Neural correlates of compassion - An integrative systematic review

Novak, Lukas; Malinakova, Klara; Mikoska, Petr; van Dijk, Jitse P.; Tavel, Peter

Published in:
International Journal of Psychophysiology

DOI:
10.1016/j.ijpsycho.2021.12.004

International Journal of Psychophysiology 172 (2022) 46–59

Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

Neural correlates of compassion – An integrative systematic review

Lukas Novak [a,b,*], Klara Malinakova [a], Petr Mikoska [a], Jitse P. van Dijk [a,b,c], Peter Tavel [a]

[a] Olomouc University Social Health Institute, Palacký University Olomouc, Olomouc, Czech Republic
[b] Department of Community and Occupational Medicine, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands
[c] Graduate School Kosice Institute for Society and Health, P.J. Safarik University in Kosice, Kosice, Slovak Republic

ARTICLE INFO

Keywords:
Compassion
Neuroanatomical bases
Empathic concern
fMRI
MRI

ABSTRACT

Compassion is a psychological construct that has received increasing attention in recent years. Even though a lot of work has been done to identify neural correlates of empathy across studies, such work has not been properly done on neural correlates of compassion. Therefore, the aim was to systematically review the literature on neural correlates of compassion.

We have searched through PsycINFO, PubMed and Web of Science for relevant articles published between 1985 and 2020. We included the studies ($n = 35$) examining the relationship between brain structure or function and compassion. Screening was performed by two authors, between whom a level of agreement was calculated. The quality of the studies was assessed by measures used in other studies as well by measures specific for our study aims. This study was conducted under PRISMA guidelines.

Our analysis revealed that the most frequent neural associations with compassion across all analysed studies can be found in the orbital part of the left inferior frontal gyrus, in the right cerebellum, the bilateral middle temporal gyrus, in the bilateral insula and the right caudate nucleus.

Our findings suggest that people displaying a lower compassion tend to have either lower neural activity or a grey matter volume in neural areas associated with reward.

1. Introduction

Together with empathy, compassion strongly influences human social interactions, especially interactions when someone seems to be in need. Although empathy refers to sharing emotions while acknowledging that another person is the cause of emotions (Singer and Lamm, 2009), compassion does not entail emotional sharing and is rather 'complementary social emotion elicited by witnessing the suffering of others and is rather associated with feelings of concern and warmth, linked to the motivation to help' (Preckel et al., 2018, p. 1).

It is assumed (Goetz et al., 2010) that the construct of compassion yields two components: compassion state or dispositional compassion (trait). A state reflects how a person is feeling or responding in the present moment. A trait, on the other hand, depicts a general tendency or how a person feels or responds most of the time (Medvedev et al., 2021, p. 637).

In general, compassion (both state and trait) has been recognised as the construct with significant evolutionary benefits. Compassion could evolve as the adaptive function that increases the human ability to effectively care for offspring and increases cooperation or prosocial behaviour (Di Bello et al., 2020; Gilbert, 2020; Goetz et al., 2010) and altruism (FeldmanHall et al., 2015). Compassionate care towards oneself and other people is supposed to foster mental health and well-being of the individual (Strauss et al., 2016) and compassion training could serve as a strategy that could prevent burnout (Klimecki et al., 2014). Moreover, compassion is likely to bring large practical advantages also in health care settings (Strauss et al., 2016), and finally fostering patient's satisfaction with health care services. Because of these practical implications, there is a growing research interest in the associations of compassion with various aspects of human life (Strauss et al., 2016).

However, despite this growing research interest (Mascaro et al., 2020), there is still a lack of studies that would systematically describe the neural circuits underlying this social emotion. The need for such systematic review work is even larger, since the results from neuroimaging studies examining neural substrates of compassion are inconsistent. For example, the study of Kim et al. (2009), reported a neural activation during a compassion state besides other areas in the medial prefrontal cortex and in the inferior parietal lobe. On the contrary,

* Corresponding author at: OUSHI - Olomouc University Social Health Institute, Palacký University Olomouc, Univerzitni 244/22, 771 11 Olomouc, Czech Republic.

E-mail address: lukas.novak@oushi.upol.cz (L. Novak).

https://doi.org/10.1016/j.ijpsycho.2021.12.004
Received 4 December 2020; Received in revised form 3 December 2021; Accepted 10 December 2021
Available online 25 December 2021

Immordino-Yang et al. (2009) found no activation of these areas.

In previous years, several meta-analysis and systematic reviews (Y. Fan et al., 2011; Lamm et al., 2011) as well as lesion studies (Shamay-Tsoory, 2015) examining neural substrates of empathy have been published. However, a systematic review or meta-analytic evidence concerning neural correlates of compassion across different methodologies is still missing. So far, two meta-analyses have been published (Hou et al., 2017; Kim et al., 2020a). The first (Hou et al., 2017) examined neural correlates of trait compassion. Nevertheless, the generalizability of the findings from this meta-analysis is crucially limited. They also used as a keyword: "empathy" for the search of neural correlates of compassion with the justification that empathy is a similar construct to compassion and that the database did not contain the word "compassion." This might explain the fact that their results correspond to the findings of studies that revealed neural activity in anterior insula and anterior cingulate cortex across empathy tasks, as described in the meta-analysis of Fan et al. (2011).

The second meta-analysis (Kim et al., 2020a) focused on the functional correlates of state compassion, but only in fMRI studies. Since only fMRI studies were included, this study did not explore the results of the structural studies (e.g. structural MRI), which also provide valuable information about neural correlates of compassion.

From a methodological perspective, systematic examination of functional neural networks underlying human behaviour usually rests on the analysis of the results of functional Magnetic Resonance Imaging (fMRI). However, the fMRI and other functional neuroimaging methods have one central limitation, that is, from the neural activity during a certain compassion task it is not possible to infer a causal connection (Shdo et al., 2018). Thus, a narrative synthesis of studies, which uses other than functional neuroimaging methods, might increase the value

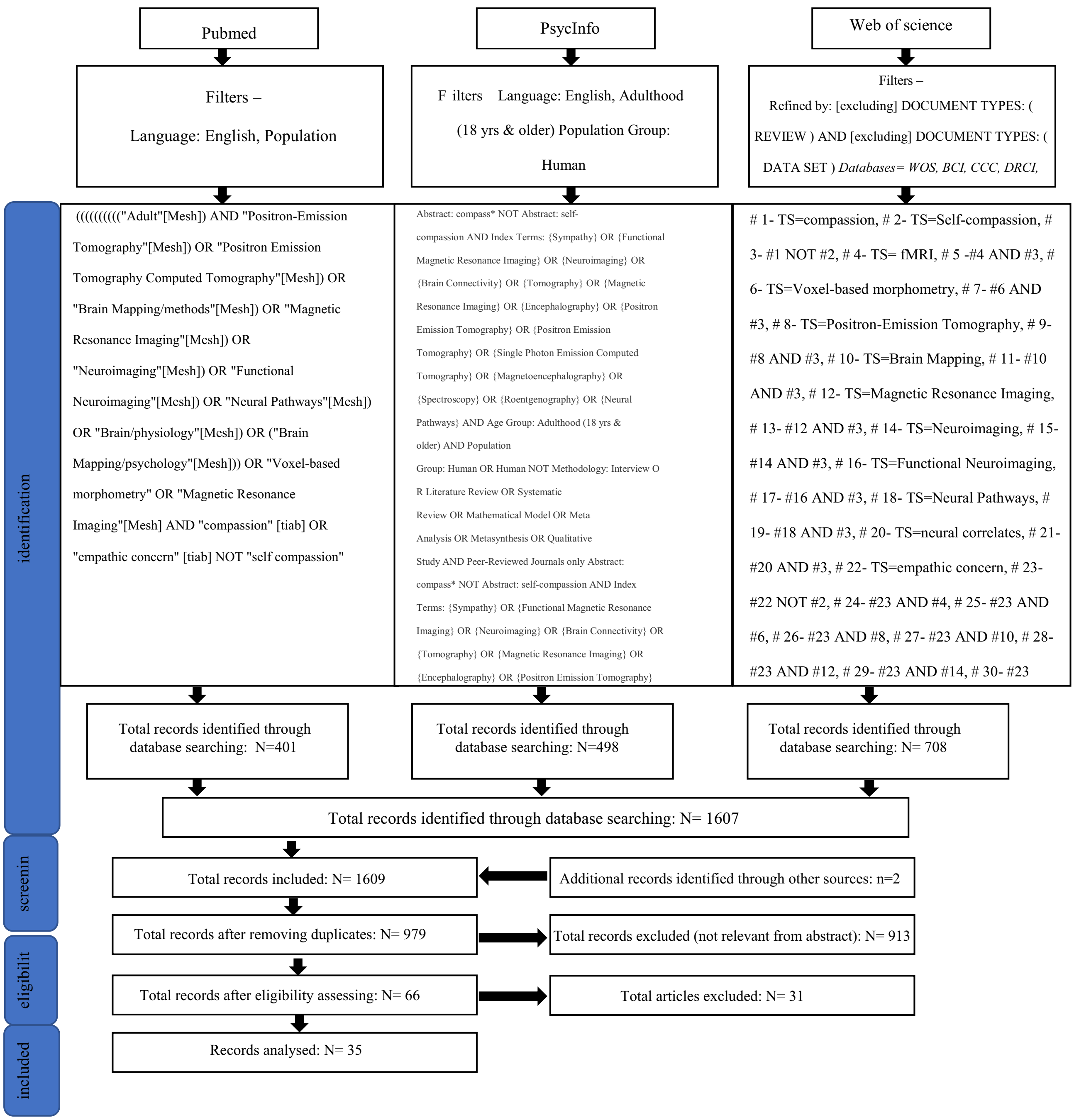

Fig. 1. Prisma diagram and syntax.

of our findings. These other methods include Magnetic resonance imaging (MRI) or Computed tomography (CT). A central characteristic of these methods is that they provide information about the neuroanatomical structures associated with some experimental tasks (structural studies). When these methods are used to explore the relationship between damaged brain structure and behaviour, they are called lesion studies. These studies can provide findings that are necessary and sufficient (Shdo et al., 2018) to infer a causal connection between brain structure and some behaviour, like compassion. Importantly, in lesion studies, it is possible to recruit and measure large cohorts (Hogeveen et al., 2016; Rankin et al., 2006), which makes the results from these studies even more informative.

Lesion studies, fMRI, as well as structural studies have limitations that may be bridged by mutual integration of these approaches. For instance, if the fMRI studies suggests that a particular part of the brain is associated with compassion, by analysis of results of lesion study we may confirm the results of neuroimaging studies and in addition make a step forward and provide a causal explanation. This is why we have decided to integrate functional neuroimaging, structural paradigm (involving health subjects) and lesion studies in our analysis. To the best of our knowledge such integrative systematic review evidence on the neuronal substrates of compassion is fully lacking. Therefore, the aim of this systematic review is to identify the neuronal correlates of compassion both state and tendency.

2. Method

2.1. Search protocol

In order to assure as much structure reliability as possible, we followed the recommendations of the PRISMA statement (Liberati et al., 2009) - see the PRISMA Flow Diagram in Fig. 1. We have searched for relevant studies in three databases: Web of Science, PubMed, and PsycINFO. Because the number of studies from 1985 using structural MRI has started to increase dramatically (Edelman, 2014) we limited our search from 1985 up to July 2020. A search algorithm consisted of the following basic terms and their synonyms: "compassion" and "neuroimaging", from which the syntax for each separate database has been made (Fig. 1).

In some studies, "empathy" and "compassion" are used interchangeably (e.g. Immordino-Yang et al., 2014). Thus, in order to facilitate the search for relevant studies, we have also searched for studies examining compassion by the 'empathic concern scale', which is part of the perhaps most widely used Interpersonal reactivity index (IRI) questionnaire developed by Davis (1983) and which is considered to measure compassion tendency (Lebowitz and Dovidio, 2015; Patil et al., 2018; Shamay-Tsoory, 2015; Shamay-Tsoory and Lamm, 2018). The search was conducted in July 2020 by the first author (LN) assisted by the third (PM) according to separate syntax for each database (see list of syntaxes in Fig. 1). The search through the databases has been done by the Thesaurus in case of PsycINFO, through MeSH terms for PubMed, and by a combination of keywords in Web of Science.

2.2. The selection of studies; inclusion and exclusion criteria

As a first step, after removing duplicates using programs Zotero and EndNote, the first author (LN) scanned through the final list of titles and abstracts, trying to select the studies for eligibility assessing. During the same time, the third author (PM) randomly selected and assessed a subset of titles and abstracts ($n = 414$), trying to choose appropriate ones for eligibility evaluation. In order to explore inter-rater reliability and in accordance with recommendations regarding the measurement of agreement between raters (McHugh, 2012), we calculated both the percentage of agreement and Cohen's Kappa (Cohen, 1960). Kappa values above 0.60 are thought to reflect a substantial level of agreement (Landis and Koch, 1977). In case of disagreement between two authors, which study to include, the first author (LN) provided rationale and decided which study to include further into eligibility assessing (see Online Supplementary material: Novak et al. (2020)). The inclusion criteria were: 1) the study reported the association between a structure of the brain or brain function and either an experience of compassion or score in the compassion questionnaire; 2) the study included adults (i.e., older than 18 years) from the healthy population. Studies examining the non-healthy population of adults were included only if there was also a control group consisting of healthy adults (typical in lesion studies). In special cases, the authors included studies ($n = 5$) in which the health status was not reported (Online Supplementary Table 3) and the study was an empirical study (conference papers with empirical data were included); 4) the study used magnetic resonance imaging (MRI), functional magnetic resonance imaging (fMRI), positron emission tomography (PET) or structural magnetic resonance imaging (MRI);

Excluded were 945 studies consisting of: 1) review articles including systematic reviews and meta-analysis; 2) theoretical articles, e.g. editorials, letters, commentaries; 3) case studies; 4) qualitative studies; 5) neuroimaging studies not referring to compassion; 6) compassion during meditation state. We also excluded studies, where the correlation between compassion and neural activity in fMRI was utilized during economic decision making and studies that linked compassion with neural activity during economic game settings in fMRI (e.g. Ogawa et al., 2018). Also, we excluded studies exploring neural substrates of self-compassion. The number of excluded studies and their reasons can be found in Table 1. As a second step, the first author reviewed the full text of the articles in order to explore whether they fit our eligibility criteria.

2.3. Data extraction

For each study, which passed through our eligibility criteria, the following information has been gathered: 1) general information regarding publication (e.g. title, year of publication, author names); 2) data concerning the study sample (e.g. number of participants, percentage of women in the sample, ethnicity, mean age), study design and measures (e.g. fMRI or lesion study, compassion measure, type of compassion inducing paradigm) and neural correlates associated with compassion. If the study reported coordinates in Talairach space, we converted them to Montreal Neurological Institute coordinate space (MNI) using the Yale online converter: http://sprout022.sprout.yale.edu/mni2tal/mni2tal.html. Due to a large methodological divergence across studies, we did not perform a meta-analysis. Across studies, not only methodological divergence, but also different neuroanatomical labelling is very frequent. It is therefore likely that this large heterogeneity of anatomical labelling would indirectly affect the results. In addition, it is not uncommon that in the study results, crucial

Table 1
Number of excluded studies with the reasons for exclusion.

Reason for exclusion	N
Absence of neural correlates or irrelevant measure (e.g. EEG)	474
Review, theoretical article, commentary, dissertation, case studies, meta-analysis, qualitative studies, theoretical article/study, review, commentary, ethnographic study, editorial, meta-analysis, systematic review.	208
Compassion has not been measured or induced	116
Paper not focussing on Compassion but on Compassion fatigue	38
Non–adult population	34
Did not fit our inclusion criteria for other reasons	30
Abstract and/or study was not found	8
Duplicate left by program	8
Methodological incompatibility, e.g. even when the compassion state has been measured, there have been other processes present that very likely masked neural activity during compassion (e.g. decision-making processes)	6
Compassion focused therapy	6
Non-human	3
Self-compassion	2

information about lateralization of the brain area activity during certain tasks is missing (e.g. Moll et al., 2007). Thus, in order to deal with both issues, we have decided to review peak voxel coordinates and relabel voxel coordinates to a more uniform form using the Automatic anatomical labelling atlas (Tzourio-Mazoyer et al., 2002) in MRIcron software (https://www.nitrc.org/projects/mricron). When a study reported neural activity related to different stimuli inducing compassion (e.g. social pain, physical pain), we reviewed peak voxel coordinates from the areas in which activity was overlapping across stimuli. Similarly, if there was a possibility to report either neural activation during compassion for innocent or compassion for responsible, we have reported neural activity during compassion for innocent. Likewise, we reviewed peak voxel coordinates related to compassion to sad or suffering faces but not to neural faces. Based on type of compassion inducing stimuli, studies were assigned into two categories: 1) written narratives; 2) video or picture observation. Consequently, neural correlates of compassion state between these two categories were explored. Descriptive statistics and other statistical calculations were performed in R 4.0.1 (R Core Team, 2020) using lpSolve (Berkelaar, 2020) and irr (Gamer et al., 2019) packages (for calculation of percentage of agreement and Cohen's Kappa). Confidence intervals (95%) for Kappa were calculated separately, according to the following formula below, where SD is standard error of the estimated κ:

$$95CI = \kappa \pm z_{\alpha/2}\, SD\, (\kappa)$$

2.4. Study quality evaluation

2.4.1. Data acquisition

Theoretical articles (Preckel et al., 2018) identify the Orbitofrontal cortex (OFC) as one of the regions activated during compassion. However, tissue-air interfaces may result in false magnetic field gradients in the orbitofrontal region, with a subsequent deprivation of signal and image perversion. This issue is more significant at high magnetic fields and for rapid Gradient-Echo based sequences, for instance Echo-Planar-Imaging (EPI), particularly used in studies applying fMRI to detect brain activity (Moccia et al., 2017). Strategies exist to prevent the occurrence of these problems (Moccia et al., 2017) and so it is important to identify in each fMRI study, whether some strategies have been used to optimize the quality of structural MRI image in the orbitofrontal part of the cortex during fMRI scanning.

2.4.2. Compassion assessment

Regarding other criteria, we also evaluated whether participants were told to generate compassion deliberately or whether the compassion score was obtained by a questionnaire measuring participant tendencies to experience compassion. Besides that, we registered whether the participants were told, what the word: "compassion" or other words labelling the same construct was referring to.

2.4.3. Confounding variables

Because a number of studies reported a possible association of socioeconomic status with compassion (Callister and Plante, 2017; Piff and Moskowitz, 2018; Stellar et al., 2012), we also evaluated whether socioeconomic status was considered. We did not use established quality measures protocols, because with respect to our study aims, much stricter criteria for evaluating study quality were needed. As there are gender differences in neural activity during compassion (Mercadillo et al., 2011), another indicator of a study quality was the proportion of female participants in the sample and in turn, the generalizability of its findings.

2.4.4. Sample size

During the quality assessment, we also evaluated a sample size. Based on recommendations of David et al. (2013), an analysed study was labelled as "1" if the number of subjects was ≥16.

3. Results

3.1. Inter-rater reliability results

In percentages, 96.40% of agreement between authors was found; Cohen's Kappa test revealed that there was significant agreement between raters with the following Kappa value: K = 0.72; 95% CI [0.58–0.85]; $p < 0.001$. Thus, our inter-rater reliability results suggest a high level of agreement between authors.

3.2. Socio-demographic results

The data from the 35 studies was analysed (Table 2). The first study concerning neural correlates of compassion was published in 2006. Age median of the total sample ($n = 2956$) was: 27.68 years old with median SD = 4.32. Percentage of female participants in all studies ranged from 100% (Klimecki et al., 2013, 2014; Majdandžić et al., 2016) to 0% (Hein et al., 2010). Across all studies, 50% of all participants were female (median = 50%). One study did not report the number of female and male respondents (Simon-Thomas et al., 2012). In total, 45.71% ($n = 16$) of studies reported a percentage of right-handed participants. In addition, 17.14%, ($n = 6$) of studies reported the ethnicity of participants. Furthermore 8.57% ($n = 3$) of all studies reported the socio-economic status.

Almost all studies reported that their subjects (in control groups) were in general health (i.e., good general health, absence of psychiatric or neurological diseases). However, several fMRI studies: 14.70% ($n = 5$) did not report the health status of the participants. Two structural MRI studies (5.88%) did not specify what exactly the notion "healthy" meant. Most patients in the structural studies (studies using structural MRI or CT) consisted of either Alzheimer's disease or Frontotemporal dementia. For detailed information, see the Online Supplementary Table 1.

3.3. General neurobiological underpinnings of compassion: General results

Across all 35 studies, in total, 98 neuroanatomical and functional locations associated with compassion (both state and tendency) have been identified. For further information regarding frequency of association and other details see Online Supplementary material 2: Novak et al. (2020).

3.4. Neurobiological substrates of compassion tendency

The analysis of fMRI studies, which examined compassion tendency ($n = 6$) revealed relatively frequent activation in left insula (50.0%) see Fig. 3.

Similarly, results from structural studies ($n = 11$) which explored compassion tendency in both healthy and psychiatric participants showed most frequently an association with the right insula (36.4%), left insula and right caudate nucleus (27.3%) - see Figs. 3 and 2. Interestingly, two structural MRI studies of Takeuchi et al., (2016) and Banissy et al., (2012), reported a negative correlation between brain structure and compassion tendency in: left precentral gyrus, right lingual gyrus, left ACG, left precuneus, left IFG - pars opercularis. Finally, one study (Bernhardt et al., 2014) found no relationship between compassion tendency and cortical thickness in left and right insula and left medial frontal despite the fact that these locations were regions of interest of the study. For further results see Online Supplementary table 3.

Subsequent analysis of structural studies ($n = 5$) examining compassion tendency in brain lesion patients revealed that most frequent neural association has been observed in the left insula (60.0%) – Fig. 3, followed by: right insula, left IFG - pars orbitalis, left and right caudate nucleus, left MCA, left putamen, right midcingulate cortex and left thalamus (40.0%). However, one study (Hogeveen et al., 2016) did

Table 2
Displays results and basic information about studies, which examined neuroanatomical bases of compassion.

study	Total number of participants from which data were analysed	Neuroimaging method	Independent measures; triggers measures of compassion or method of inducing compassion	Dependent measure: Compassion	Findings summary
Rankin et al. (2006)	143	MRI	correlation between grey matter tissue density and IRI - EC	IRI - EC	empathic concern positively correlated with grey matter tissue density in right MTG; right caudate nucleus; right IFG - pars orbitalis; right olfactory cortex
Moll et al. (2007)	12	fMRI	short scenarios inducing compassion, guilt, etc.	post scanning rating (0–4) of compassion felt	compassion > neutral agency → right cerebellum; left MTG; right MTG; right MFG; left middle frontal gyrus; left ACG; left MOG; right parahippocampal gyrus; left STG; left ventral pallidum
Kédia et al. (2008)	29	fMRI	affective and control stories	following fMRI session 1–7 Likert scale → compassion ratings to each story	compassion (someone harms someone) > self-anger (I harm myself) → increase activity in left MTG; right MTG; left precuneus; left MFG
Immordino-Yang et al. (2009)	13	fMRI	narratives about real people's lives inducing compassion	self-report button press in fMRI to indicate strength of induced compassion	compassion > neutral →left insula; right insula; left MTG; right MTG; left MCA; left SMG; left ACG; left hippocampus; left PCG; right hypothalamus; right SMG; left mesencephalon; right mesencephalon; posterior cingulate cortex
Kim et al. (2009)	21	fMRI	facial pictures (sad, neutral)	self-report button press in fMRI (scale 1–10)	Compassion attitude towards sad faces > neutral attitude towards sad faces → left and right insula; left IFG - pars orbitalis; right cerebellum; right caudate nucleus; right IFG - pars orbitalis; left putamen; right ACG; left IFG - pars triangularis; right putamen; left and right SMA; left SMG; left cerebellum; SMA; right thalamus; right Rolandic operculum; left SN/VTA; right SN/VTA; left STP; right STP; left globus pallidus; left periaqueductal grey; left GR,
Zahn et al. (2009)	16	fMRI	narratives inducing compassion	IRI-EC; after scanning rating of emotion (compassion and other) most strongly associated with narrative (i.e., compassion - Yes/ No).	empathic concern scale → right ACG
Hein et al. (2010)	16	fMRI	observation of the video of in-group and out-group pain	empathic concern scale Batson, (1997 in Herin et al., 2010)	compassion during video observation no in-group or out-group conditions → left insula
Lang et al. (2011)	22	?#?	hearing negative sounds displaying human suffering	IRI – EC	Empathic concern positively correlated with activity in left insula left thalamus right thalamus during hearing of suffering of others (pain)
Mercadillo et al. (2011)	24	fMRI	pictures representing suffering	button press indicating feeling of compassion (Yes/no)	compassion > neutral → left IFG - pars orbitalis; right MTG; left and right IFG - pars triangularis; left SMA; left precentral gyrus; left MOG; right precentral gyrus; left SPL; right STG; left IPL; right SPL; left IFG - pars opercularis
Simon-Thomas et al. (2012)	16	fMRI	affective pictures	self-reported intensity of experience of compassion	compassion provoking pictures (harm and suffering) > neutral pictures → activation in right cerebellum; right IFG - pars orbitalis
Bruneau et al. (2012)	37	fMRI	narratives depicting other persons in pain (social and physical)	self-report scale (1–4) in fMRI after story was presented	no relationship between compassion and neural activity
Banissy et al., 2012	118	MRI	correlation between grey matter volume and IRI – EC	IRI - empathic concern	There has been found a negative correlation between Empathic Concern and grey matter volume in the left ACG; left precentral gyrus; left precuneus; left IFG - pars opercularis
Klimecki et al., 2013	28	fMRI	video observation (depicting people in distress)	compassion questionnaire	right IFG - pars triangularis; right putamen; right GR; right SFG - orbital part right SN/ VTA; left IOG; right globus pallidus; right IOG
Immordino-Yang and Singh, 2013	13	fMRI	narratives about real people's lives inducing compassion	self-report button press in fMRI to indicate strength of induced compassion	compassion for physical and social pain > neutral → left MTG; right MTG; right ITG
Bernhardt et al., 2014	94	MRI	correlation between cortical thickness and IRI - EC	IRI – EC	there has been found no correlation between cortical thickness between IRI - EC and brain structure in left insula and left MFG

(*continued on next page*)

Table 2 (*continued*)

study	Total number of participants from which data were analysed	Neuroimaging method	Independent measures; triggers measures of compassion or method of inducing compassion	Dependent measure: Compassion	Findings summary
Fehse et al., 2015	18	fMRI	narratives from everyday life events inducing compassion	self-report button press in fMRI (felt/did not feel)	compassion for innocent > compassion for responsible → left insula; left MCA; right ACG; left parahippocampal gyrus; left fusiform gyrus; left hippocampus; left mOFC; right postcentral gyrus; right paracentral lobule
Immordino-Yang et al., 2014	47	fMRI	narratives about real people's lives inducing compassion	self-report button press in fMRI (scale 1–4)	compassion > neutral → left insula; left STP
Klimecki et al., 2014	25	fMRI	video observation	compassion questionnaire	compassion training > memory training during observation of suffering → left and right IFG - pars orbitalis; right MFG; left IFG - pars triangularis; left ACG; left and right OFC, left ventral striatum
Kraus et al., 2014	25	MRI	correlation between grey matter volume and IRI – EC	IRI – EC	Empathic concern positively correlated with grey matter volume in left parahippocampal gyrus
Engen and Singer, 2015	15	fMRI	video observation	not reported	voluntary generating compassion > passive watching → left insula; left IFG - pars orbitalis; right cerebellum; left MTG; right MTG; right caudate nucleus; left putamen; right MFG; Cerebellar vermis; left caudate nucleus; right ACG; left IFG - pars triangularis; left middle frontal gyrus; left SMA; left ACG; left precentral gyrus; left cerebellum; right SMA; left precuneus; left PCG; left mOFC; left MFG; left SFG - orbital part; right hypothalamus; left SPL; right mOFC; left olfactory cortex; left paracentral lobule
Mercadillo et al., 2015	24	fMRI	pictures representing suffering	button press indicating feeling of compassion (Yes/no)	compassion > social cues → right cerebellum; left FG; left hippocampus; right amygdala; right MOG
Kanske et al., 2015	178	fMRI	correlation between brain activity during observation of affective video depicting person, telling sad story	Likert scale (compassion) induced	compassion experienced during observation of the negative video story did vary with activity in left IFG - pars orbitalis; right cerebellum; right MFG; Cerebellar vermis; left caudate nucleus; right IFG - pars triangularis; left middle frontal gyrus; left SMA; left SMG; left cerebellum; left precuneus; left SN/VTA; right STG; left lingual gyrus; right ventral striatum
Majdandžić et al., 2016	30	fMRI	photo and symbol indicating degree of pain in the person in the photo	post scanning IRI and its part - empathic concern scale	empathic concern score correlated with activity in left insula pain > no- pain
Takeuchi et al., 2016a, 2016b	777	MRI	correlation of brain structure and compassion score in (Temperament Character Inventory)	compassion vs. revengefulness in Temperament Character Inventory	regional GM density (rGMD) of right lingual gyrus negatively correlated with compassion
Chen et al., 2016	64	MRI	correlation between insular glioma (L, R) and IRI (EC)	IRI – EC	patients with left and glioma has significantly lower empathic concern score in comparison to both healthy controls and posterior glioma control
Baez et al., 2016	49	MRI	correlation between empathic concern measured by one question (i.e., "how sad do you feel for the hurt person?") and regional grey matter volume	one empathic concern question (i.e., "how sad do you feel for the hurt person?" scale: −9 to 9 ranging	significant association have been revealed between empathic concern score and grey matter volume in right GR, (beta value = 0. 31)
Dermody et al., 2016	71	MRI	correlation between IRI - EC and grey matter intensity	IRI - EC rated by caregiver (no explanation, who exactly caregiver is)	decrease of empathic concern was associated with decrease density of grey matter volume in: left insula; left IFG - pars orbitalis; left MTG; left MCA; left putamen; left precentral gyrus; right midcingulate cortex; left MOG; left thalamus; right precentral gyrus; left orbitorfontal cortex; left postcentral gyrus
Ashar et al., 2017	66	fMRI	listening to stories displaying suffering of another person/s, observing pictures of suffering individual while listening to story about him.	rating of compassion in scanner (scale 1–5)	compassion > empathic distress → right caudate nucleus; left caudate nucleus; left middle frontal gyrus; left SMA; left ACG; right GR; left SMG; left precentral gyrus; orbital part of right and left SFG; right

(continued on next page)

Table 2 (*continued*)

study	Total number of participants from which data were analysed	Neuroimaging method	Independent measures; triggers measures of compassion or method of inducing compassion	Dependent measure: Compassion	Findings summary
					SMA; left precuneus; right precentral gyrus; right STP; right postcentral gyrus; right mOFC; left lingual gyrus; left paracentral lobule; left IPL; left IFG - pars opercularis; right lingual gyrus
Valk et al., 2017	307	MRI	correlation between compassion score (Likert scale) and grey matter volume after several months of compassion training	Likert scale (compassion)	compassion increase (measured by socio-affective video task) after three month of training was associated with thickness in right insula; left IFG - pars orbitalis; right IFG - pars triangularis; left FG; right ITG; right olfactory cortex; right parahippocampal gyrus; right STP; right amygdala; right MTP
Weng et al. (2018)	24	fMRI	observation of neutral faces and negative (suffering)	compassion training induces changes - no questionnaire	compassion group post-training > Reappraisal group post -training, negative pictures > neutral pictures → Activation < right amygdala, < right insula and right SFG - orbital part
Hogeveen et al. (2016)	166	CT	correlation between brain structure and compassion scale (IRI -EC)	IRI - EC - completed by participants	no relationship found between brain lesions in Anterior insula; IFG; ventromedial PFC; ACC and empathic concern scale
Shdo et al. (2018)	275	MRI	correlation of brain structure and IRI - EC score	IRI - EC - completed by participant's informant	IRI - EC correlated with grey matter volume in: left insula; right insula; left and right IFG - pars orbitalis; right caudate nucleus; left putamen; left caudate nucleus; right putamen; right GR; orbital part of both right and left SFG; right subcallosal area
Patil et al. (2018)	79	MRI	correlation between empathic concern score and enlargement in regions of interest e.g. Right insular cortex	IRI – EC	positive association has been found between score in EC and enlargement in: right insula; right MFG; Cerebellar vermis; left middle frontal gyrus; right SMA; right IFG - pars opercularis; right lingual gyrus
Sturm et al. (2018)	80	MRI	correlation between grey matter volume and IRI – EC	IRI – EC	lower empathic concern was associated with reduced grey matter volume in left and right caudate nucleus; left MCA; right midcingulate cortex; left and right thalamus
Miller et al. (2020)	34	TMS	Group difference in compassion state after TMS application over right MTG	Likert scale (1–7) indicating the degree of experienced compassion	There was no difference between the experimental group and control group in compassion after TMS application

Abbreviations: IFG (inferior frontal gyrus); SN/VTA (substantia nigra/ventral tegmental area); SFG (superior frontal gyrus); PFC (prefrontal cortex); ACC (anterior cingulate cortex); IRI – EC (interpersonal reactivity index – empathic concern scale); GM (grey matter); CT (Computed tomography); MRI (Magnetic resonance imaging) fMRI (functional magnetic resonance imaging) middle temporal gyrus (MTG), medial frontal gyrus (MFG), supplementary motor area (SMA), anterior cingulate gyrus (ACG), midcingulate area (MCA), gyrus rectus (GR), supramarginal gyrus (SMG), middle occipital gyrus (MOG), fusiform gyrus (FG), superior temporal gyrus (STG), superior temporal pole (STP), inferior temporal gyrus (ITG), posterior cingulate gyrus (PCG), medial orbitofrontal cortex (mOFC), superior parietal lobule (SPL), inferior parietal lobule (IPL), Inferior occipital gyrus (IOG), middle temporal pole (MTP), transcranial magnetic stimulation (TMS).

not find any relationship between compassion tendency and neural structure.

Fig. 2: displays axial and sagittal view on right caudate nucleus frequently associated with compassion in structural studies. MNI co-ordinates ($x = 10$, $y = 13$, $z = -3$) were obtained from Shdo et al. (2018).

Interestingly, the biggest differences between fMRI studies examining neural activation in compassion state and compassion tendency has been observed in the right cerebellum (compassion state 40.0% vs. compassion tendency 0.0%). In summary, our results suggest that compassion tendency and compassion state have across both fMRI and structural studies differences, but also an overlapping neural substrate (e.g. in left IFG - pars orbitalis - see Fig. 3). The results concerning neurobiological substrates of compassion state can be found in Online Supplementary material 2. It has to be noted that only one fMRI study (Weng et al., 2018) reported deactivations (in right amygdala and insula) during compassion state.

3.5. *Neuronal differences associated with different paradigms*

We also explored the effect of different compassion inducing stimuli on neural activity during the compassion state. We found that written or heard narratives about misfortunates of others ($n = 8$) were more frequently associated with neural activity in the left and right MTG (in 50% of cases), compared to studies ($n = 10$) that used video or pictures (10% of all cases).

The comparison of video or picture observation with written or heard narratives revealed that the left IFG pars orbitalis and triangularis were activated by video or picture observation (40.0%) but not by written or heard narratives (0.0%). Differences were also observed in the activation of the right cerebellum (40.0% for observation vs. 12.5% for narratives), right IFG pars orbitalis (see Fig. 2 in the main text) and left SMA (30.0% for observation vs. 0.0% for narratives). Similar frequencies of activation in the left insula (40.0% for pictures or videos displaying misfortunates of others vs. 37.5% for written or heard narratives) have also been found- see Online Supplementary Table 8.

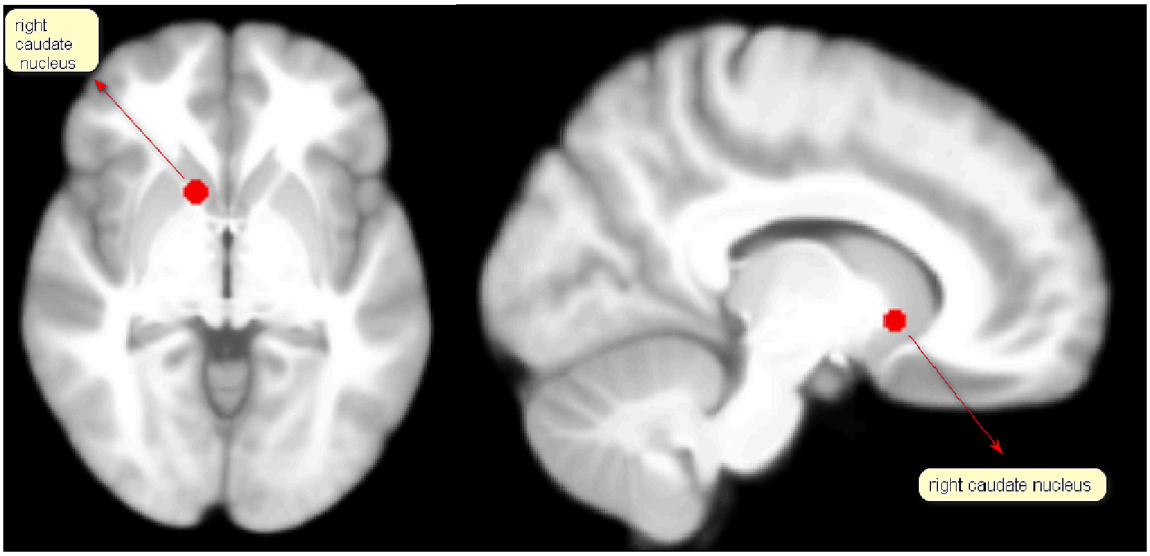

Fig. 2. Right caudate nucleus.

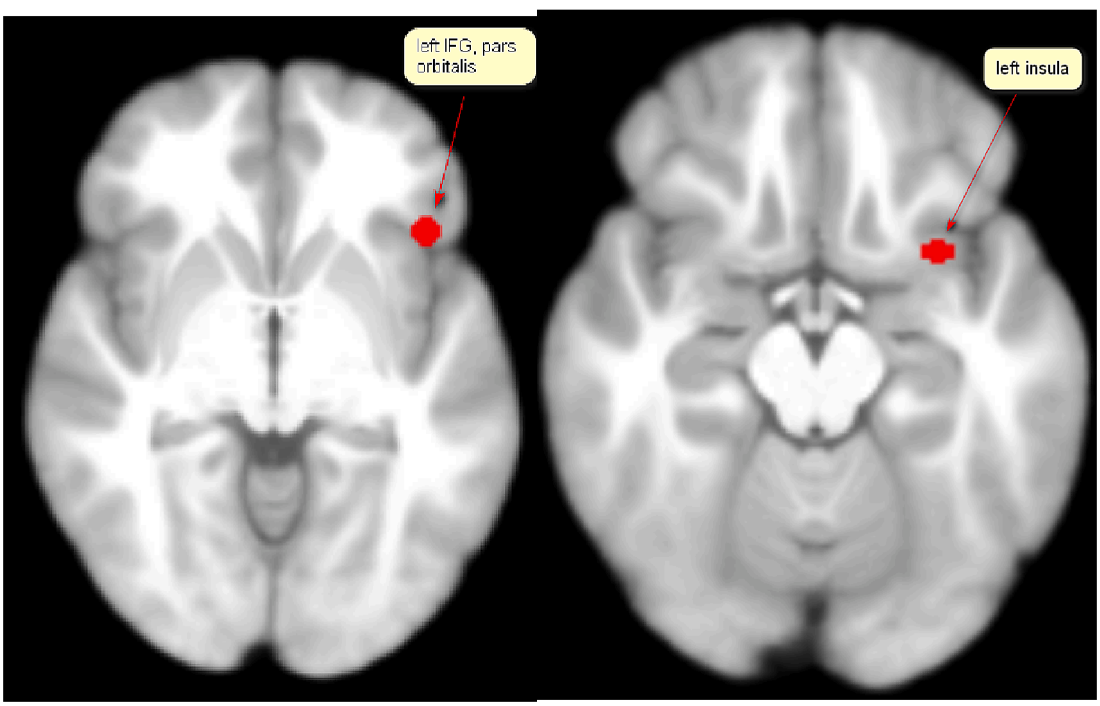

Fig. 3. Axial view on two neural areas most frequently associated with compassion. On the left side the left inferior frontal gyrus (neural area second most frequently associated with compassion) (MNI: x = 46, y = 20, z = −2). On the right side it displays the left insula (part of the brain most frequently associated with compassion) (MNI: x = −32, y = 12, z = −16). MNI coordinates were obtained from Kim et al., (2009). All T1 images in our systematic review were acquired from Fan et al., (2014, 2016) with permission.

3.6. Quality assessment results

3.6.1. Comparison of quality rated vs. non-rated studies

In total, 50.0% of all studies ($n = 17$) met at least one of our quality measures criteria. In order to distinguish between lower and higher quality studies, we have computed quartiles based on quality rating score (see Table 3).

Studies, which reached scores located on the third quartile (Q3) and above (three or more points), were labelled as higher quality. On the other hand, because first (Q1) and the second (Q2) quartiles did not differ in their values, studies obtaining scores that were located below Q3 were considered as lower quality. Additionally, studies, which did not report at least one of our quality measures criteria and which thus cannot be scored, we labelled as non-rated studies.

Even though the numbers of rated and non-rated studies were the same, among the quality rated studies a larger homogeneity of findings compared to quality non-rated studies has been observed. Among the quality rated studies, 20 neural locations associated with compassion in three or more times, compared to non-rated studies among which only 7 neural areas were associated with compassion in three or more times has been found. Thus, larger methodological homogeneity seems to contribute to the homogeneity of the results.

Among the higher quality studies (Q3 and above, $n = 5$), neural association with compassion state was observed in: right STP (the majority

Table 3
Studies that met at least one of our quality measures criteria.

Study	OFC/vmPFC -correction	Socio-economic status	Generalizability (gender)	Provided conceptualization of compassion	Compassion state measuring	Total score	Sample size
Q3 studies							
Mercadillo et al., 2015		1	2	1	1	5	1
Valk et al., 2017			1	1	1	3	1
Ashar et al., 2017			1	1	1	3	1
Kim et al., 2009			1	1	1	3	1
Zahn et al., 2009	1		1		1	3	1
Q2and Q1 studies							
Takeuchi et al., 2016a, 2016b		1	1			2	1
Simon-Thomas et al., 2012		1			1	2	1
Engen and Singer, 2015	1			1		2	
Fehse et al., 2015					1	1	1
Kanske et al., 2015					1	1	1
Immordino-Yang et al., 2014					1	1	1
Immordino-Yang and Singh, 2013					1	1	
Bruneau et al., 2012					1	1	1
Immordino-Yang et al., 2009					1	1	
Kédia et al., 2008					1	1	1
Moll et al., 2007					1	1	
Weng et al., 2018				1		1	1

Note: Studies were rated as follows: OFC correction = 1; Socioeconomic status =1; Generalizability: 45–55% of female participants = 2, 40–60% of female participants = 1; Participants were told what compassion means =1; Participants indicated whether/or how strongly they felt compassion during the experimental task (Compassion state measuring) =1. Sample size: number of subjects ≥16 = 1. We reported Generalizability (gender) only in fMRI studies, because with exception of 2 studies (Bernhardt et al., 2014; Patil et al., 2018) structural studies were very balanced with respect to gender proportion.

(60.0%) of all 5 studies found neural activity in this location); furthermore, neural activity was found in the left IFG - pars orbitalis, right insula, right cerebellum, right caudate nucleus, left SMA, right ACG, left SMG, right SMA, left FG and right amygdala (all locations at least mentioned in 40.0% of cases) - for further results see Online Supplementary Table 5 and Online Supplementary material 2.

In order to explore the differences between lower and higher quality studies, we compared the results from the lower quality studies to the higher quality studies. Compared to the Q3 studies, the Q1 and Q2 studies found neural association with compassion state in: right STP (60.0% in higher quality studies vs 0.0% in lower quality studies), right caudate nucleus, right SMA and left FG (40.0% vs. 5.6%) and right amygdala (40.0% vs. – 0.0%). A relative consistency of results can be observed regarding the right cerebellum (40.0% vs. 36.4%).

4. Discussion

The aim of this systematic review was to identify neural correlates of compassion across relevant structural MRI, CT and fMRI studies. Data from 2922 participants revealed 98 neural locations associated with compassion. We found that compassion tendency has been most frequently associated with neural activity in the left insula among fMRI studies. Results from the structural studies indicated frequent neuroanatomical associations between compassion tendency and grey matter volume in left and right insula and right caudate nucleus. Among higher quality studies, we observed most frequent neural association with compassion state in the right STP and further regions such as left IFG - pars orbitalis, right insula, right cerebellum, right caudate nucleus, left SMA, right ACG, left SMG, right SMA, left FG and right amygdala.

4.1. Reasons for heterogeneity of neural findings

We found a large divergence of neuroanatomical findings across both structural and fMRI studies. There might be several reasons for such a divergence: 1) the effect of social desirability, 2) empathizing with another person, instead of generating compassion, 3) random noise due to a small sample size, 4) differences in compassion inducing stimuli and 5) non-balanced proportion of females and males.

4.1.1. Divergence of findings

We found the findings to be divergent and we have three explanations for this. First, divergence of findings can be partially explained by different role self-report vs. informant report have effects on social desirability. It has been shown that the empathic concern scale (used in the majority of studies measuring compassion tendency) correlates with social desirability (Laurent and Hodges, 2009). Additionally, it has been shown that there is a relationship between the brain structure and social desirability (Andrejević et al., 2017). While taking into account that no study which used empathic concern scale statistically controlled for social desirability, it is possible that in participants filling in questionnaires on their own, related neural association partially reflect neural correlates of social desirability. This however, might not be the case, if the compassion questionnaire was filled in by the participant's informant. Taken together, the heteronomous neural results across the studies can be partially explained as an effect of social desirability.

Second, an alternative reason for the divergence of the results may be that participants were empathizing with another person, instead of generating compassion. Even though that compassion and empathy as different abilities, recruits different neural networks (Preckel et al., 2018) and that the general population considers notion of "compassion" as synonyms to "empathy" (Lamm et al., 2019) in a dominant number of studies researchers did not declare that they advise participants what they should do exactly in the fMRI, i.e., whether they should empathize or generate compassion.

Third, perhaps the most important explanation is that many neuroimaging results can to some degree reflect a random noise as a result of a small sample used. Positive predictive value (PPV) reflects post study probability of detecting true effect (Ioannidis, 2005) and PPV is largely influenced by sample size (Button et al., 2013). Therefore, the smaller the sample size, the lower is the chance that the detected neural activity represents a true neural activity. Taken together, a low power of the study associated with a small sample size (Cremers et al., 2017) indirectly increases Type I error (see David et al., 2013). Thus, the results of the studies examining neural correlates of compassion that use too small sample sizes need to be interpreted with caution, because they can reflect random noise instead of a true effect. An important question is, however, what exactly does "too small sample" mean. On this question the recent neuroscientific community has no consensus opinion. Although as a few as 13 subjects is considered to be below optimal (David et al., 2013), some researchers recommend using between 16 and 32 participants (see David et al., 2013) and according to others, in some cases it is necessary to use around 80 participants (Geuter et al., 2018). In this context it is important to note that four studies (Engen and Singer, 2015; Immordino-Yang et al., 2009; Immordino-Yang and Singh, 2013; Moll et al., 2007) in our systematic review, examined data from less than 16 participants. In these four studies, the results might be distorted. However, none of our high-quality studies had a sample size below 16, the minimum sample size (David et al., 2013). This finding underlines the importance of our results from higher quality studies; it suggests that these results are more likely to be reliable compared to results from studies that used a smaller sample.

4.1.2. Compassion inducing stimuli

Heterogeneity of results may be partially explained by differences in compassion inducing stimuli, i.e., by differences in sensory inputs (written narratives vs. picture observations). This explanation is in line with results from previous studies (Lamm et al., 2011) examining similar abilities (e.g. empathy) as well as with results from our systematic review, as both suggest that different stimuli impute is associated with a different neural response.

4.1.3. Generalizability: Gender

Divergence in neural findings might be also partially explained by a non-balanced proportion of females and males in research samples. As mentioned in the methods section, it has been observed that neural activity during compassion state towards sad facial expressions differs between genders (Mercadillo et al., 2011).

4.2. Neurobiological substrates of compassion

4.2.1. Role of insula during compassion

We found that across all studies, the general neuroanatomical substrate most frequently associated with compassion was found in the left insula. In more detail, across fMRI and structural studies the insular cortex was the most frequently or the second most frequently identified region associated with compassion. Importantly, evidence from the majority of the lesion studies, which allow us to infer a causal connection between brain and behaviour (Shdo et al., 2018), also showed that the insula was the most frequently associated with decreased compassion tendency. The role of the insular cortex during compassion has several interpretations: 1) processing of pleasure, 2) processing awareness of one's own affective state, 3) processing of negative emotions.

4.2.1.1. Reward processing. First, left and right insula was thought to play an important role in processing pleasure and positive emotions (Naqvi et al., 2007). This could possibly imply that during the compassion state, the left insula contributes to a processing of positive emotions. According to the theory (Klimecki et al., 2013) the compassion state should be associated with feelings of warmth and positive emotions. Thus, our findings may support the theory that compassion is associated with positive emotions. Despite the previously mentioned role of the insula in processing pleasure, theoretical work and reviews do not identify the insular cortex as the part of the compassion network (Preckel et al., 2018; Singer and Klimecki, 2014). Instead of its involvement in compassion, the insula is rather linked to the processing of empathy (see Shamay-Tsoory and Lamm, 2018).

4.2.1.2. Processing of awareness of one's own affective state. An alternative interpretation of the role of the insula (especially its anterior part) during compassion state can rest on the production of one's own awareness of affective state. Specifically, the function of the insular cortex could rest on the representation of internal states (e.g. hunger or cold) by integration of various interceptive signals from the body (Murphy et al., 2017). This integration of various body signals allows the insula to produce awareness of one's own emotional state (Gu et al., 2013). The lesion study of Hogeveen et al. (2016) revealed that grey matter volume loss in the anterior insula disrupts the awareness of one's own emotions.

4.2.1.3. Processing of negative emotions. In contrast to the first explanation linking insula to positive emotions, the role of insula during the compassion state might also primarily rely on the processing of negative emotions. In line with this explanation, some studies suggest that insula is a part of the neural network processing negative emotions (Knutson et al., 2013). Moreover, negative emotional stimuli (e.g. presentation of suffering human faces) are used to induce compassion in participants. Thus, instead of positive emotions, the role of insula during a compassion state might in fact rest on the processing of negative emotions.

4.2.1.4. Processing of both positive and negative emotions. It is, however, important to note that during the compassion state, the insula might process both positive and negative emotions, but in different time periods. This integrative role of insula is supported by behavioral studies suggesting that compassion is frequently experienced as both positive and negative emotion (Condon and Barrett, 2013) This is also supported by neuroimaging studies indicating that the degree of interoceptive awareness related to both positive and negative emotions is associated with activation in insula (Pollatos et al., 2007). In summary, during the compassion state, the insula might process both positive and negative emotions evoked in different times during the compassion state.

4.2.1.5. Concluding remarks on the role of insula during compassion. Taken together, it is possible that while in functional studies the left insula activity can reflect (1) the integration processes of sensory input and (2) the awareness of participants of their experienced compassion towards other, processing of positive and/or negative emotions (3), in lesion studies insular damage did not allow participants to effectively integrate incoming sensory inputs, so the representation of compassion feeling in their awareness is likely to be impaired.

4.2.2. Role of cerebellum during compassion state

4.2.2.1. Negative emotion processing. It is worth noting that the relationship between the right cerebellum and compassion state is missing in theoretical and review articles concerning neural substrates of compassion (Preckel et al., 2018; Singer and Klimecki, 2014). Despite this absence of a clear link between compassion state and right cerebellum in previous theoretical work, neuroimaging evidence (Schmahmann, 2019) documents a direct link from cerebellum to social cognition and also documents functional connection between cerebellum and parts of the neural circuit involved in compassion state i.e., insula - its anterior part respectively (Nomi et al., 2016). Through this connection with the anterior insula, the compassion state might be related to the cerebellum. Several studies document that patients with degenerative diseases of the cerebellum and its projections have heavily impaired emotion recognition (Hoche et al., 2016), especially negative emotion recognition (D'Agata et al., 2011). Therefore, the role of the cerebellum in the compassion neural network can rest on recognizing the negative affective state in a suffering person, which is a necessary condition for compassion state to occur.

4.2.3. IFG and its role during compassion

We observed a relative consistency of the neuroanatomical and functional association with compassion state in the left IFG - pars orbitalis. The neuroanatomical structure of the orbital part of the left IFG has a stronger relationship to brain function compared to the right cerebellum. Results from lesion studies also indicate that the orbital part of the left IFG was frequently associated with compassion tendency.

Interpretation of the function of the IFG can be the following: 1) proper naming and identifying of one's own emotional state and 2) sense of agency processing. Lastly mentioned can be found in the Online Supplementary discussion.

4.2.3.1. Naming and identifying of one's own emotional state. Functionally, the role of the IFG in a compassion state may rest on the role of language in naming and describing one's own feelings. Problems in naming and identifying emotions is one of the core aspects of alexithymia, which represents impaired ability to identify and express experienced emotions (Hobson et al., 2018). Additionally, it has been found that lesions in the left orbital part of the IFG together with pars triangularis and opercularis were associated with difficulty in identifying one's own feelings and with naming of objects (Hobson et al., 2018). Thus, it is possible that the role of the orbital part of the IFG during compassion rests on the proper naming and identifying of one's own emotional state. In other words, it is possible that the more neural activity or grey matter volume an individual in the orbital part of the left IFG displays, he or she is better able to identify his or her feelings including compassion.

4.2.4. Caudate nucleus, left putamen and their role in compassion

The neuroanatomical association between the compassion tendency and the left putamen in conjunction with bilateral caudate nucleus in lesion studies may indicate the functional importance of this circuit for trait compassion. Association between the caudate nucleus and the left putamen is partially in line with work from Preckel et al. (2018) and Singer & Klimecki (Singer and Klimecki, 2014) that links anatomical subparts of these areas with compassion. These subparts include: ventral striatum (SN/VTA) and nucleus accumbens, which are part of the neural circuit associated with affiliative behaviour and reward (Preckel et al., 2018; Singer and Klimecki, 2014). Additionally, parts of this system increase their activity when an individual experiences pleasure from e.g. listening to music (Zatorre and Salimpoor, 2013) or from eating high fat sweet food (Lenoir et al., 2007). Thus, our findings are congruent with the previously mentioned theory linking compassion to positive feelings (Preckel et al., 2018). Interestingly, neural activity in the nucleus accumbens (NaCC) - part of the mesolimbic reward system (Arias-Carrión et al., 2010) – is associated with helping behaviour (Meulen et al., 2016). It is therefore possible that during confrontation with compassion provoking stimuli (e.g. suffering face), participants felt a desire to relieve distress of this suffering individual. This explanation corresponds to the theory of compassion, which suggests that an inherent feature of compassion is the desire to help (Preckel et al., 2018). Taken together, it is possible that individuals high in trait compassion benefit more from helping others than individuals with low trait compassion, because brain areas in the reward system are more active in response to helping others.

4.2.5. Neural differences between compassion state and trait

Interestingly, in almost 50% of cases, the neural activity in the right cerebellum has been found in fMRI studies examining compassion state. In contrast, only one structural study found an association between the right cerebellum and compassion trait. One explanation for such a divergence of findings is that a bigger cortical thickness may not strictly imply greater neural activity as diagnosed by fMRI. Indeed, it has been argued that brain anatomical structure does not strictly determine the neural networks dynamics (Batista-García-Ramó and Fernández-Verdecia, 2018). Collectively, a complex relationship between brain structure and function might be one of the reasons why findings from fMRI and structural studies are not homogenous.

4.2.6. Structural imagining: Comparison of the results from healthy subjects with results from lesion studies

This study also revealed differences in structural findings between neurological patients and healthy subjects: while the left insula was the neural area most frequently associated with trait compassion in patients with a neurological disease, in the healthy subjects, the same area, but in the opposite hemisphere, was most frequently linked with compassion. These differences in laterality can be possibly explained by the age-related changes in functional connectivity. Indeed, there are studies indicating that the structure of functional brain networks changes with increasing age (Geerligs et al., 2015). Particularly in networks associated with social emotions (Oliveira Silva et al., 2018) such as the default mode network (Bagarinao et al., 2019). This explanation can also be supported by the fact that in our study there was a large difference between healthy subjects and neurological patients: while the median age in healthy participants was 24.0, the median age in respondents suffering from some brain disease was 64.0.

5. Strengths and limitations

One of the strengths of this systematic review is that we integrated results from both functional as well as from lesion studies. Such integration increased the confidence in the results from the functional studies and allowed us to suggest a causal connection between particular brain circuits and compassion. Another strength of our study rests on the fact that by uniforming different anatomical labelling atlases, we reduced the heterogeneity of the findings, which in turn increases the reliability of our results. Finally, the substantially high inter-rater reliability during the study selection process suggests that our inclusion and exclusion criteria were precisely formulated, and our findings are more likely to be replicable.

Our study also has some limitations. First, because the results from many functional studies have a correlative nature (score in trait compassion was correlated with brain activity), the interpretation of their results as referring to neural bases of trait compassion might not be necessarily correct. That is a correlation between a neural activity and a score in a trait compassion questionnaire does not necessarily imply that neural activity during a certain task is directly related to compassion. Second, is the use of Automatic anatomical labelling atlas, which smaller neural areas, e.g. ventral striatum, relabels to a bigger shape, e.g. Putamen. This, however, seems to be a general problem associated with anatomical labelling of small neural areas. Third, we excluded studies that investigated both compassion states with decision making at the same time. This implies that we did not examine the extent to which neural activity during compassion is influenced by some situational factors (e.g. decision-making processes). Fourth, our results might be affected by the results of the studies that used smaller sample sizes, as their results are likely to be less reliable compared to the results from the studies that used bigger sample sizes. Therefore, we highlight the results from our higher quality studies since they met - according to some recommendations - requirements for minimal sample size.

5.1. Implications

Our findings have several implications: first, our results have a great influence for scientists who want to measure compassion via fMRI while aiming to decrease type II error. It is usual that fMRI studies analyse neural data from a smaller brain region, so-called regions of interest (ROI). Identifications of a ROI are usually based on the previous findings or the theoretical assumptions. It has been argued that one of the possible ways to decrease the type II error in neuroimaging research is to use ROI analysis instead of another frequently used type of analysis i.e., whole brain analysis (Cremers et al., 2017). Thus, our results could be helpful in compassion research in identifying ROI while decreasing the type II error.

Second, future studies examining neural correlates of compassion should include socioeconomic status, alexithymia, empathy and social desirability as the possible variables that may confound findings. Additionally, the definition of compassion provided to the participants, when they are required to judge the intensity of compassion, is crucial to reduce risk of misunderstanding. This procedure might in turn significantly increase the reliability of the results. Third, as our systematic review evaluated only the affective component of compassion, future studies might also explore its cognitive component (Kim et al., 2020a; Longe et al., 2010; Lutz et al., 2020). Finally, despite the fact that pioneering articles questioning the reliability of research findings due to low study power were published years ago, neuroimaging studies that are recently published still utilize suboptimal sample sizes. This highlights the importance of review processes and journal publication requirements in the following way: the journal guidelines should demand from researchers to report procedures ensuring that proper statistical power was used (for recommendation of such strategies see: Cremers et al., 2017).

From the practical point of view, the identification of neural areas associated with compassion can have important implications not only for patients who in general suffer from deficits in compassion, but also for individuals suffering from malevolent tendencies such as psychopathy. Many of these individuals are characterised by a lack of compassion (Robinson et al., 2007) probably contributing to their delinquent behaviour (Hunter et al., 2007). Neural areas identified in our study could be neuromodulated by e.g. Transcranial Magnetic Stimulation (TMS), which might in turn stimulate compassion in such individuals. It can be speculated that in combination with compassion training via meditation (Leiberg et al., 2011), the neuromodulation could possibly represent a strategy how to decrease the risk of recidivism in delinquents.

5.2. Conclusions

Our systematic review integrating the results from both structural and functional studies underlines the importance of the neural networks associated with reward in both state and trait compassion. In more detail, it links biliterate caudate nucleus, middle temporal gyrus and right cerebellum to compassion trait, while the insula and orbital parts of the Inferior frontal gyrus to both state and trait compassion.

Funding

This study was supported by the Grant Agency of the Czech Republic, project Biological and Psychological Aspects of Spiritual Experience and Their Associations With Health (Contract No. 19-19526S) and by the Sts Cyril and Methodius Faculty of Theology of the Palacký University Olomouc internal project Determinants of Health from a Spiritual, Psychological, Social and Biological Point of View (grant number IGA-CMTF- 2020-006) and by Palacký University Olomouc Young Researcher Grant, project The efficacy, effectiveness, and use of Emotion-Focused Therapy in counselling for university students: an experimental study (Contract No. JG 2020 006).

Open Science Data

All Online supplementary tables and other online research materials are available on the Open Science Framework website: https://osf.io/fwsjq/, DOI: doi:10.17605/OSF.IO/FWSJQ.

Declaration of competing interest

None declared.

Acknowledgement

We are grateful to prof. Fan Lingzhong for allowing us to use the T1 images from the Brainnetome Atlas (Fan et al., 2014, 2016) - http://atlas.brainnetome.org/download.html - for our analytical purposes.

Appendix A. Supplemenatry data

References

Andrejević, M., Meshi, D., van den Bos, W., Heekeren, H.R., 2017. Individual differences in social desirability are associated with white-matter microstructure of the external capsule. Cognit.Affect. Behav. Neurosci. 17 (6), 1255–1264. https://doi.org/10.3758/s13415-017-0548-2.

Arias-Carrión, O., Stamelou, M., Murillo-Rodríguez, E., Menéndez-González, M., Pöppel, E., 2010. Dopaminergic reward system: a short integrative review. Int. Arch. Med. 3, 24. https://doi.org/10.1186/1755-7682-3-24.

Ashar, Y.K., Andrews-Hanna, J.R., Dimidjian, S., Wager, T.D., 2017. Empathic care and distress: predictive brain markers and dissociable brain systems. Neuron 94 (6), 1263–1273.e4. https://doi.org/10.1016/j.neuron.2017.05.014.

Baez, S., Morales, J.P., Slachevsky, A., Torralva, T., Matus, C., Manes, F., Ibanez, A., 2016. Orbitofrontal and limbic signatures of empathic concern and intentional harm in the behavioral variant frontotemporal dementia. Cortex 75, 20–32. https://doi.org/10.1016/j.cortex.2015.11.007.

Bagarinao, E., Watanabe, H., Maesawa, S., Mori, D., Hara, K., Kawabata, K., Yoneyama, N., Ohdake, R., Imai, K., Masuda, M., Yokoi, T., Ogura, A., Taoka, T., Koyama, S., Tanabe, H.C., Katsuno, M., Wakabayashi, T., Kuzuya, M., Ozaki, N., Sobue, G., 2019. Reorganization of brain networks and its association with general cognitive performance over the adult lifespan. Sci. Rep. 9 (1), 11352. https://doi.org/10.1038/s41598-019-47922-x.

Banissy, M.J., Kanai, R., Walsh, V., Rees, G., 2012. Inter-individual differences in empathy are reflected in human brain structure. NeuroImage 62 (3), 2034–2039. https://doi.org/10.1016/j.neuroimage.2012.05.081.

Batista-García-Ramó, K., Fernández-Verdecia, C.I., 2018. What we know about the brain structure–function relationship. Behav. Sci. 8 (4), 39. https://doi.org/10.3390/bs8040039.

Berkelaar, M., 2020. LpSolve: (R package version 5.6.15) [Computer software]. https://CRAN.R-project.org/package=lpSolve.

Bernhardt, B.C., Klimecki, O.M., Leiberg, S., Singer, T., 2014. Structural covariance networks of the dorsal anterior insula predict females' individual differences in empathic responding. Cereb. Cortex 24 (8), 2189–2198. https://doi.org/10.1093/cercor/bht072.

Bruneau, E.G., Dufour, N., Saxe, R., 2012. Social cognition in members of conflict groups: behavioural and neural responses in arabs, israelis and south americans to each other's misfortunes. Philos. Trans. Roy. Soc. B: Biol. Sci. 367 (1589), 717–730. https://doi.org/10.1098/rstb.2011.0293.

Button, K.S., Ioannidis, J.P.A., Mokrysz, C., Nosek, B.A., Flint, J., Robinson, E.S.J., Munafò, M.R., 2013. Power failure: why small sample size undermines the reliability of neuroscience. Nat. Rev. Neurosci. 14 (5), 365–376. https://doi.org/10.1038/nrn3475.

Callister, E.S., Plante, T.G., 2017. Compassion predictors in undergraduates: a Catholic college example. Pastor. Psychol. 66 (1), 1–11. https://doi.org/10.1007/s11089-016-0729-x.

Chen, P., Wang, G., Ma, R., Jing, F., Zhang, Y., 2016. Multidimensional assessment of empathic abilities in patients with insular glioma. Cogn. Affect. Behav. Neurosci. 16 (5), 962–975. https://doi.org/10.3758/s13415-016-0445-0.

Cohen, J., 1960. A coefficient of agreement for nominal scales. Educ. Psychol. Meas. 20, 37–46. https://doi.org/10.1177/001316446002000104.

Condon, P., Barrett, L.F., 2013. Conceptualizing and experiencing compassion. Emotion (Washington, D.C.) 13 (5), 817–821. https://doi.org/10.1037/a0033747.

Cremers, H.R., Wager, T.D., Yarkoni, T., 2017. The relation between statistical power and inference in fMRI. PLOS ONE 12 (11), e0184923. https://doi.org/10.1371/journal.pone.0184923.
D'Agata, F., Caroppo, P., Baudino, B., Caglio, M., Croce, M., Bergui, M., Tamietto, M., Mortara, P., Orsi, L., 2011. The recognition of facial emotions in spinocerebellar ataxia patients. Cerebellum 10 (3), 600. https://doi.org/10.1007/s12311-011-0276-z.
David, S.P., Ware, J.J., Chu, I.M., Loftus, P.D., Fusar-Poli, P., Radua, J., Munafò, M.R., Ioannidis, J.P.A., 2013. Potential reporting bias in fMRI studies of the brain. PLOS ONE 8 (7), e70104. https://doi.org/10.1371/journal.pone.0070104.
Davis, M.H., 1983. Measuring individual differences in empathy: evidence for a multidimensional approach. J. Pers. Soc. Psychol. 44 (1), 113–126. https://doi.org/10.1037/0022-3514.44.1.113.
Dermody, N., Wong, S., Ahmed, R., Piguet, O., Hodges, J.R., Irish, M., 2016. Uncovering the neural bases of cognitive and affective empathy deficits in Alzheimer's. J. Alzheimers Dis. 53 (3), 801–816. https://doi.org/10.3233/JAD-160175.
Di Bello, M., Carnevali, L., Petrocchi, N., Thayer, J.F., Gilbert, P., Ottaviani, C., 2020. The compassionate vagus: a meta-analysis on the connection between compassion and heart rate variability. Neurosci. Biobehav. Rev. 116, 21–30. https://doi.org/10.1016/j.neubiorev.2020.06.016.
Edelman, R.R., 2014. The history of MR imaging as seen through the pages of radiology. Radiology 273 (2S), S181–S200. https://doi.org/10.1148/radiol.14140706.
Engen, H.G., Singer, T., 2015. Compassion-based emotion regulation up-regulates experienced positive affect and associated neural networks. Soc. Cogn. Affect. Neurosci. 10 (9), 1291–1301. https://doi.org/10.1093/scan/nsv008.
Fan, L., Li, H., Yu, S., Jiang, T., 2016. Human brainnetome atlas and its potential applications in brain-inspired computing. In: Amunts, K., Grandinetti, L., Lippert, T., Petkov, N. (Eds.), Brain-Inspired Computing. Springer International Publishing, pp. 1–14. https://doi.org/10.1007/978-3-319-50862-7_1.
Fan, L., Wang, J., Zhang, Y., Han, W., Yu, C., Jiang, T., 2014. Connectivity-based parcellation of the human temporal pole using diffusion tensor imaging. Cereb. Cortex 24 (12), 3365–3378. https://doi.org/10.1093/cercor/bht196.
Fan, Y., Duncan, N.W., de Greck, M., Northoff, G., 2011. Is there a core neural network in empathy? An fMRI based quantitative meta-analysis. Neurosci. Biobehav. Rev. 35 (3), 903–911. https://doi.org/10.1016/j.neubiorev.2010.10.009.
Fehse, K., Silveira, S., Elvers, K., Blautzik, J., 2015. Compassion, guilt and innocence: An fMRI study of responses to victims who are responsible for their fate. Soc. Neurosci. 10 (3), 243–252. https://doi.org/10.1080/17470919.2014.980587.
FeldmanHall, O., Dalgleish, T., Evans, D., Mobbs, D., 2015. Empathic concern drives costly altruism. NeuroImage 105, 347–356. https://doi.org/10.1016/j.neuroimage.2014.10.043.
Gamer, M., Lemon, J., Puspendra, I., 2019. irr: Various Coefficients of Interrater Reliability and Agreement. https://CRAN.R-project.org/package=irr.
Geerligs, L., Renken, R.J., Saliasi, E., Maurits, N.M., Lorist, M.M., 2015. A brain-wide study of age-related changes in functional connectivity. Cerebral Cortex 25 (7)), 1987–1999. https://doi.org/10.1093/cercor/bhu012 (New York, N.Y.: 1991).
Geuter, S., Qi, G., Welsh, R.C., Wager, T.D., Lindquist, M.A., 2018. Effect size and power in fMRI Group. BioRxiv 295048. https://doi.org/10.1101/295048.
Gilbert, P., 2020. Compassion: from its evolution to a psychotherapy. Front. Psychol. 11 https://doi.org/10.3389/fpsyg.2020.586161.
Goetz, J.L., Keltner, D., Simon-Thomas, E., 2010. Compassion: an evolutionary analysis and empirical review. Psychol. Bul 136 (3), 351–374. https://doi.org/10.1037/a0018807.
Gu, X., Hof, P.R., Friston, K.J., Fan, J., 2013. Anterior insular cortex and emotional awareness. J. Comp. Neurol. 521 (15), 3371–3388. https://doi.org/10.1002/cne.23368.
Hein, G., Silani, G., Preuschoff, K., Batson, C.D., Singer, T., 2010. Neural responses to ingroup and outgroup members' suffering predict individual differences in costly helping. Neuron 68 (1), 149–160. https://doi.org/10.1016/j.neuron.2010.09.003.
Hobson, H., Hogeveen, J., Brewer, R., Catmur, C., Gordon, B., Krueger, F., Chau, A., Bird, G., Grafman, J., 2018. Language and alexithymia: Evidence for the role of the inferior frontal gyrus in acquired alexithymia. Neuropsychologia 111, 229–240. https://doi.org/10.1016/j.neuropsychologia.2017.12.037.
Hoche, F., Guell, X., Sherman, J.C., Vangel, M.G., Schmahmann, J.D., 2016. Cerebellar. Cerebellum 15 (6), 732–743. https://doi.org/10.1007/s12311-015-0746-9.
Hogeveen, J., Bird, G., Chau, A., Krueger, F., Grafman, J., 2016. Acquired alexithymia following damage to the anterior insula. Neuropsychologia 82, 142–148. https://doi.org/10.1016/j.neuropsychologia.2016.01.021.
Hou, X., Allen, T.A., Wei, D., Huang, H., Wang, K., DeYoung, C.G., Qiu, J., 2017. Trait compassion is associated with the neural substrate of empathy. Cognit. Affect. Behav. Neurosci. 17 (5), 1018–1027. https://doi.org/10.3758/s13415-017-0529-5.
Hunter, J.A., Figueredo, A.J., Becker, J.V., Malamuth, N., 2007. Non-sexual delinquency in juvenile sexual offenders: the mediating and moderating influences of emotional empathy. J. Fam. Violence 22 (1), 43–54. https://doi.org/10.1007/s10896-006-9056-9.
Immordino-Yang, M.H., McColl, A., Damasio, H., Damasio, A., 2009. Neural correlates of admiration and compassion. Proc. Natl. Acad. Sci. 106 (19), 8021. https://doi.org/10.1073/pnas.0810363106.
Immordino-Yang, M.H., Singh, V., 2013. Hippocampal contributions to the processing of social emotions. Hum. Brain Mapp. 34 (4), 945–955. https://doi.org/10.1002/hbm.21485.
Immordino-Yang, M.H., Yang, X.-F., Damasio, H., 2014. Correlations between social-emotional feelings and anterior insula activity are independent from visceral states but influenced by culture. Front. Hum. Neurosci. 8 https://doi.org/10.3389/fnhum.2014.00728.
Ioannidis, J.P.A., 2005. Why. PLoS Med. 2 (8), e124 https://doi.org/10.1371/journal.pmed.0020124.
Kanske, P., Böckler, A., Trautwein, F.-M., Singer, T., 2015. Dissecting the social brain: introducing the EmpaToM to reveal distinct neural networks and brain–behavior relations for empathy and Theory of Mind. NeuroImage 122, 6–19. https://doi.org/10.1016/j.neuroimage.2015.07.082.
Kédia, G., Berthoz, S., Wessa, M., Hilton, D., Martinot, J.-L., 2008. An agent harms a victim: a functional magnetic resonance imaging study on specific moral emotions. J. Cogn. Neurosci. 20 (10), 1788–1798. https://doi.org/10.1162/jocn.2008.20070.
Kim, J.J., Cunnington, R., Kirby, J.N., 2020. The neurophysiological basis of compassion: an fMRI meta-analysis of compassion and its related neural processes. Neurosci. Biobehav. Rev. 108, 112–123. https://doi.org/10.1016/j.neubiorev.2019.10.023.
Kim, J.-W., Kim, S.-E., Kim, J.-J., Jeong, B., Park, C.-H., Son, A.R., Song, J.E., Ki, S.W., 2009. Compassionate attitude towards others' suffering activates the mesolimbic neural system. Neuropsychologia 47 (10), 2073–2081. https://doi.org/10.1016/j.neuropsychologia.2009.03.017.
Klimecki, O.M., Leiberg, S., Lamm, C., Singer, T., 2013. Functional neural plasticity and associated changes in positive affect after compassion training. Cereb. Cortex 23 (7), 1552–1561. https://doi.org/10.1093/cercor/bhs142.
Klimecki, O.M., Leiberg, S., Ricard, M., Singer, T., 2014. Differential pattern of functional brain plasticity after compassion and empathy training. Soc. Cogn. Affect. Neurosci. 9 (6), 873–879. https://doi.org/10.1093/scan/nst060.
Knutson, K.M., Rakowsky, S.T., Solomon, J., Krueger, F., Raymont, V., Tierney, M.C., Wassermann, E.M., Grafman, J., 2013. Injured brain regions associated with anxiety in Vietnam veterans. Neuropsychologia 51 (4), 686–694. https://doi.org/10.1016/j.neuropsychologia.2013.01.003.
Kraus, C., Kranz, G., Pfabigan, D., Hoffmann, A., Hahn, A., Eva-Maria, S., Küblböck, M., Kasper, S., Windischberger, C., Lamm, C., Lanzenberger, R., 2014. Parahippocampal and insular gray matter volume correlates with empathic concern. 44.
Lamm, C., Decety, J., Singer, T., 2011. Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. NeuroImage 54 (3), 2492–2502. https://doi.org/10.1016/j.neuroimage.2010.10.014.
Lamm, C., Rütgen, M., Wagner, I.C., 2019. Imaging empathy and prosocial emotions. Neurosci. Lett. 693, 49–53. https://doi.org/10.1016/j.neulet.2017.06.054.
Landis, J.R., Koch, G.G., 1977. The measurement of observer agreement for categorical data. Biometrics 33 (1), 159–174. https://doi.org/10.2307/2529310. JSTOR.
Lang, S., Yu, T., Markl, A., Müller, F., Kotchoubey, B., 2011. Hearing others' pain: neural activity related to empathy. Cognit. Affect. Behav. Neurosci. 11 (3), 386. https://doi.org/10.3758/s13415-011-0035-0.
Laurent, S.M., Hodges, S.D., 2009. Gender roles and empathic accuracy: the role of communion in reading minds. Sex Roles 60 (5), 387–398. https://doi.org/10.1007/s11199-008-9544-x.
Lebowitz, M.S., Dovidio, J.F., 2015. Implications of emotion regulation strategies for empathic concern, social attitudes, and helping behavior. Emotion 15 (2), 187–194. https://doi.org/10.1037/a0038820.
Leiberg, S., Klimecki, O., Singer, T., 2011. Short-term compassion training increases prosocial behavior in a newly developed prosocial game. PLOS ONE 6 (3), e17798. https://doi.org/10.1371/journal.pone.0017798.
Lenoir, M., Serre, F., Cantin, L., Ahmed, S.H., 2007. Intense sweetness surpasses cocaine reward. PLOS ONE 2 (8), e698. https://doi.org/10.1371/journal.pone.0000698.
Liberati, A., Altman, D.G., Tetzlaff, J., Mulrow, C., Gøtzsche, P.C., Ioannidis, J.P.A., Clarke, M., Devereaux, P.J., Kleijnen, J., Moher, D., 2009. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ 339. https://doi.org/10.1136/bmj.b2700.
Longe, O., Maratos, F.A., Gilbert, P., Evans, G., Volker, F., Rockliff, H., Rippon, G., 2010. Having a word with yourself: neural correlates of self-criticism and self-reassurance. NeuroImage 49 (2), 1849–1856. https://doi.org/10.1016/j.neuroimage.2009.09.019.
Lutz, J., Berry, M.P., Napadow, V., Germer, C., Pollak, S., Gardiner, P., Edwards, R.R., Desbordes, G., Schuman-Olivier, Z., 2020. Neural activations during self-related processing in patients with chronic pain and effects of a brief self-compassion training – a pilot study. Psychiatry Res. Neuroimaging 304, 111155. https://doi.org/10.1016/j.pscychresns.2020.111155.
Majdandžić, J., Amashaufer, S., Hummer, A., Windischberger, C., Lamm, C., 2016. The selfless mind: how prefrontal involvement in mentalizing with similar and dissimilar others shapes empathy and prosocial behavior. Cognition 157, 24–38. https://doi.org/10.1016/j.cognition.2016.08.003.
Mascaro, J.S., Florian, M.P., Ash, M.J., Palmer, P.K., Frazier, T., Condon, P., Raison, C., 2020. Ways of knowing compassion: how do we come to know, understand, and measure compassion when we see it? Front. Psychol. 11 https://doi.org/10.3389/fpsyg.2020.547241.
McHugh, M.L., 2012. Interrater reliability: the kappa statistic. Biochemia Medica 22 (3), 276–282. https://doi.org/10.11613/BM.2012.031.
Medvedev, O.N., Dailianis, A.T., Hwang, Y.-S., Krägeloh, C.U., Singh, N.N., 2021. Applying generalizability theory to the self-compassion scale to examine state and trait aspects and generalizability of assessment scores. Mindfulness 12 (3), 636–645. https://doi.org/10.1007/s12671-020-01522-3.
Mercadillo, R.E., Alcauter, S., Fernández-Ruiz, J., Barrios, F.A., 2015. Police culture influences the brain function underlying compassion: a gender study. Soc. Neurosci. 10 (2), 135–152. https://doi.org/10.1080/17470919.2014.977402.
Mercadillo, R.E., Díaz, J.L., Pasaye, E.H., Barrios, F.A., 2011. Perception of suffering and compassion experience: brain gender disparities. Brain Cogn. 76 (1), 5–14. https://doi.org/10.1016/j.bandc.2011.03.019.

Meulen, M.van der, IJzendoorn, M.H.van, Crone, E.A., 2016. Neural correlates of prosocial behavior: compensating social exclusion in a four-player cyberball game (e0159045). PLOS ONE 11 (7). https://doi.org/10.1371/journal.pone.0159045.
Miller, J.G., Xia, G., Hastings, P.D., 2020. Right Temporoparietal junction involvement in autonomic responses to the suffering of others: a preliminary transcranial magnetic stimulation study. Front. Hum. Neurosci. 14 https://doi.org/10.3389/fnhum.2020.00007, 7-7.
Moccia, L., Pettorruso, M., De Crescenzo, F., De Risio, L., di Nuzzo, L., Martinotti, G., Bifone, A., Janiri, L., Di Nicola, M., 2017. Neural correlates of cognitive control in gambling disorder: a systematic review of fMRI studies. Neurosci. Biobehav. Rev. 78, 104–116. https://doi.org/10.1016/j.neubiorev.2017.04.025.
Moll, J., de Oliveira-Souza, R., Garrido, G.J., Bramati, I.E., Caparelli-Daquer, E.M.A., Paiva, M.L.M.F., Zahn, R., Grafman, J., 2007. The self as a moral agent: linking the neural bases of social agency and moral sensitivity. Soc. Neurosci. 2 (3–4), 336–352. https://doi.org/10.1080/17470910701392024.
Murphy, J., Brewer, R., Catmur, C., Bird, G., 2017. Interoception and psychopathology: a developmental neuroscience perspective. Dev. Cognit. Neurosci. 23, 45–56. https://doi.org/10.1016/j.dcn.2016.12.006.
Naqvi, N.H., Rudrauf, D., Damasio, H., Bechara, A., 2007. Damage to the insula disrupts addiction to cigarette smoking. Science 315 (5811), 531–534. https://doi.org/10.1126/science.1135926.
Nomi, J.S., Farrant, K., Damaraju, E., Rachakonda, S., Calhoun, V.D., Uddin, L.Q., 2016. Dynamic functional network connectivity reveals unique and overlapping profiles of insula subdivisions. Hum. Brain Mapp. 37 (5), 1770–1787. https://doi.org/10.1002/hbm.23135.
Novak, L., Malinakova, K., Mikoska, P., Dijk, J.P.van, Tavel, P., 2020. Neural correlates of compassion – an integrative systematic review: OSF project: Online repository of data and other supplementary materials. https://doi.org/10.17605/OSF.IO/FWSJQ.
Ogawa, A., Ueshima, A., Inukai, K., Kameda, T., 2018. Deciding for others as a neutral party recruits risk-neutral perspective-taking: Model-based behavioral and fMRI experiments. Sci. Rep. 8 (1), 12857. https://doi.org/10.1038/s41598-018-31308-6.
Oliveira Silva, P., Maia, L., Coutinho, J., Frank, B., Soares, J.M., Sampaio, A., Gonçalves, Ó., 2018. Empathy by default: correlates in the brain at rest. Psicothema 30 (1), 97–103. https://doi.org/10.7334/psicothema2016.366.
Patil, I., Zanon, M., Novembre, G., Zangrando, N., Chittaro, L., Silani, G., 2018. Neuroanatomical basis of concern-based altruism in virtual environment. Neuropsychologia 116, 34–43. https://doi.org/10.1016/j.neuropsychologia.2017.02.015.
Piff, P.K., Moskowitz, J.P., 2018. Wealth, poverty, and happiness: social class is differentially associated with positive emotions. Emotion 18 (6), 902–905. https://doi.org/10.1037/emo0000387.
Pollatos, O., Gramann, K., Schandry, R., 2007. Neural systems connecting interoceptive awareness and feelings. Hum. Brain Mapp. 28 (1), 9–18. https://doi.org/10.1002/hbm.20258.
Preckel, K., Kanske, P., Singer, T., 2018. On the interaction of social affect and cognition: empathy, compassion and theory of mind. Curr. Opin. Behav. Sci. 19, 1–6. https://doi.org/10.1016/j.cobeha.2017.07.010.
R Core Team, 2020. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing.
Rankin, K.P., Gorno-Tempini, M.L., Allison, S.C., Stanley, C.M., Glenn, S., Weiner, M.W., Miller, B.L., 2006. Structural anatomy of empathy in neurodegenerative disease. Brain 129 (11), 2945–2956. https://doi.org/10.1093/brain/awl254.
Robinson, R., Roberts, W.L., Strayer, J., Koopman, R., 2007. Empathy and emotional responsiveness in delinquent and non-delinquent adolescents. Soc. Dev. 16 (3), 555–579. https://doi.org/10.1111/j.1467-9507.2007.00396.x.
Schmahmann, J.D., 2019. The cerebellum and cognition. Neurosci. Lett. 688, 62–75. https://doi.org/10.1016/j.neulet.2018.07.005.
Shamay-Tsoory, S., 2015. The neuropsychology of empathy: Evidence from lesion studies. Revue de Neuropsychologie, Neurosci. Cognit. Clin. 7 (4), 237–243.
Shamay-Tsoory, S., Lamm, C., 2018. The neuroscience of empathy – from past to present and future. Neuropsychologia 116, 1–4. https://doi.org/10.1016/j.neuropsychologia.2018.04.034.
Shdo, S.M., Ranasinghe, K.G., Gola, K.A., Mielke, C.J., Sukhanov, P.V., Miller, B.L., Rankin, K.P., 2018. Deconstructing empathy: Neuroanatomical dissociations between affect sharing and prosocial motivation using a patient lesion model. Neuropsychologia 116, 126–135. https://doi.org/10.1016/j.neuropsychologia.2017.02.010.
Simon-Thomas, E.R., Godzik, J., Castle, E., Antonenko, O., Ponz, A., Kogan, A., Keltner, D.J., 2012. An fMRI study of caring vs self-focus during induced compassion and pride. Soc. Cogn. Affect. Neurosci. 7 (6), 635–648. https://doi.org/10.1093/scan/nsr045.
Singer, T., Klimecki, O.M., 2014. Empathy and compassion. Curr. Biol. 24 (18), R875–R878. https://doi.org/10.1016/j.cub.2014.06.054.
Singer, T., Lamm, C., 2009. The social neuroscience of empathy. Ann. N. Y. Acad. Sci. 1156 (1), 81–96. https://doi.org/10.1111/j.1749-6632.2009.04418.x.
Stellar, J.E., Manzo, V.M., Kraus, M.W., Keltner, D., 2012. Class and compassion: socioeconomic factors predict responses to suffering. Emotion 12 (3), 449–459. https://doi.org/10.1037/a0026508.
Strauss, C., Lever Taylor, B., Gu, J., Kuyken, W., Baer, R., Jones, F., Cavanagh, K., 2016. What is compassion and how can we measure it? A review of definitions and measures. Clin. Psychol. Rev. 47, 15–27. https://doi.org/10.1016/j.cpr.2016.05.004.
Sturm, V.E., Sible, I.J., Datta, S., Hua, A.Y., Perry, D.C., Kramer, J.H., Miller, B.L., Seeley, W.W., Rosen, H.J., 2018. Resting parasympathetic dysfunction predicts prosocial helping deficits in behavioral variant frontotemporal dementia. Cortex 109, 141–155. https://doi.org/10.1016/j.cortex.2018.09.006.
Takeuchi, H.T., Yasuyuki, Sekiguchi, Atsushi, Nouchi, Rui, Kotozaki, Yuka, Nakagawa, Seishu, Miyauchi, Carlos Makoto, Iizuka, Kunio, Yokoyama, Ryoichi, Shinada, Takamitsu, Yamamoto, Yuki, Hanawa, Sugiko, Araki, Tsuyoshi, Hashizume, Hiroshi, Kunitoki, Keiko, Sassa, Yuko, Kawashima, Ryuta, 2016. Differences in gray matter structure correlated to nationalism and patriotism. Sci. Rep. 6, 29912. https://doi.org/10.1038/srep29912.
Takeuchi, H., Taki, Y., Sekiguchi, A., Nouchi, R., Kotozaki, Y., Nakagawa, S., Miyauchi, C.M., Iizuka, K., Yokoyama, R., Shinada, T., Yamamoto, Y., Hanawa, S., Araki, T., Hashizume, H., Kunitoki, K., Sassa, Y., Kawashima, R., 2016. Differences in gray matter structure correlated to nationalism and patriotism. Sci. Rep. 6 (1), 29912. https://doi.org/10.1038/srep29912.
Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., Mazoyer, B., Joliot, M., 2002. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation ofthe MNI MRI single-subject brain. NeuroImage 15 (1), 273–289. https://doi.org/10.1006/nimg.2001.0978.
Valk, S.L., Bernhardt, B.C., Trautwein, F.-M., Böckler, A., Kanske, P., Guizard, N., Collins, D.L., Singer, T., 2017. Structural plasticity of the social brain: Differential change after socio-affective and cognitive mental training. Sci. Adv. 3 (10), e1700489 https://doi.org/10.1126/sciadv.1700489.
Weng, H.Y., Lapate, R.C., Stodola, D.E., Rogers, G.M., Davidson, R.J., 2018. Visual attention to suffering after compassion training is associated with decreased amygdala responses. Front. Psychol. 9, 771. https://doi.org/10.3389/fpsyg.2018.00771.
Zahn, R., de Oliveira-Souza, R., Bramati, I., Garrido, G., Moll, J., 2009. Subgenual cingulate activity reflects individual differences in empathic concern. Neurosci. Lett. 457 (2), 107–110. https://doi.org/10.1016/j.neulet.2009.03.090.
Zatorre, R.J., Salimpoor, V.N., 2013. From perception to pleasure: music and its neural substrates. Proc. Natl. Acad. Sci. 110 (Supplement 2), 10430–10437. https://doi.org/10.1073/pnas.1301228110.