【3.6】

**3.6每日一篇 | 外刊精读**

**deception** in Alzheimer’s research：Brain fog  
   
**doctored**.  
   
【1】ALZHEIMER’S DISEASE affects more than 30m people worldwide, mostly the elderly. After the age of 65, the chance of developing it doubles every five years. By 85, the odds are one in three. Its **symptoms**, which include memory loss, difficulty with basic tasks and **depression**, **progressively** worsen. As global life **expectancy** rises, so will cases of Alzheimer’s, making it one of the big public-health challenges of an ageing world.  
   
【2】There is no **cure**. Between 1995 and 2021, around $42bn was **poured** into more than 1,000 **clinical** **trials**. Yet only a **handful** of drugs has made it to market. Even those mostly treat the **symptoms** of the disease, rather than stop it.Panda Foreign Magazine Intensive Reading:Respect for Originality, Piracy Must Be Punished  
   
【3】The leading **explanation** of Alzheimer’s is the “**amyloid** **hypothesis**”, which suggests that **deposits** of beta-**amyloid**, a type of **protein**, **accumulate** between **neurons** and **disrupt** their function. But the theory remains **controversial**: all brains with Alzheimer’s show beta-**amyloid** **plaques**, yet not everyone with these **plaques** experiences **cognitive** decline. Whether **amyloid** build-up causes Alzheimer’s, or is merely a **symptom**, remains **unresolved**.  
   
【4】In “**doctored**” Charles Piller, a science journalist, details how **groupthink** and **dishonesty** steered Alzheimer’s research off course. In 2006 a Nature paper by researchers at the University of Minnesota appeared to provide a major **breakthrough**. The study **claimed** that a **subtype** of beta-**amyloid** caused memory **impairment**. It quickly became one of the most **cited** papers and **inspired** hundreds of millions of dollars in public-research **grants**. Another influential paper **published** in 2012 by scientists **associated** with Cassava Sciences, a biotech firm, bolstered the **amyloid** theory by **linking** **insulin** **resistance** to **amyloid** plaque **formation**. The finding **fuelled** a wave of research into the idea of Alzheimer’s being a “**diabetes** of the brain” that could be managed with drugs. There was just one problem—both studies were based on **falsified** data.  
   
【5】“**doctored**” follows Mr Piller’s **investigation** into the **deception**. Central to the story is a group of image sleuths, with a sharp eye for **manipulated** **pixels** of Western blots (a lab **technique** used to study **proteins**, which were **doctored** in the studies). Some **chapters** read like a scientific whodunnit. In one, Mr Piller has to work hard to earn the trust of a **reluctant** **whistleblower**. In another, he travels to Prague for a private meeting with a group of image detectives with cryptic pseudonyms.Panda Foreign Magazine Intensive Reading:Respect for Originality, Piracy Must Be Punished  
   
【6】Despite clear evidence of **manipulated** research results, journals and regulators were slow to act. Mr Piller **blames** powerful backers of the **amyloid** **hypothesis** who ignored red flags. It was only in June 2024—two years after **allegations** first **surfaced**—that the Nature paper was retracted by its authors. Cassava Sciences, while **denying** wrongdoing, stopped **trials** of its Alzheimer’s drug, Simufilam, in November after it failed to show **clinical** **benefits**.  
   
【7】These papers’ **consequences** go beyond the lab. For patients and their families, **experimental** treatments often **represent** a final **lifeline**. Encouraging people to pin their hopes on medicines that are **ineffective**, or even **unsafe**, is a **betrayal**. Fixation on a theory offering **limited** success in human **trials** may also have **diverted** **resources** from other more **promising** **therapies**.  
   
【8】Since 2023 the Food and Drug Administration, America’s drug **regulator**, has **approved** two new medicines that **modestly** slowed **cognitive** decline by **attacking** the **amyloid** **plaques**. They also come with dangerous side-effects for some, which include brain **swelling** and bleeding. Mr Piller remains **sceptical** of these treatments. So will many of his readers, after his **gripping** story of medical **groupthink** and **warped** **incentives**.

**①短语**：

1.原文：Between 1995 and 2021, around $42bn was poured into more than 1,000 clinical trials.

词典: **pour into 向…投入大量金钱；大量投资于**

例句：The government has **poured** millions **into** the education system.

政府已在教育系统投入数百万。

2.原文：In “Doctored” Charles Piller, a science journalist, details how groupthink and dishonesty steered Alzheimer’s research off course.

词典: **off course 错误的，不正确的**

例句：Officials warned that global trade rows could still knock the economy **off course**.

官员们警告称，全球贸易争端仍可能导致经济偏离轨道。

3.原文：Mr Piller blames powerful backers of the amyloid hypothesis who ignored red flags.

词典: **red flag危险信号；预警**

例句：The abnormal bleeding is your body’s own **red flag** of danger.

非正常的出血是你的身体发出的危险信号。

**②长难句**

1. 原文：**The leading explanation of Alzheimer’s is the “amyloid hypothesis”**, **which** suggests **that** deposits of beta-amyloid, a type of protein, accumulate between neurons and disrupt their function.

分析：本句包含一个定语从句和一个宾语从句。主句为“**The leading explanation of Alzheimer’s is the “amyloid hypothesis”**”；“**which** suggests...”为非限制性定语从句，which指代the“amyloid hypothesis”；“**that** deposits... function”为宾语从句，作suggests的宾语。

译文：**关于阿尔茨海默病的主流解释是“淀粉样蛋白假说”，该假说认为，一种名为β淀粉样蛋白的物质在神经元之间积聚，从而破坏其功能。**

1. 原文：**The finding** **fuelled a wave of research** into the idea of Alzheimer’s being a “diabetes of the brain” **that** could be managed with drugs.

分析：本句包含一个同位语从句。主句为“**The finding** **fuelled a wave of research**”，“**The finding** **fuelled a wave of research**”为同位语从句，对the idea进行解释说明。

译文：**这一发现推动了关于阿尔茨海默症是“大脑糖尿病”且可用药物治疗的研究浪潮。**

**③写作技巧：**

The finding fuelled a wave of research into the idea of Alzheimer’s being a “diabetes of the brain” that could be managed with drugs.

**这一发现推动了关于阿尔茨海默症是“大脑糖尿病”且可用药物治疗的研究浪潮。**

生词：fuel v.给…提供燃料；加强，刺激

n. 燃料

**fuel本义为“燃料”，其固定搭配“add fuel to (a conflict or debate)”表示“火上浇油”。**

**fuel作动词时，表示“给…提供燃料”，可以进一步引申为“促进，增强，推动”。在写作中想要表达“A加剧或推动B”，我们可以用A fuels B或B is fuelled by A。**

**fuel与猜测、谣传、恐惧等不好的事情一起出现，可以替代cause/ lead to/trigger，表示“引起，加剧”。**

例句：Fuelled by the wide spread of Internent, on-line learning has taken off in recent years.

近年来，在互联网广泛普及的推动下，线上学习开始兴起。

**④背景知识：**

阿尔茨海默症的发病机理复杂，至今其确切机制仍未完全明晰，“β淀粉样蛋白（Aβ）假说”一直是研究中的关键路径。然而，一项被视为该领域里程碑式的研究，却被证实存在严重的造假行为。

1907年，阿洛伊斯·阿尔茨海默 (Alois Alzheimer) 描述了第一例以他的名字命名的痴呆症病例，他在一名患有痴呆症的患者脑中发现了淀粉样斑块和神经原纤维缠结。后来，George Glenner于1984 年推进了Aβ的生化解剖，他发现Aβ是阿尔茨海默病患者脑中淀粉样斑块的关键成分。1991年，研究人员发现了第一个与早发型家族性阿尔茨海默病相关的β淀粉样前体蛋白（APP）基因突变，由此支持了Aβ假说。1992年，John Hardy和Gerald Higgins正式提出“淀粉样蛋白级联假说”，认为Aβ的沉积是阿尔茨海默病的始动事件，引发一系列病理事件，包括神经原纤维缠结的形成、神经元细胞死亡，最终导致痴呆。这一假说的正式提出促使学界投身于针对Aβ产生和聚集的研究中，但一直没能取得突破性进展。直到2006年，一篇发表在Nature上的文章似乎给事情突然带来了转机。

这项来自美国明尼苏达大学神经学家Sylvain Lesné与Karen H. Ashe的研究发现了一种可溶性56-kDa Aβ集合体，命名为Aβ\*56，它在中年小鼠的大脑中累积。研究认为，Aβ\*56 是通过突触功能的变化而不是直接导致神经变性来损害记忆的。这项研究的发现，似乎提供了一个更具体、更有希望的治疗靶点，促使阿尔茨海默氏症研究的重点从不溶解的纤维状Aβ斑块转移到作为认知能力下降主要因素的特定可溶性Aβ寡聚体。学界对这一观点广泛接受，大量工作开始投入相关的研究中，该论文被引数已经达到2300余次。论文的作者也因此功成名就，Karen H. Ashe获得了著名的神经科学波坦金奖，而Sylvain Lesné也成为了明尼苏达大学神经科学研究生项目的领导者。而这一年，也恰好是阿尔兹海默症被发现的100周年。

2022年，美国范德比尔特大学的神经学家Matthew Schrag在调查与抗Aβ药物Aduhelm相关的研究论文时，发现Lesné那项研究中的图像，似乎存在一些问题。他将证据提交给Science杂志后，Science对相关的文献开展了数个月的审查。最终发现，Lesné 数篇论文中70多张图片，可能都有篡改的嫌疑。分子生物学家、知名法医图像顾问Elisabeth Bik指出，作者似乎“将来自不同实验的图片进行了拼接，以此生成了这些图表。他们所得到的实验结果可能并不如预期，因此数据可能被人为修改，以更贴合其理论假设。”这意味着，数百万美元的政府研究经费可能在这项研究及其衍生的相关工作中打了水漂。如今，部分阿尔茨海默病研究领域的专家开始质疑， Lesné的发现是否在过去6年间将整个研究领域导向了错误的道路，也进一步延缓了阿尔茨海默病治疗进展的步伐。

段落大意：

【1】阿尔茨海默病影响广泛，成为老龄化社会面临的重大公共卫生挑战之一。

【2】阿尔茨海默病尚无治愈方法，药物多只能缓解症状。

【3】阿尔茨海默病主流解释存争议，病因尚不明确。

【4】皮勒揭露阿尔茨海默病研究存在造假行为。

【5】《篡改》记录了皮勒对造假的调查过程。

【6】期刊和监管机构对造假行动迟缓，论文终被撤回。

【7】造假论文影响深远，误导患者，浪费资源。

【8】FDA批准阿尔茨海默病新药，但副作用大。