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the 1990s, the number of people in the world who are illiterate has increased from 1.2 billion to 1.5 billion.

There is a growing awareness that illiteracy is a barrier to economic development and social progress. The United Nations Development Programme (UNDP) has estimated that illiteracy costs the world economy \$100 billion each year. The World Bank has estimated that illiteracy costs the world economy \$150 billion each year.

The United Nations Educational, Scientific and Cultural Organization (UNESCO) has estimated that illiteracy costs the world economy \$200 billion each year. The International Labour Organization (ILO) has estimated that illiteracy costs the world economy \$250 billion each year.

The World Health Organization (WHO) has estimated that illiteracy costs the world economy \$300 billion each year. The World Trade Organization (WTO) has estimated that illiteracy costs the world economy \$350 billion each year.

The World Bank has estimated that illiteracy costs the world economy \$400 billion each year. The International Monetary Fund (IMF) has estimated that illiteracy costs the world economy \$450 billion each year.

The United Nations Development Programme (UNDP) has estimated that illiteracy costs the world economy \$500 billion each year. The World Bank has estimated that illiteracy costs the world economy \$550 billion each year.

The International Labour Organization (ILO) has estimated that illiteracy costs the world economy \$600 billion each year. The World Health Organization (WHO) has estimated that illiteracy costs the world economy \$650 billion each year.

The World Trade Organization (WTO) has estimated that illiteracy costs the world economy \$700 billion each year.

The United Nations Development Programme (UNDP) has estimated that illiteracy costs the world economy \$750 billion each year.

The World Bank has estimated that illiteracy costs the world economy \$800 billion each year. The International Labour Organization (ILO) has estimated that illiteracy costs the world economy \$850 billion each year.

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The United Nations Development Programme (UNDP) has estimated that illiteracy costs the world economy \$1,000 billion each year. The World Bank has estimated that illiteracy costs the world economy \$1,050 billion each year.

The International Labour Organization (ILO) has estimated that illiteracy costs the world economy \$1,100 billion each year. The World Health Organization (WHO) has estimated that illiteracy costs the world economy \$1,150 billion each year.

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第 1 章

帕金森病的历史

第一节 发现帕金森之旅

詹姆士·帕金森 (James Parkinson)

1817年，有个英国的内科医生，名叫詹姆士·帕金森 (James Parkinson)，发现了一种奇怪的病症，患者们总是手抖、脚抖。

于是，詹姆士·帕金森把这一类病症记录了下来，还给它起了个名字，叫“震颤麻痹”。

帕金森病

1877年，法国的神经病学家夏尔科 (Charcot) 为了纪念他，首先提出把这种病叫作“帕金森病”。于是，帕金森医生的名字就这么和这种病绑在了一起，流传了

两百多年。估计他自己都没想到，自己会因为发现这个“手足抖动”的毛病而名垂青史！

4 月 11 日为“世界帕金森病日”

欧洲帕金森病联合会觉得，James Parkinson 医生的发现太重要了，值得好好庆祝一下。于是决定把他的生日——4 月 11 日，定为“世界帕金森病日”。从 1997 年开始，每年的这一天，全世界的医生、患者和家属们都会聚在一起，分享帕金森病的经验，互相鼓励！



第二节 帕金森的现在与未来

左旋多巴的传奇登场

1957 年，瑞典科学家阿尔维德·卡尔松（Arvid Carlsson）首次发现了多巴胺（DA）——一种在大脑中发挥重要作用的神经递质。他进一步研究发现，帕金森综合征的主要病因是大脑中多巴胺的缺乏。凭借这些开创性的研究成果，他在 2000 年荣获诺贝尔生理学或医学奖。

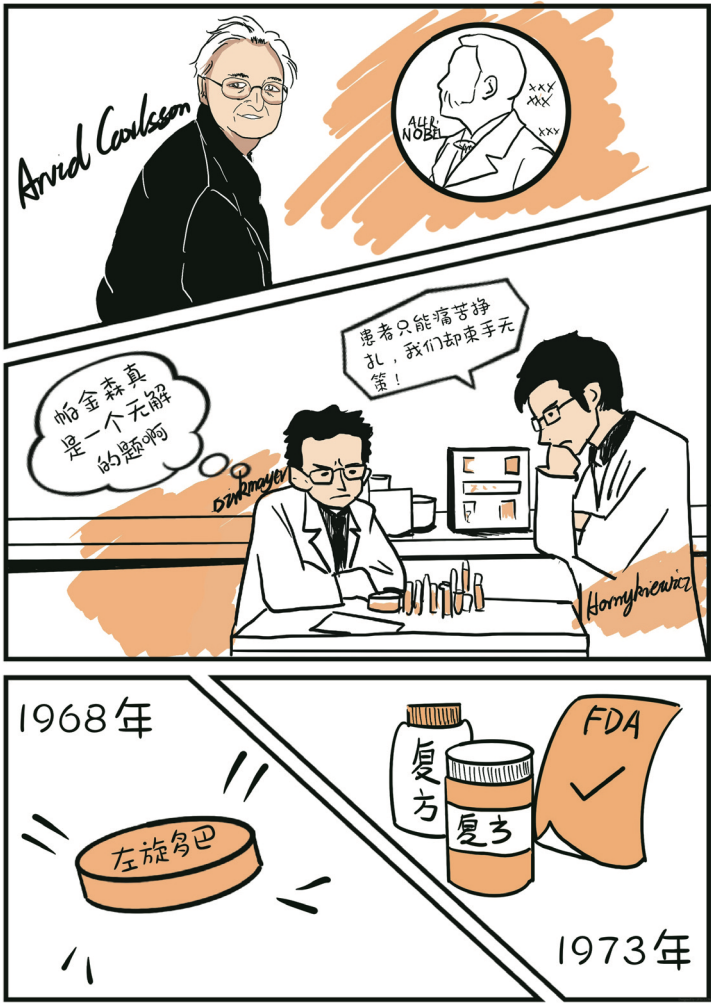
1961 年，匈牙利科学家 Birkmayer 和 Hornykiewicz 苦恼于帕金森患者的治疗。在经过反复探索后，首次尝试了左旋多巴的临床试验。当给帕金森病患者注射左旋多巴后，患者的症状竟然奇迹般地改善了。这就好比在

黑暗中突然点亮了一盏明灯，让医生们看到了治疗帕金森病的希望。

1968 年，Cotzias 及其团队发现，帕金森病患者在口服左旋多巴后，其运动功能障碍得到了显著改善，疗效令人瞩目。这一成果标志着左旋多巴治疗帕金森病的新纪元正式开启。同年，左旋多巴也获得了美国食品药品监督管理局（FDA）的批准，正式进入临床应用阶段。

1973 年，由苧丝肼、卡比多巴和左旋多巴组成的复方制剂获得了美国食品药品监督管理局（FDA）的批准。这种复方制剂减少了左旋多巴在外周的代谢，从而提高了其生物利用度和耐受性。

目前，此类复方制剂已成为大多数帕金森病患者的主要用药选择，也开启了此后数十年帕金森病治疗的黄金时代。

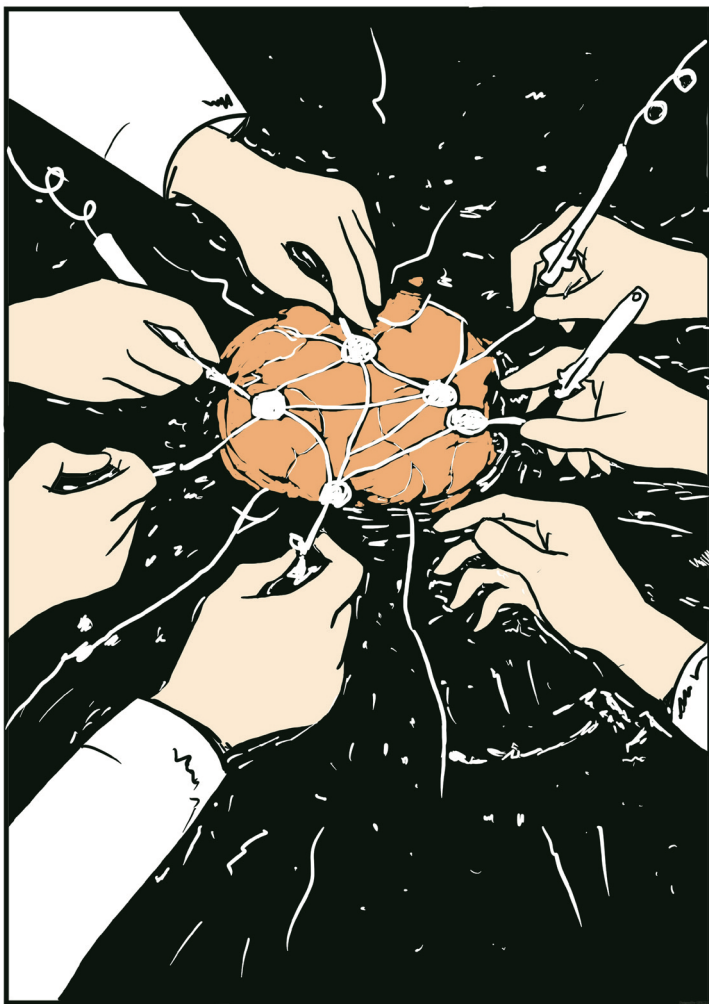


DBS 脑深部电刺激术

1987年，法国神经外科专家贝纳比德 (Benabid) 教授有了新发现，高频电刺激可以消除特发性震颤的颤抖。突发奇想：用电刺激大脑深部会不会缓解帕金森病患者症状呢？结果，当他把电极插入患者大脑的丘脑底核位置（位于中脑黑质与丘脑之间）；在功能上，丘脑底核参与调控运动的起始、稳定和执行等过程。当丘脑底核发生病变时，会导致一系列运动障碍疾病，如帕金森病就与丘脑底核的功能异常密切相关，患者常出现震颤、强直、运动迟缓等症状。）当遇到高频电脉冲刺激时，患者的震颤竟然神奇地停止了。这一发现就像一颗“重磅炸弹”，彻底改变了帕金森病的治疗格局。脑深部电刺激术（DBS）从此成了外科治疗帕金森病的“王牌手段”，它通过植入电极，持续释放微弱的电脉冲，抑制大脑中异常活跃的神经细胞，从而缓解患者的运动症状。

帕金森病治疗的“双剑合璧”

左旋多巴和脑深部电刺激术，就像是帕金森病治疗领域的“双剑合璧”，各有各的“拿手好戏”。左旋多巴主要适用于早期患者，通过补充多巴胺来改善症状，让患者的生活质量得到显著提升。而脑深部电刺激术则更适合那些药物疗效不佳或出现严重副作用的中晚期患者，它不仅能有效控制震颤、僵硬等症状，还能减少药物的使用量。



干细胞治疗

干细胞治疗现在还只是在“试用阶段”，就像一个还在实习的超级英雄，但它的潜力可不得了！比如，从患者自己的身体里提取干细胞，然后把它们变成大脑需要的“超级细胞”，再移植回去。听起来是不是很神奇？就好像给大脑送快递一样，直接把“修复材料”送到需要的地方，给大脑做了一场“内部修复”。

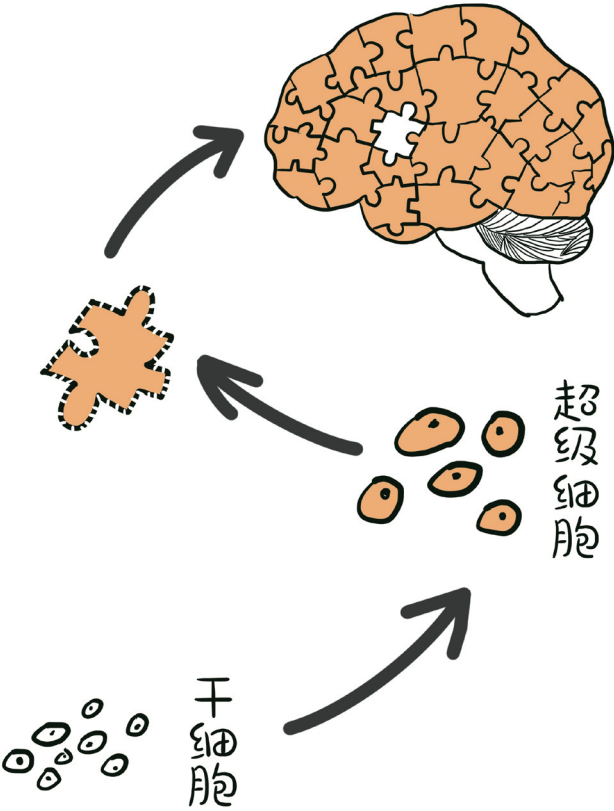
虽然现在干细胞治疗还在“实习期”，但科学家们已经看到了它的巨大潜力。未来，它很有可能成为对付帕金森病的“主力英雄”，让那些被“帕金森病”困扰的人们重新找回健康和快乐。

但是，目前干细胞的分化靶向分化问题，还有待科学家进一步研究解决。

精准治疗——“私人定制”的未来

医生及科学家们发现帕金森病的发病机制和基因突变密切相关，提出一个大胆的设想：未来帕金森病的治疗可能会进入“私人定制”模式。这就好比给每个患者的病情“量体裁衣”，专门定制一套治疗方案，而不是“一刀切”。他们正在研究针对不同基因突变的靶向药物，这就好比给每个患者准备了一把“专属钥匙”，专门用来打开治愈之门。

未来，帕金森病的治疗将不再是“盲人摸象”，而是“有的放矢”。科学家们就像是在给每个患者量身打造一套“盔甲”，让帕金森病这个“捣蛋鬼”无处遁形。有了这样的“私人定制”治疗，患者的病情肯定能得到更好的控制，生活也会更加美好！





第 2 章

帕金森病的基础

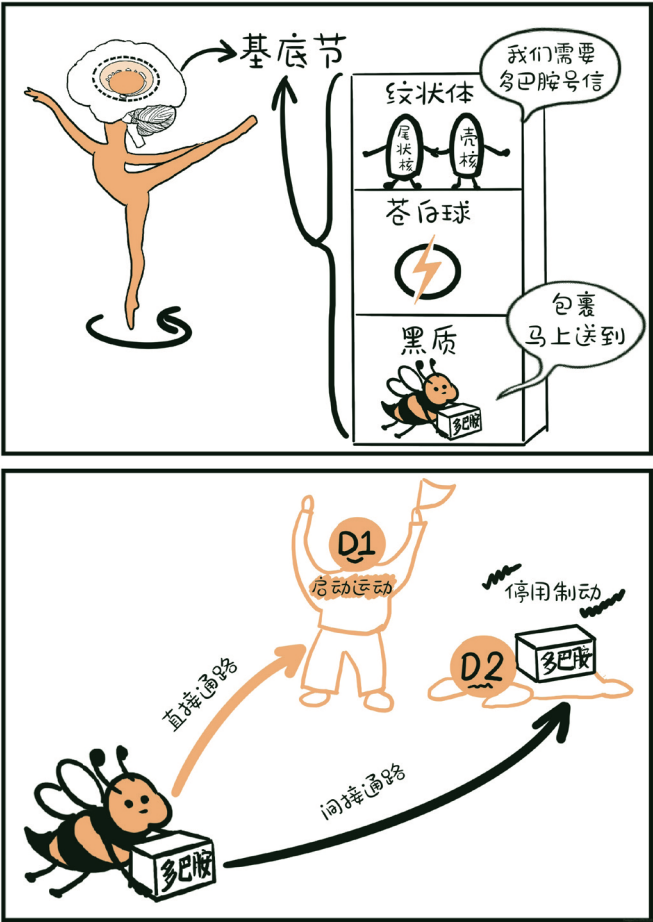
第一节 遇见基底节

大脑里有个超级重要的“指挥中心”，叫基底节。它专门负责指挥我们的身体运动，让我们的手脚能灵活地动起来。不过，帕金森病偏偏就喜欢扰乱这个“指挥中心”。黑质是基底节里的一个关键部位。

黑质：帕金森病的“主战场”

正常情况下，黑质里的多巴胺能神经元就像一群勤劳的小蜜蜂制造多巴胺（DA），通过黑质纹状体这条通路，把一种“神奇物质”即多巴胺绝大部分送到纹状体。多巴胺就像润滑油一样，让基底节的运动调节功能顺畅无比。可是在帕金森病患者身上，这些勤劳的小蜜蜂“罢工”了，导致多巴胺的产生减少，输送系统也出

了大问题。结果，身体的运动调节功能也跟着乱套了。

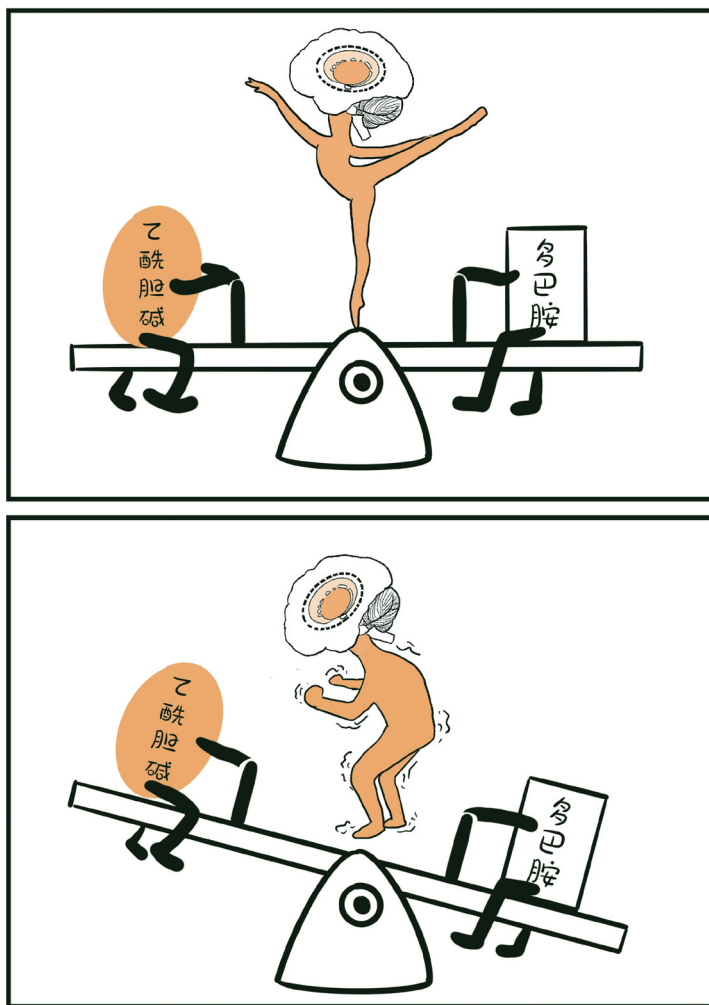


多巴胺和乙酰胆碱的“跷跷板”

基底节里还有另一个重要的“小伙伴”——乙酰胆碱。多巴胺和乙酰胆碱（两种神经介质）就像一对“跷跷板”，它们之间的平衡对基底节的运动功能至关重要。正常情况下，它们俩配合得非常好，身体的运动也自然流畅。但在帕金森病患者身上，多巴胺水平已经降得很低（大约 80% 以上），乙酰胆碱系统就显出“太强势”了。这种失衡就像跷跷板一头重一头轻，导致基底节的运动调节功能失去平衡，彻底乱了套，皮质 - 基底节 - 丘脑 - 皮质环路也跟着“罢工”，结果就是患者出现颤抖、肌张力增高、手脚不灵活、动作变慢等一系列典型症状。

帕金森病与基底节的“恩怨情仇”

总的来说，帕金森病和基底节的“恩怨情仇”主要体现在黑质多巴胺能神经元的变性、丧失，以及由此导致产生多巴胺水平下降和递质失衡。这些变化就像一场“完美风暴”，让基底节的运动调节功能逐步崩溃，导致了帕金森病患者的运动障碍和其他症状（便秘、阳痿、情绪抑郁、出汗异常等）。



第二节 为何会患帕金森病

帕金森病（PD）是一种慢性神经系统退行性疾病，其核心问题在于大脑中一种名为“多巴胺”（DA）的化学信使（神经递质）严重短缺。尽管科学家尚未完全揭开PD的所有谜团，但经过多个国家的专家长期研究，尤其近来数十年的病因学研究，已逐步找出与病因相关的因素：比如遗传、环境、衰老等多重因素交织作用的结果。

多巴胺：大脑的“动作指挥官”

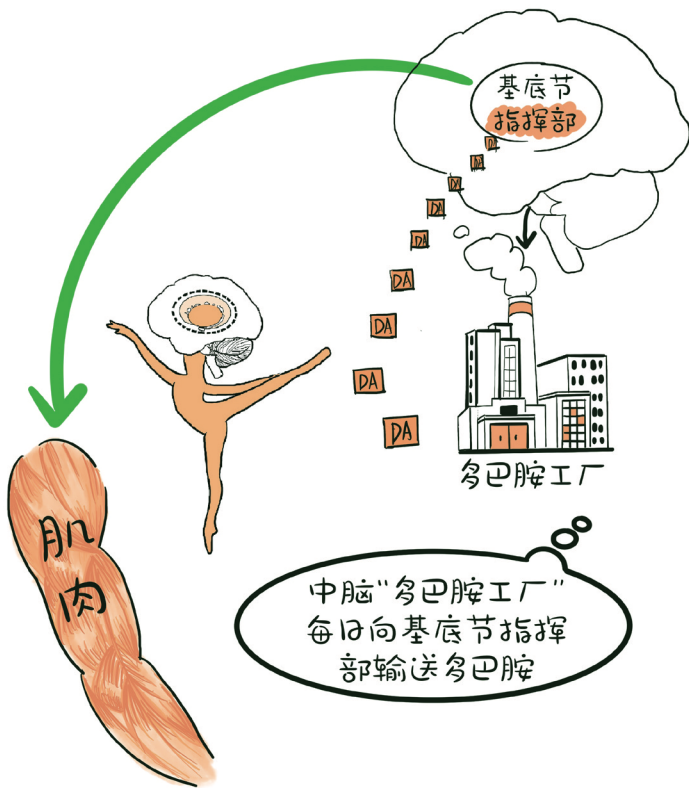
在健康人的大脑中，多巴胺如同一位精准的“动作指挥官”，由中脑的特定的黑质神经细胞生产，并通过“神经高速公路”输送到基底神经节（大脑的动作控制

中心)。它负责协调肌肉运动,确保我们能够流畅地完成走路、写字、端杯子,以及姿势、步态的协调活动等日常动作。

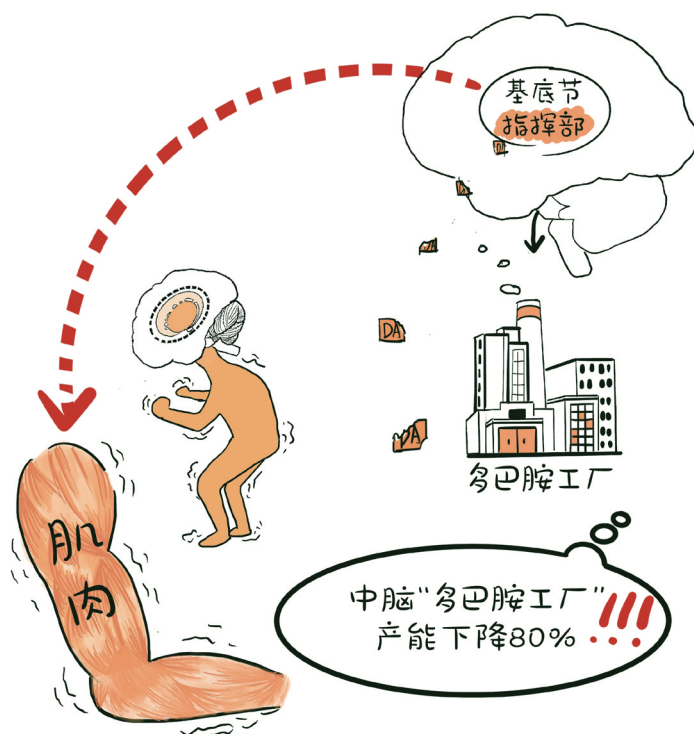
然而,在帕金森病患者中,生产多巴胺的神经细胞会逐渐死亡。当这些细胞损失超过80%、多巴胺水平暴跌时,基底神经节对运动的调控功能丧失,便会“罢工”,导致身体动作失控,出现颤抖、肌肉僵硬、动作迟缓等典型症状。值得注意的是,大脑在早期会启动“备用方案”(无症状代偿期),通过剩余细胞超负荷工作代偿功能,这一过程可能持续数年,直到多巴胺“库存不足”时,才会显现帕金森病的症状。

目前,医学界可通过PET-CT扫描技术,直接观察大脑纹状体内多巴胺D2受体的变化,或检测多巴胺运载体的数量,从而评估患病风险,并帮助区分PD与其他类似疾病(如帕金森综合征、帕金森叠加综合征)。

正常大脑



帕金森大脑



“三大嫌疑”病因：环境、基因与衰老

环境毒素：潜伏的“隐形杀手”

约 20% 的 PD 患者发病与长期接触环境毒素密切相关。工业污染、农药残留、装修材料释放的挥发性有机物（如甲醛）、重金属（锰、铅、铜、铁）等，均可能穿透血脑屏障，毒害黑质神经元。例如：锰暴露——电焊工、矿工等职业群体因长期吸入含锰粉尘，PD 发病率显著升高；农药与除草剂——某些有机氯农药（如百草枯）被证实可破坏多巴胺能神经元。流行病学研究还发现，吸烟与 PD 发病无显著关联，但接触有色金属或化学毒素的人群需格外警惕。

已经发现环境因素与帕金森病的发病有关，我国提倡青山绿水多么重要！工业污染、食品与水源的安全对帕金森病的发病潜在的危害可想而知。

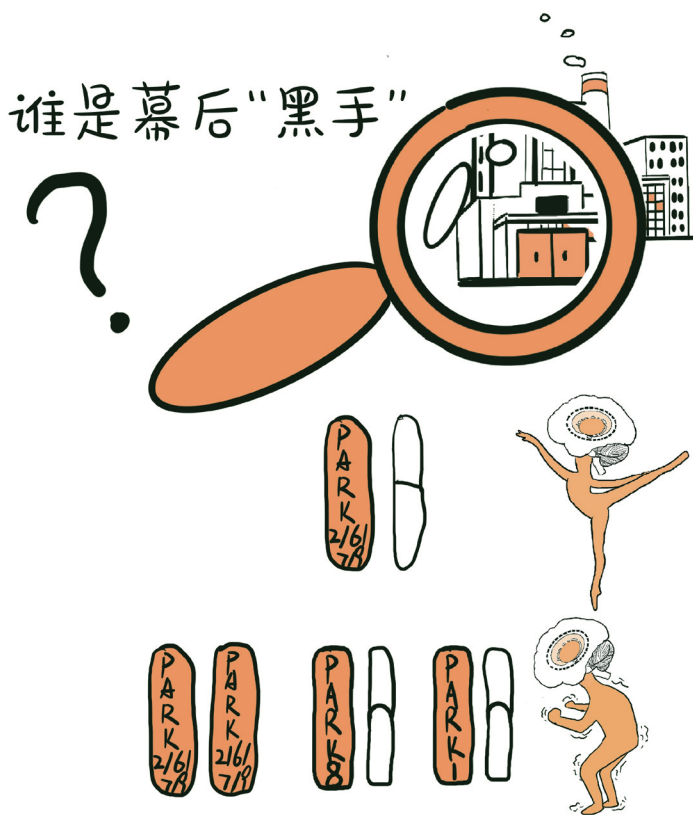


20%的患者是被“重金属小分队”暗算的！它们伪装成工业废气、装修毒气，溜进大脑搞破坏。

遗传基因：家族中的“暗码”

约 10% ~ 15% 的 PD 患者存在明确的遗传倾向，尤其是青少年型帕金森病患者，其发病多由基因突变直接导致。目前科学家已发现 16 个与 PD 相关的易感基因（PARK1 ~ PARK16），主要分为两类：显性遗传基因（如 PARK1、PARK8）——若父母一方携带致病突变，子女有 50% 概率患病；隐性遗传基因（如 PARK2、PARK6）——需父母双方同时传递缺陷基因才会发病。

值得注意的是，绝大多数 PD 患者为散发性病例（无家族史），但遗传因素可能通过增加个体对毒素或衰老的敏感性间接促成疾病。例如，PD 患者的近亲患病风险是普通人的 2 ~ 3 倍，提示某些基因可能像“薄弱开关”，让大脑更易受外界攻击。



知识点秒懂

显性遗传 = 抽到“基因王牌”直接中招

隐性遗传 = 集齐两张“卧底卡”才能中招

基因突变 = 突然崩出BUG，与家族遗传无关

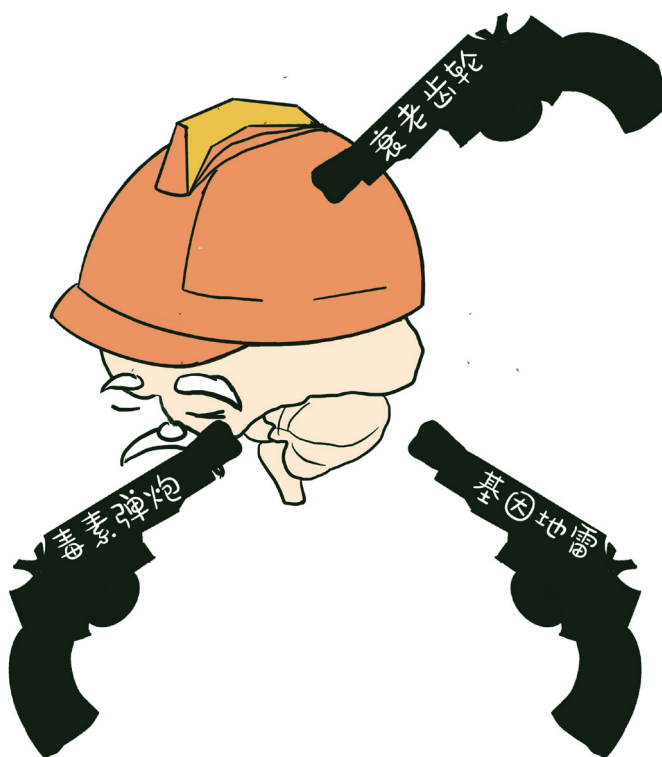
年老衰退：不可忽视的“加速器”

60 岁后，PD 发病率随年龄增长显著上升，本病患者主要是中老年人群。衰老本身会导致神经细胞自然死亡，但为何仅部分老年人患病？科学家认为，衰老与前述环境或遗传风险因素存在“协同效应”——好比年久失修的建筑，若再遭遇暴风雨、地震（毒素）或地基缺陷（基因问题），便更容易坍塌。

病因的“组合拳”假说

目前主流观点认为，PD 的发病是多重因素“联手作案”的结果：基因易感性——某些人先天性携带脆弱的多巴胺生产系统；环境毒素暴露——毒素持续侵蚀本已脆弱的神经细胞；衰老削弱修复能力——年龄增长使大脑难以修复损伤。这一理论可解释为何同卵双胞胎中一人患病而另一人可能健康（环境差异），或为何某些高污染地区人群患病率更高（基因与环境叠加）。

衰老Buff与大脑的三重围剿



预防与研究：未来可期

尽管 PD 病因复杂，但已有明确的风险防控策略：

（1）远离毒素：避免长期接触重金属、农药，新房装修后充分通风。

（2）关注家族史：有 PD 亲属的人群可考虑基因筛查，定期进行神经科体检。

（3）早期干预：在无症状代偿期，通过药物或康复训练延缓病情进展。

the 1990s, the number of people in the world who are illiterate has increased from 1.2 billion to 1.5 billion.

There are many reasons for this. One is that the population of the world is growing so fast that the number of people who are illiterate is increasing. Another reason is that the quality of education is so poor that many people who are literate are not able to read and write. A third reason is that many people who are literate are not able to use the skills they have learned in a productive way.

There are many ways to improve the quality of education. One way is to provide more teachers and more schools. Another way is to provide more training for teachers. A third way is to provide more materials for students. A fourth way is to provide more opportunities for students to practice their skills.

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