·基础研究·

跑轮和跑台预运动对磨牙缺失大鼠学习记忆能力的影响

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【摘要】 **目的** 观察跑轮和跑台两种不同预运动方式对磨牙缺失大鼠学习记忆能力的影响。**方法** 选取 32 只 3 月龄健康雄性 SD 大鼠,将所有大鼠按照随机数字表法分为对照组(C 组)、磨牙缺失组(ML 组)、跑轮预运动磨牙缺失组(W-ML 组)、跑台预运动磨牙缺失组(T-ML 组),每组 8 只。T-ML 组和 W-ML 组大鼠进行为期 1 周的预运动训练,对 T-ML 组大鼠进行跑台预运动干预,对 W-ML 组大鼠进行跑轮预运动干预。ML 组和 C 组大鼠在正常鼠笼里自由饲养。运动结束后,T-ML、W-ML 组和 ML 组大鼠均接受单侧磨牙拔除手术。1 周后,采用被动回避反射实验来评价各组大鼠的学习记忆能力。**结果** 在训练阶段,C 组、ML 组、W-ML 组、T-ML 组的潜伏期Ⅰ分别为(58.00±11.41)s、(65.33±11.39)s、(64.33±14.06)s、(63.33±14.32)s。在实验阶段,C 组、ML 组、W-ML 组、T-ML 组的潜伏期Ⅱ分别为(300.00±0.00)s、(69.21±12.19)s、(300.00±0.00)s、(300.00±0.00)s。训练阶段,4 组大鼠的潜伏期Ⅰ间比较,差异无统计学意义($P>0.05$)。实验阶段,与 C 组比较,ML 组大鼠潜伏期Ⅱ显著降低($P<0.05$);与 ML 组比较,W-ML 组和 T-ML 组潜伏期Ⅱ显著升高($P<0.05$),W-ML 组与 T-ML 组间比较,差异无统计学意义($P>0.05$)。**结论** 跑台和跑轮两种不同预运动方式均可改善磨牙缺失后大鼠的学习记忆能力。

【关键词】 跑轮; 跑台; 预运动; 磨牙缺失; 学习记忆能力

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Exercise can promote cognition and memory after molar loss

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【**Abstract**】 **Objective** To observe the effect of wheel running and treadmill running on the cognitive functioning of rats after the extraction of a molar. **Methods** Thirty-two Sprague-Dawley rats were randomly divided into a control group (group C, $n=8$), a molar extraction group (ML group, $n=8$), a wheel running pretreatment group (W-ML group, $n=8$) and a treadmill running pretreatment group (T-ML group, $n=8$). The rats in the T-ML and W-ML groups practiced wheel running and treadmill running for 1 week, then they and the rats in the ML group received molar extraction surgery. One week later, a passive avoidance test was used to evaluate the cognitive functioning of all of the rats. **Results** No significant differences were found in the groups' average latency I times, but the average latency II time of the ML group was significantly shorter. There was no significant difference in the average latency II times of the T-ML and W-ML groups. **Conclusion** Either wheel running or treadmill running can promote learning and memory after molar loss by oral surgery, at least in rats.

【**Key words**】 Exercise; Treadmill running; Molar extraction; Cognition; Memory; Dental surgery

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随着中国老年人口数量的不断增加,老龄化问题也越来越严重[1-2]。其中,不少老年人存在着由牙齿缺失所引发的一系列口腔问题。临床研究表明,磨牙缺失是老年痴呆的重要危险因素之一[3-6]。有研究表明,老年痴呆的程度与其磨牙丢失的数目呈正比[7]。流行病学与动物实验研究表明,磨牙缺失与啮齿类动物学习记忆能力的下降密切相关[8-10]。Kato 等[11]研究表明,大鼠磨牙缺失后可引起胆碱能系统失调,从而导致其学习记忆能力下降。Pang 等[12]研究表明,磨牙

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缺失大鼠学习记忆能力的显著下降与其脑部一氧化氮等内源性气体增多关系密切。神经生理学和生物化学研究表明,运动可从多方面促进学习记忆能力[13-16]。Aguiar 等[17]研究表明,运动可增加神经突触的可塑性和脑源性神经营养因子(brain-derived neurotrophic factor,BDNF)的数目,从而促进大鼠的学习记忆能力。Radák 等[18]研究表明,运动可通过减小氧化应激水平,促进大鼠的学习记忆能力。但运动是否能改善磨牙缺失导致的认知功能障碍仍有待于深入研究。基于上述研究背景,本研究采用 1 周的预运动训练作为干预手段,观察跑轮和跑台两种不同的预运动方式对磨牙缺失后大鼠学习记忆能力的影响,旨在为运动干预磨牙缺失导致的认知功能障碍提供行为学实验证据。

材料与方法

一、动物与实验分组

32 只成年雄性 Sprague-Dawley(SD)大鼠,体重 275~345 g,由北京市北医三院实验动物中心提供。动物实验已通过动物伦理委员会的批准。将大鼠按照随机数字表法分为对照组(C 组),磨牙缺失组(ML 组),跑轮预运动磨牙缺失组(W-ML 组)和跑台预运动磨牙缺失组(T-ML 组),每组 8 只。其中,C 组为空白对照组,ML 组大鼠接受上颌磨牙缺失手术,T-ML 组和 W-ML组大鼠分别接受 1 周的跑台和跑轮预运动后再接受上颌磨牙缺失手术。

二、跑轮和跑台预运动训练

T-ML 组和 W-ML 组大鼠分别进行 1 周的跑台和跑轮预运动,W-ML 组大鼠在跑轮鼠笼里自由运动 1 周,T-ML 组大鼠在跑台上运动,设定跑台坡度为 0°,跑台速度为 15 m/min,每日 1 h,共 7 d。ML 组和 C 组大鼠在正常鼠笼里自由饲养。本研究中所有大鼠均为单笼饲养。

三、磨牙缺失手术

T-ML 组、W-ML 组和 ML 组接受上颌磨牙缺失手术[19]。大鼠经腹腔注射水合氯醛(350 mg/kg)全身麻醉后,在上颌部涂抹适量 1% 碘伏消毒。使用特制手术钳将上颌的磨牙挺松,并使用小手术钳将其拔除;在此操作中,应尽量完整拔除磨牙。整个手术过程中应做好消毒工作,避免细菌感染。术后各组大鼠正常饲养,并给予充足水源。

四、学习记忆能力的评价

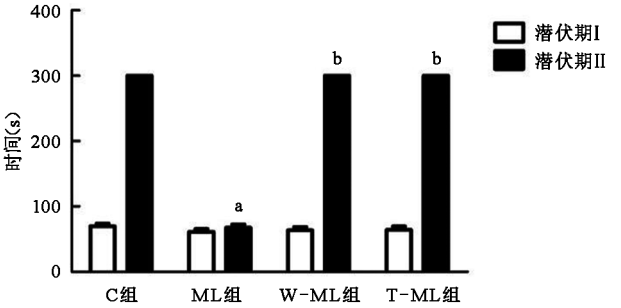
1 周后,本实验通过被动回避反射实验来评价大鼠的学习记忆能力[20]。被动回避反射实验中所用到的实验装置是大鼠穿梭箱。大鼠穿梭箱由大小相等的明室和暗室两部分组成。明室有灯光射入,暗室则无任何光源射入。两室之间有活动滑门,可控制大鼠在明暗室之间活动。暗室底部铺装有铜栅,通电后可以产生电流,本实验中将电流设置为 2.5 mA。被动回避反射实验分为训练阶段和实验阶段。首先,在训练阶段中记录大鼠从从明室到暗室的时间,即为“潜伏期Ⅰ”。此时,给予大鼠电刺激,持续时间 8 s。实验阶段,观察大鼠从明室再次进入暗室的时间,即为“潜伏期Ⅱ”。实验中的全部操作应在安静的房间中单独进行,实验过程中避免外界光源的照射,实验后采用酒精对大鼠穿梭箱进行消毒除味。

五、统计学分析

采用 Graphpad Prism 5 软件对相关数据进行整理和分析。所有数据采用($\bar{x}\pm s$)形式表示。两组间比较采用独立样本 t 检验,$P<0.05$表示差异有统计学意义。

结　果

在训练阶段,C 组、ML 组、W-ML 组、T-ML 组的潜伏期Ⅰ分别为(58.00±11.41)s、(65.33±11.39)s、(64.33±14.06)s、(63.33±14.32)s;在实验阶段,C 组、ML 组、W-ML 组、T-ML 组的潜伏期Ⅱ分别为(300.00±0.00)s、(69.21±12.19)s、(300.00±0.00)s、(300.00±0.00)s。训练阶段,4 组大鼠的潜伏期Ⅰ间比较,差异无统计学意义($P>0.05$)。实验阶段,与 C 组比较,ML 组大鼠潜伏期Ⅱ显著降低($P<0.05$);与 ML 组比较,W-ML 组和 T-ML 组潜伏期Ⅱ显著升高($P<0.05$),W-ML 组与 T-ML 组间比较,差异无统计学意义($P>0.05$)。详见图 1。



注:与 C 组潜伏期Ⅱ比较,[a]$P<0.05$;与 ML 组潜伏期Ⅱ比较,[b]$P<0.05$

图 1　各组大鼠在训练阶段及实验阶段的潜伏期比较

讨　论

牙齿缺失对脑功能的影响越来越受到人们的关注[21-23]。口腔临床医学研究表明,磨牙缺失可导致脑部受损,从而影响脑的正常发育及其学习记忆能力[24-25]。神经生物学研究亦表明,磨牙缺失还可在活体动物层次对其脑功能产生不良影响,比如学习、重复记忆等能力下降[26]。Terasawa 等[27]研究表明,磨牙缺失可通过胆碱能系统功能失调导致学习记忆能力下

降。本研究结果也表明磨牙缺失后大鼠的学习记忆能力下降。Oue 等[28]研究表明,磨牙缺失后导致的学习记忆能力下降,可能与脑部神经元数目的丢失有关。Kubo 等[29]认为磨牙缺失可下调突触小泡蛋白的表达水平,从而导致认知功能障碍。因此,我们推测磨牙缺失后大鼠学习记忆能力的下降可能与脑部神经元丢失、突触小泡蛋白的表达下降有关。

运动可通过减小氧化应激水平、减小炎症反应、促进神经突触可塑性等改善学习记忆能力[30-33]。此外,运动还可促进学习记忆能力。Choi 等[34]研究表明,跑台运动可促进大鼠脑部神经前体细胞和成熟神经元的再生能力,从而促进其学习记忆能力。因此,本研究分别对磨牙缺失大鼠进行为期 1 周的跑轮和跑台预运动训练,结果表明主动跑轮和被动跑台两种不同的预运动方式均可促进磨牙缺失大鼠的学习记忆能力。因此,我们可以推测预运动促进磨牙缺失后学习记忆能力恢复与预运动通过增加神经元的抗损伤能力和脑内多巴胺等神经递质的基础含量有关。值得一提的是,Lin[35]等研究表明,与跑台运动比较,跑轮运动是一种主动的、自发的运动形式,因而对大鼠的学习记忆能力具有更好的促进作用。但在本研究中,大鼠在磨牙缺失前分别进行跑轮和跑台预运动,此后其学习记忆能力差异无显著性差异,其可能原因是,本研究采用被动回避反射评价大鼠在 300 s 内的学习记忆能力,而 300 s之后是否有差异未予比较;此外,跑轮和跑台两种不同的预运动方式改善磨牙缺损后的学习记忆能力是否在其他认知行为学模型中有不同效果,是否在分子或细胞水平有内在机制差异等还需进一步深入研究。

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Long-term outcomes of microfracture of the shoulder

BACKGROUND AND OBJECTIVE The incidence of glenohumeral chondral defects reported incidentally at arthroscopy has been within the range of five to 17%. As microfracture has been used in knee surgery, this study was designed to determine the effect of this procedure on patients with articular cartilage defects at the glenohumeral joint.

METHODS This retrospective review included consecutive patients with chondral defects of the humeral head and/or glenoid who received microfracture surgery after failed conservative treatment. Participants were contacted by phone for postoperative assessments, including a visual analogue scale (VAS) for pain, the Single Assessment Numeric Evaluation (SANE), subsequent surgery, willingness to undergo the surgery again, the Simple Shoulder Test (SST), the American Shoulder and Elbow Surgeons (ASES) form and the Short Form-12 (SF-12). The average follow-up time was 10.2 years.

RESULTS Of the 13 patients available for follow-up, three had progressed to failure, with 10 available for follow-up questionnaires. The adjusted VAS scores were significantly improved at long-term follow-up as compared with baseline ($P=0.004$), as were scores on the ASES ($P=0.009$) and SST ($P=0.009$). Survivorship was 93.8% at one year, 87.5% at three years and 76.6% at nine years.

CONCLUSION This study of patients with shoulder joint chondral defects, treated with microfracture, found a reoperation rate of 28.6% and a long-term clinical failure rate of 24.2%.

【摘自:Wang KC, Frank RM, Cotter EJ, et al. Long-term clinical outcomes after microfracture of the glenohumeral joint. average 10-year follow-up. Am J Sports Med, 2018, 46 (4): 786-794.】