

失眠相关神经通路结构连接异常的磁共振研究进展

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摘 要

失眠是一种常见的睡眠障碍, 其发病机制与大脑多个神经通路的功能及结构连接异常密切相关, 其中又以边缘系统 - 皮质 - 基底神经节通路和前额叶 - 纹状体通路的异常最为突出。而结构连接作为神经通路的解剖学基础, 其异常可能是功能改变和临床症状产生的根源。既往研究已证实, 失眠患者在上述神经通路的重要组成脑区存在明显结构异常。边缘系统 - 皮质 - 基底神经节通路中的眶额叶、海马和丘脑等关键脑区的结构变化可能通过影响情绪调节和觉醒控制导致失眠。前额叶 - 纹状体通路中的尾状核、壳核和伏隔核能够通过调控多巴胺和腺苷等神经递质维持睡眠 - 觉醒周期的平衡, 其结构改变会打破这一平衡, 进而引发失眠。因此, 本文聚焦于结构连接层面, 综述并深入探讨边缘系统 - 皮质 - 基底神经节通路和前额叶 - 纹状体通路中多脑区的结构异常, 导致睡眠 - 觉醒调节障碍, 最终诱发失眠的具体机制。

关键词

失眠, 边缘系统 - 皮质 - 基底神经节通路, 前额叶 - 纹状体通路, 神经影像学

Advances in Magnetic Resonance Imaging (MRI) Research on Structural Connectivity Abnormalities in Neural Pathways Associated with Insomnia

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Abstract

Insomnia is a prevalent sleep disorder whose pathogenesis is closely associated with aberrant functional and structural connectivity across multiple neural pathways in the brain, with the most prominent alterations observed in the limbic-cortical-basal ganglia circuit and the prefrontal-striatal pathway. As the anatomical substrate of neural pathways, abnormal structural connectivity is considered to underlie functional alterations and the emergence of clinical symptoms. Accumulating neuroimaging evidence has demonstrated marked structural abnormalities in the key constituent regions of these two pathways among patients with insomnia. Structural changes in core nodes of the limbic-cortical-basal ganglia circuit, including the orbitofrontal cortex, hippocampus, and thalamus, may contribute to insomnia by impairing emotional regulation and arousal control. Within the prefrontal-striatal pathway, the caudate nucleus, putamen, and nucleus accumbens maintain the homeostasis of the sleep-wake cycle via regulating neurotransmitters such as dopamine and adenosine; structural alterations in these regions can disrupt this balance and precipitate the onset of insomnia. Accordingly, this review focuses on the dimension of structural connectivity, systematically summarizes and elaborates the mechanisms by which structural abnormalities across multiple brain regions in the two aforementioned pathways induce sleep-wake dysregulation and ultimately lead to the development of insomnia.

Keywords

Insomnia, Limbic-Cortical-Basal Ganglia Circuit, Fronto-Striatal Circuit, Neuroimaging

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1. 前言

失眠(insomnia)是一种以入睡困难、睡眠维持障碍、早醒、睡眠时间不足或睡眠效率低下为特征的睡眠障碍[1]。失眠在普通人群中的发病率较高,我国成年人失眠的发生率约为9.2%~11.2%,而在老年人群中,这一比例高达30%~40%[2]。失眠也是痴呆、抑郁症、焦虑症、糖尿病及心血管疾病等多种慢性疾病的重要危险因素[3]。近年来,神经影像学研究揭示失眠与大脑多种神经环路的功能及结构连接密切相关[4],其中边缘系统-皮质-基底节神经通路和前额叶-纹状体通路在失眠中发挥重要作用。本文基于解剖投射与核心功能双维度标准划分两条通路并分别论述:边缘系统-皮质-基底神经节通路指以海马、杏仁核等边缘结构为起点,经眶额叶投射至丘脑及基底节(尾状核、壳核)的闭合环路[5],主要负责情绪整合与全身性觉醒调控;前额叶-纹状体通路则界定为前额叶皮层(尤其是内侧前额叶与眶额叶)与纹状体亚区(伏隔核、尾状核、壳核)之间的双向投射[6],侧重奖赏评估与睡眠-节律的门控调节。两通路在眶额叶及腹侧纹状体存在解剖重叠,但功能偏倚各异。将其拆分为两个子系统讨论,旨在避免笼统分析掩盖功能异质性,前者更多对接“过度觉醒”假说,后者则为“奖赏-动机失衡”及节律门控障碍提供结构注解;同时,两条通路在连接组学中具有相对独立的拓扑属性,分别讨论有助于揭示各自在失眠发病中的差异化贡献,也为后续亚型分型与靶点筛选提供明确依据。现有神经影像学对失眠神经机制的研究多聚焦于功能连接异常,且已有充分论述,但结构连接作为神经通路的物理基础,其异常可能是功能改变和临床症状产生的根源。因此,本文聚焦于结构连接层面,旨在深入探讨上述两种通路的结构连接异常

及其与失眠神经生物学机制的内在联系。

2. 失眠的神经生物学机制

睡眠-觉醒周期的调节主要依赖于促觉醒和促睡眠两大系统[7]的动态平衡,以及促进觉醒的神经递质(如乙酰胆碱、去甲肾上腺素、多巴胺、组胺及食欲素等)和促进睡眠的神经递质(如 γ -氨基丁酸、褪黑素和腺苷等)发挥的协同作用[8]。而在失眠患者中,这一动态平衡可能被打破[9]。睡眠主要分为快速动眼睡眠和非快速动眼睡眠两个阶段。研究表明, γ -氨基丁酸(GABA)是大脑中主要的抑制性神经递质,通过抑制觉醒系统促进非快速动眼睡眠[10]。失眠患者中 GABA 水平的下降可能会削弱对于觉醒系统的抑制功能,从而导致过度觉醒状态[11]。过度觉醒假说是解释失眠的重要理论之一。该假说认为,失眠患者往往表现为躯体、皮质以及认知活动的过度觉醒状态,这种状态被认为是失眠发生的关键因素[12]。失眠的神经生物学机制涉及睡眠-觉醒周期调节失衡、神经递质紊乱以及过度觉醒等多个层面。随着神经影像学技术的进展,该技术为探究失眠的神经机制提供了新型非侵入性研究方法。研究发现,失眠患者中与过度觉醒相关的脑区,如前额叶皮质、下丘脑、海马和基底神经节区域表现出广泛的结构异常[13]-[15],而这些脑区可以归属于大脑中不同的神经通路。

3. 常用结构影像研究技术及其局限性

当前失眠脑结构连接的神经影像学研究主要依赖基于体素的形态测量学(voxel-based morphometry, VBM)与弥散张量成像(diffusion tensor imaging, DTI)。VBM 通过在全脑体素水平定量计算灰质体积与密度差异[16],已被广泛用于识别失眠患者眶额叶、海马、丘脑等关键脑区的灰质萎缩特征,但其结果易受分割算法、平滑核大小等预处理参数,以及皮层厚度、表面积与脑沟折叠模式个体差异的多重影响,仅能反映大体形态学改变,既无法区分神经元丢失、胶质细胞异常等微观病理机制,并且对伏隔核等小体积深部核团的细微结构变化检测效力也较为有限。DTI 基于水分子扩散的各向异性特征,通过各向异性分数等指标定量评估白质纤维束完整性[17],结合纤维束追踪技术可重建前额叶-纹状体、丘脑-额叶及内囊等关键通路的结构连接,为揭示白质微结构损伤提供了核心方法。然而该技术基于高斯扩散模型的固有假设,限制了其对轴突密度、髓鞘退变等精细微结构特征的检测灵敏度,同时难以精准解析纤维交叉、分叉等复杂解剖场景,纤维追踪结果也易受种子点选择、算法阈值设置的干扰。新兴的弥散峰度成像(diffusion kurtosis imaging, DKI)可通过量化非高斯扩散特征提升早期白质病理改变的检测敏感性,能够在一定程度上弥补传统 DTI 的技术局限[18],为后续研究提供了更优的技术选择。

4. 失眠相关神经通路结构连接异常

失眠的发病机制与特定神经通路的结构异常密切相关[19][20],主要体现在神经通路中关键灰质节点的体积改变与连接脑区间的白质纤维束完整性受损[4]。研究表明,失眠患者大脑白质完整性的破坏具有区域性特征,主要集中于额纹状通路、额丘脑通路、皮质-皮质网络及边缘系统,其中以内囊、放射冠、上纵束等纤维束的异常最为显著[21]。而在众多受累通路中,边缘系统-皮质-基底节神经通路与前额叶-纹状体通路的异常对睡眠-觉醒周期调节的影响极为重要[22][23],二者的关键灰质节点形态改变与白质纤维束完整性损伤是失眠病理机制中具有代表性的神经影像学特征。

4.1. 边缘系统-皮质-基底神经节通路结构连接异常

Haynes 等[5]首次提出边缘系统-皮质-基底节神经通路模型,其涵盖前额叶、顶叶、枕叶、扣带回、丘脑、海马、岛叶、杏仁体等脑区以及尾状核、壳核等基底节结构。近年来,该通路在失眠中的作用逐渐被揭示。吴筠凡等[22]对原发性失眠患者的脑网络展开研究,发现位于该神经通路的右侧眶内额上回、右

侧海马、右侧尾状核和双侧丘脑等核心节点的拓扑属性表现出显著的异常变化。这些结果提示, 该通路关键脑区的异常可能是失眠发病的核心环节。

眶额叶作为边缘系统的重要组成部分, 在情绪调节、奖励处理和决策制定中起到关键作用[24] [25]。眶额叶皮层接收包括丘脑、杏仁核在内的觉醒系统的广泛投射[26], 这种特殊的神经连接为其参与觉醒调控提供了结构基础。近年神经影像学研究显示, 失眠患者的左眶额叶灰质体积减少与失眠严重程度[15]以及较早觉醒[27]均呈负相关。Falgàs 等[28]研究表明, 腹侧眶额叶较小的皮层体积与更严重的失眠水平相关。此外, 值得注意的是, 眶额叶还参与热舒适度评估和最佳睡眠温度识别, 当该区域出现异常时, 患者可能无法准确感知适宜睡眠的环境温度, 进而诱发失眠, 这可能是失眠的潜在机制之一[27] [29]。

海马作为大脑中与认知表现和记忆形成密切相关的关键区域, 同样在睡眠-觉醒周期的调节中扮演着重要角色[30]。多数研究提示慢性失眠患者的海马体积表现出异常变化[31]。Riemann 等[32]研究发现, 失眠患者双侧海马体积显著减少。类似的, Koo 等[13]研究表明, 海马体积与睡眠质量和觉醒指数呈负相关。然而, 关于海马体积变化的研究结果并不一致。Leerssen 等[33]研究发现, 失眠患者与健康对照组之间的双侧海马体积并无显著差异。这种不一致性可能与研究方法、样本特征(如失眠持续时间、是否伴有认知功能障碍)以及海马的解剖和功能异质性有关[34]。

丘脑作为上行网状激活系统的关键部分, 在觉醒和睡眠控制中起双重作用[35]。丘脑的活动与非快速眼动睡眠到清醒的过渡、非快速眼动睡眠中出现的觉醒现象以及个体的警觉程度密切相关[36]-[38]。在睡眠期间丘脑能够筛选并投射信息到大脑皮层, 以维持睡眠的稳定性[39]。研究发现, 失眠患者双侧丘脑灰质体积显著减少[40], 会呈现出萎缩状态[13]。此外, 丘脑和皮质区域之间的结构连接异常也是导致失眠的潜在因素。Kang [41]等研究证明, 失眠患者左侧丘脑-额下回三角部白质束完整性降低, 且患者的认知损伤可能与该区域结构连接性降低及结构异常有关。

综上所述, 边缘系统-皮质-基底节神经通路的结构连接异常可能是诱发失眠的重要神经生物学机制。而眶额叶、海马和丘脑作为该回路的关键节点, 其体积和结构连接异常可能通过影响睡眠-觉醒周期控制, 进而导致失眠的发生。

4.2. 前额叶-纹状体通路结构连接异常

神经影像学研究为前额叶-纹状体通路的结构异常提供了直接证据: 一方面, 失眠患者眶额叶皮层的灰质体积显著降低[15] [27], 且额叶区域的灰质体积减少与前内囊中白质束完整性的降低有关[42]; 另一方面, Chen 等[23]选择纹状体作为种子点, 采用基于种子的分类和 DTI 概率束造影方法来评估失眠患者的白质连接, 研究发现前额叶-纹状体通路的结构连接强度下降, 且该下降与 PSQI 评分呈负相关。这一发现不仅证实了前额叶-纹状体通路结构异常与失眠的关联, 也为失眠诊断提供了潜在的影像学生物标志物。

前额叶-纹状体通路在睡眠-觉醒周期的调节、觉醒控制和执行功能中发挥着重要作用[43], 该通路的异常与失眠的病理生理学密切相关[44] [45]。纹状体是一个高度异质性的结构, 由空间上不重叠的三个区域组成: 尾状核、壳核和伏隔核[46]。它们在睡眠-觉醒周期的调节中扮演不同的角色: 背侧纹状体(尾状核和壳核)主要增强觉醒, 而腹侧纹状体(伏隔核)则促进睡眠[47]。

尾状核被认为是睡眠调节的关键脑区之一, 通过参与奖励感觉处理和皮质兴奋性调节[48]睡眠。研究证实, 尾状核的结构异常与失眠密切相关, 失眠患者的尾状核体积存在显著变化[49], 且该体积变化与睡眠持续时间呈正相关[50], 提示尾状核体积异常可能直接影响睡眠时长。

壳核作为背侧纹状体的组成部分之一, 接收来自多个皮层区域的传入信号, 并通过抑制性 GABA 能投射到苍白球和丘脑, 从而调节唤醒水平并促进皮质活动和觉醒[51]。在失眠人群中, 壳核的结构改变同

样与疾病显著相关:慢性失眠患者的壳核常表现出萎缩性变化,且这种变化与较高的觉醒率显著相关[13]。类似地,在心理生理学和反常性失眠患者中,也观察到壳核和尾状核体积减小的现象[49]。

伏隔核作为腹侧纹状体的核其在睡眠-觉醒周期调节中的作用更依赖神经递质的动态调控,且该作用已被大量动物实验所证实[52][53]。多巴胺和腺苷是调节睡眠-觉醒周期至关重要的两种神经递质,它们均在伏隔核中呈现高表达特性[54]。其中,多巴胺通过增强动机行为和奖赏效应参与觉醒维持,而腺苷则通过浓度积累抑制神经活动,促进睡眠稳态的建立,二者通过复杂的交互作用,共同介导睡眠-觉醒周期的动态平衡[55]。近年来,相关研究逐渐从动物模型扩展到人类失眠患者。Shao 等人[56]发现,失眠患者的右侧伏隔核体积显著增大,且双侧伏隔核与左内侧前额叶皮层之间的静息态功能连接增强,且这种功能连接的增强与患者的匹兹堡睡眠质量指数(Pittsburgh sleep quality index, PSQI 评分)呈显著相关。此外,伏隔核和内侧前额叶皮层中的多巴胺水平在清醒和快速眼动睡眠期间显著升高,而在非快速眼动睡眠期间则明显降低[57]。这些结果提示,伏隔核-内侧前额叶皮层通路的异常可能在睡眠-觉醒周期的调节中发挥了重要作用。

神经影像学研究揭示了前额叶-纹状体通路的结构异常在失眠中的关键作用,纹状体的灰质体积改变及其白质连接异常可能直接导致睡眠质量下降;左眶额叶灰质体积减少和前内囊白质束完整性受损,进一步破坏了额纹状体网络的拓扑结构;而额纹状体白质连接强度与失眠严重程度的负相关性,更为失眠提供了客观影像学生物标志物。这些发现从结构-功能多模态影像层面,系统阐释了前额叶-纹状体通路异常在失眠中的核心机制。

5. 失眠患者异质性及其对研究结果的影响

失眠患者群体的高度异质性,是导致当前神经影像学研究结果不一致、部分结论难以稳定重复的核心原因。其一,临床表型与病程异质性显著:入睡困难型、睡眠维持障碍型、早醒型等不同临床亚型,以及病程长短、症状严重程度的差异,可能对应差异化的脑结构连接异常模式,但多数研究将失眠患者作为同质群体整体分析,既掩盖了不同亚型特有的神经生物学机制,也是海马体积等指标在不同研究中结果存在分歧的关键因素。其二,共病混杂效应突出:失眠与抑郁症、焦虑症的精神共病率极高,且常伴随高血压、糖尿病等慢性躯体代谢疾病,而上述疾病本身即可诱发前额叶、海马、纹状体等脑区的结构改变。多数研究未对共病状态进行严格匹配与分层分析,导致脑结构异常的疾病归因存在明显混杂。其三,药物干扰因素未得到充分控制:长期使用苯二氮草类催眠药物或抗抑郁药物本身可能影响脑结构可塑性,但不同研究对用药人群的纳入与排除标准差异较大,且鲜有研究对药物种类、剂量及疗程进行分层,使得观察到的结构改变难以明确区分是疾病本身的病理特征还是药物作用的结果。因此,在解读现有文献结论及设计未来研究时,需充分考量上述混杂因素对结果效度的影响,以提升研究结论的可靠性与临床转化价值。

6. 总结

现有神经影像学研究已证实,边缘系统-皮质-基底神经节通路与前额叶-纹状体通路中眶额叶、海马、丘脑及纹状体等关键节点的灰质形态异常及白质纤维束完整性损害与失眠的发生密切相关,为过度觉醒等病理机制提供了结构层面的支撑。但当前研究以横断面观察为主,普遍存在因果时序不明、样本异质性较高、微观病理机制阐释不足、结构异常可逆性证据匮乏等局限。未来可围绕“通路结构损伤是失眠的前置易感因素”、“前额叶-纹状体连接强度可作为认知行为疗法或药物疗效的预测生物标志物,指导个体化治疗选择”、“不同失眠亚型存在特异性结构损伤模式”三个可检验假说开展前瞻性研究。临床层面可整合关键脑区体积与白质连接指标构建影像评估模型,用于失眠高危人群早期预警与生

物学亚型划分, 指导个体化干预, 推动失眠诊疗向精准化方向发展。

参考文献

- [1] 赵佳丽, 汤永红, 夏凤娟. 神经递质对原发性失眠的作用研究进展[J]. 中国临床神经科学, 2024, 32(2): 194-198.
- [2] 卢玉俊, 于小刚, 代晶晶, 等. 失眠机理的中西医研究进展[J]. 中国社区医师, 2021, 37(14): 8-9.
- [3] Aquino, G., Benz, F., Dressle, R.J., Gemignani, A., Alfi, G., Palagini, L., *et al.* (2024) Towards the Neurobiology of Insomnia: A Systematic Review of Neuroimaging Studies. *Sleep Medicine Reviews*, **73**, Article ID: 101878. <https://doi.org/10.1016/j.smr.2023.101878>
- [4] Van Someren, E.J.W. (2021) Brain Mechanisms of Insomnia: New Perspectives on Causes and Consequences. *Physiological Reviews*, **101**, 995-1046. <https://doi.org/10.1152/physrev.00046.2019>
- [5] Haynes, W.I.A., Clair, A., Fernandez-Vidal, S., Gholipour, B., Morgiève, M. and Mallet, L. (2018) Altered Anatomical Connections of Associative and Limbic Cortico-Basal-Ganglia Circuits in Obsessive-Compulsive Disorder. *European Psychiatry*, **51**, 1-8. <https://doi.org/10.1016/j.eurpsy.2018.01.005>
- [6] Gopinath, K., Ringe, W., Goyal, A., Carter, K., Dinse, H.R., Haley, R., *et al.* (2011) Striatal Functional Connectivity Networks Are Modulated by fMRI Resting State Conditions. *NeuroImage*, **54**, 380-388. <https://doi.org/10.1016/j.neuroimage.2010.07.021>
- [7] Dopheide, J.A. (2020) Insomnia Overview: Epidemiology, Pathophysiology, Diagnosis and Monitoring, and Nonpharmacologic Therapy. *The American Journal of Managed Care*, **26**, S76-S84. <https://doi.org/10.37765/ajmc.2020.42769>
- [8] Jones, B.E. (2019) Arousal and Sleep Circuits. *Neuropsychopharmacology*, **45**, 6-20. <https://doi.org/10.1038/s41386-019-0444-2>
- [9] Levenson, J.C., Kay, D.B. and Buysse, D.J. (2015) The Pathophysiology of Insomnia. *Chest*, **147**, 1179-1192. <https://doi.org/10.1378/chest.14-1617>
- [10] España, R.A. and Scammell, T.E. (2011) Sleep Neurobiology from a Clinical Perspective. *Sleep*, **34**, 845-858.
- [11] Morgan, P.T., Pace-Schott, E.F., Mason, G.F., Forselius, E., Fasula, M., Valentine, G.W., *et al.* (2012) Cortical GABA Levels in Primary Insomnia. *Sleep*, **35**, 807-814. <https://doi.org/10.5665/sleep.1880>
- [12] Riemann, D., Spiegelhalder, K., Feige, B., Voderholzer, U., Berger, M., Perlis, M., *et al.* (2010) The Hyperarousal Model of Insomnia: A Review of the Concept and Its Evidence. *Sleep Medicine Reviews*, **14**, 19-31. <https://doi.org/10.1016/j.smr.2009.04.002>
- [13] Koo, D.L., Shin, J., Lim, J., Seong, J. and Joo, E.Y. (2017) Changes in Subcortical Shape and Cognitive Function in Patients with Chronic Insomnia. *Sleep Medicine*, **35**, 23-26. <https://doi.org/10.1016/j.sleep.2017.04.002>
- [14] Qiu, M., Vetrivelan, R., Fuller, P.M. and Lu, J. (2010) Basal Ganglia Control of Sleep-Wake Behavior and Cortical Activation. *European Journal of Neuroscience*, **31**, 499-507. <https://doi.org/10.1111/j.1460-9568.2009.07062.x>
- [15] Altena, E., Vrenken, H., Van Der Werf, Y.D., van den Heuvel, O.A. and Van Someren, E.J.W. (2010) Reduced Orbitofrontal and Parietal Gray Matter in Chronic Insomnia: A Voxel-Based Morphometric Study. *Biological Psychiatry*, **67**, 182-185. <https://doi.org/10.1016/j.biopsych.2009.08.003>
- [16] Ashburner, J. and Friston, K.J. (2000) Voxel-Based Morphometry—The Methods. *NeuroImage*, **11**, 805-821. <https://doi.org/10.1006/nimg.2000.0582>
- [17] Macey, P.M., Kumar, R., Woo, M.A., *et al.* (2008) Brain Structural Changes in Obstructive Sleep Apnea. *Sleep*, **31**, 967-977.
- [18] Marrale, M., Collura, G., Brai, M., Toschi, N., Midiri, F., La Tona, G., *et al.* (2015) Physics, Techniques and Review of Neuroradiological Applications of Diffusion Kurtosis Imaging (DKI). *Clinical Neuroradiology*, **26**, 391-403. <https://doi.org/10.1007/s00062-015-0469-9>
- [19] Jespersen, K.V., Stevner, A., Fernandes, H., Sørensen, S.D., Van Someren, E., Kringelbach, M., *et al.* (2019) Reduced Structural Connectivity in Insomnia Disorder. *Journal of Sleep Research*, **29**, e12901. <https://doi.org/10.1111/jsr.12901>
- [20] Fasiello, E., Gorgoni, M., Scarpelli, S., Alfonsi, V., Ferini Strambi, L. and De Gennaro, L. (2022) Functional Connectivity Changes in Insomnia Disorder: A Systematic Review. *Sleep Medicine Reviews*, **61**, Article ID: 101569. <https://doi.org/10.1016/j.smr.2021.101569>
- [21] Sanjari Moghaddam, H., Mohammadi, E., Dolatshahi, M., Mohebi, F., Ashrafi, A., Khazaie, H., *et al.* (2021) White Matter Microstructural Abnormalities in Primary Insomnia: A Systematic Review of Diffusion Tensor Imaging Studies. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, **105**, Article ID: 110132. <https://doi.org/10.1016/j.pnpbp.2020.110132>
- [22] Wu, Y., Liu, M., Zeng, S., Ma, X., Yan, J., Lin, C., *et al.* (2018) Abnormal Topology of the Structural Connectome in

- the Limbic Cortico-Basal-Ganglia Circuit and Default-Mode Network among Primary Insomnia Patients. *Frontiers in Neuroscience*, **12**, Article 860. <https://doi.org/10.3389/fnins.2018.00860>
- [23] Chen, L., Shao, Z., Xu, Y., Wang, S., Zhang, M., Liu, S., *et al.* (2021) Disrupted Frontostriatal Connectivity in Primary Insomnia: A DTI Study. *Brain Imaging and Behavior*, **15**, 2524-2531. <https://doi.org/10.1007/s11682-021-00454-3>
- [24] Rolls, E.T., Cheng, W. and Feng, J. (2020) The Orbitofrontal Cortex: Reward, Emotion and Depression. *Brain Communications*, **2**, fcaa196. <https://doi.org/10.1093/braincomms/fcaa196>
- [25] Kringelbach, M.L. (2005) The Human Orbitofrontal Cortex: Linking Reward to Hedonic Experience. *Nature Reviews Neuroscience*, **6**, 691-702. <https://doi.org/10.1038/nrn1747>
- [26] Rolls, E.T. (1996) The Orbitofrontal Cortex. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences*, **351**, 1433-1444. <https://doi.org/10.1098/rstb.1996.0128>
- [27] Stoffers, D., Moens, S., Benjamins, J., van Tol, M., Penninx, B.W.J.H., Veltman, D.J., *et al.* (2012) Orbitofrontal Gray Matter Relates to Early Morning Awakening: A Neural Correlate of Insomnia Complaints? *Frontiers in Neurology*, **3**, Article 105. <https://doi.org/10.3389/fneur.2012.00105>
- [28] Falgàs, N., Illán-Gala, I., Allen, I.E., Mumford, P., Essanaa, Y.M., Le, M.M., *et al.* (2021) Specific Cortical and Subcortical Grey Matter Regions Are Associated with Insomnia Severity. *PLOS ONE*, **16**, e0252076. <https://doi.org/10.1371/journal.pone.0252076>
- [29] Raymann, R.J. and Van Someren, E.J. (2008) Diminished Capability to Recognize the Optimal Temperature for Sleep Initiation May Contribute to Poor Sleep in Elderly People. *Sleep*, **31**, 1301-1309.
- [30] Bird, C.M. and Burgess, N. (2008) The Hippocampus and Memory: Insights from Spatial Processing. *Nature Reviews Neuroscience*, **9**, 182-194. <https://doi.org/10.1038/nrn2335>
- [31] Joo, E.Y., Kim, H., Suh, S. and Hong, S.B. (2014) Hippocampal Substructural Vulnerability to Sleep Disturbance and Cognitive Impairment in Patients with Chronic Primary Insomnia: Magnetic Resonance Imaging Morphometry. *Sleep*, **37**, 1189-1198. <https://doi.org/10.5665/sleep.3836>
- [32] Riemann, D., Voderholzer, U., Spiegelhalter, K., Hornyak, M., Buysse, D.J., Nissen, C., *et al.* (2007) Chronic Insomnia and MRI-Measured Hippocampal Volumes: A Pilot Study. *Sleep*, **30**, 955-958. <https://doi.org/10.1093/sleep/30.8.955>
- [33] Leerssen, J., Wassing, R., Ramautar, J.R., Stoffers, D., Lakbila-Kamal, O., Perrier, J., *et al.* (2019) Increased Hippocampal-Prefrontal Functional Connectivity in Insomnia. *Neurobiology of Learning and Memory*, **160**, 144-150. <https://doi.org/10.1016/j.nlm.2018.02.006>
- [34] Ma, X., Jiang, G., Tian, J., Liu, M., Fang, J., Xu, Y., *et al.* (2020) Convergent and Divergent Functional Connectivity alterations of Hippocampal Subregions between Short-Term and Chronic Insomnia Disorder. *Brain Imaging and Behavior*, **15**, 986-995. <https://doi.org/10.1007/s11682-020-00306-6>
- [35] Wijdicks, E.F.M. (2019) The Ascending Reticular Activating System. *Neurocritical Care*, **31**, 419-422. <https://doi.org/10.1007/s12028-019-00687-7>
- [36] Balkin, T.J. (2002) The Process of Awakening: A PET Study of Regional Brain Activity Patterns Mediating the Re-Establishment of Alertness and Consciousness. *Brain*, **125**, 2308-2319. <https://doi.org/10.1093/brain/awf228>
- [37] Falahpour, M., Chang, C., Wong, C.W. and Liu, T.T. (2018) Template-Based Prediction of Vigilance Fluctuations in Resting-State fMRI. *NeuroImage*, **174**, 317-327. <https://doi.org/10.1016/j.neuroimage.2018.03.012>
- [38] Zou, G., Xu, J., Zhou, S., Liu, J., Su, Z.H., Zou, Q., *et al.* (2019) Functional MRI of Arousals in Nonrapid Eye Movement Sleep. *Sleep*, **43**, zsz218. <https://doi.org/10.1093/sleep/zsz218>
- [39] Del Felice, A., Formaggio, E., Storti, S.F., Fiaschi, A. and Manganotti, P. (2012) The Gating Role of the Thalamus to Protect Sleep: An f-MRI Report. *Sleep Medicine*, **13**, 447-449. <https://doi.org/10.1016/j.sleep.2011.07.021>
- [40] Li, M., Wang, R., Zhao, M., Zhai, J., Liu, B., Yu, D., *et al.* (2018) Abnormalities of Thalamus Volume and Resting State Functional Connectivity in Primary Insomnia Patients. *Brain Imaging and Behavior*, **13**, 1193-1201. <https://doi.org/10.1007/s11682-018-9932-y>
- [41] Kang, J.M., Joo, S.W., Son, Y., Kim, H., Ko, K., Lee, J.S., *et al.* (2018) Low White-Matter Integrity between the Left Thalamus and Inferior Frontal Gyrus in Patients with Insomnia Disorder. *Journal of Psychiatry and Neuroscience*, **43**, 366-374. <https://doi.org/10.1503/jpn.170195>
- [42] Spiegelhalter, K., Regen, W., Prem, M., Baglioni, C., Nissen, C., Feige, B., *et al.* (2013) Reduced Anterior Internal Capsule White Matter Integrity in Primary Insomnia. *Human Brain Mapping*, **35**, 3431-3438. <https://doi.org/10.1002/hbm.22412>
- [43] Lu, F., Liu, C., Lu, S., Tang, L., Tie, C., Zhang, J., *et al.* (2017) Disrupted Topology of Frontostriatal Circuits Is Linked to the Severity of Insomnia. *Frontiers in Neuroscience*, **11**, Article 214. <https://doi.org/10.3389/fnins.2017.00214>
- [44] Cano, G., Mochizuki, T. and Saper, C.B. (2008) Neural Circuitry of Stress-Induced Insomnia in Rats. *The Journal of*

- Neuroscience*, **28**, 10167-10184. <https://doi.org/10.1523/jneurosci.1809-08.2008>
- [45] Nofzinger, E.A., Buysse, D.J., Germain, A., Price, J.C., Miewald, J.M. and Kupfer, D.J. (2004) Functional Neuroimaging Evidence for Hyperarousal in Insomnia. *American Journal of Psychiatry*, **161**, 2126-2128. <https://doi.org/10.1176/appi.ajp.161.11.2126>
 - [46] De Havas, J.A., Parimal, S., Soon, C.S. and Chee, M.W.L. (2012) Sleep Deprivation Reduces Default Mode Network Connectivity and Anti-Correlation during Rest and Task Performance. *NeuroImage*, **59**, 1745-1751. <https://doi.org/10.1016/j.neuroimage.2011.08.026>
 - [47] Qiu, M., Liu, W., Qu, W., Urade, Y., Lu, J. and Huang, Z. (2012) The Role of Nucleus Accumbens Core/Shell in Sleep-Wake Regulation and Their Involvement in Modafinil-Induced Arousal. *PLOS ONE*, **7**, e45471. <https://doi.org/10.1371/journal.pone.0045471>
 - [48] Jiang, C., Cai, S. and Zhang, L. (2023) Functional Connectivity of White Matter and Its Association with Sleep Quality. *Nature and Science of Sleep*, **15**, 287-300. <https://doi.org/10.2147/nss.s406120>
 - [49] Emamian, F., Mahdipour, M., Noori, K., Rostampour, M., Mousavi, S.B., Khazaie, H., *et al.* (2021) Alterations of Subcortical Brain Structures in Paradoxical and Psychophysiological Insomnia Disorder. *Frontiers in Psychiatry*, **12**, Article 661286. <https://doi.org/10.3389/fpsyt.2021.661286>
 - [50] Jones, N.F. and Ikuta, T. (2022) Sleep Duration Is Associated with Caudate Volume and Executive Function. *Brain Imaging and Behavior*, **16**, 2601-2607. <https://doi.org/10.1007/s11682-022-00715-9>
 - [51] Vetrivelan, R., Qiu, M., Chang, C. and Lu, J. (2010) Role of Basal Ganglia in Sleep-Wake Regulation: Neural Circuitry and Clinical Significance. *Frontiers in Neuroanatomy*, **4**, Article 145. <https://doi.org/10.3389/fnana.2010.00145>
 - [52] Barik, S. and de Beaurepaire, R. (2005) Dopamine D3 Modulation of Locomotor Activity and Sleep in the Nucleus Accumbens and in Lobules 9 and 10 of the Cerebellum in the Rat. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, **29**, 718-726. <https://doi.org/10.1016/j.pnpbp.2005.04.020>
 - [53] Oishi, Y., Xu, Q., Wang, L., Zhang, B., Takahashi, K., Takata, Y., *et al.* (2017) Slow-Wave Sleep Is Controlled by a Subset of Nucleus Accumbens Core Neurons in Mice. *Nature Communications*, **8**, Article No. 734. <https://doi.org/10.1038/s41467-017-00781-4>
 - [54] Oishi, Y. and Lazarus, M. (2017) The Control of Sleep and Wakefulness by Mesolimbic Dopamine Systems. *Neuroscience Research*, **118**, 66-73. <https://doi.org/10.1016/j.neures.2017.04.008>
 - [55] 刘炜. 伏隔核在睡眠觉醒调节中的作用[D]: [博士学位论文]. 上海: 复旦大学, 2012.
 - [56] Shao, Z., Xu, Y., Chen, L., Wang, S., Zhang, M., Liu, S., *et al.* (2020) Dysfunction of the NAc-mPFC Circuit in Insomnia Disorder. *NeuroImage: Clinical*, **28**, Article ID: 102474. <https://doi.org/10.1016/j.nicl.2020.102474>
 - [57] Léna, I., Parrot, S., Deschaux, O., Muffat-Joly, S., Sauvinet, V., Renaud, B., *et al.* (2005) Variations in Extracellular Levels of Dopamine, Noradrenaline, Glutamate, and Aspartate across the Sleep-Wake Cycle in the Medial Prefrontal Cortex and Nucleus Accumbens of Freely Moving Rats. *Journal of Neuroscience Research*, **81**, 891-899. <https://doi.org/10.1002/jnr.20602>