| 1 | Structural and functional brain correlates of suicidal ideation and |
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| 2 | behaviours in depression: A scoping review of MRI studies |
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Abstract

26 Identifying and integrating the neural correlates of suicidal ideation and behaviors is crucial to expand the knowledge and develop targeted strategies to prevent suicide. This review aimed to 27 describe the neural correlates of suicidal ideation, behavior and the transition between them, 28 using different magnetic resonance imaging (MRI) modalities, providing an up-to-date 29 overview of the literature. To be included, the observational, experimental, or quasi-30 experimental studies must include adult patients currently diagnosed with major depressive 31 disorder and investigate the neural correlates of suicidal ideation, behavior and/or the transition 32 using MRI. The searches were conducted on PubMed, ISI Web of Knowledge and Scopus. Fifty 33 34 articles were included in this review: 22 on suicidal ideation, 26 on suicide behaviors and two on the transition between them. The qualitative analysis of the included studies suggested 35 alterations in the frontal, limbic and temporal lobes in suicidal ideation associated with deficits 36 in emotional processing and regulation, and in the frontal, limbic, parietal lobes, and basal 37 ganglia in suicide behaviors associated with impairments in decision-making. Gaps in the 38 literature and methodological concerns were identified and might be addressed in future studies. 39

Keywords: depression, suicide behaviors, suicidal ideation, magnetic resonance
imaging, scoping review.

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44 **1. Introduction**

Suicide is a major public health concern, accounting for more than 700,000 deaths every year (World Health Organization, 2021). At time of death by suicide, major depressive disorder (MDD) is one of the most frequent diagnoses (Moitra et al., 2021; Nock et al., 2009). In fact, death by suicide is 20-fold higher in MDD patients than in the general population (Ösby et al., 2001). For each death, there are an even higher number of suicide attempts. In depression, compared to patients without depression, the odds ratio for lifetime and past-year prevalence of suicide attempts were 3.45 and 7.34, respectively (Cai et al., 2021).

The suicide pathway is a complex process that ranges from suicidal ideation, communicated (or not) verbally or non-verbally, suicide attempts and death by suicide (Wasserman et al., 2012). This process is influenced by multiple interacting biological, psychological, environmental, and situational factors (Wasserman et al., 2012). Suicidal ideation is considered a major risk factor for suicide (Franklin et al., 2017), and its presence in MDD is associated with worse treatment response (Lopez-Castroman et al., 2016).

In the past decades, multiple non-invasive neuroimaging tools, such as magnetic resonance 58 imaging (MRI), have been used to investigate the suicidal brain in vivo in multiple psychiatric 59 disorders (Bani-Fatemi et al., 2018; Cox Lippard et al., 2014; Desmyter et al., 2011; Schmaal 60 61 et al., 2020). Although suicidal symptoms might be identified in multiple psychiatric disorders, previous reviews on their neuroimaging correlates reported inconsistent findings across 62 disorders (Dominguéz-Baléon et al. 2018; Schmaal el et al., 2020), which might be partially 63 explained by the specific characteristics of the different diagnoses. In fact, there is evidence of 64 different clinical characteristics of suicide behavior across psychiatric disorders (Nakagawa et 65 al., 2011). To date, only one review (Zhang et al., 2014) focused on MDD alone, reporting 66 abnormalities in the frontal-striatal circuits associated with suicide behavior. Two meta-67 analyses reported no morphometric abnormalities (Jollant et al., 2018; Rentería et al., 2017), 68

while alterations in the activation of the insula and fusiform gyrus during different tasks were 69 70 associated with suicide behaviors in depression (Li et al., 2020). Nevertheless, the amount of literature available at the time of publication was small, with 14 studies included in the review, 71 and 16 and 7 in the brain structure and function meta-analyses, respectively. Contrary to the 72 findings of previous meta-analyses, a recent pooled mega-analysis from the Enhancing 73 NeuroImaging Genetics through Meta Analysis (ENIGMA) MDD Consortium revealed a 74 decreased volume in the bilateral thalamus and the right pallidum and lower cortical surface 75 area in the left inferior parietal lobe in patients with previous suicide attempts in MDD (Campos 76 et al., 2021). Moreover, no previous review or meta-analysis, to our knowledge, has focused on 77 78 the neural correlates of suicidal ideation in adult patients with MDD only.

Suicidal ideation is a red flag for clinical concern and an important part of suicide risk 79 assessment, given that it is the first step of the suicidal pathway (Wasserman et al., 2012). It is 80 81 highly dependent on the patient collaboration and clinician expertise, given it is usually assessed through clinical interviews and self-report instruments (Lotito & Cook, 2015). Even though 82 active suicidal ideation constitutes one of the best predictors of suicide attempts (Franklin et 83 al., 2017), only one third of patients with suicidal ideation will act on their thoughts (Kessler et 84 al., 1999), which suggest different profiles between suicide ideators and attempters. Taking that 85 86 into consideration, Klonsky, and May (2014) proposed that suicide research and theory should follow an ideation-to-action framework, suggesting that the development of suicidal ideation 87 and the transition from ideation to behaviors may be distinct processes, with distinct 88 explanations, and consequently different predictors. Given the ethical issues associated with the 89 study of this transition within the same person, comparing suicide attempters and ideators 90 (suicide attempters vs. suicide ideators) may bring new insights on specific processes of suicidal 91 thoughts and behaviors. Neuroimaging techniques, such as MRI, might be crucial to identify 92 neural signatures of suicidal ideation and behaviors, and consequently help developing models 93

94 to identify the individuals with higher risk for suicide as well as targeted treatments and 95 prevention strategies for future attempts. Even though, the number of neuroimaging studies 96 following this approach is small and no previous review compiled the neural correlates of the 97 transition from suicide ideation to attempt.

Finally, literature reviews and meta-analyses are essential to synthetise and integrate the 98 findings available in the literature, which is particularly useful when there is high heterogeneity 99 in the published studies as in the field of neuroimaging and suicidology. This type of scientific 100 approach allows the field to move forward by developing new theories and identifying gaps in 101 the literature. The present review aimed to describe the neural correlates of suicidal ideation, 102 103 behaviors and transition between them in MDD, using MRI, to provide an up-to-date and comprehensive overview of the literature. Compared to the most recent literature reviews on 104 the field (e.g., Schmaal et al., 2020), this review focuses on MDD alone, given that different 105 106 psychiatric disorders might have unique neurobiological characteristics underlying suicide as stated above. Moreover, we explored for the first time the neural correlates of the transition 107 between suicidal ideation and attempt. Given the broad focus of this review on the neural 108 correlates of different steps on the suicide pathway, MRI modalities and analyses, as well as 109 the complexity and heterogeneity of our research questions and the literature available, a 110 111 scoping review may be the most beneficial approach to provide an up-to-date overview (Munn et al., 2018). 112

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114 **2. Methods**

The present scoping review follows the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for Scoping Reviews (PRISMA-ScR). The PRISMA-ScR checklist is available in the Supplementary Material (Table S1). The protocol of this review was registered with the Open Science Framework (https://osf.io/6z3cx/).

120 **2.1 Literature search**

The literature search was conducted on PubMed, ISI Web of Knowledge and Scopus from 121 February 1st to September 28th 2022 using the following terms: (depress* or major depressive 122 disorder) and (suicide* or suicidal thoughts or death thoughts or suicidal ideation or suicide 123 ideators or suicide attempt or suicide behavior or parasuicide) and (neuroimaging or brain 124 image or magnetic resonance imaging or MRI or functional magnetic resonance imaging or 125 functional MRI or fMRI or resting-state fMRI or functional connectivity or diffusion MRI or 126 DTI or white matter or structural connectivity or structural MRI or gray matter or cortical 127 thickness or volume). See detailed search strategy for each database in the Supplementary 128 129 Material (Table S2). To complement our searches, the reference lists of included studies and relevant reviews and meta-analyses on this topic were manually checked. 130

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132 **2.2 Eligibility criteria**

The eligibility criteria are summarized in Table 1. To be included in this review, the studies 133 must report brain structural and functional correlates of suicidal ideation, attempt and transition 134 between them in adult patients currently diagnosed with MDD. The data must be acquired with 135 MRI in at least one of the following modalities: structural, diffusion, resting-state, and task-136 related functional MRI (fMRI). Studies were excluded when including patients diagnosed with 137 other psychiatric, neurologic disorders or comorbidities, did not clearly define suicidal ideation, 138 attempt, or used the broad term "suicidality" without any detailed definition. Suicidality is a 139 broader term including suicide ideation, attempt and death, which lacks specificity and 140 141 confounds the findings of the studies (Meyer et al., 2010).

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143 **2.3 Article selection and data extraction**

144 After the primary searches, the results were uploaded to Rayyan (Ouzzani et al., 2016) to 145 remove duplicates. Then, a two-step screening process was implemented. First, titles and abstracts of all publications were screened against the eligibility criteria by 3 independent reviewers (RV, ARF, DR). If a decision could not be made based on the title and abstract, the article was retained for full text screening. Full text of all publications included at first screening were then examined in detail to determine eligibility. Any disagreement between reviewers was solved through discussion and consulting a fourth reviewer (MPP). The authors of the publications were contacted by the reviewers, when necessary. Neither one of the reviewers were blind to the journal's title, authors' names, or institutions.

A standardized data extraction form was created using Google Forms (see Figure S1), and the three independent reviewers (RV, ARF, DR) extracted the relevant data of the included manuscripts.

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157 **3. Results**

158 **3.1 Main findings**

Through the literature search detailed above 2375 articles were identified. From these, 816 159 duplicated papers were excluded using Rayyan (Ouzzani et al., 2016). Then, the titles and 160 abstracts of the 1559 were examined. From these, 87 articles were kept for full text screening, 161 from which 50 articles met the eligibility criteria to be included in this review. These studies 162 163 were categorized according to the suicide pathway (ideation, attempt or transition) and MRI modality (structural, diffusion, and fMRI). Regarding the suicide pathway, studies were 164 categorized according to the main comparisons of the statistical analysis performed: patients 165 with suicidal ideation vs. controls with or without MDD or direct correlations with suicidal 166 ideation scale score were classified as suicide ideation; patients with history of suicide attempt 167 vs. controls with and without MDD were classified as suicide attempt; and patients with suicide 168 ideation vs. patients with history of previous suicide attempt were classified as transition 169 between suicidal ideation and attempt. Thus, there were 22 studies on suicidal ideation, 26 170

studies focused on suicide attempts, and two on the transition from ideation to action. Regarding 171 MRI modality, the different studies used the following analysis: gray and white matter volumes 172 using voxel-based morphormetry or Freesurfer, magnetization transfer ratio, cortical thickness, 173 and structural covariance network for structural MRI; tract-based spatial statistics, deterministic 174 and probabilistic tractography, graph theory and network-based statistics (NBS) for diffusion 175 MRI; seed-based analysis, independent component analysis, regional homogeneity (ReHo), 176 amplitude of low frequency fluctuation (ALFF), NBS, and graph theory for resting-state fMRI; 177 and brain activation and connectivity (psychophysiological interactions analysis) for task-based 178 fMRI. Figure 1 displays the PRISMA flow diagram of the study selection process, providing 179 180 information on the reasons of exclusion.

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182 **3.2 Studies' characteristics**

The studies included in this review were published between 2005 and 2022 (see Figure 2). Most 183 of the studies (80%) were conducted in Asia, whereas the remaining studies were conducted in 184 North America and Europe. Patients' samples were recruited in Psychiatric Departments of 185 Hospitals, mostly in outpatient wards. Healthy control samples were commonly recruited from 186 the community. From 39 studies indicating medication status, 22 (~56%) included medication 187 188 free patients (drug-naïve or washout) and 17 (~44%) included patients under any pharmacotherapy. The characterization of the samples is detailed in Tables S3, S4 and S5 for 189 the included studies focusing on suicide attempts, ideation, and transition between them, 190 191 respectively.

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193 **3.3 Suicide ideation**

From the 22 studies focusing on the neural correlates of suicide ideation, two used structuralMRI, three diffusion MRI, and 13 fMRI (only resting state). Four studies combined more than

one MRI modality, specifically two combined structural and resting-state fMRI, one structural
and diffusion MRI, and one diffusion and resting-state fMRI. The results of the qualitative
synthesis are summarized in Table 2.

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200 3.3.1. Structural MRI

Taylor and collaborators (2015) found a decrease in the cortical thickness of the insula, caudal 201 middle frontal gyrus, superior parietal, and temporal gyri in suicide ideators compared to 202 depressed controls. Abnormalities in gray matter volume were also described in suicide 203 ideators, particularly in the lingual gyrus (Wang et al., 2021). Moreover, a study considering 204 205 the severity of suicidal ideation reported not only a decrease in the gray matter volume of frontal 206 areas, but also an increased structural connectivity between them in severe and mild suicide ideators when compared to controls (He et al., 2022). Nevertheless, two studies reported no 207 differences in gray matter volume in cortical and subcortical regions (Kim et al., 2019; Taylor 208 et al., 2015). 209

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211 3.3.2 Diffusion MRI

Despite the different diffusion metrics used in the included studies, in general suicide ideators 212 exhibited decreased fractional anisotropy, being the corpus callosum, the anterior thalamic 213 radiation and the corona radiata the most reported (Chen, et al., 2021a; Reis et al., 2022; Taylor 214 et al., 2015). Moreover, two studies using NBS identified subnetworks disrupted in suicide 215 ideators, comprising frontal and occipital regions, as well as the basal ganglia in the left 216 217 hemisphere (Chen et al., 2021a; Myung et al., 2016). Myung and collaborators (2016) described decreased structural connectivity in suicide ideators compared with both depressed and non-218 depressed controls, whereas Chen and collaborators (2021a) only found this difference among 219 220 suicidal ideators and non-depressed controls. Finally, mixed findings were reported regarding the brain topological organization. Specifically one study reported no differences in the graph 221

theory metrics between suicide ideators and controls (with and without MDD) (Chen et al.,
2021a), whereas the other reported decreased small worldness, global efficiency and modularity
only between suicide ideators and controls without MDD (Liu et al., 2021).

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226 **3.3.3 Functional MRI**

227 **3.3.3.1 Resting-state**

Abnormalities in the functional connectivity of different brain regions were reported in suicide 228 ideators (Du et al., 2017; Fan et al., 2022; Li et al., 2022a; Li et al., 2022b; Qiao et al., 2020; 229 Wei et al., 2018; Yang et al., 2022a). At the cortico-cortical level, there was a decreased 230 231 functional connectivity between the right anterior cingulate cortex (ACC) and the medial orbitofrontal cortex (OFC) and right middle temporal gyrus (Du et al., 2017), as well as an 232 increased dynamic functional connectivity (i.e., increased switch between two regions) between 233 the left posterior cingulate cortex (PCC) and the left inferior frontal gyrus in suicide ideators 234 (Li et al., 2022a). At the subcortico-cortical level, a decreased functional connectivity was 235 described not only between the right amygdala and the left postcentral gyrus, left precentral 236 gyrus, left superior and right middle temporal gyrus, and right angular gyrus, but also between 237 the left amygdala and the right precentral gyrus and left inferior parietal lobule in suicide 238 239 ideators (Li et al., 2022b; Yang et al., 2022b). Also, an increased functional connectivity was found between the bilateral amygdala and the bilateral precuneus, as well as between the left 240 amygdala, the left frontal gyrus, and bilateral caudate nuclei for suicidal ideators (Wei et al., 241 242 2018; Yang et al., 2022b). Interestingly, different subnetworks associated with suicidal ideation were identified using NBS, consistently including regions as the OFC, PCC, middle temporal 243 gyrus, and postcentral gyrus (Chen et al., 2022b; Kim et al., 2017; Reis et al., 2022). These 244 studies described a decrease in the functional connectivity in the identified subnetworks in 245 patients with depression and suicidal ideation. Abnormalities in the functional connectivity of 246

resting-state visual networks (Reis et al., 2022) as well as in the stability and temporal 247 248 variability of the default-mode network (DMN) were also reported in suicidal ideators (Ouvang et al., 2022). Two studies did not find any differences between groups in the ALFF (Li et al., 249 2018a; Wang et al., 2021), whereas one study reported increased ALFF in the left cuneus and 250 decreased ALFF in the right cuneus (Chen, et al., 2021). Moreover, a decrease in the ReHo of 251 the right cuneus and right OFC and an increase in the ReHo of the left middle temporal gyrus 252 253 and right middle frontal gyrus was associated with suicidal ideation (Chen et al., 2021b; He et al., 2022). Regarding the brain topological organization, mixed findings were described (Chen, 254 et al., 2021b; Yang et al., 2022b). On one hand, Chen and collaborators (2021b) reported 255 256 decreased global efficiency in suicide ideators compared to controls with MDD, whereas compared to controls without MDD, suicide ideators showed increased global efficiency and 257 decreased assortativity and transitivity. No differences between the groups were found for other 258 259 graph theory metrics (e.g., small wordlness, normalized characteristic path length). On the other hand, Yang and colleagues (2022b) described a decreased global connectivity and small 260 worldness, but an increased normalized characteristic path in suicide ideators compared to 261 controls without MDD. 262

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264 **3.4 Suicide attempt**

From the 26 studies focusing on the neural correlates of suicide attempt, 9 used structural MRI, 4 diffusion MRI, and 11 fMRI (9 resting-state and two task-based). Two studies combined more than one MRI modality, specifically one combined structural and diffusion MRI, and the other structural and resting-state fMRI. The results of the qualitative synthesis are summarized in Table 3.

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272 **3.4.1 Structural MRI**

273 Most of the studies reported decreased gray matter volumes in suicide attempters compared with depressed and non-depressed controls in both cortical and subcortical structures (Jollant 274 et al., 2018; Lee et al., 2016; Lee et al., 2018; Peng et al., 2014; Yang et al., 2020). In 275 accordance, suicide attempters showed a decreased magnetization transfer ratio and cortical 276 surface in parietal and frontal cortices, respectively (Chen et al., 2015; Kang et al., 2020a). At 277 the subcortical level, Kang and collaborators (2020b) found that suicide attempters had a 278 decreased volume in the putamen, hippocampus, amygdala, pallidum and thalamus compared 279 to controls with MDD. Nevertheless, two studies found an increased gray matter volume in the 280 281 calcarine fissure (Yang et al., 2020), postcentral gyrus and OFC (Kang et al., 2020a) in suicide attempters when compared to depressed controls. Additionally, Kang and collaborators (2020b) 282 also reported an increased cortical surface in the postcentral gyrus and occipital regions. Only 283 one study explored the role of white matter hyperintensities in suicide attempts in depression, 284 reporting no statistically significant differences between groups in the deep white matter 285 hyperintensities, but increased periventricular hyperintensities in suicide attempters (Ehrlich et 286 al., 2005). Two studies did not find statistically significant differences in gray and white matter 287 volume, or cortical thickness, between suicide attempters and controls (Jia et al., 2010; Jollant 288 et al., 2018). 289

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291 3.4.2 Diffusion MRI

Diffusion MRI studies consistently showed decreased fractional anisotropy in suicide attempters compared to depressed and non-depressed controls (Chen, et al., 2021c; Jia et al., 2010, 2014; Olvet et al., 2014; Zhang et al., 2021). Additionally, the studies also reported decreased axial diffusivity (Jia et al., 2010), and increased mean and radial diffusivity (Jia et al., 2010; Zhang et al., 2021) associated with suicide attempts. The anterior limb of the internal capsule (Jia et al., 2010, 2014), the corpus callosum (Chen et al., 2021c), the forceps minor and
major, the inferior fronto-occipital fasciculus and the cingulum bundle (Zhang et al., 2021) were
described as disrupted in patients with history of suicide attempts. Recently, Chen and
colleagues (2021c) identified a subnetwork, comprising mainly frontal and parietal regions,
with increased structural connectivity in suicide attempters compared with healthy controls.
Moreover, these authors did not find differences in the topological parameters of the brain
structure, such as global efficiency, modularity, and small worldness (Chen et al., 2021c).

304

305 3.4.3 Functional MRI

306 **3.4.3.1 Resting-state**

Several authors reported alterations in the functional connectivity of the OFC, ACC, and 307 amygdala at rest (Chen et al., 2021d; Kim et al., 2017; Qiu et al., 2020; Shu et al., 2022) in 308 309 suicide attempters versus controls with and without depression. On the one hand, there was a decreased functional connectivity between the right OFC and the left rectus, left inferior parietal 310 lobule, left ACC, and left calcarine sulcus (Chen et al., 2021d; Yang et al., 2020), as well as 311 between the subgenual ACC and the right caudate nucleus, the pregenual ACC, the left insula, 312 and the left superior medial frontal gyrus (Qiu et al., 2020). On the other hand, increased 313 314 functional connectivity was reported between the left amygdala and the right insula, the left OFC, the right amygdala, and the left middle temporal gyrus (Kim et al., 2017), as well as 315 between the subgenual ACC and frontal brain regions in suicide attempters (Qiu et al., 2020). 316 Increased functional connectivity was also found between the dorsomedial prefrontal cortex 317 (PFC) and the left frontal and the right temporal regions in suicide attempters (Chen et al., 318 2021d). Interestingly, two studies employing NBS approaches identified subnetworks showing 319 a decreased functional connectivity only when suicide attempters were compared with healthy 320 controls (Wagner et al., 2019; Weng et al., 2019). Both subnetworks included motor and 321

322 somatosensory regions. Moreover, Weng and collaborators (2019) reported an increase in 323 suicide attempters in the ALFF and ReHo in the left superior parietal gyrus and the right 324 putamen, respectively. Compared to patient's controls, suicide attempters also showed a 325 decrease in the ALFF in the right angular gyrus and in the ReHo of the right superior temporal 326 gyrus and right OFC (Weng et al., 2019). Other authors (Yang et al., 2022b) described a 327 decrease as well in the ReHo of the PCC.

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329 3.4.3.2 Task-based

Richard-Devantoy and collaborators (2016) used a Go/No Go task to explore brain function 330 331 during response inhibition in suicide attempters, reporting decreased activation in the precuneus and PCC during the Go/No-Go contrast in suicide attempters compared to healthy controls. No 332 differences were reported among the patients' groups. Another study investigated the neural 333 correlates of risk and loss aversion in suicide attempters, focusing on the activation of the 334 following brain regions: OFC, ventromedial PFC, ACC, insula, midbrain, striatum, and 335 amygdala (Baek et al., 2017). Compared to controls with depression, suicide attempters showed 336 a decreased activation in the ACC during loss aversion (Baek et al., 2017). Moreover, a 337 decreased activation in the ACC and amygdala during loss aversion, as well as decreased 338 339 activation in the insula during risk aversion were described only when suicide attempters were compared with controls without depression (Baek et al., 2017). 340

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342 **3.5 Transition from ideation to action**

Two studies focused on the transition of suicidal ideation to action in patients with depression.
Both used fMRI (one resting-state and one task-based). The results of the qualitative synthesis
are summarized in Table 4.

347 **3.5.1 Functional MRI**

348 **3.5.1.1 Resting-state**

Compared with suicide ideators, suicide attempters showed a decreased ALFF, particularly in bilateral parietal regions, and an increased ALFF in limbic regions, such as the left hippocampus and parahippocampal gyrus (Wagner et al., 2021). Interestingly, similar findings were described for suicide attempters when compared with controls with and without depression, and no differences between suicide ideators and controls were reported (Wagner et al., 2021).

354

355 **3.5.1.2 Task-based**

Ai and colleagues (2018) used the tower of London and the faces tasks to investigate the neural correlates of executive function and emotional processing, respectively, in patients with and without suicide attempts and ideation. Compared with suicide ideators and controls, suicide attempters showed an increased activation in the insula (under a very liberal threshold) and a decrease in the activation of the bilateral fusiform gyri during executive planning and processing of emotional faces, respectively (Ai et al., 2018). No differences between suicide ideators and controls were described (Ai et al., 2018).

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364 **3.6 Summary findings**

Figure 3 integrates the findings of all the included studies in this review organized by the 365 following lobes: frontal, temporal, parietal, occipital, insular, limbic (i.e., cingulate, 366 parahippocampal, hippocampus, amygdala, septal area, thalamus, and hypothalamus), basal 367 ganglia (i.e., striatum, globus pallidum, caudate nucleus, putamen, nucleus accumbens, 368 subthalamic nuclei, substantia nigra) and cerebellum. For suicidal ideation studies, alterations 369 in frontal, temporal and limbic lobes were the most reported across studies but were even more 370 evident when using fMRI (75% frontal, 56% temporal, and 50% limbic). For suicide attempt, 371 alterations in frontal and limbic lobes were recurrently reported across studies (frontal lobe: 372

36% structural, 60% diffusion, and 67% fMRI; limbic lobe: 45% structural, 40% diffusion and
83% fMRI). Moreover, alterations in the basal ganglia and parietal lobe were also highly
reported (basal ganglia: 18% structural, 60% diffusion, and 25% fMRI; parietal lobe: 55%
structural, 20% diffusion and 50% fMRI). Only two studies compared suicide attempters and
ideators, both used fMRI and reported differences mainly in the occipital lobe.

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379 **4. Discussion**

In the present study, a scoping review of the literature on the neural correlates of suicidal 380 ideation, attempt and the transition between them was performed, aiming to provide an up-to-381 382 date and comprehensive overview of the published MRI studies on this topic. A total of 50 studies were included in this review. Specifically, 22 studies focused on the neural correlates 383 of suicidal ideation, 26 studies on suicide attempts, and two on the transition from ideation to 384 action, using structural, diffusion and functional MRI. The interest on this topic has increased 385 throughout the years, with half of the studies included in this review published in the last 3 386 years. 387

Overall, the studies included in this review pointed to the involvement of different brain lobes, 388 for instance, frontal, temporal, parietal, and limbic lobes, and basal ganglia. Both suicide 389 390 attempters and ideators displayed alterations in frontal and limbic lobes, mainly in the OFC, the ACC and the amygdala (Baek et al., 2017; Chen et al., 2021b; Colle et al., 2015; Du et al., 2017; 391 He et al., 2022; Kang et al., 2020a; Kang et al., 2020b; Kim et al., 2017; Li et al., 2018a; Liao 392 et al., 2018; Qiao et al., 2020; Qiu et al., 2020; Reis et al., 2022; Shu et al., 2022; Taylor et al., 393 2015; Wagner et al., 2019; Weng et al., 2019; Yang et al., 2022b; Yang et al., 2020). These 394 regions have been previously implicated in decision-making, cognitive control, and emotional 395 processing and regulation (Rolls et al., 2018). Therefore, the abnormalities described in these 396 regions might be more associated with deficits in emotional processing and regulation linked 397

with suicidal ideation and impairments in decision-making contributing more to suicideattempts.

400

401 4.1 Suicidal ideation

To our knowledge, no review nor meta-analysis focused on the neural correlates of suicidal ideation in patients diagnosed with MDD only. Based on the studies included in this review, frontal, temporal and limbic lobes showed structural and functional alterations associated with suicidal ideation. The regions of these lobes are connected and involved in emotional processing and regulation as well as self-referential processing, which are disrupted in MDD (Li et al., 2018b; Mitchell, 2011; Park et al., 2019).

Two resting-state functional MRI studies included in this review reported altered functional 408 connectivity between prefrontal and temporal regions and amygdala in suicidal ideation (Li et 409 410 al., 2022b; Yang et al., 2022a). These regions integrate bottom-up and top-down brain circuits, and its maladaptive functioning may cause biases in attention, processing, and memory 411 typically associated with MDD (Disner et al., 2011), which in turn would lead to emotional 412 dysregulation. In fact, these biases have been also previously linked to suicidal ideation 413 414 (Wenzel & Beck, 2008). Accordingly, abnormal patterns of brain activation in the prefrontal 415 cortex have been shown during emotional processing and regulation in a sample of adolescents with suicidal ideation, suggesting deficits in the recruitment of top-down circuits (Miller et al., 416 2018). Moreover, abnormalities in the white matter microstructure of corpus callosum and 417 418 anterior thalamic radiation, involved in the emotional response (Coenen te al., 2012; Lungu & Stip, 2012), were also associated with suicidal ideation in MDD (Taylor et al., 2015; Chen et 419 420 al., 2021a; Reis et al., 2022).

Interestingly, some of the regions included in the lobes identified as altered for suicidal ideationin this review, such as the medial PFC and temporal regions, belong to the DMN. This network

has been consistently described as impaired in MDD (Kaiser et al., 2015; Li et al., 2018b) and
its main regions have been correlated with rumination in patients with depression (Zhou et al.,
2020). Moreover, rumination has been linked to suicidal ideation (Rogers & Joiner, 2017).
Indeed, in the comprehensive review of Schmaal and collaborators (2020), it was suggested that
frontal, limbic and temporal lobes were involved in the generation of suicidal ideation by
enhancing the negative internal states and rumination.

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430 **4.2 Suicide attempts**

A previous review suggested that a fronto-striatal circuit, including the OFC, ACC, and striatum, had a key role in suicide for depression (Zhang et al., 2014), whereas meta-analyses reported no morphometric differences and brain activation changes in the insula and fusiform gyrus between suicide attempters and controls during different tasks (Jollant et al., 2018; Li et al., 2020; Rentería et al., 2017). In contrast, a previous ENIGMA MDD Consortium study described structural abnormalities in the thalamus, pallidum and inferior parietal lobule in suicide attempters compared to non-attempters (Campos et al., 2021).

In this scoping review, the studies included suggest alterations mainly in frontal and limbic 438 lobes and basal ganglia, and in a lesser extent in the parietal lobe. The regions of these lobes 439 440 are included in frontoparietal and frontostriatal networks, both disrupted in MDD (Li et al., 2018b). These networks have been implicated in executive functions and reward processing (Li 441 et al., 2018b; Uddin et al., 2019). Interestingly, inhibition and decision-making are the only 442 443 neurocognitive abilities that differentiated suicide attempters and ideators (Saffer & Klonsky, 2018). In accordance, suicide behaviours were proposed as a decision-making dysfunction 444 displayed by neglecting decision-relevant information and alterations in delay discounting 445 (Dombrovski & Hallquist, 2017), as well as less inhibitory control (Mann & Risk, 2020). 446 Indeed, decreased cortical surface (Kang et al., 2020a), magnetization transfer ration (Chen et 447

al., 2015), and functional connectivity at rest (Yang et al., 2020) were described in
frontoparietal regions involved in response inhibition (Menon, 2011). Compared to control
patients, suicide attempters with MDD have more commission errors in Go/No-Go response
inhibition task, but no alterations were found in the brain activity between the groups (RichardDevantoy et al., 2016). Schmaal and collaborators (2020) also suggested that regions of the
frontoparietal network might be facilitators of suicide behaviors due to their role in cognitive
control, cognitive flexibility, and decision-making.

Not surprisingly, basal ganglia were also associated with suicide attempts in MDD. The studies 455 included in this review reported abnormal volumes (Kang et al., 2020b), as well as altered white 456 457 matter microstructure and functional connectivity between frontal cortex and these subcortical structures (Jia et al., 2010, 2014; Qiu et al., 2020). Basal ganglia have an important role not 458 only in motor control, but also in reward-related behavior and emotions (Lanciego et al., 2012; 459 460 Li et al., 2018b). Elderly suicide attempters with MDD, who had a lower gray matter volume in the putamen, prefer immediate rewards rather than larger delayed ones (Dombrovski et al., 461 2011). Moreover, suicide attempters have increased loss aversion, suggesting that they might 462 overestimate the likelihood of future negative events and use suicide to avoid them (Baek et al., 463 2017). Decreased insula activity was associated to their risk aversion and heightened negative 464 465 valuation of expected loss, whereas decreased ACC was associated with potential gains in the loss aversion task (Baek et al., 2017). 466

467 Taken together, the alterations in the brain structure and function present in suicide attempters 468 with MDD seem to be associated with deficits in decision-making probably due to impairments 469 in cognitive control and reward systems. Importantly, other neurobiological mechanisms such 470 as the serotoninergic system and the hypothalamic-pituitary-adrenal (HPA) axis, have been 471 linked to suicidal behaviors (Orsolini et al., 2020). Dysregulations in the serotonergic system and the HPA axis have been shown in suicide attempters (Pandey, 2013; Pompili et al., 2010),

- 473 which might also help to explain the reported alterations in brain structure and function.
- 474

475 **4.3 Transition from suicidal ideation to attempt**

Ninety-six percent (n=48) of the studies included in this review focus on suicidal ideation or 476 attempts alone but including patients with both suicidal ideation and attempt. In fact, only 6 477 studies focusing on suicidal ideation excluded patients with history of previous suicide 478 attempts, and no study focusing on suicide attempts controlled for suicidal ideation severity. 479 Therefore, it is difficult to be confident about the common and differential brain alterations 480 481 across suicidal ideation and behaviors. May and Klonsky (2016) showed that the most cited risk factors for suicide were associated with suicidal ideation but did not distinguish suicide 482 ideators from attempters. Nevertheless, not every person with suicidal thoughts will attempt 483 suicide (Nock et al., 2009). Therefore, Klonsky and May (2014) proposed an ideation-to-action 484 framework, aiming to better understand the transition from suicidal ideation to behavior. Two 485 studies followed the ideation-to-action framework reporting differences in the functional brain 486 patterns of suicidal ideators and attempters (Ai et al., 2018; Wagner et al., 2021), suggesting 487 widespread dysfunction in brain activity and connectivity were contributing to the transition 488 489 from ideation to action. More studies following this framework are required.

490

491 **4.4 Gaps and methodological concerns**

Suicidality related features, such as timeframe between suicide attempt and assessment (i.e., lifetime, past year), amount and lethality of the attempts, family history of suicide, and severity of suicidal ideation, are underexplored and might be moderating the relationship between suicide risk and brain function and structure. Colle and collaborators (2015) described a decrease in the gray matter of hippocampus in suicide attempters, however, these findings only

remained for patients with history of previous suicide attempts in the past month (not for 497 498 lifetime suicide attempts) compared with non-attempters. Another study exploring the morphological alterations associated with suicide behaviors, reported no differences among 499 suicide attempters and control patients when combining two samples (Jollant et al., 2018). 500 Nevertheless, the same authors reported increased gray matter volume in the caudate nucleus 501 among patients with and without history of previous suicide attempts using violent means and 502 503 decreased gray matter volume in temporal gyrus, dorsomedial PFC, and putamen in patients with family history of suicide attempts (Jollant et al., 2018). Moreover, patients with mild and 504 severe suicidal ideation showed differences in gray matter volume and structural connectivity 505 506 (He et al., 2022).

Other gaps and methodological concerns were identified among the included studies. For 507 instance, suicidality measures were highly heterogeneous for ideation and behaviors. Across 508 509 studies, multiple tools of measurement (e.g., medical records and/or interviews, self-reported questionnaires) were used to assess suicidal ideation and behaviours. Moreover, a recent study 510 revealed that nearly one-third of the participants responded inconsistently across measures of 511 suicide attempt, which may lead to misleading categorizations depending on the tool used (Hom 512 et al., 2019). Similar findings were also described for single-items to assess suicidal ideation 513 514 and planning (Ammerman et al., 2021). On top of that, van Velzen and collaborators (2022) also showed reduced effect sizes for the comparison between interrupted, aborted, and actual 515 suicide attempts compared to using only actual suicide attempts, highlighting the importance 516 of using specific and consistent definitions for suicide attempts. The heterogeneity of 517 timeframe of these tools, that could vary from past month to lifetime for suicide attempts and 518 519 from past week to past month for suicidal ideation, is also concerning. Given that suicidal ideation displays a rapid onset and short duration (Kleiman & Nock, 2018), that is not captured 520 by the current available scales (Gratch et al., 2021). Although the current research methods of 521

measurement bring interesting and valuable findings to the field, introducing new measurement
approaches, such as ecological momentary assessment, and pairing it with MRI might shed light
on the development of suicidal ideation.

Still, longitudinal studies are missing, and they are crucial to better understand the suicide 525 pathway and to identify individual at risk, as highlighted by several reviews on the suicidal 526 527 brain (Bani-Fatemi et al., 2018; Desmyter et al., 2011; Schmaal et al., 2020). These studies 528 should include short-term intervals of assessments, and if possible, hour-to-hour assessments to map the suicidal ideation fluctuations in the brain as suggested by Ballard and colleagues 529 (2021). Moreover, more studies investigating alterations in the brain structure and function of 530 531 pharmacological and non-pharmacological treatments for suicide are needed to expand the knowledge on its therapeutic mechanisms, determine predictors of treatment response and 532 develop new treatments. A few studies emerged showing promising findings. Specifically, 533 534 alterations in the functional connectivity between DMN and precuneus network after individual target-transcranial magnetic stimulation, and within ACC and frontoparietal network after 535 ketamine treatment in patients diagnosed with depression and suicidal ideation were reported 536 (Chen et al., 2019; Tang et al., 2021). 537

As highlighted by Campos and collaborators (2021), and confirmed in this review, the current literature available in the field includes studies with small samples sizes, multiple MRI methodologies and analyses, heterogenous measurements, and lack of clinical information wich might be on the basis of the lack of reproducibility across studies and the small effect sizes reported. Hence, well-powered studies accounting for the issues detailed above are needed to avoid reaching biased conclusions, and further enhance their reproducibility.

544

545 **4.5 Limitations**

As a scoping review, there was no formal assessment of the methodological quality of the 546 547 included studies. This review did not mean to provide a systematic review or meta-analyses of the available literature, but an up-to-date overview of the literature on the brain structural and 548 functional alterations associated with suicidal ideation and behaviors. Nonetheless, there was 549 an effort to reduce the heterogeneity between the samples of the included studies by using the 550 following inclusion criteria: patients currently depressed (not euthymic), adults, and clearly 551 552 stating how history of suicidal attempts and ideation were defined or measured. The effects of medication of the included studies cannot be discarded, given that only 22 studies reported to 553 use medication-free patients (drug-naïve patients or washout). We also included studies 554 555 reporting differences between suicide attempters and ideators and controls without depression (i.e., healthy controls). The inclusion of these studies might hamper the final conclusions, given 556 that we cannot guarantee that the differences are due to the presence of ideation/attempt or due 557 558 to depression itself. Moreover, several studies followed hypothesis driven approaches, either using regions of interest or seed-based analysis which might be biasing the conclusions of this 559 review. It is important to highlight that the heterogeneity of suicidality measures, MRI 560 modalities and its analyses complicated the identification of common and differential brain 561 alterations across suicide behaviors and ideation, preventing the possibility to perform a meta-562 563 analysis with this data. This remains an open question for future work when further and more homogeneous studies are available. Overall, caution is needed when interpreting the findings 564 of this review, given that its findings are hampered by the same biases of the included studies, 565 566 which can lead to misleading conclusions.

567

568 **5 Conclusion**

569 In sum, this review aimed to offer an overview and up-to-date picture on the MRI studies 570 focusing on suicidal ideation, behavior and the transition between them in depression. Fifty

studies met the eligibility criteria and were included in this review. Their findings were 571 572 summarized in Figure 3 pointing to alterations in frontal, limbic and temporal lobes in suicidal ideation and alterations in frontal, limbic, parietal lobes, and basal ganglia in suicide behaviors. 573 Gaps in the literature and methodological concerns were identified, which might be important 574 to address in future studies, in order to expand the knowledge on the neurobiological correlates 575 of the suicidal process. Nevertheless, it is important to highlight that the suicidal process is a 576 577 very complex and heterogenous one, and the information provided by neuroimaging techniques, specifically MRI, is only a small piece of the big puzzle. 578

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580 6. Conflicts of interest

The authors declare that the research was conducted in the absence of any commercial orfinancial relationships that could be construed as a potential conflict of interest.

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584 7. Authors' contributions

RV, MPP and JMB contributed to the concept and design the study. RV performed the literature searches and wrote the first draft of the manuscript. RV, ARF and DR screened the studies against the eligibility criteria of this review and extracted its data. MPP solved any disagreement between the reviewers. All the authors contributed for the following and final versions of the manuscript.

590

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1016

1018 **10 Figures captions**

- 1019 Figure 1. PRISMA flow diagram. Retrieved from Page, M. J., McKenzie, J. E., Bossuyt, P. M.,
- 1020 Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan,
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1025

Figure 2. Number of MRI studies on suicidal ideation and behaviors published by 3-year
periods. This figure only shows the studies included in this review. Abbreviations: MRI, magnetic
resonance imaging.

1029

Figure 3. Summary findings of the review. A) Percentage of suicidal ideation studies reporting
findings in the frontal, temporal, parietal, insular, limbic, basal ganglia, and cerebellar lobes.
B) Percentage of suicidal attempt studies reporting findings in the frontal, temporal, parietal,
insular, limbic, basal ganglia, and cerebellar lobes. C) Percentage of transition studies reporting
findings in the frontal, temporal, parietal, insular, limbic, basal ganglia, and cerebellar lobes.

11 Tables

Table 1. Eligibility criteria for the review

| Inclusion criteria | Exclusion criteria | | | | |
|--|--|--|--|--|--|
| Published on peer-reviewed journals; | Gray literature; | | | | |
| English language; | Case reports, conference abstracts, protocol papers, | | | | |
| Empirical studies; | letters, editorials, opinion pieces, theoretical papers, | | | | |
| Humans; | reviews, and studies with computational methods or | | | | |
| Adult patients, aged 18-65 years old; | purely qualitative designs; | | | | |
| Current diagnosis of major depressive disorder, | Animal studies; | | | | |
| according to DSM or ICD; | Post-mortem studies; | | | | |
| Brain MRI acquisition; | Adolescents (<18) or elderly people (>65); | | | | |
| Assessment of suicidal ideation and/or attempt; | Other psychiatric and/or neurologic disorders | | | | |
| Group comparison or association between suicidal | diagnoses; | | | | |
| ideation or attempt and an MRI measure. | Other neuroimaging tools; | | | | |
| | Focus on non-suicidal self-injury; | | | | |
| | No assessment of suicidal ideation or attempt, using | | | | |
| | the broad term suicidality without any specification, | | | | |
| | not indicating how suicidal ideation or attempt were | | | | |
| | measured; | | | | |
| | Not measuring the association between suicidal | | | | |
| | ideation and/or attempt and the MRI measure. | | | | |
| | | | | | |

Abbreviations: DSM, Diagnostic and Statistical Manual of Mental Disorders; ICD, International Classification of
 Diseases; MRI, magnetic resonance imaging.

Table 2. Main findings of the studies on suicidal ideation.

| Author (Year) | MRI methods | p-value corrections | Main findings | Secondary findings |
|---------------|---|--|--|---|
| STRUCTURAL | | | | |
| Taylor (2015) | GM volume and cortical thickness Freesurfer | p <.05, FDR corrected | <u>ROI – GM volume: bilateral OFC, cingulate cortex, insula, amygdala, parahippocampi, thalamus, and basal ganglia; Cortical thickness: cortical regions</u> SI vs DC: No differences in the GM volume. ↓ cortical thickness in the L insula, L caudal middle frontal gyrus, L superior parietal gyrus, and L superior temporal gyrus. SI vs HC: No differences in the GM volume, nor cortical thickness. | |
| Kim (2019) | LSV Freesurfer | p<.05, FDR corrected | <u>ROI</u> – bilateral amygdala, caudate, hippocampus, pallidum, putamen, and thalamus SI vs DC/HC : No differences in the LSV. | |
| _ | | p<.001, Gaussian Random Field corrected | | SI : BSSI score was positively correlated with L pallidum LSV. |
| Wang (2021) | GM volume VBM | p-value corrected with cluster-based statistics ^a | <u>Whole brain</u> SI vs DC: \downarrow GM volume in the R lingual gyrus. | |
| He (2022) | GM volume Freesurfer Structural covariance network | p<.05, FDR corrected | <u>ROI - Cingular opercular network regions</u> Severe SI vs DC: ↓ GM volume in the L ACC and R inferior OFC. ↑ SC between the R inferior OFC and R ventral PCC; R ventral PCC and R superior frontal gyrus; and R superior frontal gyrus and R postcentral gyrus. Mild SI vs DC: ↓ GM volume in the R inferior OFC. ↑ SC between the R inferior OFC and R ventral PCC; and the R ventral PCC and R superior frontal gyrus. Severe SI vs HC: ↓ GM volume L ACC, L superior frontal Gyrus, L middle temporal gyrus, bilateral postcentral gyrus, R inferior OFC, and R PCC. ↑ SC between the L ACC and L postcentral gyrus, and L superior frontal gyrus; L superior frontal gyrus and L middle temporal gyrus; R inferior OFC and R ventral | |

| | | | PCC; R ventral PCC and R superior frontal gyrus; and | |
|----------------------|---------------------------------|--------------------------------|---|------------------------------------|
| | | | R superior frontal gyrus and R postcentral gyrus. | |
| | | | Mild SI vs HC: \downarrow GM volume in the L ACC, L | |
| | | | superior frontal gyrus, and R inferior OFC. ↑ SC | |
| | | | between the L superior frontal gyrus and L middle | |
| | | | temporal gyrus: and L ACC and L superior frontal | |
| | | | ovriis | |
| | | | Severe SI vs Mild SI · GM volume in the R inferior | |
| | | | OFC \uparrow SC between the R inferior OFC and R ventral | |
| | | | PCC. | |
| Kang (2022) | GM volume | p<.05, uncorrected | ROI - bilateral dmPFC, dlPFC, vmPFC, vlPFC, OFC, | |
| | CAT | | and ACC | |
| | | | MDD: SSI score was positively correlated with GM | |
| | | | volume of the L dlPFC and R dmPFC. | |
| DIFFUSION | | | | |
| Taylor (2015) | FA and RD maps | p<.05, TFCE | Whole brain | |
| • | TBSS | corrected ^a | SI vs DC: \downarrow FA in the L posterior corona radiata and | |
| | | | \uparrow RD in the R anterior that amic radiation. | |
| | | | SI vs HC: FA in the splenium of the CC R | |
| | | | corticospinal tract and R anterior thalamic radiation: | |
| | | | and \uparrow RD in the L superior longitudinal fasciculus | |
| | | n < 05 FDP | POI CaH CaC superior and posterior corona | |
| | | p<.05, TDR | radiata CC ALIC PLIC anterior and posterior | |
| | | conceleu | the lamic radiation | |
| | | | $\frac{\text{unather factors}}{\text{SL}_{\text{vac}} \mathbf{DC}/\text{UC}} + \mathbf{E} \mathbf{A} \text{ and } \mathbf{A} \mathbf{DD} \text{ in the series redicts}$ | |
| | | | Si vs DC/HC : \downarrow FA and \mid KD in the corona radiata, | |
| N (2017) | | 0.5 | CgH, and anterior thalamic radiation. | |
| Myung (2016) | Probabilistic tractography | p<.05, non- | Whole brain | |
| | NBS | parametric | SI vs DC/HC: \downarrow SC in a subnetwork including L | |
| | Graph theory: nodal, strength | correction method ^a | frontal and occipital regions, and basal ganglia. | |
| | and degree, clustering, and | p<.05, FDR | | SI: SSI score was positively |
| | ragional efficiency and | corrected | | correlated with betweenness |
| | betweenness centrality | | | centrality of the L rostral middle |
| | betweenness centranty | | | frontal gyrus. |
| Chen (2021a) | Generalized Q-Sampling: | p<.05, FDR | Whole brain | <u>.</u> |
| | GFA, and NQA maps | corrected | SI vs DC: \downarrow GFA and NQA in the CC and ACC. No | |
| | Graph theory: global | | differences in graph theory measures. | |
| | efficiency, normalized shortest | | SI vs HC: \downarrow GFA in the CC and ACC. \downarrow NOA in the | |
| | | | ACC. No differences in graph theory measures | |
| | | | | |

| | and characteristic path length, and small worldness NBS | p<.05, non- parametric correction method ^a | Whole brain SI vs DC: No differences in the SC of any subnetwork. | |
|--------------------|---|---|--|---|
| Liu (2021) | Deterministic tractography Graph theory: normalized shortest path length, normalized clustering coefficient, small worldness, global and local efficiency, rich-club, and modularity NBS | p-value corrected with Bonferroni | SI vs HC: ↓ SC of the frontal subnetwork. Whole brain SI vs DC: No differences in the topological parameters. ↓ betweenness centrality in the L fusiform gyrus. SI vs HC: ↓ small worldness, global efficiency, and modularity. | |
| Reis (2022) | FA, AD, MD, and RD maps TBSS | p<.05, TFCE corrected ^a | Whole brain MDD: BSSI score was negatively correlated with FA in the genu of the CC and R anterior corona radiata. | |
| FUNCTIONAL | | | | |
| Resting-state fMRI | | | | |
| Du (2017) | Seed-based FC Seed: R rostral ACC | p<.05, Bonferroni corrected | <u>Whole brain</u> SI vs DC/HC: \downarrow intrinsic FC between the R rostral ACC and the medial OFC and the R middle temporal pole. | |
| | | p<.05, uncorrected | | SI: SSI score was positively correlated with intrinsic FC between the R rostral ACC and the middle temporal pole. |
| Kim (2017) | NBS Graph theory: node strength, betweenness centrality, | p<.05, non- parametric correction method ^a | <u>Whole brain</u> SI vs DC: \downarrow FC in a subnetwork including frontal and temporal regions and basal ganglia. | <u>i</u> |
| | regional efficiency | p<.05, FDR corrected | | SI: SSI score was negatively correlated with FC of the regions of the subnetwork, node strength, clustering coefficients, and regional efficiency in the bilateral thalamus and L OFC. |
| Li (2018a) | Static and dynamic ALFF | p<.05, Bonferroni corrected | <u>ROI – R dorsal ACC, L inferior temporal gyrus, L</u> <u>hippocampus/parahippocampal gyrus and L OFC</u> SI vs DC: No differences in the static ALFF. \downarrow dynamic ALFF in the L OFC, L inferior temporal | |

| | | | gyrus, L hippocampus/parahippocampus gyrus and R dorsal ACC. SI vs HC: ↑ in the static ALFF in the R dorsal ACC and L inferior temporal gyrus; ↓ dynamic ALFF in the R dorsal ACC and L hippocampus/parahippocampal | |
|-------------|--------------------------------------|-------------------|---|--|
| Liao (2018) | Static and dynamic | p<.05, Bonferroni | <u>Whole brain</u> | |
| | connectomics | corrected | SI vs DC: No differences in the overall static | |
| | Graph theory: network | | connectomics. \downarrow static nodal efficiency in the R insula. | |
| | efficiency and small worldness | | \uparrow overall network strength and network efficiency in dynamic connectomics \uparrow dynamic nodal efficiency in | |
| | - | | the L inferior OFC, R fusiform gyrus, R postcentral | |
| | | | gyrus and R superior parietal gyrus. | |
| | | | SI vs HC: ↓ overall network strength and efficiency | |
| | | | in static connectomics; \downarrow static nodal efficiency in the | |
| | | | R insula. \uparrow overall network strength and efficiency in | |
| | | | the L superior frontal medial gyrus | |
| Wei (2018) | Seed-based FC | p<.05. Bonferroni | ROI –bilateral precuneus/cuneus | |
| | Seed: bilateral amygdala | corrected | SI vs DC/HC: ↑ FC between bilateral amygdala and | |
| | | | bilateral precuneus/cuneus. | |
| Qiao (2020) | Seed-based FC (static and | p<.05, Bonferroni | <u>ROI – static FC: L habenula-L putamen, L</u> | SI: No correlation between BSSI |
| | dynamic) Seed: bilateral habenula | corrected | cerebellum, R precentral gyrus, R habenula-R | score and static and dynamic FC in the regione with differences |
| | Seed. bhateral habenula | | gyrus bilateral precupeus R babenula-I superior | between groups |
| | | | temporal gyrus, L angular gyrus and L postcentral | between groups. |
| | | | gyrus | |
| | | | SI vs DC/HC: \downarrow static FC between R habenula and R | |
| | | | precuneus, and L IFG; ↑ static FC between L habenula | |
| | | | and L cerebellum. ↓ dynamic FC between L habenula and R lingual gyrus and R habenula and L postcentral | |
| | | | ovrus: ↑ dynamic FC between L habenula and L | |
| | | | precuneus and R habenula and R superior temporal | |
| | | | gyrus. | |

| Chen (2021b) | Seed-based FC Seed: bilateral amygdala, hippocampus, thalamus, visual and motor cortices, ACC, PCC and precuneus ALFF ReHo Graph theory: clustering and normalized clustering coefficient; characteristic and normalized characteristic path length, local and global efficiency, transitivity, assortativity, and small worldness | p<.05, FDR corrected p<.05, non- parametric correction method ^a | Whole brain SI vs DC: ↓ ALFF in the L cuneus and ↑ ALFF in the R middle temporal pole gyrus. ↓ ReHo in the R cuneus and ↑ ReHo in the L middle temporal gyrus. ↓ global efficiency. SI vs HC: ↑ global efficiency, ↓ assortativity and transitivity. ROI - bilateral amygdala, hippocampus, thalamus, visual and motor cortices, ACC, PCC and precuneus SI vs DC: ↑ FC in the R and L hippocampus. Whole brain SI vs DC: ↓ FC in a subnetwork including frontal, parietal, and occipital regions, as well as parahippocampal gyrus. | |
|--------------|--|--|--|---|
| | NBS | | SI vs HC: No differences in the FC of any subnetwork. | |
| Tang (2021) | ICA: inter-network connectivity | p<.05, FDR corrected | DMN, anterior and posterior salience, visual, precuneus, thalamus cerebellum, sensorimotor, motor, language, and L central executive networks SI vs HC: ↓ FC between DMN and precuneus networks; ↑ FC between DMN and thalamus cerebellum and sensorimotor networks; between L central executive and sensorimotor networks; and between sensorimotor and precuneus networks. | SI: Positive correlation between the changes in the BSSI score and the changes in the FC in DMN-precuneus network (due to IT-TMS therapy). |
| Wang (2021) | ALFF | p<.001, Gaussian Random Field corrected | Whole brain SI vs DC: No differences in the ALFF. | |
| Fan (2022) | Cerebral blood flow-based FC Seed: Bilateral visual cortices, precuneus, PCC, striatum, L supplementary motor area, L inferior temporal gyrus, L superior temporal gyrus, and L insula | p<.05, Bonferroni corrected | Whole brain SI vs DC: ↑ FC between the L precuneus and L middle temporal gyrus; L supplementary motor area and R OFC; R striatum and the bilateral medial PFC. ↓ FC between the L visual cortex and the bilateral sensorimotor cortex. SI vs HC: ↓ FC between the L visual cortex and the bilateral sensorimotor cortex. | |
| He (2022) | ReHo | p<.05, uncorrected | ROI - Cingular opercular network regions MDD: MADRS item 10 score was negative correlated with ReHo of the R inferior OFC and positively correlated with ReHo of the R middle frontal gyrus. | |

| Li (2022a) | Seed-based dynamic FC Seed: Bilateral dorsal and ventral PCC | p<.05, Bonferroni corrected | ROI – L dorsal PCC and L fusiform gyrus, L ventralPCC and L IFG, and R ventral PCC and L IFGSI vs DC: \uparrow dynamic FC variability between the Lventral PCC and the L IFG.SI vs HC: \uparrow dynamic FC variability between the Lventral dorsal PCC and the L fusiform gyrus, and theR ventral PCC and the L IFG. | MDD: SSI score was positively correlated with the dynamic FC variability between the L ventral PCC and the L IFG. SI: No significant correlation between SSI scores and dynamic FC |
|----------------------|---|---|---|---|
| Li (2022b) | Seed-based FC Seed: Bilateral amygdala | p<.05, Bonferroni corrected | <u>ROI – L amygdala and L middle frontal gyrus, L</u> medial superior frontal gyrus, L inferior and superior parietal lobule, R precentral gyrus; R amygdala and L middle temporal gyrus, L precentral gyrus, R angular gyrus, and L postcentral gyrus SI vs DC: ↑ FC between the L amygdala and the L medial superior frontal gyrus and L middle frontal gyrus; and R amygdala and L middle temporal gyrus. ↓ FC between the L amygdala and the L inferior parietal lobule and R precentral gyrus; and the R amygdala and L precentral gyrus, R angular gyrus and L postcentral gyrus. | |
| Ouyang (2022) | Temporal Correlation Coefficient | p<.05, FDR corrected | <u>Whole brain</u> MDD: HDRS item 3 score was negatively correlated with the temporal correlation coefficient of the DMN. | |
| Reis (2022) | ICA DMN, salience, central executive, precuneus, sensorimotor, basal ganglia, high and primary visual networks NBS | TFCE, p<.05 corrected ^a | Whole brain MDD: BSSI score was positively correlated with FC between the high visual network and the R inferior occipital gyrus and negatively correlated with the L precuneus and L cerebellum. BSSI score was positively correlated with FC between the primary visual network and R cuneus, and negatively correlated with the L OFC. | _ |
| | | p<.05, non- parametric correction method ^a | Whole brain MDD: BSSI score was negatively correlated with the FC of a subnetwork including frontal, temporal, occipital and cerebellar regions. | |
| Yang (2022a) | Seed-based FC Seed: bilateral lateral and medial amygdala Graph theory | p<.05, FDR corrected | <u>Whole brain</u> SI vs DC: \uparrow FC between the L lateral amygdala and the bilateral caudate; \downarrow FC between the R lateral amygdala, the L postcentral gyrus, R superior temporal gyrus and L middle temporal gyrus. | |

| (small worldness), lambda (normalized characteristic path length), and gamma (normalized clustering coefficient) | and the L caudate; ↓ FC between the amygdala and L superior frontal gyrus, the amygdala and the L parahippocampal gyru L middle temporal gyrus, and the R media and the L superior temporal gyrus. <u>ROI - bilateral superior frontal gyri, parahi</u> gyri, basal ganglia, amygdala, L hippod <u>OFC, L superior temporal gyrus, R postcer</u> SI vs DC: ↓ global connectivity. SI vs HC: ↓ global connectivity and sig lambda. | R lateral L medial s, and the amygdala <u>pocampal</u> <u>impus, L</u> ral gyrus ha, and \uparrow |
|--|---|--|
| P< | c.05, uncorrected | SI: SSI score was negatively correlated with sigma. |

1043 Footnotes: a, similar to p<.05 family-wise error rate corrected. Abbreviations: ACC, anterior cingulate cortex; AD, axial diffusivity; ALFF, amplitude of low frequency 1044 fluctuation; ALIC, anterior limb of the internal capsule; BSSI, Beck Scale for Suicidal Ideation (self-report); CAT, Computational Anatomy Toolbox; CC, corpus callosum; 1045 CgC, cingulate portion of the cingulum bundle; CgH, hippocampal portion of the cingulum bundle; DC, patient control group; dlPFC, dorsolateral prefrontal cortex; DMN, 1046 default mode network; dmPFC, dorsomedial prefrontal cortex; FA, fractional anisotropy; FC, functional connectivity; FDR, false discovery rate; fMRI, functional magnetic 1047 resonance imaging; GFA, generalized fractional anisotropy; HC, healthy control group; HDRS, Hamilton Depression Rating Scale; ICA, independent component analysis; IFG, inferior frontal gyrus; IT-TMS, individual targeted-transcranial magnetic stimulation; GM, gray matter; L, left; LSV, local shape volume; MD, mean diffusivity; MDD, major 1048 depressive disorder; NBS, network-based statistics; NQA, normalized quantitative anisotropy; OFC, orbitofrontal cortex; PCC, posterior cingulate cortex; PLIC, posterior limb 1049 1050 of the internal capsule; R, right; ReHo, regional homogeneity; RD, radial diffusivity; ROI, region of interest; SI, suicidal ideation group; SC, structural connectivity; BSSI, 1051 Scale for Suicidal Ideation (interview); TBSS, tract-based spatial statistics; TFCE, threshold-free cluster enhancement; VBM, voxel-based morphometry; WM, white matter; 1052 vlPFC, ventrolateral prefrontal cortex; vmPFC, ventromedial prefrontal cortex.

1053

Table 3. Main findings of the studies on suicidal behavior.

| Author (Year) | MRI methods | p-value corrections | Main findings | Secondary findings |
|-------------------------------|---|---|---|--|
| STRUCTURA | L | | | |
| Ehrlich (2005) | Deep WMH and periventricular hyperintensities Modified Fazekas 4-point rating scale | p<.05, uncorrected | Whole brain SA vs DC: ↑ periventricular hyperintensities. No differences in deep WMH. | SA: No correlation between lethality or number of SA and the presence, severity, or number of WMH. |
| Jia (2010) | WM and GM volume VBM | p <.05, FWE corrected | <u>Whole brain</u> SA vs DC/ HC: No differences in GM or WM volume. | |
| Peng (2014) | GM Volume VBM | p<.05, FDR corrected | Whole brainSA vs DC: \downarrow GM volume in the L PCC.SA vs HC: \downarrow GM volume in the R middle temporal gyrus and \uparrow GM volume in the R parietal lobe. | |
| Chen (2015) | MTR maps | Voxel p<.005, AlphaSim corrected p <.05 | Whole brainSA vs DC/HC: \downarrow MTR in the L inferior parietal lobule and Rsuperior parietal lobule.ROI – Bilateral caudate nucleusSA vs DC/HC:No MTR differences. | |
| Colle (2015) | GM Volume SACHA | p<.05, uncorrected | <u>ROI - Bilateral hippocampi</u> SA (past month and lifetime) vs DC: \downarrow GM volume in the hippocampus. | Past month SA vs DC: ↓ GM volume in the hippocampus. Lifetime SA vs DC: No differences in the GM volume of the hippocampus. Past month vs Lifetime SA: No differences in the GM volume of the hippocampus. |
| Lee (2016) | GM Volume VBM | p<.001, uncorrected | $\frac{\text{Whole brain}}{\text{SA vs DC: }} \downarrow \text{GM volume in the L angular gyrus and R cerebellum.}$ | |
| Lee (2018) | GM Volume VBM | p<.001, uncorrected | <u>Whole brain</u> SA vs HC: \downarrow GM volume in the L middle frontal gyrus, L IFG, L ACC, R middle temporal gyrus, L cerebellum, R precentral and postcentral gyrus. | |
| Jollant (2018) Jena sample | WM and GM Volume | p<.05, TFCE corrected | $\frac{\text{Whole brain}}{\text{SA vs DC: }} \downarrow \text{GM volume in the R dmPFC cortex.}$ | SA with violent means vs. SA without: ↑ GM in the bilateral caudate nuclei. |

| VBM | | | SA vs HC: No differences in the GM volume. | Family history of suicide vs No | | |
|-----------------------------------|---|---|--|--|--|--|
| Jollant (2018) Montreal sample | WM and GM Volume VBM | p<.05, TFCE corrected | Whole brain SA vs DC/ HC: No differences in GM or WM volume. | temporal gyri, L temporal gyrus extending to fusiform gyrus, R dmPFC, and L putamen. | | |
| Kang (2020a) | Cortical thickness, surface area, and cortical volume Freesurfer | p<.05, FDR corrected | <u>ROI – cortical regions</u> SA vs DC: \uparrow cortical surface areas of the L postcentral and L lateral occipital areas and \downarrow cortical surface areas of the L superior frontal area; \uparrow cortical volumes of the L postcentral and the L lateral OFC. No differences in cortical thickness. | SA: No differences between number of SA and risk-rescue rating score and the surface area/cortical volume of the areas with significant results between groups. | | |
| Kang (2020b) | LSV Freesurfer | Non-parametric procedure to estimate the p- value ^a | <u>ROI</u> – bilateral amygdala, caudate nuclei, hippocampi, pallidum, putamen, and thalamus SA vs DC: ↓ LSV in the L putamen, L hippocampus, L amygdala and bilateral pallidum and thalamus. SA vs HC: ↓ LSV in the bilateral amygdala, pallidum and putamen, and L caudate nucleus and L hippocampus. | SA: Negative correlation between BSSI score and LSV of bilateral thalamus. | | |
| Yang (2020) | GM volume VBM | Bonferroni corrected p- value | ROI – R inferior OFC, L rectus gyrus, L superior temporal pole, Lpostcentral gyrus, L calcarine fissure, bilateral amygdala, L insulaand L caudate nucleusSA vs DC: ↓ GM volume in the R inferior OFC, L caudate nucleus,and ↑ GM volume in the L calcarine fissure.SA vs HC: ↓ GM volume in the R inferior OFC, L rectus gyrus, Lsuperior temporal pole, L postcentral gyrus, bilateral amygdala, Linsula, L caudate nucleus and ↑ GM volume in the L calcarine fissure. | SA: Negative correlation between the GM volume of the R inferior OFC and the Nurses' Global Assessment of Suicide Risk Scale score. | | |
| DIFFUSION | | | | | | |
| Jia (2010) | FA, AD and RD maps | p <.05, FWE corrected | Whole brainSA vs DC: \downarrow FA and AD of the L ALIC and the R lentiform nucleus.SA vs HC: \downarrow FA and AD of the L ALIC and \downarrow FA and \uparrow RD of theR frontal lobe (subgyral WM).ROI - bilateral lentiform nucleus, hippocampus, and thalamusSA vs DC: \downarrow FA and \uparrow RD of the R lentiform nucleus. | | | |
| Jia (2014) | Deterministic tractography Seed: L ALIC | p<.05, Bonferroni corrected | ROI – L medial frontal cortex, L OFC and L thalamusSA vs DC: \downarrow mean percentage of projecting fibers from the L ALICto the L OFC, and the L thalamus; \downarrow mean FA in the fibersprojecting from L ALIC to the L medial frontal cortex.SA vs HC: \downarrow mean percentage of projecting fibers from the L ALICto the L medial frontal cortex.SA vs HC: \downarrow mean percentage of projecting fibers from the L ALICto the L medial frontal cortex.SA vs HC: \downarrow mean percentage of projecting fibers from the L ALICto the L medial frontal cortex, L OFC, and L thalamus; \downarrow mean FA | | | |

| | | | in the fibers projecting from L ALIC to the L medial frontal cortex, | |
|----------------------------------|------------------------|------------------------|---|---|
| | | | | |
| Olvet (2014) | FA and ADC maps | p<.05, TFCE | Whole brain | |
| | TBSS | corrected ^a | SA vs DC/HC: No differences in FA and ADC. | |
| | | p<.01, | Whole brain | |
| | | uncorrected | SA vs DC: \downarrow FA in the R dmPFC. No differences in ADC. | |
| | | p<.05, | ROI - medial OFC, dmPFC, rostral and caudal ACC | |
| | | uncorrected | SA vs DC: \downarrow FA in the bilateral dmPFC. No differences in ADC. | |
| Chen (2021c) | Generalized Q- | p<.05, FDR | Whole brain | |
| | Sampling: GFA, | corrected | SA vs DC: \downarrow GFA and NQA in the corpus callosum and precuneus; | |
| | NQA maps | | \downarrow GFA in the cuneus. | |
| | Graph theory: global | | SA vs HC: \downarrow GFA and NQA in the corpus callosum and the caudate | |
| | efficiency, normalized | | nucleus. | |
| | shortest and | p<.05, non- | Whole brain | |
| | characteristic path | parametric | SA vs DC: No differences in the topological parameters. No | |
| | length, modularity, | correction | differences in the SC of any subnetwork. | |
| | normalized clustering | method ^a | SA vs HC: \uparrow SC in a subnetwork including frontal and parietal | |
| | coefficient, and small | | regions. No differences in the topological parameters. | |
| | NBS | | | |
| Zhang (2021) | FA AD MD and | n< 05 | ROI – forcens major and minor bilateral anterior thalamic | |
| Linang (2021) | PD mans | p<.05, Bonferroni | radiation arcuate fasciculus corticospinal tract CaC CaH IEOE | |
| | ND maps | corrected | inferior and superior longitudinal fasciculus, uncinate fasciculus | |
| | tractography | concella | SA vs $\mathbf{DC} \cdot \mid \mathbf{EA}$ forcers major $\uparrow \mathbf{MD}$ and \mathbf{RD} in the forcers minor | |
| | uaciography | | LIEOE and L CaC | |
| | | | \mathbf{L} in \mathbf{L} CgC. SA ve $\mathbf{HC} + \mathbf{L}$ in the forces major \uparrow MD and PD in the forces | |
| | | | minor and L IFOF | |
| FUNCTIONAL | | | | |
| Resting-state f | - /RI | | | |
| Kang (2017) | Seed-based EC | n< 005 | Whole brain | SA: SSI score was positively correlated |
| $\mathbf{Kang}\left(2017\right)$ | Seed: bilateral | p<.005, | SA vs DC: \uparrow EC between L amygdala and R insula and L OEC \uparrow | with EC between R amygdala and R |
| | amvgdala | unconcetted | EC between R amygdala and L middle temporal gyrus | parahippocampal gyrus |
| Ι οο (2010) | Seed based EC | n< 05 EDP | POL regions of the Harvard Oxford atlases | All SSI score was negatively correlated |
| LUC (2017) | ROI-to-ROI | corrected | SA vs HC \uparrow EC between R anterior parahippocampal games and L | with EC between medial prefrontal |
| | Seed: medial frontal | contentu | posterior parahippocampal gyrus: D tomporooccipital part of | cortex and R supplementary meter |
| | cortex, R | | inferior temporal gurus and D frontal ave field. EC between | cortex and K supplementary motor |
| | supplementary motor | | method composal gyrus and R supplementary meter cortex. | CUITCA. |
| | cortex, R anterior and | | Whole broin | |
| | L posterior | | | |

| | parahippocampal gyri, temporooccipital part of R inferior temporal gyrus, R frontal eye field (significant results ROI-to-ROI analysis) | | SA vs HC: \uparrow FC between L posterior parahippocampal gyrus and R uncus; R frontal eye field of dorsal attention network and R fusiform gyrus. | |
|--|---|---|--|--|
| Wagner (2019) Jena and Montreal sample | Graph theory: clustering coefficients, global efficiency, assortativity, rich-club coefficients NBS | p<.05, FDR corrected p<.05, FWE corrected | Whole brain SA vs DC: ↑ rich-club coefficients for higher degree nodes. No differences in the other topological parameters. SA vs HC: ↓ assortativity and ↓ rich-club coefficients for lower degree nodes. Whole brain SA vs HC: ↓ FC in the identified subnetwork, including frontal, parietal, occipital and temporal regions, and parahippocampal gyrus. | |
| Weng (2019) | Seed-based Seed: bilateral visual and motor cortices, PCC, amygdala, hippocampi, thalamus, ALFF ReHo Graph theory: clustering and normalized clustering coefficients, local and global efficiency, characteristic and normalized characteristic path length, small worldness and transitivity NBS | p<.05, FDR corrected p<.05, non- parametric correction method ^a | Whole brainSA vs DC: \uparrow ALFF in the L superior parietal gyrus and \downarrow ALFF inthe R angular gyrus. \uparrow ReHo in the R putamen and \downarrow ReHo in the Rsuperior temporal gyrus and R superior and inferior OFC. Nodifferences in the topological parameters.SA vs HC: \downarrow ALFF in the bilateral thalamus. \downarrow ReHo in the bilateralthalamus. \downarrow characteristic path length, lambda, assortativity, andtransitivity.ROI – bilateral visual and motor cortices, PCC, amygdala,hippocampi, and thalamus.SA vs DC: \uparrow FC in the L hippocampus and bilateral thalamus.SA vs HC: \downarrow FC in the bilateral thalamus and motor cortex.Whole brainSA vs DC: No differences in the FC of any subnetwork.SA vs HC: \downarrow FC in a subnetwork including pre and postcentral gyriand temporal regions. | |

| Qiu (2020) | Seed-based FC Seed: pregenual, anterior and posterior subgenual ACC | Voxel p<.001 with cluster p <.05, Gaussian Random Field corrected | Whole brainSA vs DC: \downarrow FC between anterior subgenual ACC and R caudatenucleus, \downarrow FC between the pregenual ACC and L insula and Lsuperior medial frontal gyrus; \uparrow FC between the anterior subgenualACC and L frontal inferior (tri) frontal and L superior medial frontalgyri, \uparrow FC between the posterior subgenual ACC and L superior | |
|--------------|---|---|---|--|
| | | p<.05, uncorrected | medial frontal gyrus. | SA: SSI score was positively correlated with FC between pregenual ACC and L superior frontal gyrus. No correlation between number of SA and FC. DC: SSI score was positively correlated with FC between pregenual ACC and L superior frontal gyrus, and negatively correlated with anterior subgenual ACC and superior frontal gyrus. |
| Shu (2020) | fALFF | p<.01, AlphaSim corrected | <u>Whole brain</u> SA vs HC: \uparrow fALFF in the L posterior cerebellum, R ACC, L caudate nucleus and L superior frontal cortex. | |
| | | p<.05, uncorrected | | SA: SSI score was positively correlated with mean fALFF in the L superior frontal gyrus and R ACC. |
| Yang (2020) | Seed-based FC Seed: R inferior OFC, L caudate nucleus, L calcarine fissure | p<.0019, Bonferroni corrected | <u>ROI – R inferior OFC: L rectus gyrus and left inferior parietal</u> <u>lobule; L caudate nucleus: L middle frontal gyrus</u> SA vs DC: ↓ FC between R inferior OFC and L rectus gyrus, and L inferior parietal lobule. SA vs HC: ↓ FC between R inferior OFC and L inferior parietal lobule. | |
| Chen (2021d) | FC strength Seed-based FC Seed: R OFC, and bilateral dmPFC | Voxel p <.001, with a cluster p<.05, FWE corrected | Whole brainSA vs DC:FC strength in the R OFC and bilateral dmPFC;FCbetween R OFC and L ACC and L calcarine sulcus;FC betweenthe R OFC and the R middle frontal gyrus; andFC between thebilateral dmPFC and the L middle frontal gyrus, and R inferiortemporal gyrus.SA vs HC:FC strength in the bilateral hippocampus, R inferiorand occipital gyrus. | |
| Shu (2022) | Seed-based FC Seed: bilateral ACC and precuneus | p<.001, AlphaSim corrected | Whole brain SA vs HC: ↓ FC between R subgenual ACC and L posterior cerebellum; ↓ FC between L subgenual ACC and occipital lobe; | |

| | | | FC between R precuneus and R middle frontal cortex/precentral gyrus. | |
|--------------------------------|---|--|--|--|
| | | p<.05, uncorrected | | SA: SSI score was negatively correlated with FC between R subgenual ACC and L posterior cerebellum. |
| Yang (2022b) | ReHo | p<.05 | Whole brain SA vs DC: ↓ ReHo in the R PCC. SA vs HC: ↓ ReHo in the L PCC and R PCC/precuneus. | MDD: HDRS item 3 score was positively correlated with ReHo in the R PCC. |
| Task fMRI | | | | |
| Richard- Devantoy (2016) | Brain activation Task: Go/No-Go Task | Voxel p<.001, uncorrected, with cluster p<.05, FWE corrected | Whole brain SA vs DC: No differences in activation during response inhibition. SA vs HC: ↓ activation in the precuneus and middle/PCC during Go vs. No-Go contrast (response inhibition). | SA: Beck Suicide Intent Scale score was positively correlated with the activation in the medial thalamus during response inhibition. |
| Baek (2017) | Brain activation Task: Monetary Decision-Making Task (risk and loss aversion) | p<.01 with Tukey's test | <u>ROI - OFC, vmPFC, ventral ACC, insula, midbrain, striatum and amygdala</u> SA vs DC: ↓ activation of the subgenual ACC for potential gain contrast (loss aversion). SA vs HC: ↓ activation of the subgenual ACC and L amygdala for potential gain and loss contrasts, respectively (loss aversion); ↓ activation of the L insula for subjective value of probabilistic loss contrast (risk aversion). | |
| | | p<.001, uncorrected | | SA: The L insula activity was negatively correlated with subjective value of probabilistic loss (risk aversion). The R amygdala, bilateral insula, L middle temporal gyrus, and L globus pallidus activity was negatively correlated with the subjective value of probabilistic gain (risk aversion). |

1056 Footnotes: a, similar to p<.05 family-wise error rate corrected. Abbreviations: ACC, anterior cingulate cortex; AD, axial diffusivity; ADC, apparent diffusion coefficient; ALFF, 1057 amplitude of low frequency fluctuation; ALIC, anterior limb of the internal capsule; BSSI, Beck Scale for Suicidal Ideation (self-report); CgC, cingulate portion of the cingulum 1058 bundle; CgH, hippocampal portion of the cingulum bundle; DC, patient control group; dmPFC, dorsomedial prefrontal cortex; FA, fractional anisotropy; fALFF, fractional 1059 amplitude of low frequency fluctuation; FC, functional connectivity; FDR, false discovery rate; fMRI, functional magnetic resonance imaging; FWE, family-wise error rate; GFA, generalized fractional anisotropy; HC, healthy control group; HDRS, Hamilton Depression Rating Scale; IFG, inferior frontal gyrus; IFOF, inferior fronto-occipital 1060 1061 fasciculus; GM, gray matter; L, left; LSV, local shape volume; MD, mean diffusivity; MDD, major depressive disorder; MTR, magnetization transfer ratio; NBS, network-1062 based statistics; NQA, normalized quantitative anisotropy; OFC, orbitofrontal cortex; PCC, posterior cingulate cortex; R, right; ReHo, regional homogeneity; RD, radial 1063 diffusivity; ROI, region of interest; SA, suicide attempt group; SI, suicidal ideation group; SC, structural connectivity; BSSI, Scale for Suicidal Ideation (interview); TBSS,

tract-based spatial statistics; TFCE, threshold-free cluster enhancement; VBM, voxel-based morphometry; WM, white matter; WMH, white matter hyperintensities; vmPFC, ventromedial prefrontal cortex.

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| 1068 | Table 4. Main | findings of | the studies | on the t | ransition | between | suicidal | ideation | and be | ehavior. |
|------|---------------|-------------|-------------|----------|-----------|---------|----------|----------|--------|----------|
|------|---------------|-------------|-------------|----------|-----------|---------|----------|----------|--------|----------|

| Author (Year) | MRI methods | p-value corrections | Main findings | Secondary findings |
|------------------|--|-------------------------|---|---|
| FUNCTIONA | L | | | |
| Resting-state f | MRI | | | |
| Wagner (2021) | ALFF Graph theory: degree centrality | p<.05, FWE corrected | ROI – ALFF: R dIPFC, R vIPFC, bilateral inferior and superior parietal lobes, precuneus, angular, supramarginal, postcentral, fusiform, and superior temporal gyri, occipital cortices, hippocampi, and R thalamus; degree centrality: R dIPFC, R vIPFC, R superior parietal cortex, bilateral angular gyrus, and bilateral occipital cortices SA vs SI: ↓ ALFF in the bilateral angular gyrus, L inferior parietal cortex, L occipital cortex, R precuneus, R supramarginal, R superior parietal cortex, and R postcentral gyrus; and ↑ ALFF in the L parahippocampal gyrus, L hippocampus, and R fusiform gyrus. ↓ degree centrality in the L occipital cortex, R IFG, and R angular gyrus. SA vs DC: ↓ ALFF in the R IFG, R cuneus, bilateral angular and supramarginal gyrus, superior parietal cortex and occipital cortex; and ↑ ALFF in bilateral hippocampus and fusiform gyrus. ↓ degree centrality in the R IFG, R superior parietal cortex, R superior parietal cortex, and bilateral angular gyrus. SA vs DC: ↓ ALFF in the bilateral angular gyrus, temporal cortex, supramarginal gyrus, superior parietal cortex, and bilateral angular gyrus. SA vs HC: ↓ ALFF in the bilateral angular gyrus, temporal cortex, supramarginal gyrus, angular gyrus, R paracentral lobule, L inferior and R superior parietal cortex, R inferior and middle frontal gyri, L occipital cortex, R cuneus; and ↑ ALFF in the bilateral hippocampus, R thalamus and R fusiform gyrus. ↓ degree centrality in the B Superior parietal cortex, R inferior and middle frontal gyri, L occipital cortex, R cuneus; and ↑ ALFF in the bilateral angular gyrus, occipital cortex, and R Superior parietal cortex, R inferior and middle frontal gyri, L occipital cortex, R inferior superior parietal angular gyrus, occipital cortex, and R IFG. SI vs DC: No differences in the ALFF, prove in degree centrality in the angular gyrus. | No correlation between the number of SA and ALFF and degree centrality values. |
| Task fMRI | | | | |
| Ai (2018) | Brain activation Task: Faces task; Tower of London | p<.05, FWE corrected | <u>ROI – Faces task: bilateral fusiform gyri extending to the lingual gyrus; Tower of London: L insula, L dlPFC, and L postcentral gyrus</u> SA vs SI/DC/HC: ↓ activation in the bilateral fusiform gyri extending to lingual gyrus in the processing of emotional faces. No differences between groups in the activation for executive planning. SI vs DC/HC: No differences in activation in the processing of emotional faces or executive planning. | |
| | | p<.001, uncorrected | <u>ROI - L insula, L dlPFC, and L postcentral gyrus</u> SA vs SI/DC/HC: \uparrow activation in the L insula during executive planning. | - |

- 1069 *Abbreviations:* ALFF, amplitude of low frequency fluctuation; DC, patient control group; dlPFC, dorsolateral prefrontal cortex; fMRI, functional magnetic resonance imaging;
- 1070 FWE, family-wise error rate; HC, healthy control group; IFG, inferior frontal gyrus; L, left; R, right; ROI, region of interest; SA, suicide attempt group; SI, suicidal ideation 1071 group; vIPFC, ventrolateral prefrontal cortex.