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Life Sciences
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学习与记忆

New Focus in Life Sciences

学习与记忆

6

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7 Methodological challenges for understanding cognitive development in infants

Trends in Cognitive Sciences, Volume 9, Issue 3, March 2005, Pages 92-98

Richard N. Aslin and József Fiser

婴儿认知发育研究的方法学挑战

婴儿认知发育研究基本上依靠行为水平上的描述性资料，而婴儿期是特殊能力出现的年龄阶段。尽管研究者们尝试把行为表现与大脑状况联系起来，但是认知发育机制的很大部分仍然是未知的。我们在此提出，认知发育研究必须把重点放在学习的理论，这些理论必须既能揭示（学习的）计算原理，又能揭示发育变化的各种制约要素。依据以上观点，我们在本文讨论对婴儿学习的研究方面重获重视的四个特别话题。

（张春雷 译，李葆明 校）

14 Nature and nurture in language acquisition: anatomical and functional brain-imaging studies in infants

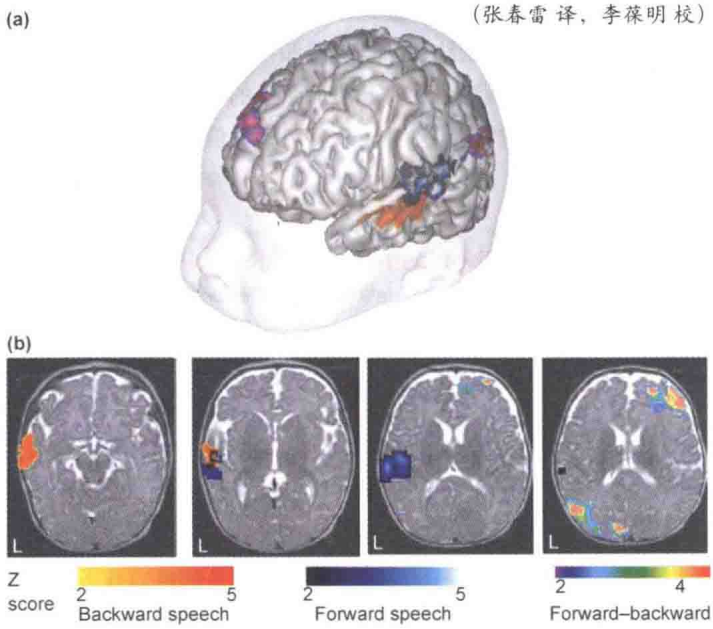
Trends in Neurosciences, Volume 29, Issue 7, July 2006, Pages 367-373

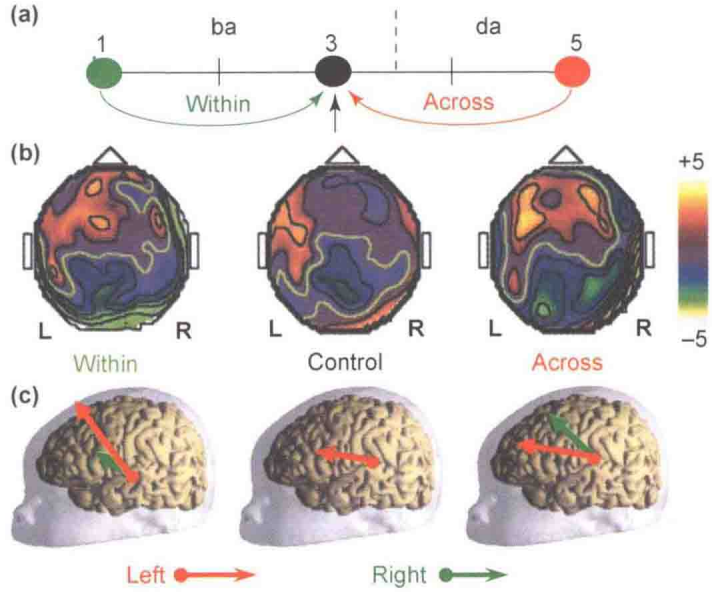
Ghislaine Dehaene-Lambertz, Lucie Hertz-Pannier and Jessica Dubois

语言获得的先天性和后天因素：婴儿脑解剖和功能的成像研究

成人言语处理依赖精密和专门化的神经网络，这些神经网络主要位于左侧大脑半球。婴儿行为学研究表明，在音韵学、韵律学和单词分割方面，相当多的学习在出生后第一年就已发生。在神经影像学技术的帮助下，我们可以跨越行为学方法，直接检测在学习之前婴儿大脑如何处理语言刺激。尽管尚没有证据表明左侧半球神经网络的言语特异性，但神经影像学研究揭示出了婴儿左侧半球在言语方面的结构和功能组织非常接近于成年人的情况，并提示这些脑区对言语信息处理的强烈偏好，这种偏好可能引导婴儿发现他们母语的特征。本综述的内容是作者在 INMED/TINS 年度学术研讨会上的发言，它是 INMED/TINS 专辑《大脑发育和神经功能紊乱的先天和后天因素》的一部分（http://inmednet.com）。

（张春雷 译，李葆明 校）





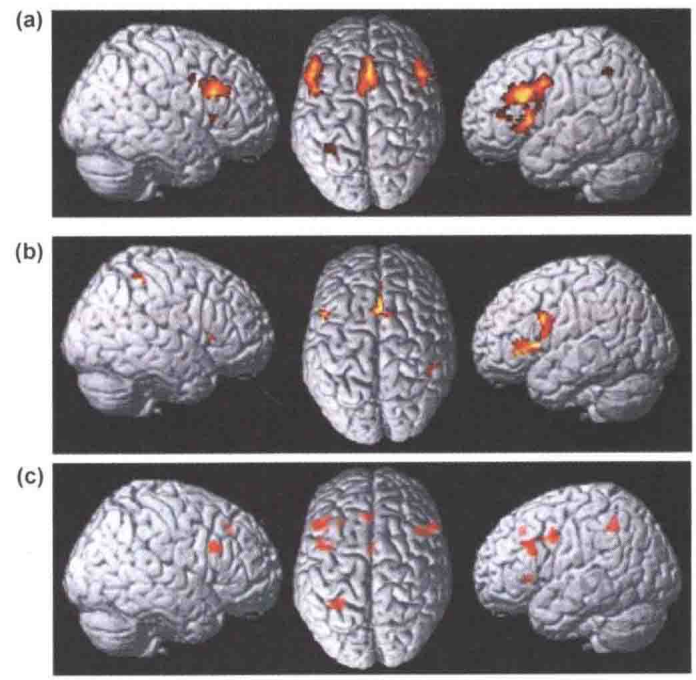
21 Dynamic auditory processing, musical experience and language development

Trends in Neurosciences, Volume 29, Issue 7, July 2006, Pages 382-390

Paula Tallal and Nadine Gaab

动态听觉处理、音乐经验及语言发展

具有语言学习障碍(LLI)的儿童是一个特殊的群体，他们中绝大多数不仅具有说和写的障碍，而且在感觉运动能力方面也有缺损，这点在动态听觉处理方面表现得尤为突出。大量的研究一直在致力于回答感觉运动缺损（尤其听觉频谱-时间处理障碍）是否是语音能力缺损的原因，从而导致言语障碍和阅读障碍。当前，这种努力的新趋势是，研究者们开始着眼于对遗传上高危婴儿进行前瞻性的长期跟踪研究，并应用电生理学、脑成像技术及其他技术评估听力训练（包括音乐训练）对于大脑语言发育和组织的效应。对发育过程中语言学习障碍机制的进一步理解必将增进我们对语言发展的个体差异的认识，并将促使更加有效的教育与干预



策略的建立。本综述的内容是作者在INMED/TINS年度学术研讨会上的发言，它是INMED/TINS专辑《大脑发育和神经功能紊乱的先天和后天因素》的一部分（http://inmednet.com）。

（陆绮 译，李葆明 校）

30 Constructing a past in infancy: a neuro-developmental account

Trends in Cognitive Sciences, Volume 10, Issue 4, April 2006, Pages 175-181

Patricia J. Bauer

婴儿如何构建过去：神经发育学的观点

回忆过去是人的一种基本能力。然而，直到不久之前婴儿还被认为缺乏这种能力。与此相反，非语言测试结果表明，婴儿到一周岁时记忆功能已处于良好的发育状态；到两周岁时，长时记忆已经非常稳定和可靠。电生理学和行为学研究的结合正在揭示随年龄而变化的脑区：这些增龄变化使得信息编码、巩固和储存过程变得更加有效；而这些过程与负责记忆的颞叶皮层的发育密切相关。这一正在形成的新理论框架适用于情景记忆和自传记忆，它强调婴儿期及之后记忆发育的关联性，为揭示童年遗忘现象带来了新的曙光。

（王玮娜 译，李葆明 校）

37 The structure and function of explanations

Trends in Cognitive Sciences, Volume 10, Issue 10, October 2006, Pages 464-470

Tania Lombrozo

解释的结构与功能

我们每个人都具备理解事物的感觉或能力。其中，如何对事物做出解释并对解释做出评估是自发的、普遍存在的基本的能力。最近的证据表明，在人们进行推理的过程中，解释事物对得出因果关系、发现非本质特性以及学习过程具有深刻的效应。这些效应来源于解释结构的两个特征：（1）通过解释，新异信息被整合到已有的知识框架体系；（2）通过这一整合，结论的产生过程得到促进或易化。因此，对解释的研究有助于揭开一些核心的认知问题的面纱，例如学习、归纳和概念表征。不仅如此，先前的一些理论忽视了已有知识和基于解释的推理所起的作用，解释对学习和推理的效应对这些理论提出了挑战。

（李奕 译，李葆明 校）

44 Modeling developmental cognitive neuroscience

Trends in Cognitive Sciences, Volume 10, Issue 5, May 2006, Pages 227-232

Gert Westermann, Sylvain Sirois, Thomas R. Shultz and Denis Mareschal

认知发育神经科学的建模

在过去的几年里，连接主义模型对认知发育理论的形成做出了巨大贡献。其中的一些模型模拟认知发育神经科学的研究思路，通过把结构变化整合到学习来探索脑发育和认知发育的相互作用。本文从这些模型中挑选两类加以描述：第一类模型通过增加或删除学习过程中的单元或连接，强调经验依赖的脑区结构重组；第二类模型通过把经验依赖的要素和结构发育因素结合在一起，强调不同脑区的逐步整合。这些模型为在不同情况下的认知发育机理提供了新的理论，为研究婴幼儿期的正常和异常认知发育及成年期的正常和受损的认知信息处理提供了一个整合的理论框架。

（彭吉云 译，李葆明 校）

50 Bridges over troubled waters: education and cognitive neuroscience

Trends in Cognitive Sciences, Volume 10, Issue 4, April 2006, Pages 146-151

Daniel Ansari and Donna Coch

波澜水面上的桥梁：教育与认知神经科学

近年来，关于认知神经科学与教育之间关系的兴趣和争议与日俱增。本文目的是进一步提升这场争论，而不是重述与教育有关的认知神经科学发现，也不是主张在这两个领域之间建立某种空想“桥梁”。为了在学生、教育家、研究人员和科学工作者之间启动一次关于互动机制的对话，我们提出在教育与认知神经科学之间建立多重“桥梁”，包括教师培训、研究人员培训和合作研究。这些“桥梁”（即，促进心智、大脑和教育研究的具体机制）既有益于教育家也有益于认知神经科学家，他们将从中获得新的理念，有助于他们提出和回答关于大脑的许多关键问题。

（伊峰 译，李葆明 校）

56 Learning under stress: how does it work?

Trends in Cognitive Sciences, Volume 10, Issue 4, April 2006, Pages 152-158

Marian Joëls, Zhenwei Pu, Olof Wiegert, Melly S. Oitzl and Harm J. Krugers

应激如何影响学习？

长期以来，应激对学习记忆影响的研究结果很不一致：既有人报道应激会易化学习记忆，也有人报道应激会损伤学习记忆。在这里，我们提出一种统一的理论，即应激只有在以下情况下才会易化学习和记忆过程：（1）应激发生的场景和时间与事件发生的场景和时间相同时，应激会易化个体对事件的学习记忆；（2）应激引起机体释放的激素和神经递质所作用的神经回路同时也是行为任务所依赖的神经回路，即当应激和行为任务在时间和空间上发生会聚时。应激激素（尤其是皮质酮）的作用机制可以解释学习过程中应激如何提高注意力、改善对相关信息的记忆。

（金新春 译，李葆明 校）

63 Learning to tell apples from oranges

Trends in Cognitive Sciences, Volume 9, Issue 10, October 2005, Pages 455-457

Manfred Fahle

如何把苹果与桔子分开？

为了完成对图像的识别，需要对图像进行正确的概念分类。没有概念分类，我们就无法把苹果与桔子区别开来。一个根本的问题是，对事物的分类能力究竟是生来就有的，还是通过后天学习获得的？如果是通过学习获得的，那么这种分辨能力在多大程度上可以泛化？最近，Notman等人的发现表明，某些特定的分类辨

别能力可以通过学习快速获得，但是很容易被刺激形式的轻微调整所弱化。与高级认知学习不同的是，这种能力的获得涉及大脑皮层的"早期"机制，无法在不同的刺激类型之间迁移。

（马梅方 译，李葆明 校）

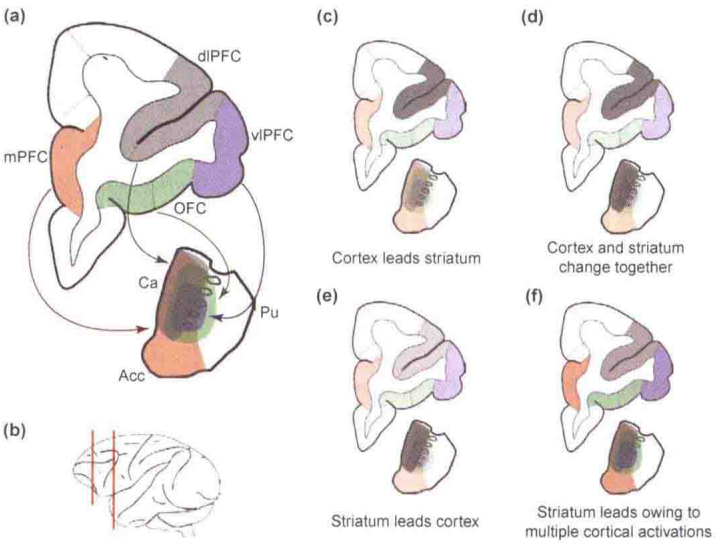
66 Who's on first? What's on second? The time course of learning in corticostriatal systems

Trends in Neurosciences, Volume 28, Issue 10, October 2005, Pages 509-511
Mark Laubach

谁先谁后？皮层纹状体系统在学习过程中的时间顺序

现已知道，前额叶皮层和基底神经节对感觉运动联合学习至关重要（例如，学会在红色交通信号灯前停下）。然而，我们对于这两个大脑结构在感觉运动联合学习过程中学习相关神经元活动的时间过程所知甚少。按照传统观点，前额叶皮层对基底神经节与学习相关的神经元活动变化起驱动作用。然而，基底神经节可能是主导的一方，它对前额叶皮层与学习相关的神经元活动起驱动作用。的确，最近的研究通过在前额叶皮层和基底神经节同时记录神经元活动，证明与学习相关的神经元活动首先在基底神经节出现。本文对这些研究做一回顾，并把这些研究工作与已知的皮层纹状体解剖学相整合。本文还提出了一些关于学习过程中皮层纹状体相互作用的、可验证的假说。

（马梅方 译，李葆明 校）



TRENDS in Neurosciences

69 A unified model for perceptual learning

Trends in Cognitive Sciences, Volume 9, Issue 7, July 2005, Pages 329-334
Aaron Seitz and Takeo Watanabe

知觉学习的一个统一模型

知觉学习指的是成年人和动物经训练后感觉能力提高的现象。先前认为，只有当注意力集中于要学习的刺激时，这种提高现象才会发生（任务相关学习）；但是，最近的研究证明，对于注意之外的刺激，感觉能力提高现象同样存在（非任务相关学习）。这里，我们提出一个统一的模型，他可以解释任务相关知觉学习和非任务相关知觉学习。根据这一模型，对任务相关刺激和非任务相关刺激感觉能力的提高，是由于任务操作触发的信号与刺激呈现触发的信号之间适时相互作用的结果。这一机制使用多重注意和强化系统，他们依赖于不同的神经调质系统。我们的这一模型有助于了解神经调质、注意力和强化学习系统之间如何相互关联。

（伊峰 译，李葆明 校）

75 How our hands help us learn?

Trends in Cognitive Sciences, Volume 9, Issue 5, May 2005, Pages 234-241
Susan Goldin-Meadow and Susan M. Wagner

手势如何帮助学习？

人们说话的时候会打手势，手势所表达的内容往往是话语里没有表达的。从这种意义上说，手势和与其相伴的言语之间是可以不匹配的。当学习者开始某项任务学习时，常常发生手势-言语不匹配现象。并且，手势-言语的不匹配现象使我们能够洞察这种转变状态下学习者所特有的脑内认知过程。手势并非只是挥挥手而已，它反映我们脑内是如何思考的。然而，有证据提示手势不仅反映我们的思考过程，而且还帮助改变思考过程。我们认为手势通过两条途径改变学习进程：通过影响学习环境间接发生作用或通过影响学习者本身而直接发生作用。

（王景 译，李葆明 校）

83 Number and language: how are they related?

Trends in Cognitive Sciences, Volume 9, Issue 1, January 2005, Pages 6-10
Rochel Gelman and Brian Butterworth

数和语言：它们是如何关联的？

数概念形成能力是否依赖于我们的语言使用能力？我们认为，计数词汇在数概念发展中扮演某种角色。我们对"自举"理论（"bootstrapping" theory）提出挑战，这一理论认为儿童在学习计数相关的词汇时，最先使用一种类似于实物列举（object-file）方法（对小的数量做出反应时的注意过程），然后才转变为真正意义的算术数字。我们对最近关于亚马逊部落（该部落只有非常有限的数字词汇）数概念的研究结果的解释同样提出质疑。在本综述中，我们列举实验数据和理论以及神经科学的相关证据，认为数概念具有个体发育起源，以及不依赖于语言的神经基础。

（彭吉云 译，李葆明 校）

88 Different molecular cascades in different sites of the brain control memory consolidation

Trends in Neurosciences, Volume 29, Issue 9, September 2006, Pages 496-505
Iván Izquierdo, Lia R.M. Bevilaqua, Janine I. Rossato, Juliana S. Bonini, Jorge H. Medina and Martín Cammarota

大脑不同部位的记忆巩固依赖不同的分子级联反应

弄清习得反应如何转变为长时记忆对理解认知非常重要。记忆巩固过程在一次回避学习模型上得到了广泛的研究。在这种学习任务中，动物（或人类）只需经历一次学习就能建立起躲避危

险的条件性反应，这一过程依赖于海马CA1区的一系列分子级联反应，这些分子事件与CA1区长时程增强过程中的分子事件非常相似。在不同时间窗内，记忆巩固同样需要杏仁核基底外侧核、内嗅皮层、顶叶皮层和扣带皮层内发生的类似分子事件。记忆巩固的许多步骤均受单氨能神经通路的调控，而单氨能神经通路与情绪知觉和情绪反应密切相关。这至少部分地解释了为什么情感记忆通常都是强烈而持久的。总之，记忆巩固不仅需要大脑复杂神经网络的参与，还需要众多的串行和/或并行的分子级联反应，即使对于一次步入回避学习这样简单的任务也不例外。我们有理由认为，这些分子级联反应可能也参与动物和人类的其他类型记忆。

（朱壁 译，李葆明 校）

98 Memory retention - the synaptic stability versus plasticity dilemma

Trends in Neurosciences, Volume 28, Issue 2, February 2005, Pages 73-78

Wickliffe C. Abraham and Anthony Robins

记忆的保持——突触稳定性还是突触可塑性？

普遍认为，学习过程中相关神经回路上突触强度变化的长时间保持使记忆得以维持。尽管最近新的研究技术取得了令人兴奋的进步，但到目前为止还不可能通过实验手段验证这一感觉上很具吸引力的假说。人工神经网络提供了另一个方法学，因为它能够不间断地观察学习和记忆保持过程中单个突触联接强度的改变。在人工神经网络模型中，如果网络在学习新信息的同时还要保持先前已储存的信息，突触联结强度需要实时地和持续地做出调整。因此，突触变化的时间长短并非一定是记忆能否保持下来的关键。相反，在真实的神经元回路中，最佳记忆保持更有可能需要突触稳定性和可塑性之间的可调控平衡。

（刘芳 译，李葆明 校）

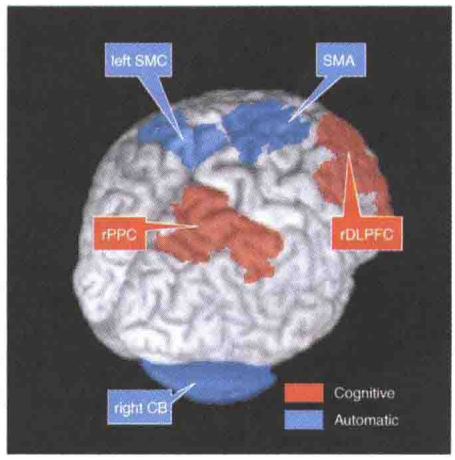
104 Remembering the time: a continuous clock

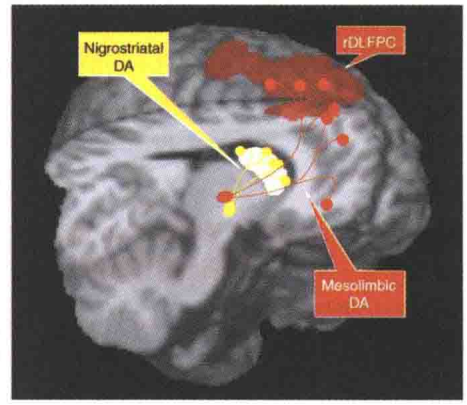
Trends in Cognitive Sciences, Volume 10, Issue 9, September 2006, Pages 401-406

Penelope A. Lewis and R. Chris Miall

记住时间：永不停歇的时钟

时间估测的神经机制是当前富有争议的主题。本文认为，大脑前额叶皮层背外侧部参与工作记忆的那些神经元，同样也被用来测量时间。支持这一观点的实验证据如下：（1）前额叶皮层背外侧部对时间感知和工作记忆都是必需的；（2）时间感知和工作记忆都受多巴胺能系统的调制，干预前额叶皮层背外侧部的多巴胺能投射对这两种行为均造成损害；（3）前额叶皮层背外侧部的神经元以时间上可预测的方式在两种行为任务的作业过程中发放；（4）这种神经元放电活动受多巴胺调制。前额叶背外侧部神经元对工作记忆和时间感知的双重参与支持这样一个观点，即前额叶皮层是不同行为任务的多用途处理器。





（李奕 译，李葆明 校）

110 αCaMKII autophosphorylation: a fast track to memory

Trends in Neurosciences, Volume 29, Issue 8, August 2006, Pages 459-465

Elaine E. Irvine, Laura S.J. von Hertzen, Florian Plattner and Karl Peter Giese

αCaMKII 自身磷酸化：记忆的快速通道

αCa^{2+}/钙调素依赖性激酶II（αCaMKII）是前脑的主要突触蛋白，它可以通过自身磷酸化转变成自主活化的状态。αCaMKII自身磷酸化被认为是介导长时程记忆（LTM）形成的机制。然而，最近的实验证据表明，突触刺激和行为训练仅仅短暂时地增加αCaMKII的自身磷酸化活动，提示αCaMKII自身磷酸化只在长时程记忆形成中起作用，并不参与长时程记忆的存储。与此相一致的是，αCaMKII自身磷酸化缺损的基因突变型小鼠在经历密集型的训练后能够建立长时程记忆，但一次性训练不能导致长时程记忆的建立。在这篇综述中，我们回顾αCaMKII自身磷酸化参与一次性训练长时程记忆形成的实验证据，并认为αCaMKII自身磷酸化可能是通过调控记忆巩固特异性相关的基因转录过程来参与长时程记忆的形成。

（陆绮 译，李葆明 校）

117 The rhinal cortex: 'gatekeeper' of the declarative memory system

Trends in Cognitive Sciences, Volume 10, Issue 8, August 2006, Pages 358-362

Guillén Fernández and Indira Tendolkar

嗅皮层：陈述性记忆系统的守门人

几乎所有关于人类陈述性记忆神经活动的研究都不是集中在记忆的编码方面，就是集中在记忆的读取方面。然而，我们在本文提出，嗅皮层的功能是把编码和读出整合为单一的操作。你对某件事情越熟悉，嗅皮层的参与就越少，它被编码到记忆的强度就越小。考虑到嗅皮层所处的解剖学位置和功能特性，这一整合完成一个重要的、必不可少的任务：把有限的编码资源从熟悉信息更多地优化分配给新异信息。我们提出一个假设，即嗅皮层通过充分地把编码和读出整合成为单一的门控操作，从而优化陈述性记忆。

（郭楠楠 译，李葆明 校）

122 Memory consolidation and reconsolidation: what is the role of sleep?

Trends in Neurosciences, Volume 28, Issue 8, August 2005, Pages 408-415

Robert Stickgold and Matthew P. Walker

记忆巩固和再巩固：睡眠在其中的作用

记忆的巩固和再巩固伴随着分子、细胞及系统水平上的序列变化，这些变化把不稳定的记忆表征转变为永久的记忆，使得记忆在很长时间内能够被激活或读出。我们将在本文讨论记忆巩固和再巩固的复杂性，并认为巩固和再巩固不应被认为是"全或无"的现象，而是一系列持续的生物适应性反应，这些反应可以长时间地增强已存储记忆的使用效率和效能，满足机体对外界变化的需求。因此，巩固和再巩固更应该被认为是记忆的组织和再组织。越来越多的研究结果表明，记忆的组织和再组织过程发生的最佳时间是在睡眠期间。

（金新春 译，李葆明 校）

130 Homeostatic plasticity and NMDA receptor trafficking

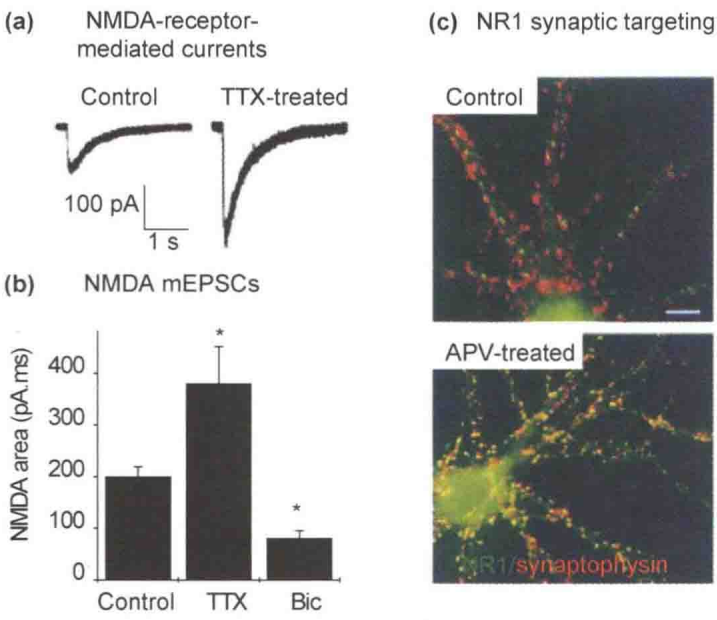
Trends in Neurosciences, Volume 28, Issue 5, May 2005, Pages 229-238

Isabel Pérez-Otaño and Michael D. Ehlers

稳态可塑性和NMDA受体的转运

学习、记忆和大脑发育与突触的长时程修饰有关，这些修饰由特定模式的神经元活动指导。这种修饰包括快速、突触特异性的Hebb突触可塑性（例如，长时程增强和长时程抑制）和其他一些持续时间更长的、对神经元网络功能维持和协调关键的修饰（例如，突触排列和总可塑性）。Hebb突触可塑性的细胞机制已经得到深入的研究，这种可塑性需要AMPA受体的转运。近来出现了一种新的概念，认为活动依赖性的NMDA受体的转运对中枢谷氨酸能突触的稳态可塑性有贡献。

（冯泽君 译，李葆明 校）



140 Human memory development and its dysfunction after early hippocampal injury

Trends in Neurosciences, Volume 29, Issue 7, July 2006, Pages 374-381

Michelle de Haan, Mortimer Mishkin, Torsten Baldeweg and Faraneh Vargha-Khadem

人类记忆的发育及早期海马损伤后的记忆缺陷

认知记忆包括对事实的长时程记忆（语义记忆）和对个人经历的长时程记忆（情景记忆）。人们普遍认为海马及其相关的内侧颞叶结构对成年人认知记忆是关键的，但这些结构在幼儿和儿童记忆中的作用知之甚少。我们认为内侧颞叶从早年开始就参与记忆，出生后第一个月的识别记忆和第一年的记忆回忆均需要内侧颞叶的参与。我们提出，记忆的正常发育存在先后次序：语义样记忆（semantic-like memory）首先出现，情景记忆随后出现，它伴随海马发育而发育。发育早期双侧海马损毁会干扰这种正常的记忆形成模式，以至情景记忆能力丧失发展机会。本综述的内容是作者在INMED/TINS年度学术研讨会上的发言，它是INMED/TINS专辑《大脑发育和神经功能紊乱的先天和后天因素》的一部分（http://inmednet.com）。

（王景 译，李葆明 校）

148 Cognitive abnormalities in post-traumatic stress disorder

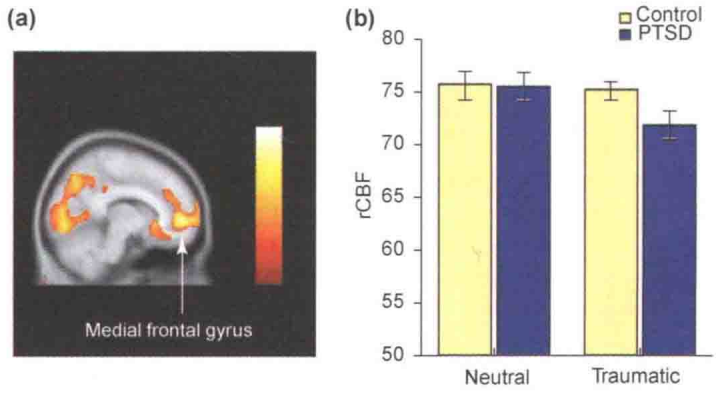
Trends in Cognitive Sciences, Volume 10, Issue 6, June 2006, Pages 271-277

Richard J. McNally

创伤后应激综合征（PTSD）的认知异常

创伤后应激综合征（PTSD）的显著特征是患者对过度恐怖事件的过度反应，它是一种记忆紊乱：患者似乎不由自主地回忆过去的痛苦经历。PTSD显著的认知异常尤其是记忆功能方面的紊乱激发了人们的研究兴趣。这些研究旨在阐明PTSD的发病机制，尤其是那些关于痛苦经历的不由自主回忆的机制。最近的研究进展提出了一个关于PTSD的病理生理学模型，这个模型的核心是前额叶皮层的反应性过低和杏仁体的反应性过高。其他研究工作也证实，PTSD病人高于平均水平的认知能力是一种保护性因素，而低于平均水平的海马体积则是一个破坏性因素。这些关于PTSD发病机制的研究既在认知层面开展，最近也在认知神经科学层面被强调。

（王玮娜 译，李葆明 校）



155 Genetic influences on language impairment and phonological short-term memory

Trends in Cognitive Sciences, Volume 9, Issue 11, November 2005, Pages 528-534
Dianne F. Newbury, Dorothy V.M. Bishop and Anthony P. Monaco

语言损伤和语音短时记忆的遗传性影响

特殊语言障碍（SLI）是指与年龄相适应的语言技巧的获得障碍。早在几年前，人们就知道SLI具有很高的遗传性。然而，SLI存在异质性，它的基因型与表型之间缺乏清晰关系，这严重阻碍了其病因的分子遗传学研究。本文回顾了近年来的一些研究。这些研究提示，如果抛开临床诊断标准，转而对以理论模型为基础的关于疾病表型的定量和认知测量（一种语音短时记忆检测），我们对SLI的遗传学基础将会有更好的理解。现已知道，语音短时记忆受损与特异基因位点突变相关联，它有可能在确定某些类型的阅读障碍和SLI方面起作用。鉴定那些最适合于作为遗传表型指标的认知障碍，将有助于我们揭开发育障碍病因的面纱。

（曲莉丽 译，李葆明 校）

162 Notch to remember

Trends in Neurosciences, Volume 28, Issue 8, August 2005, Pages 429-435
Rui M. Costa, Camilla Drew and Alcino J. Silva

记忆的形成需要Notch信号通路

长时记忆形成需要大量的不同信号分子的参与，其中一些信号分子在成年大脑功能中扮演重要角色，而其他信号分子则参与其他的生物学过程。Notch信号传递通路在不同系统中对细胞的特化和分化过程举足轻重，在发育成熟的大脑中，这条通路也处于活化状态。在本综述中，我们回顾了最近的相关研究进展，这些研究表明Notch信号通路是长时记忆的形成所必需的。同时，我们也讨论了Notch信号通路可能调控的记忆过程。此外，我们还提到了Notch信号通路在认知障碍中可能起到的作用。

（朱璧 译，李葆明 校）

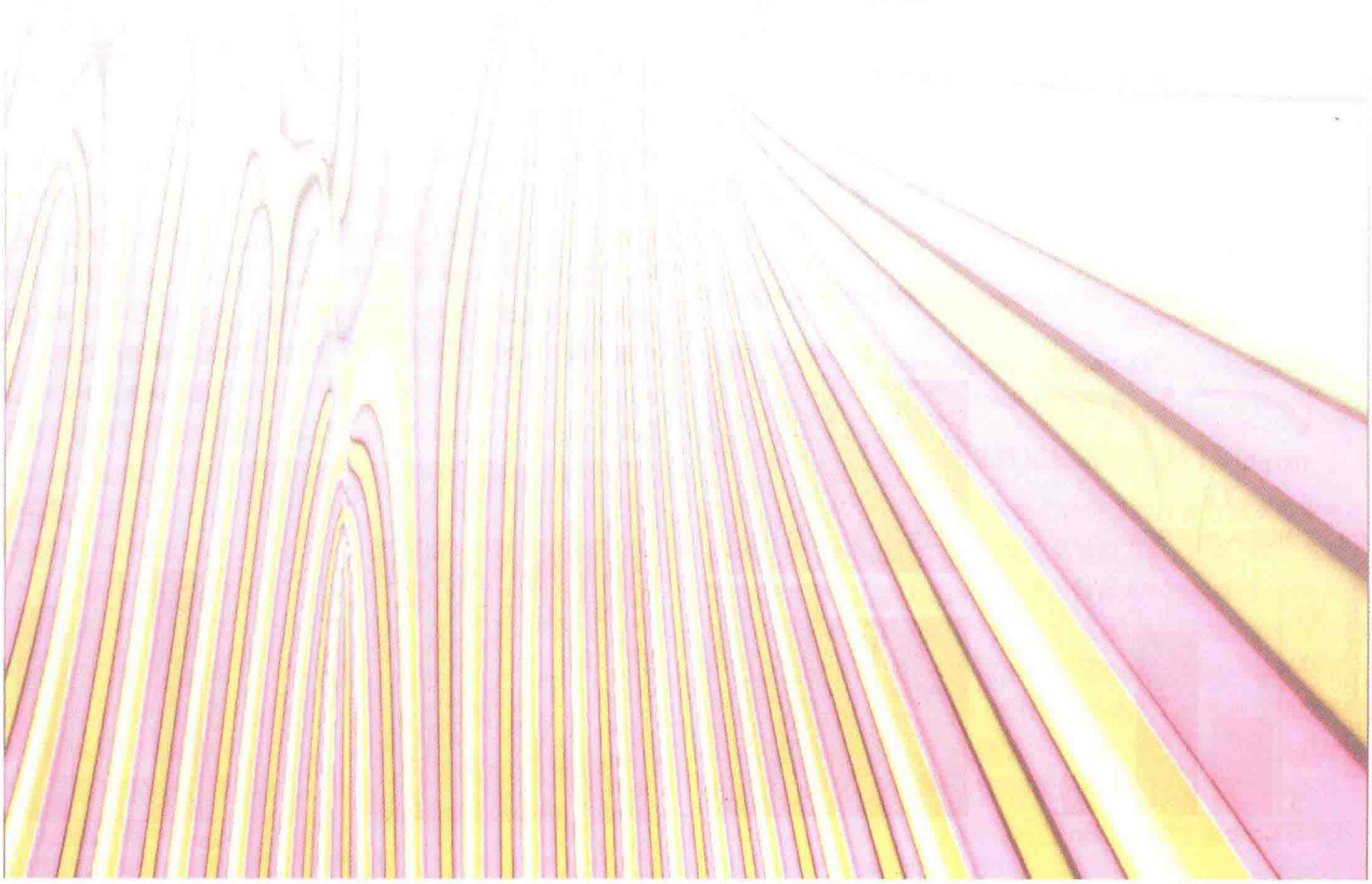
169 Protein kinase A as a therapeutic target for memory disorders: rationale and challenges

Trends in Molecular Medicine, Volume 11, Issue 3, March 2005, Pages 121-128
Amy F.T. Arnsten, Brian P. Ramos, Shari G. Birnbaum and Jane R. Taylor

蛋白激酶A作为记忆障碍的药物治疗靶点：依据和挑战

cAMP依赖的蛋白激酶A（PKA）在记忆过程中起着至关重要的作用，并被认为是治疗记忆障碍的潜在药物靶点。对于依赖于海马和/或杏仁核的长时程记忆巩固来说，PKA通路的激活非常关键。与之相反，已有的研究表明，前额叶皮层cAMP-PKA通路的激活可能损害工作记忆和执行功能。不仅如此，伏隔核PKA通路的激活可能易化药物的成瘾行为。因此，在设计针对PKA通路的记忆障碍治疗药物时，必须考虑到这些负面因素的存在。对于那些因遗传或环境因素导致cAMP-PKA全局性变化而出现的记忆障碍，PKA作为药物治疗靶点也许是最现实可行的。

（嵇晓华 译，李葆明 校）



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Methodological challenges for understanding cognitive development in infants

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Studies of cognitive development in human infants have relied almost entirely on descriptive data at the behavioral level – the age at which a particular ability emerges. The underlying mechanisms of cognitive development remain largely unknown, despite attempts to correlate behavioral states with brain states. We argue that research on cognitive development must focus on theories of learning, and that these theories must reveal both the computational principles and the set of constraints that underlie developmental change. We discuss four specific issues in infant learning that gain renewed importance in light of this opinion.

Introduction

Over the past 40 years, research on human cognitive development has revealed a set of surprisingly sophisticated competencies in infancy, given the seemingly immature and incompetent appearance of the newborn [1]. These findings emerged as a result of increasingly subtle and sensitive methods, most of which rely on behavioral responses such as visual fixations and eye movements, sucking, and a variety of psychophysiological recordings (e.g. heart rate) [2]. In the past decade, there has been a resurgence of interest in obtaining more direct recordings of brain activity (sensory-evoked potentials, event-related potentials, EEG spectra) and their hemodynamic correlates (PET, fMRI, near-infrared spectroscopy) [3,4]. These new cognitive neuroscience methods have brought infancy research much closer to the neurobiological bases of behavioral development and reduced the gap in methodologies and viewpoints between traditional sensorimotor neuroscience and developmental science.

Despite these advances, we believe that several key research strategies must be followed for substantial progress to continue. First, experimental studies of cognitive development in infants must shift from predominantly single-parameter tests that assess the presence/absence of a capacity at a particular age to multiple-parameter tests that assess the full range of an underlying mechanism across age. Second, the role of learning in accounting for cognitive development must be expanded and a computational learning framework must be developed to bring studies of infant perceptual and cognitive processing to the level of sophistication emerging in research on mature sensory and motor behavior [5,6]. Third, as learning mechanisms must be constrained to enable them to plausibly acquire the type of information that complex perceptual and cognitive processes require, theories of learning must be directed to studies that reveal these constraints. Fourth, rather than demonstrating the localization of neural activity in the nervous system, the new methods of developmental cognitive neuroscience should focus on testing directly the computational framework for how information is learned in the brain.

Here, we review the relevant data acquisition paradigms and the computational requirements for developing an adequate framework of infant learning, and we discuss how such a framework could be further constrained by the methods of cognitive neuroscience.

The power and limitations of behavioral data

Presence–absence paradigms

Nearly all studies of cognitive and language development in human infants use paradigms that can only provide group data. This is in part because of the limited duration of infant cooperation (10–15 min) and in part because infant performance is more susceptible to fluctuations in attention and motivation than adults. As a result, each infant typically provides a very few (1–4) data points per condition and statistical comparisons are made between two treatment groups (or an experimental and a control group). The paradigms used with infants (see **Box 1**) essentially provide a Yes–No answer to a given research question, such as whether ability X is present at a given age. A limitation of Yes–No data is that, even with large sample sizes, it is difficult to determine which, among the dozens of potentially relevant stimulus parameters in a given experiment, enabled the infants (as a group) to exhibit positive evidence of ability X. To clarify the roles of these parameters, additional experiments must be conducted with this binary testing method to obtain a coherent set of outcomes.

In addition, many behavioral paradigms (**Box 1**) are not only limited to providing a Yes–No answer to a given research question but also the difference (e.g. from a control group) can be in either of two directions (e.g. familiarity or novelty) [7–10]. This bidirectional outcome is not, in principle, a problem if the desired conclusion is that infants can discriminate between two

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Box 1. Behavioral paradigms and their measurement outcomes

Measures of infant cognition that rely on looking times to visual or auditory stimuli fall into three categories: preference, familiarization/habituation and violation of expectancy. Sample paradigms are shown in Figure I. In each paradigm, infants are exposed to a very small number of test trials, in some cases after being pre-exposed to several stimuli and in other cases with no pre-exposure trials (see Table I). Trials are either of fixed duration or of variable duration controlled by the infant (e.g. fixations directed away from the stimulus for less than two consecutive seconds do not result in termination of a trial). For visual studies, looking times to two or more visual stimuli serve as the dependent variable. For auditory studies, looking times to a uniform visual stimulus presented in the presence of two or more auditory stimuli serve as the dependent variable.

Table I. The limited number of data points collected from each infant

Paradigm	Number of pre-test trials	Number of test trials
Preference	0	2–12
Familiarization/Habituation	6–20	2–6
Violation of expectancy	0–4	2–6

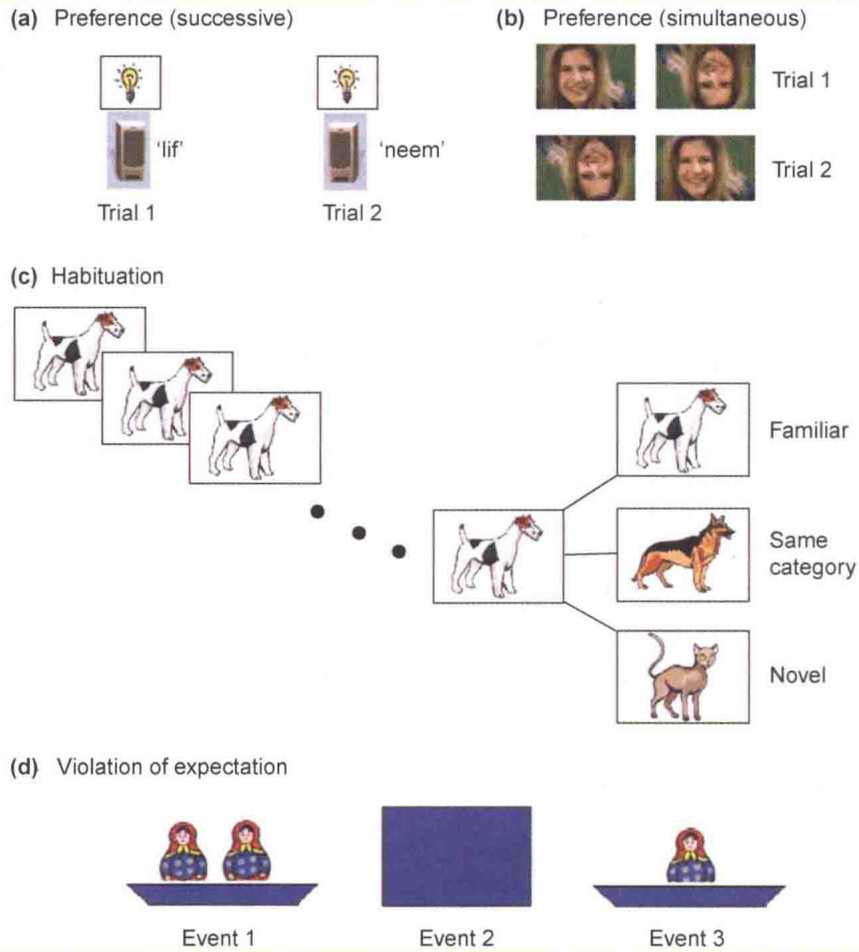

Figure I. The three major paradigms used to measure cognitive development in human infants. Preference paradigms use either successive **(a)** or simultaneous **(b)** test trials, in which a visual stimulus serves to elicit fixations. The duration of looking to the visual stimulus in the presence of two different auditory stimuli **(a)**, or to the two different visual stimuli themselves **(b)**, serves as the measure of preference. If looking times to the two types of test trials are different from each other, discrimination as well as preference can be inferred. Habituation paradigms **(c)** repeat a single visual stimulus (or a visual–auditory compound) until looking time declines to a preset criterion. Alternatively, familiarization can be of a fixed duration. Two (or more) types of test trials are then presented to assess differential recovery of looking time. Significant recovery from the last habituation trial to a test trial (compared to a no-change control) indicates discrimination. Greater recovery to one of two types of test trials reflects a familiarity or novelty preference with respect to the habituation stimulus. In a Multiple Habituation variant of this paradigm, two or more different stimuli are presented during the habituation phase, followed by test trials that are the same or different from the habituation stimuli along one common dimension. If there is no post-habituation recovery to novel test stimuli that share the common dimension, then infants are inferred to have categorized along that dimension. 'Violation of expectancy' paradigms present a series of visual events that are judged by adults to be 'impossible' because they contain properties that violate some physical or cognitive principle. For example, in **(d)** two objects are hidden behind an occluder and then a test trial reveals a single object when the occluder is removed. Longer looking times to impossible over possible test events provide evidence of some level of underlying 'knowledge'.

stimuli. But it becomes an interpretive problem when the direction of the effect is crucial to drawing a particular conclusion and cannot be predicted in advance. This can lead to post hoc explanations in a given experiment to account for a positive effect. Moreover, when a negative effect is obtained, it is not clear if it is a true failure (i.e. the absence of ability X) or rather a false negative resulting from a 'balance' of bidirectional outcomes when summed across infants in grouped data. As the novelty versus familiarity distinction is a crucial one in infant learning, this uncertainty becomes a major obstacle to gaining precise information using the paradigms of Box 1.

Stimulus–response (S–R) monotonicity

In contrast to the above 'cognitive' paradigms, there is a longstanding tradition in psychophysics and motor control

that relies on the collection of many data points from each subject under three or more stimulus conditions (multiple S–R paradigms), and these paradigms have been transferred successfully to infant research [11,12]. For example, visual acuity can be assessed in individual infants by measuring fixations to stripes that vary in width, thereby generating a psychometric function relating a stimulus variable (stripe-width) to a response (percent detection). Moreover, because every test trial can be treated as independent (except for generalized fatigue across trials), a given infant can provide dozens of trials either within or across sessions. Although group data are often the preferred way of reporting infant performance, even when sufficient within-subject data are available, having access to within-subject data makes it possible to avoid the inappropriate collapsing of data across subjects, which can erroneously characterize changes in performance with age.

Yes–No paradigms are less powerful than multiple S–R paradigms in drawing conclusions about underlying mechanisms because there is no *function* relating the putative stimulus variable to the measured response. For example, we cannot conclude in a violation-of-expectancy paradigm that a doubling of a novelty preference to condition A versus condition B means that A is twice as discriminable as B. Rather, Yes–No paradigms use quantitative data (e.g. looking times) to draw qualitative conclusions. In addition, Yes–No paradigms rely on the appropriate control of all irrelevant stimulus variables, rather than observing the systematic outcome of altering the putative stimulus variable through three or more levels.

The dilemma facing researchers who want to assess cognitive and language development in infants is that detection of a stimulus (as in a visual acuity study) is not typically the goal of their research questions. Instead, they seek to characterize what stimulus information *can* be used by infants in a specific task or how stimulus information is *learned*. This in turn means that infants must be exposed to a 'corpus' of stimulus information (either before or during the experimental session) and tested for their ability to extract from that corpus one or more types of information. In our judgment, studies of learning require more than the kinds of qualitative data provided by Yes–No paradigms because a proper understanding of underlying mechanisms demands quantitative results to test competing models. This is not to say that Yes–No paradigms are always inconclusive, but they tend to be very inefficient (requiring large sample sizes) and subject to false-negative outcomes.

In summary, future progress in studying infant cognitive development will benefit from paradigms that are more akin to those used with adults. Rich datasets from within subjects are needed so that the range of performance affected by variation along a stimulus dimension of interest can be revealed. Current Yes–No paradigms are both inefficient and potentially misleading as a characterization of development. However, even if rich datasets were available from infants, the field needs to confront the mechanisms of learning to understand how information is acquired and represented in the brain.

Information extraction: system-level mechanisms of learning

Unsupervised but not unconstrained

We propose that the fundamental limitation on progress in research on infant cognitive development is at the level of a computational theory of infant learning. By infant learning we refer to the full spectrum of knowledge acquisition: from low-level perceptual processes, such as understanding the three-dimensional layout of a scene, to high-level cognitive processes, such as language acquisition. Computational studies of infant learning must confront the following dilemma. Learning mechanisms can be made more efficient by the availability of specific feedback to direct the information–extraction process. This suggests that for domains of cognitive development where acquisition occurs rapidly, the most plausible framework for infant learning is that of supervised learning. As a result, researchers studying higher-level cognitive and language development initially used classical supervised methods to model infant development [13–15]. However, there is little evidence that specific feedback is available in the infant's natural environment to guide lower-level sensory and motor learning (other than crude after-the-fact feedback, as in reaching, that has no direct effect on the subcomponents of the reach). This suggests that either reinforcement learning [16], which relies on indirect feedback, or unsupervised learning [17,18], which relies on information structure rather than feedback *per se*, is a more plausible mechanism for infant learning. Thus, infant learning can be characterized by different 'modes': supervised learning, reinforcement learning, unsupervised learning and, in rare cases, one-shot learning. We suggest that a successful learning framework for infant development must encompass all these modes of learning because lower-level sensory and motor learning is intimately integrated into the development of higher-level cognitive functions. Without doubt, the underlying neural mechanisms by which these modes of learning operate and the biophysical basis of learning and plasticity in the brain (e.g. long-term potentiation, LTP, and long-term depression, LTD) may be diverse. However, we believe that a viable goal is to search for a unified system-level explanation of how information is extracted and represented in the brain that can account for phenomena at both lower and higher levels of cognition as well as across different domains.

A second fundamental problem with attempting to develop a framework of learning that can handle large complex problems, such as visual perception or language, is that a powerful mechanism for acquiring information must be able to deal with the exponentially large number of potentially relevant correlations available in the input. For example, in randomly ordered strings of four different elements, there are 12 possible unique pairs. But when the strings are doubled to eight different elements, the number of possible pairs increases more than fourfold to 56. This exponential increase requires an equally expanding number of sensory examples to learn the relevant pairs that are meaningful for the organism. However, under natural situations there is no realistic opportunity for infants to experience so many examples. This is called

the curse of dimensionality [19] or the computational explosion problem [20], and it is particularly insidious when considering not just adjacent pairs of elements but also nonadjacent pairs and higher-order combinations of more than two elements in any sensory or cognitive domain.

Despite the presence of the computational explosion problem, human learners have been shown to be sensitive to the statistical probabilities that define the underlying structures embedded in both sequential strings (visual and auditory) and spatial arrangements of visual elements [18,21,22]. Moreover, they automatically extract a variety of statistics, including conditional probabilities [23,24], which provide a superior metric of predictability than simple counts of the relative frequency of element co-occurrences. Importantly, this statistical learning mechanism is robust and rapid, and operates in an unsupervised mode in both adults and infants [25–27]. In addition, there is rapidly accumulating evidence that in human adults low-level perception and action is optimal in a Bayesian probability sense [5,6]. This raises the possibility that infants' internal representations of visual, auditory and other sensory inputs develop based on a general statistical learning method.

Computational bootstrapping: less is more

How can we reconcile the computational explosion problem with the empirical evidence that statistical learning operates rapidly and efficiently in both adults and infants? From adult experiments, the solution seems to involve a mechanism that generates an internal representation that only partially codes the sensory input while it reduces the redundancy of the code [28,29]. That is, when correlations among groups of elements in the input contain embedded correlations among smaller subgroups of elements, the redundant subgroups are eliminated (or downweighted) in the corresponding feature representation generated in the brain. This resembles the behavior of standard unsupervised learning algorithms that uncover the underlying causes of complex modular inputs [30,31]. However, the only way to use such a method on large real-world problems is to add a set of constraints to implicitly guide learning to acquire a minimally sufficient rather than a complete representation of the input. For infants, these constraints could be endogenous, by building in specialized mechanisms, or exogenous, by having caregivers reduce the complexity of the input itself or otherwise provide their infant with an environment that has a limited range of structures. There are examples of each of these types of constraints in different domains. For example, in language development mothers hyperarticulate their speech to infants [32] and embed words in short, grammatically simple, and prosodically salient utterances [33]. In vision, even newborns have a preference to attend to roughly face-like or slowly moving patterns [34,35].

An alternative to endogenous constraints that arise from specialized mechanisms are constraints that are the byproduct of general developmental immaturities. Originally proposed in the domain of language development, with the phrase 'less-is-more' [36], these constraints are based on the limited sensory and working-memory capacities of infants (or any naïve learner confronted with initially unfamiliar stimuli [37]; see **Box 2**). If sensory immaturities and limited working memory reduce the number of elements that can potentially be related via a statistical learning mechanism, then the computational explosion problem can be reduced or eliminated. Once 'simple' element correlations are extracted, they can in turn serve as the elements for building higher-order features. In other words, developmental immaturities allow infants to bootstrap their way to a feature hierarchy that avoids the curse of dimensionality.

An important outcome of this computational bootstrapping process is that, if the representational power of the initial set of features is sufficiently rich, the developmental feature hierarchy enables infants (and adults) to recognize both familiar and novel events. Familiar events are recognized by noting the higher-order features, whereas novel events are recognized by noting the lower-order features (and the fact that they are organized in novel ways). For example, the perception of faces is a highly efficient process of extracting familiar lower-order features and organizing them into higher-order spatial configurations [41]. When the lower-order features are presented in a novel configuration (e.g. inverted), the higher-order recognition process is disrupted, but recognition is still possible if based on the lower-order features alone. If such bootstrapping is indeed the core mechanism for developing neural representations at both higher and lower levels, then a main objective of research on learning should be to identify the set of constraints that cooperate with the statistical learning process on each level to achieve this computational bootstrapping process.

Of course, the particular mechanisms by which information is learned and represented in the brain cannot be revealed entirely by data at the behavioral level. Behavioral data provide a rich source of information about *what* infants have learned, the *contexts* in which they learn, and the *constraints* that enable learning to occur both rapidly and efficiently. However, a direct neural assessment of how information is represented in the brain requires the methods of cognitive neuroscience.

The promise and prospects of cognitive neuroscience for development

Unaddressed by the foregoing behavioral evidence of statistical learning are the neural mechanisms that underlie it and the manner in which the output of statistical learning is represented in the brain. The same

Box 2. Limitations on working memory

A number of recent studies suggest that, despite impressive long-term memory, infants have remarkably poor short-term or working memory. When the duration of retention is a few seconds, only 3–4 visual objects can be recognized [38]. When visual objects must be updated in working memory every second, then capacity is 1–2 objects [39]. And when two objects are successively hidden behind an occluder for a few seconds, the capacity of short-term memory is only one [40].

can be said about every other cognitive and linguistic skill. At issue is how the techniques of cognitive neuroscience can help to resolve these questions of neural mechanism and representation.

The seduction of neurophrenology

In the absence of direct evidence for the neural mechanisms that enable a particular cognitive or learning process, which can only come from studies of animals, the primary goal of developmental cognitive neuroscience has been to determine *where* in the brain activity is present during a particular task. Even if we ignore for the moment the enormous technical problems associated with localizing regions of activation in the brain (see **Box 3**), it is not always clear what is gained by obtaining evidence of where neural activity is located. It is important to emphasize that neural activity that is not under experimental control is merely a correlate of behavior [52]. Thus, knowing that a particular region of the brain is active during a particular behavioral/cognitive state does not 'explain' that state. Without a theory for how the brain is organized and how information is represented in it, neural correlates of behavior are no more important than a second measure of behavior. In this respect, cognitive neuroscience shares many of the methodological problems of infancy research, where knowing when a particular ability emerges does not explain how the ability came about.

There are circumstances, however, under which researchers could benefit from knowing which regions of the brain are active. First, if the same region of the brain is active across a wide age range during a given task, then it is likely that the relationship between the task and the underlying neural architecture is maintained over this developmental period. Second, if a different region of the brain is active as information is acquired, and behavioral performance changes with continued exposure, then it is likely that the underlying neural representation has also changed. Unfortunately, these goals are difficult to attain when the data are in the form of Yes–No answers. For example, if there is a left-hemisphere (LH) advantage for linguistic materials in infancy as there is in adulthood, it is seductive to conclude that the LH specialization is developmentally invariant. But without a quantitative measure of the *degree* of LH advantage, it is possible that a modest bias in infancy develops into a strong bias in

Box 3. Recent methods for assessing infant brain function

The methods of cognitive neuroscience used with adults have recently been extended successfully to infants (see **Figure II**). Building on a longstanding subfield of EEG and event-related potential methods [42], ERP source localization [43] and EEG spectra [44,45] have shown great promise for localizing brain activation in infants during stimulus events. In addition, fMRI has been extended to the assessment of language areas of the infant brain [46], and near-infrared spectroscopy (NIRS), a through-the-skull optical imaging technique, has been used to assess visual [47], cognitive [48–50] and language [51] development in infants.

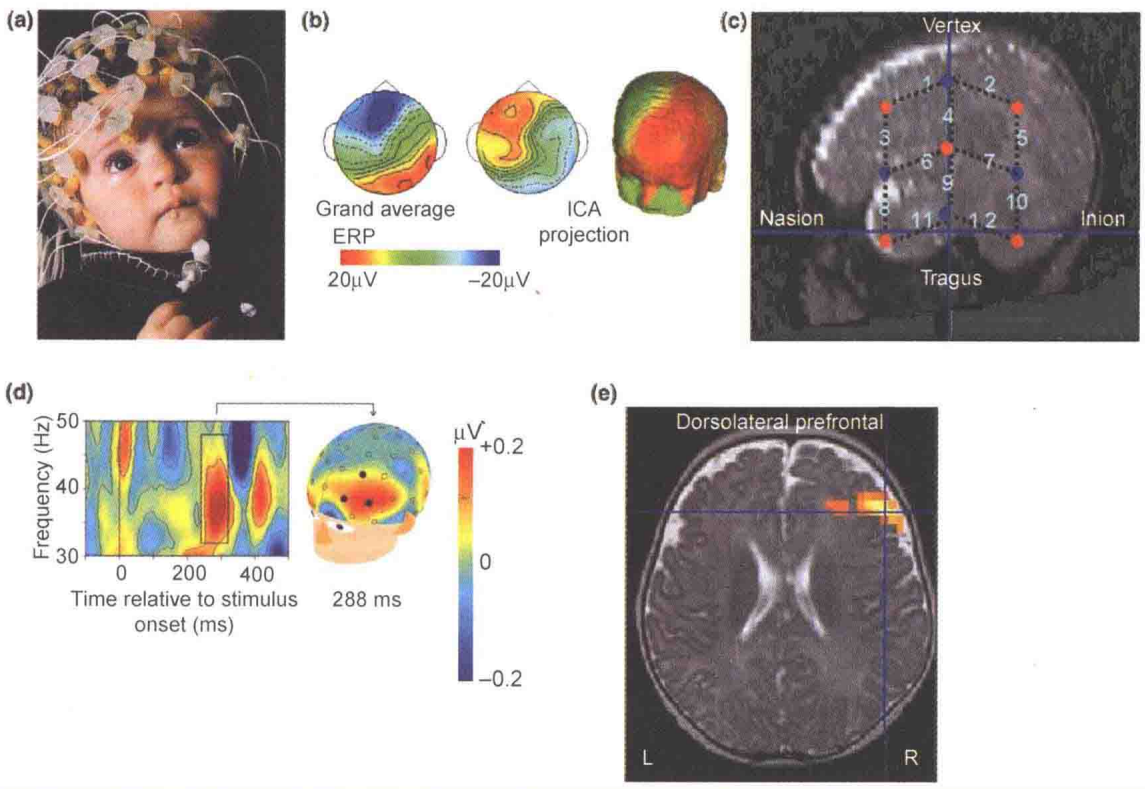

Figure II. Recent examples of the methods of cognitive neuroscience applied to human infants. **(a)** EGI 64-channel electrode net. (Photo courtesy of Charles Nelson.) **(b)** Independent components analysis (ICA) of ERPs to novel vs. familiar visual stimuli and the estimated cortical source localization. (Reproduced with permission from Ref. [43].) **(c)** Placement of near-infrared optical imaging probes used to detect hemodynamic responses from the left hemisphere of newborns presented with speech stimuli. (Reproduced with permission from Ref. [51].) **(d)** EEG spectral responses in the 40-Hz gamma band showing frontal activity to subjective contours. (Reproduced with permission from Ref. [44].) **(e)** BOLD fMRI responses from the frontal cortex to forward vs. backward speech stimuli. (Reproduced with permission from Ref. [46]).

adulthood, thereby altering the interpretation of the development of LH specialization.

The search for monotonicity in brain–behavior relationships

Our earlier point about the limitations of Yes–No paradigms in behavioral studies takes on added significance in studies of developmental cognitive neuroscience and highlights the common challenges faced by infancy researchers as they use any of the currently available dependent measures. Multiple S–R paradigms, like those used to study sensory and motor systems, provide a function relating a stimulus variable to a measured response. We believe that similar paradigms are essential in studies of brain–behavior relationships [53]. Consider the example of a specialized region in temporal cortex that is preferentially activated by faces and face-like objects. The so-called fusiform face area (FFA) may be an innate 'module' or it may emerge during development because of its capacity to represent objects that are highly familiar [54]. But without quantitative evidence for face and non-face discriminability and categorization [55], it will be very difficult to determine which of these competing theories of brain specialization is correct.

Conclusion

In this article, we have argued for four related points. First, experimental studies of cognitive development in infants require multiple S–R paradigms that help to clarify such basic issues as how infant learning is driven by a representational hierarchy that builds on familiar information to encode novel information. Second, a general learning framework of infant cognitive development is needed and it must be able to explain the unsupervised and supervised nature of learning, as well as the development of both low and high levels of information representation in the brain. Third, a promising framework includes unsupervised mechanisms that can bootstrap hierarchical representations, but such mechanisms require several evolutionarily built-in constraints on learning that enable complex tasks such as visual object recognition or language acquisition to be computationally tractable. Fourth, without a computational framework for how information is represented and learned in the brain, the localization of neural activity provided by the methods of cognitive neuroscience are of limited benefit. The goal of future studies in the field of cognitive development (see **Box 4**) should be to gather quantitative data using both behavioral and neural techniques so that detailed models of the mechanisms underlying learning can be evaluated.

Box 4. Questions for future research

- What determines when an infant pays more attention to novel versus familiar inputs? Is this dependence static or does it change as the input is repeated? Does it change with age?
- Is there a limit on the amount of information infants can take in at a glance? Is there a limit on the type of information infants can take in at a particular age? Can these limits be changed by suitable pre-training?
- How rich and detailed is the infant's representation of the environment? If the young infant's representation is impoverished, what allows it to improve with age? What does it mean that an infant 'cannot understand' an image?
- Is there a preset division of higher cortical areas or do the maps of functionally different areas develop and reorganize on demand during cognitive development? What principle determines which features will be represented in a more localized manner in the brain?
- Is there a common computational mechanism for the different types of learning, including fast one-shot learning, slow statistical learning, and the transfer of learning from one set of stimuli to another? How widespread is the mechanism (in terms of brain structures involved) by which new feature representations are acquired?

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