared to have a prepotent

response to defect, whereas lower-scoring subjects were found to have a prepotent response to cooperate. Thus, when deciding to defect, higher-scoring subjects did not have a prepotent response to override, and therefore demonstrated reduced DLPFC activity. However, when deciding to cooperate, Rilling et al.<sup>S4</sup> found increased activity in the DLPFC in higher-scoring participants. Two possible explanations were offered—subjects scoring higher in psychopathy may be exerting effortful cognitive control to opt for the morally appropriate action (cooperating), or they may be using abstract reasoning processes to determine the response that would result in the greatest long-term benefit. Thus, it may be that psychopathic individuals require greater DLPFC involvement to choose a morally appropriate option; this finding could lend support for the hypotheses regarding cognitive control *or* abstract reasoning processes.

Although we raise the possibility that our findings of increased DLPFC may be indicative of increased reliance on abstract reasoning about the moral dilemmas, alternative explanations are certainly possible. Furthermore, our data do not contradict the role of the DLPFC in cognitive control during moral decision-making, a process which appears to be gaining evidence in recent literature.<sup>S5, S6</sup>

Finally, our lack of significant findings in the behavioral responses to the moral dilemmas is in contrast to findings of increased utilitarian moral judgment in patients with lesions to the ventromedial prefrontal cortex or with frontotemporal dementia. Two important differences between psychopathic individuals and these patients should be noted. First, although there may be some overlap between brain regions that are disrupted in lesion patients and regions that have been implicated in psychopathy, there are many differences that exist in the regions involved in these two conditions and the corresponding emotional deficits likely differ. Second, the brain differences observed in psychopathy are much less pronounced than in patients who have brain

lesions, so it is likely that the emotional deficits are less severe, and may impact moral judgment to a lesser degree.

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