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肥胖症是全球范围内常见的慢性代谢性疾病，是2型糖尿病、心血管疾病及多种恶性肿瘤的重要危险因素，其发生率居高不下，严重危害人类健康。目前减重的干预方法较多，包括生活方式干预、药物治疗、减重手术等。轻度肥胖可通过生活方式调整实现体重控制，但因该病发病机制复杂，涉及能量稳态与奖赏环路失衡，多数患者长期减重应答不佳且体重反弹风险高，对于这类患者，靶向中枢奖赏环路的无创神经调控技术逐渐成为研究热点。

然而，临床上传统减重方案的长期疗效并不稳定，体重反弹率较高且针对中枢奖赏环路异常的精准干预手段有限，因此从肥胖症中枢机制出发探索安全有效的靶向干预方案十分重要，而目前尚缺乏明确的、经临床验证的无创干预方案及脑-肠轴相关机制证据。

近年来，实时功能磁共振成像神经反馈（real-time functional magnetic resonance imaging neurofeedback, rtfMRI-NF）技术快速发展，在脑功能调控与疾病干预方面展现出极大的应用潜力，通过从实时影像数据中提取脑区活动信号并转化为可视化反馈，从而对神经环路异常进行客观的靶向调控，以非侵入性方法实现深部脑区的功能重塑，可用于肥胖症等代谢性疾病的干预研究。

本研究分析了靶向肥胖症患者双侧伏隔核的rtfMRI-NF干预前后的静息态脑功能特征，通过配对样本t检验及高斯随机场校正，筛选出干预前后差异显著的分数低频振幅（fractional amplitude of low-frequency fluctuations, fALFF）脑区。其次，收集并分析患者干预前后的临床量表与血清学指标，定量资料采用配对样本*t*检验或Wilcoxon符号秩检验比较干预前后的差异，对于等级资料采用非参数检验进行比较，将所有差异显著的指标纳入Pearson相关分析，筛选出与脑功能变化相关的临床及外周关联因素，进一步探索神经反馈对脑-肠轴相关外周代谢指标的潜在调控效应。结果显示该rtfMRI-NF干预具有良好的调控效能，能有效改善肥胖症患者的不良摄食行为与脑功能异常，具有调节脑-肠轴相关外周代谢指标的潜能，有助于临床更好地探索肥胖症的无创靶向治疗方案。详见内文第12页。

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### About the cover

Obesity is a common chronic metabolic disease worldwide and an important risk factor for type 2 diabetes, cardiovascular diseases, and multiple malignant tumors. Its prevalence remains high and it poses a serious threat to human health. Currently, weight-loss interventions mainly include lifestyle modification, pharmacotherapy, and bariatric surgery. Mild obesity can be managed through lifestyle adjustment; however, because the pathogenesis of obesity is complex and involves imbalance between energy homeostasis and reward circuitry, many patients show poor long-term weight-loss responses and are at high risk of weight regain. For these patients, non-invasive neuromodulation techniques targeting the central reward circuitry have gradually become a research focus.

However, the long-term efficacy of traditional clinical weight-loss approaches is unstable, weight regain rates are high, and precision interventions for central reward circuit abnormalities remain limited. Therefore, it is important to explore safe and effective targeted interventions based on the central mechanisms of obesity. At present, however, clear, clinically validated non-invasive intervention protocols and brain-gut axis-related mechanistic evidence are still lacking.

In recent years, real-time functional magnetic resonance imaging neurofeedback (rtfMRI-NF) has developed rapidly and shown great potential in brain function modulation and disease intervention. By extracting brain activity signals from real-time imaging data and converting them into visual feedback, rtfMRI-NF enables objective targeted modulation of neural circuit abnormalities and non-invasive functional remodeling of deep brain regions, and can be used in intervention studies of metabolic diseases such as obesity.

This study analyzed resting-state brain functional characteristics before and after rtfMRI-NF intervention targeting the bilateral nucleus accumbens in patients with obesity. Using paired-sample t tests and Gaussian random field correction, brain regions with significant pre- versus post-intervention differences in fractional amplitude of low-frequency fluctuations (fALFF) were identified. In addition, clinical scale scores and serological indicators were collected and analyzed before and after intervention. Quantitative data were compared using paired-sample *t* tests or Wilcoxon signed-rank tests, and ordinal data were compared using nonparametric tests. All indicators with significant differences were included in Pearson correlation analysis to identify clinical and peripheral factors associated with brain functional changes, further exploring the potential regulatory effects of neurofeedback on brain-gut axis-related peripheral metabolic indicators. The results indicate that this rtfMRI-NF intervention has good regulatory efficacy, can effectively improve maladaptive eating behaviors and brain functional abnormalities in patients with obesity, and has the potential to modulate brain-gut axis-related peripheral metabolic indicators, which may help facilitate clinical exploration of non-invasive targeted treatment strategies for obesity. Please see text page 12.

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