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探討失智症引起的激躁症狀治療

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一、前言

神經精神症狀 (Neuropsychiatric symptoms, NPS) 在失智症的病人中普遍發生，常見的症狀為：激躁 (Agitation)、侵略行為 (Aggression)、焦慮 (Anxiety)、幻覺 (Delusion) 等，多項橫斷面研究 (Cross-sectional study) 指出，失智症病人的精神症狀中，激躁有最高的盛行率 (30 - 60 %)[1,2,3]，此外，納入三項歐洲的縱向研究 (Longitudinal study) 之系統性回顧文獻顯示，失智症病人從未有激躁至產生症狀，1年累積發生率為 18.5%；4年累積發生率為36%，也就是四年內大於三分之一的失智症病人將產生激躁症狀，且會隨著疾病的惡化，提高發生率[4]。論台灣概況，衛福部估算2019年台灣失智人口達29萬人，相當於嘉義市的人口數，並推論20年後會翻倍，且40年會超過88萬人[5]，若按照上述縱向研究結論推算，約有10萬人會發生激躁症狀，是一個相當可觀的數字。

激躁的表徵為：無目的且具運動性的煩躁不安、攻擊行為和情緒困擾，除了自身容易受傷外，執行醫療照護時也會受到影響，如：量測血壓，協助服藥等。若產生攻擊行為，謾罵、幻想等，也會影響到同住者。激躁症狀可以透過神經精神評估量表 (Neuropsychiatric Inventory, NPI)[6] 或是柯恩-曼斯菲爾德激動情緒行為量表 (Cohen-Mansfield Agitation Inventory, CMAI) [7] 來評估嚴重程度：NPI量表分為情緒及妄想兩個環節，評估病人的躁動、幻想及焦慮等程度分數，分數愈高者愈嚴重；CMAI量表則是針對躁動症狀，評估言語

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、肢體攻擊性的發作頻率來計算分數。而一項瑞典的資料庫分析數據指出，在嚴重的NPS (NPI分數 = 7 - 9) 病人族群中，追蹤了224天 (中位數)，發現相較於無NPS者，死亡率的 HR 為1.74; 95% CI = 1.44 – 2.12，有顯著差異，而且躁動症狀佔了NPS病人 61.7%[8]。從上述的研究資料來看，失智症引起的激躁不僅發生率高，也是所有神經精神症狀中盛行率最高的症狀，顯著影響著病人生活品質、照護者負擔，甚至嚴重症狀者會有較高的死亡率，因此如何治療激躁症狀，顯得重要。本文將會討論失智症引起的激躁症狀治療，以及其指引與文獻的回顧。

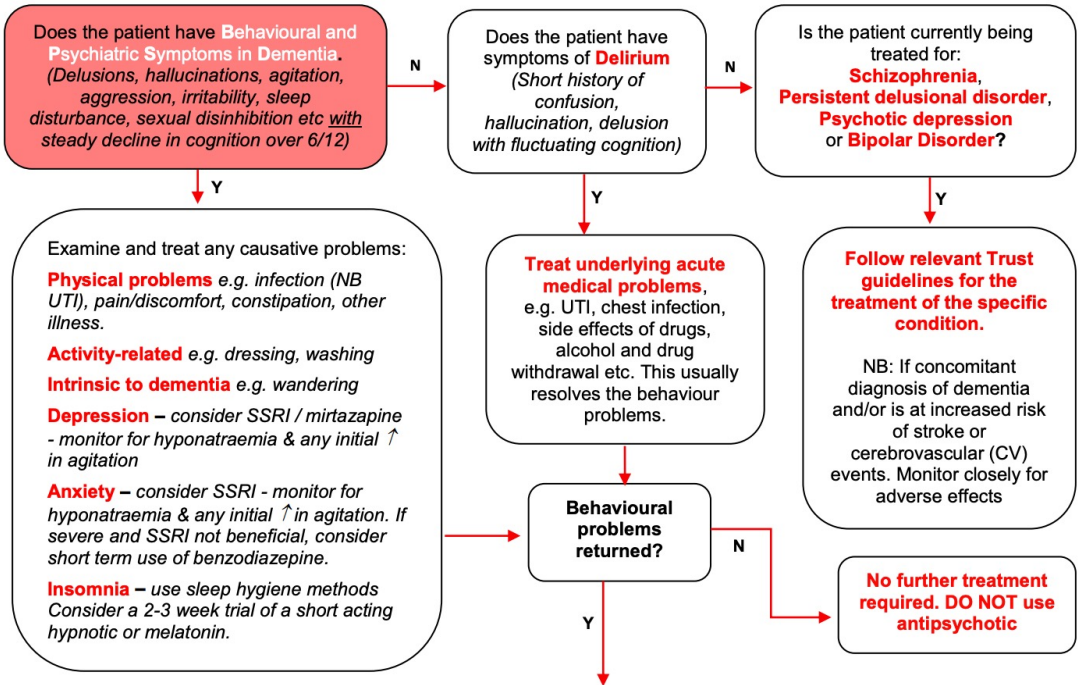
二、產生激躁症狀的原因評估 (圖一)[11]

雖然激躁症狀在失智病人中常見，但病人和家屬可能常常低估或是沒有察覺症狀的發生，所以醫療人員在每次的訪視時，可以透過詢問家屬「病人最近哪些行為會造成你的負擔？」或者「病人會不會產生幻覺，像是不存在的物體、聲音或事件？」來評估近期的激躁表現，或是認知退化的進展。激躁症狀常發生於午後到傍晚的時段，有Sundowning之稱，且大約有2/3的失智症病人有這種現象，主要跟晝夜調節有密切關係。然而，無論是美國精神醫學會 (American Psychiatric Association, APA)[10] 或是2019年英國國民健保署牛津大學健康基金會 (Oxford Health NHS Foundation Trust) 的治療指引 (Guidelines for the management of Behavioural and Psychological Symptoms of Dementia)[11]，都建議進行激躁的治療前，必須先評估產生激躁的原因為何，並對原因進行治療，直接針對激躁的介入治療多用於持續激躁症狀者。

大多數的病人產生激躁是因為感染 (Infection) 及藥物的毒性 (Medication side effect)，新的感染發生則先治療感染；藥物毒性方面，Benzodiazepines類的藥物或是其他鎮靜藥盡可能避免失智病人使用，因為會導致認知功能的退化，增加激躁行為的可能，另外，抗組織胺藥物，如：diphenhydramine有較高的中樞副作用，也必須避免；疼痛 (Pain) 也是造成激躁的原因之一，失智症病人在表達疼痛相對困難，可以透過面部表情、肢體的運動、言語改變或是情緒狀態來辨認是否有疼痛的現象，Pain Assessment in Advanced Dementia (PAINAD) 是一套幫助我們評估的工具，因此病人若有疼痛的表徵，也須以緩解疼痛為主；因年紀、失智症的影響，引起晝夜節律失調及睡眠障礙，進一步影響到激躁行為的發生，甚至是認知功能的退化，因此評估睡眠品質也是重要的一環；癡呆妄想 (Delirium) 是失智症患者常有的現象，尤其在認知退化時容易發生，其他情況像是感染、藥物毒性也都有可能造成妄想，然而與NPS不同的是，妄想通常短暫發生，不過症狀與表徵NPS相似，發生激躁時同時考慮妄想是否正在發生；情緒的問題也是因素之一，憂鬱、焦慮是否有接受適當的治療也要納入考量；最後，除了認知功能退化，較差的聽力、視力也會導致失智症患者更容易困惑，增加產生激躁行為的可能[9]。

上述幾點為造成激躁症狀的幾項因素或

共病，再進行治療的介入前，應評估共並是否已經達到良好的控制，若控制不佳，則先處理這些因素疾病，達到完善治療後，激躁行為若持續，再進一步給予病人介入治療。



圖一、治療前激躁症狀的原因評估[11]

三、治療指引回顧[11]

評估了病人產生激躁的原因，並針對原因進行治療 (如疼痛、感染、藥物毒性或是睡眠障礙等)，仍有持續的激躁行為表現，則需進行介入治療，根據2019年牛津大學健康基金會指引建議[11]，第一線介入為非藥物治療 (Non-pharmacological therapy)，非藥物治療的選擇應考量病人能夠參與介入的能力與激躁的型態，若沒有攻擊性，可考慮肢體接觸的活動 (Physical presence touch) 或是娛樂與社交活動等；行為治療可透過完成ABC量表 (ABC chart) 其中A為動機 (Antecedent)，B為 (Behavior)，C為 (Consequence)，透過分析ABC的關聯性，以更好理解行為所傳達的溝通內容；改善環境可以減少住民的睡眠干擾，讓晝夜節律回歸正常，像是白天明亮夜晚昏暗、減少環境噪音、避免干擾睡眠的藥物等；按摩、芳香療法或者音樂治療有助於舒緩情緒，也能緩解激躁症狀；聽力、視力訓練可以增加病人對於環境的感知[11]。

若是進行非藥物治療後，病人激躁症狀仍持續、嚴重甚至會危及自己與他人時，就得進行藥物治療 (Pharmacological therapy)，然而藥物治療並非取代非藥物治療，而是兩者建議並行。針對嚴重及高風險的激躁症狀

首選藥物為抗精神病藥物 (Antipsychotics)，當開始使用此類藥物進行治療時，牛津大學建議[11]每六週應評估一次利益與風險，若病人對於藥物反應不佳，則需停藥，另外，一項研究顯示，失智症病人使用抗精神病藥物的180天內累積死亡率相較於安慰劑上升3 - 12%，NNH (Number need to harm) = 8 - 50 (根據不同的藥物)，所以APA的觀點則是抗精神病藥物建議最長不要使用超過120天[12]。給藥時，所有藥物應該慢慢提高劑量至目標劑量，停藥時也須慢慢減量。藥物的首選為Risperidone 0.25 - 2mg/日，在各國，甚至TFDA也核准用於治療失智症病人具嚴重攻擊性、躁動或精神病症狀、行為障礙和其他破壞性行為障礙，而Olanzapine 2.5 - 10mg/日、Amisulpride 25 - 50mg/日、Quetiapine 12.5 - 300mg/日、Aripiprazole 5 - 15mg/日屬於二、三線用藥，若病人是巴金森氏症或是路易氏體失智症可考慮首選使用Quetiapine或是二線使用Aripiprazole。

非抗精神病藥物，像是Paracetamol 500mg - 1g/日可以用於有潛在疼痛的病人；尚未用藥治療認知障礙者，可使用乙醯膽鹼酶抑制劑 (Acetylcholinesterase Inhibitors) 或NMDA 受體拮抗劑可用於治療，如：Donepezil 5 - 10mg/日、Rivastigmine 3 - 12mg/day (分次給藥)、Galantamine 8 - 24mg/日、Memantine 5-20mg/日；Benzodiazepine類的藥物應盡量避免使用，然而，若病人處於嚴重急性的情緒壓力，建議給予Lorazepam 0.5-2mg/日(分次給藥)；抗憂鬱劑，如：Sertraline 25mg - 100mg/日、Citalopram 10 - 20mg/日、Mirtazapine 15 - 30mg/日或是Trazodone 50 - 150mg/日，用於中度至重度情緒憂鬱的病人之激躁症狀。情緒穩定劑 Carbamazepine 400mg/日 (分次給藥)，可以使用在所有其他上述藥物無效或不適用於病人時[11]。

無論使用抗精神病要或是其他類別的藥物，都需要監測副作用的發生，抗憂鬱劑需要監測血鈉、自殺意念評估以及QTc波延長，

表一、抗精神病藥物用於治療激躁症狀[11]

Antipsychotic	*Usual dose range in dementia*	*Comments*
Risperidone	0.25 – 2mg/day	• **First line** antipsychotic • Only antipsychotic licensed for use in BPSD in the UK.
Olanzapine	2.5 – 10mg/day	• **Second line** antipsychotic, where risperidone is either contraindicated or ineffective
Quetiapine	12.5-300mg/day	• Could be considered for **first line** for **patients with Parkinson's disease or Lewy Body** Dementia as lower risk of movement disorders or • May be considered **third line** where risperidone and quetiapine are ineffective or contraindicated.
Aripiprazole	5 – 15mg/day	• Could be considered **second line** for **patients with Parkinson's disease or Lewy Body** Dementia as lower risk of movement disorders *(where quetiapine ineffective or contraindicated)* or • May be considered **third line** where risperidone and quetiapine are ineffective or contraindicated.
Amisulpride	25 – 50mg/day	• Should only be considered where all other antipsychotic options have been ineffective or are contraindicated.

其中Trazodone或者Mirtazapine則要小心骨髓抑制發生，因此要定期監測血液數據；乙醯膽鹼酶抑制劑則注意心搏徐緩以及體重下降；Benzodiazepines則要小心鎮靜後的跌倒風險，以及認知退化的問題。Carbamazepine使用時則注意嚴重過敏反應Steven-Johnson syndrome。

表二、非抗精神病藥物治療激躁症狀[11]

	Treatment options	Comment
Analgesics	Paracetamol *500mg – 1g up to QDS*	• Treatment of potential pain is of great importance in dementia. Therefore, a trial of paracetamol should be considered for all patients with non-cognitive symptoms, even where there are no overt symptoms of pain. • Maximum dosage in frail patients and those weighing <50kg is 500mg QDS.
Acetylcholinesterase Inhibitors	Donepezil 5 - 10mg/day Rivastigmine 3 - 12mg/day *(in divided doses)* Galantamine 8 - 24mg/day	If not already prescribed for cognitive symptoms, then could be considered for non-cognitive symptoms, which cause significant distress or potential harm, in: • Patients with mild to moderate dementia • Patients with Lewy body dementia ** NB: Donepezil is considered first line acetylcholinesterase inhibitor for dementia within Oxford Health**
NMDA Antagonist	Memantine 5-20mg/day	If not already prescribed for cognitive symptoms, then could be considered for non-cognitive symptoms, which cause significant distress or potential harm, in: • Patients with moderate to severe dementia • Patients with mild to moderate dementia *where acetylcholinesterase inhibitors have been ineffective or contraindicated*.
Benzodiazepines	Lorazepam 0.5-2mg/day *(in divided doses)*	• Benzodiazepines should be avoided where possible • ONLY use in short term severe acute distress. • Lorazepam is the preferred choice (due to quick onset and short half-life). • High risk of sedation. Care in patients at high risk of falls
Antidepressants	SSRIs *e.g. low dose sertraline 25-100mg/day or low dose citalopram 10-20mg/day* Mirtazapine 15-30mg/day Trazodone 50-150mg/day	Low dose SSRI or mirtazapine may be helpful in patients with moderate to severe depressive symptoms. • Low dose sertraline may be a possible first line option. • Please be aware of contraindication between citalopram and all other medications known to cause QTc prolongation (this includes ALL antipsychotics). • Be aware of sedation as an adverse effect of mirtazapine Trazodone may be beneficial in patients with increased restlessness and agitation. • Be aware of sedation is a possible side effect. Care in patients at high risk of falls. • Trazodone can be given as a single or divided dosage.
Mood Stabilizers / Anticonvulsants	Carbamazepine Up to 400mg/day *(in divided doses)*	• Cautiously consider if all other treatment options *(including antipsychotics)* have been ineffective/unsuitable for the patient. • High risk of interactions with other medicines, if necessary contact pharmacy for advice. • Be aware of risk of Steven Johnsons Syndrome and stop if patient develops any unexplained rashes.

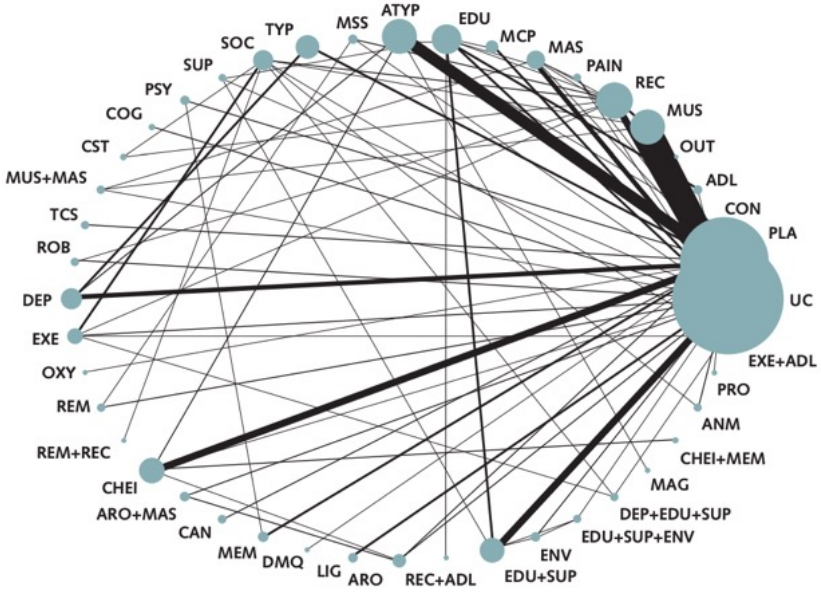
四、文獻回顧[13]

一篇2019年的系統性回顧與網絡統合分析 (Systematic Review and Network Meta-analysis) 比較用於失智症之激躁症狀的所有治療之效果，包含藥物與非藥物治療，納入了163篇隨機對照試驗，由超過兩位以上的作者進行文獻篩選、資料擷取、品質評估與結果合併，每個試驗終點都是透過Bayesian shared parameter random-effects NMA統合分析，以標準化的平均差來合併結果，最後回推出CMAI評估量表的分數，另外以surface under the cumulative ranking curve (SUCRA) values來排行治療效果，圖二為此篇文獻的網絡圖。

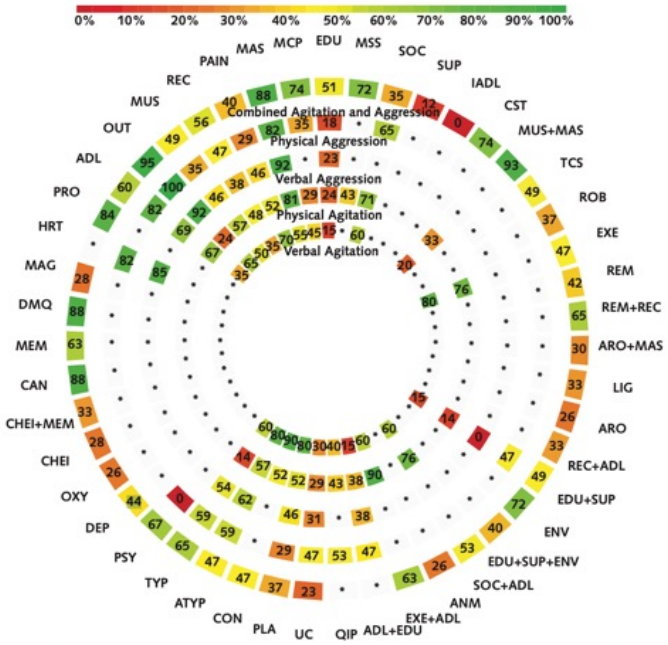
總共有23143位病人納入統合分析，納入的文獻中約50%為中度到嚴重的失智症病人，接近70%的病人已發生NPS，65%為安養機構住民，17%為住在社區的病人，75歲以上約83%(表三)。

透過網絡統合分析的排行治療效果，在激躁症狀與攻擊性 (Combined aggression and agitation) 的緩解中，戶外活動 (Outdoor activities) 的SUCRA = 95% (7% - 100%)，肢體的攻擊行為 (Physical aggression) 戶外活動之SUCRA = 100% (35% - 100%)，戶外活動 (Outdoor activities)、按摩 (Massage) 與肢體接觸治療 (Touch therapy) 對於言語的攻擊性有最好的治療效果。藥物方面，在緩解所有激躁症狀與攻擊性的效果中，抗精神病藥之SUCRA = 67%，其中典型的精神病藥物效果較好，對於言語的攻擊性，非典型抗精神病藥則有較好的效果SUCRA = 80%；抗憂鬱劑、乙醯膽鹼酶抑制劑或是NMDA受體抑制劑的SUCRA 28 - 44%，抗憂鬱劑在三者中有較好的效果 (圖三)。

若是以CMAI分數作為指標，戶外活動 (Outdoor activities) 相較於工具性日常生活活動 (Instrumental activities of daily living, IADL) 的改善下降了25.31 CMAI分數頗為顯著；音樂療法搭配按摩 (Music therapy + massage and touch therapy) 相較於IADL的改善，下降23.75 CMAI分數；藥物治療，如：典型或非典型抗精神病藥、NMDA受體抑制劑相較於IADL的改善也能下降15.93 - 16.78的MCAI分數；另外，環境改善、認知刺激等非藥物治療，在改善激躁及攻擊行為都有不錯的效果。在長照機構的次族群分析中，音樂療法搭配按摩(Music therapy + massage and touch therapy) 相較於一般照護 (Usual care)，可減少13.51的平均CMAI分數，此外，在大於80歲的次族群分析中，音樂療法搭配按摩相較於一般照護也可減少13.22平均CMAI分數。CMAI的最小臨床重要差異 (Minimal important difference) 為5.69 (0.4 SD) 與 7.11 (0.5 SD)，上述提到的治療，除了統計上有顯著之外，臨床上，激躁與攻擊行為也有顯著的緩解。綜上所述，非藥物治療的平均效果大於藥物治療，且治療的症狀較廣泛，而藥物的使用多針對特殊的病人狀況，像是肢體、言語的攻擊性分別使用不同的藥物等。



圖二、網絡統合分析之網絡圖[13]



The scale bar represents the SUCRA value for each intervention, with red indicating the lowest values (worst/least efficacious treatments) and green indicating the highest values (best/most efficacious treatments). ADL = modification of activities of daily living; ANM = animal therapy; ARO = aromatherapy; ATYP = atypical antipsychotics; CAN = cannabinoids; CHEI = cholinesterase inhibitor; CON = anticonvulsants; CST = cognitive stimulation; DEP = antidepressants; DMQ = dextromethorphan-quinidine; EDU = caregiver education; ENV = environmental modification; EXE = exercise; HRT = hormonal therapy; IADL = instrumental activities of daily living; LIG = light therapy; MAG = magnesium; MAS = massage and touch therapy; MCP = multidisciplinary care plan; MEM = memantine; MSS = multisensory stimulation; MUS = music therapy; OUT = outdoor activities; OXY = oxytocin; PAIN = pain management; PLA = placebo; PRO = propranolol; PSY = antipsychotics; QIP = quality improvement project; REC = recreation therapy; REM = reminiscence therapy; ROB = robotic pet therapy; SOC = social interaction; SUCRA = surface under the cumulative ranking curve; SUP = caregiver support; TCS = transcutaneous stimulation; TYP = typical antipsychotics; UC = usual care.
* Treatment without data on the outcome within the circle.

圖三、所有治療的SUCRA排行圖[13]

表三、失智症的激躁與攻擊行為之治療效果[13]

Treatment Comparison	MA Estimate of Studies (Participants), n*	NMA SMD (95% CrI)	MA SMD (95% CrI)	NMA SMD Reexpressed as MD on CMAI†
ADL modification vs. IADL modification	–	−1.1 (−2.14 to −0.05)	–	−15.64
Antipsychotics vs. IADL modification	–	−1.18 (−2.26 to −0.07)	–	−16.78
Cannabinoids vs. IADL modification	–	−1.51 (−2.72 to −0.29)	–	−21.47
Caregiver education + support vs. IADL modification	–	−0.99 (−1.86 to −0.11)	–	−14.08
Caregiver education vs. IADL modification	–	−1.02 (−1.91 to −0.13)	–	−14.50
Cognitive stimulation vs. IADL modification	–	−1.27 (−2.4 to −0.11)	–	−18.06
Dextromethorphan-quinidine vs. IADL modification	–	−1.5 (−2.78 to −0.2)	–	−21.33
Environmental modification vs. IADL modification	–	−1.24 (−2.27 to −0.22)	–	−17.63
Exercise vs. IADL modification	–	−0.98 (−1.89 to −0.04)	–	−13.94
Massage and touch therapy vs. aromatherapy	–	−0.74 (−1.39 to −0.1)	–	−10.52
Massage and touch therapy vs. caregiver education and support	–	−0.52 (−1.02 to −0.02)	–	−7.39
Massage and touch therapy vs. caregiver support	–	−0.92 (−1.84 to −0.01)	–	−13.08
Massage and touch therapy vs. cholinesterase inhibitors	–	−0.7 (−1.32 to −0.07)	–	−9.95
Massage and touch therapy vs. IADL modification	–	−1.51 (−2.4 to −0.62)	–	−21.47
Massage and touch therapy vs. light therapy	–	−0.67 (−1.29 to −0.05)	–	−9.53
Massage and touch therapy vs. music therapy	1 (34)	−0.52 (−0.96 to −0.08)	0.01 (−0.65 to 0.67)	−7.39
Massage and touch therapy vs. placebo	1 (80)	−0.61 (−1.19 to −0.01)	0.21 (−0.23 to 0.64)	−8.67
Massage and touch therapy vs. recreation therapy	1 (81)	−0.45 (−0.91 to −0.01)	0.07 (−0.36 to 0.5)	−6.40
Massage and touch therapy vs. social interaction	–	−0.64 (−1.22 to −0.06)	–	−9.10
Massage and touch therapy vs. usual care	6 (385)	−0.75 (−1.12 to −0.38)	−0.9 (−1.28 to −0.51)	−10.67
Memantine vs. IADL modification	–	−1.12 (−2.16 to −0.06)	–	−15.93
Multidisciplinary care plan vs. IADL modification	–	−1.26 (−2.2 to −0.31)	–	−17.92
Multidisciplinary care plan vs. usual care	4 (552)	−0.5 (−0.99 to −0.01)	−0.44 (−1 to 0.12)	−7.11
Multisensory stimulation vs. IADL modification	–	−1.22 (−2.27 to −0.18)	–	−17.35
Music therapy + massage and touch therapy vs. IADL modification	–	−1.67 (−2.85 to −0.49)	–	−23.75
Music therapy + massage and touch therapy vs. usual care	1 (34)	−0.91 (−1.75 to −0.07)	−1.71 (−2.36 to −1.05)	−12.94
Music therapy vs. IADL modification	–	−0.99 (−1.84 to −0.14)	–	−14.08
Outdoor activities vs. IADL modification	–	−1.78 (−3.39 to −0.17)	–	−25.31
Recreation therapy vs. IADL modification	–	−1.05 (−1.9 to −0.2)	–	−14.93
Recreation therapy vs. usual care	8 (474)	−0.29 (−0.57 to −0.01)	−0.26 (−0.64 to 0.12)	−4.12
Typical antipsychotics vs. IADL modification	–	−1.14 (−2.17 to −0.09)	–	−16.21

ADL = activities of daily living; CMAI = Cohen-Mansfield Agitation Inventory; CrI = credible interval; IADL = instrumental activities of daily living; MA = pairwise meta-analysis; MD = mean difference; NMA = network meta-analysis; SMD = standardized mean difference.
* Sample size adjusted for clustering when appropriate.
† Minimum clinically important difference estimated to be 5.69 at 0.4 SD and 7.11 at 0.5 SD.

表四、治療效果的次群組分析[13]

Treatment Comparison, by Subgroup	MA Estimate of Studies (Participants), n*	NMA SMD (95% CrI)	MA SMD (95% CrI)	NMA SMD Reexpressed as MD on CMAI†
Intervention in long-term care/assisted living facilities				
Cognitive stimulation vs. usual care	–	−0.94 (−1.83 to −0.04)	–	−13.37
Massage and touch therapy vs. usual care	6 (385)	−0.76 (−1.06 to −0.46)	−0.87 (−1.18 to −0.58)	−10.81
Multidisciplinary care plan vs. usual care	3 (520)	−0.49 (−0.93 to −0.05)	−0.39 (−0.92 to 0.15)	−6.97
Music therapy vs. usual care	10 (460)	−0.31 (−0.55 to −0.08)	−0.37 (−0.63 to −0.11)	−4.41
Music therapy + massage and touch therapy vs. usual care	1 (34)	−0.95 (−1.63 to −0.27)	−1.7 (−2.36 to −1.05)	−13.51
Recreation therapy vs. usual care	5 (339)	−0.36 (−0.63 to −0.09)	−0.24 (−0.6 to 0.13)	−5.12
Mean age of study participants ≥80 y				
Anticonvulsants vs. usual care	–	−0.61 (−1.2 to −0.03)	–	−8.67
Massage and touch therapy vs. usual care	6 (328)	−0.77 (−1.08 to −0.46)	−0.88 (−1.22 to −0.56)	−10.95
Multidisciplinary care plan vs. usual care	3 (279)	−0.49 (−0.95 to −0.03)	−0.38 (−0.96 to 0.2)	−6.97
Music therapy vs. usual care	12 (535)	−0.26 (−0.49 to −0.02)	−0.26 (−0.52 to 0)	−3.70
Music therapy + massage and touch therapy vs. usual care	1 (34)	−0.93 (−1.63 to −0.22)	−1.71 (−2.36 to −1.05)	−13.22
Recreation therapy vs. usual care	8 (474)	−0.34 (−0.6 to −0.07)	−0.27 (−0.59 to 0.06)	−4.83
Typical antipsychotics vs. usual care	–	−0.65 (−1.26 to −0.06)	–	−9.24
>50% of study participants female				
Massage and touch therapy vs. placebo	1 (80)	−0.81 (−1.47 to −0.13)	0.21 (−0.23 to 0.64)	−11.52
Massage and touch therapy vs. usual care	5 (291)	−0.89 (−1.33 to −0.45)	−1.07 (−1.5 to −0.64)	−12.66
Music therapy + massage and touch therapy vs. usual care	1 (34)	−0.96 (−1.84 to −0.08)	−1.7 (−2.36 to −1.05)	−13.65
Standard diagnostic criteria used to diagnose dementia				
Antipsychotics vs. placebo	3 (167)	−0.39 (−0.73 to −0.02)	−0.13 (−0.69 to 0.44)	−5.55
Atypical antipsychotics vs. placebo	9 (2777)	−0.18 (−0.32 to −0.07)	−0.25 (−0.5 to 0.01)	−2.56
Cannabinoids vs. placebo	3 (397)	−0.52 (−1.02 to −0.03)	−0.29 (−0.66 to 0.07)	−7.39
Dextromethorphan-quinidine vs. placebo	1 (218)	−0.59 (−1.01 to −0.19)	−0.45 (−1.72 to 0.81)	−8.39
Memantine vs. placebo	4 (990)	−0.25 (−0.44 to −0.05)	−0.17 (−0.41 to 0.08)	−3.56
Music therapy vs. usual care	7 (341)	−0.3 (−0.54 to −0.05)	−0.26 (−0.63 to 0.1)	−4.27
Recreation therapy vs. usual care	–	−0.45 (−0.87 to −0.03)	–	−6.40
Typical antipsychotics vs. placebo	3 (418)	−0.26 (−0.49 to −0.05)	−0.14 (−0.64 to 0.37)	−3.70

CMAI = Cohen-Mansfield Agitation Inventory; CrI = credible interval; MA = pairwise meta-analysis; MD = mean difference; NMA = network meta-analysis; SMD = standardized mean difference.
* Sample size adjusted for clustering when appropriate.
† Minimum clinically important difference estimated to be 5.69 at 0.4 SD and 7.11 at 0.5 SD.

五、結語

無論是指引或是系統性回顧告訴我們，失智症引起的激躁症狀，首選的治療是屬於非藥物的介入，藥物只能當作一種控制症狀的下策。非藥物治療，如戶外休閒活動、到公園散步或者馬路上走走與人互動、曬曬太陽等，還有透過聆聽舒緩音樂，搭配芳香按摩的肢體接觸活動，其他像認知刺激、聽力視力訓練等，相對於使用藥物，反而有非常顯著的效果，也不會受到藥物副作用的影響。藥或許可以把失智症想像成一種囚禁老年人靈魂的一種疾病，當因為腦部退化喪失各種感官時，與外界環境漸行漸遠，產生激躁的症狀像是一種掙扎，各種肢體、言語的侵略性，則是一種求救的訊號，疼痛、感染或藥物不良反應，在失智症患者不易表達的狀況下，激躁的症狀成為溝通的語言，可想而知這是個痛苦的過程。所以不管是醫療人員，家屬或是照護者，陪伴、細心照料或者溫柔的對話，增加對環境的感受，對於失智症病人而言，是一種溫暖的連結。

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