

重复经颅磁刺激在原发性失眠中的应用研究

Application Of rTMS In The
Primary Insomnia

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PART

1

重复经颅磁刺激

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简介

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1

重复经颅磁刺激简介

Introduction For Repetitive Transcranial Magnetic Stimulation

概念 Concept

► 经颅磁刺激 (transcranial magnetic stimulation , TMS)

是一种非侵入性无痛性的神经系统检测和治疗技术。

Transcranial magnetic stimulation (TMS) is a painless, non-invasive treatment method which can be effectively used in the diagnosis and treatment of neurological diseases.

► 重复性经颅磁刺激 (repetitive TMS , rTMS)

以固定的脉冲发放频率，作用在一个固定点上的刺激。



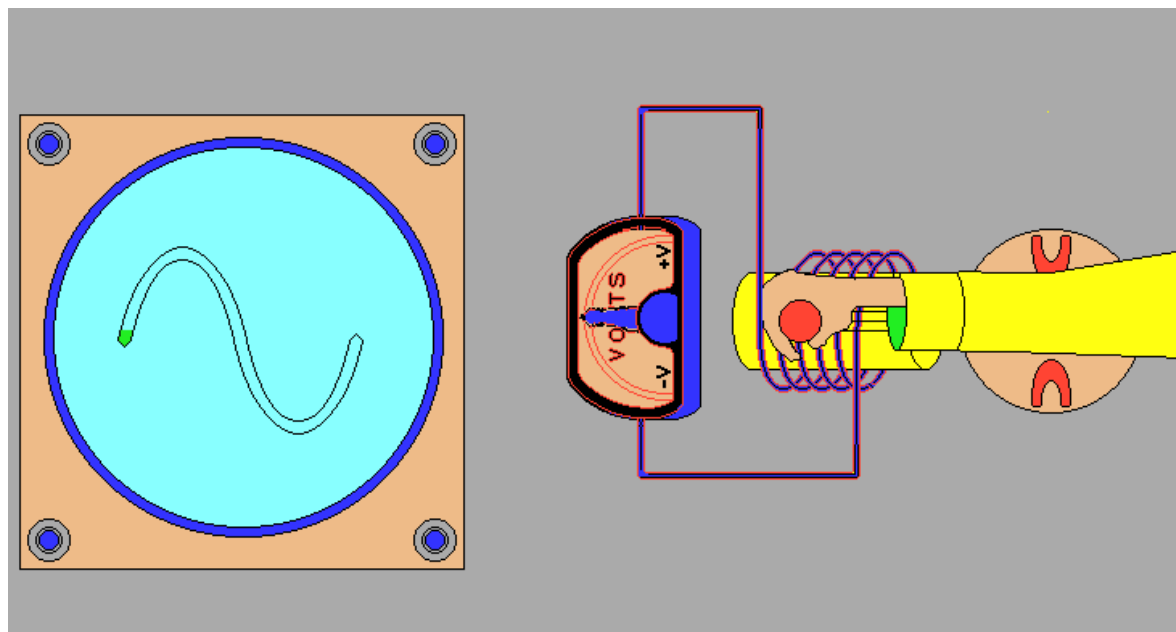
原理 Mechanism

“ The brain is a machine that runs on electricity.”

——大脑就是一台用电来工作的机器。

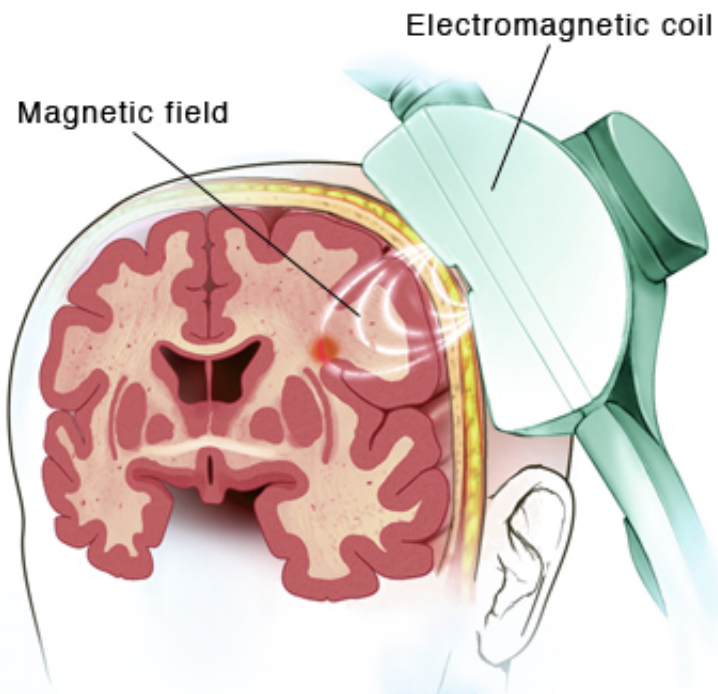


原理 Mechanism



- ▶ 法拉第电磁感应原理 (Electromagnetic induction)

原理 Mechanism



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- ▶ TMS的感应电场产生的电流密度是与其受刺激的介质的电导率成正比的。
- ▶ 在人体组织中，神经组织的电导率比较大，而在肌肉和骨骼电导率比较小，因而 TMS在肌肉和骨骼几乎不产生感应电流，而在神经系统则产生较大的感应电流。

原理 Mechanism

- ▶ TMS 仪器产生的脉冲磁场无衰减地透过颅骨作用于中枢神经系统以改变皮层神经细胞的膜电位，使之产生感应电流，超过神经细胞的刺激阈值则就会产生兴奋性或者抑制性的效果
- ▶ 从而影响脑内代谢和神经电活动，最终引起人体内一系列生理生化反应。



原理 Mechanism

▶ 分类 Classification

▶ 单脉冲经颅磁刺激 (sTMS)

-引起皮质去极化，用于电生理检查

▶ 双脉冲经颅磁刺激pTMS

-第一个刺激后神经元抑制，用于实验研究

▶ 重复性经颅磁刺激 (rTMS)

-影响大脑皮质功能，用于临床治疗

rTMS眼中的TMS设备



3

重复经颅磁刺激简介

Introduction For Repetitive Transcranial Magnetic Stimulation

历史与发展

History and Development

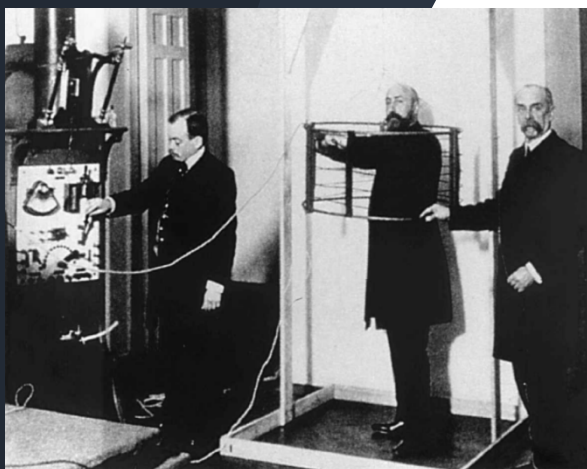


Figure 4. d'Arsonval and colleagues showing the apparatus used to induce visual phosphenes. This photograph was taken in 1911.



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重复经颅磁刺激简介

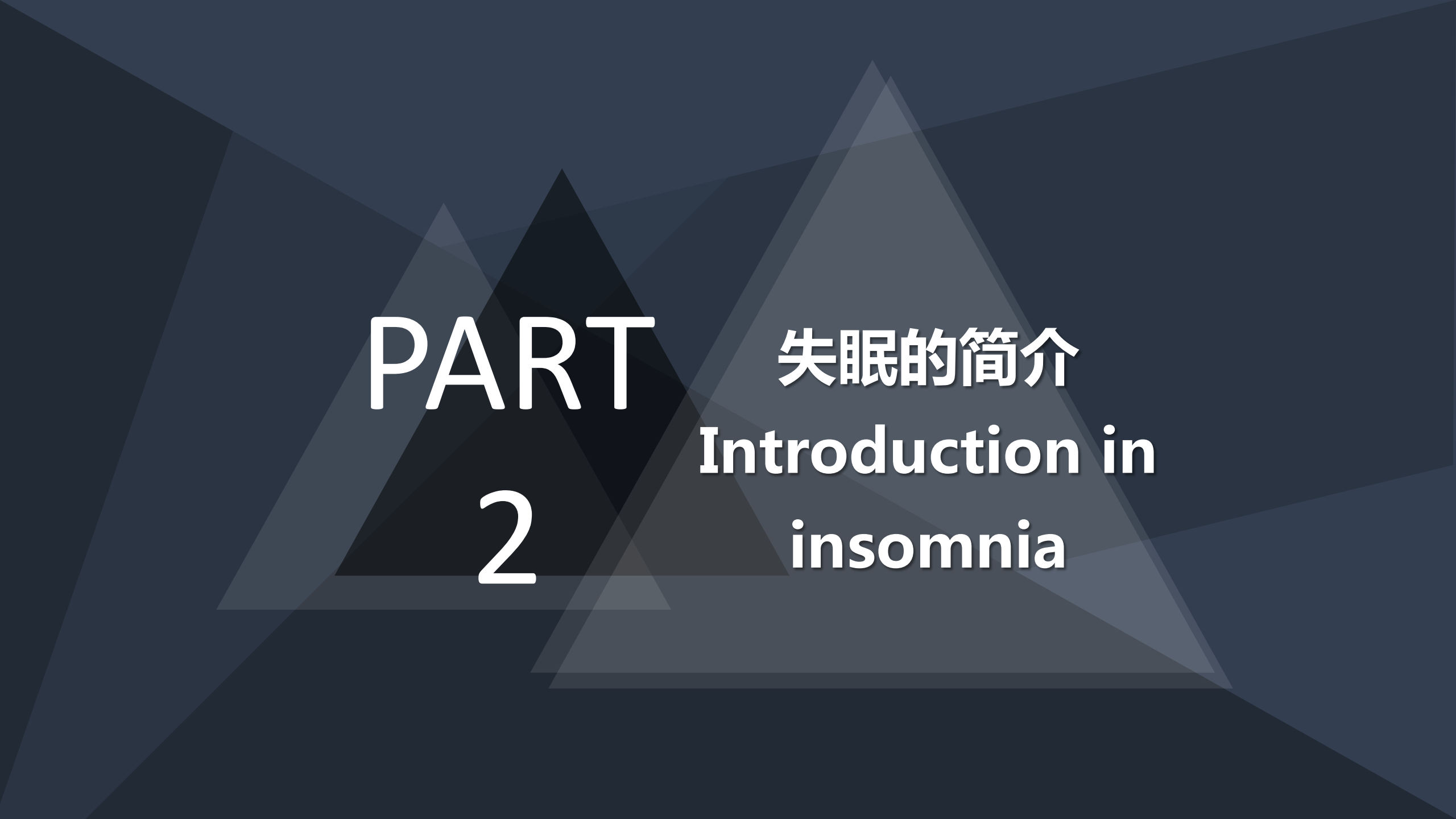
Introduction For Repetitive Transcranial Magnetic Stimulation

应用

TMS On Rehabilitation

- ▶ 运动障碍 (Motor Disability)
- ▶ 肌张力障碍 (Spasticity)
- ▶ 言语, 吞咽 (Aphasia, dysphagia)
- ▶ 认知障碍 (Cognitive Disorder)
- ▶ 昏迷促醒 (arousal)
- ▶ 其他





PART 2

失眠的简介 Introduction in insomnia

失眠 Insomnia

I

失眠的概念 Concept

2

流行病学 Epidemiology

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分类 Classification

4

症状 Symptoms

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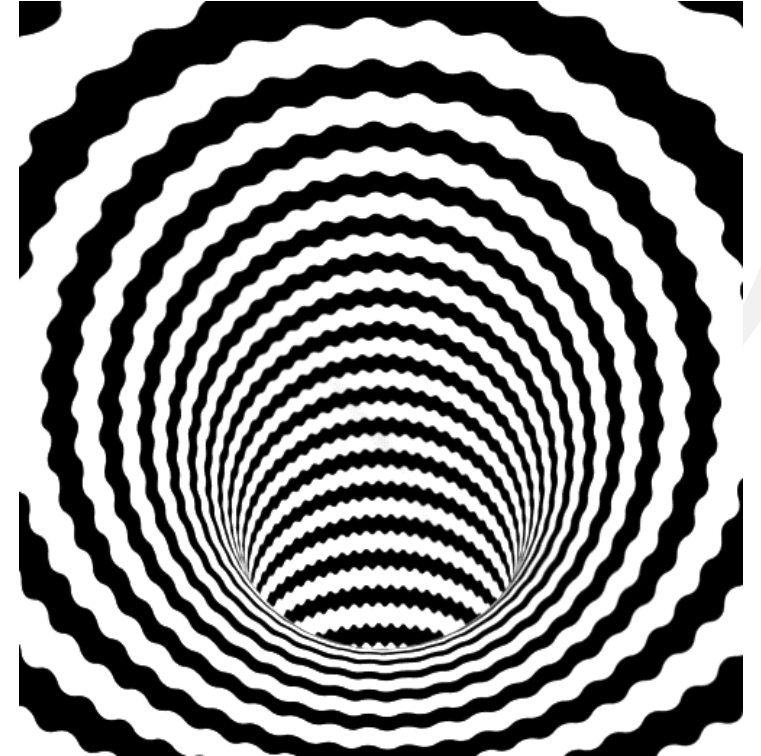
睡眠生理 The physiology of sleep

6

发病机制 Mechanism

Have you ever experienced
insomnia?

Have you ever see pictures
like these?



失眠通常指患者对睡眠时间和（或）质量不满足并影响白天社会功能的一种主观体验。
Insomnia, also known as sleeplessness, is a sleep disorder where people have trouble sleeping which will influence the social function.

2.Epidemiology



WHO的一项研究表明，全球约有27%的人遭受睡眠病症的困扰.[1]

27% people is troubled by undersleep.



33%的人出现过睡眠障碍

33% people have experienced somnipathy.



17%的人为严重失眠。

17% people are diagnosed severe insomnia.



国内研究资料显示严重失眠症的发病率为9.38%.[2]

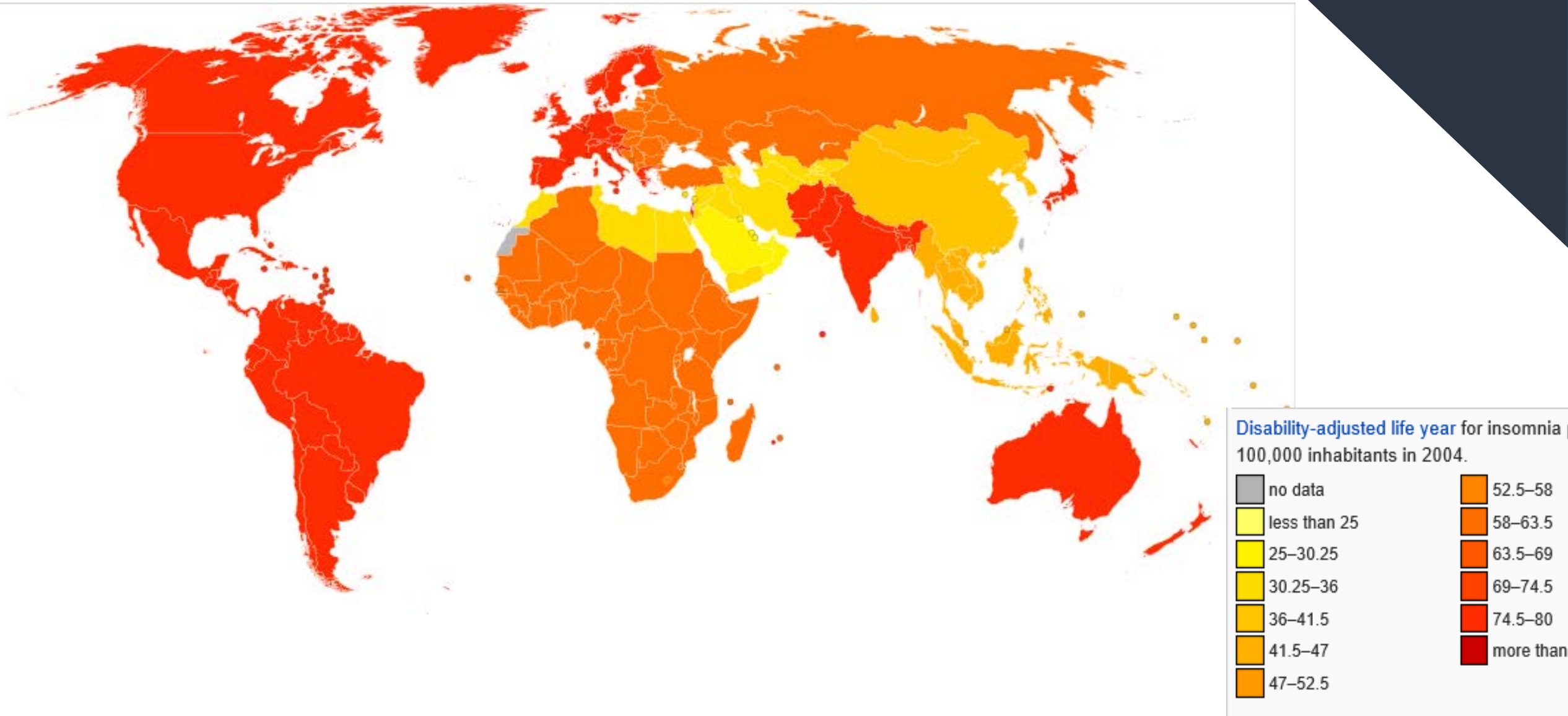
The severe insomnia people are more than 9.38%.



[1] Taylor DJ. Lichstein KIJ. Durrence HH. Insomnia as a health risk factor. Be—how Sleep Med 2013: 227—47

[2]赵忠新，张照环. 应给予睡眠更多的关注[J]. 中华神经科杂志, 2011, 44(8): 513—515.

Disability-adjusted life year for insomnia per 100,000 inhabitants in 2014.



3.失眠的分类

Classification of insomnia

短暂性失眠 (Transient insomnia)

急性失眠 (Acute insomnia)

慢性失眠 (Chronic insomnia)

失眠时间大于一个月，睡眠时间由长到短，睡眠质量日趋更差，可由脑本身疾病或其他部位疾病导致。

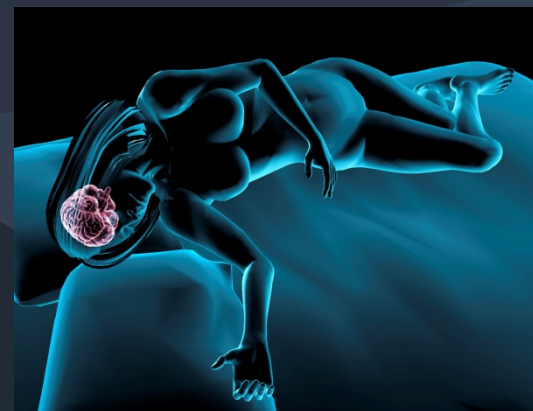
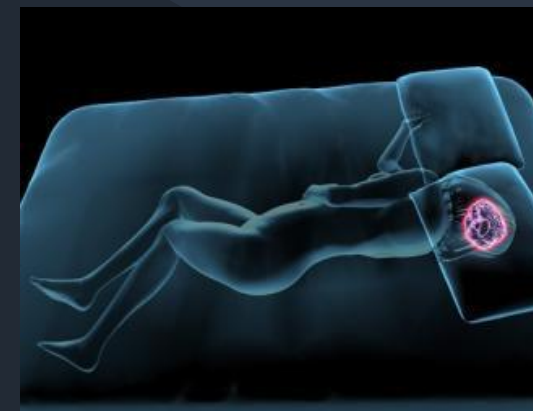
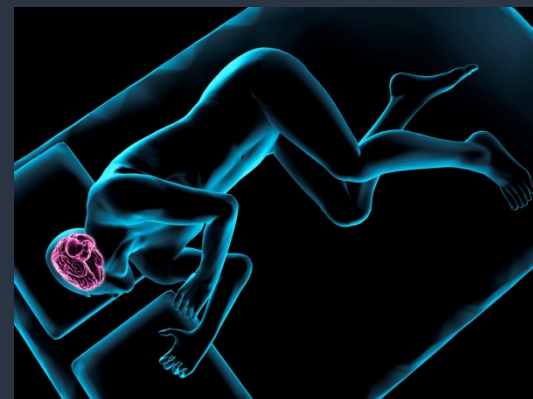
The inability to consistently sleep well for a period of more than a month, the sleep time turning less and the sleeping quality becoming worse.

◆ 原发性失眠

Primary insomnia

◆ 继发或伴发于其他原因的失眠

Caused by other diseases.



慢性失眠分类



A.原发性失眠:原发性失眠约占慢性失眠患者的1 / 4，急性或隐匿性起病，女性多于男性。



◆ **特发性失眠**：这类失眠通常始于婴儿期或低龄儿童。患者长期睡眠紊乱，但不能发现任何明确的病因，占就诊失眠患者的10%以内。



◆ **反常性失眠**：这类失眠又称睡眠状态感知不良或主观性失眠，占慢性失眠者的5%以内。



◆ **心理生理性失眠**：患者有不适当的睡眠预防行为发生，最终进展成为感觉睡眠紊乱的主要因素。



B.继发性失眠:继发于其他疾病，如脑肿瘤等。

4

Symptoms

失眠的症状

Symptoms of insomnia:

◆入睡困难（包括难以找到舒适的睡眠体位）

Difficulty falling asleep, including difficulty finding a comfortable sleeping position.

◆半夜醒后难以入睡

Waking during the night and being unable to return to sleep.

◆早晨容易醒

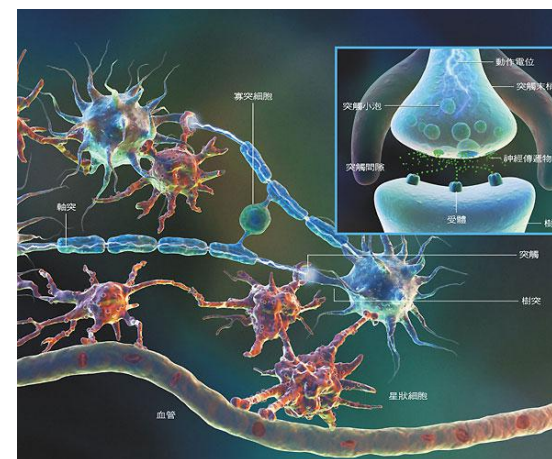
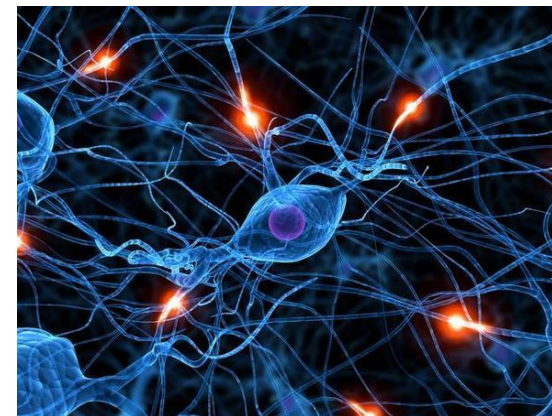
Early morning awakening

◆白天感觉疲惫、困乏、焦虑

Feeling unrefreshed upon waking daytime sleepiness, irritability or anxiety

觉醒状态的维持：

- ◆ 脑干上行网状激活系统
- ◆ 大脑皮层的感觉运动区，眶回、额叶扣带回、颞上回、海马、杏仁核、下丘脑的下行纤维。



觉醒的
维持

行为觉醒的维持

黑质多巴胺能系统

脑电觉醒的维持

蓝斑上部去甲肾上腺素能系统和脑干网状胆碱能系统

5 睡眠生理

The physiology of sleep

慢波睡眠相关脑区：

- ◆ 间脑、下丘脑后部
- ◆ 脑干上行抑制系统
- ◆ 基底前脑的视前区以及Broca斜带区

快波睡眠相关脑区：

- ◆ 脑桥被盖外侧区胆碱能神经元



慢性失眠涉及广泛的脑区异常，主要集中在包括：

Chronic insomnia is involved in wide brain areas:

◆ 前额叶

prefrontal cortex

◆ 前扣带

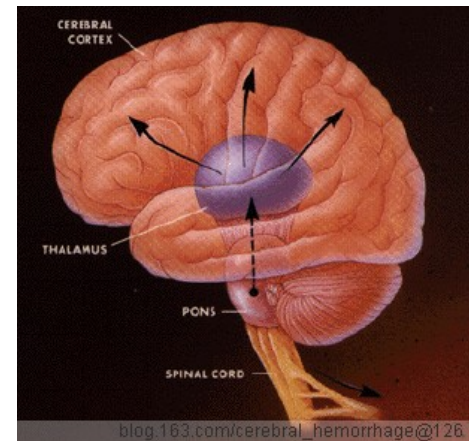
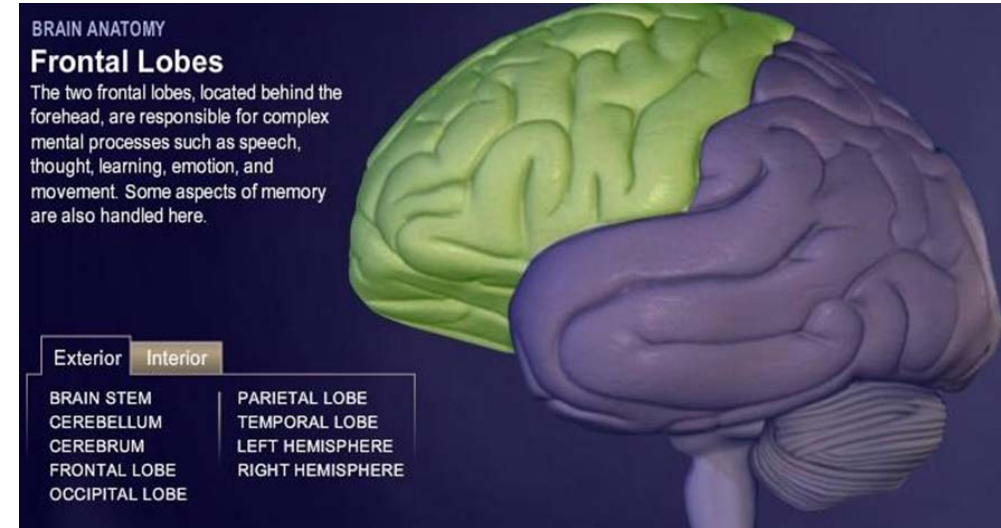
anterior cingulate

◆ 杏仁核

Cortex Amygdala

◆ 海马和丘脑等

hippocampus, and thalamus



6.失眠的病理机制

The pathology of insomnia

有关失眠的最具影响力的病理生理机制为：

◆ 神经认知 (高觉醒)模型：

认为从外周到中枢的觉醒水平的增加，尤其是皮层持久处于信息处理增强的状态而促发失眠的形成和维持

◆ 心理生物学模型：

认为中枢神经系统从觉醒中“抽身而退”的抑制能力受损或丧失是导致失眠形成的重要机制。

us SS, Rabin LA. Sleep America:managing the
is of adultchronic insomnia and associated
nditions[J]. J Affect Disord,2012,138(3): 192-212.



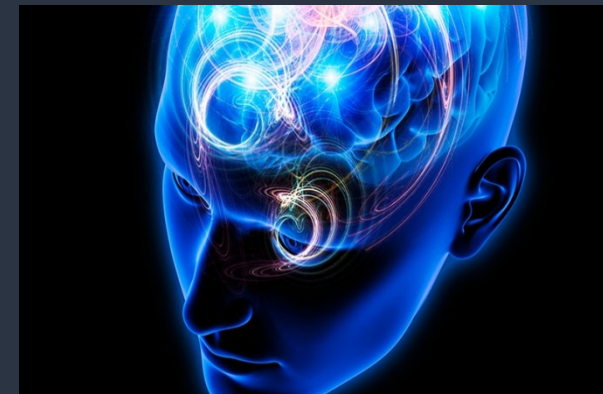
6.失眠的病理机制

The pathology of insomnia

◆脑电生理机制研究：

The researches of brain electrophysiology

采用定量脑电图描记器（EEG）证实了失眠患者中皮层高觉醒的存在，表现为睡眠起始和非快眼动(NREM)睡眠期间 β/γ 脑电活动的增加。



◆脑影像学机制研究：

The researches of brain image

磁共振波谱研究显示：失眠患者其枕叶皮质存在 γ -氨基丁酸(GABA)的减少,且患者的高失眠严重指数(insomnia severity index,ISI)与顶-枕区皮质的低水平GABA及高谷氨酸水平相关。



Meyerhoff DJ, Mon A, Metzler T, et al. Cortical gamma-aminobutyric acid and glutamate in posttraumatic stress disorder and their relationships to self-reported sleep quality [J]. Sleep, 2014, 37(5):893-900



PART

3

失眠中的应用
Application in
insomnia

重复经颅磁刺激

I

rTMS对失眠作用机制
The Mechanism of rTMS

2

禁忌症 Contraindication

3

临床研究 Clinical research

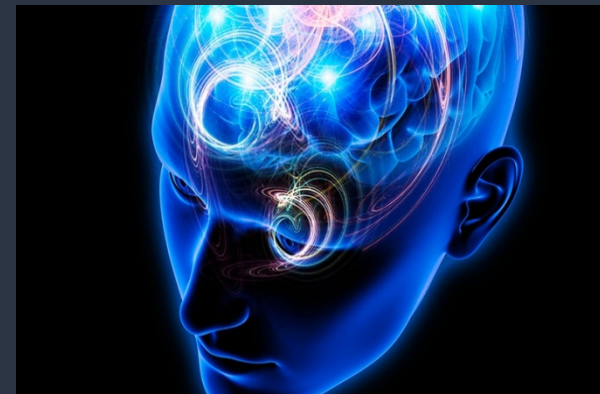
失眠的病理机制

The pathology of insomnia

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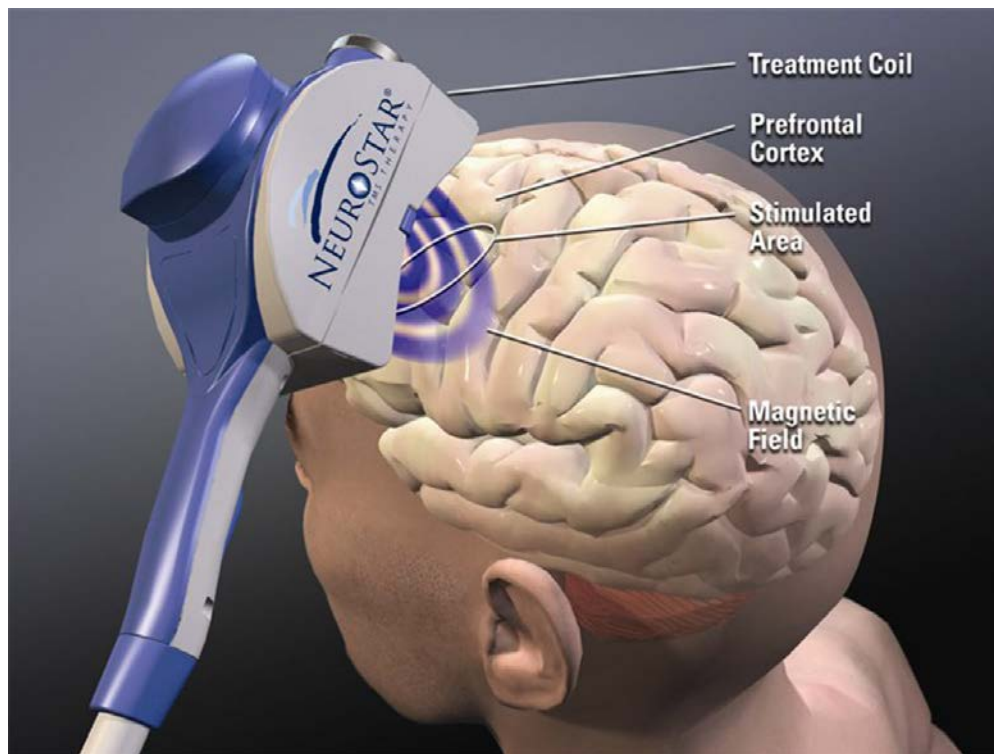
The researchs of brain image

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作用机制 Mechanism



www.neuroscienze.net

TMS可以调节大脑皮质的兴奋性:

- ▶ 高频TMS（频率 $\geq 5\text{Hz}$ ）可以增加大脑皮质的兴奋性；
- ▶ 低频TMS（频率 $\leq 1\text{Hz}$ ）则可以抑制大脑皮质兴奋从而促进睡眠。

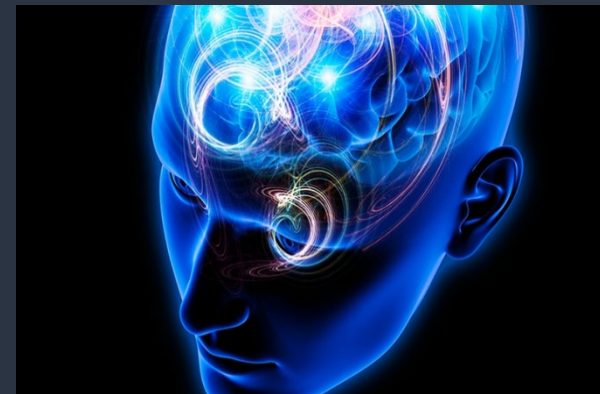
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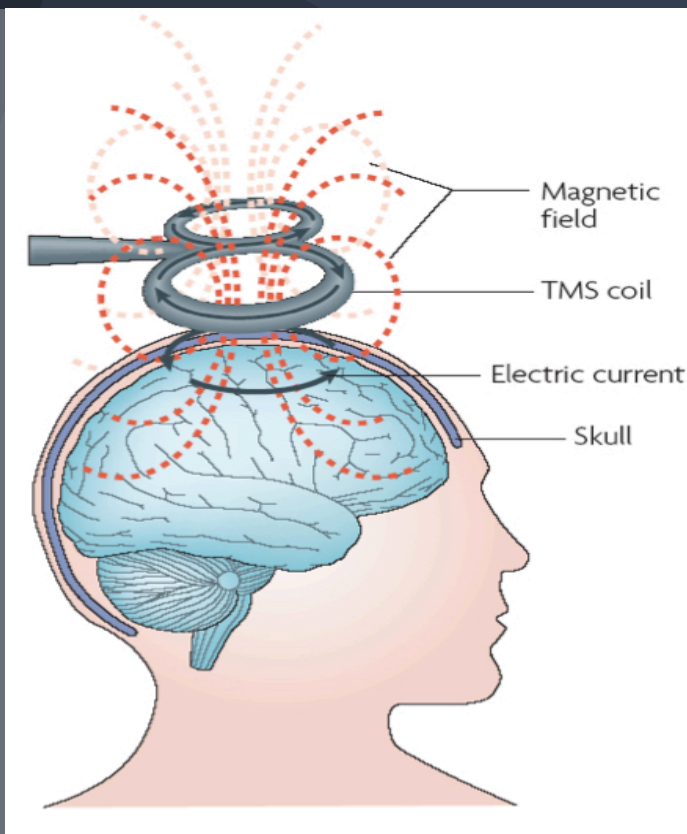
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作用机制 Mechanism



brainstimulationclinic.squarespace.com

rTMS的磁场作用

影响神经递质的释放来调节脑功能的兴奋及抑制水平,可促进5-HT和 γ -氨基丁酸 (GABA)的释放

2

禁忌症

Contraindication



颅内金属植入物、耳蜗植入物者、佩戴心脏起搏器者；

急性期的脑器质性疾病、颅内压增高患者；

孕妇和婴幼儿慎用rTMS治疗；

癫痫患者禁止使用高频、高强度刺激。

<http://image.baidu.com/>

[1]李冬,强静,刘惠苗等.经颅磁刺激治疗失眠的研究进展[J].中华物理医学与康复杂志,2015,37(2):155-157.DOI:10.3760/cma.j.issn.0254-1424.2015.02.021.

研究方法

“Hundred and twenty patients were enrolled between April and November 2011. Patients were randomly assigned to one Of the three study groups :rTMS treatment group, medication treatment group, and psychotherapy group. Each group comprised 40 patients.”

治疗方法

“stimulus frequency 1 Hz, stimulus intensity 80 % of motion, Stimulation number 30 pulses/string, string interval 2 s, total Of 60 strings, total stimulation pulses 1,800, total stimulation time 30 min. The treatment was applied once a day continuously for 2 weeks.”

Table 2 Sleep parameters before and after treatment

Group	Sleep efficiency (%)		Sleep latency (min)		Total sleep time (min)	
	Before	After	Before	After	Before	After
rTMS	66.34 ± 8.56	83.23 ± 26.23*	44.03 ± 9.25	26.15 ± 10.28*	330.24 ± 81.01	408.05 ± 68.12*
Medication	67.35 ± 9.01	86.34 ± 21.02*	39.25 ± 10.31	15.67 ± 5.05*	331.56 ± 70.12	426.14 ± 73.25*
Psychotherapy	65.12 ± 11.23	72.15 ± 30.76*	43.15 ± 11.12	30.02 ± 12.32*	328.73 ± 90.56	387.56 ± 87.47*

Table 6 Relapse and recurrence rates

Group	Relapse rate (%)	Recurrence rate within 3 months (%)
TMS	23.75 ± 7.48	36.28 ± 11.57
Medication	70.41 ± 12.35	96.34 ± 29.01
Psychotherapy	40.39 ± 16.89	56.27 ± 15.57

Data are presented as mean ± SD

临床研究 Clinical research

“在被试脑干的中缝核区域(枕骨粗隆下方1cm左右)施加刺激, 刺激参数设置1Hz,80%RMT, 1500次rTMS(持续10s间隔2s)。”

刘运洲, & 张忠秋. (2012). 中国运动医学杂志, 31(12), 1103-1106.

“刺激部位选择右背双侧前额皮层, 刺激频率为1Hz, 强度为80%静息运动阈值, 30 次为一个序列, 每序列 40 次脉冲, 序列间隔 10s, 每天 40 个序列, 1 次连续给予, 每次治疗的时间为 20 min, 每天1次,连续治疗4周。”

段妮, 张永东, & 王立涛. (2016). 国际精神病学杂志, (2), 263-265.

“线圈正面放在右侧额叶前部背外侧(DLPFC)部位并与治疗部位头皮相切。刺激频率为 1Hz, 刺激强度为80% 静息运动阈值, 刺激数为30 脉冲/序列, 序列间隔时间2秒, 共60个序列, 总刺激数为1800脉冲。每天1次, 共14d。”

刘彩兴, 王婷婷, & 孙忠国. (2016). 中国药物依赖性杂志, 25(2), 206-208.

3

临床研究

文献第一作者	频率(HZ)	刺激强度 (%)	脉冲 (脉冲/序列)	序列数	序列间隔 (s)	刺激部位
刘永洲	1	80	30	50	10	中缝核区域
段妮	1	80	40	40	10	右背双侧前额皮层
刘彩兴	1	80	30	60	2	右背双侧前额皮层

PART

4

重复经颅磁刺激

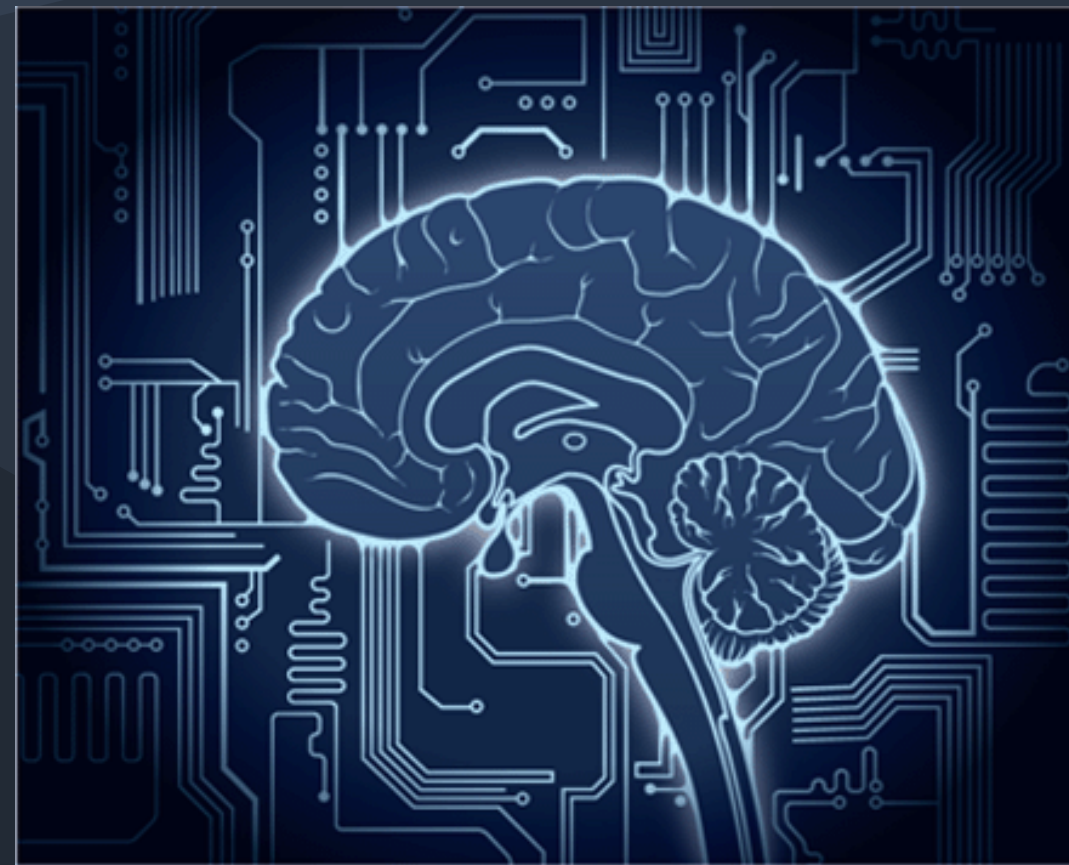
Repetitive Transcranial
Magnetic Stimulation

优势和不足

Advantages and
disadvantages

经颅磁刺激的优势 Advantages

1. 高效安全
2. 无痛无创
3. 克服了电流不能进入颅脑的缺陷
4. 兴奋更多水平方向的神经元
5. 应用广泛



Khedr EM, Farweez HM Islam H. Therapeutic effect of repetitive transcranial magnetic stimulation on motor function in Parkinson's disease patients. Eur J Neurol, 2003, 10(5): 567-572.

经颅磁刺激的不足 Disadvantages

1. 头痛
2. 恶心
3. 癫痫发作
4. 情绪改变
5. 内分泌影响
6. 对学习能力的影晌
7. 价格



Shimamoto H, Takasaki K, Shigemori M, Imaizumi T, Ayabe M, Shoji H.
Therapeutic effect and mechanism of repetitive transcranial magnetic
stimulation in Parkinson's disease. J Neurol, 2001, 248 Suppl 3:III48-52.

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