

情绪特异性还是普遍性？ ——抑郁患者抑制控制损伤的 ALE 元分析*

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摘 要 抑制控制能力受损是影响抑郁症发病的关键因素之一,但这种损伤是情绪特异性的还是普遍性的尚不明确。本研究采用激活似然估计法(ALE),整合任务态脑成像研究,分析和比较情绪性与非情绪性抑制控制任务下重度抑郁(Major Depressive Disorder, MDD)患者与健康对照组的脑激活差异。经文献检索与筛选,共纳入 19 项研究,133 个有效坐标。结果发现:(1)在情绪性抑制控制任务中,MDD 患者右侧额中回出现补偿性激活,左侧额中回和右侧额下回激活减弱;(2)在非情绪性抑制控制任务中,未发现跨研究一致的差异脑区。该结果提示,MDD 患者的抑制控制能力损伤可能是情绪特异性的,损伤脑区主要集中于前额叶。研究结果为探索抑制控制在抑郁症发生和维持中的作用提供了方向性启发,并为开发基于抑制控制的靶向干预提供了参考。

关键词 抑郁症,抑制控制,神经机制,ALE 元分析,情绪特异性

分类号 B845; B842

1 前言

抑郁症作为一种发病率极高的心理疾病,影响着全球超过 3 亿人(Perini et al., 2019),其高复发率和致残率不仅严重损害患者的社会功能,也为临床治疗带来严峻挑战(Friedrich, 2017; Martínez-Amorós et al., 2021)。因此,探索抑郁症的发病机制,为抑郁症治疗方案的开发提供理论依据,具有重要现实意义。

临床研究发现抑郁患者常表现出负性情绪注意偏向、不自觉的消极记忆反刍、甚至会出现自残、自杀的意念或行为,而这些症状往往与患者的抑制控制能力受损有关(Peckham et al., 2010; Shen et al., 2025; Shimony et al., 2021)。抑制控制是指个体抑制与目标无关的干扰、想法或行为的心理过程(Cristofori et al., 2019),它不仅与抑郁症的临床症状有关,还可以预测有家族抑郁史群体的抑郁症首发风险、抑郁缓解患者的复发风险以及抗抑郁治疗

的疗效(Galkin & Peshkovskaya, 2021; Stevens et al., 2023; Taylor et al., 2025)。这些都表明抑制控制是影响抑郁症发生和维持的关键因素之一,但具体影响机制却尚不清楚。

Joormann 和 Gotlib (2010)提出的抑郁症认知模型指出,抑郁患者难以抑制情绪性信息,因而持续受到负面情绪的困扰,并逐步发展成严重的情绪障碍。该模型侧重强调抑制控制损伤通过影响个体的情绪加工过程,促进抑郁症的产生和加重。然而,抑郁患者不仅持续性情绪低落,往往还伴随明显的认知功能损伤(Perini et al., 2019; Zacková et al., 2021)。抑制控制既是情绪管理的关键机制,也是认知功能的重要组成成分(Shetty et al., 2025)。患者抑制控制能力的损伤可能不仅影响情绪加工过程,更可能对认知与情绪系统均产生负面影响,呈现出普遍性的广泛损伤。因此,抑郁患者的抑制控制损伤究竟是情绪特异性还是普遍性的成为理解其对抑郁症作用机制的关键问题。然而,以往研究往往仅

收稿日期: 2025-12-08

* 全国教育科学规划国家一般基金(BBA250050)资助。

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关注其中的一个侧面,较少系统性比较抑郁患者情绪性与非情绪性抑制控制能力的损伤情况。梳理已有研究,也难得出明确结论。情绪性抑制控制能力常通过情绪性抑制控制任务进行测量,它是指个体对具有情绪效价的材料(如悲伤的面孔、负性词汇、情绪性图片等)执行抑制过程,例如情绪性 Stroop 任务。相应的,个体抑制字母、数字、中性词汇、图片等中性情绪材料就反映了个体的非情绪性抑制控制能力。从行为结果来看,抑郁患者难以抑制情绪性信息,在情绪性 Stroop 任务、情绪性定向遗忘等抑制控制任务中表现差于健康对照组(Quigley et al., 2020; Yang et al., 2016),而在经典 Stroop 任务、Go-NoGo 任务等非情绪性抑制控制任务中常与健康对照组无显著的行为表现差异(Cane et al., 2023; Tozzi et al., 2020),这些结果似乎表明抑郁患者的抑制控制损伤是情绪特异性的。然而,从脑成像研究结果来看,在非情绪性抑制控制任务中,抑郁患者与健康对照组在前额叶、扣带回等与抑制控制高度相关的脑区存在差异性激活(Kikuchi et al., 2012; Wagner et al., 2006),支持普遍性损伤的观点。不仅如此,汇总以往研究发现,在抑制控制任务中,抑郁患者与健康对照组激活差异脑区与差异方向也缺乏一致性,其损伤的潜在神经机制并不明晰。基于此,本研究聚焦于任务态脑成像研究,通过激活似然估计法(Activation Likelihood Estimation, ALE),系统比较重性抑郁障碍(Major Depressive Disorder, MDD)患者在情绪性与非情绪性抑制控制任务中与健康对照组(Health Controls, HC)脑激活模式的差异,以识别以往研究中统一的脑区激活模式(Tolomeo & Yu, 2022),并揭示其抑制控制受损的特性及潜在神经机制,为抑郁症临床诊疗提供参考。

1.1 MDD 患者情绪性抑制控制的损伤及相关脑区

情绪性抑制控制是探讨 MDD 患者情绪特异性损伤的核心维度,研究虽然发现 MDD 患者较难抑制情绪性信息,但不同研究所报告的脑激活模式并不一致(Colich et al., 2016; Nishizawa et al., 2019),因而难以确定其情绪性抑制控制损伤的神经机制。

在抑制控制相关脑区上,研究结论不一。首先,在抑制控制的核心脑区前额皮层上,研究发现 MDD 患者与 HC 激活的差异方向不一致。具体而言,在情绪性 Stroop 任务中,尽管行为表现没有显著差异,但在恐惧情绪条件下, MDD 患者较 HC 左前额叶激活增强(Matsubara et al., 2014; Nishizawa

et al., 2019)。Dichter 等人(2009)发现,在负性情绪刺激下, MDD 患者在中、下、眶额叶皮层比 HC 激活程度更高。研究者们认为,这并不代表 MDD 患者的抑制控制能力更强,相反,这恰恰表明其情绪性抑制功能受损,为了成功抑制情绪信息,需要付出更多主观努力,补偿性增强前额叶的激活程度(Matsubara et al., 2014; Yang et al., 2016)。但也有部分研究认为, MDD 患者前额叶功能直接受损,不存在补偿性激活。如,在情绪干扰任务、情绪性 Go-NoGo 任务中, MDD 患者的前额叶激活程度降低(Colich et al., 2016; Korgaonkar et al., 2013)。甚至有研究发现前额叶激活强度随着抑郁严重程度的升高呈阶梯式下降: Carew 等人(2013)让 MDD 患者、抑郁风险者和 HC 抑制由负面自传体记忆凝练的句子,结果发现,在抑制负面回忆时, HC 背外侧前额叶的激活最强,抑郁风险组次之,而 MDD 患者最弱。综上所述,前额叶激活差异模式的不同,模糊了 MDD 患者情绪性抑制控制能力受损程度及受损的心理机制,因此,需加以整合分析。

其次,大量协助完成抑制控制过程的脑区,也表现出激活差异。核磁研究表明,在对工作记忆中的负性信息进行移除时, MDD 患者的背侧前扣带回、顶叶和双侧岛叶皮质激活程度更高(Foland-Ross et al., 2013)。在抑制负性图像时,抑郁高风险群体右中扣带回、左侧尾状核激活程度更高(Lisiecka et al., 2012)。其中,扣带回、岛叶皮质与认知监控有关(Botvinick et al., 2001),顶叶与认知资源分配有关(Tyler et al., 2015),尾状核与目标导向的行为选择有关(Grahn et al., 2008)。然而,有些研究结果却与之相反。Liu 等人(2021)采用情绪性 Go-NoGo 任务发现,在负性情绪刺激下, MDD 患者下顶叶、内侧顶叶、后侧额叶和中扣带回等脑区的激活水平降低。Alders 等人(2019)也发现, MDD 患者在抑制各情绪效价信息时,均表现出前扣带回、顶上小叶、右边缘上回(冲突监控, Thiebaut de Schotten et al., 2011)、中央后脑回(动作反馈, Smith & Nichol, 2009)和颞中回(情绪整合, Mansueto et al., 2025)激活水平的降低。这些激活脑区与激活差异方向的不一致,使得确定 MDD 患者情绪性抑制控制损伤的内部心理过程和神经机制变得较为困难,因此需进行整体性梳理。

杏仁核与情绪加工息息相关,分析 MDD 患者情绪性抑制控制能力的变化必然需要关注杏仁核的激活情况(Zuo et al., 2018)。研究表明,在加工情

绪性信息时, MDD 患者往往表现出杏仁核激活的增强(Jaworska et al., 2015), 代表患者对情绪信息过度反应, 情绪弹性减弱(Barbour et al., 2020)。而在抑制情绪性信息时, MDD 患者的杏仁核激活并未表现出统一的趋势。Beauregard (2007)发现, 当要求 MDD 患者对悲伤情绪信息进行情绪管理时, 其背侧前扣带回、后侧颞叶、杏仁核等区域激活显著增强。Chechko 等人(2013)也发现, 在情绪性 Stroop 任务中, 患者的杏仁核激活强于 HC。但 Loeffler 等人(2018)同样采用情绪性 Stroop 任务和情绪管理任务, 并未发现 MDD 患者与 HC 在杏仁核激活上的差异。情绪性抑制控制任务中, 杏仁核激活水平不仅与 MDD 患者对情绪性信息的加工有关, 还与前额叶皮层的调节有关(Zuo et al., 2018), 杏仁核激活情况的不一致反应的不仅是患者情绪加工的异常, 可能也代表其前额叶对杏仁核调控能力削弱, 预示着其情绪性抑制控制的缺陷。

1.2 MDD 患者非情绪性抑制控制能力的损伤及相关脑区

除了情绪性抑制控制外, MDD 患者在非情绪性抑制控制上是否也存在缺陷, 是回答其抑制控制能力是否存在普遍性损伤的关键。然而, 相关研究结果却存在争议。在行为指标上, 许多研究并未报告 MDD 患者与 HC 明显的差异(Cane et al., 2023; Diler et al., 2014; Tozzi et al., 2020), 部分神经生理机制研究也声称在抑制控制任务上, MDD 患者与 HC 脑区激活不存在显著差异(Cane et al., 2023; Davey et al., 2012)。甚至有研究发现其前额皮层激活比 HC 更强(Korgaonkar et al., 2013; Wagner et al., 2006)。然而, 有研究发现了相反的结果。Kikuchi 等人(2012)采用 Stroop 任务发现, MDD 患者额中回等区域的激活强度显著降低。Halari 等人(2009)采用 Stop-Signal 任务发现 MDD 患者右侧背外侧前额叶、额下回皮层激活降低。这说明, MDD 患者前额叶抑制功能是否受损, 不能一概而论, 需整合多项研究, 分析其中统一的激活模式, 才能更好确定。

在协助前额叶完成抑制控制的脑区上, 相关研究也存在差异。有研究表明, 在 NoGo 条件下, 抑郁群体在左侧颞上回和左尾状核激活程度更强(Aarts et al., 2013)。同样是 Go-NoGo 任务, Tozzi 等人(2020)发现 MDD 患者仅在角回激活程度更强。角回与注意定向关系密切(Lojowska et al., 2025)。Korgaonkar 等人(2013)采用多种认知控制任务进行探究, 结果发现, 在 Go-NoGo 任务上, MDD 患者的

背侧前扣带回激活强度更大。这种多个脑区的差异化激活, 使得研究难以锁定与 MDD 患者抑制控制能力改变相关的关键脑区, 因而对其是否损伤也难得出统一结论。

总的来看, 目前虽然有大量研究支持 MDD 患者情绪性抑制控制能力的损伤, 但非情绪性抑制控制能力是否损伤存在争议, 无法确定这种损伤是情绪特异性的还是普遍性的。并且, MDD 患者与 HC 在两种抑制控制任务中的大脑激活模式的差异均存在许多不一致, 其背后的神经机制难以确定。因此本研究采用 ALE 元分析的方法, 分析和比较 MDD 患者与 HC 在情绪性与非情绪性抑制控制任务中大脑激活模式的差异, 揭示 MDD 患者抑制控制能力损伤的特性及神经机制。

2 方法

为确保研究方法的科学性, 依据 PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses)指南开展了文献检索、筛选、分析和结果报告等过程(Page et al., 2021)。并且为确保研究的可追溯性, 对研究内容在预见心理学预注册平台进行了预注册, 注册编号为 202511.00051。

2.1 文献检索

本研究检索了知网、万方、维普、Sinomed、Google Scholar、Pubmed、PsychoINFO、Web of Science、Elsevier、Scopus 数据库, 检索目标为数据库中 2025 年 8 月 6 日之前与抑郁群体抑制控制有关的脑成像研究文献。检索包含三组关键词: 第一组是抑郁相关词, 包括 Depression、Depressive Disorder、Depressive Symptom、Major Depressive Disorder、抑郁、抑郁情绪、抑郁症状; 第二组是抑制控制相关词, 包括 Inhibition、Inhibitory Function、Cognition、Cognitive Control、Stroop、Flanker、Stop-Signal、Intentional Forgetting、Directed Forgetting、Think-NoThink、抑制、抑制控制、认知控制; 第三组是脑成像相关词, 包括 Magnetic Resonance Imaging、functional Magnetic Resonance Imaging、fMRI、Positron Emission Tomography、PET、functional Near-Infrared Spectroscopy、fNIRS、神经机制、磁共振、脑成像。为避免遗漏, 影响研究可靠性, 本研究还检索了相关主题的综述及元分析文献的参考文献列表(Diener et al., 2012; Li et al., 2025; Piani et al., 2022; Wan et al., 2024; Yan et al., 2022; Zacková et al., 2021)。

2.2 文献筛选和编码

针对检索所得文献,进行了两阶段的筛选。第一阶段,基于文章的标题和摘要进行初步判断,纳入和排除标准如下:1)仅纳入包含抑郁群体的研究,对于以其他精神障碍群体、非人类为研究对象的文章予以排除;2)仅纳入任务态磁共振研究、fNIRS 或 PET 研究,对于行为、脑电和静息态、结构像磁共振研究予以排除;3)仅纳入实证研究,对综述、元分析及个案研究予以排除。第二阶段,基于全文内容对符合以上标准的文献进一步筛选,具体纳入和排除标准如下:1)仅纳入研究对象为重性抑郁患者的文章,对于研究对象为阈下抑郁、抑郁缓解期、抑郁风险者等的文章不予纳入;2)考虑到抑制控制能力具有发展性特征(Rey-Mermet et al., 2018),本研究仅纳入研究对象年龄在 16~60 范围的文章;3)仅纳入提供有效空间坐标的文章,对于未提供标准空间坐标(Talairach 或 MNI)或未提供 MDD 患者与 HC 在抑制相关任务上脑激活差异坐标的文章不予纳入。

对最终纳入分析的文献,进行系统编码,并记录关键信息,包括文章标识(第一作者与发表时间)、性别比、样本量、年龄、研究所用范式、MDD 患者筛选标准、量表及得分、分析方式(全脑分析或兴趣区分析)、行为结果、脑激活差异方向(MDD > HC 或 MDD < HC)、坐标类型(情绪性(E)或非情绪性(N))及相应坐标值。其中,情绪性坐标是指在情绪性抑制任务中,抑制控制条件下 MDD 患者与 HC 激活的差异脑区坐标;非情绪性坐标依此类推。根据脑激活的差异方向和坐标类型将有效坐标分为 E-MDD > HC、E-MDD < HC、N-MDD > HC、N-MDD < HC 四组。为确保编码的准确性和合理性,由第一与第二作者依据上述标准先后独立进行文献筛选和编码。对所提取坐标及其属性进行对比后发现,两名编码者之间的一致性系数达到 95.49%,针对编码中不一致的 4.51%部分,由第一、第二与第三作者逐一进行对比分析与深度讨论,最终达成共识,确定了纳入分析的 133 个有效坐标。

2.3 激活似然估计法(ALE)

数据分析使用 GingerALE 2.6.3 软件进行,该软件由 Turkeltaub 等人(2002)开发,它可以通过汇总多个研究报告的激活坐标,计算脑区激活重叠的统计显著性,从而识别跨研究一致的脑激活模式。当前研究统一采用 MNI 空间坐标体系,对文献中提取的 Talairach 坐标通过 GingerALE 2.6.3 转换为 MNI 空间坐标,再执行数据分析。首先,依据上述

分组分别对四组坐标进行单一分析,统计方法为 Uncorrected p , 阈值设定为 $p < 0.0001$,最小团块设为 200 mm^3 。最后,将分别对比情绪与非情绪性抑制控制任务下, MDD > HC 的激活脑区的异同和情绪与非情绪性抑制控制任务下, MDD < HC 的激活脑区的异同。本研究中, N-MDD < HC、N-MDD > HC 的单一分析结果不存在统一激活的大脑区域,无法执行对比分析。

2.4 出版偏倚

为了评估因阴性结果而未发表的文献是否会削弱当前研究的解释力,采用 FSN (Fail-Safe-N)方法评估当前元分析结果的稳健性(Acar et al., 2018)。FSN 方法的基本思想是:估算需要加入多少个零结果的假想研究,才能使当前元分析结果不再显著。理想情况下,某一簇类的 FSN 越高,表明其结果越稳健,但也不应超过设定的上限,以防结果由少数几个研究主导(何全兴 等, 2025)。因此,参考前人研究设定了 FSN 的下限与上限,下限为研究总数的 30%,上限通过以下公式计算:(对某簇有贡献的研究数/0.05) - (该 ALE 分析中包含研究数)(何全兴 等, 2025; Acar et al., 2018; Fascher et al., 2024)。假想研究坐标依据 Acar 等人(2018)提供的代码 (<https://github.com/NeuroStat/GenerateNull>), 通过 R 4.5.0 生成。

2.5 异质性检验

研究虽严格选取以符合临床诊断标准的重性抑郁患者为研究对象的文献,研究群体异质性较低,但纳入分析研究采用的实验范式多样,具有一定异质性。因此,本研究采用敏感性分析,逐一排除不同实验范式的研究再进行 ALE 分析,将所得结果与未排除任何实验范式的分析结果进行比较,以确定范式异质性对结果的影响。

2.6 兴趣区分析研究的影响

考虑到抑制控制所涉及的脑区在学界已具有基本共识(Kang et al., 2022),本文参考 Gentili 等人(2019)的研究,未排除针对这些脑区进行兴趣区分析的研究,但这些研究仍可能过度凸显特定脑区的作用。因此,剔除基于兴趣区分析提取的坐标后,再次执行 ALE 分析,以检验兴趣区分析研究可能的影响。

3 结果

3.1 纳入文献和样本特征

通过关键词检索,共检索到 28402 篇文献,最

终筛选出 19 篇文献纳入分析, 提取出 133 个坐标点, 涉及被试 823 名, 其中 MDD 患者有 393 名(详细文献筛选过程见图 1, 纳入分析文章信息见表 1 和表 2)。19 篇文献中 11 篇涉及情绪性抑制控制, 12 篇涉及非情绪性抑制控制, 其中 4 篇文献与两者均有关。情绪性抑制控制研究涉及 422 名被试, 其中 MDD 患者有 207 名(女性 134 名, 男性 63 名, 其中一项研究未报告剔除无效数据后的性别比), 共提供 99 个有效坐标点。其中 $MDD > HC$ 的坐标点 40 个, 涉及 9 项研究; $MDD < HC$ 的坐标点 59 个, 涉及 5 项研究。非情绪性抑制控制研究涉及 576 名被试, 其中 MDD 患者有 273 名(女性 164 名, 男性 81 名, 其中 2 项研究未报告剔除无效数据后的性别比), 提供 34 个有效坐标点。其中 $MDD > HC$ 的坐标点 23 个, 涉及 10 项研究; $MDD < HC$ 的坐标点 11 个, 涉及 3 项研究。

3.2 元分析结果

3.2.1 MDD 患者情绪性抑制控制与 HC 的差异

对从 11 项研究中提取的 2 组情绪性抑制控制有关的脑激活坐标(组 1: $E-MDD > HC$; 组 2: $E-MDD < HC$)分别进行单一分析, 结果如图 2 和表 3 所示。结果显示, 与 HC 相比, 在情绪性抑制控制任务中, MDD 患者右侧额中回(34, 38, 32)激活增强; 右侧额下回(50, 14, 18)、左侧额中回(-36, 40, 16)皮层激活削弱。

3.2.2 MDD 患者非情绪性抑制控制与 HC 的差异

对从 12 项研究中提取的 2 组非情绪性抑制控制有关的脑激活坐标(组 1: $N-MDD > HC$; 组 2:

$N-MDD < HC$)分别进行单一分析, 结果并未发现 MDD 患者较 HC 统一激活增强或削弱的脑区。

3.2.3 出版偏倚结果

采用 FSN 方法评估当前研究结果受出版偏倚影响的程度, 结果表明, MDD 患者与 HC 的差异脑区右侧额中回(34, 38, 32)、左侧额中回(-36, 40, 16)、右侧额下回(50, 14, 18)的 FSN 值均处于相应的上限与下限之间(详见表 3), 表明本研究结果较为稳健, 不易受出版偏倚的影响。

3.2.4 异质性检验结果

敏感性分析结果表明, 在情绪性抑制控制任务中, 剔除定向遗忘范式、情绪性 Stroop 范式、Go-NoGo 范式、情绪负启动范式、思想抑制任务、返回抑制范式中的任一范式, MDD 患者仍在右侧额中回皮层激活高于 HC, 与原分析结果一致; 但剔除 Oddball 范式或 Think\No-Think 范式后, 这一共同激活的差异脑区消失, 意味着结果主要受到这两个范式影响。在剔除 Go-NoGo 范式或情绪性 Stroop 范式后, MDD 患者在左侧额中回、右侧额下回皮层激活低于 HC, 与原分析结果一致; 而剔除 Oddball 范式或思想抑制任务的研究后, 这一共同激活的差异脑区消失, 说明原分析结果主要受这两个范式影响, MDD 患者主要在这两个范式中表现出相应脑区的激活不足。

就非情绪性抑制控制任务而言, 剔除任一涉及的研究范式, 均未出现 MDD 患者与 HC 存在激活差异的脑区, 与原结果一致, 说明原分析中的阴性结果并非受到范式异质性的影响。

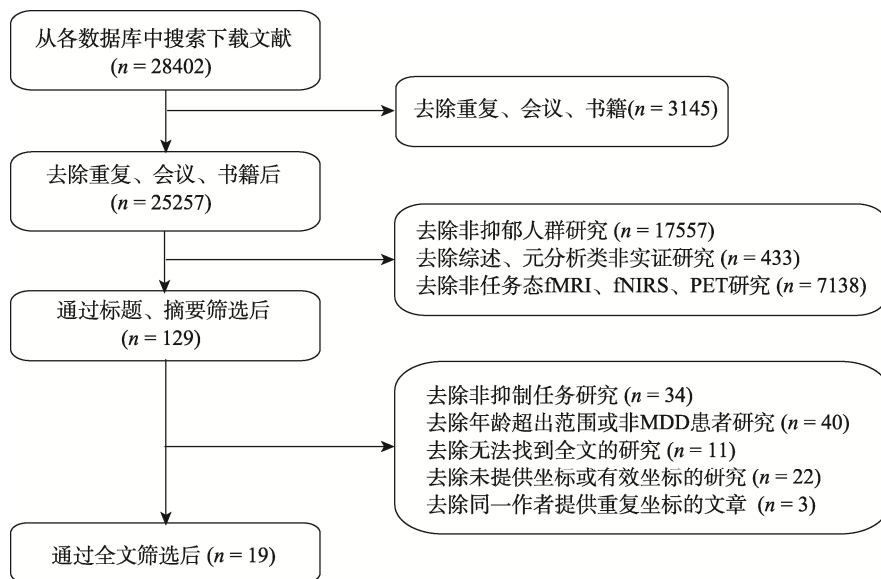


图 1 文献筛选流程图

表 1 纳入分析文章的被试信息表

作者	抑郁症诊断与评分				样本量		性别比(女/男)		年龄(Mean ± SD/Range)	
	诊断标准	量表	抑郁组 Mean (SD)/Median (Range)	健康组 Mean (SD)/Median (Range)	抑郁组	健康组	抑郁组	健康组	抑郁组	健康组
Liu et al. (2021)	DSM-IV	BDI-II	33.00 (12.00~49.00)	3.50 (0~21.00)	30	34	23/7	22/12	27.97 ± 8.16	26.53 ± 9.29
Wang et al. (2008)	DSM-IV	HAM-D	19.90(5.30)	0.55(0.80)	19	20	12/7	13/7	39.30 ± 9.00	36.50 ± 10.50
Chechko et al. (2013)	DSM-IV	BDI HAM-D	31.70(8.20) 22.70(5.00)	1.40(2.60)	18	18	13/5	13/5	36.50 ± 10.80	36.00 ± 10.30
Eugène et al. (2010)	DSM-IV	BDI-II	29.00(10.4)	1.00(1.60)	12	12	6/6	8/4	34.40 ± 11.70	33.80 ± 9.90
Yang et al. (2016)	DSM-IV	BDI HAM-D	16.80(8.70) 21.30(5.40)	5.50(4.10) 2.60(1.40)	16	16	9/7	10/6	32.00 ± 8.24	30.00 ± 8.98
Elliott et al. (2002)	DSM-IV	HAM-D MADR	23.10(3.90) 31.30(5.20)	—	10	11	—	—	42.20 ± 8.30	37.60 ± 9.70
Carew et al. (2013)	DSM-IV	BDI-II HAM-D	30.30(9.40) 15.40(3.90)	8.80(6.50)	15	16	15/0	16/0	16.00~24.00	16.00~24.00
Dai et al. (2018)	DSM-IV	BDI-II HAM-D PHQ-9	35.86(10.12) 23.43(2.94) 21.00(5.80)	2.12(1.62) 1.76(1.12) 1.09(1.26)	30	33	23/7	21/12	48.77 ± 11.88	48.85 ± 12.86
Sacchet et al. (2017)	DSM-IV	BDI	31.10(9.50)	1.80(2.20)	16	16	9/7	8/8	31.50 ± 8.90	31.70 ± 10.00
Dichter et al. (2009)	DSM-IV	BDI	26.90(4.90)	0.70(1.20)	14	15	7/7	9/6	34.80 ± 14.30	30.80 ± 9.60
Fales et al. (2008)	DSM-IV	HAM-D	20.00(2.30)	0.30(0.60)	27	24	17/10	12/12	33.40 ± 8.00	36.40 ± 9.00
Alders et al. (2019)	DSM-IV	MADR	30.00(6.00)	1.00(2.00)	48	30	33/15	22/8	34.70 ± 12.20	33.20 ± 9.80
Simeonova et al. (2022)	DSM-IV	HAM-D	23.20(5.00)	2.70(3.00)	24	26	15/9	18/8	37.70 ± 14.00	39.00 ± 12.40
Langenecker et al. (2007)	DSM-IV	BDI-II HAM-D	25.00(9.70) 20.40(7.60)	1.20(1.80) 1.10(2.00)	16	17	—	—	41.00 ± 12.20	34.20 ± 11.00
Richard-Devantoy et al. (2016)	DSM-IV	HAM-D-24	29.60(5.20)	0.80(1.30)	22	27	15/7	17/10	41.30 ± 11.40	33.80 ± 7.10
Korgaonkar et al. (2013)	DSM-IV	HAM-D	19.20(3.10)	1.30(1.40)	30	30	18/12	18/12	41.20 ± 15.80	35.70 ± 14.10
Wagner et al. (2006)	DSM-IV	HAM-D	23.50(4.90)	—	16	16	16/0	16/0	40.30 ± 9.70	38.80 ± 9.10
Crane et al. (2016)	DSM-IV	HAM-D	20.76(7.25)	0.85(1.90)	18	54	11/7	38/16	34.28 ± 11.69	33.80 ± 11.56
Matthews et al. (2009)	DSM-IV	BDI-II	15.00~43.00	0~3.00	12	15	—	—	19.00~35.00	19.00~37.00

注：DSM-IV = Diagnostic and Statistical Manual of Mental Disorders; HAM-D = Hamilton Depression Scale; BDI = the Beck Depression Inventory; MADR = Montgomery-Asberg Depression Rating Scale, PHQ-9 = Patient Health Questionnaire-9.

表 2 纳入分析文章的研究信息表

作者	任务类型	差异方向	分析方式	坐标类型	行为结果
Liu et al. (2021)	E-GNG	MDD < HC	全脑	E	ACC; MDD < HC
Wang et al. (2008)	E-OB	MDD < HC	Both	E	RT; MDD < HC
Chechko et al. (2013)	E-stroop	Both	全脑	E	ACC (Neg); MDD < HC
Eugène et al. (2010)	NAP	MDD > HC	Both	E	No
Yang et al. (2016)	DF	MDD > HC	全脑	E	DFE (Neg); MD < HC
Elliott et al. (2002)	E-GNG	MDD > HC	兴趣区	E	No
Carew et al. (2013)	TS	Both	全脑	E	—
Dai et al. (2018)	IOR	MDD > HC	兴趣区	Both	IOR (Neu); MDD > HC
Sacchet et al. (2017)	TNT	MDD > HC	全脑	Both	No
Dichter et al. (2009)	OB	Both	全脑	Both	No
Fales et al. (2008)	Stroop	Both	全脑	Both	No
Alders et al. (2019)	Stroop	MD < HC	全脑	N	No
Simeonova et al. (2022)	Stroop n-back	MDD > HC	全脑	N	ACC; MD < HC
Langenecker et al. (2007)	GNG	MDD > HC	全脑	N	Rejections; MDD > HC
Richard-Devantoy et al. (2016)	GNG	MDD > HC	全脑	N	No
Korgaonkar et al. (2013)	GNG	MDD > HC	Both	N	No
Wagner et al. (2006)	Stroop	MDD > HC	兴趣区	N	No
Crane et al. (2016)	GNG	MDD < HC	全脑	N	No
Matthews et al. (2009)	SST	MDD > HC	全脑	N	No

注：任务类型中，NAP = 情绪负启动范式；IOR = 返回抑制范式；TNT = 压抑遗忘范式；OB = Oddball 范式；TS = 思维压抑任务；GNG = Go-NoGo 任务；SST = Stop-Signal Task；前缀 E-代表情绪性任务。行为结果中，ACC = 准确率；RT = 反应时；DFE = 定向遗忘效应；IOR = 返回抑制效应；Neg = 在负性情绪信息上表现出差异；Neu = 在中性信息上表现出差异；No = MDD 患者与 HC 在抑制控制行为指标上无显著差异。Both 代表该研究包含此列所代表的两种属性。

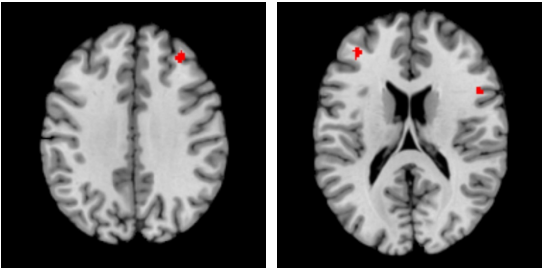


图 2 情绪性抑制控制任务下，MDD > HC 的脑区(左)和 MDD < HC 的脑区(右)

3.2.5 兴趣区分析研究的影响

剔除基于兴趣区分析提取的坐标后，分析结果与当前结果一致，排除了兴趣区分析的潜在影响(详见表 4)。

4 讨论

抑制控制能力损伤既是抑郁症发生的潜在机制，也是抗抑郁治疗的重要切入点。但 MDD 患者的抑制控制能力损伤是情绪特异性的还是普遍性的，研究结果却存在争议。本研究采用激活似然估计法，分别对 MDD 患者情绪性与非情绪性抑制控制相关的脑成像研究进行元分析，探索其抑制控制能力损伤的特性及神经机制。

4.1 MDD 患者情绪性抑制控制能力受损

元分析结果表明，在情绪性抑制控制任务中，MDD 患者相比 HC 右侧额中回皮层激活增强，但左侧额中回激活减弱。根据以往研究，在处理消极

表 3 MDD 患者与 HC 在情绪性抑制控制任务中脑区激活差异

脑区	左/右脑	MNI (x, y, z)	体积(mm ³)	ALE	布尔德曼区	贡献研究数	FSN
MDD > HC (k = 9)							
额中回	右	34, 38, 32	312	0.0151	BA9	2	3 < 21 < 31
MDD < HC (k = 5)							
额中回	左	-36, 40, 16	232	0.0131	BA10	2	2 < 12 < 35
额下回	右	50, 14, 18	320	0.0174		2	2 < 26 < 35

表 4 排除兴趣区分析坐标后 ALE 分析结果

脑区	左/右脑	MNI(x, y, z)	体积(mm ³)	ALE	布尔德曼区	贡献研究数
MDD > HC (k = 7)						
额中回	右	34, 38, 32	328	0.0151	BA9	2
MDD < HC (k = 5)						
额中回	左	-36, 40, 16	232	0.0131	BA10	2
额下回	右	50, 14, 18	320	0.0174		2

情绪时, 大脑的右侧脑区激活程度高于左侧脑区(Henriques & Davidson, 1991; Wheeler et al., 1993), 而相比健康群体, MDD 患者更易表现出这种右侧偏侧化(Fu et al., 2022; Javaheripour et al., 2023)。当前研究结果与以往研究相一致, 并进一步揭示了这种右侧偏侧化与 MDD 患者情绪性抑制控制能力受损有关。前额叶是抑制控制的关键脑区(Sridhar et al., 2024); 右侧前额叶更与消极情绪处理息息相关(Imajo et al., 2024)。右侧前额叶激活增强意味着 MDD 患者为了完成情绪性抑制付出了更多的认知努力, 然而行为结果却与 HC 无差异(Chechko et al., 2013), 甚至表现出更长的抑制反应时或更低的记忆抑制效应(Yang et al., 2016; Zheng et al., 2023), 表明这种激活增强是一种补偿性激活, 预示着 MDD 患者情绪性抑制控制能力受损。另外, 左侧前额叶与积极情绪调控有关(Buhle et al., 2014; Palser et al., 2025), 抑制积极情绪信息或面部表情时, 健康群体往往表现出左侧前额皮层激活的增强(Ochsner & Gross, 2004; Palser et al., 2025), 本研究中 MDD 患者相较 HC 左侧额中回激活减弱, 表明其抑制积极情绪信息的能力同样受损。

有趣的是, MDD 患者的右侧额中回激活增强, 而其右侧额下回激活却有所减弱, 这可能与两个脑区在抑制控制过程中的分工不同有关: 额中回主要与较高级别的自上而下的控制有关, 包括任务目标维持、冲突监控及抑制网络的策略性调节等(Apšvalka et al., 2022; Ehliis et al., 2024); 而额下回皮层则参与更具体的抑制执行过程, 是前额皮层-基底节-丘脑环路的重要调控节点(Boen et al., 2022; Zhuang et al., 2023)。MDD 患者右侧额中回激活增强, 但其下行脑区额下回激活并未相应增强, 反而有所减弱, 这可能代表 MDD 患者额中回皮层的调控能力下降, 也可能是其额下回皮层存在功能缺陷无法响应上级皮层的抑制指令。两种可能都表明右侧额中回与额下回之间的功能连接异常很可能是 MDD 患者情绪性抑制控制损伤的关键机制。

需要指出的是, 虽然元分析结果在情绪性任务层面表现出一定一致性, 但具体激活模式仍可能受到任务范式差异的影响, 因此, 当前结果更适合被理解为“跨多种情绪性抑制任务出现的前额叶异常倾向”, 而非完全不受范式影响的普遍机制。

此外, 对于协助完成抑制控制的脑区(如, 顶叶、尾状核、扣带回等), 本研究并未发现 MDD 患者与 HC 跨研究一致的差异, 这可能与这些脑区的激活易受任务特征或患病特征的调节有关。已有研究显示, 顶叶主要参与认知资源分配(Tyler et al., 2015), 尾状核与行为选择及动作抑制有关(Grahn et al., 2008), 而这些脑区仅参与抑制控制的部分子过程, 且激活程度受认知负荷或抑制类型的影响(Grahn et al., 2008; Torralbo et al., 2016)。本研究主要探究 MDD 患者抑制控制损伤的普遍特征, 涵盖多种抑制范式, 这可能导致这些脑区难以呈现跨研究一致的激活。除此之外, 不同抑郁亚型的脑神经机制存在差异。例如, 扣带回激活异常在高反刍水平的抑郁个体中更为常见(Sheena et al., 2021; Zhou et al., 2020), 而岛叶激活异常与抑郁严重程度有关, 尤其在重度或伴焦虑共病患者中更为稳定(Schnellbacher et al., 2022; Sindermann et al., 2022)。当前研究主要纳入无共病 MDD 患者, 而 MDD 患者的临床异质性可能使上述脑区的功能异常难以被凸显, 从而未表现出一致性激活。

尽管大量研究发现在处理负性情绪信息时, MDD 患者的杏仁核激活异常(Barbour et al., 2020; Jaworska et al., 2015), 但当前元分析结果并未发现 MDD 患者在情绪性抑制控制任务中相较于健康人群杏仁核激活的差异。这可能是前额皮层补偿性上调的结果, 即 MDD 患者通过额外的认知努力, 经由前额皮层下调了杏仁核的激活水平, 减少了对情绪刺激的情绪反应。另一种可能是, 当前研究群体的杏仁核激活水平不存在稳定差异。Tamm 等人(2022)经过大样本研究(> 2 万, 平均年龄 64 岁)发现, 在控制人口统计学变量后, MDD 患者杏仁核激

活的异常程度与其抑郁症状不存在预测关系。然而, Ferri 等人(2017)发现, 较严重的难治性抑郁症患者在加工情绪信息时, 其杏仁核的激活程度较低, 并且这种杏仁核功能钝化预测了 52 周后患者病情的严重程度。由此可见, MDD 患者杏仁核激活是否异常, 可能受到抑郁严重程度的调节。本研究纳入的研究群体仅包含重性抑郁症患者, 且主要集中在中度抑郁水平, 其杏仁核结构可能还未出现功能性变异, 因而未呈现出跨研究一致的差异激活。

4.2 未发现 MDD 患者非情绪性抑制控制能力的损伤脑区

在非情绪性抑制控制任务中, 当前研究未发现 MDD 患者较健康群体存在稳定的激活差异脑区, 并且敏感性分析也表明这种阴性结果与纳入研究的范式异质性无关, 结合行为结果与以往研究, MDD 患者的非情绪性抑制控制任务反应时、正确率常与健康群体无差异(Cane et al., 2023; Tozzi et al., 2020), 初步提示 MDD 患者的非情绪性抑制控制能力未见稳定异常。不过, 考虑到当前研究纳入的非情绪性抑制控制的研究数量与坐标数量相对有限, 未来仍需更多实证研究进一步验证这一结果。

综上所述, 现有证据更倾向于支持 MDD 患者的抑制控制能力存在情绪特异性损伤, 且损伤主要集中在前额皮层。这一结果可为后续开展 MDD 患者抑制控制训练以及前额叶靶向干预研究提供参考。

4.3 研究局限

尽管严格遵循 ALE 元分析的方法, 当前研究仍存在若干局限性。首先, 研究群体局限于重性抑郁症患者, 未纳入其他如: 抑郁风险者、阈下抑郁者、抑郁缓解期患者等群体, 这一方面导致最终纳入分析的文献数量较少, 另一方面也使研究结论的可推广性受限。考虑到不同病程 MDD 患者可能存在不同的生理与心理特征, 未来研究可纳入更多抑郁亚群进行更全面的分析。其次, 最终纳入群体的性别比例并不均衡, 女性患者多于男性, 这可能使男性患者在抑制控制任务上脑激活模式的特征无法凸显, 未来研究可以考虑将性别作为关键变量, 分别探讨男、女性 MDD 患者在抑制控制任务中共同与独特的脑激活模式。最后, 本研究仅针对任务态核磁研究进行了 ALE 元分析, 无法明确脑区间的协同作用, 未来研究可从功能连接的角度, 进行更深入的探究, 为抑郁症的诊断、治疗提供更丰富的生理机制的参考。

5 结论

通过 ALE 元分析的方法, 当前研究探索了 MDD 患者抑制控制能力损伤的特性及相应的神经机制。研究结果表明, 在情绪性抑制控制任务中, MDD 患者表现出右侧额中回的补偿性激活和右侧额下回、左侧额中回皮层的激活降低; 而在非情绪性抑制控制任务中, 未发现 MDD 患者与健康群体的差异脑区。这意味着 MDD 患者抑制控制能力损伤可能是情绪特异性的。研究结果不仅为探讨抑制控制对抑郁症的影响机制提供了方向性启发, 也为抑郁症认知训练及脑磁刺激干预方案的开发提供了理论参考。

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Emotion-specific or general? An ALE meta-analysis of inhibitory control impairments in patients with depression

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Abstract

Impaired inhibitory control is considered one of the key factors contributing to the progression of depression. Cognitive models of depression propose that deficits in inhibitory control weaken individuals' ability to regulate emotional information, thereby sustaining negative affect and exacerbating depressive symptoms. However, because patients with depression exhibit both emotional disturbances and widespread cognitive impairments, explaining inhibitory control deficits solely from an emotion-processing perspective may not fully capture their role in the pathophysiology of depression. Therefore, it is necessary to systematically integrate existing evidence to determine whether inhibitory control impairments in depression are primarily emotion-specific or reflect a more generalized cognitive dysfunction, thereby clarifying the pathways through which inhibitory control contributes to the onset and maintenance of depression. The present study conducted a meta-analysis to synthesize neuroimaging findings from emotional and non-emotional inhibitory control tasks in patients with depression, aiming to identify the characteristics and neural mechanisms of inhibitory control deficits.

Specifically, this study conducted an Activation Likelihood Estimation (ALE) meta-analysis of task-related neural activation differences between patients with major depressive disorder (MDD) and healthy controls (HC) during emotional and non-emotional inhibitory control tasks. Following a systematic literature search and rigorous screening, 19 task-based fMRI studies were included, involving 393 individuals with MDD and reporting 133 activation foci. Based on task type (emotional vs. non-emotional) and the direction of activation difference (MDD > HC vs. MDD < HC), these foci were classified into four datasets: emotional-MDD > HC, emotional-MDD < HC, non-emotional-MDD > HC, and non-emotional-MDD < HC. All coordinates were transformed into Montreal Neurological Institute (MNI) space prior to analysis, with Talairach coordinates reported in the original studies converted to MNI coordinates using GingerALE 2.6.3. Single ALE analyses were performed for each dataset using an uncorrected threshold of $p < 0.0001$ and a minimum cluster size of 200 mm³. Because the non-emotional-MDD < HC and non-emotional-MDD > HC datasets showed no significant convergent activation, contrast analyses between emotional and non-emotional inhibitory control tasks could not be performed.

The results showed that, during emotional inhibitory control tasks, individuals with MDD exhibited compensatory hyperactivation in the right middle frontal gyrus (34, 38, 32), and decreased activation convergence in the left middle frontal gyrus (-36, 40, 16) and right inferior frontal gyrus (50, 14, 18) relative to HC. By contrast, no significant convergent activation was observed for non-emotional inhibitory control tasks.

This meta-analysis advances our understanding of the pathophysiology of depression by revealing the characteristics of inhibitory control deficits. The findings indicate that depression is characterized by altered recruitment of prefrontal regions during emotional inhibitory control, supporting the view that inhibitory control deficits in depression are closely linked to emotional processing dysfunction. These results highlight a potential pathway through which impaired inhibitory control may contribute to the persistence of depressive symptoms and may inform the development of targeted cognitive and neurobiological interventions.

Keywords Major Depressive Disorder, inhibitory control, neural mechanism, ALE meta-analysis, emotion-specific