

综述：小鼠实验研究中的新奇食物

赵恩威

对于人类而言，新奇食物往往能带来好奇和嘴馋的反应；而对于像小鼠这样不能呕吐的啮齿类动物而言，新奇食物同时还是稳定的焦虑来源，尤其是当它们很饿的时候。经由小鼠这一动物模型来看待新奇食物这个现象，或许能够进一步理解好奇、饥渴、焦虑这三个现象之间的联系。本研究旨在系统调查基于小鼠的实验研究对于新奇食物的关注，以探索这一主题未来可能的研究方向。

1. 综述

总的来说，涉及小鼠进食行为的实验研究中，新奇食物的存在感呈现逐渐下降的趋势。二十世纪末，基于小鼠的实验研究曾流行过将食物新奇性作为自变量来操纵，对其本身进行探讨。(Cheney & Miller, 1997; Cooper & Francis, 1979; Kronenberger & Médioni, 1985; Stephens, 1973)。如(Stephens, 1973)的研究中同时将食物新奇性和环境新奇性作为自变量，来探索二者对于小鼠进食行为的影响。其得出的结论是：新奇食物和新奇环境都会抑制进食，并且效果差不多。二者叠加时，会产生最强的抑制效果。(Kronenberger & Médioni, 1985)则是对比了不同品系的小鼠在摄入水和糖水溶液上的差异。(Cooper & Francis, 1979)则是为小鼠同时提供了熟悉食物和新奇食物的选项，观察其进食行为。(Cheney & Miller, 1997)更是深入探索小鼠是更容易接受草莓味还是薄荷味的新奇食物。

但近年来，更多的研究是将新奇食物（往往连同新奇环境）作为实验中的常量，以稳定地诱导出饥饿小鼠的焦虑状态(Bannerman et al., 2002; Chen et al., 2003; Deacon, 2011; Deacon & Rawlins, 2005; Finger et al., 2010; Keane et al., 1988; Liu et al., 2012)。Deacon 等人较早将新奇食物和新奇环境同时应用于诱发小鼠的焦虑状态，并于 2011 发表了一个新奇抑制进食测试(Hyponeophagia Test, HT)协议，详细说明了这个行为测试的实施细节(Deacon, 2011)。Finger 等人受 Deacon 等人的启发，在其研究中设置了高新奇环境+新奇食物，和低新奇环境+新奇食物两个条件（其中，环境新奇性主要是通过改变环境的亮度来操纵）(Finger et al., 2010)。这一研究发现，在高新奇环境+新奇食物的条件下，小鼠的进食行为出现了地板效应，进食延迟都接近了设定的无效阈值；而在低新奇环境和新奇食物的条件中，小鼠的进食延迟才出现了比较合适的个体间差异。此外，上述已提到的 Stephens 的研究还开创了另一个应用新奇环境和新奇食物来诱导小鼠焦虑状态的流

派(Chen et al., 2003; Keane et al., 1988; Liu et al., 2012; Stephens, 1973)。虽然这一流派通常被称为新奇食物摄入测试 (Novel Food Consumption Test, NFCT)，但由于测试的环境是一个新的塑料盒子，所以对小鼠而言，环境的新奇性仍然是存在的。相较于 HT, NFCT 的特点是新奇食物比较统一，都是常规小鼠饲料粉末化之后，加水或者油调和成的糊状物。而 HT 中，新奇食物则更加多样化，包括甜化牛奶糊、葵花籽、甜玉米等。此外，HT 的环境新奇程度通常高于 NFCT 的新的塑料盒子。

在借助小鼠的进食行为来诱导其焦虑状态的行为测试中，HT 和 NFCT 其实算是相对小众的。更主流的新奇抑制进食范式 (Novelty Suppressed Feeding, NSF) (Samuels & Hen, 2011)和新奇致进食困难测试 (Novelty-Induced Hypophagia Test, NIHT) (Dulawa & Hen, 2005; Merali et al., 2003)中则是显性地保持食物的熟悉性的同时，仅借助新奇环境来诱导出焦虑状态。

基于以上综述，本文认为基于小鼠的实验研究对于新奇食物本身的关注还很有限。考虑到对于小鼠而言，新奇食物这一现象不光是信息饥渴和物质饥渴的交接处，同时还是饥饿时稳定的焦虑来源，通过使用小鼠这一拥有完善的遗传学工具的模式动物来研究新奇食物，或许能帮助我们精确地捕捉到好奇、饥饿、焦虑这三个宏观现象之间的某种深刻的联系。

2. 方法

本综述采用了 I-View-U 工作流¹，接下来将对起点文献积累和终点文献确定部分的方法进行介绍。

在起点文献积累阶段，本研究首先进行了语言模型辅助检索。在这一阶段一共使用了 9 种语言模型检索工具，所使用的检索句一共迭代了 5 次，并且所有检索均在 2025 年 4 月 30 日完成。随后，本研究开展了多种子相关文献探索，先后使用了 Research Rabbit 和 Litmap 这两个探索工具。接着在学术文献数据库的检索中，本研究先后于 2025 年 4 月 30 日和 2025 年 5 月 1 日在 Web of Science 和 Pubmed 这两个数据库中进行检索，后者所应用的检索句较前者更为完善。在本研究的单种子相关文献探索中，一共利用了两个种子和三种类型的相关性文献探索工具。终点文献的确认上主要接住了 Google Scholar 的引文网络。具体方法细节见下方表一。

¹ 关于 I-View-U 工作流的详情，请访问 <https://github.com/a1256844492/I-View-U>

当前综述的不足主要有两点：（1）语言模型辅助检索中最终迭代的检索句只是应用在了 Grok DeeperSearch 上。如果能够再在另一个工具中应用并对照结果会是更为理想的；（2）语言模型辅助检索所应用的检索句受到了语言模型幻觉的影响，使用了“Novel Food Intake Test”，但实际的收集的文献中并未出现该标签。这一标签可能影响了搜索的效果。未来对于本综述的更新要考虑在语言模型辅助检索的检索句中进行对应修改。

表一 起点文献积累和终点文献确定的方法细节

调查步骤	检索句/种子文献/终点文献	使用的工具
语言模型辅助检索	what's the development history of Novel Food Intake Test paradigm based on mice model? 2025.4.30	Scispace (https://scispace.com/) , Perplexity pro search (https://www.perplexity.ai/) , Concensus (https://consensus.app/search/) , Ai2 Scholar QA (https://qa.allen.ai/chat) Elicit (https://elicit.com/)
	I want to find a chronological account of the development of the Novel Food Intake Test paradigm as it has been used exclusively in mice, including key methodological milestones, seminal studies, variations in protocol, and the ways its use or interpretation have changed within mouse behavioral neuroscience 2025.4.30	Undermind (https://www.undermind.ai/)
	I want to know the chronological development of the Novel Food Intake Test paradigm as it has been used exclusively in mice, including key methodological milestones, seminal	ChatGPT Deep Research (https://chatgpt.com/) Gemini Deep Research (https://gemini.google.com/app) Perplexity pro search

	<p>studies, variations in protocol, and the ways its use or interpretation have changed within mouse behavioral neuroscience</p> <p>2025.4.30</p>	
	<p>I want to know the chronological development of the Novel Food Intake Test paradigm as it has been used exclusively in mice, including key methodological milestones, seminal studies, variations in protocol, and the ways its use or interpretation have changed within mouse behavioral neuroscience. Novel Food Intake Test paradigm may sometimes be included as part of Novelty-Suppressed Feeding paradigm. As long as studies employing the label of Novelty-Suppressed Feeding paradigm manipulated not only the novelty of environments but also the novelty of food, these studies could also be regraded as having adopted the Novel Food Intake Test paradigm.</p> <p>2025.4.30</p>	Perplexity pro search
	<p>I want to know the chronological development of the Novel Food Intake Test</p>	<p>Grok 3 deeper search (https://grok.com/?referrer=website)</p>

	<p>paradigm as it has been used exclusively in mice, including key methodological milestones, seminal studies, variations in protocol, and the ways its use or interpretation have changed within mouse behavioral neuroscience. Novel Food Intake Test paradigm may sometimes be included as part of Novelty-Suppressed Feeding paradigm. As long as studies employing the label of Novelty-Suppressed Feeding paradigm manipulated not only the novelty of environments but also the novelty of food, these studies could also be regraded as having adopted the Novel Food Intake Test paradigm. Include both peer-reviewed studies and gray literature; cover all fields of application (such as anxiety, reward, metabolism, etc.)</p> <p>2025.4.30</p>	
多种子相关文献探索		<p>Research Rabbit (https://researchrabbitapp.com/home)</p> <p>Litmap (https://app.litmaps.co/)</p>
学术数据库检索	(mice OR mouse) AND (novel OR novelty OR "novelty-suppressed feeding" OR nsf) AND (food OR nourishment	Web of Science (https://access.clarivate.com/)

	<p>OR sustenance OR meals) AND (consumption OR feeding OR eating) AND (experiment OR test OR trial OR protocol OR guideline)</p> <p>2025.4.30</p>	
	<p>(mice OR mouse) AND (novel OR novelty OR "novelty-suppressed feeding" OR nsf OR neophobia) AND (food OR nourishment OR sustenance OR meals) AND (consumption OR feeding OR eating OR intake) AND (experiment OR test OR trial OR protocol OR guideline)</p> <p>2025.5.1</p>	<p>Pubmed (https://pubmed.ncbi.nlm.nih.gov/)</p>
单种子相关文献探索	<p>Exploring food neophobia in mice: unraveling behavior and implications for laboratory research</p>	<p>Google Scholar (https://scholar.google.com/)</p> <p>Semantic Scholar (https://www.semanticscholar.org/me/research)</p> <p>Openalex (https://openalex.org/)</p>
	<p>A non-peptide oxytocin receptor agonist, WAY-267,464, alleviates novelty-induced hypophagia in mice: Insights into changes in c-Fos immunoreactivity</p>	<p>Google Scholar</p> <p>Web of Science</p>
终点文献确定	<p>Latagliata, E. C., Puglisi-Allegra, S., Ventura, R., & Cabib, S. (2018). Norepinephrine in the medial pre-frontal cortex supports accumbens shell responses to a novel palatable food in food-</p>	<p>Google Scholar</p>

	restricted mice only. Frontiers in Behavioral Neuroscience, 12, 7.	
--	--	--

参考文献

- Bannerman, D. M., Deacon, R. M. J., Offen, S., Friswell, J., Grubb, M., & Rawlins, J. N. P. (2002). Double dissociation of function within the hippocampus: Spatial memory and hyponeophagia. *Behavioral Neuroscience*, 116(5), 884–901. <https://doi.org/10.1037/0735-7044.116.5.884>
- Chen, S. W., Xin, Q., Kong, W. X., Min, L., & Li, J. F. (2003). Anxiolytic-like effect of succinic acid in mice. *Life Sciences*, 73(25), 3257–3264. <https://doi.org/10.1016/j.lfs.2003.06.017>
- Cheney, C. D., & Miller, E. R. (1997). Effects of forced flavor exposure on food neophobia. *Applied Animal Behaviour Science*, 53(3), 213–217. [https://doi.org/10.1016/S0168-1591\(96\)01160-4](https://doi.org/10.1016/S0168-1591(96)01160-4)
- Cooper, S. J., & Francis, R. L. (1979). Food-choice in a food-preference test: Comparison of two mouse strains and the effects of chlordiazepoxide treatment. *Psychopharmacology*, 65(1), 89–93. <https://doi.org/10.1007/BF00491985>
- Deacon, R. M. J. (2011). Hyponeophagia: A Measure of Anxiety in the Mouse. *Journal of Visualized Experiments (JoVE)*, 51, e2613. <https://doi.org/10.3791/2613>
- Deacon, R. M. J., & Rawlins, J. N. P. (2005). Hippocampal lesions, species-typical behaviours and anxiety in mice. *Behavioural Brain Research*, 156(2), 241–249. <https://doi.org/10.1016/j.bbr.2004.05.027>
- Dulawa, S. C., & Hen, R. (2005). Recent advances in animal models of chronic antidepressant effects: The novelty-induced hypophagia test. *Neuroscience & Biobehavioral Reviews*, 29(4), 771–783. <https://doi.org/10.1016/j.neubiorev.2005.03.017>
- Finger, B. C., Dinan, T. G., & Cryan, J. F. (2010). Leptin-deficient mice retain normal appetitive spatial learning yet exhibit marked increases in anxiety-related behaviours. *Psychopharmacology*, 210(4), 559–568. <https://doi.org/10.1007/s00213-010-1858-z>
- Keane, P. E., Simiand, J., Morre, M., & Biziere, K. (1988). *Tetrazepam: A BenzodiazepinewhichDissociatesSedationfrom OtherBenzodiazepinAactivitiesI. Psychopharmacological Profilein Rodents.*
- Kronenberger, J. P., & Médioni, J. (1985). Food neophobia in wild and laboratory mice (*Mus musculus domesticus*). *Behavioural Processes*, 11(1), 53–59. [https://doi.org/10.1016/0376-6357\(85\)90102-0](https://doi.org/10.1016/0376-6357(85)90102-0)

- Liu, S., Chen, S. W., Xu, N., Liu, X. H., Zhang, H., Wang, Y. Z., & Xu, X. D. (2012). Anxiolytic-like Effect of α -Asarone in Mice. *Phytotherapy Research*, 26(10), 1476–1481. <https://doi.org/10.1002/ptr.4596>
- Merali, Z., Levac, C., & Anisman, H. (2003). *Validation of a Simple, Ethologically Relevant Paradigm for Assessing Anxiety in Mice*.
- Samuels, B. A., & Hen, R. (2011). Novelty-Suppressed Feeding in the Mouse. In T. D. Gould (Ed.), *Mood and Anxiety Related Phenotypes in Mice: Characterization Using Behavioral Tests, Volume II* (pp. 107–121). Humana Press. https://doi.org/10.1007/978-1-61779-313-4_7
- Stephens, R. J. (1973). Proceedings: The influence of mild stress on food consumption in untrained mice and the effect of drugs. *British Journal of Pharmacology*, 49(1), 146P.