



The role of social norms, empathy, and religiosity in assisted dying decisions: an fMRI study

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Abstract

Medical assistance in dying (MAiD) is gaining legal and social acceptance; yet it remains ethically controversial and challenging for healthcare professionals. This functional MRI study examines how social norms and empathy influence MAiD decisions in 59 Australian medical students while evaluating hypothetical assisted-dying scenarios. Participants' decisions generally aligned with the legal framework. MAiD was approved when eligibility criteria were met (normative cases) and denied when they were not (nonnormative cases). Nonnormative scenarios elicited greater activation in frontoparietal brain regions involved in response selection and inhibition, consistent with increased decision difficulty. These scenarios elicited heightened activity in the precuneus, temporoparietal junction, and angular gyrus, along with stronger functional connectivity between the anterior hippocampus and the precuneus, suggesting greater reliance on memory retrieval and mentalizing. Normative scenarios were associated with increased amygdala activity, particularly among less religious participants, suggesting a role for negative affective salience. Greater activity in the ventromedial prefrontal cortex, and connectivity between the anterior cingulate cortex and this region, suggest positive feelings related to compassion when a clinician can legally approve an assisted dying request. Normative scenarios were also associated with reduced connectivity between the anterior cingulate cortex and the anterior insula, particularly in those with higher trait affective empathy, suggesting that doctors might feel a reduction in their patients' pain. The findings provide the first empirical evidence of the neural mechanisms underlying decision-making in bioethical cases involving death as the outcome, highlighting distinct contributions and potential risk factors for medical practitioners in normative and nonnormative MAiD clinical situations.

Keywords Medical assistance in dying (MAiD) · Empathy · Decision-making · fMRI · Social norms

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Introduction

The evolution of medical science has not only extended human life but also introduced complex ethical dilemmas surrounding end-of-life care. Among these, medical assistance in dying (MAiD) has emerged as a contentious issue that challenges traditional medical ethics, legal frameworks, and societal and moral values (Lizzio-Wilson et al., 2023; Wibisono et al., 2022; 2024). In Western liberal democracies, an increasing number of countries have legalized MAiD, reflecting an emphasis on patient autonomy and the right to die with dignity. In the United States, MAiD is currently permitted in 12 states, underscoring a broader shift in both public policy and societal attitudes towards end-of-life decision-making. Public opinion also appears to support this shift. According to a 2023 Pew Research Center survey, a substantial majority of Americans (71%) believe that mentally capable adults enduring unbearable pain with no hope

of improvement have a right to end their lives. This statistic underscores a societal inclination towards respect for personal autonomy in the face of terminal illness and suffering.

Nevertheless, while public acceptance grows, the practical implementation of MAiD remains challenging for healthcare practitioners. In clinical practice, these professionals are often at the forefront of decision-making, tasked with evaluating patient eligibility, engaging in difficult conversations, and potentially administering life-ending medications. Consequently, healthcare professionals frequently face significant ethical challenges, torn between their professional duty to preserve life (as mandated by the Hippocratic Oath to “do no harm”), and their responsibility to respect patient autonomy. Even when practitioners support the legalization of MAiD, a significant proportion preferred to transfer responsibility for the procedure to another medical professional (Zenz et al., 2015). The degree of autonomy afforded to patients adds complexity to these decisions, because it is contentious in the context of variable states, family support, and resources for palliative care (Wibisono et al., 2022). Empirical studies also reveal a disparity between physicians’ conceptual endorsement of MAiD and their behavioral willingness to administer it (Campbell et al., 2022; Hetzler et al., 2019). Recent surveys have shown that 86% of healthcare providers would care for patients contemplating MAiD, while only 67% would participate in the final act (Davidson et al., 2022). This reluctance often stems from moral distress, ethical conflicts, and fear of professional repercussions (Crane et al., 2023; Wibisono et al., 2022). The weight of such decisions has been associated with increased risks of mental health issues, including depression and anxiety (Tran et al., 2014; Milner et al., 2015; Fink-Miller & Nestler, 2018).

The experience of decision-making is expected to be moderated by several personal and situational factors (Wibisono et al., 2022). The present research focused on the professional and legal norms intended to guide MAiD decisions as a critical situational factor in practitioners’ experiences (Lizzio-Wilson et al., 2023; Wibisono et al., 2024). Such norms include formal laws that specify permitted and prohibited behaviors, as well as groups’ formal and informal social standards for behavior, such as practitioners’ professional rules or standards regarding what is expected in providing assisted dying services.

Neural responses involved in MAiD decision making

Despite these challenges, a research gap exists in the literature regarding medical practitioners’ decision-making. There is a need to elucidate the underlying cognitive and neural mechanisms as well as dispositional characteristics that can influence the MAiD decision-making process. Therefore, the purpose of this study was to examine medical students’ decisions on whether to approve hypothetical assisted dying

requests in the Australian context. We use functional MRI (fMRI) and questionnaire data about trait empathy and religiosity to examine the neural mechanisms and individual differences in responding to normative and nonnormative patient requests. These methods allow a deeper understanding of how individual dispositions and values intersect with social norms to shape decisions. Furthermore, they can reveal the neural signatures of ethical decision-making and conflicts under conditions of high or low normativity and different levels of trait empathy. Such an understanding is crucial for developing effective strategies and policies that support healthcare providers, enabling them to fulfill their roles without compromising their well-being or professional integrity.

MAiD decisions place substantial cognitive and emotional demands on healthcare professionals (Wibisono et al., 2022). Based on this past research, we expected that deciding whether to approve a MAiD request likely engages neural systems implicated in conflict monitoring, emotional distress, and empathic processing. A large body of work in cognitive neuroscience points to the anterior cingulate cortex (ACC) as a critical node in this network, particularly the anterior midcingulate (amCC), which acts as a dynamic integrator that actively synthesizes signals of pain, negative emotion, and cognitive demand to guide adaptive behavior (Shackman et al., 2011). This integrative capacity is most profound in the social domain, where the ACC emerges as a central hub for empathy, enabling people to share and understand another’s suffering and shape our responses through distinct downstream circuits (Smith et al., 2021). It is precisely this convergence of functions—processing suffering, resolving conflict, and facilitating empathy—that makes the ACC a vital neuroanatomical nexus for investigating the multifaceted nature of MAiD decisions.

The role of empathy and religiosity in MAiD decisions

Dispositional factors may also play a role in shaping MAiD decisions. One such factor is empathy, which plays a critical role in health care by improving patients’ outcomes, trust and satisfaction (Decety, 2020). Empathy comprises interrelated dimensions (cognitive and emotional), each supported by relatively distinct neural circuits which have different functions (Decety & Jackson, 2004; Eres et al., 2015; Gamble et al., 2024). Cognitive empathy refers to a person’s ability to understand another person’s mental state and perspective, which helps professionals to make informed and supportive decisions about requests to end life (see also Crane et al., 2023; Wibisono et al., 2022). Higher levels of cognitive empathy may facilitate a deeper understanding of the patient’s needs and enable a more comprehensive approach to MAiD decision-making, especially when evaluating the patient’s suffering and wishes.

In addition, an emotional motivation to alleviate distress can lead practitioners to create a more emotionally supportive atmosphere around the patient's care. Compassionate healthcare practitioners may be more inclined to understand and accept requests for MAiD, especially when patients experience significant suffering. Emotional empathy refers to the capacity to resonate with another person's emotions, including pain. Higher levels of emotional empathy can lead to empathic distress (Decety & Lamm, 2009) and increase the likelihood of physician burnout (Crane et al., 2023; Decety & Li, 2025; Gleichgerrcht & Decety, 2013; Wilkinson et al., 2017). Studies have shown that practitioners experiencing higher empathic distress may be less willing to engage in or endorse MAiD, as the emotional toll becomes a significant barrier (Milner et al., 2015). To investigate these distinct emotional dimensions, we examined key brain regions implicated in processing emotional salience, such as anterior insula (AI), ACC, and amygdala (Cunningham & Brosch, 2012; Menon et al., 2010; Uddin et al., 2019). This network, which increases attention to important changes in the environment and motivates avoidance of dangerous or noxious stimuli, plays a critical role in moral decision-making (Yoder & Decety, 2018). Finally, neural regions involved in compassionate concern and relieving suffering, such as the striatum and ventromedial prefrontal cortex (vmPFC) (Ashar et al., 2017; Decety & Porges, 2011; Jensen et al., 2020), may be implicated in decisions to approve MAiD.

Religiosity is another significant factor influencing healthcare professionals' support for MAiD (Grove et al., 2022; Wibisono et al., 2022). Higher levels of religious belief are associated with lower support for MAiD because religiously affiliated physicians often view assisted dying as incompatible with their moral and ethical framework (Guzowski et al., 2024; Mimarakis et al., 2025). This is particularly the case if their faith emphasizes the sanctity of life or considers suicide to be a violation of divine law. This core belief creates a perceived clash with the principles of patient autonomy that underpin MAiD. In other cases, MAiD may be understood as a legitimate and merciful last resort to uncontrollable suffering when all other medical and palliative interventions have failed. In the present research, we explored the role of personal religiosity in practitioners' hypothetical decisions on whether to offer assisted dying services, both behaviorally and in fMRI data.

Current study

In the context of medical ethics, social norms are often formalized through legal and professional frameworks that delineate the boundaries of acceptable practice. In

this study, we operationalize *normative* scenarios as those that conform to the specific eligibility criteria for MAiD, also referred to as Voluntary Assisted Dying (VAD), under Australian law (e.g., terminal illness and unbearable suffering). By contrast, *nonnormative* scenarios refer to cases that fall outside these established legal and professional standards. Although these scenarios necessarily differ along clinical dimensions such as suffering and terminality, it is important to emphasize that within the medical profession, such dimensions are not merely potential confounds. Rather, they constitute the very criteria by which social and legal norms are defined. Thus, the distinction between normative and nonnormative requests reflects the extent to which practitioners adhere to the structured standards of their professional community. All scenarios are listed in the Supplementary Materials. Using fMRI, we can gain insight into how these two types of scenarios differ in their engagement of cognitive and/or emotional processes, which could help clarify how practitioners approach these decisions. Furthermore, examining how neural responses vary as a function of individual differences in religiosity and trait empathy, and in relation to alignment with the normative framework, will help to clarify how personal values and personality traits shape responses to these scenarios.

Method

Participants

A total of 62 health science students from the University of Melbourne were recruited for this study. This sample size was determined a priori to ensure a final usable sample of approximately 59 participants after a typical 5% attrition rate common in neuroimaging (e.g., due to excessive head motion), providing sufficient statistical power ($1 - \beta = .80$, $\alpha = .05$) to detect medium-sized brain-behavior correlations of at least $r = .35$. In the context of 7 T fMRI, which offers superior signal-to-noise ratio, this sample represents a sample larger than typically seen in ethical decision-making fMRI studies.

All participants were screened for MRI safety. Among them, two were excluded owing to incomplete structural MRI data, and one was excluded due to excessive head motion, leaving 59 participants in the final dataset (1 non-binary, 28 females, and 30 males; $M_{\text{age}} = 24$ years, $SD = 3.71$). The study lasted approximately 2 hr. Participants were paid AUD \$200 in compensation. The study was approved by the ISN Human Research Ethics Committee (approval number 201207).

Experimental design and procedure

Prior to the scan, participants' demographic information was collected (including age, gender identity, education level, religion, and area of specialty), and the Questionnaire of Cognitive and Affective Empathy (QCAE; Reiners et al., 2011) was used to assess cognitive and affective empathy. All measures are given in full in the supplementary materials.

During the fMRI experiment, participants were presented with 60 assisted-dying scenarios. These scenarios were shown one at a time and consisted of two distinct categories. One category, normative scenarios, included 30 assisted dying requests, with a typical example being the following: "A woman is in severe physical pain with terminal cancer. She asks for voluntary assisted dying services." It should be noted that different Australian states have different criteria for assisted dying. In all cases, the terse descriptions do not do justice to the detailed interviews that practitioners are required to conduct. However, in the details given, the normative stimuli conformed to the eligibility criteria for voluntary assisted dying at the time of writing.

The other category, nonnormative scenarios, also comprised 30 cases but focused on atypical requests that included details falling outside the acceptable criteria for assisted dying eligibility. A typical example of this

category is, "A man is in mild physical pain with early-stage cancer. He asks for voluntary assisted dying services." The scenarios were adapted from previous research (Wasserman et al., 2005). We modified them to ensure that 1) participants could read each scenario within 5 s; and 2) normative and nonnormative euthanasia scenarios were matched on average word length. These changes minimize potential confounds related to reading time or stimulus length in the observed differences in brain activation between the conditions. After each scenario, participants subsequently rated the following two questions inside the MRI scanner (Fig. 1): 1) Would you grant VAD in this scenario? (1 for yes, 2 for no); 2) How confident are you about your decision? (1 = not confident, 9 = very confident). All 60 scenarios were presented in a pseudorandom order twice (one time each in each run so 120 trials in total). Following MRI scanning, participants were asked to complete the Duke University Religious Index (DUREL, Koenig & Büssing, 2010) to assess religiosity.

Materials

A full copy of the measures is included in the supplementary materials.

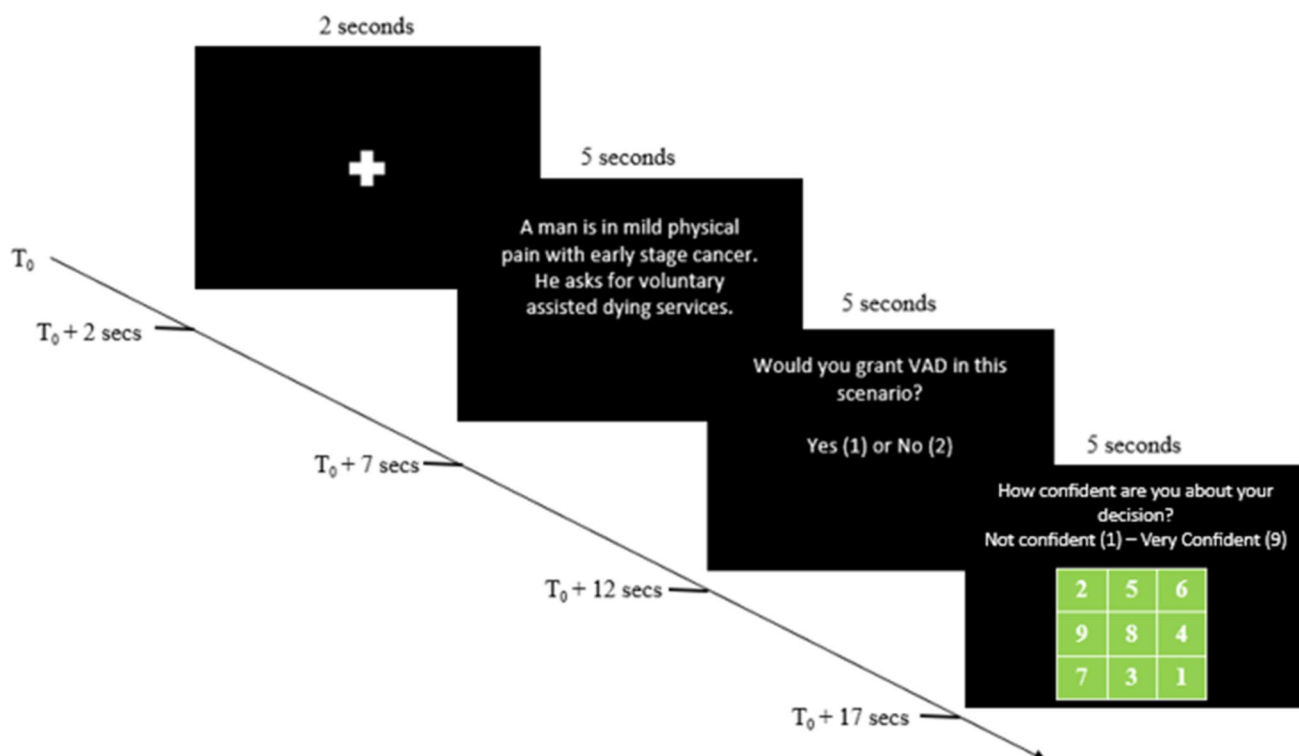


Fig. 1 Schematic Representation of a Sample Trial

Demographic questions

Demographic information was collected prior to the MRI session and included questions on age, gender, education, religion, and area of specialty.

Questionnaire of cognitive and affective empathy

To assess empathy, three subscales (perspective taking, emotion contagion, and proximal responsivity) from the Questionnaire of Cognitive and Affective Empathy (QCAE; Reniers et al., 2011) were used. Cognitive empathy was assessed by using the Perspective Taking subscale, which measures the ability to adopt the perspective of others (e.g., “I can easily work out what another person might want to talk about”: from 1, strongly disagree, to 4, strongly agree). Affective empathy was measured using two subscales: emotion contagion (e.g., “People I am with have a strong influence on my mood”), and proximal responsivity (e.g., “I often get emotionally involved with my friends’ problems”). Items were averaged such that higher scores indicate greater empathy. The emotion contagion items have a high Cronbach’s alpha of 0.84, as did the proximal responsivity items ($\alpha = 0.77$). However, perspective taking items had a moderate reliability level ($\alpha = 0.65$; Reniers et al., 2011).

Religiosity

Religiosity was measured using the Duke University Religion Index (DUREL), a validated five-item scale that assesses three dimensions of religiosity: organizational religious activity, nonorganizational religious activity, and intrinsic religiosity (Koenig & Büssing, 2010). Participants completed this questionnaire after the MRI component. Participants rated five questions on a 6-point Likert scale, with higher scores indicating stronger religious involvement. Example items included: “How often do you attend church or other religious meetings?” (organizational religious activity), “How often do you spend time in private religious activities, such as prayer, meditation, or Bible study?” (nonorganizational religious activity), and “My religious beliefs are what really lie behind my whole approach to life” (intrinsic religiosity). Items were averaged to create a single index. The DUREL was chosen for its brevity and multidimensionality, providing a comprehensive assessment of participants’ religious involvement, which could influence their perspective toward assisted dying. The items had a high reliability coefficient ($\alpha = 0.93$).

MRI acquisition

A 7 T Magnetom system (Siemens Healthcare, Erlangen, Germany) with a 32-channel head coil (Nova Medical Inc,

Wilmington MA) was used to acquire brain images. First, a 5-min MP2RAGE scan (Marques et al., 2010) was conducted to acquire a T1-weighted whole brain structural image for anatomical reference, using 1-mm isotropic resolution, repetition time (TR) = 5,290 ms, echo time (TE) = 2.8 ms, inversion time (TI) 1 = 700 ms, flip angle (FA) 1 = 8°, TI2 = 2700 ms, FA2 = 10°.

The functional images were acquired using a multiband gradient echo planar imaging (EPI) sequence, with parallel imaging acceleration (Moeller et al., 2010). A total image acceleration factor of 12 (two by parallel and six by multiband) and blipped controlled aliasing was used to achieve whole brain coverage with 1.6-mm isotropic spatial resolution, and a temporal resolution of 800 ms with 1,300 repetitions per run (two runs in total) (Polimeni et al., 2016). Field of view (FOV) = 208 mm, TE = 22.2 ms, and flip angle = 45° were specified. The phase encoding direction was posterior to anterior, to avoid signal pile up in the frontal cortex. Two sets of spin-echo EPI scans with matching resolution to the fMRI scans but with opposing phase encoding directions were acquired to correct for distortion of the magnetic field using the PEPOLAR approach.

MRI preprocessing

Preprocessing of anatomical and functional data was run using fMRIPrep v23.1.4 (Esteban et al., 2019; 2020). The detailed descriptions in the two sections below were adapted from boilerplate documentation generated by fMRIPrep.

Structural data preprocessing

The T1-weighted (T1w) image was corrected for intensity nonuniformity (INU) with N4BiasFieldCorrection (Tustison et al. 2010), distributed with ANTs (Avants et al. 2008). The T1w image was then skull-stripped with a Nipype implementation of the antsBrainExtraction.sh workflow (from ANTs), using OASIS30ANTs as the target template. Brain tissue segmentation of cerebrospinal fluid (CSF), white matter (WM), and gray matter (GM) was performed on the brain-extracted T1w using the FSL fast function (Zhang et al., 2001). Brain surfaces were reconstructed using recon-all (FreeSurfer 7.3.2; Dale et al., 1999), and the brain mask estimated previously was refined with a custom variation of the method from Mindboggle to reconcile ANTs-derived and FreeSurfer-derived segmentations of the cortical gray-matter (Klein et al., 2017). Volume-based spatial normalization to standard space was performed through nonlinear registration with the antsRegistration routine from ANTs, using brain-extracted versions of both the participant’s T1w reference and the T1w template. The MNI152NLin6Asym template,

accessed via TemplateFlow (23.0.0, Ciric et al., 2022), was used as the target for normalization.

Functional MRI data preprocessing

For each of the two functional neuroimaging runs in which participants responded to the MAiD scenarios, the following preprocessing was performed. First, a reference volume and its skull-stripped version were generated by aligning and averaging 1 single-band reference image. Head-motion parameters with respect to the BOLD reference (transformation matrices, and six corresponding rotation and translation parameters) were estimated before any spatiotemporal filtering using *mcfliirt* from FSL (Jenkinson et al., 2002). The confound time series derived from head motion estimates were retained for use as confound regressors in the general linear model (GLM) first-level analysis. A B_0 -nonuniformity map (or *fieldmap*) was estimated based on the two echo-planar imaging (EPI) references using the *topup* command from FSL (Andersson et al., 2003). The estimated fieldmap was then aligned with rigid-registration to the target EPI (echo-planar imaging) reference run. The field coefficients were mapped on to the reference EPI using the transform. BOLD runs were slice-time corrected to 0.371s (midpoint of slice acquisition range 0–0.743 s) using *3dTshift* from AFNI (Cox & Hyde, 1997).

The BOLD reference was then co-registered to the T1w reference using *bbregister* from FreeSurfer, which implements boundary-based registration (Greve & Fischl, 2009). Co-registration was configured with six degrees of freedom. The BOLD time-series were resampled into standard space, generating a preprocessed BOLD run in MNI152N-Lin6Asym space. All resamplings can be performed with a single interpolation step by composing all the pertinent transformations (i.e., head-motion transform matrices, susceptibility distortion correction when available, and co-registrations to anatomical and output spaces). Gridded (volumetric) resamplings were performed using *antsApplyTransforms* from ANTs, configured with Lanczos interpolation to minimize the smoothing effects of other kernels (Lanczos, 1964). Nongridded (surface) resamplings were performed using *mri_vol2surf* from FreeSurfer.

A set of physiological regressors was extracted to allow for component-based noise correction (aCompCor) (Behzadi et al., 2007; Muschelli et al., 2014). For aCompCor, three probabilistic masks (CSF, WM, and combined CSF+WM) were generated in anatomical space. The implementation differs from that of Behzadi et al. in that instead of eroding the masks by 2 pixels in BOLD space, a mask of pixels that likely contain a volume fraction of gray matter (GM) is subtracted from the aCompCor masks. This mask is obtained by dilating a GM mask extracted from the FreeSurfer's *aseg* segmentation, and it ensures components are not extracted

from voxels containing a minimal fraction of GM. Finally, these masks are resampled into BOLD space and binarized by thresholding at 0.99 (as in the original implementation). Components are also calculated separately within the WM and CSF masks. The time series of the 5 aCompCor components with the largest singular values from the separate WM and CSF masks were retained for use as confound regressors in the GLM analysis. Principal components were estimated after high-pass filtering of the preprocessed BOLD time-series (using a discrete cosine filter with 128 s cutoff); thus, regressors corresponding to this filtering approach were also included in the GLM.

Functional MRI analysis

Univariate analysis

Univariate analyses were conducted using FSL FEAT. Input data had been preprocessed and normalized in *fMRIprep*; the only additional preprocessing run in FSL was a 5-mm smoothing kernel. For the main analyses, the first-level model for each of the two runs included two primary regressors: one representing trials with normative scenarios, and a second representing trials with nonnormative scenarios. Each event was represented as a boxcar function beginning at stimulus onset and lasting 10 seconds; this time window included the description of the scenario and the choice but not the confidence rating. These events were convolved with a double-gamma hemodynamic response function (HRF). Temporal derivatives for each regressor were also included in the model to accommodate variability in the HRF. Additionally, regressors of no interest were added, which were computed in *fMRIprep*: 6 motion parameters, 10 aCompCor regressors (5 components from white matter and 5 components from CSF), and 15 cosine basis functions to achieve high-pass filtering. Any nonsteady state regressors computed by *fMRIprep* were also included in the model. First-level cope (contrast of parameter estimate) maps for the two primary regressors were entered into a fixed-effects model to combine estimates across the two runs. A contrast between non-normative and normative trials was also computed on these second-level results. For whole-brain analyses, cope maps reflecting contrasts of interest were entered into a mixed-effects model using FLAME1 to estimate group-level effects. A voxel threshold of $z > 3.1$ was applied together with a cluster threshold of $p < 0.05$ implemented using Gaussian random field theory in FEAT.

To test whether differences between nonnormative and normative scenarios observed in the primary model were driven by differences in response confidence rather than from qualitative differences in how the two types of trials are judged, we constructed an alternative model controlling for

confidence. Three regressors were entered into the model: one representing all trials with equal weightings, a second in which the scenario type was varied parametrically (1 = nonnormative, -1 = normative), and a third in which confidence rating was entered as a parametric modulator. Note that when trial type is modeled parametrically, it is not possible to separate which effects are driven by normative scenarios and which by nonnormative scenarios. We verified however that differences between scenario types (without accounting for confidence) were nearly identical with this approach vs. our primary analysis. It also provides a more statistically robust approach for modeling task condition alongside an additional parametric regressor (confidence) that is independent of condition. As in the primary model, only the 10-s time window during which the decisions were made was modeled, excluding the subsequent time window during which confidence was judged. Further, this model included the same regressors of no interest (temporal derivatives, motion parameters, CompCor regressors, cosine basis function regressors, and nonsteady state regressors as needed) as in the primary model.

Region of interest analyses

A priori region-of-interest (ROI) analyses were conducted to test predictions about specific brain regions hypothesized to be involved, based on prior studies. The ACC and AI were both defined using the Neurosynth automated meta-analysis database (Yarkoni et al., 2011). Association test maps for the terms “anterior cingulate” and “anterior insula” were downloaded from the Neurosynth Web interface (www.neurosynth.org). Arbitrary thresholds were applied to limit the activations to the region in question, with thresholds of $z > 9$ applied for anterior cingulate and $z > 10$ applied for anterior insula. Note that the ACC ROI included both the dorsal ACC (also known as the anterior midcingulate, or aMCC) and the more anterior pregenual ACC. A similar approach was used to define the mentalizing network, using the term “mentalizing” and applying a threshold of $z > 7$. The mentalizing network ROI primarily identified voxels in dmPFC, precuneus, and temporo-parietal junction (TPJ); note that although the full map also included a large cluster in vmPFC, this cluster was so far ventral that most voxels were excluded from our whole-brain mask due to signal dropout issues. To ensure that reported results did not depend on the arbitrary choice of threshold on the Neurosynth meta-analysis maps, we also report results using a more lenient threshold in which the required z statistic was lowered by 1 (ACC: $z > 8$, AI: $z > 9$, mentalizing: $z > 6$). These leniently-defined ROIs were then trimmed as needed to remove voxels that obviously did not conform to standard anatomical definitions of the named regions. The reward system ROIs (vmPFC and striatum) were obtained from www.kablelab.com,

identified based on a meta-analysis which identified a core “valuation system” that tracks subjective value (Bartra et al., 2013). This vmPFC ROI is located in a less ventral region than the vmPFC cluster from the mentalizing ROI, so was less vulnerable to signal dropout, but some voxels that were excluded from the whole-brain mask at the group level were excluded from the ROI here as well. ROIs for amygdala, hippocampus, and precuneus were extracted from the Harvard-Oxford atlas provided with FSL. All voxels with more than a 25% probability of being in the intended region, and where the intended region was the most likely label, were included. To confirm that these analyses were not dependent on a specific choice of threshold, secondary analyses using thresholds of 50% probability and 0% probability are also reported. Anterior hippocampus and posterior hippocampus were separated at $y = -21$, following Poppenk et al. (2013), because these regions were expected to have different connectivity patterns.

Functional connectivity analyses

A generalized psychophysiological interaction (gPPI) analysis (McLaren et al., 2012) was conducted to assess how functional connectivity between a defined seed region and other regions changed depending on the context (i.e., processing normative vs. nonnormative scenarios). Regressors for the gPPI analysis were constructed using AFNI. The average time series in the seed region was extracted from the data that had been preprocessed in fMRIPrep and smoothed in FSL (using a 5-mm FWHM Gaussian kernel). This time series was then detrended and up-sampled by a factor of 10. A gamma function HRF was deconvolved from the time series using the AFNI 3dTfitter command. This deconvolution approach used a combination of penalty functions (based on the raw time series and its first and second derivatives) with a penalty weight of -2 , and Lasso regularization with $\lambda = -6$, following the suggested parameters from the 3dTfitter help file. To create the physiological regressor, the deconvolved time series of the ROI was reconvolved with a gamma HRF and down-sampled back to the original TR length. The psychological regressors for gPPI (normative and nonnormative) were computed by up-sampling the raw regressors, convolving them with a gamma HRF and down-sampling back to the TR length. The gPPI regressors were created by multiplying the up-sampled raw psychological regressor for normative and nonnormative trials with the deconvolved time series of the seed region, convolving with a gamma HRF, and then down-sampling back to the TR length. Finally, all down-sampled regressors were then input back into FEAT as part of a new first-level analysis. Input data were the same as for the univariate analysis, i.e., data that had been preprocessed by fMRIPrep. Other than

application of a 5-mm smoothing kernel, no additional pre-processing was done.

The first-level FEAT model for each run included psychological and PPI regressors for each condition, and the physiological regressor, for a total of five regressors. The temporal derivatives of the two psychological regressors were computed by FEAT and included in the model, and temporal filtering was applied to the psychological regressors. The same nuisance regressors were used as in the univariate model, i.e., 6 motion parameters, 10 aCompCor parameters, and 15 cosine basis function regressors. Data from the two runs were combined in a second-level fixed effects analysis, where contrasts of interest were computed. These second-level contrast estimates then served as inputs to the final group-level analysis, which was run using the FLAME1 mixed effects model. As for the univariate analysis, secondary PPI models were run to control for trialwise confidence. These models included seven primary regressors: a physiological regressor, as well as psychological and PPI regressors representing 1) all trials, 2) all trials parametrically modulated by trial type (1 = nonnormative, −1 = normative), and 3) all trials parametrically modulated by confidence level. The same regressors of no-interest were included in this model as in other first-level models.

PPI analyses are known to yield noisier parameter estimates relative to univariate analyses (Di & Biswal, 2017), likely due to the high level of collinearity among regressors. We elected to increase sensitivity primarily by running voxelwise analyses masked with specific target brain regions rather than a whole-brain mask, limiting the search space and making cluster correction less stringent. While not preregistered, connectivity between seed regions and the specified target regions were motivated by specific findings from prior literature. These analyses maintained the standard voxelwise threshold of $z > 3.1$, cluster corrected to $p < .05$. Findings from whole-brain PPI analyses with a lowered voxelwise threshold of $z > 2.3$ ($p < .01$) are also reported. This is an alternative approach used in some prior published work (Cohen et al., 2019) for dealing with the reduced signal-to-noise ratio in PPI. Despite having a nominal corrected $p < .05$, it is also associated with an elevated false-positive risk (Eklund et al., 2016). A lowered voxelwise threshold of $z > 2.3$ within a target ROI was used for some analyses but this was intended specifically as a more lenient thresholding choice with weaker inferential value.

Results

Behavioral results

Participants were more likely to approve MAiD requests under normative conditions compared with nonnormative

conditions. Specifically, under normative conditions, where the patient's circumstances were aligned with the legal guidelines for MAiD, participants responded "yes" to grant the request 93% of the time compared with 12% in nonnormative conditions where the patient's situation deviated from the typical criteria ($t(58) = -24.82$, $p < 0.001$; $d = -3.23$, 95% CI of mean difference $[-87.9\%, -74.8\%]$). Furthermore, participants reported higher confidence in their decisions when evaluating normative scenarios ($M = 7.35$, $SD = 1.54$) compared with nonnormative scenarios ($M = 6.75$, $SD = 1.14$), suggesting that participants felt more certain when the request aligned with legal and social criteria ($t(58) = -2.67$, $p = 0.01$; $d = 0.35$, 95% CI of mean difference $[-1.06, -0.15]$) (Fig. 2). Decision response times did not significantly differ between nonnormative ($M = 1,167$ ms, $SD = 355$ ms) and normative ($M = 1,078$ ms, $SD = 356$ ms) scenarios ($t(58) = 1.85$, $p = .069$, $d = 0.24$, 95% CI of mean difference $[-7.12$ ms, 184.02 ms]).

Whole-brain univariate analysis

To examine differences in processing between normative and nonnormative trials, a whole-brain univariate analysis was conducted. Regions that showed increased activity for nonnormative vs. normative scenarios included frontoparietal areas supporting response selection and executive function bilaterally in premotor cortex, pre-supplementary motor area (pre-SMA), and caudate, with clusters extending into dorsolateral prefrontal cortex (dlPFC) and intraparietal sulcus. Furthermore, heightened activation for nonnormative scenarios was detected in regions of the default-mode network, specifically the bilateral precuneus, right posterior cingulate cortex, and bilateral angular gyrus (Fig. 3; Table 1). While activity in these regions may reflect mentalizing and/or self-referential thought, these regions are also involved in high-fidelity memory retrieval. We report below an analysis that examines task-dependent connectivity with hippocampus to better understand the functional coupling of these activations. The reverse contrast (normative > nonnormative) revealed significantly greater activation in the subgenual anterior cingulate (subgenual ACC), mid-insula, and amygdala, as well as postcentral gyrus, regions that process emotional and pain salience (Fig. 3; Table 1).

Because responses to normative trials were generally provided with higher confidence than responses to nonnormative trials, we ran an additional analysis examining whether these findings are maintained when controlling statistically for response confidence. The key effects listed in Table 1 from the primary analysis were largely preserved when examining effects of trial type in this analysis, although with slightly different cluster extent (Supplementary Fig. 1; Supplementary Table 1). This included reliably greater activity for

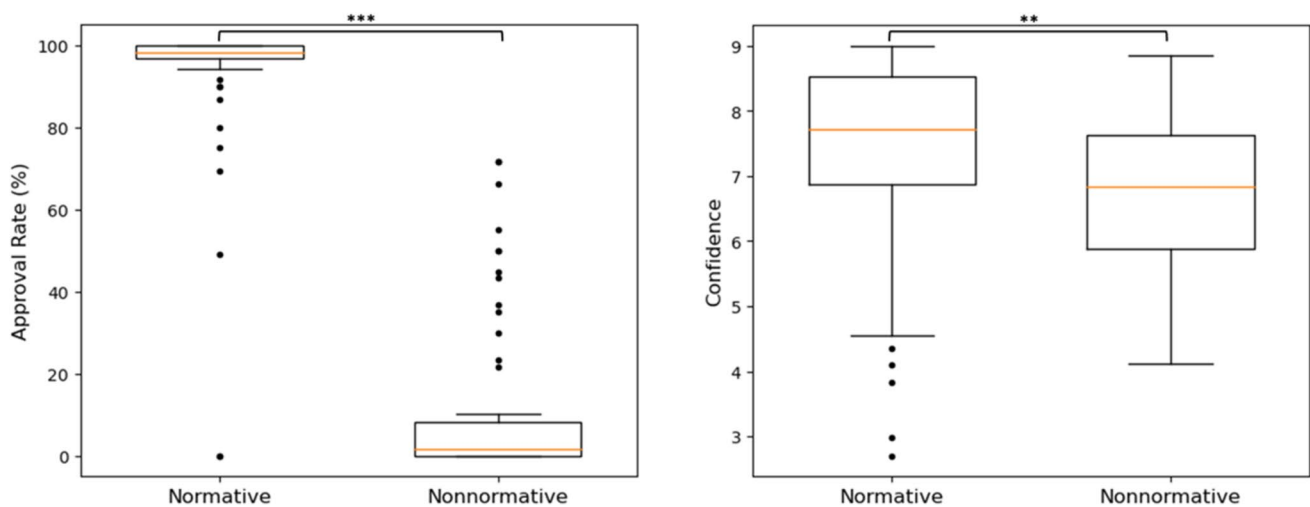


Fig. 2 Approval Rate and Confidence Rating for Normative and Nonnormative Scenarios

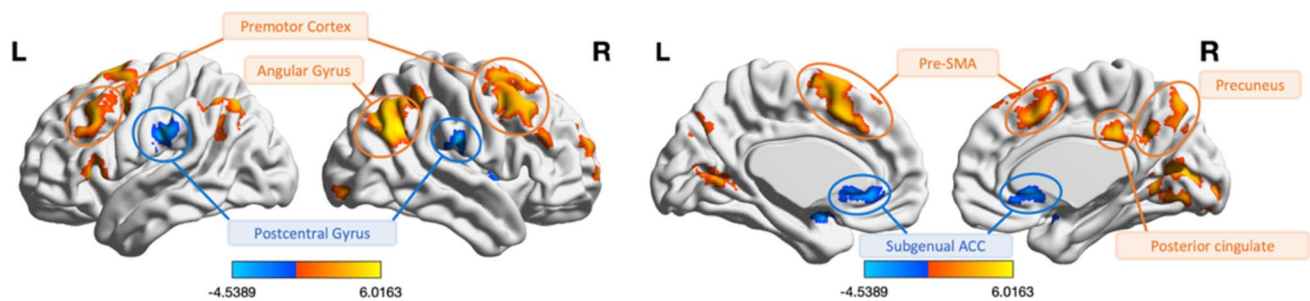


Fig. 3 Whole-Brain Analysis Showing Differences in Brain Response: Non-Normative Scenarios > Normative Scenarios

nonnormative trials in bilateral angular gyrus (corresponding to clusters 1 and 4 in Table 1), right IPS (as in cluster 1), left pre-SMA (as in cluster 3), precuneus and posterior cingulate (as in clusters 6, 11, and 14), right caudate (as in cluster 10), and occipital cortex (as in cluster 5). Thus, we can still conclude that nonnormative scenarios appear to more strongly engage brain regions related to response selection and executive function as well as nodes of the default-mode network. In the reverse contrast, reflecting greater activity during normative trials, effects in left somatosensory cortex (cluster 1) and bilateral mid-insula (clusters 2 and 3) were still robust when controlling for confidence level. Effects of trialwise confidence are also described in supplementary materials (Supplementary Fig. 2; Supplementary Table 2).

Effects of social norms in regions of interest

Many of the effects identified in the whole-brain univariate analysis comparing nonnormative and normative scenarios were detected in regions associated with cognitive

processing, including those implicated in evaluating the information presented against stored knowledge retrieved from memory and resolving conflicting elements. We further hypothesized that normative and nonnormative scenarios would differentially engage brain regions involved in emotional processing and empathy. An ROI analysis in the anterior insula (AI), a key region involved in affective empathy (Decety, 2015; Eres et al., 2015), showed greater activation during evaluation of nonnormative requests ($t(58) = 2.2$, $p = 0.032$, $d = 0.29$, 95% CI of mean difference: [0.37, 7.88]). This difference was negatively correlated with affective empathy ($r = -0.313$, $p = 0.016$, 95% CI of r [-0.53, -0.06]), indicating that the overall nonnormative > normative effect is driven by participants scoring lower on affective empathy (Fig. 4A). These results are not dependent on the arbitrary threshold chosen for the anterior insula ROI, as both the main effect ($t(58) = 2.01$, $p = 0.049$, $d = 0.26$, 95% CI of mean difference: [0.02, 6.99]) and the correlation with affective empathy ($r = -0.312$, $p = 0.016$, 95% CI of r [-0.53, -0.06]) remain significant when a more lenient threshold is applied, yielding a larger

Table 1 Cluster peaks with significantly greater hemodynamic response when viewing nonnormative scenarios compared to normative scenarios

Cluster Number	Brain Regions	Peak Coordinates			Z max	Cluster Size (Voxels)
		X	y	l		
Greater Response for non-normative > normative scenarios						
1	Right angular gyrus	48	−56	32	6.02	1717
	Right temporoparietal junction	56	−64	30	5.55	
	Right inferior parietal lobule	38	−70	40	4.61	
	Right supramarginal gyrus	46	−42	56	4.43	
	Right intraparietal sulcus	40	−42	48	4.19	
2	Left middle frontal gyrus (Premotor cortex)	−28	4	56	5.21	1610
	Left supplementary motor area	−10	18	66	4.91	
	Left pre-SMA	−4	18	46	4.83	
	Left middle frontal gyrus (premotor cortex)	−46	8	50	4.79	
	Right pre-SMA	8	12	50	3.96	
3	R middle frontal gyrus (premotor cortex)	40	24	50	5.06	1438
	R middle frontal gyrus (premotor cortex)	26	6	60	4.7	
	R dorsolateral prefrontal	so	34	22	4.16	
4	R primary visual cortex	10	−72	10	5.45	935
	R primary visual cortex	16	−92	−6	5.15	
	R extrastriate visual cortex	−16	−54	2	4.58	
	R extrastriate visual cortex	12	−70	−4	4.1	
5	L angular gyrus	−42	−60	40	4.8	605
	L supramarginal gyrus	−50	−48	50	4.65	
6	R precuneus	2	−70	56	4.35	304
	R precuneus	8	−74	40	4.06	
	L precuneus	−6	−70	36	3.8	
7	R caudate	18	8	14	5.52	301
8	L middle frontal gyrus (premotor cortex)	−46	24	42	4.49	277
9	L caudate	−16	2	18	5.45	243
	L caudate	−14	14	8	5	
10	R frontal pole	16	62	24	4.16	178
11	L inferior frontal gyrus, pars triangularis	−54	24	4	4.53	149
12	L pre-SMA	−8	38	60	4.12	130
	R pre-SMA	6	32	62	3.82	
13	R posterior cingulate/precuneus	2	−54	32	4.09	101
14	R posterior cingulate	4	−34	36	4.12	79
15	R cerebellum	34	−60	−30	3.95	76
16	L cerebellum	−22	−82	−28	4	63
17	L thalamus	−6	−20	12	3.93	62
Greater Response for normative scenarios> non-normative scenarios						
1	L somatosensory cortex	−62	−20	28	4.46	143
2	R mid-insula	38	6	6	4.54	141
3	R somatosensory cortex	56	−20	24	4.52	130
4	L insula/amygdala	−28	4	−18	4.26	105
	L orbitofrontal cortex	−18	8	−18	4.14	
5	R subgenual ACC	2	22	−4	4.12	83
	L subgenual ACC	−2	32	−8	3.87	

ROI. However, the main effect of trial type in this region is greatly attenuated when response confidence was included as a covariate: when both variables are included in the model, as described for the whole-brain analysis above, this effect is no longer significant ($t(58) = 0.52$, $p = 0.60$, $d = 0.07$, 95% CI of mean difference $[-1.42, 2.44]$). At the same time, the effect of confidence is highly significant ($t(58) = -4.87$, $p < 0.001$, $d = 0.63$, 95% CI of mean difference $[-2.69, -1.12]$), suggesting that the univariate effect in AI is driven primarily by response confidence. Nevertheless, the correlation between effect of trial type in this region and affective empathy remains significant ($r = -0.258$, $p = 0.049$, 95% CI of mean difference $[-0.48, -0.002]$).

We also examined whether activity differed between normative and nonnormative stimuli in other emotion-processing regions. There was no difference in activation in ACC, another region associated with affective empathy, across conditions ($t(58) = 0.13$, $p = 0.897$, $d = 0.02$, 95% CI of mean difference $[-1.86, 2.12]$). Greater activation during evaluation of normative requests was found in the primary amygdala ROI ($t(58) = -3.36$, $p = 0.001$, $d = 0.45$, 95% CI of mean difference $[-3.1, -0.82]$), consistent with

the whole-brain results suggesting greater emotional salience for normative trials. This effect correlated positively with overall religiosity ($r = 0.33$, $p = 0.010$, 95% CI of r $[0.08, 0.54]$); as greater activity during normative trials is reflected in negative values, this means that the overall difference is most apparent in less religious participants (Fig. 4B). While the primary amygdala ROI was defined using a 25% probabilistic threshold, both the main effect and the correlation with religiosity remained robust when applying alternative 50% and 0% probabilistic thresholds for the amygdala ROI ($p < .001$ for both mean differences; $p < .013$ for both correlations). Finally, we examined the main (25% probabilistic threshold) ROI in the analysis controlling for trial-level confidence. Both the main effect of trial type ($t(58) = -2.31$, $p = .025$, $d = -0.3$, 95% CI of mean difference $[-1.51, -0.11]$) and the correlation between this effect and religiosity ($r = 0.31$, $p = .016$, 95% CI of r $[0.06, 0.53]$) remained robust, while the effect of confidence was marginal ($t(58) = 1.81$, $p = .075$, $d = 0.24$, 95% CI of mean difference $[-0.04, 0.77]$). Thus, while lower confidence may partly contribute to the increased activity in amygdala during normative trials, such trials also appear to be associated

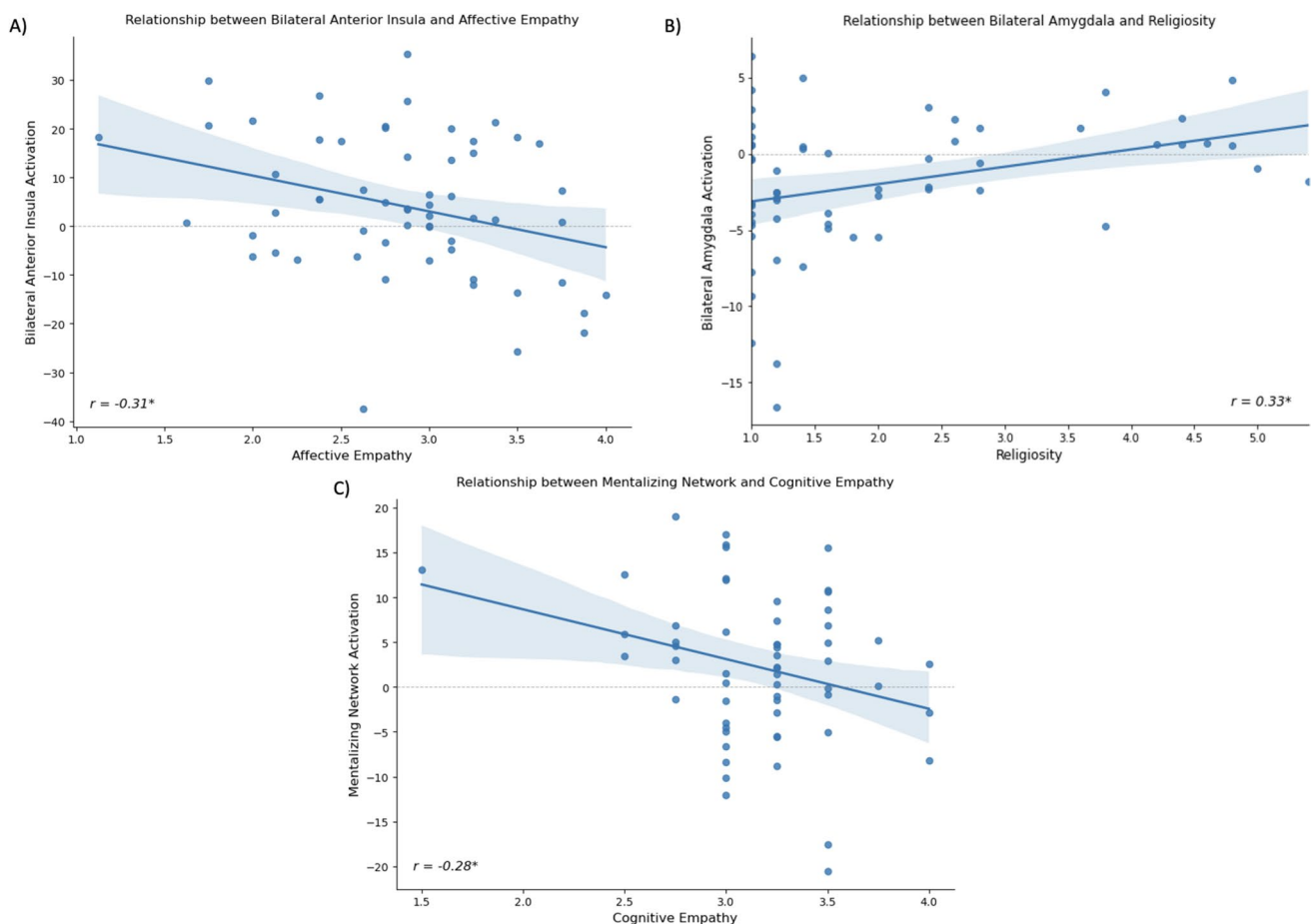


Fig. 4 Relationships Between **A)** Bilateral Anterior Insula and Affective Empathy; **B)** Bilateral Amygdala and Religiosity; **C)** Mentalizing Network and Cognitive Empathy

with higher levels of amygdala activation when controlling for judged confidence level.

As possible markers of compassionate responding, we examined the hemodynamic response in the vmPFC ROI (Decety & Porges, 2011; Jensen et al., 2020), which showed greater activation during the evaluation of normative requests ($t(58) = -2.23$, $p = 0.03$, $d = -0.29$, 95% CI of mean difference $[-10.02, -0.54]$), and in the striatum ROI, which showed no difference between conditions ($t(58) = 0.4$, $p = 0.69$, $d = 0.05$, 95% CI of mean difference $[-0.99, 1.48]$). The vmPFC response was not robust to including trialwise confidence in the model, ($t(58) = -1.17$, $p = .25$, $d = 0.15$, 95% CI of mean difference $[-3.75, 0.98]$), but the effect of trialwise confidence was also not significant ($t(58) = 1.19$, $p = .24$, $d = 0.15$, 95% CI of mean difference $[-0.58, 2.28]$). Thus, the effects of confidence may contribute to neural activity in this region but do not appear to be the primary driver.

To understand the impact of cognitive empathy, we examined activity in an ROI from Neurosynth representing the mentalizing network, including the dmPFC, precuneus, and bilateral TPJ (Decety & Lamm, 2007). Averaging across all voxels in this network, activity was greater for nonnormative trials ($t(58) = 2.02$, $p = 0.048$, $d = 0.26$, 95% CI of mean difference $[0.02, 4.33]$), and the effect varied based on participants' cognitive empathy ($r = -0.28$, $p = 0.035$, 95% CI of r $[-0.5, -0.02]$), such that the overall difference in scenario types was driven by participants scoring lower on cognitive empathy (Fig. 4C). When a more lenient threshold was used to identify the mentalizing network, the main effect of scenario type (nonnormative vs. normative) remained significant ($t(58) = 2.58$, $p = .012$, $d = 0.34$, 95% CI of mean difference $[0.57, 4.54]$), while the correlation between this effect and cognitive empathy was a weak trend ($r = -0.216$, $p = .1$, 95% CI of r $[-0.45, 0.04]$). Similarly, in the original ROI, in the analysis controlling for trialwise confidence, the main effect of scenario type was significant ($t(58) = 2.63$, $p = .011$, $d = 0.34$, 95% CI of mean difference: $[0.41, 3.06]$), while the effect of confidence was not ($t(58) = 0.63$, $p = .53$, $d = 0.08$, 95% CI of mean difference $[-0.64, 1.24]$). Here, the correlation between the effect of scenario type and cognitive empathy was marginal ($r = -0.24$, $p = .066$, 95% CI of r $[-0.47, 0.02]$).

Effects in the mentalizing network varied by region, however. When separately examining the four regions contributing most strongly to this network (dmPFC, precuneus, and left and right TPJ), increased activity during nonnormative scenarios was apparent in right TPJ ($t(58) = 5.68$, $p < .001$, $d = 0.74$, 95% CI of mean difference: $[6.32, 13.21]$), left TPJ ($t(58) = 2.44$, $p = 0.018$, $d = 0.32$, 95% CI of mean difference $[0.76, 7.68]$), and precuneus ($t(58) = 2.89$, $p = .005$, $d = 0.38$, 95% CI of mean difference $[1.51, 8.28]$), but not apparent in dmPFC ($t(58) = -1.73$, $p = .088$, $d = 0.22$, 95% CI

of mean difference $[-7.06, 0.51]$), with a trend going in the opposite direction. However, the correlation with cognitive empathy was only significant in dmPFC ($r = -0.27$, $p = .042$, 95% CI of r $[-0.49, -0.01]$), with no significant correlations in precuneus ($r = -0.21$, $p = .11$, 95% CI of r $[-0.44, 0.05]$), left TPJ ($r = -0.07$, $p = .6$, 95% CI of r $[-0.32, 0.19]$) or right TPJ ($r = -0.04$, $p = .77$, 95% CI of r $[-0.29, 0.22]$). These differences in activation by region were consistent across both robustness checks (using a more lenient ROI threshold and controlling for trial-wise confidence), with the TPJ and precuneus effects remaining significant and the dmPFC trend remaining nonsignificant in both cases. Full statistics for these checks are reported in Supplementary Tables 3a and 3b.

Functional connectivity analyses with hippocampal seed region

As noted, one possible interpretation of activity differences in regions such as precuneus and angular gyrus is that participants engaged in greater memory retrieval when evaluating nonnormative scenarios. If this were the case, the functional coupling between hippocampus and these default mode network regions should likewise increase on nonnormative trials. The left hippocampus was selected based on its greater involvement in episodic retrieval, while the right hippocampus is more associated with spatial memory (Burgess et al., 2002). Prior literature also suggests that connectivity between the left anterior hippocampus and precuneus is the pairing most strongly modulated by the need to engage memory retrieval processes in a naturalistic context, alongside greater univariate activity in regions including the precuneus, angular gyrus, and hippocampus (Ren et al., 2018). Thus, we used a left anterior hippocampus seed (Fig. 5A), and for our primary analysis, limited the target search space to the precuneus.

A cluster in precuneus showed significantly higher connectivity with anterior hippocampus during nonnormative relative to normative trials (peak voxel: 2, -66 , 48, $z = 3.67$, corrected $p = .033$, cluster extent = 19 voxels). The primary result applied a 25% probabilistic threshold to both ROIs, but this result was robust across alternative thresholding choices: the cluster remained significant when both ROIs were thresholded at 50% (peak voxel: 2, -66 , 48, $z = 3.61$, corrected $p = .021$, cluster extent = 17 voxels) and was marginal when both ROIs were thresholded at 0% (peak voxel: 2, -66 , 48, $z = 3.51$, corrected $p = .088$, cluster extent = 14 voxels). This PPI result was similarly robust when controlling for trialwise confidence, yielding the following cluster when ROIs were defined based on a 25% threshold: peak voxel: 8, -66 , 50, $z = 3.96$, corrected $p = .009$, cluster extent = 29 voxels. An exploratory whole-brain PPI analysis using the anterior

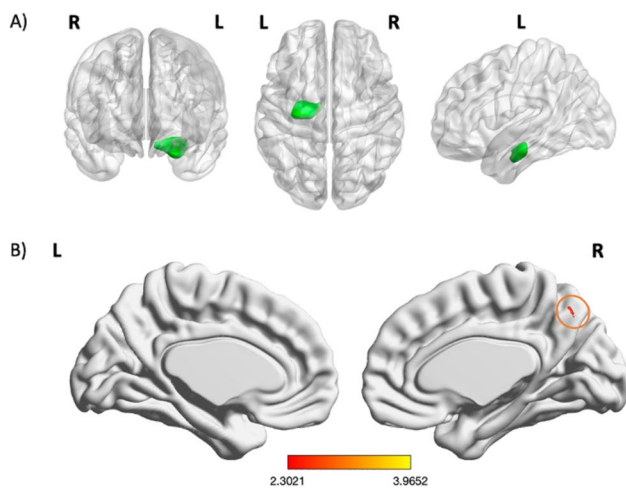


Fig. 5 A) Left Anterior Hippocampus as the Seed Region and B) gPPI Connectivity Between Hippocampus and Precuneus

hippocampus seed, with a reduced voxelwise threshold of $z > 2.3$, similarly showed a significant cluster in precuneus (peak voxel: 2, -78, 52, $z = 3.74$, corrected $p = .0499$, cluster extent = 156 voxels) (Fig. 5B). These findings suggest that people are engaging in memory retrieval processes more strongly during nonnormative trials.

Functional connectivity analyses with ACC as the seed region

To investigate whether neural markers of trait empathy are differentially engaged across conditions, we conducted a second functional connectivity analysis using the ACC as the seed region (Fig. 6A). The ACC is likely to be critically involved in processes central to medical assistance in dying (MAiD), including negative affect, pain, and cognitive control (Shackman et al., 2011). In particular, the aMCC subdivision of the ACC is consistently engaged during these states, supporting its proposed role in resolving complex

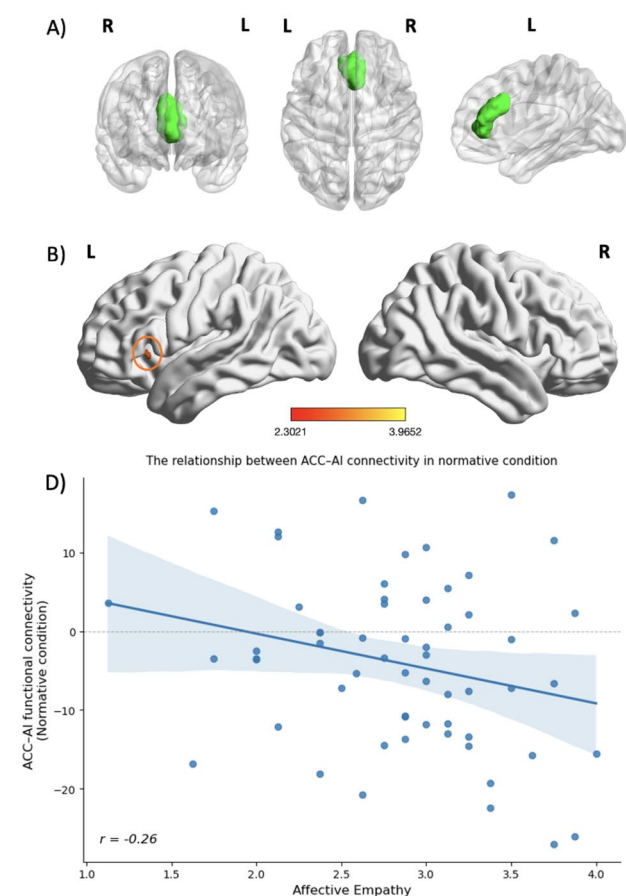
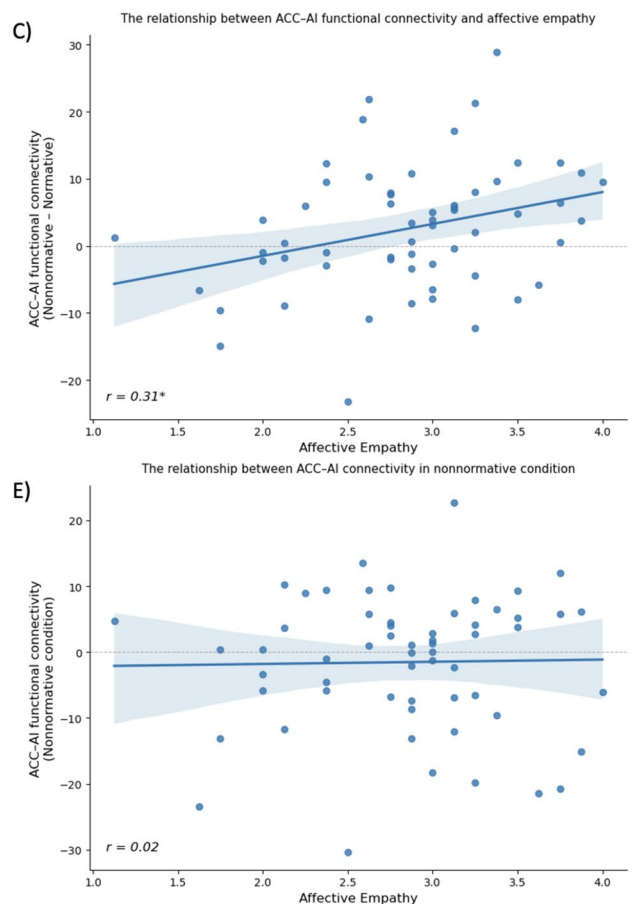


Fig. 6 A) Anterior Cingulate Cortex (ACC) as the Seed Region; B) gPPI Connectivity Between ACC and Anterior Insula (AI); C) The Relationship Between ACC–AI Functional Connectivity and Affective Empathy; D) The Relationship Between ACC–AI Connectivity



in Normative Condition and Affective Empathy; E) The Relationship Between ACC–AI Connectivity in Nonnormative Condition and Affective Empathy

and uncertain decisions (Shackman et al., 2011). Moreover, the ACC is a core region for empathy and for processing others' emotional states (Smith et al., 2021; Gamble et al., 2024; Lamm et al., 2011), making it especially relevant in the deeply interpersonal, emotionally charged context of MAiD decisions. Furthermore, there is reason to expect that the connectivity between ACC and AI might be associated with empathic reactions. Previous literature finds that ACC and bilateral AI are typically both associated with empathy for pain (Lamm et al., 2011), with AI processing salient emotional responses that are subsequently communicated to ACC to initiate behavioral responses (Medford & Critchley, 2010). Thus, we first focused on AI as a target region for this PPI analysis.

When limiting the search space to the Neurosynth-derived bilateral AI mask, a significant effect was apparent in left AI with a $z > 3.1$ voxelwise threshold (peak voxel $-36, 22, 0$, $z = 3.97$, corrected $p = .005$, cluster extent = 16 voxels). An exploratory whole-brain PPI analysis with a lowered voxelwise threshold of $z > 2.3$ similarly showed only one cluster centered in left AI, extending into left ventrolateral prefrontal cortex (peak voxel $-36, 22, 0$, $z = 3.97$, corrected $p = .002$, cluster extent = 257 voxels). An additional sensitivity analysis using more liberal definitions of both seed and target regions than in our primary analysis confirmed that this effect was not dependent on arbitrary thresholding choices: using a $z > 3.1$ voxelwise threshold and a bilateral AI prethreshold mask, but defining both the seed region and the target mask with the critical z threshold lowered by 1, the cluster centered in AI was still significant (peak voxel $-36, 22, 0$, $z = 3.81$, corrected $p = .009$, cluster extent = 15 voxels).

To confirm that this effect holds bilaterally across the anterior insula, we also examined the PPI effect averaged across a bilateral ROI of this region, and again found that the functional coupling between ACC and AI was significantly stronger when participants evaluated nonnormative scenarios compared to normative ones ($t(58) = 2.06$, $p = 0.044$, $d = 0.27$, 95% CI of mean difference $[0.08, 5.02]$). Consistent with prior work establishing these two regions as central to affective empathy, participants who scored higher on the dispositional measure of affective empathy showed a greater difference in ACC-AI connectivity across conditions ($r = 0.31$, $p = 0.018$, 95% CI of r $[0.06, 0.52]$; Fig. 6C). To understand this relationship better, we then examined the effect in each condition separately and found that the modulation was driven by the normative condition: higher affective empathy was associated with weaker ACC-AI connectivity in the normative condition to a nearly significant degree ($r = -0.256$, $p = 0.05$, 95% CI of r $[-0.48, 0]$; Fig. 6D), whereas no relationship with affective empathy was apparent during the nonnormative condition ($r = 0.02$, $p = 0.88$, 95% CI of r $[-0.24, 0.27]$; Fig. 6E). This suggests a

reduction of negative affective responses for highly empathic individuals in the normative condition.

Sensitivity analyses using more lenient ROI thresholds yielded broadly consistent results. When both the ACC seed region and the AI target ROI are defined using more lenient thresholds, the main effect of condition is slightly weakened to a marginal effect ($t(58) = 1.96$, $p = .055$, $d = 0.25$, 95% CI of mean difference $[-0.06, 4.93]$), and the correlation with affective empathy remains significant ($r = .31$, $p = .018$, 95% CI of r $[0.06, 0.52]$), driven primarily by a significant effect in the normative condition ($r = -0.263$, $p = .044$, 95% CI of r $[-0.49, -0.01]$). Thus, it does not appear that the observed effects are due to the arbitrary thresholding choices, although the main effect shifted enough to change from just under the threshold for statistical significance to just over the significance threshold.

The increased connectivity between ACC and AI on non-normative trials does not appear to be entirely independent from the lower confidence with which decisions were typically made for nonnormative scenarios. Specifically, after controlling for trialwise confidence, there was no longer a significant PPI effect of scenario condition emerging from a voxelwise analysis in the AI target region, although there were also no reliable effects of confidence here. Similarly, no effect of condition in AI emerged from an exploratory whole-brain PPI analysis with a lowered $z > 2.3$ voxelwise threshold, although in this analysis, a significant effect was apparent in right occipital cortex (peak voxel: $32, -82, 6$, $z = 4.19$, corrected $p = .013$, cluster extent = 197 voxels). This whole-brain analysis also did not show significant effects as a function of trialwise confidence. Finally, to test whether there was even weak evidence that the condition effect is maintained when controlling for confidence, we tried limiting the search space to the left AI (based on where the original voxelwise effect was located) and also lowered the voxelwise threshold to $z > 2.3$. Here, an effect with the same peak voxel as the original effect reported above did emerge as statistically significant (peak voxel $-36, 22, 0$, $z = 3.24$, corrected $p = .044$, cluster extent = 17 voxels), suggesting that the condition effect is weakened but not entirely eliminated when controlling for trialwise confidence. Notably, unlike when examining univariate effects in AI, trialwise confidence does not itself predict increased ACC-AI connectivity even at this very lenient threshold. Thus, there appears to be a weak increase in ACC-AI connectivity specific to nonnormative trials and unrelated to confidence, although this result should be interpreted with caution.

An analysis averaging across the entire bilateral AI ROI was also run for the PPI model that controlled for trialwise confidence. Here, the effect of scenario type did not reach statistical significance ($t(58) = 1.42$, $p = 0.16$, $d = 0.18$, 95% CI of mean difference $[-0.42, 2.49]$), nor did the effect of confidence itself ($t(58) = -1.02$, $p = 0.31$).

The difference between nonnormative and normative trials in the ACC-AI connectivity effect when controlling for trial-wise confidence still correlated with affective empathy, however ($r = 0.31$, $p = 0.016$, 95% CI of r [0.06, 0.53]). These results reinforce the conclusion above that confidence may play a partial role in driving overall differences in ACC-AI connectivity between nonnormative and normative trials. It also appears that correlations between this effect and affective empathy are likely not driven by differences in confidence between nonnormative and normative trials.

Finally, we defined a second target region, vmPFC, for the PPI analysis seeded in ACC. Examination of the functional connectivity between these regions was motivated by work showing that the pregenual ACC tends to co-activate with vmPFC during compassionate responses, whereas the dorsal ACC tends to co-activate with the anterior insula during empathic responses (Klimecki et al., 2014). The ACC ROI that we used includes both dorsal and pregenual ACC. Additionally, ACC-vmPFC connectivity being modulated by condition would follow from the difference in univariate activity by condition that was observed in vmPFC, discussed above. A voxelwise analysis masked with the vmPFC ROI did not show a significant result at the $z > 3.1$ voxelwise threshold but did show a negative effect (i.e., normative > nonnormative) at the exploratory $z > 2.3$ threshold (peak voxel: $-2, 44, 6$; $z = 3.14$, corrected $p = .006$, cluster extent = 56 voxels). When averaging findings across the entire vmPFC ROI, connectivity between ACC and vmPFC was also found to be significantly stronger during the normative condition compared to the nonnormative condition ($t(58) = -2.17$, $p = .034$, $d = -0.28$, 95% CI of mean difference $[-6.38, -0.25]$). Notably, these effects are in the same direction as the univariate effect in vmPFC.

This effect was robust to using a more lenient definition of the ACC seed region. Specifically, the voxelwise effect masked by the vmPFC ROI was significant at both a $z > 3.1$ voxelwise threshold (peak voxel $-8, 46, -6$; $z = 3.28$, corrected $p = .025$, cluster extent = 4 voxels) and $z > 2.3$ voxelwise threshold (same peak, corrected $p = .005$, cluster extent = 61 voxels). The effect likewise remained significant when averaging across the entire vmPFC ROI target region, ($t(58) = -2.15$, $p = .036$, $d = -0.28$, 95% of mean difference CI $[-6.7, -0.23]$).

However, as with the univariate effect in vmPFC, effects of condition on ACC-vmPFC connectivity were not robust to controlling for trialwise confidence. Specifically, no reliable effects emerged from the voxelwise analysis, whether with a $z > 3.1$ voxelwise threshold or a $z > 2.3$ voxelwise threshold. Similarly, averaging across the vmPFC ROI, the difference between normative and nonnormative trials was no longer significant ($t(58) = -1.39$, $p = .17$, $d = -0.18$, 95% CI of mean difference $[-2.92, 0.52]$). Still, the effect of trialwise confidence was also not significant, either in the voxelwise

analysis, or averaging across the ROI, ($t(58) = 0.64$, $p = .52$, $d = 0.08$, 95% CI of mean difference $[-0.84, 1.63]$). Together, these results suggest that increased ACC-vmPFC connectivity in normative trials is not independent from differences in confidence between conditions, but it does not appear to be driven primarily by increased confidence.

Discussion

Decisions about whether to provide MAiD are highly challenging and stressful, requiring healthcare practitioners to consider professional duty, ethical principles, personal moral values, and respect for patients' autonomy. This study is the first to investigate the cognitive and neural mechanisms underlying hypothetical MAiD decision-making in medical students. Moreover, we examined how these processes are influenced by social norms and individual dispositions towards empathy and religiosity.

We found that decisions generally aligned with the normative context: requests for assisted dying services were approved in 93% of normative cases but only in 12% of nonnormative cases. While this strong correspondence between scenario type and decision could suggest a simple response confound, the neural data reveal a more nuanced evaluative process. Brain regions showing greater activation during nonnormative scenarios include the posterior nodes of the default mode network (precuneus, posterior cingulate, and angular gyrus). Engagement of these regions reflects mentalizing or introspection, i.e., participants thinking more about others' viewpoints or drawing upon their personal values more when evaluating nonnormative scenarios. However, activity in these regions, more so than in anterior default network nodes, can also reflect memory retrieval processes (Raichle, 2015). Indeed, the increased functional coupling observed between the anterior hippocampus and precuneus during nonnormative trials supports the interpretation that memory may be differentially engaged between conditions. Nonnormative scenarios also elicited increased activity in frontoparietal brain regions and the pre-SMA. While these regions are typically associated with response inhibition (Simmonds et al., 2008), in the context of MAiD, this activity may reflect a professional "gatekeeping" function. Practitioners must exert effort to override an intuitive compassionate impulse to assist the patient, ensuring adherence to regulatory and legal standards. The concurrent increase in hippocampal-precuneus functional connectivity suggests that this inhibitory process is not merely motoric but is grounded in a deliberate, memory-informed evaluation of professional norms.

Finally, the increased activation for nonnormative scenarios in regions often associated with executive function (e.g.,

intraparietal sulcus) suggests increased attentional engagement. Specifically, these activations suggest that nonnormative scenarios are more difficult for participants to adjudicate and that they needed to devote more effort to analyzing the situation and the rules before making their decisions.

A rich literature supports the interpretation that this process plays a stronger role in MAiD decision making under nonnormative conditions. Early work found default-mode regions to be associated with the subjective experience of recollection (Rugg & Vilberg, 2013) and source memory (Lundstrom et al., 2005). Other studies have associated the precuneus with the vividness of memory retrieval and the angular gyrus with retrieval precision (Richter et al., 2016). Furthermore, connectivity between the precuneus and the anterior hippocampus predicts confidence in memory retrieval and the subjective experience of memory for context (Ren et al., 2018; Foudil & Macaluso, 2024). In the present study, memory retrieval suggests that participants are drawing on their personal experiences or recalling MAiD-related criteria learned earlier during their medical training.

Beyond the cognitive demands, there is evidence that emotional processing also plays an important role. Specifically, normative scenarios more strongly engaged the amygdala and other regions often associated with negative sensations. This activity suggests that the dire situations described by the normative scenarios may carry greater emotional salience for the participants. Notably, the effect in the amygdala was stronger among participants who were lower in religiosity. Generally, less religious individuals tend to perceive death with greater affective intensity (e.g., finding death to be scarier) compared with those higher in religiosity (Jong et al., 2018). Consequently, making a decision involving a person close to death may evoke a more pronounced emotional response for these individuals.

However, normative scenarios also engaged vmPFC more strongly and led to increased connectivity between ACC and vmPFC, which may indicate *positive* emotions associated with relieving someone's suffering (Decety & Li, 2025; Decety & Porges, 2011; Jensen et al., 2020). This effect may be related to feelings of compassion, driven by the ability to help relieve suffering from a person in pain. Prior work has shown that the vmPFC is associated with empathic care (Ashar et al., 2017; Decety & Cowell, 2015). The vmPFC was also found to be activated among women who choose to endure pain themselves to relieve a romantic partner's pain (López-Solà et al., 2018). Lesion studies have documented that damage to vmPFC is associated with a reduced willingness to give money to help someone who is suffering (Beadle et al., 2018). Thus, the compassionate aspects of being allowed to approve a request in the normative case may be reflected in increased vmPFC activation. Engagement of this pathway during normative scenarios may facilitate

acceptance by reflecting concern for the patient's needs and a drive to alleviate their suffering. At the same time, a shallower explanation that the vmPFC activation reflects positive feelings related to decisions being easier (i.e., made with higher confidence) in normative scenarios cannot be ruled out, because neither the univariate effect in vmPFC nor the ACC-vmPFC connectivity effect were robust to controlling for trialwise confidence. Further work will be needed to more carefully address this issue.

There was also evidence that brain responses suggestive of empathic distress were stronger during nonnormative scenarios. Specifically, the functional connectivity between ACC and anterior insula was stronger during these scenarios, particularly in participants with high levels of trait affective empathy, consistent with those regions tending to co-activate when a person resonates with another's pain (Decety & Lamm, 2009; Lamm et al., 2011). We also find that individual differences were driven by reduced connectivity in the normative scenarios among participants with higher affective empathy, suggesting that negative affect related to empathizing with a person in pain is significantly reduced in these people when one is allowed to help relieve that pain. In contrast, the functional connectivity in the non-normative scenarios was not affected by affective empathy.

The overall difference in ACC-AI connectivity between nonnormative and normative conditions may be partly driven by confidence; in a model controlling for confidence, the effect of condition became weaker and was only statistically significant when strong assumptions based on the primary analysis were applied alongside a lenient voxelwise threshold. Still, there was no evidence of a direct effect of confidence on connectivity between these regions. Additionally, when controlling for response confidence, individuals with more affective empathy still showed a greater difference in connectivity between nonnormative and normative scenarios. Thus, while not conclusive, it is reasonable to propose a tentative conclusion that the connectivity effect reflects reduced empathic distress when one is allowed to relieve a patient's suffering.

Notably, there was also increased univariate activity in anterior insula in the nonnormative condition. However, this effect does appear to be driven primarily by the decision difficulty (i.e., lower levels of confidence) generated by nonnormative trials, as adding trialwise confidence as an additional regressor wiped away the effect of trial type in this region, while there was a strong direct effect of confidence on brain response in anterior insula. Thus, univariate activity in the anterior insula may reflect the unpleasantness of making a difficult decision, apart from this region's role in empathy. Unlike the connectivity effect, the degree of increased activity in anterior insula on nonnormative trials was also greater in those with *lower* affective empathy. Thus, to the extent that this effect is specific to the task at hand, it may

be indicative of medical students feeling internal distress at having to decline a request from a hypothetical patient with a nonnormative request. Those with lower affective empathy may be more focused on their own discomfort at denying such a request.

Finally, greater activity was detected in brain regions associated with mentalizing during nonnormative scenarios. The whole-brain result indicated such an effect in the precuneus and bilateral angular gyrus, and ROI analyses found similar effects in the precuneus and bilateral TPJ. In the dmPFC, a different brain region associated with mentalizing, such an effect was apparent specifically among individuals lower in dispositional cognitive empathy. One possible explanation for this effect is a need to understand why someone whose condition is relatively less severe (i.e., in a nonnormative scenario) would request MAiD. It may be that people who struggle with cognitive empathy must work harder to try to understand the mental state of a hypothetical patient in this situation, leading to greater engagement of brain regions that effectuate this processing.

Theoretical and practical implications

The results of this fMRI study underscore the importance of social norms in bioethical decisions (Wibisono et al., 2022;2024). Engagement of the vmPFC and its functional connectivity with the ACC during normative decisions suggests that granting requests aligns with intuitive, compassion-oriented motivation, potentially reinforcing the rewarding nature of alleviating suffering (Decety & Li, 2025; Decety & Porges, 2011). By contrast, activation of frontoparietal control networks and the pre-SMA during nonnormative scenarios likely reflects the cognitive demands of “gatekeeping,” indicating that denying requests requires the effortful inhibition of a compassionate impulse to adhere to regulatory criteria. Additionally, involvement of the Default Mode Network and hippocampal coupling in these nonnormative cases suggests that when external rules constrain intuitive response, decision-makers must increasingly rely on internal retrieval of professional standards and personal moral schemas.

From a practical standpoint, the results highlight a potential risk factor for moral injury and burnout. Nonnormative scenarios elicited greater functional connectivity between the ACC and anterior insula, which might reflect empathic distress (Decety & Lamm, 2009). This suggests that denying a request, even when legally justified, imposes a measurable emotional burden. Conversely, reduced ACC-AI connectivity during normative trials among participants with higher trait affective empathy suggests that medical training should focus not on reducing empathy, but on reappraising it. A well-documented medical literature finds that medical

students undergo a process of developing “clinical detachment” or “detached concern” (Halpern, 2003). This process involves learning to regulate one’s own affective response to patient suffering to maintain objective decision-making and prevent empathy distress and burnout. Our neural data suggest that making meaningful decisions, i.e., those aligned with professional and compassionate norms, can actually help regulate the practitioner’s own affective responses. Understanding these neural signatures of professionalization may inform training programs that foster sustainable empathy in end-of-life care, helping protect nurses, students, and physicians from moral injury when navigating nonnormative cases.

While the vmPFC activation in normative cases may reflect a reward associated with relieving suffering, the finding that this reward signal is reliably lower in nonnormative cases, coupled with insular distress, places the practitioner in a difficult emotional position. Healthcare institutions should also acknowledge that the emotional demands of MAiD evaluations vary considerably depending on practitioners’ personal dispositions, including religiosity, empathy, and moral values. Support mechanisms, such as structured debriefing sessions, may be critical for helping practitioners process the physiological arousal and internal cognitive conflicts revealed by these neural signatures.

Strengths and limitations

A key strength of this research is that it represents the first known examination of the neural mechanism underlying decision-making in the context of MAiD, with a sample of health care practitioners in training. However, several limitations should be acknowledged. First, the participants lacked real-world experience in handling MAiD requests, and the introduction of assisted dying was comparatively recent. Future research should extend this work by including experienced clinicians who have encountered such ethical challenges in their practice. Their repeated exposure may either heighten sensitivity to the moral and ethical dimensions of MAiD, or lead to desensitization as their decisions become routinized. Second, because the study was conducted in Australia, the generalizability of findings may be limited. Cultural norms, moral values, religious beliefs, and legal frameworks vary across countries and can significantly influence decision-making processes related to MAiD, potentially leading to different neural and behavioral responses in other contexts. Cross-cultural comparative research would help clarify how these contextual factors shape both neural and behavioral responses in MAiD-related decisions.

The results from the functional connectivity analyses provide important additional insight into how brain regions interact during complex bioethical evaluations.

However, these findings were derived using more permissive statistical thresholds than those used in the univariate analyses, whether using pre-threshold masks consistent with prior literature but not pre-registered, or applying reduced voxelwise thresholds. As a result, the observed pathways, such as the ACC–AI and hippocampus–precuneus couplings, should be considered exploratory. Future research with larger cohorts and pre-registered hypotheses will be necessary to confirm the specificity of these functional circuits.

Another potential limitation of the current design is the inherent overlap between the normative status of a request and its clinical severity (e.g., terminality and intensity of suffering). However, the observed neural dissociation supports an interpretation centered on social norm processing. Specifically, normative scenarios, characterized by intense suffering, engaged emotional salience regions, whereas nonnormative scenarios, characterized by lower suffering, elicited greater activation in the frontoparietal control network and the pre-SMA. This suggests that denying a request based on legal criteria is not an easier or less salient decision, but rather an effortful process. Furthermore, increased functional coupling between the anterior hippocampus and the precuneus during nonnormative trials (Fig. 5) suggests greater reliance on memory retrieval, likely reflecting participants actively recalling and applying formal VAD criteria to adjudicate atypical requests. Together, these findings demonstrate that professional norms shape the cognitive architecture of decision-making by engaging control and retrieval systems when legal standards are not met.

Finally, regarding the ecological validity of the study, it is important to consider the legal context in which these decisions occur. In Australia, MAiD legislation mandates a rigorous process involving at least two independent medical assessments (a coordinating and a consulting practitioner). The requirement for independent verification ensures that the final outcome reflects multiple practitioners' perspectives. Given the constraints of a functional neuroimaging study, participants here made decisions in isolation. This design mirrors the individual nature of the assessments made by each clinician but does not capture the collaborative and longitudinal aspects of real-world clinical practice. In clinical settings, a doctor has access to the patient's full medical history, engages in multiple face-to-face consultations, and may discuss the case with palliative care specialists. The nature of the scenarios used in an fMRI environment necessarily simplifies this complexity to accommodate the constraints of the neuroimaging environment. Future research could improve ecological validity by providing more detailed case files or simulating the consultative phase of the MAiD process.

Conclusions

This study is among the first to use functional neuroimaging to investigate the cognitive and neural mechanisms underlying MAiD decision-making. By identifying the factors and individual dispositions that modulate neural responses when medical practitioners evaluate hypothetical MAiD scenarios, our findings can inform the development of improved medical training and support systems for real-world decision-making in these ethically challenging situations. This empirical contribution is particularly timely given the evolving legal and ethical landscape surrounding end-of-life care. Future research should build on these findings by investigating decision-making in more realistic clinical contexts.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.3758/s13415-026-01452-y>.

Authors' contributions P.M., W.L., and J.D. conceived and designed the study. P.M. collected the data. J.C., M.S.C., and J.D. conducted the data analysis. All authors contributed to the interpretation of the results. J.C., M.S.C., & J.D. wrote the first draft of the manuscript. All authors commented on previous versions of the manuscript.

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Data availability All data, files and codes to replicate this study can be accessed on OSF at <https://osf.io/tx2nf/overview>. The raw and first level-fMRI data were too large to upload to OSF but can be accessed by contacting the corresponding author on pascal.mollenberghs@gmail.com.

Declarations

Ethics approval The study was approved by the ISN Human Research Ethics Committee (approval number 201207).

Consent to participate All participants provided written consent prior to participating in the study.

Consent for publication All authors read and approved the final manuscript.

Conflicts of interest/Competing interests The authors declare no conflict of interest.

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