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慢性失眠障碍患者钙调蛋白、神经递质与多导睡眠图的相关性

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[摘 要] 目的：慢性失眠障碍(chronic insomnia disorder，CID)是一种常见的睡眠障碍性疾病，可引起多种健康问题。神经递质，尤其是γ-氨基丁酸(gamma-aminobutyric acid，GABA)、谷氨酸(glutamic acid，Glu)、5-羟色胺(5-hydroxytryptamine，5-HT)在睡眠调节中发挥关键作用，而钙调蛋白(calmodulin，CaM)参与其调控过程。然而，目前尚缺乏关于CaM及相关神经递质水平与多导睡眠图(polysomnography，PSG)参数间相关性的系统性研究，上述指标对CID的诊断价值亦不明确。本研究旨在比较CID患者与健康体检者的上述生化指标差异，分析其与PSG参数的相关性，并评估其对CID的诊断效能，以期为CID的辅助诊断提供新的血液生物标志物，并探索其临床应用潜力。**方法：**纳入2017年1月至2019年4月于南华大学附属第二医院神经内科就诊的CID患者103例，同期的健康体检者102例为健康对照(healthy controls，HCs)。采用双抗体夹心酶联免疫吸附试验(enzyme-linked immunosorbent assay，ELISA)检测2组血清GABA、Glu、5-HT水平，比较2组差异，并分析上述指标与PSG参数的相关性，进一步绘制受试者操作特征(receiver operating characteristic，ROC)曲线评估其诊断效能。**结果：**与HCs组相比，CID组血清CaM、GABA、5-HT水平和GABA与Glu的比值(GABA/Glu)均显著降低，而Glu水平显著升高(均P<0.05)。在CID组，血清GABA/Glu与N3期睡眠持续时间呈正相关(r=0.225，P=0.022)，血清5-HT水平与睡眠效率呈正相关(r=0.215，P=0.029)。血清CaM、GABA/Glu和5-HT诊断CID的曲线下面积(areas under the curve，AUC)分别为0.616、0.609和0.790(均P<0.05)。其中，5-HT的诊断效能最佳，AUC为0.790；当血清5-HT水平低于125.249 ng/mL时，诊断CID的准确率达79.0%。基于上述3个指标构建的Logistic回归联合诊断模型可显著提升诊断效能，AUC[95% 置信区间(confidence interval，*CI*)]达0.800(0.739~0.861)，敏感度为81.4%，特异度为68.0%(P<0.01)。**结论：**CID患者血清CaM、GABA、5-HT水平和GABA/Glu均显著降低，Glu水平显著升高。CID患者血清GABA/Glu与N3期持续时间呈正相关，5-HT水平与睡眠效率呈正相关。血清CaM、GABA/Glu及5-HT对CID具有诊断价值，基于3者的联合诊断模型的诊断效能强于单个指标。

[关键词] 慢性失眠障碍；钙调蛋白；γ-氨基丁酸；谷氨酸；5-羟色胺；多导睡眠图

Correlations of calmodulin and neurotransmitters with polysomnographic parameters in patients with chronic insomnia disorder

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ABSTRACT

Objective: Chronic insomnia disorder (CID) is a common sleep disorder that can cause a variety of health problems. Neurotransmitters, particularly gamma-aminobutyric acid (GABA), glutamate (Glu), and 5-hydroxytryptamine (5-HT), play key roles in sleep regulation, and calmodulin (CaM) is involved in their regulatory processes. However, systematic studies examining the correlations of CaM and related neurotransmitter levels with polysomnographic (PSG) parameters are currently lacking, and the diagnostic value of these indicators for CID remains unclear. This study aims to compare biochemical indicators between patients with CID and healthy controls (HCs), analyze their correlations with PSG parameters, and evaluate their diagnostic performance for CID, with the goal of identifying novel blood biomarkers for the auxiliary diagnosis of CID and exploring their potential clinical applications.

Methods: A total of 103 patients with CID who attended the Department of Neurology of the Second Affiliated Hospital of University of South China between January 2017 and April 2019 and 102 HCs who underwent health examinations during the same period were enrolled. Serum levels of CaM, GABA, Glu, and 5-HT were measured by enzyme-linked immunosorbent assay (ELISA) and compared between the 2 groups. Correlations between these indicators and PSG parameters were analyzed, and receiver operating characteristic (ROC) curves were generated to evaluate their diagnostic performance.

Results: Compared with the HC group, the CID group had significantly lower serum CaM, GABA, and 5-HT levels and ratio of GABA to Glu (GABA/Glu), but significantly higher Glu levels (all $P<0.05$). In the CID group, the serum GABA/Glu was positively correlated with N3 sleep duration ($r=0.225$, $P=0.022$), and serum 5-HT levels were positively correlated with sleep efficiency ($r=0.215$, $P=0.029$). The areas under the curve (AUCs) for serum CaM, the GABA/Glu, and 5-HT in diagnosing CID were 0.616, 0.609, and 0.790, respectively (all $P<0.05$). Among these indicators, 5-HT demonstrated the best diagnostic performance, with an AUC of 0.790. At a serum 5-HT cutoff value of less than 125.249 ng/mL, the diagnostic accuracy for CID was 79.0%. A combined diagnostic model constructed using Logistic regression based on these 3 indicators significantly improved diagnostic performance, yielding an AUC of 0.800 [95% confidence interval (*CI*) 0.739 to 0.861], a sensitivity of 81.4%, and a specificity of 68.0% ($P<0.01$).

Conclusion: Patients with CID had significantly lower serum CaM, GABA, and 5-HT levels and GABA/Glu and significantly higher Glu levels. In patients with CID, the serum GABA/Glu was positively correlated with N3 sleep duration, whereas the serum 5-HT level was positively correlated with sleep efficiency. Serum CaM, the GABA/Glu, and 5-HT have diagnostic value for CID, and a combined diagnostic model incorporating all 3 indicators has better diagnostic performance than any individual indicator.

KEY WORDS chronic insomnia disorder; calmodulin; gamma-aminobutyric acid; glutamate; 5-hydroxytryptamine; polysomnography

慢性失眠障碍(chronic insomnia disorder，CID)是临床上最常见的睡眠障碍之一，以入睡困难、睡眠维持困难或早醒为主要特征，并伴有日间功能损害。作为一种常见的睡眠障碍，CID全球成人的患病率约为1/3[1]，可引发多种健康问题，包括认知功能减退[2]、焦虑抑郁[3]、免疫功能紊乱[4]、肥胖风险增

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加[5]、衰弱[6]等。

研究[7-8]表明，神经递质在睡眠调节中起关键作用。γ-氨基丁酸(gamma-aminobutyric acid，GABA)是广泛存在的抑制性神经递质，而谷氨酸(glutamic acid，Glu)作为主要兴奋性神经递质，可在谷氨酸脱羧酶的作用下转化为GABA。二者共同调控睡眠-觉醒周期，其功能紊乱可能导致睡眠障碍。GABA与Glu的比值(GABA/Glu)可用来评估中枢神经系统功能兴奋-抑制平衡[9]。5-羟色胺(5-hydroxytryptamine，5-HT)，又称血清素，作为“睡眠诱导因子”，参与睡眠启动与维持、认知、情绪调节等功能[10]，其水平变化与睡眠密切相关[11-12]。钙调蛋白(calmodulin，CaM)是一种高度保守的钙结合蛋白。近年来，越来越多的研究[13-14]提示钙信号通路在睡眠-觉醒调控中发挥关键作用。研究[15-17]证实，Ca^{2+}/CaM依赖性通路对睡眠具有重要的调节作用，且CaM参与神经递质调控过程。多导睡眠图(polysomnography，PSG)是客观量化CID患者睡眠结构、识别主客观睡眠差异的临床金标准。然而，目前缺乏CaM及神经递质(GABA、Glu、5-HT)与CID患者PSG参数的相关性研究，亦未明确其对CID的诊断价值。

本研究旨在比较CID患者与健康对照者血清CaM、GABA、Glu及5-HT水平差异，分析上述血液指标与PSG参数的相关性，并评估CaM、GABA/Glu及5-HT对CID的诊断价值。

1 对象与方法

1.1 伦理声明

本研究为横断面研究，研究方案已获南华大学附属第二医院(以下简称“我院”)伦理委员会批准(审批号：2016-02-0001)。所有研究对象均签署书面知情同意书。

1.2 对象

纳入2017年1月至2019年4月于我院神经内科就诊的103例CID患者为CID组，另在我院体检中心招募同期健康体检者作为健康对照(healthy controls，HCs)组。所有研究对象均由2名经过培训的高年资神经内科医师根据国际睡眠障碍分类第3版修订本(International Classification of Sleep Disorders, 3rd Edition: Text Revision，ICSD-3-TR)[18]中慢性失眠的诊断标准进行评估。

CID组纳入标准：1)年龄为18~80岁；2)符合ICSD-3-TR中慢性失眠的诊断标准；3)经PSG确诊；4)受教育年限≥7年，无认知理解障碍；5)签署知情同意书。

HCs组纳入标准：1)年龄为18~80岁；2)匹兹堡睡眠质量指数(Pittsburgh sleep quality index，PSQI)评分≤5且无失眠相关主诉；3)受教育年限≥7年，无认知理解障碍；4)签署知情同意书。

CID组及HCs组排除标准：1)合并神经系统疾病(如急性脑卒中、癫痫、阿尔茨海默病、帕金森病)；2)合并中重度精神疾病(如抑郁、焦虑)；3)合并其他睡眠障碍(如不宁腿综合征、睡眠行为异常、中重度阻塞性睡眠呼吸暂停低通气综合征)；4)近期有重大情感创伤史或使用精神活性药物；5)处于妊娠期或哺乳期。为控制人口学变量的影响，对HCs组与CID组研究对象在年龄、性别上进行了匹配。

1.3 方法

1.3.1 一般临床资料收集

收集所有参与者的性别、年龄等人口统计学特征。

1.3.2 血清样本采集与检测

采集所有参与者清晨空腹肘前静脉血3 mL，以3 000 r/min离心20 min，收集血清0.5 mL，于−80 ℃冰箱保存备用。采用双抗体夹心酶联免疫吸附试验(enzyme-linked immunosorbent assay，ELISA)检测血清CaM、GABA、Glu及5-HT水平。人CaM ELISA试剂盒、5-HT ELISA试剂盒均购自武汉伊莱瑞特生物科技股份有限公司，人GABA ELISA试剂盒和谷氨酸检测试剂盒均购自南京建成生物工程研究所有限公司。所有操作步骤严格按照说明书执行。

1.3.3 CID组睡眠状况的评估

对CID组患者进行一整夜的PSG监测，评估患者的睡眠状况。PSG的判读依据ICSD-3-TR。主要纳入的PSG参数包括呼吸相关参数[睡眠呼吸暂停低通气指数(apnea-hypopnea index，AHI)、最低血氧饱和度]和睡眠结构参数[入睡后清醒时间、总睡眠时间、睡眠效率、睡眠潜伏期、快速眼动(rapid eye movement，REM)期潜伏期、清醒期持续时间、REM

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期和非快速眼动(non-rapid eye movement，NREM)期(NREM的1、2、3期简称为N1期、N2期、N3期)的持续时间，以及各睡眠时间占总睡眠时间的比例]。

1.4 统计学处理

所有数据采用SPSS 26.0统计学软件及Free Statistics (2.2.0)软件进行统计分析。数据集完整无缺失值，数据处理原则如下：符合正态分布的计量资料以均数±标准差表示，组间比较采用独立样本t检验；非正态分布的连续变量以中位数(第1四分位数，第3四分位数)表示，组间比较采用Mann-Whitney U检验；分类变量以频数(构成比)表示，组间比较采用χ^2检验。采用Pearson积差相关分析法进行相关性分析。基于Logistic回归构建联合诊断模型。为评估各指标和联合诊断模型的判别效能，绘制受试者操作特征(receiver operating characteristic，ROC)曲线，并报告曲线下面积(area under the curve，AUC)。P<0.05为差异有统计学意义。

2 结 果

2.1 基本情况

根据纳入及排除标准，共纳入103例CID患者、102例HCs。2组在性别及年龄的分布上差异均无统计学意义(均P>0.05)。CID组血清CaM、GABA、5-HT水平及GABA/Glu均显著低于HCs组(均P<0.05)，而Glu水平显著高于HCs组(P<0.05，表1)。

2.2 CID组血液指标与PSG参数相关性

采用Pearson积差相关分析法分析血清指标CaM、GABA、Glu、GABA/Glu、5-HT与PSG参数的相关性结果显示，CID组患者的GABA/Glu与N3期睡眠持续时间呈正相关(r=0.225，P=0.022)，血清5-HT水平与睡眠效率呈正相关(r=0.215，P=0.029；表2、图1)。

表1 CID组和HCs组的人口学特征及血液指标比较

Table 1 Comparison of demographic characteristics and blood indices between the CID group and the HCs group

组别	n	男性/[例(%)]	年龄/岁	CaM/(pg·mL^{-1})	GABA/(nmol·L^{-1})	Glu/(μmol·L^{-1})	GABA/Glu	5-HT/(ng·mL^{-1})
CID组	103	45(43.7)	52.6±11.8	36.5±8.5	3 231.6±1421.5	59.0±27.9	57.0(35.8, 91.3)	103.6±47.01
HCs组	102	45(44.1)	51.5±13.1	39.8±6.9	3 783.0±2 191.9	51.6±24.3	70.2(45.4, 116.6)	152.6±43.4
总体人群	205	90(43.9)	52.1±12.5	38.2±7.9	3 506.0±1 861.5	55.3±26.4	62.3(39.2, 107.0)	128.0±51.4
$t/U/\chi^2$		0.004	0.385	9.359	4.575	4.022	7.326	60.068
P		0.951	0.536	0.003	0.034	0.046	0.007	<0.001

正态分布的计量资料以均数±标准差表示，组间比较采用独立样本t检验；非正态分布的连续变量以中位数(第1四分位数，第3四分位数)表示，组间比较采用Mann-Whitney U检验；分类变量以频数(构成比)表示，组间比较采用χ^2检验。CID：慢性失眠障碍；HCs：健康对照；CaM：钙调蛋白；GABA：γ-氨基丁酸；Glu：谷氨酸；5-HT：5-羟色胺。

2.3 血液指标对CID患者的诊断效能

通过ROC曲线分析评估血清CaM、GABA/Glu及5-HT对CID的诊断价值(表3)。血清CaM、GABA/Glu、5-HT的AUC[95%置信区间(confidence interval，CI)]分别为0.616(0.539~0.692)、0.609(0.533~0.686)、0.790(0.726~0.854)(均P<0.01)。结果表明血清CaM、GABA/Glu、5-HT对区分CID患者与健康人群均具有统计学意义，其中5-HT的诊断效能最优。当血清5-HT截断值为125.249 ng/mL时，Youden指数为0.551，敏感度为75.7%，特异度为79.4%，诊断准确率为79.0%。基于Logistic回归构建的联合诊断模型(Model 1)可显著提升诊断效能，AUC为0.800(0.739~0.861)，敏感度为81.4%，特异度为68.0%。

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表2　CID组血清指标与PSG参数的相关性分析

Table 2　Correlation analysis of the blood indices and PSG parameters in CID group

PSG参数	CaM/(pg·mL^{-1})	GABA/(nmol·L^{-1})	Glu/(μmol·L^{-1})	GABA/Glu	5-HT/(ng·mL^{-1})
AHI	−0.020	0.057	0.094	−0.046	0.089
最低血氧饱和度	−0.053	−0.050	0.058	−0.016	−0.007
入睡后清醒时间	0.029	−0.090	0.098	−0.106	−0.101
总睡眠时间	−0.142	0.097	0.010	0.085	0.110
睡眠效率	−0.072	0.068	−0.135	0.118	0.215*
睡眠潜伏期	0.138	−0.051	0.045	−0.033	−0.118
REM期潜伏期	−0.056	−0.003	0.045	0.017	−0.116
清醒期持续时间	0.061	−0.103	0.016	−0.072	−0.075
REM期持续时间	−0.058	0.161	0.074	0.118	0.138
REM期占比	0.119	0.136	−0.087	0.174	0.086
NREM期					
N1期持续时间	−0.085	0.062	0.015	−0.015	0.059
N1期占比	−0.040	0.007	0.013	−0.064	−0.061
N2期持续时间	−0.079	0.024	0.006	−0.053	0.040
N2期占比	−0.028	−0.104	0.007	−0.180	−0.115
N3期持续时间	−0.034	0.079	−0.037	0.225*	0.104
N3期占比	0.022	0.011	−0.039	0.164	0.071

采用Pearson积差相关分析法进行相关性分析。*P<0.05。AHI：睡眠呼吸暂停低通气指数；REM：快速眼动；NREM：非快速眼动。

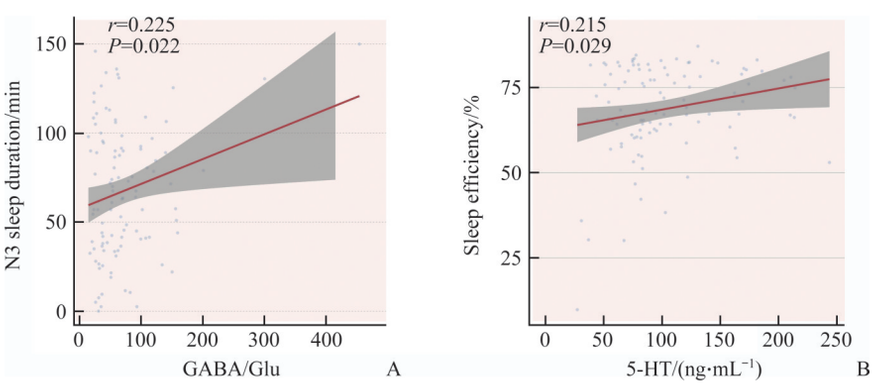


图1　CID组患者血清GABA/Glu及5-HT水平与PSG参数的相关性散点图

Figure 1　Scatter plots of correlations between serum biomarkers and PSG parameters in the CID group

A: Scatter plots of correlation between the serum GABA/Glu and N3 sleep duration in the CID group. B: Scatter plots of correlation between serum 5-HT levels and sleep efficiency in the CID group. PSG: Polysomnography; CID: Chronic insomnia disorder; GABA: Gamma-aminobutyric acid; Glu: Glutamic acid; 5-HT: 5-Hydroxytryptamine.

表3　血液指标诊断CID的效能

Table 3　Diagnostic efficacy of blood indices for CID

指标	AUC(95% *CI*)	截断值	敏感度	特异度	Youden指数	*P*
CaM/(pg·mL^{-1})	0.616(0.539~0.693)	43.350	0.845	0.363	0.208	0.004
GABA/Glu	0.609(0.532~0.686)	39.276	0.350	0.843	0.193	0.007
5-HT/(ng·mL^{-1})	0.790(0.726~0.854)	125.249	0.757	0.794	0.551	<0.001
Model 1	0.800(0.739~0.861)		0.814	0.680	0.494	<0.001

Model 1：CaM、GABA/Glu、5-HT联合诊断模型。*CI*：置信区间。

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3 讨 论

CID已成为潜在的健康风险因素，可能导致患者出现认知功能减退、焦虑抑郁及免疫力下降，严重影响患者生活质量[19]。本研究发现CID患者血清GABA、GABA/Glu及5-HT水平显著低于健康人群，而Glu水平显著升高，与课题组既往研究[20]及动物实验[21-23]结论一致。在失眠模型中，大鼠下丘脑与海马区中GABA和5-HT含量降低，Glu水平升高；经酸枣仁干预后，上述神经递质异常得到逆转，睡眠效率明显提高，失眠症状显著缓解[21]。机制研究[22]表明，GABA水平下降与Glu升高可诱发失眠，而五味子乙素通过上调GABA/Glu可发挥镇静作用。此外，睡眠剥夺动物模型的5-HT含量亦显著降低[23]，进一步支持神经递质紊乱与睡眠障碍的关联。

PSG是评估睡眠障碍的客观金标准，可提供睡眠结构、睡眠连续性和睡眠效率等多维度参数。本研究采用PSG检测患者的客观睡眠情况，并分析神经递质水平与PSG参数的相关性。结果显示，GABA/Glu与N3期睡眠持续时间呈正相关。N3期为深睡眠期，慢波成分比较多，又称为慢波睡眠期，是身体修复和记忆巩固的关键阶段。脑内GABA及Glu水平可能参与睡眠时相转换，在睡眠节律调节中发挥重要作用。动物实验[24]表明，GABA能神经元在慢波睡眠中放电频率显著增高。此外，靶向激活GABA能神经元可缩短小鼠睡眠潜伏期，增加小鼠慢波睡眠持续时间和皮层脑电图的慢波活动[25]。人群研究[26]亦证实，补充GABA可缩短睡眠潜伏期，延长慢波睡眠时间。上述证据提示，GABA/Glu可能通过调节慢波睡眠机制影响N3期时长。此外，5-HT水平与PSG睡眠效率呈正相关。自脑内5-HT睡眠诱导作用理论提出以来[27]，研究[28-30]逐步揭示5-HT通过调节睡眠稳态系统发挥作用。本研究结果进一步支持了5-HT能信号在维持睡眠效率中的生理意义。

钙调蛋白作为Ca^{2+}受体蛋白，其依赖性通路[如钙调蛋白依赖性蛋白激酶II(calmodulin-dependent protein kinase II，CaMKII)]已被证实在睡眠调节中发挥关键作用。Wang等[31]阐述了细胞内Ca^{2+}信号通过激活CaMKII参与睡眠诱导和维持的分子机制，并指出CaMKII及其多位点磷酸化状态可能是连接神经元瞬时钙动力学与长时程睡眠-觉醒动态的关键桥梁。基因敲除研究[32]表明，*CaMKIIα*/*β*缺失可抑制睡眠稳态恢复。进一步的研究[13]发现，CamKII信号转导是在睡眠剥夺后触发中丘脑联合核可塑性和恢复NREM睡眠稳态所必需的。另有研究[14]发现，CaM不仅在睡眠时长的控制中起重要作用，还参与了睡眠需求的稳态调节。既往研究[15-17]显示CaM参与神经递质调控，结合本课题组既往的研究[15]发现CID患者血清CaM水平下降，且与GABA/Glu呈相关性，提示CaM可能通过调节神经递质平衡参与睡眠调控，但具体机制需深入探索。

本研究通过ROC分析证实5-HT等生物标志物对CID具有良好的诊断价值，并进一步构建CaM、GABA/Glu与5-HT的联合诊断模型，AUC达0.800，敏感度与特异度均有一定的提高，提示多指标联合有助于提升辅助诊断效能，具有一定转化潜力。

本研究的优势在于首次系统评估了CID患者血清中CaM、GABA、Glu、5-HT水平及GABA/Glu与PSG参数的相关性及其诊断效能，为CID的筛查及诊断提供了新方向，具有一定的临床转化潜力，并为钙信号通路参与慢性失眠的神经化学失衡提供了新的临床证据。

本研究存在一定局限性。首先，样本量偏小，且为单中心设计，可能限制结论的外推性。其次，横断面观察无法确定生化异常与失眠之间的因果关系。再次，PSG仅监测单夜，首夜效应可能干扰睡眠参数的稳定性。最后，联合诊断模型缺乏外部验证，其泛化能力尚需多中心队列进一步验证。

综上所述，本研究发现CID患者血清CaM、GABA、5-HT水平及GABA/Glu显著降低，Glu水平显著升高。CID患者血清GABA/Glu与N3期持续时间呈正相关，5-HT水平与睡眠效率呈正相关。血清CaM、GABA/Glu及5-HT对CID具有诊断价值，3者联合诊断模型的诊断效能最强。

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参考文献

[1] Perlis M, Posner D, Riemann D, et al. Insomnia[J]. Lancet, 2022, 400(10357): 1047-1060. https://doi.org/10.1016/S0140-6736(22)00879-0.

[2] Olsen L, McCubbins H, Moore R, et al. Sleep deprivation: cognitive decline and hippocampal neuroinflammation[J]. Sleep, 2023, 46(Supplement_1): A89-A90. https://doi.org/10.1093/sleep/zsad077.0202.

[3] Bean C, Ciesla J. Naturalistic partial sleep deprivation leads to greater next-day anxiety: the moderating role of baseline

©Journal of Central South University (Medical Science). All rights reserved.

anxiety and depression[J]. Behav Ther, 2021, 52(4): 861-873. https://doi.org/10.1016/j.beth.2020.10.008.

[4] Garbarino S, Lanteri P, Bragazzi N, et al. Role of sleep deprivation in immune-related disease risk and outcomes[J]. Commun Biol, 2021, 4: 1304. https://doi.org/10.1038/s42003-021-02825-4.

[5] Akhlaghi M, Kohanmoo A. Sleep deprivation in development of obesity, effects on appetite regulation, energy metabolism, and dietary choices[J]. Nutr Res Rev, 2025, 38(1): 4-24. https://doi.org/10.1017/s0954422423000264.

[6] 郑宇, 周冰倩, 龚妮, 等. 老年人睡眠与衰弱双轨迹[J]. 中南大学学报(医学版), 2023, 48(4): 621-627. https://doi.org/10.11817/j.issn.1672-7347.2023.220544.
ZHENG Yu, ZHOU Bingqian, GONG Ni, et al. Dual trajectory of sleep and frail in elderly people[J]. Journal of Central South University. Medical Science, 2023, 48(4): 621-627. https://doi.org/10.11817/j.issn.1672-7347.2023.220544.

[7] Simon C, Hayar A, Garcia-Rill E. Developmental changes in glutamatergic fast synaptic neurotransmission in the dorsal subcoeruleus nucleus[J]. Sleep, 2012, 35(3): 407-417. https://doi.org/10.5665/sleep.1706.

[8] Chen X, Jia X, Zhang Y, et al. The combined use of gamma-aminobutyric acid and walnut peptide enhances sleep in mice [J]. Ann Palliat Med, 2021, 10(10): 11074-11082. https://doi.org/10.21037/apm-21-2798.

[9] 王升旭, 李求实. 睡眠剥夺对大鼠脑组织氨基酸类神经递质含量的影响[J]. 第一军医大学学报, 2002, 22(10): 888-890. https://doi.org/10.3321/j.issn:1673-4254.2002.10.008.
WANG Shengxu, LI Qiushi. Effects of sleep deprivation on gamma-amino-butyric acid and glutamate contents in rat brain [J]. Journal of First Military Medical University, 2002, 22(10): 888-890. https://doi.org/10.3321/j.issn:1673-4254.2002.10.008.

[10] 宋卫科, 郑荐, 杨晓樨. 血清IGF-1, 5-HT及TNF-α水平与帕金森病伴发抑郁的相关性[J]. 临床与病理杂志, 2020, 40(12): 3171-3176. https://doi.org/10.3978/j.issn.2095-6959.2020.12.013.
SONG Weike, ZHENG Jian, YANG Xiaoxi. Correlation between serum IGF-1, 5-HT and TNF-α levels and Parkinson's disease with depression[J]. Journal of Clinical and Pathological Research, 2020, 40(12): 3171-3176. https://doi. org/10.3978/j.issn.2095-6959.2020.12.013.

[11] Wang HR, Gu YQ, Khalid R, et al. Herbal medicines for insomnia through regulating 5-hydroxytryptamine receptors: a systematic review[J]. Chin J Nat Med, 2023, 21(7): 483-498. https://doi.org/10.1016/S1875-5364(23)60405-4.

[12] 胡俊航, 许菲, 王桐生, 等. 茯神水煎液对PCPA致失眠小鼠5-HT系统和GABA表达的影响[J]. 中国中药杂志, 2025(6): 1581-1591. https://doi.org/10.19540/j.cnki.cjcmm.20241101.401.
HU Junhang, XU Fei, WANG Tongsheng, et al. Effect of Fushen Decoction on 5-HT system and GABA expression in mouse model of PCPA-induced insomnia[J]. China Journal of Chinese Materia Medica, 2025(6): 1581-1591. https://doi.org/10. 19540/j.cnki.cjcmm.20241101.401.

[13] Lee S S, Liu Q, Cheng A H R, et al. Sleep need-dependent plasticity of a thalamic circuit promotes homeostatic recovery sleep[J/OL]. Science, 2025, 388(6753): eadm8203[2025-04-10]. https://doi.org/10.1126/science.adm8203.

[14] Wang YM, Cao SY, Tone D, et al. Postsynaptic competition between calcineurin and PKA regulates mammalian sleep-wake cycles[J]. Nature, 2024, 636(8042): 412-421. https://doi.org/10.1038/s41586-024-08132-2.

[15] Wei J, Zhang M, Zhu Y, et al. Ca(2+) -calmodulin signalling pathway up-regulates GABA synaptic transmission through cytoskeleton-mediated mechanisms[J]. Neuroscience, 2004, 127 (3): 637-647. https://doi.org/10.1016/j.neuroscience.2004.05.056.

[16] Zhong W, Hutchinson T, Chebolu S, et al. Serotonin 5-HT3 receptor-mediated vomiting occurs via the activation of Ca^{2+}/CaMKII-dependent ERK1/2 signaling in the least shrew (Cryptotis parva) [J/OL]. PLoS One, 2014, 9(8): e104718[2025-04-10]. https://doi.org/10.1371/journal.pone.0104718

[17] Mockett B, Guévremont D, Wutte M, et al. Calcium/calmodulin-dependent protein kinase II mediates group I metabotropic glutamate receptor-dependent protein synthesis and long-term depression in rat hippocampus[J]. J Neurosci, 2011, 31(20): 7380-7391. https://doi.org/10.1523/JNEUROSCI.6656-10.2011.

[18] Sateia MJ. International Classification of Sleep Disorders, 3rd Edition: Text Revision[M]. Darien: American Academy of Sleep Medicine, 2023.

[19] Medalie L, Cifu AS. Management of chronic insomnia disorder in adults[J]. JAMA, 2017, 317(7): 762. https://doi.org/10.1001/jama.2016.19004.

[20] 苏婷, 高威, 李华欣, 等. 失眠患者血清钙调蛋白及GABA/Glu水平检测及其意义[J]. 中风与神经疾病杂志, 2021, 38(5): 407-410. https://doi.org/10.19845/j.cnki.zfysjjbzz.2021.0108.
SU Ting, GAO Wei, LI Huaxin, et al. Detection and significance of the level of serum calmodulin and GABA/Glu in insomnia patients[J]. Journal of Apoplexy and Nervous Diseases, 2021, 38(5): 407-410. https://doi.org/10.19845/j.cnki.zfysjjbzz.2021.0108.

[21] Xiao FQ, Shao S, Zhang HY, et al. Neuroprotective effect of Ziziphi Spinosae Semen on rats with p-chlorophenylalanine-induced insomnia via activation of GABAA receptor[J]. Front Pharmacol, 2022, 13: 965308. https://doi.org/10.3389/fphar.2022.965308.

[22] Li N, Liu JL, Wang MY, et al. Sedative and hypnotic effects of Schisandrin B through increasing GABA/Glu ratio and upregulating the expression of GABAA in mice and rats[J]. Biomed Pharmacother, 2018, 103: 509-516. https://doi.org/10.1016/j.biopha.2018.04.017.

[23] Sun YJ, Zhang N, Qu Y, et al. Shuangxia decoction alleviates p-chlorophenylalanine induced insomnia through the modification of serotonergic and immune system[J]. Metab Brain Dis, 2020, 35 (2): 315-325. https://doi.org/10.1007/s11011-019-00499-w.

[24] Alam MA, Kostin A, Siegel J, et al. Characteristics of sleep-active neurons in the medullary parafacial zone in rats[J/OL]. Sleep, 2018, 41(10): zsy130[2025-04-10]. https://doi.org/10.1093/sleep/zsy130.

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[25] 冯首花, 王艳秋, 庄慧魁. 中枢神经系统γ-氨基丁酸能神经元对睡眠-觉醒调控作用的研究进展[J]. 神经解剖学杂志, 2021, 37(3): 347-351. https://doi.org/10.16557/j.cnki.1000-7547.2021.03.016.
FENG Shouhua, WANG Yanqiu, ZHUANG Huikui. Research progress on the regulation of γ-aminobutyric acid neurons in central nervous system on sleep-wake[J]. Chinese Journal of Neuroanatomy, 2021, 37(3): 347-351. https://doi.org/10.16557/j.cnki.1000-7547.2021.03.016.

[26] Yamatsu A, Yamashita Y, Pandharipande T, et al. Effect of oral γ-aminobutyric acid (GABA) administration on sleep and its absorption in humans[J]. Food Sci Biotechnol, 2016, 25(2): 547-551. https://doi.org/10.1007/s10068-016-0076-9.

[27] Koella WP, Feldstein A, Czicman JS. The effect of para-chlorophenylalanine on the sleep of cats[J]. Electroencephalogr Clin Neurophysiol, 1968, 25(5): 481-490. https://doi.org/10.1016/0013-4694(68)90158-2.

[28] 崔素颖, 秦宇, 张永鹤. 睡眠调控与睡眠调节药物研究进展[J]. 中国药理学与毒理学杂志, 2022, 36(11): 801-811. https://doi.org/10.3867/j.issn.1000-3002.2022.11.001.
CUI Suying, QIN Yu, ZHANG Yonghe. Research progress in sleep regulation and sleep modulating agents[J]. Chinese Journal of Pharmacology and Toxicology, 2022, 36(11): 801-811. https://doi.org/10.3867/j.issn.1000-3002.2022.11.001.

[29] Chowdhury B, Abhilash L, Ortega A, et al. Homeostatic control of deep sleep and molecular correlates of sleep pressure in *Drosophila*[J/OL]. eLife, 2023, 12: e91355[2025-04-10]. https://doi.org/10.7554/elife.91355.

[30] Cespuglio R. Serotonin: its place today in sleep preparation, triggering or maintenance[J]. Sleep Med, 2018, 49: 31-39. https://doi.org/10.1016/j.sleep.2018.05.034.

[31] Wang Y, Minami Y, Ode KL, et al. The role of calcium and CaMKII in sleep[J]. Front Syst Neurosci, 2022, 16: 1059421. https://doi.org/10.3389/fnsys.2022.1059421.

[32] Yang WW, Shi JY, Li CG, et al. Calcium/calmodulin-dependent protein kinase II α and β differentially regulate mammalian sleep [J]. Commun Biol, 2025, 8: 11. https://doi.org/10.1038/s42003-024-07449-y.

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