Do fibromyalgia patients feel older than they really are? An observational study

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ABSTRACT

Objective. *This study aimed to test the hypothesis that fibromyalgia patients feel older than their actual age and to investigate the associations between their subjective age and clinical parameters such as cognition, depression, anxiety, widespread pain, sleep, and fatigue.*

Methods. *This observational cross-sectional study enrolled 176 patients with newly diagnosed fibromyalgia and 89 controls. Subjective age was determined by asking the question "how old do you feel?", and the difference between the physiological and subjective ages was calculated. Depression, anxiety, fatigue, sleep cognition, and widespread pain levels in the subjects were evaluated, and multivariate stepwise regression analysis was used to determine the factors explaining the variation in the difference between actual and subjective age.*

Results. *Of the fibromyalgia patients, 75% felt older than their actual age, whereas 45% of the controls felt younger. Regression analysis revealed that depression, widespread pain, and fatigue explained nearly half of the variation in the subjective age and the difference between actual and subjective age.*

Conclusion. *Fibromyalgia patients feel older than their actual age, and this subjective age is associated with depression, widespread pain, and fatigue. Further studies should investigate usage of subjective age perception in differential diagnosis of fibromyalgia.*

Introduction

Fibromyalgia (FM) is characterised by widespread musculoskeletal pain, sleep disorders fatigue and many other symptoms that worsen the quality of life (1, 2). There is no specific diagnostic tool for FM. However, diagnostic criteria have been defined and are completely dependent on the patient's complaints (3, 4). While the diagnostic criteria have shown high sensitivity and specificity in studies (3), the majority of patients can be misdiagnosed in clinical practice if the differential diagnosis is not considered (5-7).

The age that a person actually feels is called the subjective or felt age. This self-perceived age may be younger, the same as, or older than the chronological age (8). While younger individuals tend to feel a bit older, the geriatric community typically feels younger than their birth age (8, 9). The concept of "subjective age" has recently attracted attention in gerontology (8, 10). In geriatric patients, feeling young means lower rates of depression and cognitive decline, higher physical functioning, faster walking speed, greater grip strength, and a better quality of life (11-13). However, subjective age has not yet been investigated with respect to any specific disease.

Since there are no studies in the literature, we based our hypothesis on our clinical experience and hypothesised that FM patients feel older than their actual age. Therefore, this study examined differences in age perception by comparing subjective age feeling between FM patients and a control group. We also investigated whether subjective age is associated with depression, cognition, fatigue, anxiety, widespread pain, or sleep problems based on previous studies.

Material and methods

Study design, ethics, and registration

The study was an observational, descriptive, cross-sectional study. The Clinical Studies Ethics Committee of Gaziosmanpasa Training and Research Hospital approved the study (no. 64/2019, 8 May 2019). After ethics approval, the study was registered at clinicaltrials.gov (no. NCT03966820, 29

May 2019). All participants provided informed consent in compliance with the Declaration of Helsinki.

Sample size

Initially, 10 patients were recruited into each group (The control group consisted of patients with back, neck, shoulder, elbow or knee pain), and their subjective ages were recorded. The effect size of older subjective age rates was 0.34 for this pilot sample. Using G-Power (ver. 3.1.9.2., Germany) with $\alpha = 0.05$, power = 0.80, and an allocation ratio of 2:1, the total sample size was calculated as 244 subjects (163 FM patients and 81 controls) (Fig. 1).

Between 29 May 2019 and 28 January 2020, 176 FM patients and 89 controls were enrolled in the study after visiting the physical medicine and rehabilitation outpatient clinic in Istanbul, Turkey. Patients aged >18 years who were newly diagnosed with FM using the 2016 revised 2010/2011 FM diagnostic criteria were included in the FM group. The control group consisted of patients with pain in one body region who applied to the outpatient clinic. Pain duration and diagnosis of the control group were also recorded. Patients with a definite diagnosis, whose physical examination and necessary diagnostic tests were completed, were included in the control group. The exclusion criteria for both groups were the presence of anaemia, vitamin D deficiency, endocrine diseases such as diabetes mellitus or thyroid diseases, rheumatic or systemic autoimmune diseases, infectious or inflammatory diseases, malignancy, neurological diseases, severe cardiovascular diseases, uncontrolled psychiatric disorders, pregnancy, or lactation. Patients on any pharmacological or non-pharmacological therapy for FM in the 6 months before the study were also excluded. All participants with missing data (missing completely at random) for any measurement were also excluded (14).

Measurements

Demographic data, including age, sex, height, weight, body mass index, marital status, education level, income, and duration of pain, were recorded.

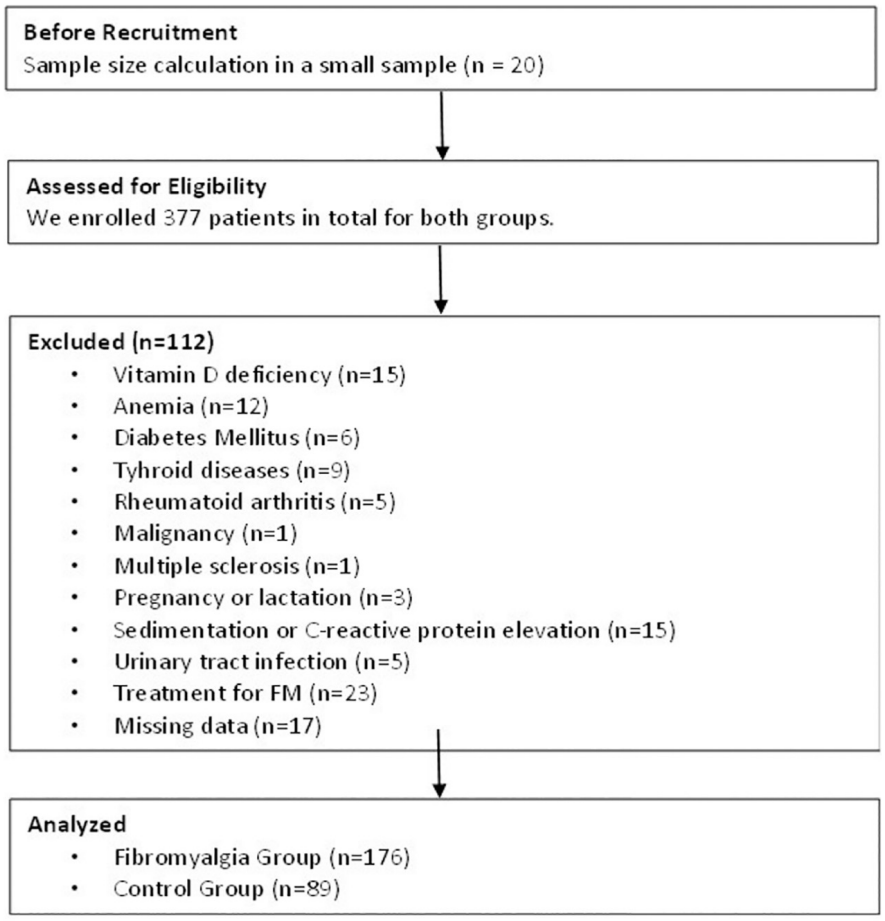

Fig. 1. Flowchart of the study.

After taking a history and establishing a trust relationship with the patient, the physician asked the patient "How old are you?" The second question was "How old do you feel?" If the patient did not provide a number, the physician asked for a definite number. Answers of feeling older or younger were not accepted. This single item measure of felt-age is a well-established reliable and valid method to measure subjective age feeling, cross-culturally (15). Then, the patient was asked to answer "How often did you feel that (subjective) age during the last week?" using a 4-point Likert-scale: (1) rarely, (2) sometimes, (3) often, and (4) always.

The difference between the actual and subjective ages was calculated by subtracting the subjective age from the actual age. Negative values indicated feeling older and positive values feeling younger than the actual age. An age difference of "0" indicated feeling the same age.

The Mini-Mental State Examination (MMSE) evaluates cognitive function (16) in six domains: orientation (10 points), registration of new information (3 points), attention and calculation (5 points), recall (3 points), language (8 points), and visuospatial construction/copying (1 point). The maximum score is 30 points. A score below 23/24 points is considered to indicate cognitive impairment (17, 18). The validity of the MMSE in the Turkish population has been established (19).

The Beck Depression Inventory (BDI) is a self-reported questionnaire commonly used to evaluate the level of depression. The BDI consists of 21 items, each with a score ranging from 0 to 3 points (20, 21). The Beck Anxiety Inventory (BAI) consists of 21 self-reported questions, each with a score ranging from 0 to 3 points that measure the level of anxiety. The highest score on both the BAI and BDI is 63 points, with higher scores indicating greater levels of anxiety or depression, respectively (22).

Quality of sleep was evaluated using the Pittsburgh Sleep Quality Index (PSQI), a self-reported questionnaire that evaluates sleep during the past month. It consists of 19 items in seven categories: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disorders, use of sleep medications, and daytime dysfunction. Scores for each category range from 0 to 3 points. The maximum total score is 21 points, and higher scores indicate poorer sleep quality (23, 24).

The severity of fatigue was evaluated using the Fatigue Severity Scale (FSS), a nine-item self-reported questionnaire. The score range for each item is 1–7 points, with 1 point indicating "strong disagreement" and 7 points "strong agreement". The final score is the mean score of the nine items, and 4 points or higher indicates severe fatigue (25).

The severity of FM was evaluated using the Revised Fibromyalgia Impact Questionnaire (FIQ-R). The FIQ-R has 21 questions in three domains: function, overall impact, and symptoms. Scores range from 0 to 10 points, with 10 indicating the worst outcome over the past 7 days (26, 27).

In the FM patients, the widespread pain index (WPI), symptom severity scale (SSS), and polysomatic distress score (PDS; Fibromyalgia Symptom Score) were calculated according to the 2016 revised 2010/2011 FM diagnostic criteria (3).

Statistical Analysis

Statistical analyses were performed using SPSS v. 20.0 (IBM, Armonk NY, USA). Data distribution was examined using the Shapiro-Wilk test and histograms. Continuous variables are expressed as means ± standard deviation (SD) with ranges, and categorical variables are expressed as numbers and percentages. The participants were grouped according to their subjective age: feeling older, the same as, or younger than their actual age. The groups were compared using the independent samples *t*-test for continuous variables and the chi-square test or Fisher's exact test, where applicable, for categorical variables. Pearson correlation coefficients were used to evaluate the association between continuous variables (coefficients were classified as follows: ± 1 as "perfect", above ± 0.7 as "strong", between ± 0.69 and 0.3 as "moderate", and below ± 0.29 as "weak") (28). One-way analysis of variance (ANOVA) followed by *post-hoc* analysis with Bonferroni adjustment was used to compare groups with different levels of education (p-adjusted = 0.008). Multivariate stepwise linear regression analysis was conducted to explore the association of the actual age-subjective age difference with other variables adjusted with age and gender. The multivariate regression model included independent variables were those with p-values <0.05 in the univariate analyses (weight, height, BMI, pain duration, WPI, SSS, BDI, BAI, FSS, FIQ-R, PSQI, MMSE scores). p-values <0.05 were considered statistically significant.

Table I. Demographic characteristics of the fibromyalgia patients and controls.

	FM group (n=176)	Control group (n=89)	p-value
Age, years (mean ± SD)	37.3 ± 9.9 (18 – 65)	36.3 ± 10.7 (18 – 67)	0.473
Gender, Woman, n (%)	164 (93 %)	81 (91 %)	0.528
Weight, kg (mean ± SD)	69.9 ± 10.2 (53 – 88)	69.7 ± 10.8 (53 – 100)	0.839
Height, m (mean ± SD)	1.61 ± 0.61 (1.49 – 1.75)	1.61 ± 0.65 (1.49 – 1.75)	0.773
BMI, kg/m^2 (mean ± SD)	27.21 ± 4.60 (19.59 – 37.72)	27.03 ± 4.81 (19.59 – 42.54)	0.765
Employed, n (%)	66 (38%)	30 (34%)	0.544
Education, n (%)			
Primary School	35 (20%)	25 (28%)	
Middle School	62 (35%)	36 (40%)	0.172
High School	47 (27%)	18 (20%)	
University	32 (18%)	10 (12%)	
Marital Status, n (%)			
Single	5 (3%)	11 (12%)	
Married	158 (90%)	70 (79%)	0.104
Widow	13 (7%)	8 (9%)	
Children, yes n (%)	143 (81%)	72 (81%)	0.945

FM: fibromyalgia; SD: standard deviation; BMI: body mass index.
p-value statistically significant at <0.05 (Independent Samples t-test, Fisher's exact test and χ^2 test were used).

Results

The study included 176 patients diagnosed with FM and 89 controls. There were no significant differences in demographic characteristics between the two groups (Table I). Table II presents the mean ± SD subjective age and frequency of feeling this subjective age. The majority of the FM patients (75%) reported feeling older, whereas 44.9% of the controls reported feeling younger, than their chronological age. The number of patients feeling older than their real age was significantly (p<0.001) greater among the FM patients than controls. The frequency of the subjective age feeling for the last week was similar between the groups (p=0.926).

Table III shows the pain duration and MMSE, BDI, BAI, PSQI, FSS, FIQ-R, WPI, SSS, and PDS scores. All scores (except pain duration, the registration and copying sub-scores of the MMSE and use of sleep medication subscale of the PSQI) differed significantly between the FM and control groups. The diagnosis of the control group was as follows: low back pain (n=34, 38.2%), non-specific neck pain (n=17, 19.1%), rotator cuff syndrome (n=13, 14.6%), patellofemoral syndrome (n=10, 11.2%), lateral epicondylitis (n=9, 10.1%), plantar fasciitis (n=6, 6.7%). In control group, patients with chronic pain subgroup (≥6 months), (n=26, 29.2%) reported significantly higher results of self-perceived older age compared to non-chronic patients (p<0.001).

Upon comparing patients with chronic pain subgroup (n=26) to FM group (n=176) for all variables, actual age-subjective age difference was significantly higher in FM group (p=0.003). Although MMSE-registration, MMSE-copying, PSQI-Use of sleep medications and PSQI-Daytime dysfunction

Table II. Subjective age, actual-subjective age difference, felt age groups and frequency of the feeling values of the participants.

	FM group (n=176)		Control group (n=89)		*p*-value
	n (%)	Mean ± SD (min-max)	n (%)	Mean ± SD (min-max)	
Age, years		37.3 ± 9.9 (18-65)		36.3 ± 10.7 (18-67)	0.473
Subjective age, years		46.4 ± 15.5 (18-100)		33.0 ± 10.4 (18-60)	**<0.001**
Age difference (actual – subjective)		9.2 ± 14.2 (-65 – 33)		3.3 ± 6.8 (-10 – 27)	**<0.001**
Subjects feeling					
Older	132 (75%)		11 (12%)		
Same age	22 (12.5%)		38 (43%)		**<0.001**
Younger	22 (12.5%)		40 (45%)		
Frequency of felt age					
Rarely	5 (3%)		2 (2%)		
Sometimes	12 (7%)		8 (9%)		0.926
Often	89 (50%)		44 (50%)		
Always	70 (40%)		35 (39%)		

FM: fibromyalgia; SD: standard deviation.
p-value statistically significant at <0.05 (Independent Samples t-test, Fisher's exact test and χ^2 test were used).

Table III. Clinical parameters of the FM patients and controls.

	FM group (n=176) Mean ± SD (min-max)	Control group (n=89) Mean ± SD (min-max)	*p*-value
Duration of pain, months	36.2 ± 27.8 (3-144)	4.9 ± 3.2 (1-20)	**<0.001**
WPI	10.9 ± 2.9 (4-18)		
SSS	7.5 ± 1.7 (4-11)		
PDS	18.4 ± 3.2 (12-28)		
FIQ-R			
Function	57.2 ± 9.0 (35-73)		
Overall	18.4 ± 1.9 (14-20)		
Symptoms	69.3 ± 9.1 (49-89)		
Total FIQ-R Scores	72.1 ± 5.8 (59-86)		
MMSE			
Orientation	7.7 ± 1.0 (5-10)	8.9 ± 1.0 (6-10)	**<0.001**
Registration	2.9 ± 0.4 (1-3)	2.8 ± 0.4 (2-3)	0.594
Attention and Calculation	2.8 ± 0.7 (2-5)	3.4 ± 0.7 (2-5)	**<0.001**
Recall	1.6 ± 0.6 (1-3)	2.0 ± 0.6 (1-3)	**<0.001**
Language	6.9 ± 0.6 (6-8)	7.3 ± 0.6 (6-8)	**<0.001**
Copying	0.9 ± 0.3 (0-1)	0.9 ± 0.4 (0-1)	0.370
Total MMSE Scores	22.7 ± 1.5 (20-27)	25.2 ± 1.6 (22-29)	**<0.001**
BDI	20.4 ± 6.8 (8-41)	2.6 ± 2.9 (0-11)	**<0.001**
BAI	27.6 ± 6.7 (9-46)	16.3 ± 4.8 (5-30)	**<0.001**
PSQI			
Subjective Sleep Quality	2.1 ± 0.9 (0-3)	1.0 ± 0.7 (0-3)	**<0.001**
Sleep Latency	1.6 ± 0.7 (0-3)	0.4 ± 0.7 (0-3)	**<0.001**
Sleep Duration	1.2 ± 0.6 (0-3)	0.8 ± 0.6 (0-2)	**<0.001**
Habitual Sleep Efficiency	1.4 ± 0.5 (1-2)	0.5 ± 0.5 (0-2)	**<0.001**
Sleep Disorders	1.8 ± 0.6 (0-3)	1.0 ± 0.4 (0-2)	**<0.001**
Use of Sleep Medications	0.2 ± 0.4 (0-1)	0.1 ± 0.4 (0-2)	0.527
Daytime Dysfunction	0.4 ± 0.7 (0-2)	0.1 ± 0.3 (0-1)	**0.002**
Total PSQI Score	8.5 ± 1.6 (4-12)	3.9 ± 1.5 (1-8)	**<0.001**
FSS	6.1 ± 0.7 (4.4-7)	4.3 ± 0.7 (3-6)	**<0.001**

FM: fibromyalgia; SD: standard deviation; WPI: widespread pain index; SSS: symptom severity scale; PDS: Polysomatic Distress Scores; MMSE: mini-mental state examination; BDI: Beck depression inventory; BAI: Beck anxiety inventory; PSQI: Pittsburgh sleep quality index; FSS: fatigue severity scale; FIQ-R: Revised fibromyalgia impact questionnaire.
p value statistically significant at <0.05 Independent Samples t-test were used).

were similar between the two groups ($p>0.05$), we found significantly higher BDI scores ($p<0.001$), higher BAI scores ($p<0.001$), higher PSQI scores ($p<0.001$) and higher FFS scores ($p<0.001$) and lower MMSE scores ($p<0.001$) in FM group.

The level of education was low in both groups; more than half of the participants graduated from primary or middle school. However, the mean scores for subjective age and actual age-subjective age difference were similar between the FM and control groups according to the level of education (subjective age: $p=0.468$ and $p=0.900$; actual age-subjective age difference: $p=0.824$ and $p=0.604$, respectively). The mean MMSE scores were also similar between the FM and control groups according to the level of education ($p=0.598$ and $p=0.045$, respectively).

Pearson correlation analysis revealed that the WPI, PDS, MMSE, BDI, BAI, PSQI, FIQ-R total, and FSS scores were correlated with the actual age-subjective age difference in the FM patients (Table IV). In the controls, only the FSS score was significantly correlated with the actual age–subjective age difference scores ($r=-0.369$, $p<0.001$).

Table V presents the results of the multivariate stepwise linear regression analysis adjusted for age and gender.- The independent variables associated with the actual age–subjective age difference were the WPI, BDI, and FSS scores. The coefficient of determina-

Table IV. Correlation between age-subjective age difference and clinical parameters in FM patients.

		Age- subjective age difference	
		r	*p*-value
Duration of pain		0.047	0.532
WPI		**-0.588**	**<0.001**
SSS		-0.090	0.235
PDS		**-0.581**	**<0.001**
MMSE	Orientation	0.210	**0.001**
	Registration	0.004	0.951
	Attention and Calculation	0.197	**0.001**
	Recall	0.217	**<0.001**
	Language	0.137	**0.026**
	Copying	0.003	0.957
	Total MMSE Scores	**0.316**	**<0.001**
BDI		**-0.528**	**<0.001**
BAI		**-0.401**	**<0.001**
PSQI	Subjective Sleep Quality	-0.213	**<0.001**
	Sleep Latency	-0.209	**0.001**
	Sleep Duration	-0.136	**0.027**
	Habitual Sleep Efficiency	-0.259	**<0.001**
	Sleep Disorders	-0.229	**<0.001**
	Use of Sleep Medications	-0.043	0.483
	Daytime Dysfunction	-0.166	0.007
	Total PSQI Score	**-0.335**	**<0.001**
FSS		**-0.500**	**<0.001**
FIQ-R	Function	-0.087	0.251
	Overall	-0.033	0.664
	Symptoms	-0.123	0.103
	Total FIQ-R Scores	-0.154	**0.041**

FM: fibromyalgia; WPI: widespread pain index; SSS: symptom severity scale; PDS: Polysomatic Distress Scores; MMSE: mini-mental state examination; BDI: Beck depression inventory; BAI: Beck anxiety inventory; PSQI: Pittsburgh sleep quality index; FSS: fatigue severity scale; FIQ-R: Revised fibromyalgia impact questionnaire. *p*-value statistically significant at <0.05.

Table V. Age and gender adjusted multivariate stepwise linear regression analysis of factors affecting age-subjective age difference in fibromyalgia patients.

	B	SE	β	t	*p*-value
Age-Subjective age difference*					
Constant	48.392	7.747		6.246	<0.001
WPI	-2.458	0.298	-0.506	-8.508	<0.001
BDI	-0.534	0.123	-0.256	-4.358	<0.001
FSS	-3.216	1.258	-0.152	-2.592	0.010

* F=6.717, R=0.661, R^2=0.438. β: standard regression coefficient; B: partial regression coefficient; SE: standard error; WPI: widespread pain index; BDI: Beck Depression Inventory; FSS: fatigue severity scale.

tion of the actual age-subjective age difference was 0.438, indicating that these three factors explain 43% of all variation in this difference.

Discussion

This study found that 75% of the FM patients felt older than their actual age, whereas the majority of the controls reported that they felt younger or the same age. The subjective feeling of older age was moderately correlated with depression, widespread pain, and fatigue in patients with FM.

Chronic stress caused by chronic pain in fibromyalgia patients results in shortened telomere lengths, and shortened telomere lengths have been shown to be associated with higher levels of depression and pain in fibromyalgia patients (29). Previous studies showed that shorter telomere lengths, self-perceived aging, and widespread pain were associated with mortality in cancer patients (30, 31). Additionally, subjective age was found to be associated with higher rates of mortality in older adults (32). Recent studies showed an increase was detected for all-cause mortality in FM patients (33). Considering these results and the conclusion of our study, further studies are needed to search for an association between premature aging, subjective aging and mortality in FM patients (34).

Interestingly, in our study, pain duration did not appear to be significantly correlated with the actual age–subjective age difference in the FM group and control group. But in control group, patients with chronic pain (≥6 months) reported older felt age. The perceived intensity of pain seems more important than the pain duration in terms of subjective age (35). Fatigue severity was significantly correlated with the actual age–subjective age difference in both the FM and control groups. Subjective age has been evaluated mainly in the field of geriatrics. Depression, quality of life, and cognition have been found to be related to subjective age; however, fatigue has not been investigated, and its relationship with subjective age should be clarified in future studies (8-10). Quality of sleep was found to be correlated with the actual age–subjective age difference only in the FM group. The results were similar to a study comparing sleep quality and subjective age in middle-aged and older adults (36). Although the mean age scores of the subjects were similar between the FM and the control group, we found no correlation between sleep quality and subjective age in the control group.

There was a significant correlation between the actual age-subjective age difference and MMSE scores in the FM group, but the regression analysis did not reveal cognition as a predictive variable. FM patients had lower MMSE scores than those of the controls, despite similar levels of education. The mean MMSE score of the FM patients

in our study was lower than that of the FM patients in the study by Rodríguez-Andreu *et al*. (37), but similar to that in the study by Can *et al*. (38).

Although there were moderate correlations of the actual age-subjective age difference with individual sleep, fatigue, depression, and cognition scores, as measured by the PDS, FSS, BDI, and MMSE, respectively, the SSS score showed no correlation. This was interesting, as fatigue, cognition, and depression are components of the SSS. Their weighted impact on the total SSS score may not be reflected sufficiently, since the maximum score for each of the items in the SSS is only 1 point (3). In this study, we verbally asked the subjects "how old do you feel?" to determine their subjective age, similar to other studies (9, 39). By contrast, Eibach *et al*. asked their participants to complete a written statement (40). There may be differences between verbal and written replies, as a written reply allows more time for contemplation and the possibility of changing the answer.

In this study, the FM patients had a higher rate of feeling older compared with the controls, which may provide a diagnostic clue. Further studies are needed to determine the rate of an older subjective age in FM compared with other chronic conditions that may cause depression, widespread body pain, or fatigue. We found a weak correlation between an older subjective age and the impact of FM, which suggests that the older the subjective age, the greater the impact of FM on a patient.

To our knowledge, the concept of subjective age has not been previously investigated in any disease. Although subjective age and quality of life or depression were previously found to be related, especially in the elderly (12), this study is the first to investigate subjective age in a chronic disease.

There are some limitations to our study. Firstly, healthy volunteers were not included in the present study, since the subjective age rates were assessed for this age in larger populations in the previous studies (9, 15). Although this can be seen as a limitation, the present study included other patient groups who applied to the outpatient clinic with musculoskeletal pain as a control group. Secondly, A control group consisting of patients with depression might provide more information on the effect of depressive mood on subjective age, independent of pain. Thirdly, this study did not determine the subjective age of FM patients prospectively. Evaluating changes in subjective age in response to treatment may be beneficial. Lastly, by using different questionnaires that evaluate cognitive function other than MMSE, the relationship between subjective age and cognition can be revealed more clearly in further studies.

This study suggests that FM patients feel older than their actual age compared with controls, and this subjective age is associated with depression, widespread body pain and fatigue. Further studies should investigate usage of subjective age perception in differential diagnosis of FM from other musculoskeletal and rheumatologic diseases.

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