Sensory Stimulation for Nursing-Home Residents: Systematic Review and Meta-Analysis of Its Effects on Sleep Quality and Rest-Activity Rhythm in Dementia

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Keywords

Sensory stimulation · Multi-sensory environments · Sleep efficiency · Rest-activity rhythm · Circadian rhythm

Abstract

Introduction: Disrupted sleep-wake cycles might be associated with an exacerbation of behavioural disturbances and accelerate disease progression in dementia. The effect of sensory stimulation for improving sleep quality is unclear.

Methods: A systematic literature search was performed and all studies examining the effects of a sensory stimulation intervention (i.e. bright light, massage, acupuncture, animal-assisted interventions) on rest-activity rhythm (RAR) and/or nocturnal restlessness in nursing-home residents with dementia were included. **Results:** Sensory stimulation was shown to improve nocturnal behavioural restlessness as well as sleep duration and continuation, but the effect on the number of awakenings, RAR, and daytime sleep was negligible. Notable was the high heterogeneity between studies regarding treatments and patients' characteristics and sleep parameters. **Conclusion:** Sleep quality and nocturnal restlessness in nursing-home residents with dementia may benefit from sensory stimulation. An environment with sensory

stimulation may prevent or improve sleep disturbances in nursing homes, and thereby contribute to a better quality of life for their patients.

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Introduction

An estimated 50 million people worldwide live with dementia, and this number is expected to increase to 152 million by 2050 [1]. People with dementia prefer to live at home as long as possible, but institutionalization is often called for after the development of sleep disturbances and related behavioural and psychological symptoms (BPSD) such as anxiety, hallucinations, and aggression [2]. On average, sleep disturbances occur in 23% (range 0–85%) of people with dementia living in nursing homes, and residents with dementia using psychotropic drugs are more likely to experience sleep disturbances [3]. The severity of sleep disturbance increases with dementia severity, negatively affecting quality of life [4].

The most common sleep disturbances in nursing-home residents with dementia are difficulties falling or staying asleep, waking up too early in the morning, and

excessive daytime sleepiness [5]. These disturbances can lead to disrupted sleep-wake cycles (the rest-activity rhythm) [5, 6]. Sleep disturbances and a disrupted rest-activity rhythm (RAR) are among the most distressing behaviours for people with dementia, their relatives, and caregivers [7, 8]. Sleep quality is a requirement for well-being in people with dementia [4, 9] and fragmented sleep is closely related to cognitive decline (e.g., memory impairment), neuropsychiatric disorders (e.g., depression), functional decline, and morbidity and mortality in dementia [10–12]. Therefore, it is important to treat sleep disturbances in nursing-home residents who have dementia, in order to improve their sleep quality and RAR, which may reduce other BPSD and improve their quality of life [4, 13].

Treating sleep disturbances with sleep medication (usually benzodiazepine derivatives) can have adverse effects, such as confusion, and also exacerbates daytime sleepiness and night-time awakenings [14]. The preferred method to improve sleep in dementia, cognitive behavioural therapy [15], appears effective in mild dementia [16] but is not compatible with the cognitive and physical capacities of people with moderate-to-severe dementia [11]. Instead, stimulating residents during the day with activities that fit their individual cognitive and physical capacities can be helpful in regulating RAR [17, 18].

Sensory stimulation has become increasingly popular in nursing homes and appears to be a promising approach for ameliorating mood disturbances and behavioural problems in moderate-to-severe dementia [19–21]. Sensory stimulation involves stimulating one (uni-sensory stimulation [USS], e.g. light therapy) or more (multi-sensory stimulation [MSS], e.g., Snoezelen®) primary senses [22], and aims to prevent sensory deprivation by creating an enriched environment in a non-directive manner [18]. Sensory stimulation is based on the assumption that the primary sensory systems (i.e., visual, auditory, olfactory, gustatory, and tactile) can still be activated in the advanced stages of dementia [23, 24]. Sensory stimulation is the only person-centered approach which can be implemented by adjusting the nursing-home environment and is suitable for people with severe dementia [25]. Sensory stimulation may also work as a “Zeitgeber” to improve sleep disturbances and RAR in dementia [6].

However, to date, evidence for its effectiveness is scarce and contradictory [26–28]. Possible explanations for the lack of evidence are the high heterogeneity between studies regarding the target population, intervention characteristics (e.g., duration and intensity), and methodology. The aim of this systematic review and meta-analysis, with

P	Participants	Dementia
I	Intervention	Sensory stimulation
C	Comparisons	Standard care/no intervention
O	Outcome	Sleep quality, circadian rhythm, sleep disturbances

Fig. 1. PICO search model.

extensive subgroup analysis, was to examine the effectiveness of sensory stimulation on the sleep quality and RAR of nursing-home residents with dementia, with a focus on different uni-sensory components.

Methods

Search Strategy

A systematic literature search was conducted on December 3, 2019. The PICO search model was used to identify research terms (Fig. 1). Studies were extracted from; PubMed, The Cochrane Library, PsycINFO, Embase, and CINAHL. The search terms differed slightly between the different databases. For an overview, see the online supplementary Material (for all online suppl. material, see www.karger.com/doi/10.1159/000509433). The review is registered with the International Prospective Register of Systematic Reviews (PROSPERO; registration No. 104104).

Study Selection

After completing the literature search, duplicates were removed. All remaining studies were selected by 2 independent reviewers according to the inclusion and exclusion criteria (Table 1). We screened title and abstract first and full text second. Disagreements between the authors were discussed after the first selection and again after the second selection until agreement was reached.

Quality Assessment

The criteria from the Cochrane Collaboration tool (CCT) [29] and the Risk of Bias in Nonrandomized Studies of Interventions (ROBINS-I) tool [30] were used to assess the methodological quality of randomized controlled trials (RCTs) and non-RCTs, respectively. Risk of bias was ranked as low, moderate, high, or no information in RCTs, and low, moderate, serious, critical, or no information in non-RCTs. Eighteen studies also reported outcomes other than sleep, e.g., mood [31–48]. For these studies, the quality assessment of some domains of the CCT and ROBINS-I (e.g., blinding of participants and outcome assessment, missing data, and selective reporting) was based only on sleep and rest-activity outcomes, i.e., actigraphy data and observational data. All selected studies were evaluated independently by 2 authors. Differences in assessment between these authors were resolved by consensus.

Outcomes

The primary and secondary outcomes were measured using wrist-worn activity monitors (Actiwatch). Primary outcomes were RAR and nocturnal awakening. RAR was described by 3

Table 1. Inclusion and exclusion criteria for systematic search

Inclusion criteria	Exclusion criteria
Articles including experimental research design; RCT, non-RCT, quasi experimental, cross-over design, pre-post studies with control	Other publication types than articles including reviews or published comments/replies on articles, single case studies, without control
Publication year 1990–2019	Publication year <1990
Articles written in English	Articles not written in English
Human studies	Animal studies
Diagnosis of dementia (all subtypes) according to DSM-IV/V and NINCDS-ADRD or ICD-10	Other neurologic diseases (Korsakov, MS, Parkinson, Huntington) or no clear diagnosis
Intervention study; sensory based and applied to individuals or in a group performed by staff members of researchers (not family caregivers) at a nursing home	No intervention study or combinations of pharmacological interventions with sensory stimulations. Intervention performed by family caregivers at home or daycare
Sensory stimulation interventions/multisensory environments	Other forms of stimulation (psychopharmacological and medical treatments including DBS and EEG)
Referring to sleep and/or circadian rhythm disturbances	Outcomes other than sleep
Standardized outcome measures	Non-standardized outcome measures

nonparametric variables [49]; relative amplitude (RA), inter-daily stability (IS), and interdaily variability (IV). RA was calculated as the (normalized) difference between the means of the most active 10-h period (M10) and the least active 5-h period (L5) in the average 24-h pattern [49]. Higher values indicated a larger difference between daytime activity and nocturnal rest, and thus a stronger rhythm (range 0–1). IS was a measure of the degree of resemblance between activity patterns over multiple days [49]. Higher values indicated a more stable rhythm (range 0–1). IV represents fragmentation of periods of rest and activity [49]. Higher values indicated a more fragmented rhythm (range 0–2). Nocturnal awakening was described by 2 variables; the number of nocturnal awakenings (NA) and wake after sleep onset (WASO, i.e., minutes awake during the night after sleep onset).

The secondary outcomes were total sleep time (TST) night (duration of sleep at night in hours [between 8 p.m. and 8 a.m.]), TST day (duration of daytime sleep in hours from wake up to bedtime), sleep efficiency (SE; the proportion of actual sleep time in hours compared with hours lying in bed during the night) and sleep onset latency (SoL; minutes awake after going to bed).

The tertiary outcomes were sleep disturbance observations (SDO) and sleep quality observations (SQO) during the night (8 p.m. to 8 a.m.). SDO was measured with the Neuropsychiatric Inventory – night-time behaviour (NPI-K) [50], the Nursing Home Behaviour Problem Scale [51], the Behavioural Pathology in Alzheimer's Disease Rating Scale – activity disturbance (Behave-AD) [52], and sleep diaries recording behavioural restlessness. SQO was measured with the Pittsburgh Sleep Quality Index (PSQI) [53], Behave-AD – diurnal rhythm scale [52], and the Depressive Symptom Assessment for Older Adults – sleep impairment and cyclic function scales (DSAOA) [54]. In addition, sleep diaries were used about daytime sleepiness, early morning awakenings, awakenings during the night, and nocturnal sleep time, and were based on observations by nursing staff.

Main Effects

Data analysis was performed using Comprehensive Meta-Analysis® v3.0 [55]. Effect sizes for all sleep outcomes with a control group were calculated with a between-group Hedges' *g* and 95% confidence intervals (CIs). For studies with a pre-post or cross-over design, a within-group Hedges' *g* and 95% CIs were calculated. We examined the effects as observed immediately after a maximum 3-month intervention (post-test). Follow-up effects >1 week after intervention completion were not examined as few studies reported them.

To calculate pooled effect sizes and standard errors, we extracted the reported means, standard deviations (SDs), and number of participants for each group (intervention and control group) for each sleep measurement. Each study provided only 1 effect size. For studies with ≥2 intervention groups and 1 control group (as was the case in 4 studies [45, 56–59]), the intervention groups were combined into a single intervention score by pooling means, SDs, and sample sizes using the formulae proposed in the Cochrane Handbook [60]. When means and SD were missing, effect sizes were calculated using *p* values, sample sizes, and correlations. When exact *p* values were missing, we assumed a *p* value of 0.5 for non-significant (ns) results and 0.05 for significant results. We estimated effect sizes under the conservative assumption of a pre-post correlation of 0.7 [61]. Mean effect sizes were calculated according to the random-effects model. Heterogeneity was tested with the *I*² statistic, the *Q* test, and the examination of funnel plots.

Publication bias was tested with Egger's test [62] and by inspecting the funnel plot. If the Egger's test was significant (e.g., *p* < 0.05, one-sided), the estimated effect sizes were adjusted for publication bias by using the trim-and-fill procedure of Duval and Tweedie [63] with the random-effects model.

Subgroup Effects and Regression Analysis

Subgroup analyses were performed for the outcomes related to RAR and nocturnal behavioural disturbances (IV, IS, RA, WASO,

Fig. 2. Flow diagram of literature search.

SoL, and SDO). For these outcomes, we examined the effect of differences in study design and quality, intervention type, and disease comorbidity (sleep disturbances, agitation, and depression) on reported effect sizes. A mixed-effects model was used in the subgroup analyses. Pooled effect sizes within subgroups were calculated with the random-effects model, and the fixed-effects model was used to test the difference between subgroups. Several meta-regression analyses were performed to examine the relationship between study characteristics (e.g., disease duration in hours and weeks and lux used in light interventions) and population characteristics (sex, dementia severity, and dementia type) and the combined effect size across all studies. The p values were corrected for the number of subgroup ($p \leq 0.0125$) and regression ($p \leq 0.008$) analyses.

Results

Study Selection

After the first search, 2,536 references were extracted from PubMed (462), The Cochrane Library (102), PsycINFO (224), Embase (1,499), and CINAHL (249). After removing duplicates, 1,695 references were screened based on title and abstract. Disagreement (a rate of 3%) between the reviewers was discussed and resulted in the selection of 121 articles. After full-text screening, disagreement (a rate of 6%) between the reviewers was discussed, and 29 studies were included for further analysis,

Table 2. Study, intervention, and participant characteristics of included studies

First author [ref.], year	Country	Females, N (%)	Design	Intervention	Control	Duration	Specific inclusion/exclusion criteria	Dementia type and severity ^d	Sleep and RAR outcomes and results	ITT dropout rate	Quality ^a a b c d e f
Alparslan [68], 2019	Turkey	15 (40)	within subjects	BLT (afternoon) 10,000 lux vertical light box	standard light (ns)	7 days, 30 min/day follow-up: 2 weeks, comparison with pretreatment	E: eye diseases, changes in medication	AD 100% ns	TST night**,\$§ Daytime inactivity status** Daily activity intensity	Yes 0%	+/-
Ancoli-Israel [83], 2002	USA	77 (75)	RCT	BLT (morning, evening) >2,500 lux vertical light box	evening dim red light: <300 lux	10 days, 2 h/day	E: eye diseases	Type: ns 12.8±8.8 (0–30 70% <20) moderate-severe	Amplitude Mesor Acrophase (morning*)	No 34%	+ - + + -
Ancoli-Israel [84], 2003	USA	92 (68)	RCT	BLT (morning, evening) >2,500 lux vertical Light box	evening dim red light: <300 lux	10 days, 2 h/day	E: eye diseases, psychiatry	AD 100% 12.8±8.8 (0–22) mild-severe	TST night Daytime alertness Amplitude Mesor Acrophase	No 22%	+ - + + -
Ancoli-Israel [85], 2003	USA	92 (68)	RCT	BLT (morning, evening) >2,500 lux vertical light box	evening dim red light: <300 lux	10 days, 2 h/day	E: eye diseases, psychiatry	AD 100% 12.8±8.8 (0–22) mild-severe	TST day TST night WASO night NA Average length of NA WASO day % Sleep day % Sleep night % Wake day % Wake night # Daytime naps Duration of naps Length of time between naps Mean duration of wake bouts night Mean duration of wake bouts day* Mean duration of sleep bouts night* Mean duration of sleep bouts day	No 22%	+ - + + -
Buettner [31], 2002	USA	70 (ns)	between/within subjects	recreational therapy, biking	usual care	2 days/week, 1 h/day for 10 weeks	I: depression	Type: ns (0–24) mild-severe	Chart review sleep disturbances**	No 41%	-
Burns [32], 2009	UK	48 (67)	RCT	BLT (morning) 10,000 lux vertical light box	standard light 100 lux	14 days, 2 h/day	I: sleep disturbance, agitation E: eye disease	AD 44% Vascular 33% LBD 12% Mixed 9% 5.1±5.6 (ns) moderate-severe	TST night (actigraphy – raw data missing in article) TST night (observation – raw data missing in article) M10** L5	Yes 0%	+ - - - - ?
Dowling [57], 2005	USA	70 (81)	RCT	BLT (morning, afternoon) >2,500 lux vertical light box	standard light 150–200 lux	10 weeks, 5 days/week, 2 h/day	I: sleep disturbance E: eye diseases	AD 100% 7±7 (0–23) mild-severe	SE (%) night TST night NA Duration of awakenings Amplitude Wake time night Wake time day Mean Activity Score night Mean Activity Score day R ² Acrophase	No Unclear	? + - - + ? -

Table 2 (continued)

First author [ref.], year	Country	Females, N (%)	Design	Intervention	Control	Duration	Specific inclusion/ exclusion criteria	Dementia type and severity ^d	Sleep and RAR outcomes and results	ITT dropout rate	Quality ^a a b c d e f
Dowling [56], 2005	USA	46 (78)	RCT	BLT (morning, afternoon) >2,500 lux vertical light box	standard light 150–200 lux	10 weeks, 5 days/week, 2 h/day	I: sleep disturbance E: eye diseases	AD 100% 6.7±6.8 (0–23) mild-severe	IS IV NA SE Amplitude RA TST night L5 M10 R ² Acrophase Day wake time	Yes Unclear	? + - - + ? -
Dowling [58], 2008	USA	50 (86)	RCT	BLT (morning, afternoon) >2,500 lux vertical light box	standard light 150–200 lux	10 weeks, 5 days/week, 2 h/day	I: sleep disturbance E: eye diseases	AD 100% 9.3±7.9 (0–23) mild-severe	Amplitude IS IV RA TST night NA TST day L5 M10 Acrophase R ² Night sleep bout duration Night wake bout duration Day sleep bout duration Day wake bout duration # Daytime sleep bouts Daytime Total Activity Score Day/night sleep ratio	No Unclear	? + - - + ? -
Edwards [33], 2014	USA	72 (75)	within subjects (pre-post)	animal-assisted intervention: aquarium	usual care	all day for 8 weeks	-	Type: ns 6.4±6 (0–20) moderate-severe	NPI-K*	No 1.3%	-
Fetveit [86], 2003 Fetveit [87], 2004	Norway	18 (86)	within subjects	BLT (morning/ 6,000–8,000 lux vertical light box	usual care	14 days, 2 h/day follow-up: 4 weeks, comparison with pretreatment	I: sleep disturbance E: eye diseases	Type: ns 11.7±4.2 (6–18) moderate-severe	SE %* Sol.* WASO* TST night SDO* Sleep wake disturbances night* Sleep wake disturbances early morning Sleep wake disturbances day* Sleep wake disturbances evening Early morning awake* Time in bed* Total wake time** Mesor* Acrophase L5 M10 Light/dark ratio Day activity Night activity* Total 24 h* Time in bed	No 38.9%	-

Table 2 (continued)

First author [ref.], year	Country	Females, N (%)	Design	Intervention	Control	Duration	Specific inclusion/ exclusion criteria	Dementia type and severity ^d	Sleep and RAR outcomes and results	ITT dropout rate	Quality ^a a b c d e f
Figuiro [34], 2014	USA	35 (77)	within subjects	low-level bluish-white light 324±190 lux vertical lamp in bedroom	standard light (ns)	4 weeks, 12 h/day	I: sleep disturbance E: eye diseases	AD 100% 7.7±2.3 (12–24) mild-severe	SE* TST* SoL IS IV PSQI** CL* CS** Phasor magnitude**	No 28.6%	–
Fontana Gasto [35], 2003	Switzerland	20 (69)	within/ between subjects	dawn-dusk simulation therapy : 0.1–200 lux vertical lamp in bedroom	dim red light <5 lux	3 weeks, 5 days/week, 45 min/day follow-up: 3 weeks comparison with pretreatment	I: sleep disturbance E: eye diseases	AD 77% Vascular 15% LBD 7.7% 14±5 (ns) mild-severe	IS IV RA Sleep duration Sleep latency L5* M10 Time in bed Nocturnal activity # Wake bouts # Immobile phases # Immobile epochs	No 35%	–
Harris [36], 2012	USA	40 (80)	within subjects (pre-post)	massage	usual care	2 days, 3 min/day	I: sleep disturbance	AD 50% Vascular 15% LBD 2.5% Mixed 2.5 ns: 30% 10.56 ±7.31 (0–26) mild-severe	Night-time sleep Sleep latency SE NA WASO Daytime inactivity Day/night sleep ratio	No, 6%	+
Ito [37], 2001	Japan	28 (57)	within subjects (cross-over)	BLT (morning) 3,000 lux horizontal	standard light (ns)	4 weeks, 2 h/day	–	AD 100% 10.14±7.3 mild-severe	NA % Sleep day % Sleep night # Naps at daytime	No ns	?
Kwok [38], 2013	China	22 (74)	within subjects (pre-post)	acupuncture	usual care	6 weeks, 12 sessions, 2/week, 30 min/day	I: sleep disturbance E: psychiatry, medica- tion changes	AD26.3% Mixed 26.3% + 15.8% Vascular 5.3% LBD 5.3% ADAS-Cog score: 27.28±10.93 mild	TST* SE SoL WASO NA Resting time*	No 14%	–
van Lieshout- van Dal [39], 2018	NL	18 (50)	quasi- experimental cross-over	biodynamic lighting 7,500 lux horizontal 2,700–6,500 K lamp in common area	standard light (ns)	3 weeks, 12 h/day	I: neuropsychiatric symptoms E: eye disease	AD33% FTD 5.5% Korsakov 5.5% ns: 55% Severity: ns	NPI-K	No 36%	–
Lyketsos [40], 1999	USA	15 (93)	RCT (cross-over)	BLT (morning) 10,000 lux vertical light box	dim light (ns)	4 weeks, 1 h/day	E: sleep disturbance, eye disease, depression	AD 80% Vascular 20% 6.4±6.8 (ns) moderate-severe	TST*	Yes 46.7%	? + + + +
Mishima [41], 1994	Japan	24 (ns)	experimental (between/ within subjects)	BLT (morning) 3,000–5,000 lux vertical light box	healthy older adults	4 weeks, 2 h/day follow-up: 2 weeks, comparison with pretreatment	I: insomnia, sleep or behavioral disturbances	ns	TST night**,\$\$ (observations) TST day* (observations) TST*,\$ (observations)	No Unclear	?
Mishima [69], 1998	Japan	22 (ns)	RCT (cross-over)	BLT (morning) 5,000–8,000 lux light box	dim light 300 lux	2 weeks, 2 h/day	I: sleep disturbances	AD 45% Vascular 55% 9 severe	AD: night-time activity (counts/day; actigraphy) Vascular: night-time activity** (counts/day; actigraphy)	No Unclear	? ? + + + ?

Table 2 (continued)

First author [ref.], year	Country	Females, N (%)	Design	Intervention	Control	Duration	Specific inclusion/ exclusion criteria	Dementia type and severity ^d	Sleep and RAR outcomes and results	ITT dropout rate	Quality ^a a b c d e f
Moyle [66], 2018	Australia	415 (43)	RCT	robotic seal toy	usual care	15-min sessions, 3 afternoons/week for 10 weeks follow-up: 5 weeks, comparison with pretreatment	E: psychiatry	AD 18% Vascular 10% FTD 0.3% Korsakov 0.7% LBD 0.7% ns: 28.7% ns	TST day TST night Step count day* Step count night [§] Physical activity day [§] Physical activity night*, [§] Awake hours day Awake hours night Lying down hours day Lying down hours night	Yes 4.3%	+ - + + + ?
Nowak [42], 2008	USA	20 (100)	2-factor experimental design with repeated- measures	blue-green light (afternoon), 12,000 lux vertical cap visor	dim red light 5 lux (vertical)	daily for 2 weeks, 30 min/day	I: sleep disturbance	AD 100% 1.96±2.86 (ns) severe	SoL SE Sleep duration Night-time awakenings	No 4.8%	? ? - + + +
Onega [43], 2018	USA	60 (72)	2 × 2 × 2 mixed-model repeated- measures	BLT (morning/evening) 10,000 lux vertical light box	250 lux	30 min twice a day, 5 days/week for 8 weeks	I: depression E: eye diseases	Type: ns 7.22±6.85 (0-22) mild-severe	DSAOA-sleep impairment DSAOA-cyclic functions	No 15.5%	-
Riemersma- van der Lek [44], 2008	NL	189 (90)	RCT	BLT ±1,000 lux vertical 9 a.m. to 6 p.m. ceiling-mounted light fixtures with Plexiglas diffusers	<400 lux	15 months-3.5 years 9 h/day for 6 weeks for synthesis	-	AD 23.8% ns: 24.8% 14±7 (0-30) mild-severe	SE SoL Total sleep duration* Duration of awakenings Nocturnal restlessness (actigraphy) Duration uninterrupted sleep epochs	Yes >50%	+ + + + + +
Rodriguez- Mansilla [45], 2013	Spain	120 (26)	RCT	acupuncture and massage	usual care	3 months, 5 days/week, 20 min/day follow-up: 2 months, comparison with pretreatment	-	AD 18.6% Vascular 8.7% Mixed 6% Severity: ns	SDO**	No 7.5%	+ + + + + +
Sadlin [46], 1992	USA	10 (10)	within subjects	BLT (evening) 1,500-2,000 lux vertical light box	standard light	7 days, 2 h/day follow-up: 1 week, comparison with pretreatment	I: sundowners E: eye diseases	Type: ns 0.6±1.1 (ns) severe	RA* IS* IV Total sleep disturbances clinical rating* Sundowning score*, [§] Acrophase Mesor Night-time awakenings %*	No Not clear	-
Sloane [59], 2007	USA	103 (47)	experimental cross-over (between/ within subjects)	BLT (morning, evening, daytime) 2,500 lux horizontal ceiling-mounted illumination	standard light 500 lux	3 weeks, 4 h/day or 13 h/day	E: eye diseases	Type: ns Severity: ns	TST night* Amplitude IV IS # Night-time sleep bouts Observed daytime sleepiness Acrophase** Mesor	No 35.9%	-
Suzuki [47], 2010	Japan	28 (71)	experimental	massage (afternoon)	usual care	30 sessions over 6 weeks, 5 times 20 min/week	-	AD 86% Vascular 14% 5.68±6 (ns) moderate-severe	Behave-AD diurnal rhythm disturbance Behave-AD activity	No 30%	-
Swansdottir [67], 2006	Iceland	47 (ns)	case control (within/ between subjects)	music	usual care	6 weeks, 3 days/week, 30 min/day follow-up: 4 weeks, comparison with pretreatment	-	AD 100% ns moderate-severe	Behave-AD diurnal rhythm disturbance Behave-AD activity*	No 19.1%	+/-

Table 2 (continued)

First author [ref.], year	Country	Females, N (%)	Design	Intervention	Control	Duration	Specific inclusion/ exclusion criteria	Dementia type and severity ^d	Sleep and RAR outcomes and results	ITT dropout rate	Quality ^a a b c d e f
Takeda [88], 2017	Japan	22 (47)	within subjects	aroma	same procedure without aroma	20 days, 1–2 h/day (evening)	I: sleep disturbance	Type: ns 6.0±6.5 (ns) moderate-severe	Sleep latency TST night** SE WASO Early morning awakening Duration of the longest sustained sleep period*	No 13.6%	-
Van Someren [70], 1997	NL	29 (52)	RCT	BLT (daytime) 790–2,190 lux horizontal ceiling-mounted illumination	standard light 110–1,106 lux	3 weeks, >2 h/day	E: eye disease	AD 55% Vascular 10% Korsakov 6.9% moderate-severe	IS** IV** Amplitude M10*	No 24.1%	-
Wahnschaffe [48], 2017	Germany	15 (58)	within subjects	biodynamic lighting +400 lux, 3,000–6,500 kelvin ceiling-mounted illumination	standard light (ns)	2 weeks, 12 h/day	-	AD 25% Vascular 25% ns: 50% 12.1± 9.2 (ns) mild-severe	RA IS IV	Yes 20%	-

BLT denotes outcomes categorized in the outcome groups used for synthesis. Mild (≥ 21), moderate (13–20), severe (≤ 12). * $p \leq 0.05$, ** $p \leq 0.01$ (direct effect), $^{\dagger} p \leq 0.05$, $^{\ddagger} p \leq 0.01$ (follow-up effect). NL, The Netherlands; ns, not specified; I, inclusion criteria; E, exclusion criteria; ITT, intention-to-treat analysis; AD, Alzheimer's disease; FTD, frontotemporal dementia; LBD, Lewy bodies dementia; BLT, bright-light therapy; Behave-AD, Behavioural Pathology in Alzheimer's Disease Rating Scale; DSAOA, Depressive Symptom Assessment for Older Adults; NPI-K, Neuropsychiatric Inventory – night-time behaviour; PSQI, Pittsburgh Sleep Quality Index; MMSE, Mini-Mental State Examination; RAR, rest-activity rhythm; IS, interdaily stability; IV, interdaily variability; RA, relative amplitude; NA, number of night-time awakenings; SE, sleep efficiency; Sol, sleep onset latency; SDO, sleep disturbance observations; WASO, wake after sleep onset; TST, total sleep time; #, number.

^a Quality of bias assessment with CCT (a = selection bias, b = performance bias, c = detection bias, d = attrition bias, e = reporting bias, f = other bias) and ROBINS-1 (overall assessment): +, low risk of bias; +/-, moderate risk of bias; - high/serious risk of bias.

^b Direct effect = during intervention period or immediately after intervention period.

^c Follow-up effect = 1–5 weeks post-intervention.

^d According to the MMSE scale.

including 27 for synthesis. Figure 2 presents a flow diagram of the search results according to the PRISMA guidelines [64].

Study Characteristics

Table 2 represents details of the study characteristics. The 29 studies included a total of 1,717 nursing-home residents with dementia, ranging between 10 and 415 participants per study. Ten studies used a RCT design. Eight studies used a non-RCT design with a control group and 11 studies used a pre-post design. Most studies were from the USA, followed by Europe and Asia.

Ten to 100% of the participants within each study were females. Dementia types were as follows: 18–100% of the participants were diagnosed with AD, 10–33% with vascular dementia, 0.7–12% with Lewy bodies dementia, 0.3–5.5% with frontotemporal dementia, and 2.5–9% with mixed dementia. Dementia severity was measured in 946 participants (55% of the total sample), with a mean Mini Mental State Examination (MMSE) [65] score between 0.6 and 12.8, which corresponds to moderate-to-severe dementia. Comorbid sleep or mood disorders at the time of inclusion were diagnosed in 401 (23% of the total sample) and 148 (9% of the total sample) participants, respectively. TST night (i.e., 8 a.m. – 8 p.m.), measured with actigraphy in 851 participants (50% of the total sample), was 7.4 h (95% CI 4.8–11.9 h). In the remaining 866 participants (50%), the severity of sleep disturbances preintervention was not reported. Participant dropout rates during the intervention period ranged from 0 to 50%.

Two studies applied MSS as outside recreational activities and robotic toy therapy [31, 66] 2–3 times/week for 10 weeks. Other studies applied USS as light ($n = 20$), massage ($n = 3$), acupuncture ($n = 2$), music ($n = 1$), animal-assisted ($n = 1$) and aromatherapy ($n = 1$). Regarding light therapy, 15 studies applied bright light (1,000–12,000 lux vertical), 3 studies applied a high light intensity but lower than bright light (<750 lux vertical), and 2 studies applied biodynamic lighting (400–750 lux horizontal, 2,700–6,500 K). Most studies ($n = 13$) placed light boxes in front of the resident with dementia for 0.5–2 h/day. Seven studies examined the effect of ceiling-mounted illumination or independent lamps in a common room for all-day exposure. The dosage and duration of the light interventions varied between 30 min and 13 h per day for 1 week to 15 months. In most studies, light exposure started between 7.00 or 10.00 a.m. [46]. Fourteen of the 20 studies (70%) excluded patients with severe visual disturbances.

Fig. 3. Graphical representation of risk of bias in RCTs and non-RCTs included in the qualitative analysis.

Risk of Bias within Studies

Disagreement between the reviewers of risk of bias based on the CCT and ROBINS-I tool were discussed (RCTs: disagreement rate 22.6 %; non-RCTs: 43.8%) and resolved (Fig. 3). Only 3 studies were judged to have a low risk of bias [36, 44, 66] and 2 a moderate risk of bias [67, 68]. The remaining studies were evaluated as having a high/serious/critical risk of bias ($n = 16$), or else varied between a low and high risk of bias ($n = 5$) depending on outcome. In 3 studies [37, 41, 69], there was not enough information to evaluate the risk of bias.

Synthesis of Results: Main Effects

Twenty-seven studies ($n = 1,238$, 72%) were available for synthesis (Fig. 2). One study [32] was excluded because of missing raw data. USS ($n = 1,006$, 59%) had significant small positive effects on RAR combined, RA, TST night, and SE. USS had significant small negative effects on WASO

and SoL (Table 3) and a significant medium negative effect on SDO and SQO. IS/IV, NA, SoL, and TST day did not significantly postintervention compared to usual care. The heterogeneity within most of the outcomes varied between medium and large. MSS ($n = 226$, 13%) had no significant effect on any of the outcome variables [31, 66].

Additional Analysis: Differences between Study, Intervention, and Patient Characteristics

Regarding the observations by nursing staff (subjective outcomes), the combined effect size was medium with medium heterogeneity. When considering actigraphic measurements (objective outcomes), the combined effect size was low with medium heterogeneity (Table 4). Effect sizes of the combined sleep outcomes did not differ between subjective and objective measurement methods ($Q = 0.71$, $p = 0.40$, $nc = 29$). The combined effect size of RCTs was medium with medium heterogeneity.

Table 3. Main post-test effects of USS

Outcomes	Nc (Np)	Hedges' g (95% CI)	I ² (95% CI)	NNT
<i>Primary outcomes</i>				
<i>Rest-activity rhythm</i>				
RA	7 (268)	0.37* (0.07 to 0.67)	59* (5 to 82)	4.85
IS	6 (174)	0.39 (-0.14 to 0.92)	86** (71 to 93)	4.59
IV	6 (174)	-0.63 (-1.29 to 0.03)	90** (80 to 95)	2.91
RAR (combined)	8 (278)	0.41* (0.02 to 0.80)	78** (57 to 89)	4.39
<i>Nocturnal awakenings</i>				
WASO	8 (413)	-0.29* (-0.54 to -0.04)	70** (37 to 85)	6.17
# Awakenings	5 (184)	-0.17 (-0.43 to 0.08)	4 (-388 to 81)	10.42
<i>Secondary outcomes</i>				
TST night	15 (593)	0.38** (0.22 to 0.54)	44 (-4 to 70)	4.72
SE	9 (350)	0.48** (0.24 to 0.72)	50* (-7 to 78)	3.76
SoL	8 (280)	-0.25* (-0.46 to -0.05)	33 (-51 to 70)	7.14
TST day	2 (106)	-0.04 (-0.22 to 0.13)	0 (-2,854,734 to 100)	45.45
<i>Tertiary outcomes</i>				
SDO	6 (276)	-0.57** (-0.96 to -0.12)	67** (22 to 86)	3.18
SQO	7 (221)	-0.61** (-1.02 to -0.20)	71** (38 to 87)	2.99
Actography combined	19 (840)	0.39** (0.21 to 0.56)	63** (39 to 77)	4.59
Observations combined	11 (473)	-0.63** (-0.92 to -0.35)	70** (44 to 84)	2.91
All outcomes combined	25 (1006)	0.47** (0.31 to 0.63)	64** (45 to 76)	3.85
RCTs	8 (476)	0.67** (0.30 to 1.05)	77** (39 to 83)	2.75

RAR, rest-activity rhythm; RA, (relative-) amplitude; IS, interdaily stability; IV, interdaily variability; WASO, wake up after sleep onset; TST, total sleep time; SE, sleep efficiency; SoL, sleep (onset) latency; SDO, sleep disturbance observations; SQO, sleep quality observations; RCTs, randomized controlled trials; CI, confidence interval; Nc, number of comparisons; Np, number of participants; NNT, number needed to treat. * $p \leq 0.05$, ** $p \leq 0.01$.

Subgroup analysis revealed significantly higher effect sizes for IV ($Q = 14.61$, $p \leq 0.01$), IS ($Q = 19.34$, $p \leq 0.001$), and SDO ($Q = 5.30$, $p \leq 0.05$) in RCTs versus non-RCTs. In studies with a low/moderate risk of bias, the effect sizes were significantly higher for WASO ($Q = 13.64$, $p \leq 0.001$) and SDO ($Q = 9.79$, $p \leq 0.01$) when compared to studies with a high/serious risk of bias. No significant subgroup differences were found for other sleep outcomes. No significant differences in sleep parameters were found for intervention type and inclusion or exclusion criteria. For details of the effect sizes and heterogeneity within each group, see online supplementary Additional file 2.

Meta-regression analysis revealed no significant relationship between the effectiveness of USS on sleep and any of the following predictors: gender, dementia severity (MMSE score), intervention duration (h/week and total of weeks), intervention dosage (lux of light interventions). For details of the coefficients, see Table 5. The effect sizes did not differ between the different dementia types ($Q = 3.82$, $p = 0.58$, $nc = 22$) and dropout rates ($Q = 4.22$, $p = 0.52$, $nc = 22$).

Publication Bias

Visual inspection of the funnel plots and execution of Egger's test indicated possible publication biases for IV ($t_4 = 2.79$, $p \leq 0.05$) and TST night ($t_{13} = 2$, $p \leq 0.03$). According to the trim-and-fill procedure [63], 5 studies measuring IV ($n = 1$) and TST night ($n = 4$) were missing.

When the estimated missing effect sizes were imputed using the trim-and-fill algorithm [63], adjusted effect sizes for IV ($g = 0.77$, 95% CI 0.11–1.43) became larger and significant, and for TST night ($g = 0.28$, 95% CI 0.12–0.43) the adjusted effect size became smaller but remained significant.

Discussion

The aim of this review and meta-analysis was to examine the effectiveness of MSS and USS on sleep quality and RAR. USS including visual and tactile stimulation were effective for improving sleep quality and RAR (effect size 0.47). More specifically, visual and tactile stimulation for

Table 4. Posttest effects of USS on rest-activity rhythm (IS, IV, and RA), WASO, SoL, and SDO - subgroup analysis

Sleep parameter	Design		Study quality		Intervention type		Inclusion criteria	
	RCT	non-RCT	low/moderate risk of bias	high/serious risk of bias	no light	light	yes	no
RAR-IV								
Nc (Np)	2 (52)	4 (122)	1 (35)	5 (87)	0	6 (174)	3 (55)	3 (119)
g (95% CI)	-1.54 (-4.51 to 1.44)	-0.25 (-0.64 to 0.15)	-0.03 (-0.68 to 0.62)	-0.76 (-1.53 to 0.02)	n.a.	-0.63 (-1.29 to 0.03)	-0.34 (-0.95 to 0.26)	-0.99 (-2.37 to 0.39)
I ² (95% CI)	97** (92 to 99)	66* (1 to 88)	n.a.	92** (83 to 96)	n.a.	90** (84 to 96)	74* (11 to 92)	95** (90 to 98)
p value	≤0.01		0.315		n.a.		0.835	
RAR-IS								
Nc (Np)	2 (52)	4 (122)	1 (35)	5 (139)	0	6 (174)	3 (55)	3 (119)
g (95% CI)	1.08 (-1.04 to 3.21)	0.09 (-0.12 to 0.31)	0.00 (-0.65 to 0.65)	0.47 (-0.14 to 1.08)	n.a.	-0.39 (-0.14 to 0.92)	0.09 (-0.19 to 0.37)	0.75 (-0.39 to 1.88)
I ² (95% CI)	95** (86 to 98)	0 (-5205 to 12)	n.a.	88** (75 to 94)	n.a.	86** (71 to 93)	0 (87 to 98)	94** (85 to 97)
p value	≤0.001		0.403		n.a.		0.095	
RAR-RA								
Nc (Np)	4 (156)	3 (112)	2 (105)	5 (163)	0	7 (268)	3 (115)	4 (153)
g (95% CI)	0.51* (0.08 to 0.94)	0.25 (-0.19 to 0.68)	0.31 (-0.12 to 0.73)	0.42 (-0.02 to 0.85)	n.a.	0.39* (0.07 to 0.70)	0.46** (0.17 to 0.74)	0.32 (-0.17 to 0.81)
I ² (95% CI)	54 (-39 to 85)	60 (-99 to 89)	0 (n.a.)	73** (32 to 89)	n.a.	60* (7 to 82)	0 (-4245 to 95)	76** (36 to 91)
p value	0.069		0.697		n.a.		0.489	
WASO								
Nc (Np)	4 (305)	4 (108)	4 (274)	4 (139)	3 (97)	5 (316)	6 (213)	2 (200)
g (95% CI)	-0.34 (-0.77 to 0.09)	-0.22 (-0.48 to 0.04)	-0.49** (-0.75 to -0.22)	-0.14 (-0.38 to 0.10)	-0.09 (-0.36 to 0.17)	-0.39* (-0.76 to -0.02)	-0.24* (-0.45 to -0.04)	-0.34* (-1.01 to -0.33)
I ² (95% CI)	85** (62 to 94)	15 (-562 to 89)	24 (-94 to 70)	46 (-63 to 82)	0 (-141,092 to 80)	81** (57 to 91)	0 (-403 to 69)	95** (84 to 98)
p value	0.826		≤0.001		0.233		0.913	
SoL								
Nc (Np)	2 (142)	6 (138)	2 (169)	6 (111)	3 (97)	5 (183)	7 (153)	1 (129)
g (95% CI)	-1.01 (-2.46 to 0.45)	-0.16 (-0.35 to 0.04)	-0.30 (-0.63 to 0.03)	-0.25 (-0.54 to 0.05)	-0.22 (-0.49 to 0.05)	-0.32 (-0.66 to 0.03)	-0.21 (-0.46 to 0.06)	-0.40** (-0.64 to -0.15)
I ² (95% CI)	79* (-360 to 72)	0 (-798 to 45)	28 (-89 to 72)	41 (-49 to 77)	0 (-5886 to 93)	57 (-17 to 84)	32 (-59 to 71)	n.a.
p value	0.067		0.424		0.627		0.206	
SDO								
Nc (Np)	1 (111)	5 (165)	2 (149)	4 (127)	4 (248)	2 (28)	1 (10)	5 (266)
g (95% CI)	-0.81** (-1.22 to -0.40)	-0.50* (-0.94 to -0.06)	-0.87** (-1.22 to -0.52)	-0.33 (-0.37 to 0.07)	-0.52* (-0.94 to -0.10)	-1.43 (-3.79 to 0.94)	-3.00 (-5.61 to 0.41)	-0.51** (-0.86 to -0.16)
I ² (95% CI)	n.a.	60* (8 to 85)	0 (-3,944,552 to 100)	42 (-73 to 80)	73* (23 to 90)	n.a.	n.a.	64* (6 to 86)
p value	≤0.05		≤0.01		0.360		≤0.05	

RAR, rest-activity rhythm; IV, interday variability; IS, interday stability; RA, (relative) amplitude; WASO, wake up after sleep onset; TST, total sleep time; SoL, sleep (onset) latency; SDO, sleep disturbance observations; CI, confidence interval; Nc, number of comparisons; Np, number of participants; n.a., not available. * $p \leq 0.05$, ** $p \leq 0.01$.

Table 5. Regression coefficients of characteristics of the interventions and target population

Predictor	B	95% CI	SE	p value
Female gender, %	0.75	−0.42 to 1.92	0.60	0.209
Dementia severity (MMSE mean score)	0.01	−0.05 to 0.06	0.03	0.743
Intervention duration (h/week)	0.00	−0.00 to 0.00	0.00	0.581
Intervention duration (total weeks)	−0.04	−0.06 to −0.10	0.04	0.299
Intervention dosage (lux)	0.00	−0.00 to 0.00	0.00	0.624

There were 13 comparisons and 482 patients (28% of the total sample).

a minimum of 30 min/day for 2 weeks was found to effectively reduce NA, SoL, and sleep disturbance, and improve nocturnal sleep duration and SE. Only 2 studies examined MSS in relation to sleep quality [31, 66], but none examined its effect on RAR. In the following paragraphs, we discuss the effects of USS on RAR and sleep quality for varying study characteristics.

Rest-Activity Rhythm. USS using light therapy (a minimal intensity of 790 lux) was only effective in strengthening the circadian rhythm (RA) in residents without severe eye diseases and in RCTs with a high risk of bias [46, 70], but did not improve fragmentation in the 24-h RAR (IV) or IS over multiple days. The effect on the RA could be attributed to dementia severity and study quality. The 2 studies with positive effects included only residents with moderate-to-severe dementia [46, 70]. More severe circadian rhythm disturbances are associated with more severe dementia, leaving more room for improvement. Reliable measurement of RA, IS, and IV requires >7 days of actigraphic recording [71], which was not achieved in 4 of the 7 studies [38, 46, 58, 70].

Sleep Quality. Consistent with recent reviews [26, 72, 73], our meta-analysis revealed significant positive effects of USS using light therapy or acupuncture on TST night. Only light therapy was effective in improving SE and SoL, and decreasing the duration of awakenings, although the effects were small. Previous meta-analyses [74, 75] and reviews [73, 76] examining light therapy found mixed results regarding TST, SoL, early morning awakening, and daytime sleepiness. In all reviews and meta-analyses, the short-term effects on SE (%) and continuation (WASO) were robust, especially in samples of nursing-home residents with moderate-to-severe dementia [76]. This supports evidence for the effectiveness of visual and tactile stimulation to improve sleep quality in nursing-home residents with dementia.

Night-Time Restlessness. Nursing staff observed less behavioural restlessness during the night when residents with dementia received light therapy, acupuncture, massage

therapy, and animal-assisted interventions. The effects were medium to large, as in previous reviews [26, 56–58, 74, 76, 77], and larger in RCTs with a low risk of bias than in those with a high risk of bias. No differences in effects were found between dementia patients with and dementia patients without a diagnosis of mood and/or sleep disorders. It remains a challenge to evaluate the efficacy of USS on night-time restlessness of patients with or without mood and/or sleep disorders because in most articles, the severity of sleep disturbances preintervention was not described clearly.

Factors Affecting the Efficacy of Sensory Stimulation. In contrast to a previous meta-analysis [74], dementia severity, dementia type, gender, treatment duration, and light intensity (lux values) were not related to the effectiveness of sensory stimulation. One reason could be that, in the selected studies, only 28% of the data were available for analysis, due to the incomplete description of interventions and the characteristics of participants. Consequently, the statistical power of the meta regression analyses was limited. Dropout rates during the intervention periods were normally distributed between the studies and no association with effect sizes was found, suggesting that the effects of dropout on the results were limited affected.

In summary, sensory stimulation (in particular, visual and tactile stimulation) can have a small to medium positive effect on the duration of nocturnal awakenings, SE, and SoL, and thereby improve the total sleep duration and quality. We speculate that higher arousal during the day, in combination with a higher circadian amplitude, might lead to longer uninterrupted sleep during the night. These positive effects were observed in both actigraphic results and behaviour observations by nursing staff. This is an important and clinically relevant finding because nocturnal awakenings, in particular, can be a precursor for disorientation, anxiety, wandering during the night, and waking up other residents, all of which were reported as distressing for nursing staff [4, 7, 8, 78]. Because improvements in sleep quality can be beneficial for both

nursing-home residents and staff, implementing sensory stimulation interventions in nursing homes is recommended. In addition, treatment of nocturnal awakenings might be valuable in preventing further deterioration of behavioural disturbances and cognitive decline [10, 79].

This meta-analysis has several limitations. First, we did not control for the timing aspect of sensory interventions, while the daily routine and optimal timing may stabilize the circadian rhythm on its own [80]. Second, because of the small sample size and the large differences in sleep outcomes, measurement instruments, and procedures between studies, the results of the subgroup and regression analyses should be interpreted with caution. However, the extensive subgroup analysis is a valuable addition to earlier reviews and meta-analyses.

In order to make the studies more comparable and increase the level of knowledge about improving sleep in nursing-home residents with dementia, it is important to set up a standard protocol for researchers to apply the same intervention and measuring instruments. Based on this review and meta-analysis and past research, we recommend the use of both actigraphy (especially nonparametric variables like RA, IS, and IV [81]) and standardized observation scales to measure sleep disturbances in dementia (e.g., NPI-K or Behave-AD subscales: activity and diurnal rhythm disturbances [82]). More research using RCTs with sufficient methodological quality is needed to examine the effect of MSS and USS on the sleep quality and RAR in nursing-home residents with dementia with or without comorbid sleep disturbances, and to examine the differences between sensory stimulation interventions with or without light therapy. In this way, establishing implementation guidelines for nursing homes and analyzing the costs and benefits of different types of sensory stimulation interventions will become possible in the future.

Conclusion

The purpose of this study was to examine the effectiveness of MSS and USS on the RAR and sleep quality of nursing-home residents with dementia, while focusing on the different uni-sensory components. This is the first systematic review and meta-analysis which has investigated the high heterogeneity across studies with regard to interventions and patient characteristics. We found that sensory stimulations like bright light, massage, acupuncture, and animal-assisted interventions are effective for reducing nocturnal awakenings, SoL, and SDO, and improving nocturnal sleep duration and SE. Clinically relevant is the

possibility that longer sleep duration and continuation might be associated with less agitated and aggressive behaviour during the night. To strengthen the RAR, only bright-light therapy seemed effective. The effect of MSS on the rest-activity rhythm and sleep quality remained unclear. Despite its exploratory nature, this study offers valuable insights into the understanding and treatment of sleep disturbances in nursing-home residents with dementia and points out directions for future research.

Statement of Ethics

The review is registered with the International Prospective Register of Systematic Reviews (PROSPERO; registration No. 104104).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

A.J.P. made substantial contribution to the conception, design, acquisition, analysis and interpretation of data and drafted the entire manuscript. E.J.A.S., M.V.M and Y.Z. contributed to designing the study, interpreting the data and revising the manuscript for important intellectual content. A.S. contributed to the methods and data-analysis and was involved in revising the manuscript for important intellectual content. All authors read and approved the final manuscript.

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