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ORIGINAL ARTICLE



Childhood and adult attention deficit hyperactivity disorder symptoms in fibromyalgia: associations with depression, anxiety and disease impact

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ABSTRACT

Objective: The first aim of this study was to determine the prevalence of childhood and current attention deficit hyperactivity disorder (ADHD) symptoms in patients with fibromyalgia. The second aim is to assess the role of depression and anxiety on the relationship between childhood and adult ADHD symptoms with disease impact in this population.

Methods: Sixty-four patients with fibromyalgia were compared to matched 58 healthy controls. All participants completed the Wender Utah Rating Scale (WURS), Adult ADHD Self-Report Scale (ASRS), Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI) and Fibromyalgia Impact Questionnaire (FIQ). Results: Patients with fibromyalgia had significantly higher mean scores of depression (BDI), anxiety (BAI), childhood ADHD symptoms (WURS) and adult ADHD symptoms (ASRS total, ASRS hyperactivity/impulsivity subscale and ASRS attention deficit subscale) than the control group. Fibromyalgia impact (FIQ) was significantly correlated with depression (BDI; r = 0.57, p < .001), anxiety (BAI; r = 0.56, p < .001) and childhood ADHD symptoms (WURS; r = 0.41, p < .001) in fibromyalgia group. There was no significant correlation between fibromyalgia impact (FIQ) and adult ADHD symptoms (ASRS total or sub-scale scores). Hierarchical multiple regression indicated that childhood ADHD symptoms (WURS), anxiety (BAI) and depression (BDI) predicted fibromyalgia impact. Both anxiety (BAI) and depression (BDI) mediated the relationship between childhood ADHD symptoms (WURS) and fibromyalgia impact (FIQ).

Conclusion: Childhood ADHD symptoms may be a contributory factor to poorer functioning in the patients with fibromyalgia. The relationship was more pronounced in the presence of depression and anxiety symptoms. Evaluation of childhood and adult ADHD symptoms in patients with fibromyalgia is important for recognition and treatment of ADHD comorbidity and also for attenuating the severity of the disease.

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KEYWORDS

Fibromyalgia; ADHD symptoms; attention deficit and hyperactivity; fibromyalgia impact; depression; anxiety

Introduction

Fibromyalgia (FM) is an extra-articular rheumatic disease characterised by widespread musculoskeletal pain (Wolfe et al. 2010). Fatigue, sleep disturbance, cognitive impairment, depressive mood and medically unexplained physical symptoms are common in FM (Geisser et al. 2008; Rutledge et al. 2009). Prevalence in the general population varies between 2.9% and 4.7%, predominantly affecting female gender (Branco et al. 2010). Cognitive complaints are seen approximately in 70% of patients with FM and contribute to disability related to disease (Katz et al. 2004). In addition to subjective complaints, objective reports of cognitive impairment detected by neuropsychological tests were reported, including executive functions, attention, working, semantic and episodic memory (Mease et al. 2009; Montoro et al. 2015). It has been suggested that distraction is the most significantly deteriorated cognitive impairment domain in FM and is a predictive factor for impaired memory function (Leavitt and Katz 2006). Reduced vigilance and attention deficit in FM patients have also been reported to be associated with emotional distress, sleep dysfunction and pain intensity (Miró et al. 2015).

In addition to cognitive symptoms, the frequency of lifetime and current psychiatric comorbidities, mainly mood disorders and anxiety disorders, are relatively high in patients with FM (Gündüz et al. 2018). The lifetime prevalence of mood disorders was found to be between 65% and 70%, the frequency of anxiety disorder to be 35-68% and the rate of any psychiatric disorder was reported to be 81%. Presence of both psychiatric comorbidities and psychiatric symptoms negatively affect pain and quality of life in patients with FM (Arnold et al. 2004; Lichtenstein et al. 2018). Besides the similarities in pathophysiology, due to common clinical characteristics such as increased frequency of depressive symptoms, elevated risk for psychiatric comorbidity and good response to antidepressant therapy; it has been suggested that FM should be included in the category of affective spectrum disorders along with some other psychiatric disorders including attention deficit hyperactivity disorder (ADHD; Gardner and Boles 2011).

There has been an increased interest in ADHD symptoms and ADHD comorbidity in patients with FM. In an earlier small study, patients with FM were reported to have higher rates of ADHD symptoms both in adulthood and in childhood when compared to other pain disorder groups (Krause et al. 1998). In a recent

study, possible diagnosis of ADHD assessed by Adult ADHD Self-Report Scale (ASRS) in patients with FM was more prevalent than the control group and possible ADHD comorbidity was shown to have a significant impact on disease severity (Van Rensburg et al. 2018). Childhood ADHD symptoms were also found to be more common in patients with FM than healthy controls (Reyero et al. 2011). Moreover, the rate of diagnosis of FM is higher in ADHD patients with cognitive complaints, when compared to control groups (Golimstok et al. 2015). A recent study conducted in Turkey reported ADHD comorbidity for one-third of patients with FM (Yılmaz and Tamam 2018). The reports on the clinical and phenomenological features suggest that there may be shared pathophysiological mechanisms of FM and ADHD. Some authors suggested a common mechanism of cognitive impairment associated with dysfunction of dopaminergic pathways in FM and ADHD (Arnsten 2006; Kravitz and Katz 2015).

Despite the overlap in clinical features, the current literature on the effect of childhood and current ADHD symptoms on the severity of disease in FM is very limited. To our knowledge, there is no study investigating the moderating role of depression and anxiety symptoms on the relationship between childhood and adulthood ADHD symptoms and severity of illness in patients with FM. The current study sought to meet these shortcomings in the literature and expand the available knowledge on the areas of research regarding ADHD symptom comorbidity in FM and possible factors affecting this relationship which may affect the clinical manifestations and impact of FM. A better understanding of the link between ADHD symptoms and FM is important for the need to recognise and offer better treatments that will eventually help improve the course of disease.

In this study, we evaluated differences in frequency of childhood and current ADHD symptoms between patients with FM and a healthy control group, and assess association of these symptoms with disease impact in patients with FM. We also evaluated the mediating roles of depression and anxiety in the relationship between childhood and current ADHD symptoms in patients with FM. In accordance with the studies reviewed above, we hypothesised that: (1) FM group would exhibit higher levels of childhood and adult ADHD symptoms compared to healthy participants; (2) high childhood and adult ADHD symptoms would be associated with more severe anxiety and depression and a greater impact of illness [as measured by Fibromyalgia Impact Questionnaire (FIQ)]; (3) both depression and anxiety would have mediator effects on the relationship between ADHD symptoms and disease impact. We considered that the disability and clinical manifestations associated with FMS may have a greater effect on depression and anxiety, therefore ADHD symptoms. Further analyses were conducted to assess the relative magnitude of associations of childhood and adult ADHD symptoms with depression and anxiety in each group.

Methods

Participants

Seventy-two female patients with FM were recruited consecutively from the pain section of physical medicine and rehabilitation unit in Bagcilar Training and Research Hospital in Istanbul/Turkey between July 2017 and September 2017. The procedure was in line with Helsinki Declaration and the study was approved by the local ethics committee of Bagcilar Training and Research Hospital. Written and oral informed consents were obtained from the patients and control subjects. Data collection and assessment procedures were both conducted blindly, groups were randomly

assigned. The diagnosis of FM was given by physical examination and investigation based on the 2010 criteria of the American College of Rheumatology (Wolfe et al. 2010). These criteria were (a) a widespread pain index (WPI) >7 and symptom severity (SS) scale score of \geq 5; or WPI of 3–6 and SS scale score of >9; (b) the symptoms should be present at a similar level for at least three months; and (c) another disorder that would otherwise explain the pain should be excluded. All patients were screened by the same clinician, who has extensive experience in managing patients with FM and other chronic pain disorders. Participants were invited to complete questionnaires after they consented the study. Exclusionary criteria were being under 18 years of age, illiterate, having severe hearing or vision impairment, clinical diagnoses of intellectual disability, psychotic disorder or dementia according to medical records or clinical history. Overall 64 patients were included to statistical analysis due to 8 participants with missing data. Fifty-eight healthy volunteers with matched sociodemographic characteristics were recruited. The healthy control group was composed of the hospital workers and patients' relatives. In addition to not having any kind of pain disorder, the control group was subject to the same exclusionary criteria as for the patients.

Measures

Wender Utah Rating Scale

The Wender Utah Rating Scale (WURS) is a 61-item self-report assessment scale for ADHD, in which the adult patient recalls his or her childhood behaviour. Items fall into three factors; dysthymia, oppositional-defiant behaviour and school/work problems. Five possible responses are scored from 0 to 4 points. Those above the cut-off value of 46 points are retrospectively diagnosed with ADHD in childhood (Ward et al. 1993). The Turkish validity and reliability study of the scale was performed by Öncü et al. (2005). Cronbach's alpha coefficients were 0.90 and 0.93 for original and translated versions.

Adult ADHD Self-Report scale

ASRS is a screening tool for ADHD developed by the World Health Organisation (Kessler et al. 2005). Two subscales assessing 'attention deficit' and 'hyperactivity' consist of nine items each. The guestions aim to determine how often each symptom occurs within the last six months and the answers are scored between 0 and 4 points. Those who score more than 24 points on any of the two subscales are considered to fall in the category 'highly likelihood of ADHD', those with 17-23 points are 'likely ADHD' and those who score 0-16 are not considered as a candidate for ADHD. The Turkish validity and reliability study of the scale was performed by Dogan et al. (2009). Cronbach's alpha coefficients were 0.70 and 0.88 for original and translated versions.

Beck Depression Inventory

The Beck Depression Inventory (BDI) was developed in 1961 by Beck et al. and composed of 21 questions or items, each with four possible responses (Beck, Steer, et al. 1988). Each response is assigned a score ranging from zero to three, indicating the severity of the symptom. Individual questions of the BDI assess mood, pessimism, sense of failure, self-dissatisfaction, guilt, punishment, self-dislike, self-accusation, suicidal ideas, crying, irritability, social withdrawal, body image, work difficulties, insomnia, fatigue, appetite, weight loss, bodily preoccupation and loss of libido. Items 1 to 13 assess symptoms that are psychological in nature, while items 14 to 21 assess more physical symptoms. It was translated



into Turkish and its reliability was recalculated Hisli (1988) for the Turkish population. Cronbach's alpha coefficients were 0.93 and 0.80 for original and translated versions.

Beck Anxiety Inventory

The Beck Anxiety Inventory (BAI) consists of 21 self-report items with a Likert scale ranging from total scores of 0 to 63. It was developed in 1988 and a revised manual was published in 1993 with changes in scoring (Beck, Epstein, et al. 1988). The scores correlate with the level of anxiety and are classified as minimal anxiety (0 to 7), mild anxiety (8 to 15), moderate anxiety (16 to 25) and severe anxiety (30 to 63). The Turkish validity and reliability study of the scale was conducted by Ulusoy et al. (1998). Cronbach's alpha coefficients were 0.92 and 0.93 for original and translated versions.

Fibromyalgia Impact Questionnaire

The FIQ was developed in 1991 by Burckhardt et al. to assess a spectrum of problems related to FM and associated variables of outcome (Burckhardt et al. 1991). It is composed of self-administered 10 items which measure physical functioning, work status, depression, anxiety, sleep, pain, stiffness, fatigue and wellbeing. The first item consists of 10 sub-items and are rated on a 4-point Likert type scale and scores on each guestion can range from 0 (always) to 3 (never). The final scores for each item of the FIQ should range from 0 (no impairment) to 10 (maximum impairment) and the total maximum score is 100, which represents the maximum impact of disease. The FIQ was modified in both 1997 and 2002; however, the Turkish validity and reliability study conducted by Sarmer et al. (2000) covered the original version, hence utilised in this study. Cronbach's alpha coefficients were 0.95 and 0.72 for original and translated versions.

Statistical analysis

Statistical analysis was performed using the software programme SPSS for Windows version 23.0. Prior to test differences between groups and model tests, assumptions of normal distribution of Kolmogorov-Smirnov variables were tested by Demographical characteristics of the study groups were compared with Chi-square analyses on categorical data and Student t-test on the continuous variables. Total scores of the clinical scales and subscales (BDI, BAI, WURS, ASRS) were compared with multivariate analysis of variance. Partial squared eta (n^2) was used as effect size indicator. Pearson correlation analysis was used to investigate the relationship between measurement variables in the FM and control groups. Group difference in correlation coefficients were tested with Fisher's Z statistics. By taking FIQ score as dependent variable, hierarchical regression analysis was performed to determine the predictors of FIQ score in patients with FM. In order to determine the effect of the WURS mean score on FIQ score was included in the first block, ASRS score in the second block, BAI score in the third block and BDI score in the fourth block of regression analysis. Significance level was set at 0.05.

Results

Comparison of demographic and clinical variables between groups

The mean ages of the groups were 39.75 ± 10.33 for the patient group and 39.6 ± 8.75 for the control group (t = 0.224, p = .823). There was no significant difference between patients with FM and healthy controls in demographic characteristics (Table 1). Compared to the control group, patients with FM reported

Table 1. Demographic characteristics of patients with fibromyalgia and healthy controls.

	Patients (n = 64)	Controls ($n = 58$)	χ2	p Value
Female	64 (100.0%)	58 (100.0%)		
Education			.106	.745
Primary School	39 (60.9%)	37 (63.8%)		
High School/Bachelor/Master	25 (39.1%)	21 (36.2%)		
Work status			.030	.863
Yes	33 (51.6%)	29 (50.0%)		
No	31 (48.4%)	29 (50.0%)		
Monthly income			.720	.698
Low	14 (21.9%)	13 (22.4%)		
Middle	46 (71.9%)	39 (67.2%)		
High	4 (6.3%)	6 (10.3%)		
Marital status			.133	.715
Married	49 (76.6%)	46 (79.3%)		
Single	15 (23.4%)	12 (20.7%)		

Data presented as n (%); χ 2: chi square; p: p value (statistical significance).

Table 2. Depression, anxiety, WURS, ASRS and ASRS subscale scores in patients with fibromyalgia and healthy controls.

	Patients (n = 64)	Controls ($n = 58$)	F	p Value	η^2
Depression	19.70 ± 10.69	8.21 ± 5.68	53.386	<.0001	0.308
Depression - cognitive	11.81 ± 7.08	5.46 ± 3.99	36.101	<.0001	0.231
Depression - somatic	7.89 ± 4.47	2.74 ± 2.45	60.379	<.0001	0.335
Anxiety	23.77 ± 13.36	8.86 ± 6.11	60.646	<.0001	0.336
WURS	29.03 ± 14.05	18.48 ± 10.04	22.334	<.0001	0.157
ASRS	31.52 ± 9.61	21.31 ± 7.90	40.55	<.0001	0.253
ASRS-hyperactivity	14.89 ± 5.76	11.17 ± 4.96	14.445	<.0001	0.107
ASRS-attention deficit	16.63 ± 5.59	10.14 ± 4.59	48.471	<.0001	0.288

Data presented as $M \pm SD$; WURS: Wender Utah Rating Scale; ASRS: Adult ADHD Screening Scale; HC: healthy controls; M: mean; SD: standard deviation; t: Student's *t*-test. ****p* < 0.001.

Table 3. Breakdown of depression and anxiety scores according to severity.

	Patients (n = 64)	Controls ($n = 58$)	χ2	p Value
Depression group			44.293	p < .001
0-13 scores	18 (28.13%)	51 (87.93%)		
14-63 scores	46 (71.88%)	7 (12.07%)		
Anxiety group			43.634	p < .001
0–7 scores	7 (10.94%)	26 (44.83%)		
8-15 scores	15 (23.44%)	23 (39.66%)		
16-25 scores	11 (17.19%)	9 (15.52%)		
26-63 scores	31 (48.44%)	0 (0.00%)		

Data presented as n (%); γ 2: chi square.

significantly higher scores on clinical scales and subscales (Table 2). According to Chi-Square Test results, FM patients were more likely to have moderate to severe scores (14-63) in BDI (71.88%) than control group (12.07%). FM patients were more likely to have moderate scores (16-25) in BAI (17.19%) and high scores (26-63) in BAI (48.44%) than the control group (15.52%, 0.00%, respectively; Table 3).

Results of correlation analysis between clinical variables

Correlation analyses of clinical scales in both FM patients and the control group, as well as comparisons of correlation coefficients between groups were reported on Table 4. In the FM group, analyses showed significant correlations between all clinical scales, except between FIQ scores and ASRS scores. In the control group, all clinical scale and subscale scores were found to be correlated between each other. There were no significant differences on correlation coefficients between the groups (Table 4).

Table 4. Correlations between measurement variables in patients with fibromyalgia and healthy controls.

		1.	2.	3.	4.	5.	6.
1. FIQ	FM	1					
	Controls	_					
2. Depression	FM	.571***	1				
•	Controls	_	1				
	Z (p)	_	n/a				
3. Anxiety	FM	.562***	.581***	1			
,	Controls	_	.541**	1			
	Z (p)	_	0.314 (.541)	n/a			
4. WURS	FM	.406***	.616* [*] **	.445***	1		
	Controls	_	.459**	.400**	1		
	Z (p)	_	1.197 (.116)	0.295 (.384)	n/a		
5. ASRS	FM	.239	.546* [*] **	.518* [*] **	.494***	1	
	Controls	_	.386**	.354**	.572**	1	
	Z (p)	_	1.106 (.134)	1.095 (.137)	-0.587 (.279)	n/a	
6. ASRS-HA	FM	.195	.421* [*] *	.452* [*] **	.489***	.852***	1
	Controls	_	.320**	.353**	.490**	.841**	1
	Z (p)	_	0.631 (.264)	.636 (.262)	-0.007 (.497)	0.209 (.417)	n/a
7. ASRA-AD	FM	.210	.505* [*] **	.425* [*] **	.345***	.841* [*] **	.433***
	Controls	_	.318*	.228	.455**	.812**	.368**
	Z (p)	_	1.219 (.112)	1.192 (.117)	-0.706 (.240)	0.493 (.311)	0.417 (.338)

FIQ: Fibromyalgia Impact Questionaire; WURS: Wender Utah Rating Scale; ASRS: Adult ADHD Screening Scale; M: mean; SD: standard deviation. **p < .01. ***p < .001.

Table 5. Associations of childhood attention deficit hyperactivity disorder symptoms with fibromyalgia impact (model 1) and mediator role of anxiety (model 2) and depression (model 3) in patients with fibromyalgia.

	β	t	p Value	F	R^2	AR ²
Model 1				12.203	.16	.15
WURS	.41	3.493	.001			
Model 2				16.171	.35	.33
WURS	.19	1.676	.099			
Anxiety	.48	4.122	.000			
Model 3				15.507	.33	.31
WURS	.09	.652	.517			
Depression	.52	3.890	.000			
Dependent variable: Fibromyalgia impact						

WURS: Wender Utah Rating Scale; ASRS: Adult ADHD Screening Scale; p:p value (statistical significance). Statistically significant tests are reported in bold.

Association of childhood ADHD symptoms, anxiety and depression with impact of disease

A hierarchical multiple regression was implemented to predict impact of disease (FIQ) on childhood ADHD symptoms (WURS), anxiety (BAI) and depression (BDI) in the FM group. The regression model summary is shown in Table 5. The hierarchical multiple regression revealed that childhood ADHD (WURS) contributed significantly to the regression model, (F(1,62) =12.203, p < .01) and $(R^2 = .16)$. The second model found that anxiety (BAI) ($\beta = .48$, p < .001) also contributed significantly to the regression model. In addition, when anxiety (BAI) was included in the model the main effect of childhood ADHD (WURS) on FM syndrome (FIQ) disappeared. In the third model with the addition of depression (BDI), it was found that depression (BDI) (β = .52, p < .001) contributed significantly to the regression model. in the third model, the main effect of childhood ADHD (WURS) on FIQ was non-significant.

Discussion

In this case-control study, both childhood ADHD and adulthood ADHD symptoms were found to be more prevalent in patients with FM than the control group. ADHD symptoms in childhood were associated with disease impact in these adult patients with FM; however, adult ADHD symptoms were not found to be associated with disease severity. We also found that both depression

and anxiety mediated the relationship between childhood ADHD symptoms and disease impact in FM group. To our knowledge, this is the first study that examines the association of childhood ADHD symptoms with disease impact and investigates the role of depression and anxiety in this association in FM.

As expected, FM patients exhibited greater levels of childhood and adult ADHD symptoms compared with healthy controls. Higher incidence of both childhood and adult ADHD symptoms in patients with FM in this study is in line with previous data (Reyero et al. 2011; Golimstok et al. 2015; Van Rensburg et al. 2018). A recent study demonstrates this symptom-based comorbidity at the clinical level as well (Yılmaz and Tamam 2018). Cognitive symptoms, emotion regulation problems and disturbances in dopaminergic pathways in the central nervous system have been suggested as indicators of potential pathophysiological mechanisms of FM and ADHD (Bou Khalil et al. 2018). Patients with FM often report cognitive problems in memory, concentration or planning (Kratz et al. 2019). The problems are sometimes referred as fibrofog, similar to mental fog that is often described by patients with depression. Cognitive problems may partly be contributing the high ADHD symptom scores in our sample.

Regarding the relationship of childhood and adult ADHD symptoms with depression and anxiety in FM patients, our initial hypotheses were confirmed. On the other hand, magnitude of the correlations of these variables did not differ between FM and healthy group. Intuitively, one would expect stronger correlation with depression and anxiety in FM group but our analyses showed it was not the case in our sample. The lack of difference in magnitudes may be related to the additional role of ADHD symptoms in emotion regulation. In developmental perspective, emotion regulation is a key component in response to ADHD symptoms that leads to vulnerability for depression and anxiety (Christiansen et al. 2019). Emotion regulation is also a major aspect of coping with pain. In our sample, ADHD symptoms may have led to dysfunctional coping mechanisms and contributed to depression and anxiety in FM patients (Agar-Wilson and Jackson 2012).

Our findings suggesting a link between childhood ADHD symptoms and FM moderated by depression is in line with a possible shared mechanism that may have an impact on quality of life in patients with FM. Future studies will need to address the link between ADHD symptoms and objective and subjective cognitive functions in this clinical group. Although our study supports the suggestion of common pathophysiology, it has also demonstrated the effect of childhood ADHD symptoms on disease impact in patients with FM. When examining childhood ADHD, somatosensory dysfunction is an entity encountered along the disease course (Scherder et al. 2008). Dysfunction in pain processing in children with ADHD may lead to a tendency towards or exacerbation of FM symptoms in adulthood. Additionally, ADHD symptoms in childhood may augment the impact of pain in the following years by intensifying the experience of pain due to difficulty in regulating emotional experience (Koechlin et al. 2018; Steinberg and Drabick 2015). People with early life adversities show altered pain processing and are at increased risk of developing ADHD (Ackerman et al. 1998). Depression and anxiety symptoms in FM patients were associated with a history of childhood traumatic events. Bou Khalil et al. (2018) suggested that early life adversities may be linked to emotional dysregulation that can lead to an overlap syndrome between FM and ADHD. According to this model, increased negative biases, disinhibition and distractibility present as clinical features in FM and ADHD. In our findings, the mediating role of depression and anxiety symptoms can be explained as part of a possible overlap syndrome. That is, shared features of emotional dysregulation (including anxiety and depression) between ADHD and FM may play role in pathophysiology of both conditions.

Both anxiety and depression are well known factors to increase risk for pain and disability in FM, furthermore similar findings in this study support the current literature. In patients with FM, depressive disorder is the most frequent comorbid psychiatric condition with prevalence figures up to 20-80% (Fietta et al. 2007). Previous research indicated that depressive symptoms without a formal diagnosis of depressive disorder often accompany FM (Kato et al. 2006). When accompanied by depression, patients with FM are observed to report somatic symptoms and pain more commonly (Thieme et al. 2004). An asserted mechanism on how depression exacerbates pain in FM is the pain inhibition hypothesis (de Souza et al. 2009). Similarly, although the incidence of anxiety disorders in patients with FM is quite high when compared to those without anxiety, the association of anxiety levels and anxiety disorders with the severity of pain in FM and the effect of disease is relatively less clear (Raphael et al. 2006). Patients with FM accompanied by anxiety reported more somatic complaints and more tender point sum scores were found in these individuals than those without anxiety disorders (Thieme et al. 2004). In line with the current literature, our study showed the negative effect of high levels of anxiety on FM impact. The physiological reaction accompanying anxiety might be the underlying cause to decrease pain threshold and increase the soreness of pain in these patients (Schmidt and Cook 1999). In addition, depression and anxiety may increase the severity of the disease by means of affecting pain modulation through neurobiological mechanisms in which neurotransmitters such as serotonin and noradrenaline are involved (Blackburn-Munro and Blackburn-Munro 2001; Porro 2003).

In our study, ADHD symptoms measured by ASRS were not associated with pain and disability in FM, in contrast to the findings of van Rensburg et al. (2018). The regression analyses revealed that the impact of childhood ADHD symptoms on FM was mediated by depression and anxiety. Longitudinal follow-up studies examining ADHD have found that depressive and anxiety disorders are highly associated with ADHD symptoms occurring in the childhood (Uchida et al. 2018). Similarly, both depression and

dysthymia are often seen together with adult ADHD, with incidence of depressive disorder as 18.6-53.3% (Kessler et al. 2006; Torgersen et al. 2006). Furthermore, ADHD comorbidity in individuals with depressive disorder varies between 9% and 16% (McIntosh et al. 2009). Anxiety disorder is another common comorbidity in individuals with ADHD. The diagnosis of ADHD is often delayed in the context of comorbid anxiety when the symptoms complicate the clinical picture, possibly due to inhibition of impulsivity when feeling on the edge (Schatz and Rostain 2006). In a recent study, 28% of the individuals referred to a tertiary clinic for mood and anxiety assessment have been reported to manifest clinically undetected ADHD (Sternat et al. 2016). Emotion regulation problems in the children with ADHD may be the underlying condition for the development of depression and anxiety symptoms in their later life (Steinberg and Drabick 2015).

One of the main limitations of our study was the retrospective assessment of childhood ADHD symptoms along with self-report basis scale measurement of current adulthood ADHD symptoms lacking clinical interview (psychiatric evaluation). It should be noted that ADHD symptoms in the adulthood can easily be confused with many other psychiatric disorder symptoms. Therefore, it is difficult to determine whether the symptoms of attention deficit observed in FM are specific to FM or are a manifestation of ADHD itself. Due to the cross-sectional nature of our study, the impact of confounding factors may have been more pronounced. In this study, it was not possible to rule out possible confounding factors such as medication use, sleeping habits, eating behaviour or physical exercise as the data on those measures were not collected. Longitudinal studies are required to investigate the role of confounders more clearly. Using standardised clinical interviews will help ruling out the confounding effect of personality traits or bipolar disorder. Unfortunately, it is not possible to determine whether childhood ADHD symptoms lead to depressive symptoms in later life and therefore aggravation of pain in patients with FM because of the design of the study. Also, conducting the research only in female subjects creates problems in terms of generalisation of outcomes. On the other hand, a strength of our study is the relatively large size of the patient sample and a consideration of subclinical ADHD symptoms that may have an impact on clinical features of FM.

Taken together, the results of this study suggest that adult ADHD symptoms are not associated with the FM impact. However, childhood ADHD symptoms are found to play a role in the exacerbation of symptoms in the FM group. This effect was mediated by depression and anxiety symptoms. The interplay between childhood ADHD symptoms, vulnerability to depression and anxiety may be implicated in the development of FM. Longitudinal and epidemiological studies on children and adolescents with ADHD may help to determine if ADHD in childhood is an actual risk factor for disease impact in FM in adulthood. Our findings stress the importance of clinical evaluation of childhood and adulthood ADHD symptoms in patients with FM for treatment of probable ADHD comorbidity. Recognising and treating ADHD symptoms are also important for attenuating the severity of the disease in FM patients.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

References

- Ackerman PT, Newton JE, McPherson WB, Jones JG, Dykman RA. 1998. Prevalence of post-traumatic stress disorder and other psychiatric diagnoses in three groups of abused children (sexual, physical, and both). Child Abuse Negl. 22(8):759–774. doi: 10.1016/S0145-2134(98)00062-3
- Agar-Wilson M, Jackson T. 2012. Are emotion regulation skills related to adjustment among people with chronic pain, independent of pain coping? EJP. 16(1):105–114. doi:10.1016/j. ejpain.2011.05.011
- Arnold LM, Hudson JI, Hess EV, Ware AE, Fritz DA, Auchenbach MB, Starck LO, Keck PE. 2004. Family study of fibromyalgia. Arthritis Rheum. 50(3):944–952. doi:10.1002/art.20042
- Arnsten A. 2006. Fundamentals of attention-deficit/hyperactivity disorder: circuits and pathways. J Clin Psychiatry. 67 (Suppl. 8): 7–12.
- Beck AT, Epstein N, Brown G, Steer RA. 1988. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol. 56(6):893–897. doi:10.1037/0022-006X.56.6.893
- Beck AT, Steer RA, Carbin MG. 1988. Psychometric properties of the Beck Depression Inventory: twenty-five years of evaluation. Clin Psychol Rev. 8(1):77–100. doi:10.1016/0272-7358(88)90050-5
- Blackburn-Munro G, Blackburn-Munro R. 2001. Chronic pain, chronic stress and depression: coincidence or consequence? J Neuroendocrinol. 13(12):1009–1023. doi:10.1046/j.0007-1331. 2001.00727.x
- Bou Khalil R, Khoury E, Richa S. 2018. The comorbidity of fibromyalgia syndrome and attention deficit and hyperactivity disorder from a pathogenic perspective. Pain Med. 19(9): 1705–1709. doi:10.1093/pm/pny142
- Branco JC, Bannwarth B, Failde I, Abello Carbonell J, Blotman F, Spaeth M, Saraiva F, Nacci F, Thomas E, Caubère J-P, et al. 2010. Prevalence of fibromyalgia: a survey in five European countries. Semin Arthritis Rheum. 39(6):448–453. doi:10.1016/j. semarthrit.2008.12.003
- Burckhardt CS, Clark SR, Bennett RM. 1991. The fibromyalgia impact questionnaire: development and validation. J Rheumatol. 18(5):728–733.
- Christiansen H, Hirsch O, Albrecht B, Chavanon ML. 2019. Attention-deficit/hyperactivity disorder (ADHD) and emotion regulation over the life span. Curr Psychiatry Rep. 21(3):17. doi: 10.1007/s11920-019-1003-6
- de Souza JB, Potvin S, Goffaux P, Charest J, Marchand S. 2009. The deficit of pain inhibition in fibromyalgia is more pronounced in patients with comorbid depressive symptoms. Clin J Pain. 25(2):123–127. doi:10.1097/AJP.0b013e318183cfa4
- Dogan S, Öncü B, Varol-Saraçoglu G, Küçükgöncü S. 2009. Erişkin dikkat eksikliği hiperaktivite bozukluğu kendi bildirim ölçeği (ASRS-v1. 1): türkçe formunun geçerlilik ve güvenilirliği. Anadolu Psikiyatri Dergisi. 10(2):77–87.
- Fietta P, Fietta P, Manganelli P. 2007. Manganelli, fibromyalgia and psychiatric disorders. Acta Biomed. 78(2):88–95.
- Gardner A, Boles RG. 2011. Beyond the serotonin hypothesis: mitochondria, inflammation and neurodegeneration in major depression and affective spectrum disorders. Prog Neuropsychopharmacol Biol Psychiatry. 35(3):730–743. doi:10. 1016/j.pnpbp.2010.07.030

- Geisser ME, Donnell CS, Petzke F, Gracely RH, Clauw DJ, Williams DA. 2008. Comorbid somatic symptoms and functional status in patients with fibromyalgia and chronic fatigue syndrome: sensory amplification as a common mechanism. Psychosomatics. 49(3):235–242. doi:10.1176/appi.psy.49.3.235
- Golimstok AM, Fernandez MC, Garcia Basalo MM. 2015. Adult attention-deficit and hyperactivity disorder and fibromyalgia: a case-control study. Neuro Open J. 2(2):61–66.
- Gündüz N, Polat A, Erzincan E, Turan H, Sade I, Tural Ü. 2018. Psychiatric comorbidity and childhood trauma in fibromyalgia syndrome. Turk J Phys Med Rehab. 64(2):91–99. doi:10.5606/tftrd.2018.1470
- Hisli N. 1988. Beck Depresyon Envanterinin Geçerliliği Üzerine Bir Çalışma. Psikoloji Dergisi. 22:118–126.
- Kato K, Sullivan PF, Evengård B, Pedersen NL. 2006. Chronic widespread pain and its comorbidities: a population-based study. Arch Intern Med. 166(15):1649–1654. doi:10.1001/archinte.166. 15.1649
- Katz RS, Heard AR, Mills M, Leavitt F. 2004. The prevalence and clinical impact of reported cognitive difficulties (fibrofog) in patients with rheumatic disease with and without fibromyalgia. J Clin Rheumatol. 10(2):53–58. doi:10.1097/01.rhu.0000120895. 20623.9f
- Kessler RC, Adler L, Ames M, Demler O, Faraone S, Hiripi EVA, Howes MJ, Jin R, Secnik K, Spencer T, et al. 2005. The World Health Organization Adult ADHD Self-Report Scale (ASRS): a short screening scale for use in the general population. Psychol Med. 35(2):245–256. doi:10.1017/S0033291704002892
- Kessler RC, Adler L, Barkley R, Biederman J, Conners CK, Demler O, Faraone SV, Greenhill LL, Howes MJ, Secnik K, et al. 2006. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. AJP. 163(4):716–723. doi:10.1176/ajp.2006.163.4.716
- Koechlin H, Coakley R, Schechter N, Werner C, Kossowsky J. 2018. The role of emotion regulation in chronic pain: a systematic literature review. J Psychosom Res. 107:38–45. doi:10.1016/j.jpsychores.2018.02.002
- Kratz A, Williams D, Clauw D, Whibley D, Sliwinski M. 2019. (117) Characterizing fibrofog in daily life: ambulatory cognitive functioning in adults with fibromyalgia and matched controls. J Pain. 20(4):S5–S6. doi:10.1016/j.jpain.2019.01.036
- Krause KH, Krause J, Magyarosy I, Ernst E, Pongratz D. 1998. Fibromyalgia syndrome and attention deficit hyperactivity disorder: is there a comorbidity and are there consequences for the therapy of fibromyalgia syndrome? J Musculoskel Pain. 6(4): 111–116. doi:10.1300/J094v06n04 10
- Kravitz HM, Katz RS. 2015. Fibrofog and fibromyalgia: a narrative review and implications for clinical practice. Rheumatol Int. 35(7):1115–1125. doi:10.1007/s00296-014-3208-7
- Leavitt F, Katz RS. 2006. Distraction as a key determinant of impaired memory in patients with fibromyalgia. J Rheumatol. 33(1):127–132.
- Lichtenstein A, Tiosano S, Amital H. 2018. The complexities of fibromyalgia and its comorbidities. Curr Opin Rheumatol. 30(1): 94–100. doi:10.1097/BOR.0000000000000464
- McIntosh D, Kutcher S, Binder C, Levitt A, Fallu A, Rosenbluth M. 2009. Adult ADHD and comorbid depression: a consensus-derived diagnostic algorithm for ADHD. Neuropsychiatr Dis Treat. 5:137–150. doi:10.2147/ndt.s4720
- Mease P, Arnold LM, Choy EH, Clauw DJ, Crofford LJ, Glass JM, Martin SA, Morea J, Simon LEE, Strand CV, et al. 2009. Fibromyalgia syndrome module at OMERACT 9: domain



- construct. J Rheumatol. 36(10):2318-2329. doi:10.3899/jrheum. 090367
- Miró E, Martínez MP, Sánchez Al, Prados G, Lupiáñez J. 2015. Men and women with fibromyalgia: relation between attentional function and clinical symptoms. Br J Health Psychol. 20(3): 632-647. doi:10.1111/bjhp.12128
- Montoro CI, Duschek S, Muñoz Ladrón de Guevara C, Fernández-Serrano MJ, Reyes del Paso GA. 2015. Aberrant cerebral blood flow responses during cognition: implications for the understanding of cognitive deficits in fibromyalgia. Neuropsychology. 29(2):173-182. doi:10.1037/neu0000138
- Öncü B, Ölmez Ş, Şentürk V. 2005. Wender-Utah Derecelendirme Ölçeği Türkçe Formunun Erişkin Dikkat Eksikliği Ve Hiperaktivite Bozukluğu'nda Geçerlik ve Güvenilirlik Çalışması. Türk Psikiyatri Deraisi. 16(4):252-259.
- Porro CA. 2003. Functional imaging and pain: behavior, perception, and modulation. Neuroscientist. 9(5):354-369. doi:10.1177/ 1073858403253660
- Raphael K, Janal MN, Nayak S, Schwartz JE, Gallagher RM. 2006. Psychiatric comorbidities in a community sample of women with fibromyalgia. Pain. 124(1):117-125. doi:10.1016/j.pain.2006.
- Reyero F, Ponce G, Rodriguez-Jimenez R, Fernandez-Dapica P, Taboada D, Martin V, Navio M, Jimenez-Arriero MA, Hoenicka J, Palomo T. 2011. High frequency of childhood ADHD history in women with fibromyalgia. Eur Psychiatry. 26(8):482-483. doi:10. 1016/j.eurpsy.2010.03.012
- Rutledge DN, Mouttapa M, Wood PB. 2009. Symptom clusters in fibromyalgia: potential utility in patient assessment and treatment evaluation. Nurs Res. 58(5):359-367. doi:10.1097/NNR. 0b013e3181b499d2
- Sarmer S, Ergin S, Yavuzer G. 2000. The validity and reliability of the Turkish version of the Fibromyalgia Impact Questionnaire. Rheumatol Int. 20(1):9-12. doi:10.1007/s002960000077
- Schatz DB, Rostain AL. 2006. ADHD with comorbid anxiety: a review of the current literature. J Atten Disord. 10(2):141-149. doi:10.1177/1087054706286698
- Scherder EJ, Rommelse NN, Bröring T, Faraone SV, Sergeant JA. 2008. Somatosensory functioning and experienced pain in ADHD-families: a pilot study. Eur J Paediatr Neurol. 12(6): 461-469. doi:10.1016/j.ejpn.2007.11.004
- Schmidt NB, Cook JH. 1999. Effects of anxiety sensitivity on anxiety and pain during a cold pressor challenge in patients with

- panic disorder. Behav Res Ther. 37(4):313-323. doi:10.1016/ S0005-7967(98)00139-9
- Steinberg EA, Drabick DA. 2015. A developmental psychopathology perspective on ADHD and comorbid conditions: the role of emotion regulation. Child Psychiatry Hum Dev. 46(6): 951-966. doi:10.1007/s10578-015-0534-2
- Sternat T, Mohamed M, Furtado M, Canzonieri A, Armata RS, Epstein I, Cameron C, Katzman MA. 2016. SSRI treatment response may predict undetected attention deficit hyperactivity disorder in depressed patients. Paper presented at: Anxiety and Depression Association of America Annual Conference: March 31- April 3, 2016. Philadelphia (PA).
- Thieme K, Turk DC, Flor H. 2004. Comorbid depression and anxiety in fibromyalgia syndrome: relationship to somatic and psychosocial variables. Psychosom Med. 66(6):837-844. doi:10. 1097/01.psy.0000146329.63158.40
- Torgersen T. Giervan B. Rasmussen K. 2006. ADHD in adults: a study of clinical characteristics, impairment and comorbidity. Nordic Psychiatry. 60(1):38-43. doi:10.1080/ 08039480500520665
- Uchida M, Spencer TJ, Faraone SV, Biederman J. 2018. Adult outcome of ADHD: an overview of results from the MGH longitudinal family studies of pediatrically and psychiatrically referred youth with and without ADHD of both sexes. J Atten Disord. 22(6):523-534. doi:10.1177/1087054715604360
- Ulusoy MN, Şahin NH, Erkmen H. 1998. Turkish version of the Beck anxiety inventory: psychometric properties. J Cogn Pschother. 12:163-172.
- Van Rensburg R, Meyer HP, Hitchcock SA, Schuler CE. 2018. Screening for adult ADHD in patients with fibromyalgia syndrome. Pain Med. 19(9):1825-1831. doi:10.1093/pm/pnx275
- Ward MF, Wender PH, Reimherr FW. 1993. The Wender Utah Rating Scale: an aid in the retrospective diagnosis of childhood attention deficit hyperactivity disorder. Am J Psychiatry. 150(6): 885-890. doi:10.1176/ajp.150.6.885
- Wolfe F, Clauw DJ, Fitzcharles M-A, Goldenberg DL, Katz RS, Mease P, Russell AS, Russell IJ, Winfield JB, Yunus MB. 2010. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care Res. 62(5):600-610. doi:10.1002/acr.20140
- Yılmaz E, Tamam L. 2018. Attention-deficit hyperactivity disorder and impulsivity in female patients with fibromyalgia. Neuropsychiatr Dis Treat. 14:1883–1889. doi:10.2147/NDT. S159312