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SHORT REPORT

Multisite pain, pain frequency and pain severity are associated with depression in older adults: results from the ActiFE Ulm study

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Abstract

Background: there is ample literature showing pain and depression are related. However, different dimensions of pain have been used in former studies.
Objective: the objective of the study was to compare the strength of the association of different pain dimensions with depression in older adults.
Methods: assessments including evaluation of pain (severity, frequency, chronicity, quality, pain medication, painful body sites) and depression (measured by the Hospital Anxiety and Depression Scale) were performed in an observational study in community dwelling older adults (sample mean age 76, $n = 1130$) in Germany. The associations of different dimension of pain with depression were assessed using descriptive and multivariate methods.
Results: the number of painful body areas was most significantly associated with self-reported late life depression (OR 1.20, CI 1.11–1.31). Pain severity and frequency (OR 1.12, CI 1.01–1.23 and OR 1.18, CI 1.01–1.37) were also associated with depression; quality and duration were not. Except for severity (OR 1.12, CI 1.02–1.24) associations of pain dimensions were strongly reduced when controlling for relevant confounders and gender was an effect modifier.
Conclusions: multisite pain, pain severity and frequency were the best predictors of late life depression. Clinicians should be especially aware of depressive disorders when older patients are complaining of pain in multiple areas across the body.

Keywords: *chronic pain, depression, community dwelling, older adults*

Introduction

In 2006 Pepersack *et al.* postulated that Geriatricians failed to recognise more than half of the depressed patients who were later diagnosed by a psychogeriatrician [1]. In general, the association of pain and depression is still highly suspected by clinicians although it has been questioned recently. Strong correlations have mostly been found in women, less so in men [2] while in a recent longitudinal study stronger correlations have been found in men than in women [3]. In 1988, Rudy *et al.* have challenged the direct relationship and have argued that reduced perceptions of control and personal

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mastery were necessary for the development of depressive symptoms in pain patients [4]. This behavioural model has been confirmed in a group of elderly subjects as opposed to younger subjects [5], although other authors have not been able to demonstrate any influence of age [6]. Pain in younger women seemed to be rather mediated by functional impairment, while for older women mastery was more important [7]. More recently, a lower degree of neuroticism was found to mediate the relationship between pain and depression [8]. However, mastery and other confounders might no longer alter the relationship after controlling for time-stable factors such as life experiences and others [9].

What is the reason for the diversity of the results? First, cohorts differed according to sex, age or clinical diagnoses. Second, not all models have been controlled for relevant confounders and third multiple qualities (mostly severity) of pain have often been used as 'the clinical pain symptom' [10]. However, current state of the art pain questionnaires not only evaluate pain severity but also ask for frequency, duration, chronicity, quality and the different body areas involved. We, therefore, examined the relationship of different dimensions of pain with depression in older adults.

Methods

The ActiFE Ulm (Activity and Function in the Elderly in Ulm) study is a population-based cohort study in older people aged 65 years and older, located in Ulm and adjacent regions in Southern Germany. A detailed description of the cohort is published elsewhere [11]. In total, 7,624 inhabitants were randomly contacted by mail and asked for participation. Exclusion criteria were severe deficits in cognition, vision or hearing that precluded the accomplishment of most assessments or serious German language difficulties. Between March 2009 and April 2010, 1,506 non-institutionalised eligible individuals agreed to participate and underwent the baseline assessments. All participants provided written informed consent. The study was approved by the ethical committee (No. 312/08).

Assessments

Affective state was assessed using the Hospital Anxiety and Depression Scale (HADS) [12]. Subscores were calculated and the D-HADS (Depression subscore) was used. For logistic regression, a common cut-off score of eight and above was used to classify participants as depressed [13].

Pain was assessed using a structured questionnaire available in German language [14]. The questionnaire includes the following items: a list of 13 body areas including an open question on any missing area and questions on pain

- severity in the last 7 days at the most painful site (visual analogue or numerical rating scale from 0 to 10)
- chronicity (four-point scale: pain since days, weeks, months, years)
- frequency in the last 7 days (six-point scale: from never to always)
- quality (pain attacks/breakthrough pain, continuous pain, both)

For comorbidity, a total number of 21 chronic conditions were used. Prevalent conditions were added up without giving weights and a total count was used as confounder. The score is based on the functional comorbidity index published by Groll *et al.* [15].

Social network was measured using the 6-item Lubben social network scale [16], a brief instrument designed to evaluate the size, perceived support and perceived confidant social network, differentiating between friends and neighbours.

Other potential confounders considered were age, gender, body mass index, a 10-item activities of daily living score [11] (ADL) and cognition (Mini Mental State Exam, MMSE) [17].

Statistical analysis

Full data with regard to the main outcome and influencing parameters were obtained from 1,130 participants. For continuous variables, means and standard deviations were calculated. Because tests for normality (Kolmogorov–Smirnov, Q–Q plots) revealed no significant difference from the normal distribution and because the assumption of homogeneity of variance was met, parametric tests (*t*-tests) were performed. For categorical items, frequencies were obtained and a χ^2 test was performed.

To assess the strengths of the associations, multiple logistic regression analysis was used. Odds ratios, confidence intervals and *P*-values are reported. The area under the receiver operating characteristic (ROC) curve represents the goodness of the model fit [18]. Since no assumptions about differences in influence on the dependent variable can be made a priori and since our approach is of exploratory nature, all variables were included at once.

Because of the cross-sectional nature of the study disentangling mediation and confounding effects would rely mostly on conceptual theories. We, therefore, decided to address confounding issues before paying attention to potential mediation concerns [19]. Established criteria for confounding were used [20]. Potential confounders considered are reported above. Only comorbidity and social network satisfied all three conditions for confounding, apart from age and gender, and were included in the full model. Anxiety, although available and mentioned in former models as associated with pain and depression, was not considered a confounder because of its high correlation with depression ($r_p = 0.47$). All analyses were performed using SAS 9.2.

Results

In bivariate analyses (Table 1), individuals classified as depressed had significantly higher pain severity scores ($M = 4.8$, $SD = 2.27$ versus $M = 4.0$, $SD = 2.21$; $T = 4.36$; $P < 0.001$), more multisite pain ($M = 3.7$, $SD = 2.85$ versus

Table 1. Patient characteristics ($n = 1130$)

Parameter	Depression	
	NO ($n = 959$)	YES ($n = 171$)
Anthropometric characteristics		
Body mass index, mean (±SD)	27.84 (±4.13)	27.46 (±4.92)
Age, mean (±SD)	75.74 (±6.61)	75.83 (±6.74)
Male sex, *n* (%)	545 (56.8%)	67 (39.2%)
Physical health		
Comorbidity (disease counts)[a], mean (±SD)	5.75 (±3.18)	9.08 (±3.41)
Basic activities of daily living[b], *n* (%)		
Dependent in one or more ADLs	32 (3.34%)	13 (7.60%)
Instrumental activities of daily living[b], *n* (%)		
Dependent in one or more IADLs	126 (13.14%)	35 (20.47%)
Mental health		
Mini Mental Status, mean (±SD)	27.77 (±2.24)	27.50 (±2.42)
Depression (DHADS), mean (±SD)	3.72 (±2.71)	5.71 (±3.44)
Pain dimensions		
Pain severity, mean (±SD)	4.1 (±2.19)	4.9 (±2.26)
Multisite pain, mean (±SD)	3.25 (±2.01)	4.26 (±2.58)
Chronicity, *n* (%)		
Days	30 (3.1%)	3 (1.8%)
Weeks	63 (6.6%)	15 (8.8%)
Months	180 (18.8%)	30 (17.5%)
Years	686 (71.5%)	123 (71.9%)
Quality, *n* (%)		
Breakthrough pain	720 (75.1%)	121 (70.8%)
Continuous pain	101 (10.5%)	22 (12.9%)
Continuous and breakthrough pain	138 (14.4%)	28 (16.4%)
Frequency (last seven days), *n* (%)		
Never/rarely	335 (35.0%)	41 (23.9%)
Sometimes/often	442 (46.1%)	79 (46.2%)
Very often/always	182 (18.9%)	51 (29.8%)

Multisite pain was asked using a list of 14 body areas. Pain severity was rated on an 11-point scale, chronicity on a 4-point Likert scale and frequency on a 6-point Likert scale. The dimensions of pain quality are shown.
DHADS, depression subscale of the HADS; depression was defined as having eight or more points in the depression subscale of the Hospital Anxiety and Depression scale (HADS); SD, standard deviation.
[a]Extended functional comorbidity index (Groll *et al.* [15]).
[b]10-item assessment including IADL and ADL tasks, participants with considerable difficulties has 10 and more points in the total score.

$M = 2.6$, $SD = 2.23$; $T = 6.51$; $P < 0.001$) and higher pain frequency levels with 29.8% ($n = 51$) versus 18.9% ($n = 182$) reporting to 000 (χ^2_2; 95% = 13.515, $P = 0.001$).

In logistic regression controlled for age and sex (Table 2, model 1), multisite pain was most clearly associated with depression (OR 1.20, CI 1.11–1.31, $P < 0.001$). Pain severity (OR 1.12, CI 1.01–1.23, P = 0.027) and frequency (OR 1.18, CI 1.01–1.37, $P = 0.033$) were also still significantly associated.

Adding the two other relevant confounders' comorbidity and social network (both strongly associated with depression, $P < 0.001$) into a full model (Table 2, model 2) decreased the associations of multisite pain and pain frequency. Severity remained almost unchanged (OR 1.12, CI 1.02–1.24, $P = 0.028$).

When stratifying for gender, results for female sex changed slightly (small model: multisite pain: OR 1.18, CI 1.05–1.32, $P = 0.004$; pain severity: OR 1.16, CI 1.01–1.33, $P = 0.031$; full model: pain severity: OR 1.18, CI 1.02–1.36, $P = 0.025$), while results for male sex were substantially altered (small model: multisite pain: OR 1.23, CI 1.08–1.40, $P = 0.002$; frequency: OR 1.43, CI 1.15–1.78, $P = 0.002$; full model: frequency: OR 1.32, CI 1.06–1.64, $P = 0.013$). Severity was no longer significant in males with regard to both models (OR 1.08, CI 0.94–1.25—OR 1.09, CI 0.94–1.27, $P = 0.277$–0.281; data not shown in the tables).

Discussion

Multisite pain, pain frequency and severity were the best predictors of depression in a population of community dwelling older adults. When controlling for relevant confounders, however, pain severity was the only dimension that remained significantly associated in the whole cohort. When looking at gender as an effect modifier, these results could be confirmed in females, while in males pain frequency became more important.

Studies examining the relationship of pain and depression mostly use different definitions of overall chronic pain, often influenced by duration and severity [10]. In our population of community dwelling older adults, pain severity seemed less important than multisite pain when only controlling for age and sex. A similar finding has been reported recently in a paper with a slightly different focus from the MOBILIZE-Boston study [21]. In this report, multisite pain showed stronger associations with depression than pain severity. Unfortunately, this relationship was not further examined in multivariate analyses. Another study in patients with fibromyalgia demonstrated that multisite pain was a better predictor of clinical pain intensity than the number of tender points [22]. However, depression was not used as an outcome measure.

The reduction of the association of pain and depression after accounting for relevant confounders is not surprising. Confounding by comorbidity and social network has been reported before [6, 23]. In the initially mentioned article, the authors concluded that uncontrolled comorbidity (including pain) and therapeutics might have been misleading factors [1]. Notably, the reduction was most pronounced for multisite pain. Therefore, multisite pain could be the dimension that is mostly linked to other disease entities, while pain severity is the most stable 'independent' predictor of depression, at least in females. In males, pain frequency seems to take the place of pain severity, while multisite pain also takes the back seat. The influence of gender has been demonstrated before [24] and it has been shown to even moderate the association between depression and pain-related disability [25]. Our study adds the idea of using a differential approach in males and females with respect to different types of pain in older adults. Yet, recent literature suggests that the previously established link between depression and pain might not withstand controlling for time-stable factors [9], although, in this article, the author did not disentangle different pain dimensions.

While pain severity and frequency are of importance with regard to pathological pathways the identification of multisite

Table 2. Association of different dimensions of pain with depression ($n = 1130$)

Parameters	Depression			
	DF	β-estimate (SE)	OR (95% CI)	*P*-value
MODEL 1 (AUC 0.71)				
Pain				
Severity	1	0.11 (0.050)	1.12 (1.01–1.23)	0.034
Number of painful body areas	1	0.18 (0.043)	1.20 (1.11–1.31)	<0.001
Chronicity	1	0.00 (0.130)	1.00 (0.78–1.29)	0.972
Frequency	1	0.16 (0.079)	1.18 (1.01–1.37)	0.018
Quality				
continuous		reference		
Breakthrough	1	0.12 (0.156)	1.08 (0.64–1.80)	0.453
Both qualities	1	−0.16 (0.200)	0.81 (0.42–1.59)	0.419
Age	1	0.04 (0.014)	1.05 (1.02–1.08)	0.002
Male sex	1	0.05 (0.098)	1.05 (0.72–1.54)	0.748
MODEL 2 (AUC 0.76)				
Pain				
Severity	1	0.12 (0.052)	1.12 (1.02–1.24)	0.028
Number of painful body areas	1	0.09 (0.049)	1.10 (1.00–1.20)	0.074
Chronicity	1	−0.02 (0.136)	0.98 (0.75–1.27)	0.865
Frequency	1	0.13 (0.082)	1.13 (0.97–1.32)	0.073
Quality				
Continuous		reference		
Breakthrough	1	0.10 (0.160)	0.97 (0.57–1.65)	0.505
Both qualities	1	−0.24 (0.208)	0.68 (0.34–1.37)	0.235
Age	1	0.02 (0.015)	1.02 (0.99–1.05)	0.135
Male sex	1	0.06 (0.102)	1.14 (0.75–1.73)	0.678
Comorbidity	1	0.11 (0.032)	1.15 (1.07–1.22)	<0.001
Social network	1	−0.11 (0.019)	0.89 (0.86–0.93)	<0.001

Association of independent parameters with depression in a multiple logistic regression model. All parameters that were controlled for are shown. Model 1 is controlled for age and sex. Model 2 is controlled for age, sex, comorbidity and social network. Comorbidity was calculated using a 21-item disease score. Social network was asked using the Lubben 6-item scale [16]. Depression was defined as having eight or more points in the depression subscale of the Hospital Anxiety and Depression scale (DHADS) [12]. Multisite pain was asked using a list of 14 body areas. Pain severity was rated on an 11-point scale, chronicity on a 4-point Likert scale and frequency on a 6-point Likert scale. The dimensions of pain quality are shown.

β-estimate, regression coefficient; SE, standard error; OR, odds ratio; CI, confidence interval; DF, degrees of freedom; AUC, area under the receiver operating characteristic (ROC) curve.

pain seems important with respect to the diagnostic process. In additional analyses of the ActiFE study, multisite pain was even stronger associated with anxiety and this relationship persisted after controlling for the above-mentioned confounders (not shown). Therefore, if older adults report multisite pain, physicians or nurses should be especially aware of a relevant depressive disorder (and/or anxiety).

The study has limitations. Depression was diagnosed using the HADS and comorbidity was self-reported, both without external confirmation. Other confounders that have been proposed such as neuroticism or mastery could not be included because they were not available [8, 9]. However, both parameters have been shown to rather mediate the relationship and our primary objective was to identify the most useful dimension for clinical practice. Still, relevant parameters might be missing in the current analysis.

To conclude, we believe that our results might increase the awareness of the clinician to think of depression when a patient complains of multiple painful body areas. This could be one step to improve the recognition of depression by geriatricians, an issue that has been criticised [1] five years ago.

Key points

- Multisite pain is most significantly associated with depression in older adults.
- When controlling for comorbidity and social network, only pain severity remains significantly associated with depression in the whole cohort and in females. In males, pain frequency becomes more important.
- For diagnostic purposes, physicians and nurses should be aware of a depressive disorder if older adults report pain across multiple body sites.
- The understanding of the association of pain and late life depression could be improved by disentangling the different pain dimensions and by stratifying for gender.

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Conflicts of interest

None declared.

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