Original Article

Pain in Dementia: Prevalence and Association With Neuropsychiatric Behaviors

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Abstract

Context. Pain is linked to behaviors and psychological symptoms of dementia (BPSD); however, it often remains underrecognized in this population.

Objectives. We aimed to investigate the prevalence and intensity of pain in people living in aged care homes with BPSD and by dementia subtypes and the association between pain intensity and BPSD.

Methods. A 1-year retrospective cross-sectional analysis was conducted on BPSD and the presence of pain in referrals to a national BPSD support service using the Neuropsychiatric Inventory and PainChek®, respectively. Referrals were categorized into two groups: *pain* group and *no pain* group.

Results. Of the 479 referrals (81.9 ± 8.3 years old) included in the analysis, two-thirds (65.6%) had pain identified, with almost half (48.4%) of these categorized as experiencing moderate-severe pain. Pain was highly prevalent (range: 54.6-78.6%) in all subtypes of dementia, particularly in mixed dementia and dementia with Lewy bodies. Compared with the *no pain* group, the *pain* group had 25.3% more neuropsychiatric behaviors, 33.6% higher total severity of these behaviors, and 31.4% higher total distress caused to caregivers. For all results, effect sizes were small to medium ($\eta^2p = 0.04$-0.06). Despite a high prevalence of aggressive or agitated behaviors across the entire group, the *pain* group was 3.8 times more likely to experience these behaviors than referrals not in pain.

Conclusion. There is a strong need to consider the possibility of pain as a contributor to behavioral changes in aged care residents living with dementia. J Pain Symptom Manage 2021;61:1215–1226.

Key Words

Dementia subtypes, pain, BPSD, neuropsychiatric behaviors, prevalence, association

Key Message

This retrospective cross-sectional study determines the prevalence and intensity of pain in various subtypes of dementia and examines the association of pain with neuropsychiatric behaviors. The results indicate that pain is very common in all dementia subtypes and strongly linked to agitation, aggression, and depression in this population.

Introduction

With increasing age, people are more likely to experience painful comorbidities such as osteoarthritis,[1] cancer,[2] and hip fractures[3] or to have pain secondary to altered biomedical function or neuropathy.[4] For people living with dementia (PLWD) in residential aged care homes (RACHs), the rates of experiencing pain are high, with estimates that 40–80% may

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experience chronic or acute pain at some time, yet little is known about the prevalence and intensity of pain in the different dementia subtypes.[5–8] A recent review on pain prevalence found that only few studies focused on major dementia subtypes (Alzheimer's disease [AD], vascular dementia [VaD], mixed dementia [MD], dementia with Lewy bodies [DLB]); no studies reported on frontotemporal dementia (FTD); and only one study used a valid, dementia-specific pain scale.[8]

A primary explanation of a high prevalence of pain is that those with more severe symptoms of dementia, including impaired verbal communication, have limited ability to report pain to carers and healthcare professionals. As such, pain instruments that rely on verbal communication become poor indicators of the presence, severity, and complex experience of pain.[9–11] Instead, pain instruments for this population rely on observers to evaluate pain experience, making pain assessment even more challenging.[12] Difficulty in identifying pain is associated with a corresponding high risk of under, over, or inappropriate treatment of pain.[9] Poorly treated pain is not only distressing for the person but can also impair social interactions, quality of life, appetite, and sleep[13–15] and is known to be implicated in behaviors and psychological symptoms of dementia (BPSD).[16]

BPSD are a near-universal experience for PLWD, with prevalence rates estimated to exceed 95%.[17–19] BPSD can present as a wide array of symptoms with varying degrees of functional interference and can include aggression, apathy, and depression. BPSD are frequently disruptive and distressing and may cause significant reductions in mood and quality of life for the person, their caregivers, and those around them.[20] The presence of BPSD may lead to early institutionalization, increased hospitalization, and the inappropriate use of antipsychotics with associated adverse effects including falls and death.[21,22]

There is often clinical uncertainty as to whether BPSD are directly attributable to altered neurotransmitter function, neurodegenerative changes, or to other factors such as the presence of pain, mood dysfunction, or unmet needs.[23] A multidisciplinary approach with a focus on nonpharmacological strategies and recommendations is considered the gold standard for treatment in most cases of BPSD.[23,24] In Australia, nationally funded bodies provide additional specialist BPSD support, especially in complex and severe instances where standard therapeutic strategies have proved unsuccessful.

Several studies have investigated the important association between pain and BPSD in community[10] and RACH settings[8,25–27]; however, limited research is available concerning pain in people with more severe forms of BPSD, that is, those who require specialist behavior support, using valid instruments.[27] Thus, this study aims to examine the prevalence and intensity of pain in PLWD subtypes using a technology-driven pain assessment tool and to clarify whether pain is associated with specific types of BPSD in people requiring such support services.

Methods

Ethics

Ethical approval from the University of New South Wales (UNSW) Human Research Ethics Committee (HC190049) was granted for this study. In accordance with the Declaration of Helsinki, all data were deidentified to protect confidentiality. A waiver of consent was approved as it was unfeasible to obtain consent from people supported by the service or their guardians retrospectively.

Study Design, Setting, and Population

A 1-year retrospective, observational, cross-sectional study used data collected as part of standard service delivery of Dementia Support Australia (DSA). DSA is an Australian federally funded national service that provides person-centered recommendations and support for people with BPSD.[28] Any person living in Australia with dementia and experiencing BPSD can access the support of DSA services free of charge, irrespective of age, sex, type of dementia, location, or care setting. In this 1-year period, up to 8000 referrals were supported by the service. We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement Checklist as a guide in reporting our study.[29]

Sample Size

Based on 50% assumed prevalence and 5% precision (i.e., estimate ± 2.5%) with a significance level (α) of 0.05 and a power (β) of 0.95, a sample size of 384 is required. No correction is necessary for attrition because no follow-up is required for prevalence studies.

Inclusion Criteria

People were included in the study if they had been/were 1) referred to DSA (i.e., individuals with an established, documented, or confirmed clinical diagnosis of dementia experiencing BPSD) during the study period; 2) no longer able to communicate the presence or intensity of pain in a valid and/or reliable manner (a clinical feature of advanced dementia)[30,31] that necessitate the use of observer-rated pain instrument (as judged by DSA consultants or nursing staff); 3) underwent both behavior and pain assessments using the Neuropsychiatric Inventory (NPI) and

PainChek (PainChek Adult, iOS version; PainChek Ltd., Sydney, Australia), respectively; and 4) resided in RACHs. As the characteristics of PLWD before the implementation of any behavior support were of interest, only assessments corresponding to their first point of contact with the service (i.e., intake), before any interventions or strategies were provided, are reported.

Data Source

As part of the standard provision of the DSA service, an extensive range of health, medical, and demographic data is collected by trained consultants via phone or during visits into RACHs. All data are securely stored online in a dedicated database using customer relationship management software. This database is designed to assist in the delivery of the DSA service and to facilitate the measurement of the outcomes and characteristics of those supported by the service.

Data Extraction

This study extracted and analyzed computerized records from the database for people supported by the service in the one-year period November 1, 2017, to October 31, 2018. All data were extracted and deidentified independently by a data custodian before being provided to the researchers involved in the present study. Only data explicitly mentioned in the "Methods" section were provided to the researchers. These included demographic data (e.g., age), dementia subtype (e.g., AD), location, primary language, and country of birth. Data on pain and neuropsychiatric behaviors from the validated assessment tools were also extracted.

Study Measures (Instruments)

Neuropsychiatric Behaviors. Two versions of the informant-based reliable and valid NPI are routinely administered by the service to characterize BPSD; the short version NPI-Q[32] and the nursing home version NPI-NH.[33] Both versions identify the presence (Yes/No) of 12 neuropsychiatric symptoms observed in PLWD, including aberrant motor behavior, aggression/agitation, anxiety, apathy, appetite and eating behavior, delusions, depression, disinhibition, euphoria, hallucinations, irritability, and night time behaviors. Both versions produce several equivalent indices of overall behavior, including the total number of behaviors (0-12), the total severity of these behaviors (0-48), and the total distress these behaviors cause caregivers (0-60).

In this study, more severe forms of BPSD are defined as BPSD that are sufficiently severe, complex, or difficult to manage by RACH staff to the degree that they required dementia-specific behavior support from outside the aged care home where the resident resides.[34]

Pain. Pain was measured with a psychometrically sound, artificial intelligence (AI)-based pain assessment tool, PainChek.[35] PainChek is a multimodal pain assessment medical device in the form of a point-of-care app for nonverbal adults including PLWD. The app identifies and quantifies pain through 42 items distributed across six domains including Face, Voice, Movement, Behavior, Activity, and Body. For the Face domain, PainChek uses deep learning methods (i.e., automated facial recognition and analysis) to detect facial microexpressions indicative of the presence of pain. The remaining domains are digital checklists manually completed by the user. Each item is provided with a clear operational definition to improve interrater consistency and rated on a binary level (Yes = present, No = absent). A total score across all domains between 0 and 6 represents no pain, 7 to 11 mild pain, 12 to 15 moderate pain, and 16 and above severe pain.[36] Among other factors, the tool was conceptualized around the International Association for the Study of Pain definition of pain, "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".[36,37] While pain assessments are administered as part of routine clinical practice of the DSA service, PainChek is a new tool recently added (September 2017) to the service, and hence, administered as part of a pilot trial for a portion of referrals over the studied period.

Statistical Analyses

Descriptive statistics (e.g., mean, standard deviation, frequency, percentage) were used to describe the sample demographics and assessment characteristics. For the purpose of analysis, we characterized the sample by pain status. Specifically, we categorized the referred individuals into two different groups according to the presence of pain, as identified by PainChek. These groups are

I. *Pain* group: included referrals with identified pain (PainChek score $\geq$ 7; range: 7-42)
II. *No pain* group: included referrals with no identified pain (PainChek score $\leq$ 6; range 0-6)

An independent ANOVA was completed to compare the two aforementioned groups on age, and χ^2 to compare groups on sex, dementia subtype, PainChek pain category and the presence of painful conditions/injuries acccording to PainChek items 41 and 42. The groups were subsequently compared on key outcome measures of the behavior and pain assessments.

Differences in the proportion of dementia subtype by PainChek pain categories were assessed with χ^2.

Group differences on the continuous measures of total pain score (PainChek), total number of behaviors (NPI), total severity of behaviors (NPI), and total

distress caused to caregivers (NPI) were examined with individual linear regression models controlling for the effects of age and sex.

The proportion of people with *pain* or *no pain* experiencing each of the 12 behaviors was examined with a series of independent binary logistic regressions either not controlling (unadjusted) or controlling (adjusted) for the effects of age and sex.

Post-hoc comparisons between categories of PainChek (i.e., no pain, mild pain, moderate pain, and severe pain) and total average number of behaviors, total severity of behaviors, and total distress caused were assessed with a series of independent analyses of covariance (ANCOVA) controlling for the individual effects of age and sex. Type 1 error for these comparisons was controlled through the Bonferroni-Holm adjustment.[38]

Precise *P* values were reported in the "Results", with $P < 5 \times 10^{-2}$ deemed as statistically significant. Partial eta squared (η^2p) and odds ratios were used to demonstrate measures of effect size. η^2p Values were interpreted as follows: 0.02 = small, 0.06 = medium, and 0.14 = large.[39]

All analyses were completed with the statistical package JAMOVI (version 1.0; Sydney, Australia).[40]

Results

Sample

A total of 479 people (age: 81.9 ± 8.3 years, 55.5% female) were referred to the service from 370 RACHs, who met the criteria for inclusion in the study. The study sample included a wide range of dementia subtypes, with AD being the most common type (40.9%), while the least frequent type was alcohol-related dementia (0.6%). The sample was primarily drawn from New South Wales, Victoria, and Western Australia. Other demographic characteristics are described in Table 1.

Table 1
Sample Demographics

Characteristics	$n = 479$
Age, y	
Mean (SD)	81.9 (8.3)
Median (IQR)	83.0 (77.0–88.0)
Sex, n (%)	
Female	266 (55.5)
Male	213 (44.5)
Dementia type, n (%)	
AD	196 (40.9)
DUN	159 (33.2)
VaD	61 (12.7)
MD	28 (5.9)
DLB	14 (2.9)
FTD	11 (2.3)
PDD	7 (1.5)
ARD	3 (0.6)
Location, n (%)	
New South Wales	178 (37.2)
Victoria	96 (20.1)
Western Australia	95 (19.8)
South Australia	45 (9.4)
Queensland	38 (7.9)
Tasmania	13 (2.7)
Australian Capital Territory	10 (2.1)
Northern Territory	4 (0.8)
Primary language spoken at home, n (%)	
English	392 (81.8)
Italian	28 (5.9)
Other	48 (10.0)
Unknown/missing	11 (2.3)
Country of birth, n (%)	
Australia	277 (57.8)
England	42 (8.8)
Italy	39 (8.1)
Other	113 (23.6)
Unknown/missing	8 (1.7)

IQR = interquartile range; AD = Alzheimer's disease; DUN = dementia unspecified or unknown; VaD = vascular dementia; MD = mixed dementia; DLB = dementia with Lewy bodies; FTD = frontotemporal dementia; PDD = Parkinson's disease dementia; ARD = alcohol-related dementia.

Prevalence and Intensity of Pain in Overall Sample

A total of 314 (65.6%) participants had pain (*pain* group), and 165 (34.4%) met the criteria of having no pain (*no pain* group) as identified by PainChek. In the *pain* group, 28.0% and 20.4% of the referred cases were scored on the PainChek as either being in moderate or severe pain, respectively. Between-group analyses revealed no statistical differences in demographics (e.g., age, sex), but differences in pain characteristics (e.g., painful injuries and conditions) were significant. Characteristics of *pain* and *no pain* groups are presented in Table 2.

Prevalence and Intensity of Pain in Dementia Subtypes

Among the referrals, people with MD and those with DLB (78.6% each) shared the highest prevalence of pain, followed by AD (64.3%) > VaD (62.3%) > FTD (54.6%). The prevalence of moderate-severe pain across dementia subtypes was in the range of 18.2%–35.8%. In terms of severe pain, dementia subtypes were ranked as follows: MD (17.9%) > AD (12.3%) > VaD (11.5%) > FTD (9.1%) > DLB (7.1%). Chi square analysis found no significant difference ($P = 0.467$) in pain prevalence between dementia subtypes. Table 3 provides the frequency of pain categories for each dementia subtype.

Association of Neuropsychiatric Behaviors With Pain

Controlling for the effects of age and sex, people in the *pain* group demonstrated significant group differences to those in the *no pain* group across all total measures of NPI behaviors. The *pain* group had 25.3% more behaviors, 33.6% greater total severity, and 31.4% greater total distress caused to caregivers. For all results, effect sizes were small to medium (η^2p of 0.06, 0.06, and 0.04). See Table 4 for full results.

Table 2
Characteristics of *Pain* and *No Pain* Groups

Characteristic	*Pain* Group, $n = 314$	*No Pain* Group, $n = 165$	*P* value
Age, y			6.2×10^{-1}
Mean (SD)	82.1 (8.3)	81.7 (8.2)	
Median (IQR)	83.0 (78.0–88.0)	82.0 (77.0–88.0)	
Sex, n (%)			1.54×10^{-1}
Female	167 (53.2)	99 (60.0)	
Male	147 (46.8)	66 (40.0)	
Dementia type, n (%)			3.9×10^{-1}
AD	126 (40.1)	70 (42.4)	
DUN	105 (33.4)	54 (32.7)	
VaD	38 (12.1)	23 (13.9)	
MD	22 (7.0)	6 (3.6)	
DLB	11 (3.5)	3 (1.8)	
FTD	6 (1.9)	5 (3.0)	
PDD	3 (1.0)	0 (0.0)	
ARD	3 (1.0)	4 (2.4)	
PainChek scores, M (SD), [median, IQR]			
Total score	12.41 (4.6), [11.00, 9.0-14.8]	3.8 (1.8), [4.00, 3.0-5.0]	**$<1.0 \times 10^{-16}$**
No pain	—	3.8 (1.8), [4.00]	
Mild pain	9.1 (1.4), [9.00]	—	
Moderate pain	13.2 (1.1), [13.00]	—	
Severe pain	19.7 (3.9), [16.00]	—	
PainChek category[a], n (%)			**$<1.0 \times 10^{-16}$**
No pain	0 (0.0)	165 (100)	
Mild pain	162 (51.6)	0 (0.0)	
Moderate pain	88 (28.0)	0 (0.0)	
Severe pain	64 (20.4)	0 (0.0)	
Selective PainChek items, n (%)			
Item#41: Painful injuries[b]	155 (49.4)	24 (14.5)	**7.2×10^{-14}**
Item#42: Painful medical conditions[c]	259 (82.5)	100 (60.6)	**1.5×10^{-7}**

IQR = interquartile range; AD = Alzheimer's disease; DUN = dementia unspecified or unknown; VaD = vascular dementia; MD = mixed dementia; DLB = dementia with Lewy bodies; FTD = frontotemporal dementia; PDD = Parkinson's disease dementia; ARD = alcohol-related dementia.
P values in bold font are statistically significant.
[a]PainChek category (range): no pain (0-6), mild pain (7-11), moderate pain (12-15), severe pain (16-42).
[b]Painful injuries: Injuries are known to induce pain for example falls, bed sores, active wounds.[72]
[c]Painful medical conditions: Conditions known to cause pain including currently presented for example dental infections, urinary tract infections, or previously documented chronic conditions in medical history for example arthritis.[72]

Table 5 details the association between the frequency for each NPI behavior with the presence of pain. The frequency of all NPI behaviors was greater for the *pain* group than the *no pain* group, regardless of model adjustment. Significance was observed in 6 or 7 NPI behaviors, in the unadjusted or adjusted model, respectively. Aberrant motor behavior was only shown to reach significance in the adjusted model. Aggression/agitation was the most frequently represented behavior (94.0%) for those in pain and was 3.8 times as frequent compared to those in the *no pain* group. Other behaviors with a significantly

Table 3
Prevalence of Pain and Pain Intensity Categories by Dementia Subtype

	a	b	c	d	c + d	b + c + d
Dementia Subtype	No Pain, n (%)	Mild Pain, n (%)	Moderate Pain, n (%)	Severe Pain, n (%)	Moderate-Severe Pain, n (%)	Total in Pain, n (%)
AD, $n = 196$	70 (35.7)	72 (36.7)	30 (15.3)	24 (12.3)	54 (27.6)	126 (64.3)
DUN, $n = 159$	54 (34.0)	45 (28.3)	35 (22.0)	25 (15.7)	60 (29.5)	105 (66.0)
VaD, $n = 61$	23 (37.7)	20 (32.8)	11 (18.0)	7 (11.5)	18 (29.5)	38 (62.3)
MD, $n = 28$	6 (21.4)	12 (42.9)	5 (17.9)	5 (17.9)	10 (35.8)	22 (78.6)
DLB, $n = 14$	3 (21.4)	6 (42.9)	4 (28.6)	1 (7.1)	5 (35.7)	11 (78.6)
FTD, $n = 11$	5 (45.4)	4 (36.4)	1 (9.1)	1 (9.1)	2 (18.2)	6 (54.6)
Other, $n = 10$	4 (40.0)	3 (30.0)	2 (20.0)	1 (10.0)	3 (30.0)	6 (60.0)

n = number of cases or episodes; % = frequency percentage; AD = Alzheimer's disease; DUN = dementia unspecified or unknown; VaD = vascular dementia; MD = mixed dementia; DLB = dementia with Lewy bodies; FTD = frontotemporal dementia.
Other includes Parkinson's disease dementia and alcohol-related dementia. $P = 4.7 \times 10^{-1}$ for differences among dementia subtypes.

Table 4
Group Differences on NPI Indices

	a	b	c				
NPI Measure	Pain Group, M (SD)	No Pain Group, M (SD)	% Increase	Estimate	SE	η^2p	*P* value
Total number of behaviors	5.5 (2.2)	4.4 (2.0)	25.3%	1.16	0.20	0.06	$\mathbf{2.4 \times 10^{-8}}$
Total severity of behaviors	12.0 (6.2)	9.0 (5.4)	33.6%	3.12	0.57	0.06	$\mathbf{7.3 \times 10^{-8}}$
Total distress by behaviors	15.9 (9.5)	12.1 (7.5)	31.4%	3.92	0.85	0.04	$\mathbf{5.0 \times 10^{-6}}$

M (SD) = mean (standard deviation).

$\%\ increase\ (c) = \frac{(a-b)}{a} x\ 100.$
P values in bold font are statistically significant.

increased frequency were aberrant motor behavior (52.0%), apathy (40.0%), appetite and eating (30.0%), irritability (70.0%), depression (60.0%), and hallucinations (22.0%). The prevalence of each of the 12 domains of behavior across each group is displayed in Figure 1.

Figure 2 describes post-hoc independent ANCOVAs, controlling for age and sex and multiple comparisons, between levels of pain experienced as measured by PainChek (i.e., no pain, mild pain, moderate pain, severe pain) and NPI measures of BPSD. These analyses revealed evidence of an exposure response between pain categories and BPSD frequency, severity, and distress. Specifically, people mostly experienced a greater number of BPSD, that were more severe and more distressing, with increasing pain levels. Significant differences were found for all comparisons except no pain and mild pain on the distress scale of the NPI and between moderate and severe pain for all NPI indices.

Discussion

We conducted a national retrospective cross-sectional study of aged care residents with dementia who were referred to a specialized behavior support service. This is the first study where an AI-powered pain assessment instrument was used to estimate the prevalence and intensity of pain in those with dementia (subtypes) who are experiencing BPSD. We also examined the prevalence of behaviors and their associations with pain in a cohort with sufficiently severe BPSD that a referral to an external specialist behavior support service was warranted.

In this study, nearly two-third of residents referred were identified as having pain as measured by PainChek, and of these, almost half were assessed as being in moderate-severe pain. These results showed similar or higher rates than those found in hospital, community, and residential settings.[5,9,16,41–44]

Although a high prevalence (54.6-78.6%) of pain was found across all dementia subtypes, there were no significant differences among those subtypes. This finding is consistent with the literature.[8,45] AD and VaD had a somewhat similar prevalence of pain (64.3% vs. 62.3%, respectively) and pain intensity (Table 3), perhaps because both have a partially similar pain-processing pathway that involves white matter lesions.[46,47] These lesions contribute to increased deafferentation and experience of (motivational-affective) pain.[46,48,49] This may also explain

Table 5
Associations Between Presence of Pain and Neuropsychiatric Behaviors

	Unadjusted				Adjusted[a]			
NPI Behaviors	Estimate	SE	OR	*P* value	Estimate	SE	OR	*P* value
Aberrant motor behavior	0.36	0.19	1.43	6.5×10^{-2}	0.40	0.20	1.49	$\mathbf{4.1 \times 10^{-2}}$
Aggression/agitation	1.34	0.30	3.82	$\mathbf{8.5 \times 10^{-6}}$	1.33	0.30	3.79	$\mathbf{1.0 \times 10^{-5}}$
Anxiety	0.26	0.20	1.30	1.8×10^{-1}	0.33	0.20	1.39	9.9×10^{-2}
Apathy	0.59	0.21	1.81	$\mathbf{4.8 \times 10^{-3}}$	0.61	0.21	1.84	$\mathbf{3.8 \times 10^{-3}}$
Appetite/Eating	0.60	0.23	1.81	$\mathbf{1.2 \times 10^{-2}}$	0.68	0.24	1.97	$\mathbf{4.6 \times 10^{-3}}$
Delusions	0.14	0.21	1.15	5.1×10^{-1}	0.15	0.21	1.16	5.0×10^{-1}
Depression	0.49	0.19	1.63	$\mathbf{1.2 \times 10^{-2}}$	0.50	0.20	1.64	$\mathbf{1.1 \times 10^{-2}}$
Disinhibition	0.30	0.20	1.34	1.5×10^{-1}	0.30	0.20	1.34	1.5×10^{-1}
Euphoria	0.54	0.52	1.72	3.0×10^{-1}	0.59	0.52	1.81	2.6×10^{-1}
Hallucinations	0.53	0.26	1.71	$\mathbf{4.2 \times 10^{-2}}$	0.56	0.27	1.75	$\mathbf{3.5 \times 10^{-2}}$
Irritability	0.79	0.20	2.20	$\mathbf{7.0 \times 10^{-5}}$	0.80	0.20	2.24	$\mathbf{5.8 \times 10^{-5}}$
Night-time behaviors	0.32	0.20	1.38	9.9×10^{-2}	0.32	0.20	1.38	9.9×10^{-2}

NPI = Neuropsychiatric Inventory; OR = odds ratio.
P values in bold font are statistically significant.
[a]Regression model adjusted for age and sex.

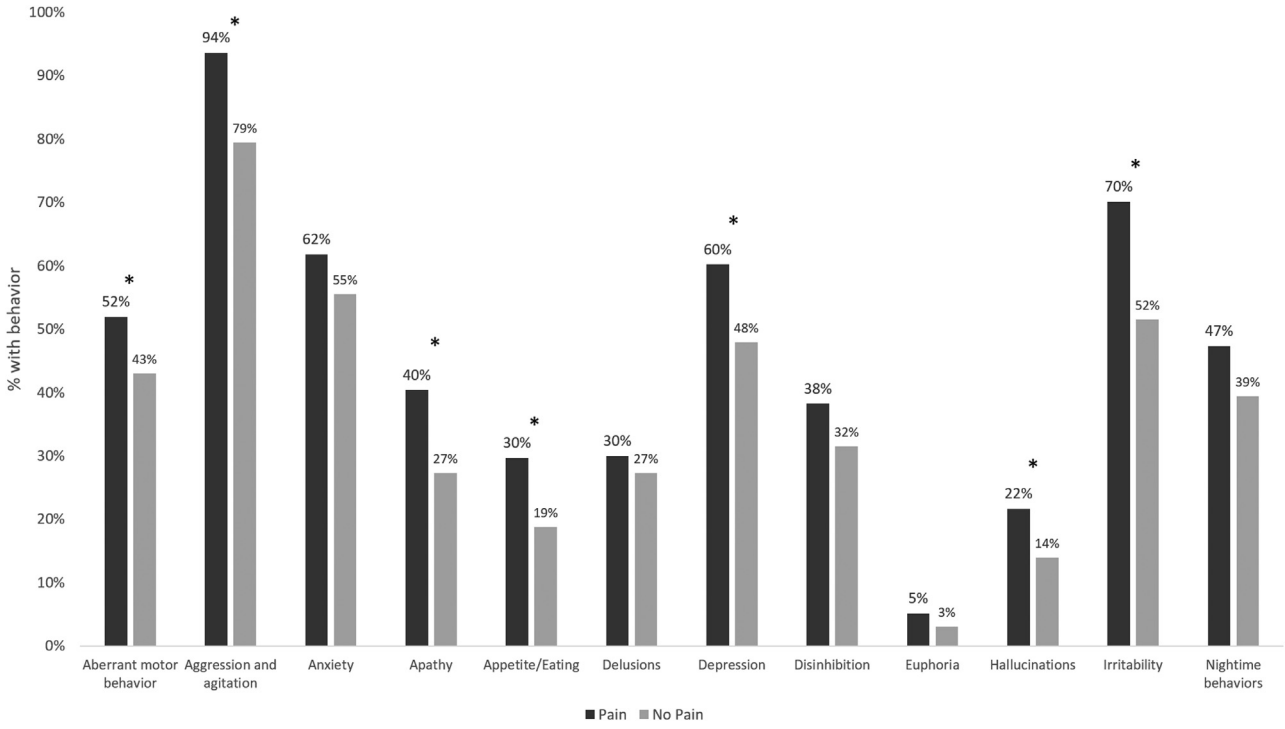

Fig. 1. Proportion (%) of people endorsing each of the 12 behavior domains of the Neuropsychiatric Inventory separated by group based on the adjusted model. Please note all percentage values were rounded to the closest row number. *Statistically significant.

the highest prevalence and intensity of pain in MD (AD + VaD) in our sample. In contrast, a significant portion (81.8%) of people with FTD recorded "no pain" (45.4%) and "mild pain" (36.4%). This is possibly because of atrophy in the prefrontal cortex, a characteristic of FTD that results in reduced (motivational–affective) pain experience.[47,49,50] This brain pathology also occurs in AD but to a much lesser extent than FTD.[47,49] Compared with previous studies,[5,45,51] we found slightly higher proportions of pain in our dementia subtypes sample, perhaps because our sample is characterized by the presence of an advanced form of dementia with significant BPSD. Other reasons include methodological variations, such as demographic characteristics, sample size, study design, setting, definition of pain, and pain assessment methods or instruments used.

Our results (Figure 2) indicate that there is a somewhat positive linear relationship between the level of pain experienced and the occurrence of BPSD. That is, the higher the pain intensity, the greater the number and severity of specific BPSD and the associated distress experienced by the carer. Despite evidence of a higher overall prevalence of behaviors, the types of behaviors exhibited by people in pain in this study are similar to profiles of behavior previously identified.[27,52] Notably,

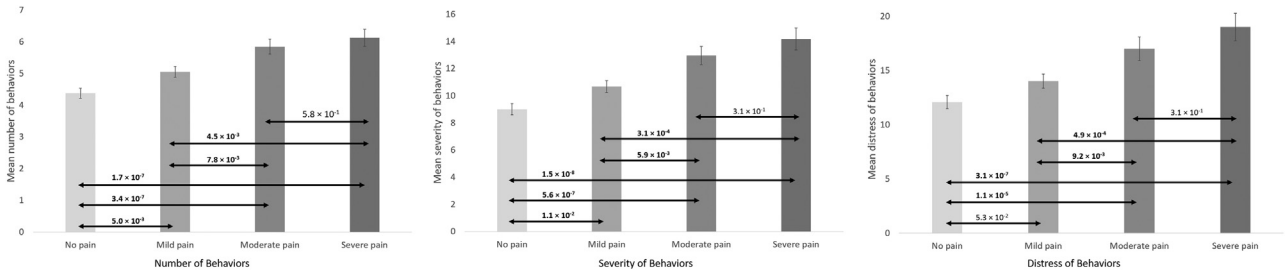

Fig. 2. Mean differences between pain assessment categories on Neuropsychiatric Inventory indices. All significance levels controlled for number of comparisons by the Holm-Bonferroni adjustment. *P* values in bold font are statistically significant.

present study groups differed most substantially on a measure of aggression/agitation, and while not always demonstrated,[53] this pattern is consistent with many studies.[52,54–56] Compared with previous literature,[27] we recorded a stronger association between pain and aggression/agitation, perhaps because of our sample characteristics and pain evaluation method. In addition, the relationship between pain and depressive symptomatology is well documented in older people without dementia.[57,58] Congruent with other studies,[22,52,59] our study suggests this relationship is maintained in those with dementia who require specialist BPSD support. Similar associations between pain and depression in PLWD are reported in the literature.[60–62] Evidence suggest that pain is associated with mood syndromes in PLWD,[14,56,63] including other behaviors such as apathy and changes to appetite, and is consistent with our study.

Our findings are not surprising given that pain is viewed as a conditioned response to perceived noxious stimuli (i.e., tissue threat), which can induce protective (avoidance) behaviors (e.g., aggression and irritability).[64] Thus, pain acts as a warning, generating nonverbal response(s) to raise attention. This appears to be a common presentation in PLWD.[16,45]

Our study design limits the interpretability of the causal nature of pain and behavior. While pain is commonly described as an antecedent of behavioral changes, it is possible that behavioral changes and pain share a common etiology. For instance, the involvement of the prefrontal cortex in many dementia subtypes is known to lead to disinhibition and a range of other behaviors.[65] However, this region is also independently implicated in the cognitive-affective pain and descending pain pathways, contributing to altered pain perceptions and experience.[66,67] This is supported by indirect evidence from studies finding a reduction in agitation for PLWD after administration of regular analgesics.[68–70]

Strengths and Limitations

To date, this is the largest study to present pain prevalence and intensity data in major dementia subtypes in the RACH setting. A strength of this study is that the DSA service used the PainChek device, a dementia-specific multidomain pain assessment tool (with strong psychometrics) that combines various technologies such as AI and smart automation.[36,71,72] Although there is an overlap between pain behaviors and BPSD, the device is unique in that it has a pain scale that includes items with clear operational definitions circumventing any ambiguity associated with interpretation during assessments.[72] Despite that, we cannot rule out completely that some neuropsychiatric symptoms (e.g., agitation) were misinterpreted as pain behaviors. Notwithstanding this, PainChek items relating to painful injuries, painful conditions, and functional/activity impairments may have helped improved pain identification.[36,73,74] If these behaviors are responsive to pain-relieving strategies/interventions (e.g., analgesics), then the trigger is likely to be pain. This approach can only be accurately evaluated in well-designed, tightly controlled studies, which is beyond the scope of this research. Unlike other observational pain scales, PainChek assigns pain intensity categories (no pain, mild pain, moderate pain, and severe pain) into a final score based on validated cutoff scores.[35,71] Given the subjective nature of pain, we acknowledge that the relationship between pain behaviors and intensity of pain is not fully understood. However, there is evidence that the number of pain behaviors observed is positively correlated with pain intensity.[75–77] Observational pain scales with robust conceptualization, multiple behavioral domains, pain-relevant items, assigned pain categories, and available cutoff scores can improve pain recognition/rating and hence the clinical utility in nonverbal PLWD.[75,76,78–81]

Our sample included residents with advanced dementia from multiple RACHs, which enhanced the homogeneity and external validity of the study. The power of the study substantially exceeded the sample size requirements, and the sample covered a wide range of dementia subtypes with reasonable proportions for the major types (AD, VaD, MD). Despite the small number of DLB and FTD cases, we did not exclude them from our sample. This is because both subtypes are epidemiologically underrepresented,[8] and hence, the need for reporting is of paramount importance in understanding the prevalence of clinical pain among these dementia subtypes. However, caution is still needed when interpreting these results. Notwithstanding this, we used various statistical methods to meet the study objectives. Other dementias were not discussed here either because of unclear etiology or the limited number in the sample.

This study is not without limitations. Ethnicity profiles of referrals were missing from the data, and therefore, the applicability of the results to the wider population may be limited. The accuracy of documentation cannot be guaranteed in retrospective studies because it largely depends on the availability of data and skills of the person involved. This is mitigated at least in part by all primary data represented in the study being collected by consultants trained in the administration of the instruments used. Medication use (e.g., analgesics) and specific comorbid pain conditions were not considered in the analysis which

could have some confounding effects on the results. Finally, we acknowledge the challenges of observational pain assessments in PLWD, such as the difficulty of differentiating pain from distress.[82] Yet, this was possibly minimized in our study by the familiarity of consultants with residents' behaviors and the use of a robust, systemized, and structured pain assessment, which was validated in RACHs.[35,36,71,83] This assessment puts less emphasis on changes in physiological indicators (e.g., temperature) because these can be influenced by confounders (e.g., medications) and may be blunt and less useful in mild-moderate or chronic pain, particularly in those with AD.[36,84–87]

Clinical Implications

The clinical implications of this study include 1) changes to behaviors in terms of their type, number, severity, and distress may prove useful in initiating formal pain assessment processes and subsequent treatment, and 2) as the source of referrals in this study was from RACHs across Australia, our findings raise the question of whether this population is receiving adequate pain control.

Conclusion

Pain is highly prevalent in residents with advanced dementia receiving support for BPSD, irrespective of the dementia subtype. Pain is also strongly linked to specific neuropsychiatric behaviors, such as agitation and aggression. Despite the noted limitations, the present study highlights the importance of the need to consider the possibility of pain as a contributor to behavioral change in PLWD. It raises the need to incorporate pain assessment and management as part of standardized behavioral assessment and treatment protocols. This would facilitate a more person-centric approach and improved clinical outcomes for PLWD who experience pain.

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Disclosures: M. A. is one of the originators of the PainChek instrument, which is marketed by PainChek Ltd. (ASX: PCK). He is also a shareholder of PainChek Ltd. He previously held the position of a Senior Research Scientist (October 2018-May 2020) at PainChek Ltd. and is currently serving the position of Research and Practice Lead at The Dementia Center. He had a granted patent titled "A pain assessment method and system; PCT/AU2015/000501" in Australia, China, Japan, and the U.S, which was assigned to PainChek Ltd. M. A. is also a PhD Candidate at School of Pharmacy and Biomedical Sciences, Curtin Univeristy. C. C. is the Director of The Dementia Center. The remaining authors have no further conflicts of interests related to the present article to disclose.

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