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# Research Status and Prospect of Aromatherapy for Senile Dementia

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## Abstract

Senile dementia is one of the most common neuropsychiatric disorders among the elderly, of which the most common cause is Alzheimer's disease (AD). The disease has a long course of development and brings heavy burden to individuals, families and society, but lacks any clinical cure. At present, dementia research is focused on exploring its effective mechanisms as well as the most effective and practical methods of prevention and treatment, health care and maintenance. This paper reviews new research on clinical and experimental uses of aromatherapy to treat senile dementia, discusses the advantages, characteristics and mechanisms of aromatherapy and the essential oils it applies, and provides references for adjuvant treatment and health care of senile dementia.

## Keywords

**Dementia, Alzheimer's Disease, Aromatherapy, Essential Oils, Research Progress**

# 芳香疗法治疗老年痴呆症的研究现状与展望

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## 摘 要

老年痴呆症是老年人最常见的神经精神障碍之一，其常见的类型就是阿尔茨海默症(AD)。该病病程长，

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给个人、家庭和社会带来沉重的负担，临床尚无根治药物。探索有效便捷的防治和保健养护方法、探讨其作用机制是目前老年痴呆症研究的重点。本文从临床和实验两方面，综述了芳香疗法及其精油对老年性痴呆症的研究进展，讨论了芳香疗法及其精油的优势特点和作用机制，并进行了研究展望，为老年性痴呆症的辅助治疗和保健养护提供参考。

## 关键词

老年痴呆症，阿尔茨海默症，芳香疗法，精油，研究进展

## 1. 引言

老年痴呆是老年人最常见的神经精神障碍之一，它是一组以认知功能损害为突出表现的临床综合征[1]。最常见的老年痴呆类型就是阿尔茨海默症(Alzheimer's disease, AD)，它是一种起病隐匿的进行性发展的神经系统退行性脑部疾病[2]，属于一种神经变性病，大概占痴呆总数的60%~80%，其他如血管疾病，脑肿瘤、脑部感染、HIV感染以及营养缺乏代谢障碍等都可以造成痴呆[3]。临床上以记忆障碍、失语、失认、失用、执行功能障碍、视空间技能损害以及人格和行为改变等全面性痴呆表现为特征，发病机制迄今未明[4]。目前全球患病人数至2050年将会达到1.15亿人，我国将达到1460万人[5]。目前老年痴呆症尚无根治药物，该病不仅病程长，给社会及家庭带来沉重的负担[6] [7]。探索有效便捷的防治和保健养护方法、探讨其作用机制是目前老年痴呆症研究的重点。

芳香疗法是一种使用植物精油，改善身体、精神和情绪的健康疗法[8]。它将气味芳香的植物或萃取的精油，通过吸嗅、涂抹、沐浴、按摩、热敷和熏蒸等各种方式作用于患者的全身或局部，用来帮助调节患者情绪，增强自愈能力，改善机体机能，缓解患者的病痛。芳香疗法可以综合考虑患者的生理、心理来进行治疗，具有独特的疗效。近年来，芳香疗法被国内外广泛应用于老年性痴呆的临床治疗，并开展了实验研究，探讨其作用机制[9] [10] [11]。本文从临床和实验两方面，综述了芳香疗法对老年性痴呆症的研究进展，讨论了芳香疗法的优势特点和作用机制，并进行了展望，以期为老年性痴呆症的辅助治疗和保健护理提供参考。

## 2. 临床研究

近年来，芳香疗法已经广泛应用于临床治疗老年痴呆，研究显示，芳香疗法能够显著减少老年痴呆患者的认知行为症状，改善激越行为和睡眠障碍，提高患者的生活质量等[12] [13]。

### 2.1. 减少认知行为症状

痴呆的行为和心理症状(BPSD)是老年痴呆患者中常见的问题。这一问题通常用药物治疗，但疗效有限，往往会引起不良反应，而芳香疗法治疗老年痴呆的BPSD具有一定的疗效，其中香蜂草精油、薰衣草精油和迷迭香精油是芳香疗法中常用于治疗老年痴呆BPSDs主要的三种精油[11] [14]。Akhondzadeh S [15]等开展了随机安慰剂对照临床试验(RCT)，观察了香蜂草精油治疗42例AD患者后的认知评分和临床痴呆评定(CDR)系统评分，结果证实香蜂草可显著提高AD患者的认知功能。Press-Sandler O等[16]采

用描述性分析方法，回顾了 7 项 RCT 临床研究，系统评价了芳香疗法治疗 BPSD 的疗效。研究共 417 名参与者，干预 10 天到 12 周，两项研究使用了香蜂草精油，另外五项使用了薰衣草精油，研究采用了喷洒和涂摩等不同的给药方法，比较了干预组和安慰剂对照组治疗前后，神经精神病学量表(NPI)、匹兹堡激越量表(PAS)、费城老年医学中心影响分级(PGCAR)评分以及科恩-曼斯菲尔德激越量表(CMAI)评分等。其中，3 项研究包括 1 项香蜂草精油[17]和 2 项薰衣草精油[18] [19]治疗有效，3 项研究[20] [21] [22]治疗无效，另外 1 项研究[23]没有得出明确的结论。结果表明，阳性研究和阴性研究之间的差异不能用研究人群、精油的类型或治疗时间的差异来解释，这一显著差异可能是源于管理方法，而当精油被应用在嗅觉系统附近时结果是积极的。

Jimbo D 等[24]评价了芳香疗法对 28 名老年痴呆患者的疗效，其中 17 人患有 AD。早上用迷迭香和柠檬精油，晚上用薰衣草和橘子精油，在 28 天的对照期之后，在接下来的 28 天里进行芳香疗法，然后再进行 28 天的冲洗期。采用 Gottfries，Brane，Steen 量表(GBSS-J)、AD 功能评估分期(FAST)、长谷川痴呆量表(HDS-R)以及触控型痴呆评估量表(TDAS)对患者进行评估。结果发现芳香疗法能够改善患者的情绪和认知表现，是一种治疗老年痴呆的有效的非药物疗法。

## 2.2. 改善激越行为

激越行为是痴呆老人常发生的一组症候群，除认知功能障碍外，还伴有语言或身体攻击、大声喊叫、藏东西、徘徊、妄想、幻觉等精神行为症状，给老人及其照顾者带来痛苦和沉重负担[25]。由于药物治疗的局限性及副作用，非药物干预为激越行为的主要干预方式。Forrester LT 等[26]系统评价了芳香疗法对痴呆患者的干预效果。由于研究者应用了多种激越症状评估工具，结果显示芳香疗法较安慰剂对痴呆患者的激越症状的影响呈现不一致的结果。其中，2 项 RCT 共 141 例临床试验研究，证实了香蜂草精油较安慰剂更好地改善了痴呆患者激越行为[17] [20]。最近，Watson K 等[27]通过 RCT 临床试验探讨了薰衣草精油和柠檬香脂对 AD 患者激越行为的影响。该研究随机选取 49 例老年痴呆患者，给予香蜂草精油、柠檬香脂和安慰剂葵花油，治疗方法为每日一次，持续两周，在开始后续治疗前进行为期两周的洗脱期。所有参与者在 10 周的时间里尝试了所有三种治疗方法，观察三组 NPI 和 CMAI 积分等的变化。研究结果支持了薰衣草精油和柠檬香脂在减少老年痴呆患者认知和激越动行为方面的效果。

Yang MH 等[28]比较了芳香穴位按摩和芳香疗法对 AD 患者躁动的影响。患者被随机分为三组：芳香按摩组 56 例(2.5%薰衣草精油 + 百会、风池、神门、内关、三阴交穴位按摩)，芳香疗法组 73 例，对照组 57 例，治疗 4 周，选用 CMAI 和心率变异性(HRV)指数进行评估。结果表明，芳香按摩比起单纯芳香治疗更加明显地改善 AD 患者的激越行为，芳香按摩和单纯芳香组患者的焦虑情绪都有所改善，使痴呆患者更加放松。

Turten Kaymaz T 等[29]运用 NPI、CMAI 和 Zarit Burden 问卷(ZBI)，研究了芳香疗法对痴呆患者躁动的影响，并评估了相关的照顾者负担。结果表明，在家中通过按摩和吸入芳香疗法治疗 4 周，明显减轻了患者的躁动、神经精神症状和护理人员的痛苦，芳香疗法防止了护理人员负担的增加。然而，另外两项在疗养院使用精油的与按摩结合的芳香疗法对照试验[30]未能提供证据支持使用纯嗅觉形式的芳香疗法来减少严重精神错乱患者的躁动。这可能与疾病的严重程度和痴呆患者的嗅觉能力受损有关[31]。

## 2.3. 改善睡眠障碍

睡眠障碍是老年痴呆患者的症状之一。李衡等[32]探讨了芳香疗法改善老年人睡眠质量的效果。将56 名老年人随机分成按摩组 18 例、嗅吸组 18 例和对照组 20 例。比较治疗 8 周后匹兹堡睡眠指数量表(PSQI)评分的差异。结果显示，芳香疗法能有效缓解和改善老年人的睡眠质量。Lee MK 等[33]采用随机对照实

验设计将 60 名受试者分成芳香疗法组(吸入一种混合了柠檬、桉树、茶树和薄荷的精油，比例为 4:2:2:1)和对照组，使用压力数值评分量表(NRS)、抑郁量表(CES-D)、睡眠质量数字评分量表(NRS)评价。结果表明，芳香疗法能够减轻压力和抑郁，改善成年人的睡眠质量。Hwang E 等[34]采用随机效应模型对 12 项研究进行荟萃分析，结果显示芳香疗法对改善睡眠质量有效，且吸入芳香疗法优于按摩治疗。因此，提出需要制定有效使用芳香疗法的具体指导方针。

## 2.4. 影响记忆力和认知能力

老年痴呆患者常见记忆力和认知能力下降。Moos M 等[35]评估了 144 名健康志愿者对薄荷、依兰的香气和无香气的认知功能，发现薄荷香味增加了受试者的记忆力，依兰香降低了受试者的记忆力。他们还发现受试者暴露于迷迭香香气后吸收的 1,8-桉树脑与认知表现和情绪之间的潜在药理关系，表明从迷迭香香气中吸收的化合物通过不同的神经化学途径独立地影响认知和主观状态[36]。Moos I [37]等比较了鼠尾草组和薰衣草与对照组对 135 例健康人记忆力的影响，发现鼠尾草组的记忆功能显著优于对照组。还有一些研究发现，柠檬香可显著改善人类的记忆力以及注意力，同时可提高认知能力[38] [39]。这些研究提示，芳香味能够影响人类记忆力，具有一定临床价值。

## 3. 实验研究

为了实证芳香疗法治疗老年痴呆症的作用，阐明其作用机制，国内外许多学者对芳香疗法使用的精油开展了体内外实验研究[11]。

## 3.1. 体内实验

在 AD 发病过程中，$A\beta$ 蛋白过表达和 Tau 蛋白过磷酸化被认为是其重要的病理机制之一。研究表明，香菜精油[40]能够减少氧化应激引起的 AD 大鼠脑内的 $\beta$ 淀粉样蛋白$(A\beta)_{1-42}$，且有神经保护作用。野蔷薇精油[41]和杜松精油[42] [43]具有抗氧化、抗炎、抗胆碱酯酶作用，能够逆转 $A\beta$ 诱导的 AD 大鼠学习障碍或记忆损伤。丁香精油[44]能够改善秋水仙碱诱导的 AD 大鼠记忆减退和线粒体功能障碍，减少神经炎症，恢复胆碱酯酶水平和抗氧化。刺果峨参精油[45]、棕尾精油[46]和薰衣草精油[47] [48]能够改善东莨菪碱诱导的大鼠记忆障碍，或预防认知缺陷，改善抑郁和焦虑。薰衣草精油及其主要成分芳樟醇[49]对 D-半乳糖和三氯化铝所致小鼠认知功能障碍起保护作用，而香茅精油[50]可提高该 AD 模型小鼠的学习和记忆能力，减轻海马组织结构的损伤，其作用可能与清除脂质过氧化产物，提高机体抗氧化能力有关。迷迭香精油[51]能够改善东莨菪碱诱导的小鼠记忆减退。迷迭香复合精油[52]能够改善慢性大脑灌注不足引起的血管性痴呆(VD)大鼠的学习记忆功能，且能够抑制其海马 CA1 区的胆碱乙酰转移酶的表达。椰子精油[53]通过活化 Akt 和 ERK 信号通路，增强神经细胞生存，防止 $A\beta$ 诱导 AD 大鼠皮质神经元的神经毒性。苏合香丸能够逆转 $A\beta_{1-42}$-介导的 AD 小鼠记忆减退，抑制海马体的 JNK，Tau 蛋白磷酸化和 p38 的表达[54]，且对果蝇 AD 有神经保护作用[55]。

国内学者开展了中药制剂与芳香疗法联合干预 AD 动物模型的相关研究。张智华等[56]采用脑康复组、脑康复组＋石菖蒲精油香熏对 AD 大鼠模型进行干预，观察了大鼠的学习记忆能力，研究发现，脑康复组＋石菖蒲精油香熏对 AD 大鼠的学习记忆能力更有促进作用，可有效防止脑萎缩。赵献敏等[57]通过天王补心丹联合迷迭香复合精油放入半导体香熏灯中，让患有血管性痴呆模型的大鼠模型来吸嗅其散发出的香味，研究发现大鼠的学习记忆能力显著提高。

## 3.2. 体外实验

体外研究表明，精油是经典的天然抗氧化剂，可抵消或抑制自由基对细胞蛋白和 DNA 的损害，影响

基因转录、细胞信号传导及其它调控功能，且多数精油都含有胆碱酯酶抑制电位，与 AD 发病机制相关[58]。例如，萘烷的辣蓼精油[59]、戟叶酸膜精油[60]和鼠尾草精油[61]通过抑制乙酰胆碱酯酶(AChE)、丁酰胆碱酯酶(BChE)、1,1-二苯基 2-苦酰肼(DPPH)、2,2-叠氮比 3-乙基苯并噻唑啉-6-磺酸(ABTS)、过氧化氢($H_2O_2$)的活性，发挥抗氧化和抗胆碱酯酶的氧化应激的作用。菖蒲精油[62]、麦冬和侧柏精油[63]、紫背天葵精油[64]以及松类植物精油及其成分[65]具有抗胆碱酯酶作用。石竹精油[66]和岩蔷薇的五种精油[67]既有抗胆碱酯酶作用，又具有抗氧化活性。薰衣草精油[47]能够通过减少 LDH 和 NO 的释放、细胞内活性氧积累和 MMP 的缺失，保护 PC12 神经细胞免受 $H_2O_2$ 诱导的细胞毒性。此外，木香精油和薰衣草精油[68]能够通过对 HEK293 细胞 AMPA 受体的作用发挥神经保护作用。这些研究结果提示，上述精油可以用于防治 AD 的食品添加剂和中草药或营养保健品的配方。

## 4. 讨论和展望

精油是一种来源于芳香植物次生代谢物，是成分极其复杂、易变、天然的混合物，主要包括萜烯类(单萜烃、倍半萜烃、氧合倍半萜烯，氧合单萜烯)、醛类、酯类和醇类酯[69]。芳香疗法利用植物精油芳香气味，经由嗅觉器官或皮肤影响人体功能。当香气分子通过吸嗅和熏蒸等进入患者的鼻腔后，作用于鼻腔上部的嗅觉细胞，通过嗅神经影响大脑嗅觉区域，使得患者的多巴胺和 5-HT 等神经化学物质快速释放，再由大脑中枢神经发出指令，来控制平衡自主神经系统，从而使得患者产生轻松、愉悦、快乐的生理状态和精神状态[70] [71]。而且，通过香气刺激嗅球，影响大脑边缘系统，或使脑干网状结构产生反应，唤醒患者情绪从而对机体产生作用，可显著对患者的情绪、记忆、认知、行为及生理等不同方面产生积极影响[9] [72]。精油分子小具有亲脂性，这使得它们极易渗透于皮肤，通过皮下脂肪下丰富的毛细血管而进入体内。当香气分子通过涂抹、按摩、热敷和沐浴等透过皮肤进入血液循环，帮助患者身心获得舒解，并达到皮肤保养目的与促进健康的功效[73]。一些精油成分如薰衣草精油中的芳樟醇，能够通过血脑屏障，减少 A$\beta$40 水平[74]，并通过与 γ-氨基丁酸(GABA)神经递质和多巴胺能系统的相互作用来抑制中枢神经系统[75]。薰衣草和迷迭香的芳樟醇和迷迭香酸具有调节 T 型钙通道的能力，有助于抗焦虑和神经保护作用[76]。而且，人体的鼻粘液或皮肤存在着 P450 酶，能够分解精油的成分，减少或消除毒性，促使有毒物质的代谢[77]。因此，芳香疗法的精油具有可吸入、渗透性好、易吸收、代谢快、安全性好以及使用方便等的优势，起到开窍化浊、疏风散寒、调和气血、扶正祛邪等治疗作用，使患者身、心、灵三者达到平衡，适合用于老年痴呆症患者的长期养护。

临床和实验研究表明芳香疗法治疗老年痴呆症是安全的，对减少患者的认知行为症状，改善激越行为和睡眠障碍，增加记忆力和认知功能等产生积极作用。一些临床研究表明其无效或疗效不明确，可能与精油选择，治疗方法，作用时间和应用部位等有关[16]，而对嗅觉缺失者更适合与按摩等其他治疗联用，提示需要研究者们做好临床试验设计，进一步开展新的多中心、大样本的 RCT 临床试验证明芳香疗法对老年痴呆的疗效，明确其疗效与剂量、扩大其适应证范围、与按摩等其他治疗及药物的协同作用等，制定出芳香疗法的安全性及疗效的行业标准等。尽管在 2013 年新加坡卫生部发布的临床实践指南中，未将芳香疗法推荐为改善老年痴呆症患者激越行为的治疗方法[78]，但在 2016 年的英国国家临床医学研究所(NICE)指南[79]推荐使用芳香疗法管理老年痴呆症行为问题。随着越来越多的临床和实验研究证据的积累，在新的临床实践指南中，芳香疗法有可能被推荐为老年痴呆的辅助治疗或养护方法之一。

中国逐渐步入老年社会，老年痴呆患者的不断增加，其伴有认知功能退化、记忆力衰退、精神行为异常甚或人格的改变等，日常生活和外出活动均受到影响。除了药物及非药物治疗，开发含有精油的中老年保健食品和饮料，在老人生活环境中的场景设置[80] [81]，对患者需求的满足，认知心理刺激以及社会情感支持等都有助于痴呆异常行为和生活质量的改善[25]。在防治老年痴呆症的同时，须要营造一个适

合老人生活的环境，做好患者的养护保健管理，改善患者的生活质量，保证患者安度晚年。

## 5. 结论

老年痴呆症是老年人最常见的神经精神障碍之一。迄今的研究表明，芳香疗法是一种安全、有效和便捷地辅助老年痴呆症防治和保健养护的方法。今后的研究需要在多中心、大样本的 RCT 临床试验的基础上，建立世界公认的老年痴呆症芳香疗法临床实践和保健养护的指南，开发出含有精油的中老年保健食品，并深入探讨芳香疗法防治老年痴呆症的作用机制，为老年性痴呆症的治疗和保健提供助力。

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