心理学报 2024, Vol. 56, No. 6, 731−744
Acta Psychologica Sinica

https://doi.org/10.3724/SP.J.1041.2024.00731

工具性喂养对 9~12 岁儿童挑食行为的影响：来自静息态功能磁共振的证据*

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摘 要 采用静息态磁共振数据结合机器学习方法在 87 名 9~12 岁儿童中探究挑食行为的神经关联, 并检验其在工具性喂养和挑食行为之间的中介作用。结果发现儿童挑食行为与右侧尾状核的局部一致性正相关。功能连接结果表明儿童挑食行为与右侧尾状核−左侧壳核功能连接正相关。预测分析结果显示上述神经发现能够较好的预测儿童挑食行为, 验证了神经结果的稳定性。这表明涉及感觉信息编码和奖赏加工的尾状核和壳核可能在儿童挑食行为的个体差异中起着关键作用。中介模型进一步显示, 工具性喂养能够通过右侧尾状核−左侧壳核功能连接负向影响儿童挑食行为。研究提供了儿童挑食行为稳健的神经基础证据, 并且为从父母喂养方式入手干预改善儿童不良的挑食行为提供理论参考。

关键词 挑食行为, 工具性喂养, 儿童, 静息态磁共振
分类号 B845

1 引言

挑食行为是儿童普遍存在的饮食问题(Chilman et al., 2023; Wolstenholme et al., 2020), 调查发现在 7~12 岁中国儿童中, 59%的儿童存在不同程度的挑食行为(Xue et al., 2015)。挑食行为是指儿童由于拒绝大量食物而导致摄入的食物种类不足(Dovey et al., 2008; Taylor & Emmett, 2019), 表现为不愿意吃某类熟悉的食物或拒绝尝试新的食物(Taylor et al., 2015)。挑食行为是喂养困难谱系中一种常见的饮食问题(McCormick & Markowitz, 2013), 会导致儿童总体食物摄入量减少(Pereboom et al., 2023), 饮食缺乏多样性还会导致营养成分缺失(Northstone & Emmett, 2013)。长此以往, 挑食行为会发展出饮食失调等问题(Machado et al., 2021), 增加肥胖发生和生长不良的风险(Demir & Bektas, 2017; Kutbi, 2021)。因此, 儿童挑食行为的研究具有现实意义, 对改善儿童的不良饮食习惯促进儿童健康成长有重要的参考价值。

儿童挑食行为的影响因素模型指出社会环境因素和认知因素是调节儿童挑食行为的关键因素(Lafraire et al., 2016)。在社会环境因素方面, 早期喂养方式被认为是儿童挑食行为最重要的“塑造者” (Brown et al., 2022; Harris et al., 2016; Taylor & Emmett, 2019)。已有研究关注父母用食物作为非营养补充目的的喂养行为, 比如将食物作为奖励来促进或巩固好的行为和表现(Lo et al., 2016; Morrison et al., 2013), 这种喂养方式被称为工具性喂养(Instrumental Feeding; Mason, 2015; Nembhwani & Winnier, 2020)。研究表明工具性喂养是非反应性喂养方式的一种, 它干扰了儿童正确识别饥饿信号和调节食欲的能力(Byrne et al., 2017; Harris et al.,

收稿日期: 2023-03-21
* 国家自然科学基金项目(32271087)资助。
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2018)，通常与不良的饮食和行为后果相关(Daniels, 2019)。以往研究表明工具性喂养与儿童挑食行为的增加有关，即父母使用食物作为奖励的频率越高，儿童的挑食水平越高(Finnane et al., 2017; Maximino et al., 2021)。例如，纵向研究发现父母在儿童 4 岁时采用工具性喂养能够预测 5 年后挑食行为的增加(Jansen et al., 2020)。Mallan 等人(2018)发现 2 岁挑食儿童的父母倾向于采用工具性喂养的方式鼓励他们吃不太喜欢的食物，但工具性喂养却预测了一年后更多的挑食行为。由此可见，工具性喂养似乎是一种不利于儿童成长的喂养方式，会增加或导致儿童的挑食行为。

除了家庭环境因素以外，儿童的大脑发育也会对其一系列行为产生影响(Plassmann et al., 2022)。挑食行为是一种可遗传的饮食行为特质(Fildes et al., 2016; Smith et al., 2017)，非稳态进食行为通过复杂的神经系统调控(Berthoud & Levin, 2012)。儿童时期是大脑神经发育的关键阶段(Fan et al., 2023; Modabbernia et al., 2021)，因此探索挑食行为的神经关联对于理解和预防儿童挑食行为至关重要。儿童挑食行为的影响因素模型首次强调认知因素对挑食行为的影响，包括对食物的感知机制、内部表征和分类系统以及情绪加工(Lafraire et al., 2016)。目前仅一篇研究探索 8~13 岁儿童挑食行为和大脑静息态功能连接之间的关系，该研究选定伏隔核、下顶叶和额极分别作为奖赏加工、反应抑制和冲动性相关脑区，结果发现冲动性功能连接(额极−伏隔核功能连接)及其与反应抑制功能连接(下顶叶−伏隔核功能连接)的差异与挑食行为负相关，这表明儿童挑食行为与奖赏、控制和冲动性相关脑区之间的功能连通性失衡有关(Chodkowski et al., 2016)。食物恐新是挑食行为的一个方面(Dovey et al., 2008)，研究发现当观看不熟悉的食物刺激时，高低食物恐新组在楔前叶、尾状核和壳核处的激活存在差异(Wolfe et al., 2015)。尾状核、壳核和伏隔核是奖赏环路的关键节点(Li, Hu et al., 2023)，参与调控对食物的“喜欢”和“想要”，决定了对食物的趋近或远离(Campos et al., 2022; Jiang et al., 2015; Morales & Berridge, 2020)。以往研究发现尾状核、壳核和伏隔核负责编码食物的主观奖赏价值，参与形成对食物的主观偏好(Hommer et al., 2013; Luo & Han, 2023; Terenzi et al., 2022; van den Bosch et al., 2014)，而且在厌恶动机驱动的行为中也发挥作用(Royet et al., 2016)，这与挑食行为的内涵相似。此外，尾状核也参与感觉信息加工(Yuan et al., 2022)，有研究表明楔前叶和尾状核是感觉加工敏感性的神经基础(Acevedo et al., 2018, 2021; Greven et al., 2019)。与之对应地，自闭症儿童普遍存在挑食行为被认为与其感官体验极其敏感相关(Klockars et al., 2021; Nimbley et al., 2022)，体现在对食物线索的味道和质地反应增强(Avery et al., 2018)。综上，儿童挑食行为可能主要与参与感觉加工敏感性以及奖赏加工相关脑区的神经活动相关。

儿童时期的神经可塑性使得脑发育容易受到养育模式等家庭环境因素的影响(Tooley et al., 2021)，例如喂养环境和策略充当着外部刺激影响儿童的大脑认知发育(Liu & Chang, 2023)。那么通过呈现奖赏食物鼓励儿童良好表现的工具性喂养可能影响儿童某认知功能相关脑区的发育。根据奖赏习惯化理论，习惯化的过程是最初对某种刺激的敏感性增加，在刺激反复出现后对其敏感性降低的过程，并且会将兴趣转向新的刺激(Benson & Raynor, 2014; Epstein et al., 2008)。同样有观点认为反复接触食物可能会导致感官特定的饱足感(Rolls et al., 1986; Temple et al., 2008)，长时间接触少量不变的食物会产生感官疲劳而导致食物偏好降低(Houston-Price et al., 2009; Lafraire et al., 2016)。因此，工具性喂养可能会影响儿童与感觉和奖赏加工相关脑区的发育，频繁呈现食物奖励可能导致儿童感觉和奖赏脑区反应疲劳。

调查发现 7~12 岁儿童挑食行为的流行性高达 59% (Xue et al., 2015)，学龄儿童仍然普遍存在挑食行为(Chao & Chang, 2017; Diamantis et al., 2023; Zhang et al., 2021)。已有研究探讨工具性喂养和挑食行为的关系大多都是在年龄较低的儿童样本中进行，并且认为工具性喂养可能会增加对奖励食物的偏好，同时对想要促进的食物的偏好降低而加剧挑食行为(Byrne et al., 2017; Harris et al., 2018)。但是没有研究验证过在父母采用食物作为奖励后儿童心理过程的变化是否与猜测一致。根据前文综述，挑食行为与儿童的感知觉加工等认知发展有关(Lafraire et al., 2016)，因此随着年龄增长，儿童的大脑发育使得认知能力不断发展，那么是否会因为认知变化而导致对食物的看法以及对父母喂养策略的反馈发生改变。基于此，有必要在学龄儿童中验证工具性喂养与挑食行为的关系，并且本研究认为在学龄儿童中二者的关联可能与以往研究的发现不同。同时，研究结合静息态磁共振数据，试图

从神经功能的角度解释工具性喂养影响挑食行为潜在的心理加工过程。从研究方法来说, 目前唯一一篇探究挑食行为静息态神经基础的研究(Chodkowski et al., 2016)采用的兴趣区到兴趣区的功能连接分析存在一定的局限性。由于目前尚无其他研究对儿童挑食行为的神经基础进行探索, 选定的兴趣区在前人研究中并未发现与挑食行为直接相关, 因此这种先验性假设兴趣区的分析方式其背后的研究依据并不充足。在儿童挑食行为研究领域尚无充足的神经方面的实证证据的情况下, 全脑层面的探索式分析更为合适。

静息态功能磁共振成像(Resting-state functional magnetic resonance imaging, RS-fMRI)是一种独立于实验任务, 反映大脑自发神经活动特征的影像学测量技术, 可以检测在放松状态下大脑内在的功能活动模式(Raichle et al., 2001; Zou et al., 2009; Zuo et al., 2010)。静息状态下大脑活动消耗总能量的 95%, 而任务诱发的活动只占用大脑 0.5%~1.0%的总能量(Fox & Raichle, 2007), 因此 RS-fMRI 被认为是识别饮食行为的神经关联很有前景的研究方法(Chen et al., 2021; Dong et al., 2014)。饮食行为由多个脑区共同参与调控, 因此探索大脑的功能连接模式是揭示挑食行为神经关联的关键手段。静息态功能连接(Resting-state functional connectivity, RSFC)反映了静息状态下大脑不同区域间的信息交流(Fox et al., 2007)。为了实现探索性分析的目的, 本研究采用基于种子点的功能连接分析方式从体素水平上探索挑食行为的神经关联(Lee et al., 2013; Yang et al., 2020)。而在选取种子点时由于尚无充足的神经证据, 因此首先探究挑食行为相关联的局部神经活动特征, 并以此与全脑其他体素进行功能连接分析, 探究挑食行为是否涉及到不同脑区间的功能协同。局部一致性(Regional homogeneity, ReHo)是衡量相邻体素间自发活动同步性程度的指标, 反映了神经活动的区域功能信息整合(Paakki et al., 2010; Zang et al., 2004), 是揭示饮食行为神经关联可靠的静息态指标(Dong et al., 2015; Gao et al., 2018)。因此, 本研究以 ReHo 和 RSFC 作为反映大脑自发神经活动的指标, ReHo 与 RSFC 结合使用被认为是从单变量水平(区域内功能同步)和多变量水平(区域间远程功能连通)两个角度识别饮食行为内在神经连接的有效方式(Gao et al., 2018; Wang et al., 2023)。此外, 本研究采用一种机器学习方法测试脑与挑食行为关联的稳定性(Chen et al., 2022)。

综上, 本研究将采用全脑探索性的相关分析结合机器学习方法探究儿童挑食行为的静息态神经关联, 提供儿童挑食行为的稳健神经生物学基础, 从神经功能的角度验证并扩展儿童挑食行为的影响因素模型。我们初步假设儿童挑食行为主要与感觉敏感性加工和奖赏加工相关脑区的活动和功能连接有关, 如楔前叶、尾状核和壳核等(假设 1)。此外, 本研究不仅验证工具性喂养与儿童挑食行为的关系, 并打算进一步从静息态功能活动的角度提供神经证据解释二者之间的作用机制, 即建立工具性喂养—静息态神经表现—挑食行为中介模型。工具性喂养可能与儿童感觉和奖赏加工脑区的发育有关, 因此本研究假设工具性喂养能够通过感觉和奖赏加工脑区的活动及功能连接影响儿童挑食行为。根据奖赏习惯化理论, 工具性喂养与感觉和奖赏加工相关脑区(如楔前叶、尾状核和壳核等)的活动和功能连接减弱有关, 导致对喜爱食物的偏好降低, 增加了吃多种食物的可能性, 挑食行为就会随之减少(假设 2)。

2 方法

2.1 被试

本实验招募来自西南地区两所小学的 129 名儿童被试。所有被试必须满足两个条件才能纳入正式分析: 完成问卷测量和静息态核磁扫描(剔除 27 名被试)以及静息态核磁数据无质量和头动较大问题(剔除 15 名被试)。经过筛选后, 87 名儿童(51%是女孩, 年龄 = 10.07 ± 0.96 岁, 年龄范围是 9~12 岁)纳入正式分析。根据 Xu 等人(2023)的计算方式, 本研究使用 G*power 软件来计算所需的样本量。根据相关文献(Finnane et al., 2017), 工具性喂养与儿童挑食行为的相关性为 0.30, 工具性喂养的标准差为 0.96, 挑食行为的标准差为 0.91。输入偏倚(α error probability) = 0.05, 统计检验力(1 − β) = 0.80, 最终得到所需样本量至少为 82 人。所有被试视力或矫正视力正常, 无色盲, 且均未报告有精神疾病史或神经病史。所有被试在实验前获得家长同意并签署知情同意书, 在实验后得到文具作为实验报酬。该研究经过心理学部学术伦理委员会批准。

2.2 行为变量测量

2.2.1 儿童挑食行为

采用儿童饮食行为问卷(Children's Eating Behavior Questionnaire)中的挑食行为维度测量家长感知到的儿童挑食行为(Wardle et al., 2001)。挑食行为维

度包含 6 个题项, 反映了对能够接受的食物范围的高度挑选倾向。这些题项评估了儿童表现出某种行为的频率(例如, 我的孩子喜欢的食物种类非常多)。评分采用 5 点计分制, 1 = 从不, 5 = 总是, 正向计分和反向计分条目交替排列, 统计分析时反向题目作反向计分处理。计算题项总分作为儿童挑食行为得分, 得分越高代表儿童的挑食行为越严重。中国版儿童饮食行为问卷已被证明具有良好的信效度(Guo et al., 2018; 曾思瑶, 2018)。本研究中挑食行为分维度的内部一致性系数为 0.76。

2.2.2 工具性喂养

工具性喂养由儿童喂养问卷(Child Feeding Questionnaire)中食物作为奖励(Food as rewards)分维度测量(Jansen et al., 2020; Zheng et al., 2016)。该维度包含两个题项, 分别是“我会给我的小孩他/她自己喜欢吃的食品来鼓励他/她好好表现”和“如果孩子表现好, 我会奖励给他/她甜食(比如: 糖果、冰淇淋、蛋糕、甜点等)”。该问卷由父母进行回答, 评分采用 5 点计分制(1 =不同意, 5 =同意), 无反向计分题。计算两个题目的总分作为父母工具性喂养的程度, 得分越高表示工具性喂养程度越高。本研究使用的工具性喂养分维度的内部一致性系数为 0.78。

2.3 静息态功能磁共振数据的采集和预处理

2.3.1 影像采集

所有影像数据均采用 3T Trio 西门子磁共振扫描仪进行采集(Siemens Medical, Erlangen, Germany)。每个被试都进行 5 分钟结构像扫描和 8 分钟的静息态磁共振的扫描。在正式扫描之前, 所有参与者都进行了 5 分钟的模拟扫描, 以适应扫描环境。在正式扫描期间, 使用泡沫垫和耳塞来减少头部运动和机器噪音。采用梯度回波平面成像序列(a gradient echo planar imaging sequence)获得静息态功能影像, 扫描参数为: 重复时间(repetition time, TR) = 2000 ms; 回波时间(echo time, TE)= 30 ms; 层数(Slices)= 33; 层厚(slice thickness)= 3.5 mm; 成像矩阵(matrix size)= 64 × 64; 翻转角(flip angle, FA)= 90°; 视场(field of view, FOV)= 224 mm × 224 mm; 体素大小(voxel size)= 3.5 mm × 3.5 mm × 3.5 mm。一共获得 180 时间点的成像。T1 加权结构像使用快速梯度回波成像序列获得(Magnetization Prepared Rapid Acquisition Gradient Echo Sequences), 使用以下扫描参数: TR = 2530 ms; TE = 3.48 ms; FOV = 256 mm × 256 mm; FA = 7°; matrix size = 256 × 256; 层间距 = 1 mm; voxel size = 1 mm × 1 mm × 1 mm。高分辨率 T1 加权结构图像是为静息态影像处理提供解剖学参考。

2.3.2 影像数据预处理

使用基于 SPM8 的脑成像数据处理与分析工具箱(Data Processing and Analysis for Brain Imaging, 简称 DPABI)对数据进行处理(Yan et al., 2016)。预处理包括以下步骤: (1)剔除每个被试前 10 个时间点的影像, 目的是为保证 BOLD 信号达到稳定状态, 排除机器启动信号不均和被试对机器环境适应过程对图像的干扰。(2)剩下的 170 个时间点的影像进行时间层校正(slice timing)以及头动校正(realignment)。(3)为排除个体大脑形状、大小等方面的差异, 方便不同被试间的比较, 将影像数据进行空间标准化(normalization), 统一到标准的蒙托利尔坐标系空间模板(Montreal Neurological Institute), 体素分辨率为 3 mm × 3 mm × 3 mm。(4)采用 6 mm 半高宽(Full width at half maximum)的平滑核进行高斯平滑(Smooth)处理(计算 ReHo 指标时不进行平滑处理)。(5)每个被试的 fMRI 图像配准到分割后的高分辨率 T1 加权解剖图像。(6)为了控制潜在的协变量对研究结果带来的影响, 采用 Friston 24 方法将 6 个头动参数(三个方向上的平移和转动)、白质、脑脊液以及全脑信号等参数进行了回归。(7)通过 0.01~0.1 Hz 频段进行低频滤波(Filer), 去除呼吸和心跳等高频信号值影响。(8)最终, 对每个被试的图像进行擦洗(Scrubbing), 在擦洗过程中剔除头动(framewise displacement, FD) > 0.5 mm 的时间点。(9)头动控制。将数据擦洗过程中剔除的时间点超过总时间点 30%的被试排除(Varangis et al., 2019), 共有 15 名被试由于坏点过多被剔除。为了确保头动与兴趣变量不存在显著相关, 计算平均头动指标(mean FD)与儿童挑食行为的相关(Li, Bian et al., 2023; Shen et al., 2017), 最终发现二者不存在显著相关(r = 0.18, p = 0.097)。最后在统计分析中, 将头动纳入协变量以进一步控制其对结果的影响(Horien et al., 2018; Waller et al., 2017)。

2.4 数据分析

2.4.1 ReHo-行为相关分析

首先使用 DPARSF 工具包(Data Processing Assistant for Resting-State fMRI)计算局部一致性系数(Regional homogeneity, ReHo)。通过计算给定体素与其 26 个相邻体素的时间序列的肯德尔和谐系数(KCC)生成单个 ReHo 图(Zang et al., 2004)。给定体素的 ReHo 值越大, 表示相邻体素之间 RS-fMRI

信号的局部同步程度越高。为了减少个体差异的影响, 通过将每个体素的 KCC 除以每个被试整个大脑的平均 KCC 来进行 ReHo 图的归一化, 并通过 Fisher 的 r-to-z 变换将 ReHo 图转换为 z 分数。最后对 ReHo 图进行空间平滑处理。为了确定与挑食行为相关的脑区, 采用全脑相关分析计算大脑每个体素与挑食行为的相关。使用 SPM 12 软件对儿童挑食行为与 ReHo 进行多重线性回归分析, 并以年龄、性别、BMI 和头动(mean FD)为协变量。采用体素水平 $p < 0.005$, 团块水平 $p < 0.05$ 的高斯随机场(Gaussian Random-Field, GRF)多重比较矫正, 以获得与儿童挑食行为显著相关的 ReHo 脑区。

2.4.2　RSFC-行为相关分析

为了探索 ReHo-行为分析发现的脑区与其他脑区的功能连通性与儿童挑食行为的关联, 本研究进行 RSFC-行为相关分析。以 ReHo 分析中发现的显著脑区为种子点, 以 6 mm 为半径定义感兴趣区, 并提取了感兴趣区内体素的时间序列。随后使用 DPABI 软件在个体水平上计算其与全脑其他体素的时间序列的相关性, 即皮尔逊相关系数 r, 将 r 值进行 Fisher z 转化。最后, 在组分析水平计算每条功能连接与挑食行为的相关, 同样在 SPM 中采用多重线性回归分析, 并以年龄、性别、BMI 和头动为控制变量。多重比较校正采用 GRF 校正, 报告通过团块水平 $p < 0.05$, 体素水平 $p < 0.005$ 矫正的显著功能连接。

2.4.3　预测分析

本研究采用一种机器学习方法——基于线性回归的交叉验证法——测试脑与挑食行为关联的稳定性(Chen et al., 2022; Kong et al., 2018; Wang et al., 2018)。传统将神经影像学指标与认知或行为评分关联起来的分析方式受到样本特点的限制, 无法确定观察到的相关结果是否可以推广到看不见的个体中, 而交叉验证法具备评估模型预测未知个体行为的能力(Cui et al., 2018; Yarkoni & Westfall, 2017)。该方法目前已得到广泛的认可并应用于认知神经科学研究以提高其研究结果的稳健性(Chen et al., 2022)。在回归模型中, 因变量为挑食行为得分, 自变量是大脑指标(与挑食行为显著相关的脑区 ReHo 和功能连接值)。首先采用四折法将数据平均分开, 接下来用其中三折的数据建立线性回归模型, 用第四折数据验证这个模型。重复这个过程四次得到一个最终的 $r_{(预测, 观测)}$值, 代表模型预测数据与真实观测数据的平均相关。为了得到模型的统计学显著性, 采用非参数测试方法, 即 1000 次置换检验来估计挑食行为与静息态脑指标之间没有关联的零假设。通过计算大于 $r_{(预测, 观测)}$的 r 值个数, 再除以数据集的个数(即 1000)得到模型的统计显著性(p 值)。

2.4.4　中介分析

采用 SPSS 中的 PROCESS 插件(Hayes & Scharkow, 2013)计算大脑自发神经活动在工具性喂养−挑食行为关系中的中介效应。具体来说, 饮食行为受大脑神经系统的指导与调控(Berthoud & Levin, 2012; Plassmann et al., 2022), 因此在建立中介模型时将静息态神经表现作为中介变量影响因变量——儿童挑食行为。而工具性喂养方式作为家庭环境方面的影响因素, 在儿童的成长发育过程中, 可能会作为外部刺激影响着大脑的发育(Tooley et al., 2021), 因此在中介模型中将工具性喂养方式作为自变量, 可能会通过影响儿童的神经发育进而影响挑食行为。综上, 工具性喂养为自变量, 挑食行为为因变量, 与挑食行为相关的脑区的 ReHo 值和功能连接值为中介变量。使用 5000 次迭代的 bootstrapping 方法评估中介效应的显著性, 如果 95%置信区间(Confidence Interval, CI)不包含零, 则表示中介效应显著。进行中介分析前, 为了对中介变量进行筛选, 将大脑信号和自变量进行偏相关分析, 以年龄, 性别和 BMI 为协变量。与自变量存在显著相关的大脑指标被选作中介变量进行进一步的中介分析。

3　结果

3.1　共同方法偏差检验

本研究采用的问卷数据来源于同一评分者, 因此可能存在共同方法偏差问题(Zhou & Long, 2004)。首先, 在施测过程中进行了必要的控制, 保护参与者的匿名性、对数据的科研用途加以解释、正反向计分等。进一步地, 采用单因素验证性因子分析对所有题项进行共同方法偏差检验(Liu et al., 2019; Podsakoff et al., 2012), 结果显示模型拟合较差, $\chi^2/df = 8.920$、CFI = 0.796、TLI = 0.714、RMSEA = 0.162、SRMR = 0.097。双因子模型的拟合指标($\chi^2/df = 1.309$、CFI = 0.974、TLI = 0.961、RMSEA = 0.06、SRMR = 0.055)显著优于单因素模型, 所以不存在严重共同方法偏差问题。

3.2　初步分析

所有变量的描述性统计和相关分析如表 1 所示。结果表明, 挑食行为没有显著的性别差异, t (85)

= 1.96, p = 0.053, 95% CI = [−0.02 3.57]。挑食行为与年龄(r = 0.05, p = 0.671, 95% CI = [−0.17 0.25]), BMI (r = −0.01, p = 0.923, 95% CI = [−0.22 0.20])和头动(r = 0.18, p = 0.097, 95% CI = [−0.03 0.38])均没有显著相关关系。

3.3 挑食行为的神经相关结果

ReHo-行为相关分析结果如图 1 和表 2 所示。挑食行为与右侧尾状核的 ReHo 值正相关(r = 0.43, p < 0.001, 95% CI = [0.25 0.59])。在控制了性别、年龄、BMI 和头动后, 预测分析的结果表明右侧尾状核($r_{(预测, 观测)}$ = 0.37, p < 0.001)的 ReHo 值能够显著预测挑食行为。

RSFC-行为相关分析结果如图 2 和表 2 所示, 结果显示挑食行为与右侧尾状核−左侧壳核之间的功能连接正相关(r = 0.43, p < 0.001, 95% CI = [0.24 0.59])。预测分析结果表明右侧尾状核−左侧壳核功能连接($r_{(预测, 观测)}$ = 0.35, p < 0.001)能显著预测儿童挑食行为。

3.4 中介模型

在控制性别、年龄、BMI 和头动后, 结果发现工具性喂养与挑食行为存在显著的负相关(r = −0.24, p = 0.026, 95% CI = [−0.45 −0.02])。接下来计算上述与挑食行为相关的神经指标与工具性喂养之间的相关性。结果显示工具性喂养与右侧尾状核处的局部一致性负相关(r = −0.22, p = 0.046, 95% CI = [−0.41 −0.001]), 与右侧尾状核到左侧壳核之间的功能连接显著负相关(r = −0.30, p = 0.006, 95% CI = [−0.49 −0.08])。这些结果表明工具性喂养、挑食行为相关的大脑自发活动/功能连接以及挑食行为三者关系密切。

表 1 所有变量的描述性统计和相关结果(N = 87)

变量	平均值	标准差	范围	1	2	3	4
1 年龄	10.07	0.96	9~12	-			
2 BMI	18.61	3.57	12.76~29.81	0.24*	-		
3 头动	0.18	0.13	0.05~0.59	−0.25*	−0.08	-	
4 挑食行为	16.10	4.28	6~28	0.05	−0.01	0.18	-
5 工具性喂养	6.47	1.76	2~10	−0.19	−0.16	−0.04	−0.26*

注: N = 样本量; $^*p$ < 0.05

表 2 儿童挑食行为与全脑 ReHo 值和功能连接的相关分析结果表

脑区	峰值点坐标			体素量	t 值
	X	Y	Z		
与 ReHo 相关的脑区					
右侧尾状核	18	21	0	139	0.54
与功能连接相关的脑区（以右侧尾状核为种子点）					
左侧壳核	−21	15	12	214	0.57

注：显著脑区的阈值设置为团块水平 p-GRF < 0.05, 体素水平 p-GRF < 0.005

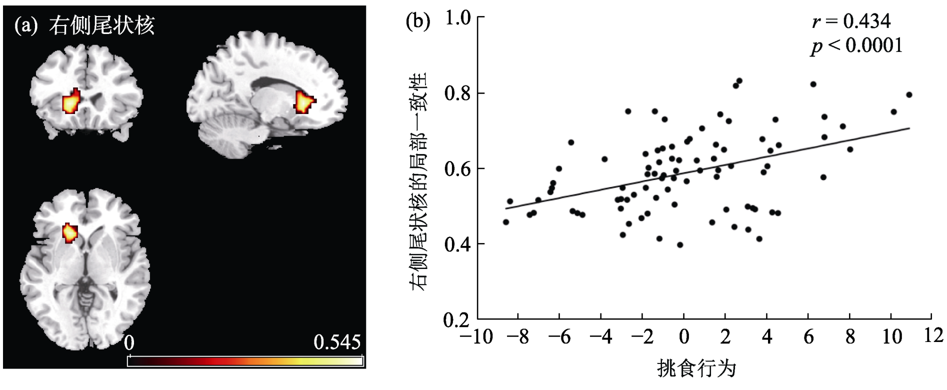

图 1 与儿童挑食行为相关的显著脑区: (a)儿童挑食行为与右侧尾状核的局部一致性正相关。颜色条表示 t 值。(b)儿童挑食行为与右侧尾状核处局部一致性相关的散点图。

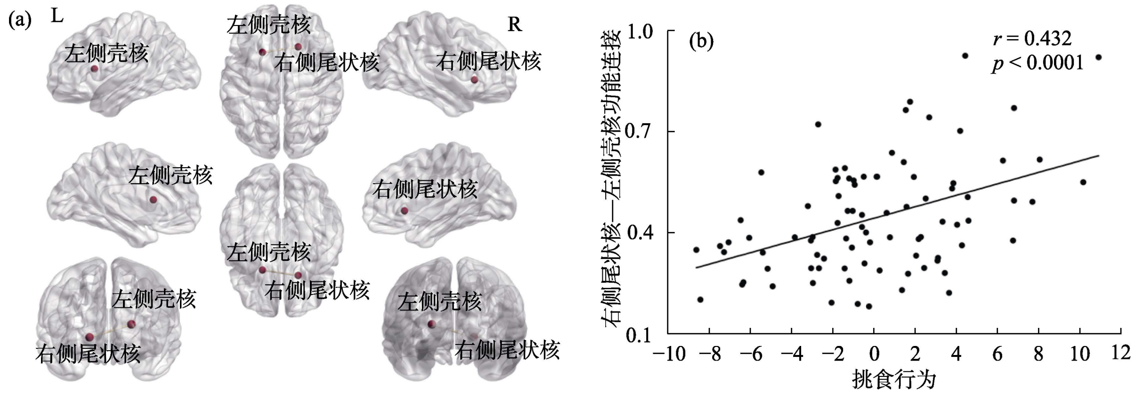

图 2　与挑食行为相关的功能连接: (a)儿童挑食行为与右侧尾状核−左侧壳核功能连接显著相关。L = 左侧; R = 右侧。(b)儿童挑食行为与右侧尾状核−左侧壳核功能连接相关的散点图。

中介结果如图 3 所示。在区域活动水平上, 结果显示右侧尾状核处的局部一致性不能中介工具性喂养对儿童挑食行为的影响(间接效应 β = −0.11, 标准误 = 0.06)。工具性喂养对挑食行为的直接影响也不显著(直接效应 β = −0.13, 标准误 = 0.09, p = 0.173)。在功能连接水平上, 工具性喂养−脑−挑食行为中介模型成立, 总效应 β = −0.24, 标准误 = 0.11, 95% CI = [−0.46 −0.03], p = 0.026, 该模型对因变量变异的解释程度 R^2 = 12.06%。结果显示工具性喂养能够通过右侧尾状核和左侧壳核之间的功能连接影响儿童挑食行为(间接效应 β = −0.16, 标准误 = 0.05, 95% CI = [−0.26 −0.06]), 同样工具性喂养对挑食行为的直接影响不显著(直接效应 β = −0.08, 标准误 = 0.10, p = 0.40)。

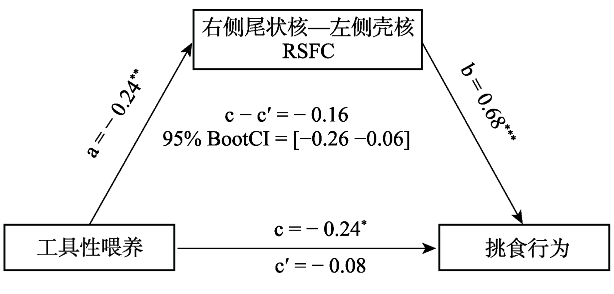

图 3　工具性喂养影响儿童挑食行为的中介模型

注：RSFC: 静息态功能连接; $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$

4　讨论

本研究采用静息态局部一致性和功能连接两个指标, 结合机器学习−交叉验证的方法探究儿童挑食行为的静息态神经基础, 并且检验了相关神经基础在工具性喂养和儿童挑食行为之间关系的中介作用。首先, 研究发现儿童挑食行为与右侧尾状核的局部一致性显著正相关。功能连接结果表明儿童挑食行为与右侧尾状核−左侧壳核之间的功能连接正相关。接着, 基于机器学习的预测分析验证了右侧尾状核的局部一致性和右侧尾状核−左侧壳核之间的功能连接与儿童挑食行为相关的稳健性。最后中介分析结果表明工具性喂养能够通过右侧尾状核−左侧壳核功能连接负向预测儿童的挑食行为。

与假设 1 一致的是, 本研究发现儿童挑食行为与奖赏相关脑区的自发神经活动相关。具体来说, 儿童挑食行为与奖赏脑区(右侧尾状核)的自发活动以及奖赏脑区之间的功能连接(尾状核−壳核)正相关。尾状核和壳核是中脑边缘奖赏网络的关键区域, 参与食物相关的奖赏加工, 并与能量稳态信号密切相互作用(Burger & Stice, 2013), 研究证实尾状核和壳核与异常进食过程有关(Zhang et al., 2019)。同时, 对高热量食物的渴求能够激活尾状核等奖赏脑区(Haber & Knutson, 2010; Pelchat et al., 2004; Stoeckel et al., 2008)。壳核被认为是奖赏加工和奖赏价值标记的核心脑区(Cromwell et al., 2005; Hori et al., 2009), 有研究表明壳核处的激活与儿童的奖赏敏感性有关(Mizuno et al., 2016)。因此, 研究发现暗示了奖赏脑区较强的反应能解释挑食行为的形成。上述神经发现印证了以往行为研究中发现的挑食儿童特定的饮食模式。前人研究发现挑食儿童会摄入更多高热量的食物(Carruth et al., 2004; Galloway et al., 2005; Taylor et al., 2016; Tharner et al., 2014), 而很少吃低奖赏价值但是高营养的食物, 例如蔬菜和水果等(Cardona Cano et al., 2015; Haszard et al., 2015; Horodynski et al., 2010)。综上, 奖赏脑区的功能活跃及其内部紧密的功能交互能够解释挑食行为的发生, 导致挑食儿童倾向于进食高奖赏价值的食物。

此外, 尾状核除了被认为是调节奖赏−食欲行

为的关键大脑结构以外(Zhang et al., 2019), 也被发现涉及感觉敏感性加工(Demarquay & Mauguière, 2016)。尾状核作为基底节的主要输入单元, 参与对感觉信息的编码加工进而影响知觉决策(Ding & Gold, 2010)。具有高感觉敏感性和高挑食行为的妥瑞氏症患者在感觉相关任务中尾状核处的激活与正常被试显著不同(Buse et al., 2016)。感觉敏感性是影响儿童挑食行为一个稳定的影响因素(Zickgraf & Elkins, 2018; Zickgraf et al., 2022)。临床研究表明挑食行为与在环境中对感觉信息的敏感程度有关(Bryant-Waugh et al., 2010; Chilman et al., 2021), 容易察觉到食物在视觉和气味等方面变化的多感官体验使得感觉敏感的个体对食物更加排斥厌恶(Cermak et al., 2010; Cunliffe et al., 2022)。尾状核与壳核间的功能连接也可能反映出的是感知觉脑区与奖赏加工脑区的功能同步性, 二者共同参与调节儿童挑食行为。儿童对食物的判断主要依赖于感知觉加工, 例如视觉和嗅觉等(Lafraire et al., 2016), 那么消极的感官决策就会导致儿童认为该食物不好吃, 即影响对食物奖赏价值的加工判断, 最终做出拒绝食物的决策。因此, 功能连接的发现表明感觉信息加工和奖赏加工对于挑食行为的重要性, 是与挑食行为紧密相关的两种认知加工过程, 能够解释儿童挑食行为的形成, 其相关脑区的功能发育也会调节挑食行为的发展。综上, 尾状核处的局部一致性以及尾状核到壳核的功能连接与儿童挑食行为之间的关联也可能是感觉敏感性与挑食行为间的关系在神经生理水平上的体现。上述发现是对儿童挑食行为影响因素模型的验证, 从神经活动的角度证实了认知功能对儿童挑食行为的影响。

与假设 2 一致的是, 本研究发现了工具性喂养与儿童挑食行为之间的负相关关系。类似地, 以往研究发现同时呈现儿童不喜欢的蔬菜和奖励会增加儿童对蔬菜的喜爱, 降低儿童挑食的可能性(Cooke et al., 2010; Wardle et al., 2003)。此外, 大多研究曾报告过相反结果, 即工具性喂养与儿童挑食行为正相关(Jansen et al., 2020)。这可能是研究者选取被试的年龄范围不同导致的。一篇关于儿童挑食行为的质性研究中提到, 一位 10 岁男孩的母亲认为相比于其他方式, 用食物作为奖励是最成功的策略(Wolstenholme et al., 2019)。与引言中提到的观点相一致, 不同年龄段的儿童神经发育程度不同(Lou et al., 2019), 使得儿童对家长喂养模式的反应不同。感官偏好并不是天生的(Lafraire et al., 2016), 大脑神经系统的发育随着年龄的增长愈发成熟使得儿童对食物的认知更加丰富, 因此当工具性喂养策略使得奖赏系统表现出对喜爱食物的反应疲劳时, 儿童的兴趣可能会转向其他食物。此外, 随着高级认知加工脑区的发育成熟(Fan et al., 2023; Tooley et al., 2021), 儿童的理解判断能力逐渐增强, 更能够理解父母采取工具性喂养策略的目的, 因此儿童很可能对喂养策略做出正向反馈, 积极配合改善自身的挑食行为。

重要的是, 本研究发现尾状核与壳核的功能连接中介了工具性喂养对儿童挑食行为的作用。具体来说, 工具性喂养频率越高, 尾状核和壳核的功能连接强度更弱, 使得儿童的挑食行为减少。从奖赏习惯化的角度解释, 食物奖励鼓励儿童做出好的行为可能意味着儿童多次接收食物奖励会形成奖赏习惯化(Benson & Raynor, 2014)。有研究表明奖赏习惯化可以阻止强迫性的奖赏寻求行为, 并且转向新的刺激(Leventhal et al., 2007)。尾状核与壳核都属于奖赏加工的关键脑区(Haruno & Kawato, 2006; Pizzagalli et al., 2009), 参与奖赏习惯化的过程(Robinson & Berridge, 2000), 并且也有研究表明尾状核到壳核的功能连接与奖赏寻求等加工过程存在相关(Arias-Carrión & Pöppel, 2007; Fuchs et al., 2006)。因此, 一个可能的解释是父母给予儿童食物奖励越多, 儿童对奖赏食物逐渐习惯化, 导致对此类食物的奖赏寻求降低, 在大脑上表现为奖赏区域之间的功能连通性降低, 饮食模式可能不会固定在对奖赏食物的摄入上, 反而有机会去尝试其他食物, 降低了挑食发生的几率。另一方面从感知觉加工的角度来说, 频繁呈现儿童偏好的食物作为奖励会导致感官饱足感, 使得儿童对奖赏食物的偏好降低(Houston-Price et al., 2009; Lafraire et al., 2016), 进而增加了选择尝试其他食物的可能性。而且这种感知觉加工“疲劳”也可能导致儿童的感官敏感性降低, 减少对以往拒绝的食物的消极感官判断, 增加了接受它们的可能性。

本研究揭示了围绕着尾状核的神经活动和功能连通性与挑食行为的紧密关联, 因此我们推断尾状核能作为识别儿童挑食行为的一个生理指标。奖赏脑区内部较强的连接从大脑自发活动的角度提供了神经证据支持行为层面上发现的儿童挑食行为对应的饮食偏好, 即挑食儿童可能会对高奖赏食物有更多的偏好和摄入。此外, 本研究创新性的提出感觉加工脑区和奖赏脑区的功能协同可能是儿

童挑食行为发生的潜在神经原因。重要的是, 本研究首次发现了工具性喂养可以通过尾状核到壳核的功能连接来影响儿童挑食行为, 解释了工具性喂养能够改善儿童挑食行为的作用原理。综上, 本研究验证并拓展了儿童挑食行为的影响因素模型。一方面, 研究结果证实了儿童挑食行为的影响因素模型中提到的社会环境因素和认知因素都会对挑食行为产生影响。另一方面, 我们进一步地发现影响因素模型中的社会环境因素和认知因素之间可能存在影响关系。由于儿童正处于大脑发育期, 因此社会环境因素可能会影响大脑的神经发育而对认知功能产生影响, 从而影响儿童挑食行为的形成与发展。此外, 研究结果在实践上有一定的参考价值, 未来可以考虑将工具性喂养作为改善儿童不健康饮食结构的干预手段。

本研究仍存在一些不足之处需要改进, 并借此提出未来研究中需要继续深入探索和拓展的方向。首先, 本研究的样本量偏小, 虽然采用机器学习方法加强了结果的稳定性, 但未来研究应该在更大的儿童样本中检验本研究结果的稳定性。除了本研究中采用的机器学习方法, 未来采用其他样本进行外部验证也是必要的。其次, 本研究仅仅是从静息态功能连接的角度提供了神经证据, 未来研究应该结合不同模态的神经研究, 例如结构态和任务态磁共振研究, 丰富儿童挑食行为神经方面的研究, 并且与静息态研究发现整合分析进一步明确儿童挑食行为的神经加工模式。第三, 本研究基于横断研究发现工具性喂养可能是改善儿童挑食行为的有效手段, 但如果想证明两者关系的因果性, 未来研究应需要采用纵向追踪的方法确定二者之间的因果关系。

5 结论

本研究采用静息态局部一致性和功能连接指标结合机器学习方法探讨了儿童挑食行为的神经基础。结果发现, 儿童挑食行为与右侧尾状核的局部一致性显著正相关, 与右侧尾状核到左侧壳核的功能连接正相关。由此揭示了感觉信息加工和奖赏加工相关脑区的神经活跃以及脑区间功能协同能够解释儿童挑食行为的个体差异, 提供了儿童挑食行为稳健的神经生物学基础, 并为该领域补充新的神经层面的实证证据。值得注意的是, 工具性喂养能够通过降低尾状核到壳核的功能连接减少儿童挑食行为。上述发现验证和拓展了儿童挑食行为的影响因素模型, 而且为通过父母的喂养方式干预改善儿童不良的挑食行为提供了理论支持。

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The impact of instrumental feeding on picky eating behavior in children aged 9 to 12: Evidence from resting-state fMRI

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Abstract

Picky eating is a common dietary issue among children characterized by lack of variety of foods consumed due to rejection of familiar (or unfamiliar) foods. The influencing factor model of picky eating behavior in children indicates that environmental and cognitive factors are key elements influencing this. Studies have found that instrumental feeding exacerbates picky eating behavior in children. However, due to the relatively young age of children in previous studies, research on the relationship between instrumental feeding and picky eating behaviors in school-aged children is insufficient. Furthermore, the brain plays a central role in guiding eating behavior; however, to date, limited neuroscientific research on the neural basis of picky eating behaviors in school-aged children exists. This study aimed to utilize resting-state functional magnetic resonance imaging (rs-fMRI) data combined with a machine learning method to explore the neural basis of picky eating behaviors in children. Additionally, it attempted to show the neural mechanisms through which instrumental feeding influences picky eating behavior.

A total of 139 children were recruited for this study. Instrumental feeding and picky eating behaviors were assessed through parent-reported measurements and rs-fMRI was conducted. A total of 87 children were included in the formal analyses as those who did not participate in the two behavioral measurements and with unqualified rs-fMRI scans were excluded. This study utilized regional homogeneity and functional connectivity to evaluate the resting-state neural substrates of picky eating behaviors. Subsequently, a machine learning method is employed to validate the stability of our results. Additionally, a mediation model was constructed to investigate the mediating role of resting-state neural substrates in the relationship between instrumental feeding and picky eating behavior.

Results showed that picky eating behavior was positively correlated with regional homogeneity in the right caudate. Functional connectivity results showed that picky eating behavior was positively correlated with functional connectivity between the right caudate and left putamen. A prediction analysis based on a cross-validation machine learning method indicated a significant correlation between picky eating behavior scores predicted by the aforementioned neural substrates (i.e., regional homogeneity in the right caudate and functional connectivity between the right caudate and left putamen) and the actual observed picky eating behavior scores. The mediation model further suggested that functional connectivity between the right caudate and left putamen could mediate the relationship between instrumental feeding and picky eating behavior. Specifically, instrumental feeding might negatively influence the functional connectivity between the right caudate and left putamen, and further reduce picky eating behavior.

By combining resting-state regional homogeneity and functional connectivity analyses, this study detected altered functional brain activity related to picky eating behaviors in children aged 9 to 12. Specifically, hyperactive neural interactions within the brain areas involved in sensory sensitivity and reward processing may explain the manifestation of picky eating behavior in children. Additionally, instrumental feeding negatively influences picky eating behavior through brain activity in regions involved in sensory sensitivity and reward processing. This study provides new insights into the resting-state neural substrates of children's picky eating behavior, extends the influencing factor model of children's picky eating behavior, and provides theoretical support for interventions to improve poor picky eating behavior in children through parental feeding practices.

Keywords picky eating behavior, instrumental feeding, children, resting-state fMRI