



Contents lists available at ScienceDirect

# Neuroscience and Biobehavioral Reviews

journal homepage: [www.elsevier.com/locate/neubiorev](http://www.elsevier.com/locate/neubiorev)



## Review

# Is there a core neural network in empathy? An fMRI based quantitative meta-analysis

Yan Fan<sup>a,b,d</sup>, Niall W. Duncan<sup>a</sup>, Moritz de Greck<sup>c</sup>, Georg Northoff<sup>a,\*</sup>

<sup>a</sup> Institute of Mental Health Research, University of Ottawa, Ottawa, Canada

<sup>b</sup> Department of Psychiatry, Otto-von-Guericke University Magdeburg, Magdeburg, Germany

<sup>c</sup> Department of Psychology, Peking University, Beijing, China

<sup>d</sup> Cluster of Excellence "Languages of Emotion" and Dahlem Institute for Neuroimaging of Emotion, Freie Universität Berlin, Berlin, Germany

## ARTICLE INFO

### Article history:

Received 22 June 2010

Received in revised form

22 September 2010

Accepted 18 October 2010

### Keywords:

Empathy

Emotion

Anterior insula

Anterior cingulate cortex

ACC

Mid-cingulate cortex

MCC

Supplementary motor area

SMA

fMRI

Meta-analysis

MKDA

## ABSTRACT

Whilst recent neuroimaging studies have identified a series of different brain regions as being involved in empathy, it remains unclear concerning the activation consistency of these brain regions and their specific functional roles. Using MKDA, a whole-brain based quantitative meta-analysis of recent fMRI studies of empathy was performed. This analysis identified the dACC-aMCC-SMA and bilateral anterior insula as being consistently activated in empathy. Hypothesizing that what are here termed affective–perceptual and cognitive–evaluative forms of empathy might be characterized by different activity patterns, the neural activations in these forms of empathy were compared. The dorsal aMCC was demonstrated to be recruited more frequently in the cognitive–evaluative form of empathy, whilst the right anterior insula was found to be involved in the affective–perceptual form of empathy only. The left anterior insula was active in both forms of empathy. It was concluded that the dACC-aMCC-SMA and bilateral insula can be considered as forming a core network in empathy, and that cognitive–evaluative and affective–perceptual empathy can be distinguished at the level of regional activation.

© 2010 Elsevier Ltd. All rights reserved.

## Contents

1. Introduction .....	00
2. Methods .....	00
2.1. Study selection .....	00
2.2. Multi-level kernel density analysis (MKDA) .....	00
2.3. Comparison between affective–perceptual and cognitive evaluative empathy .....	00
3. Results .....	00
3.1. Description of the selected studies and the balances between its categorizations .....	00
3.2. MKDA results of all empathy relevant studies .....	00
3.3. Comparison between affective–perceptual and cognitive–evaluative forms of empathy .....	00
4. Discussion .....	00
Acknowledgments .....	00
Appendix A. Supplementary data .....	00
Appendix A. Supplementary data .....	00
References .....	00

\* Corresponding author at: Mind, Brain Imaging and Neuroethics, Canada Research Chair, The Michael Smith Chair, ELJB-CIHR, University of Ottawa Institute of Mental Health Research, 1145 Carling Avenue, Room 6435, Ottawa, ON K1Z 7K4, Canada. Tel.: +1 61 3 722 6521x6959; fax: +1 61 3 798 2982.

E-mail address: [georg.northoff@rohcg.on.ca](mailto:georg.northoff@rohcg.on.ca) (G. Northoff).

URL: <http://www.imhr.ca/research/northofflab/index-e.cfm> (G. Northoff).

## 1. Introduction

Empathy, a phenomenon characterizing our understanding and sharing of others' feelings, is vital to our everyday communication and survival in a social environment (Eisenberg and Strayer, 1987). Although the definition of empathy differs somewhat from study to study (see a detailed review in Batson, 2009), it can be broadly defined as the experiencing of an affective or sensory state similar to that shown by a perceived individual, where one is aware as to whether the source of the state is oneself or another. This operational definition allows empathy to be distinguished from related concepts such as sympathy and theory-of-mind (both of which involve an understanding but no sharing of another's state), as well as emotional contagion (where there is no awareness as to whether the source of the experienced state is the self or another). Whilst an increasing number of neuroimaging studies of empathy have been carried out, these have not so far provided consistent answers to several fundamental empathy-related questions. More specifically, it remains unclear as to whether differing forms of empathy tasks and stimuli elicit common patterns of neural activation, or whether instead these produce disparate, task- or stimulus-specific, neural responses.

Studies have utilised tasks and stimuli that range across a number of domains. A variety of feelings – such as pain (Morrison et al., 2004; Singer et al., 2004), disgust (Jabbi et al., 2007; Wicker et al., 2003), and happiness (Chakrabarti et al., 2006; Hennenlotter et al., 2005; Jabbi et al., 2007) – have been used as targets for empathy, with, in addition, empathy being induced through either simple observation (Blakemore et al., 2005; Grosbras and Paus, 2006; Keysers et al., 2004; Singer et al., 2004; Singer et al., 2006; Wicker et al., 2003), imagination (Jackson et al., 2006a; Lamm et al., 2007), or evaluation (Gu and Han, 2007; Jackson et al., 2005; Moriguchi et al., 2007). This variation, and the concurrent variation in reported regions of activity, has meant that it remains unclear as to which brain regions are consistently activated in empathy, and thus whether or not there is a core network within the brain that underlies empathy across all stimulus domains.

Some empathy studies have reported that an empathic response can be evoked automatically in participants through observation, without them being aware of the goal of the experiments (Blakemore et al., 2005; Keysers et al., 2004; Singer et al., 2004; Singer et al., 2006; Wicker et al., 2003). This can be termed an 'affective–perceptual' form of empathy. In contrast, other studies have suggested that empathic responses are substantially influenced by whether or not one attends to the feelings of the target through the explicit imagination or evaluation of feelings (Fan and Han, 2008; Gu and Han, 2007; Preston et al., 2007; see more detailed review in Singer and Lamm, 2009). This 'cognitive–evaluative' form of empathy may thus potentially be differentiated from the 'affective–perceptual' form. Whether this is case or not remains unclear, however.

To effectively approach these unanswered empathy-related questions, a quantitative meta-analysis of recent fMRI studies of empathy was carried out using the MKDA approach (Kober et al., 2008a). This method allows the identification of those areas that are consistently activated in empathy across all task and stimulus domains, and thus allows the question as to whether there is a core network in empathy to be answered. The meta-analytical method also allows those regions that are active during cognitive–evaluative empathy tasks to be compared with those activated by affective–perceptual empathy tasks, revealing to what extent the brain response to these task types overlaps or differs. The approach adopted here has the advantage over the small number of prior empathy-related meta-analyses of studying activations across the whole brain, rather than any one specific region (specifically the temporoparietal junction in Decety and

Lamm, 2007; and the medial prefrontal cortex in Seitz et al., 2006).

It was hypothesised, firstly, that a set of core regions would be found to be active across all empathy task domains; and, secondly, that a differentiation would be seen between the non-core regions active in cognitive–evaluative and affective–perceptual empathy tasks. Based upon the literature, it was further hypothesised that cognitive–evaluative empathy would specifically recruit cortical midline structures such as the anterior mid-cingulate cortex (aMCC) and dorso-medial pre-frontal cortex (DMPPFC) (Lamm et al., 2007), whilst regions such as the insula and midbrain would be preferentially recruited in affective–perceptual empathy (Craig, 2009; Phan et al., 2002).

## 2. Methods

### 2.1. Study selection

A step-wise procedure was used to identify the relevant experimental articles. First, studies were selected through a standard search in PubMed (<http://www.pubmed.gov>) and ISI Web of Science (<http://apps.isiknowledge.com>), with keywords ['empathy' OR 'empathic' OR 'emotion contagion' OR 'affective theory of mind' OR 'affective mentalizing'] AND ['fMRI' OR 'magnetic resonance imaging']. Search terms other than empathy were included in order to identify any relevant studies that may have been classified as something other than empathy *per se* by the particular study authors. Next, additional studies were collected by reviewing the reference list of the relevant papers found in the first step, or through the 'related article' function of the PubMed database. Finally, the reference lists of several review articles were inspected for further relevant studies (de Vignemont and Singer, 2006; Decety and Jackson, 2004, 2006; Decety and Lamm, 2006, 2007; Eslinger, 1998; Gallese, 2001, 2003, 2007; Gallese et al., 2004; Goubert et al., 2005; Hein and Singer, 2008; Jackson et al., 2006b; Lee et al., 2008; Levenson and Ruef, 1992; Preston and de Waal, 2002; Seitz et al., 2006; Singer, 2006, 2007; Singer and Lamm, 2009).

A study was considered empathy-relevant if it required the participant to understand and share others' emotional or sensory states. We thus included all the studies which fulfilled the operational definition of empathy given above. Specifically, the empathy-relevant studies met one or more of the following criteria:

- The task required the subjects to observe the emotional or sensory state of others, although not necessarily with the explicit instruction to do so, with data being analysed in a specifically empathy-related context.
- The task required the subjects to share the emotional states of other individuals and make judgments according to others' feelings.
- The task required the subjects to imagine the others' feelings or evaluate the emotion from the others' perspective.
- The perception of others' emotional or sensory states showed activation which correlated with the dispositional measurement of one's empathy.

Other inclusion criteria were applied:

- Only studies measuring healthy adults were included; studies of patients and children were excluded. For studies comparing patients and healthy controls, the data of the healthy control group was included if detailed statistical analyses were performed on the control group alone.

- Only studies measuring neural activity in the whole brain were included; studies reporting only selected regions of interest were excluded.
- Presentation of results had been limited to regional activation changes (as revealed by task comparison or image subtraction methods, parametric designs, or brain-behavioral correction). Data on changes in functional or effective connectivity were excluded.
- Only activation data were included in the relevant analysis, whereas deactivation data were not considered.
- For studies in which coordinates referred to the Talairach space, a conversion to the Montreal Neurological Institute (MIN) standard brain was performed according to the method developed by M. Brett (Brett, 1999).

To investigate the similarities and differences between the affective–perceptual and cognitive–evaluative forms of empathy, the selected studies were categorized according to their experimental paradigms. In empathy studies which adopted an affective–perceptual task, the subjects were usually not informed about the goal of the study, but were rather asked to passively perceive a picture or film-clip depicting others' emotional or sensory experience. In some of the studies, a distraction task was employed. In cognitive–evaluative task, the subjects were explicitly asked to evaluate others' emotional or sensory states, and overt responses were required.

To control for stimulus-specific effects in the comparison between affective–perceptual and cognitive–evaluative forms of empathy, the stimulus modality of these studies were described for these two categories respectively, including the emotional or sensory feeling empathised by the subject, i.e., angry, anxiety, disgust, fear, happy, multiple emotion, pain, sad, and touch, as well as whether the stimuli were based on somatosensation. Chi-square tests were conducted to examine whether the selected empathy relevant studies were equally distributed into the affective–perceptual and cognitive–evaluative category, and whether the constitution of studies relying upon different types of stimuli differs between affective–perceptual and cognitive–evaluative empathy. Since MKDA results are also affected by the sample size and the quality of the statistical analysis of the original studies, studies in these two categories were also compared concerning their sample size and the false discovery rate correction they adopted.

## 2.2. Multi-level kernel density analysis (MKDA)

Following the MKDA approach used in several recently published meta-analyses (Etkin and Wager, 2007; Kober et al., 2008b; Wager et al., 2008; Wager et al., 2007; Wager et al., 2009), peak coordinates in a particular statistical contrast map (SCM) were collected for the selected empathy relevant studies. The MKDA approach has several important advantages: Unlike previous voxel-wise meta-analytical methods (i.e., ALE, KDA) which summarise peak coordinates directly, the MKDA algorithm first constructs activation indicator maps from the reported coordinates of each study before it summarises these activation indicator maps. This 'random effects' approach takes account of the multilevel nature of the data, and prevents the results from being biased by a large number of peak coordinates reported by a single study, thus accessing true consistency across studies. MKDA also allows the activation indicator maps entering the meta-analysis to be weighted based on the sample size and the quality of the statistical analysis used in the original study, so that larger and more rigorously performed studies can exert more influence on the meta-analytic results.

To integrate peaks across space, the peaks obtained from each SCM were convolved with a 10 mm spherical kernel and thresh-

olded at a maximum value of 1, so that multiple nearby peaks were not counted as multiple activations. This resulted in an indicator map for each SCM, where a voxel value of 1 indicates a peak in the neighbourhood, whilst 0 indicates the absence of a peak. The weighted average of all indicator maps provided a summary map, in which the weight of each SCM was the square root of the sample size multiplied by an adjusted number (1 – the SCM resulted from a random-effect analysis; 0.75 – the SCM resulted from a fixed-effects analysis) and a user defined number (1 – the SCM reported results at a corrected level, either FWE or FDR; 0.75 – the SCM reported uncorrected results). Finally, a statistical threshold was established through 5000 iterations of a Monte-Carlo procedure, and the results were reported as an MKDA statistic map at a height threshold of FWE corrected  $p < 0.05$  and a stringent threshold of uncorrected  $p < 0.001$ . To rule out the possible confounding stimuli-specific effect, the weighted proportion of contrasts activated within each cluster was also calculated for studies adopting different types of stimuli.

## 2.3. Comparison between affective–perceptual and cognitive evaluative empathy

To compare the similarities and differences between affective–perceptual empathy and cognitive–evaluative empathy, the whole database was divided into two sub-databases, with an MKDA analysis being conducted for each one of them. The two MKDA statistic maps were mounted on the same stereotaxic standard brain to indicate the overlapping and distinctive regions involved in these two tasks.

To further confirm the activation specificity across two sub-databases, separate maps constructed for each of the two task types were subtracted to yield difference maps. The same procedure was employed in the course of the Monte Carlo randomisation to establish a threshold for significant differences. The results were reported as an MKDA subtraction map at a height threshold of FWE corrected  $p < 0.05$ .

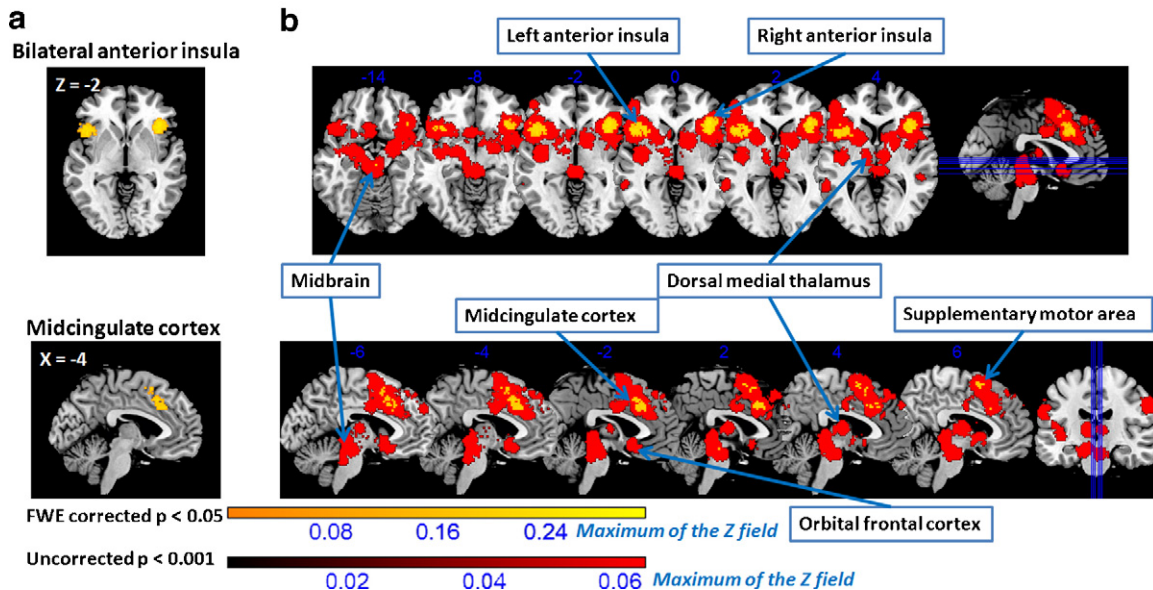
To rule out the possible confounding stimulus-specific effect in the comparison between affective–perceptual and cognitive–evaluative empathy, the weighted percentage of contrasts activated within each cluster was calculated for studies adopting different type of stimuli.

## 3. Results

### 3.1. Description of the selected studies and the balances between its categorizations

Forty studies – with 50 contrasts and 664 peak coordinates – were considered to be relevant for empathy, and thus included in our analysis (see [Supplementary Table 1](#)). Among these 50 contrasts, 32 contrasts investigating the affective–perceptual forms of empathy were compared with 18 contrasts investigating the cognitive–evaluative forms of empathy. The stimulus modality investigated in these contrasts is described in [Supplementary Table 2](#). Chi-square test showed no significant difference between contrasts investigating affective–perceptual and cognitive–evaluative forms of empathy regarding their constitution of the target feelings empathised by the subject ( $\chi^2(8) = 11.205$ ,  $p > 0.1$ ), despite there being more contrasts of empathy for pain than other feelings in both categories (in affective–perceptual empathy:  $\chi^2(8) = 26.500$ ,  $p < 0.001$ ; in cognitive–evaluative empathy:  $\chi^2(3) = 11.300$ ,  $p < 0.01$  with zero counts in several cells). Chi-square test also showed that there was no significant difference concerning the proportion of somatosensory-based stimulus and non-somatosensory based stimuli between the affective–perceptual

## MKDA results for all empathy relevant studies



**Fig. 1.** Brain regions showing consistent activation across all empathy studies, with threshold level at FWE corrected  $p < 0.05$  (yellow colour in a and b) and  $p < 0.001$  uncorrected (red colour in b). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

and cognitive–evaluative forms of empathy ( $\chi^2(1) = 0.496$ ,  $p > 0.4$ ). Moreover, no significant difference was observed between the contrasts investigating affective–perceptual and cognitive–evaluative forms of empathy concerning their sample size ( $t(48) = -0.028$ ,  $p > 0.9$ ) and the quality of their statistics (whether their results were corrected from false discovery rate or not;  $\chi^2(1) = 0.573$ ,  $p > 0.4$ ).

### 3.2. MKDA results of all empathy relevant studies

Three main clusters of activation were identified by the MKDA analysis of all the empathy relevant studies at an FWE corrected level ( $p < 0.05$ , cluster size  $> 10$  voxels). The first cluster was centred at the anterior midcingulate cortex (aMCC), with its ventral–rostral edge extending to dorsal anterior cingulate cortex (dACC) and its dorsal–caudal edge extending to supplementary motor area (SMA). This corresponds to the caudal part of Brodmann Area 32 and the rostral part of Brodmann Area 6 (adjacent to Brodmann Area 8) (see Fig. 1 and Table 1). The second and third clusters were centred at the left and right anterior insular cortex, respectively, and extended to the adjacent inferior frontal gyrus, corresponding to Brodmann Area 13 and 47 (see Fig. 1 and Table 1). Three more clusters, located at bilateral dorsal medial thalamus (DMT), medial orbital frontal cortex (OFC) and midbrain, were found at a less stringent threshold level (uncorrected  $p < 0.001$ , cluster size  $> 3273 \text{ mm}^3$ ) (see Fig. 1). In contrast to some previous studies (Benuzzi et al., 2008; de Gelder et al., 2004; Grosbras and Paus, 2006; Lawrence et al., 2006), regions from the putative mirror neuron system, such as the left inferior frontal gyrus (IFG; BA 45) and bilateral inferior parietal lobule (IPL; BA 40), were not observed in our results at a corrected level. Finally, in order to verify that the observed activation consistence was not solely contributed by a specific type of stimuli, we calculated the weighted activation proportions for contrasts investigating different feelings empathised by the subjects. The weighted activation confirmed that the activation of these three brain regions, the dACC–aMCC–SMA and the bilateral AI, was contributed by a certain percentage of contrasts investigating empathy for disgust, fear, pain, and those contrasts using more than one type of emotion as stimuli (see Table 1).

### 3.3. Comparison between affective–perceptual and cognitive–evaluative forms of empathy

The left anterior insula (BA 13) was found to be recruited in both affective–perceptual and cognitive–evaluative forms of empathy (see Table 2); this was further confirmed when the MKDA statistic maps of the two tasks were mounted together, showing a regional overlap in exactly this region (see Fig. 2). In contrast, the right anterior insula extending to right inferior frontal gyrus (BA 13/47) was found more frequently involved in affective–perceptual forms of empathy, confirmed by the MKDA subtraction analysis (see Table 2). The dorsal part of left anterior midcingulate cortex (BA 32) was more frequently activated in cognitive–evaluative rather than affective–evaluative forms of empathy, as confirmed in the MKDA subtraction analysis (see Table 2). To further ensure that the differences between the affective–perceptual and cognitive–evaluative forms of empathy were not due to the difference between two specific types of stimuli, weighted activation proportions of contrasts investigating different type of stimuli were calculated (see Table 2). These affirmed that the two brain regions differentiating the two forms of empathy, the dorsal aMCC and the right AI, were not solely contributed by contrasts from a specific type of emotion (Fig. 3).

In addition to these results on the FWE corrected level, additional regions were observed at a less stringent threshold level ( $p < 0.001$  uncorrected, cluster size  $> 3133 \text{ mm}^3$ ). The ventral part of anterior midcingulate cortex extending to right dACC, midbrain and right DMT were shown to be more frequently engaged in affective–perceptual forms of empathy; whilst the left OFC and left DMT were shown to be more frequently associated with cognitive–evaluative forms of empathy.

## 4. Discussion

A quantitative meta-analysis on fMRI studies of empathy was conducted in order to, firstly, determine the existence of a shared network of brain regions across all task and stimulus domains; and, secondly, to identify any differences in brain activation between two putative empathy types, affective–perceptual and cognitive–evaluative. As hypothesised, a collection of brain regions consis-



**Table 1**  
MKDA results of all empathy relevant studies.

Region	BA	MNI coordinates			Maxstat.	Vol.	Weighted activation proportion (%)								
		X	Y	Z			Angry	Anxiety	Disgust	Fear	Happy	Multi-emotion	Pain	Sad	Touch
							<b>2</b>	<b>1</b>	<b>4</b>	<b>2</b>	<b>5</b>	<b>11</b>	<b>21</b>	<b>2</b>	<b>2</b>
<b>Right insula/inferior frontal gyrus</b>	13/47	38	24	−2	0.32	373	0	100%	30.79%	100%	22.52%	30.32%	67.81%	0	55.25%
○ Right insula/inferior frontal gyrus	47	38	24	−8											
○ Right insula/inferior frontal gyrus	47	40	24	0											
<b>Left insula/inferior frontal gyrus</b>	13/47	−42	18	0	0.28	311	100%	0	78.92%	100%	42.92%	41.98%	65.22%	45.49%	0
○ Left insula	13	−36	16	2											
○ Left inferior frontal gyrus	47	−48	16	0											
○ Left inferior frontal gyrus	47	−42	20	−2											
<b>Left anterior mid cingulate cortex/dorsal anterior cingulate cortex</b>	32	−2	24	38	0.25	176	0	100%	20.37%	48.46%	0	21.36%	64.79%	0	0
<b>Left supplementary motor area</b>	6	−4	14	54	0.22	35	0	100%	51.16%	51.54%	0	40.46%	56.78%	0	0
○ Left supplementary motor area	6	0	14	54											
○ Left supplementary motor area	6	−8	12	48											
<b>Right supplementary motor area</b>	6	6	8	60	0.22	28	0	100%	51.16%	51.54%	0	37.14%	37.15%	0	0

Note. MNI coordinates for the most consistent peak activation foci across all empathy studies, reported at a threshold level of FWE corrected  $p < 0.05$ , cluster size  $> 10$  voxels, with their corresponding Brodmann Area (BA), the maximum statistic value (Maxstat.), the number of voxels (Vol.), and the weighted percentage of contrasts activated in each cluster calculated for each type of stimuli respectively. (The total number of contrasts for each type of stimuli is listed as bold size number below the stimuli labels.)

**Table 2**  
MKDA results of affective–perceptual and cognitive–evaluation empathy.

Region	BA	x	y	z	Maxstat.	Voxels	Weighted Activation Proportion (%)								
							Angry	Anxiety	Disgust	Fear	Happy	Multi-emotion	Pain	Sad	Touch
							<b>2</b>	<b>1</b>	<b>3</b>	<b>2</b>	<b>5</b>	<b>4</b>	<b>12</b>	<b>1</b>	<b>2</b>
<b>Affective–perceptual empathy</b>															
Right anterior insula/inferior frontal gyrus	13/47	40	24	−4	0.41	295	0	100%	39.02%	100%	22.52%	23.63%	68.96%	0	55.25%
Left anterior insula/inferior frontal gyrus	13/47	−44	18	0	0.32	84	53.9%	0	64.83%	100%	42.92%	31.87%	68.38%	100%	0
Right supplementary motor area	6	6	8	58	0.25	10	0	100%	64.83%	51.54%	0	59.47%	39.49%	0	0
<b>Cognitive–evaluation empathy</b>							<b>0</b>	<b>0</b>	<b>1</b>	<b>0</b>	<b>0</b>	<b>7</b>	<b>9</b>	<b>1</b>	<b>0</b>
Left anterior midcingulate cortex	32	−6	18	46	0.49	203			0			45.7%	72.5%	0	
Left anterior insula	13	−34	16	0	0.35	9			0			12.21%	60.99%	0	
<b>Affective–perceptual &gt; Cognitive–evaluation</b>							<b>2</b>	<b>1</b>	<b>3</b>	<b>2</b>	<b>5</b>	<b>4</b>	<b>12</b>	<b>1</b>	<b>2</b>
Right anterior insula/inferior frontal gyrus	13/47	44	28	0	0.29	34	0	100%	39.02%	100%	0	23.63%	68.96%	0	55.25%
<b>Cognitive–evaluation &gt; Affective–experiential</b>							<b>0</b>	<b>0</b>	<b>1</b>	<b>0</b>	<b>0</b>	<b>7</b>	<b>9</b>	<b>1</b>	<b>0</b>
Left anterior midcingulate cortex	32	−6	20	46	0.45	88						45.7%	72.5%		

Note. MNI coordinates for the most consistent peak activation foci within affective–perceptual forms of empathy and cognitive–evaluative forms of empathy respectively, as well as results of the subtraction between these two forms of empathy, reported at a threshold level of FWE corrected  $p < 0.05$ , cluster size  $> 10$  voxels, with their corresponding Brodmann Area (BA), the maximum statistic value (Maxstat.), the number of voxels (Vol.), and the weighted percentage of contrasts activated in each cluster calculated for each type of stimuli respectively. (The total number of contrasts for each type of stimuli is listed as bold size number below the stimuli labels.)

and exteroceptive stimuli in empathy (Lamm and Singer, 2010; Singer et al., 2009; Wiebking et al., 2010). The exact nature of this intero- and exteroceptive linkage and its mediation by the insula remain unclear however.

In a second main finding, it was revealed that the dorsal part of the aMCC on the left hemisphere was engaged more frequently in the cognitive–evaluative forms of empathy, whilst the right AI engaged more frequently in the affective–perceptual forms of empathy. Unlike the right AI, the left AI engaged in both forms of empathy (i.e., both affective–perceptual and cognitive–evaluative). The weighted activation proportion also showed that such a division of the core empathy network identified here is not restrained within one particular type of stimuli modality, providing strong evidence against an explanation for these findings through possible stimulus-specific effects. Supporting previous hypothesis, these findings provide the first piece of meta-analytic evidence confirming the distinct and associated neural bases underlying the affective–perceptual and the cognitive–evaluative forms of empathy.

The finding that an asymmetry exists between the right and left AI between the cognitive–evaluative and affective–perceptual forms of empathy reflects previous findings of functional and anatomical differences between these two regions (Craig, 2009). The right AI has been suggested to be involved in a circuit that also includes paralimbic regions such as the thalamus and PAG, and which may be involved in the evaluation of ‘bottom-up’ intero- and exteroceptive affective signals (Kober et al., 2008b), as well as being suggested to be more involved in the processing signals from the body (Craig, 2002, 2003, 2009; Critchley et al., 2004). The preferential involvement of this region in the affective–perceptual form of empathy may thus be related to this interaction with such sub-cortical regions. In contrast, the assumable further processing or linkage involved in the cognitive–evaluative form of empathy would appear to be mediated by the left AI alone. These points remain speculative at present, however.

The finding that the dorsal aMCC is involved in the cognitive–evaluative forms of empathy (and, at a lower significance level, the involvement of the ventral aMCC, extending to dACC, in the affective–perceptual forms of empathy) are in concordance with previous cytoarchitecture and receptor architecture researches highlighting the aMCC and dACC as chemoarchitecturally distinct brain structures (Palomero-Gallagher et al., 2008; Palomero-Gallagher et al., 2009; Vogt et al., 2003; Vogt and Vogt, 2003). Connectivity results (Vogt et al., 2003; Vogt and Vogt, 2003) have shown that the aMCC, extending to SMA, with its direct connection to the spinal cord and skeletal movement, plays a key role in the motor-motivation component of empathy, whilst dACC connects with limbic system, potentially coding the value of affective stimulus. Our finding suggested a dorsal ventral division of aMCC, in which the dorsal aMCC involved more in the cognitive–evaluative forms of empathy and the ventral part involved more in the affective–perceptual forms of empathy.

Although the results of the current analysis appear to give compelling support to each of the study's two hypotheses, there are naturally limitations inherent within the technique of meta-analysis, and in particular in cases such as this where there have been a slightly limited number of source studies undertaken. This shortage of source studies was particularly acute in relation to studies where empathy was induced by audio rather than visual stimuli, thus potentially restricting the applicability of the study's conclusions across all domains. However, were these findings to simply be an artifact of the stimuli type, one would not expect to see the dACC/aMCC and insula to be identified in empathy-type studies that utilise other stimuli or media. A variety of empathy-related studies not suitable for inclusion in the current meta-analysis do, however, show activations in these regions, suggesting that the

activation of these core regions is a result of there being some underlying core process, rather than a product of a particular stimulus type (Bach et al., 2008; Brune et al., 2008; Mitterschiffthaler et al., 2007; Morris et al., 1999; Sander et al., 2007; Sander and Scheich, 2005; Warren et al., 2006). Further investigation utilising non-visual stimuli aimed towards filling this particular gap is required.

Limited by insufficient studies within the domain of each emotion being empathised, we could not directly compare each emotion directly, which sets limit on our conclusion as to the vital role of the three core regions in empathy towards different emotions. However, the activation proportion clearly showed that the activation of the three core regions is not restrained by specific emotion type, which is consistent with previous findings (Lamm and Singer, 2010; Singer et al., 2009; Singer and Lamm, 2009). It should also be noted that, whilst the proportion of studies from each stimulus domain in the cognitive–evaluative and affective–perceptual classes did not differ significantly, the overall number of pain-related studies was greater than that of other empathy domains. Replication of the current results when a more extensive and balanced selection of studies becomes available may thus be warranted.

Some recent studies of empathy have suggested that there is a differentiation in the neural response to empathy-related stimuli according to gender (e.g., Derntl et al., 2010; Schulte-Ruther et al., 2008; Singer et al., 2006). With few studies of this effect available at present it was not possible to compare males and females in the current analysis. There is thus the possibility that gender differences exist in the regions forming the core-network and their activity. Those studies that do show gender differences in relevant task-types generally highlight areas outwith those identified in the current study (e.g., the amygdala (Derntl et al., 2010) and inferior frontal gyrus (Schulte-Ruther et al., 2008)), however, and so it seems likely that the overall findings described here apply to both sexes, with any specific differences existing in other, non-core, regions. Further investigation of this issue is required, however.

The nature of coordinate-based meta-analysis means that it does not take into account the deactivation information of the original studies (Salimi-Khorshidi et al., 2009). Especially concerning the subtraction analysis between the affective–perceptual and the cognitive–evaluative forms of empathy, its results could possibly be influenced if there is more deactivation within one of the two categories. The impact of deactivation regions in empathy thus needs to be investigated in future studies.

Restrained by the available fMRI studies, the majority of regions identified in our meta-analysis were located within the cortex, the involvement of sub-cortical regions was also apparent, i.e. the DMT and midbrain. That more sub-cortical regions are not flagged in our meta-analysis may be due to the relative insensitivity of fMRI to activations in these regions. As highlighted by Grimm et al. (2009, 2008), many higher brain regions correlated negatively with affective ratings, whilst subcortical networks correlate positively during the viewing of emotional material. One may wonder if the affective impact of empathy may also have a subcortical locus of control. Moreover, that such ‘lower’ brain regions are also central to empathy is supported by observation of empathy-like behaviour in mice (Chen et al., 2009; Langford et al., 2006). Further work on these regions in empathy is required in order to clarify the situation. In particular, the wider range of techniques, such as lesion or directional connectivity studies, which are available to animal rather than human studies, would provide extremely valuable insight, and may further highlight the conceptual issues in development such as the formation of attachment bonding and care giving (Panksepp, 1989/2004; Watt, 2007).

From a methodological perspective, the empathy-relevant contrasts taken in our meta-analysis usually revealed brain regions

involved in empathy in general, rather than any interaction or modulation. We thus did not choose studies that measured empathy through its interference upon another task (such as through a Stroop task Lee et al., 2008), nor by its sensitivity to other impacting factors (for example expertises, as in Cheng et al., 2007; or the reality of stimuli, as in Gu and Han, 2007), and so the impact of these factors upon our conclusions remains unknown at present. In addition, MKDA meta-analysis regards only the location of brain activation, and so is insensitive to any information about activation amplitude. This means that some variation in the degree of activation of the core regions (i.e., the dACC-aMCC-SMA and bilateral AI) may exist across the range of task and stimuli types.

To conclude, as hypothesized, MKDA meta-analysis identified a set of neural areas that are consistently activated in empathy across a various of empathy paradigms. It is suggested that these areas, the dACC-aMCC-SMA and bilateral anterior insula, support a core function underlying empathy. It was further demonstrated that the affective-perceptual and cognitive-evaluative forms of empathy are subserved by different but associated neural bases, suggesting a more detailed division of specific functions within regions of this core empathy network.

## Acknowledgments

The study was supported by a Heisenberg grant from the Salus Foundation, German Research Foundation (DFG, 304/4-1 to G.N.), the SFB/DFG (SFB 779-A6 to G.N.), and the Hope of Depression Research Foundation (HDRF) (to G.N.).

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.neubiorev.2010.10.009.

## References

- Bach, D.R., Grandjean, D., Sander, D., Herdener, M., Strik, W.K., Seifritz, E., 2008. The effect of appraisal level on processing of emotional prosody in meaningless speech. *Neuroimage* 42, 919–927.
- Batson, C.D., 2009. These things called empathy. In: Decety, J., Ickes, W. (Eds.), *The Social Neuroscience of Empathy*. MIT Press, Cambridge, MA.
- Benuzzi, F., Lui, F., Duzzi, D., Nichelli, P.F., Porro, C.A., 2008. Does it look painful or disgusting? Ask your parietal and cingulate cortex. *J. Neurosci.* 28, 923–931.
- Blakemore, S.J., Bristow, D., Bird, G., Frith, C., Ward, J., 2005. Somatosensory activations during the observation of touch and a case of vision-touch synaesthesia. *Brain* 128, 1571–1583.
- Brett, M., 1999. *The MNI Brain and the Talairach Atlas*. Cambridge Images.
- Brune, M., Lissek, S., Fuchs, N., Witthaus, H., Peters, S., Nicolas, V., Juckel, G., Tegenthoff, M., 2008. An fMRI study of theory of mind in schizophrenic patients with “passivity” symptoms. *Neuropsychologia* 46, 1992–2001.
- Carr, L., Iacoboni, M., Dubeau, M.C., Mazziotta, J.C., Lenzi, G.L., 2003. Neural mechanisms of empathy in humans: a relay from neural systems for imitation to limbic areas. In: *Proceedings of the National Academy of Sciences of the United States of America* 100, pp. 5497–5502.
- Chakrabarti, B., Bullmore, E., Baron-Cohen, S., 2006. Empathizing with basic emotions: common and discrete neural substrates. *Soc. Neurosci.* 1, 364–384.
- Chen, Q., Panksepp, J.B., Lahvis, G.P., 2009. Empathy is moderated by genetic background in mice. *PLoS ONE* 4, e4387.
- Cheng, Y., Lin, C.P., Liu, H.L., Hsu, Y.Y., Lim, K.E., Hung, D., Decety, J., 2007. Expertise modulates the perception of pain in others. *Curr. Biol.* 17, 1708–1713.
- Craig, A.D., 2002. How do you feel? Interoception: the sense of the physiological condition of the body. *Nat. Rev. Neurosci.* 3, 655–666.
- Craig, A.D., 2003. Interoception: the sense of the physiological condition of the body. *Curr. Opin. Neurobiol.* 13, 500–505.
- Craig, A.D., 2009. How do you feel–now? The anterior insula and human awareness. *Nat. Rev. Neurosci.* 10, 59–70.
- Critchley, H.D., Wiens, S., Rotshtein, P., Ohman, A., Dolan, R.J., 2004. Neural systems supporting interoceptive awareness. *Nat. Neurosci.* 7, 189–195.
- de Gelder, B., Snyder, J., Greve, D., Gerard, G., Hadjikhani, N., 2004. Fear fosters flight: a mechanism for fear contagion when perceiving emotion expressed by a whole body. *Proc. Natl. Acad. Sci. U.S.A.* 101, 16701–16706.
- de Vignemont, F., Singer, T., 2006. The empathic brain: how, when why? *Trends Cogn. Sci.* 10, 435–441.
- Decety, J., 2010. To what extent in the experience of empathy mediated by shared neural circuits? *Emotion Rev.* 2, 204–207.
- Decety, J., Jackson, P.L., 2004. The functional architecture of human empathy. *Behav. Cogn. Neurosci. Rev.* 3, 71–100.
- Decety, J., Jackson, P.L., 2006. A social-neuroscience perspective on empathy. *Curr. Dir. Psychol. Sci.* 15, 54–58.
- Decety, J., Lamm, C., 2006. Human empathy through the lens of social neuroscience. *ScientificWorldJournal* 6, 1146–1163.
- Decety, J., Lamm, C., 2007. The role of the right temporoparietal junction in social interaction: how low-level computational processes contribute to meta-cognition. *Neuroscientist* 13, 580–593.
- Derntl, B., Finkelmeyer, A., Eickhoff, S., Kellermann, T., Falkenberg, D.I., Schneider, F., Habel, U., 2010. Multidimensional assessment of empathic abilities: neural correlates and gender differences. *Psychoneuroendocrinology* 35, 67–82.
- Eisenberg, N., Strayer, J., 1987. *Empathy and its Development*. Cambridge University Press.
- Eslinger, P.J., 1998. Neurological and neuropsychological bases of empathy. *Eur. Neurol.* 39, 193–199.
- Etkin, A., Wager, T.D., 2007. Functional neuroimaging of anxiety: a meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia. *Am. J. Psychiatry* 164, 1476–1488.
- Fan, Y., Han, S., 2008. Temporal dynamic of neural mechanisms involved in empathy for pain: an event-related brain potential study. *Neuropsychologia* 46, 160–173.
- Farrow, T.F., Zheng, Y., Wilkinson, I.D., Spence, S.A., Deakin, J.F., Tarrier, N., Griffiths, P.D., Woodruff, P.W., 2001. Investigating the functional anatomy of empathy and forgiveness. *Neuroreport* 12, 2433–2438.
- Gallese, V., 2001. The ‘shared manifold’ hypothesis: from mirror neurons to empathy. *J. Conscious. Stud.* 8, 33–50.
- Gallese, V., 2003. The roots of empathy: the shared manifold hypothesis and the neural basis of intersubjectivity. *Psychopathology* 36, 171–180.
- Gallese, V., 2007. Embodied simulation: from mirror neuron systems to interpersonal relations. *Novartis Found Symp.* 278, 3–12 (discussion 12–19, 89–96, 216–221).
- Gallese, V., Fadiga, L., Fogassi, L., Rizzolatti, G., 1996. Action recognition in the premotor cortex. *Brain* 119 (Pt 2), 593–609.
- Gallese, V., Keysers, C., Rizzolatti, G., 2004. A unifying view of the basis of social cognition. *Trends Cogn. Sci.* 8, 396–403.
- Goubert, L., Craig, K.D., Vervoort, T., Morley, S., Sullivan, M.J., de C.W.A.C., Cano, A., Crombez, G., 2005. Facing others in pain: the effects of empathy. *Pain* 118, 285–288.
- Grimm, S., Boesiger, P., Beck, J., Schuepbach, D., Birmohl, F., Walter, M., Ernst, J., Hell, D., Boeker, H., Northoff, G., 2009. Altered negative BOLD responses in the default-mode network during emotion processing in depressed subjects. *Neuropsychopharmacology* 34, pp. 932–843.
- Grimm, S., Ernst, J., Boesiger, P., Schuepbach, D., Hell, D., Boeker, H., Northoff, G., 2008. Increased self-focus in major depressive disorder is related to neural abnormalities in subcortical-cortical midline structures. *Hum. Brain Mapp.*
- Grosbras, M.H., Paus, T., 2006. Brain networks involved in viewing angry hands or faces. *Cereb. Cortex* 16, 1087–1096.
- Gu, X., Han, S., 2007. Attention and reality constraints on the neural processes of empathy for pain. *Neuroimage* 36, 256–267.
- Hein, G., Singer, T., 2008. I feel how you feel but not always: the empathic brain and its modulation. *Curr. Opin. Neurobiol.*
- Hennenlotter, A., Schroeder, U., Erhard, P., Castrop, F., Haslinger, B., Stoeker, D., Lange, K.W., Ceballos-Baumann, A.O., 2005. A common neural basis for receptive and expressive communication of pleasant facial affect. *Neuroimage* 26, 581–591.
- Hynes, C.A., Baird, A.A., Grafton, S.T., 2006. Differential role of the orbital frontal lobe in emotional versus cognitive perspective-taking. *Neuropsychologia* 44, 374–383.
- Jabbi, M., Swart, M., Keysers, C., 2007. Empathy for positive and negative emotions in the gustatory cortex. *Neuroimage* 34, 1744–1753.
- Jackson, P.L., Brunet, E., Meltzoff, A.N., Decety, J., 2006a. Empathy examined through the neural mechanisms involved in imagining how I feel versus how you feel pain. *Neuropsychologia* 44, 752–761.
- Jackson, P.L., Meltzoff, A.N., Decety, J., 2005. How do we perceive the pain of others? A window into the neural processes involved in empathy. *Neuroimage* 24, 771–779.
- Jackson, P.L., Rainville, P., Decety, J., 2006b. To what extent do we share the pain of others? Insight from the neural bases of pain empathy. *Pain* 125, 5–9.
- Keysers, C., Wicker, B., Gazzola, V., Anton, J.L., Fogassi, L., Gallese, V., 2004. A touching sight: SII/PV activation during the observation and experience of touch. *Neuron* 42, 335–346.
- Kober, H., Barrett, L.F., Joseph, J., Bliss-Moreau, E., Lindquist, K., Wager, T.D., 2008a. Functional grouping and cortical-subcortical interactions in emotion: a meta-analysis of neuroimaging studies. *NeuroImage* 42, 998–1031.
- Kober, H., Barrett, L.F., Joseph, J., Bliss-Moreau, E., Lindquist, K., Wager, T.D., 2008b. Functional grouping and cortical-subcortical interactions in emotion: a meta-analysis of neuroimaging studies. *Neuroimage* 42, 998–1031.
- Lamm, C., Batson, C.D., Decety, J., 2007. The neural substrate of human empathy: effects of perspective-taking and cognitive appraisal. *J. Cogn. Neurosci.* 19, 42–58.
- Lamm, C., Singer, T., 2010. The role of anterior insular cortex in social emotions. *Brain Struct. Funct.* 214, doi:10.1007/s00429-00010-00251-00423.
- Langford, D.J., Crager, S.E., Shehzad, Z., Smith, S.B., Sotocinal, S.G., Levenstadt, J.S., Chanda, M.L., Levittin, D.J., Mogil, J.S., 2006. Social modulation of pain as evidence for empathy in mice. *Science* 312, 1967–1970.

- Lawrence, E.J., Shaw, P., Giampietro, V.P., Surguladze, S., Brammer, M.J., David, A.S., 2006. The role of 'shared representations' in social perception and empathy: an fMRI study. *Neuroimage* 29, 1173–1184.
- Lee, T.W., Dolan, R.J., Critchley, H.D., 2008. Controlling emotional expression: behavioral and neural correlates of nonimitative emotional responses. *Cereb. Cortex* 18, 104–113.
- Leslie, K.R., Johnson-Frey, S.H., Grafton, S.T., 2004. Functional imaging of face and hand imitation: towards a motor theory of empathy. *Neuroimage* 21, 601–607.
- Levenson, R.W., Ruef, A.M., 1992. Empathy: a physiological substrate. *J. Pers. Soc. Psychol.* 63, 234–246.
- Mitterschiffthaler, M.T., Fu, C.H., Dalton, J.A., Andrew, C.M., Williams, S.C., 2007. A functional MRI study of happy and sad affective states induced by classical music. *Hum. Brain Mapp.* 28, 1150–1162.
- Moriguchi, Y., Decety, J., Ohnishi, T., Maeda, M., Mori, T., Nemoto, K., Matsuda, H., Komaki, G., 2007. Empathy and judging other's pain: an fMRI study of alexithymia. *Cereb. Cortex* 17, 2223–2234.
- Morris, J.S., Scott, S.K., Dolan, R.J., 1999. Saying it with feeling: neural responses to emotional vocalizations. *Neuropsychologia* 37, 1155–1163.
- Morrison, I., Lloyd, D., di Pellegrino, G., Roberts, N., 2004. Vicarious responses to pain in anterior cingulate cortex: is empathy a multisensory issue? *Cogn. Affect Behav. Neurosci.* 4, 270–278.
- Palomero-Gallagher, N., Mohlberg, H., Zilles, K., Vogt, B., 2008. Cytology and receptor architecture of human anterior cingulate cortex. *J. Comp. Neurol.* 508, 906–926.
- Palomero-Gallagher, N., Vogt, B.A., Schleicher, A., Mayberg, H.S., Zilles, K., 2009. Receptor architecture of human cingulate cortex: evaluation of the four-region neurobiological model. *Hum. Brain Mapp.* 30, 2336–2355.
- Panksepp, J., 1989/2004. Altruism and helping behaviors, neurobiology. In: Adelman, G., Smith, B.H. (Eds.), *Encyclopedia of Neuroscience*, 3rd ed. Elsevier, New York.
- Phan, K.L., Wager, T., Taylor, S.F., Liberzon, I., 2002. Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. *NeuroImage* 16, 331–348.
- Preston, S.D., Bechara, A., Damasio, H., Grabowski, T.J., Stansfield, R.B., Mehta, S., Damasio, A.R., 2007. The neural substrates of cognitive empathy. *Soc. Neurosci.* 2, 254–275.
- Preston, S.D., de Waal, F.B., 2002. Empathy: Its ultimate and proximate bases. *Behav. Brain Sci.* 25, 1–20 (discussion 20–71).
- Salimi-Khorshidi, G., Smith, S.M., Keltner, J.R., Wager, T.D., Nichols, T.E., 2009. Meta-analysis of neuroimaging data: a comparison of image-based and coordinate-based pooling of studies. *NeuroImage* 45, 810–823.
- Sander, K., Frome, Y., Scheich, H., 2007. fMRI activations of amygdala, cingulate cortex, and auditory cortex by infant laughing and crying. *Hum. Brain Mapp.* 28, 1007–1022.
- Sander, K., Scheich, H., 2005. Left auditory cortex and amygdala, but right insula dominance for human laughing and crying. *J. Cogn. Neurosci.* 17, 1519–1531.
- Schulte-Ruther, M., Markowitsch, H.J., Shah, N.J., Fink, G.R., Piefke, M., 2008. Gender differences in brain networks supporting empathy. *NeuroImage* 42, 393–403.
- Seitz, R.J., Nickel, J., Azari, N.P., 2006. Functional modularity of the medial prefrontal cortex: involvement in human empathy. *Neuropsychology* 20, 743–751.
- Singer, T., 2006. The neuronal basis and ontogeny of empathy and mind reading: review of literature and implications for future research. *Neurosci. Biobehav. Rev.* 30, 855–863.
- Singer, T., 2007. The neuronal basis of empathy and fairness. *Novartis Found Symp.* 278, 20–30 (discussion 30–40, 89–96, 216–221).
- Singer, T., Critchley, H.D., Preusschoff, K., 2009. A common role of insula in feelings, empathy and uncertainty. *Trends Cogn. Sci.* 13, 334–340.
- Singer, T., Lamm, C., 2009. The social neuroscience of empathy. *Ann. N.Y. Acad. Sci.* 1156, 81–96.
- Singer, T., Seymour, B., O'Doherty, J., Kaube, H., Dolan, R.J., Frith, C.D., 2004. Empathy for pain involves the affective but not sensory components of pain. *Science* 303, 1157–1162.
- Singer, T., Seymour, B., O'Doherty, J.P., Stephan, K.E., Dolan, R.J., Frith, C.D., 2006. Empathic neural responses are modulated by the perceived fairness of others. *Nature* 439, 466–469.
- van der Gaag, C., Minderaa, R.B., Keysers, C., 2007. Facial expressions: what the mirror neuron system can and cannot tell us. *Soc. Neurosci.* 2, 179–222.
- Vogt, B.A., Berger, G.R., Derbyshire, S.W., 2003. Structural and functional dichotomy of human midcingulate cortex. *Eur. J. Neurosci.* 18, 3134–3144.
- Vogt, B.A., Vogt, L., 2003. Cytology of human dorsal midcingulate and supplementary motor cortices. *J. Chem. Neuroanat.* 26, 301–309.
- Wager, T.D., Barrett, L.F., Bliss-Moreau, E., Lindquist, K., Duncan, S., Kober, H., Joseph, J., Davidson, M., Mize, J., 2008. The neuroimaging of emotion. In: Lewis, M., Haviland-Jones, J.M., Barrett, L.F. (Eds.), *Handbook of Emotions*, 3rd ed. Guilford Press, New York, pp. 249–271.
- Wager, T.D., Lindquist, M., Kaplan, L., 2007. Meta-analysis of functional neuroimaging data: current and future directions. *Soc. Cogn. Affect Neurosci.* 2, 150–158.
- Wager, T.D., Lindquist, M.A., Nichols, T.E., Kober, H., Van Snellenberg, J.X., 2009. Evaluating the consistency and specificity of neuroimaging data using meta-analysis. *NeuroImage* 45, S210–221.
- Warren, J.E., Sauter, D.A., Eisner, F., Wiland, J., Dresner, M.A., Wise, R.J., Rosen, S., Scott, S.K., 2006. Positive emotions preferentially engage an auditory-motor "mirror" system. *J. Neurosci.* 26, 13067–13075.
- Watt, D., 2007. Toward a neuroscience of empathy: integrating affective and cognitive perspectives. *Neuro-Psychoanalysis* 9, 119–172.
- Wicker, B., Keysers, C., Plailly, J., Royet, J.P., Gallese, V., Rizzolatti, G., 2003. Both of us disgusted in My insula: the common neural basis of seeing and feeling disgust. *Neuron* 40, 655–664.
- Wiebking, C., Bauer, A., de Greck, M., Duncan, N.W., Tempelmann, C., Northoff, G., 2010. Abnormal body perception and neural activity in the insula in depression: an fMRI study of the depressed "material me". *World J. Biol. Psychiatry* 11, 538–549.