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Diagnosis and Treatment of Attention-Deficit Hyperactivity Disorder in Patients with Chronic Pain

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Abstract

Aims: To investigate rates of attention-deficit hyperactivity disorder (ADHD) in patients with chronic pain attending a pain clinic, the effects of a screening measure for ADHD in patients with chronic pain, and the effects of ADHD drugs on both pain and ADHD symptoms. Methods: We retrospectively surveyed 110 patients with chronic pain visiting the Anesthesiology and Pain Relief Center at the University of Tokyo in Japan, who had also consulted a psychiatrist, between April 2012 and July 2015. Results: Of the total of 110 patients with chronic pain, 35 (31.8%) were also diagnosed with ADHD, and the average Wender Utah Rating Scale (WURS) score among the ADHD patients was 39.0 ± 22.1 (n = 25). Only 36.0% of these patients exceeded the cutoff value, suggesting that 64.0% of the patients with ADHD were not identified by screening with the WURS. Twenty-six patients initiated treatment with ADHD medication, with dosage adjustment completed in 21. Of these 21 patients 20 (95.0%) had improved ADHD symptoms. Improved pain symptoms were observed in 14 patients (66.6%), with a reduction in the pain numerical rating scale of 64.7% ± 30.1%. Conclusions: This is the first study investigating the comorbidity of ADHD and chronic pain at pain clinics showing a high level of comorbidity and amelioration of pain and ADHD symptoms with treatment. Careful interpretation is required when the WURS is used to screen patients with chronic pain.

1. Introduction

Chronic pain is a condition in which the main symptom is persistent pain for
more than 3 months after the acute phase [1]. In Japan, 13.4% of the general
population (approximately 17 million people) experience this symptom [2]. This
represents a serious burden on Japanese society, with annual economic losses
amounting to 370 billion yen [3]. Chronic pain occurs and persists due to com-
plicated interactions between physical and psychosocial factors, which often
makes it difficult to treat. Therefore, it is important to find more effective treat-
ments that will improve the condition more rapidly, as this will have benefits
from both health control and socio-economic perspectives.

Recent studies report that among patients with chronic pain, there are high
numbers who have had multiple traffic accidents or who suffer from memory
problems, both of which may suggest that they have attention-deficit hyperactiv-
ity disorder (ADHD). Indeed, it has been reported that treatment with ADHD
medication (central nervous system stimulants) may effectively treat not only
attention or memory problems, but also chronic pain symptoms [4].

It has also been suggested that fibromyalgia (FM) and chronic fatigue syn-
drome (CFS) may be related to ADHD [5] [6]. Therefore, ADHD should be in-
cluded as a potential differential diagnosis during assessment for these disorders
if patients complain of widespread muscle pain, tiredness, and sleep problems
without significant physical abnormalities. A high rate of concurrent ADHD
(25% - 80%) has been reported in individuals with FM [7] [8], and it has also
been reported that 32.3% of patients with FM suffered from ADHD during early
childhood, compared with 2.5% in a control group [9]. Moreover, patients with
FM exhibit significant memory problems more often than healthy controls, and
this is reportedly due to heightened distractibility among patients with FM [10].
Similarly, 50% - 80% of patients with CFS exhibit impairments in memory, con-
centration, and attention [11]. Furthermore, it has been reported that many pa-
tients who consult a doctor for ADHD as their primary complaint have a pre-
vious diagnosis of FM or CFS [5]. Many of the patients with comorbid FM or
CFS and ADHD have shown improvements in both ADHD and pain symptoms,
when treated with ADHD medications (central nervous system stimulants) [5].

ADHD is a developmental disorder known to be associated with functional
impairments in the dopamine and noradrenaline systems, leading to disorders in
the executive, reward, and time-processing systems [12]. There are several sub-
types of ADHD, including predominantly inattentive, predominantly hyperac-
tive-impulsive, and combined subtypes, each of which persists from early child-

hood. Patients with the predominantly hyperactive-impulsive subtype are easy to recognize due to their markedly problematic behaviors [5]. In contrast, in patients with the predominantly inattentive subtype, their ADHD symptoms are often masked by symptoms of depression and anxiety, meaning that their ADHD symptoms are often not correctly diagnosed and escape clinical awareness [5] [7]. The symptoms of ADHD can be improved with ADHD medications such as methylphenidate (a central nervous system stimulant) and atomoxetine (a non-central nervous system stimulant).

Given that medications for ADHD may improve chronic pain symptoms of the musculoskeletal system (e.g., lower back pain) among patients with FM and CFS, these medications may shed light on the treatment and management of chronic pain, which are often difficult. However, there are only a few previous reports on rates of patients with FM [8] [9] or CFS [13] who are also diagnosed with ADHD. Similarly, the limited studies performed to date have reported varied results with regard to the effects of central nervous stimulant treatments for ADHD on pain symptoms [5] [6] [7]. To our knowledge, there have been no reports on the rates of patients with chronic pain in the musculoskeletal system who are also diagnosed with ADHD, or on their responsiveness to treatment. Furthermore, although some studies have reported the effects of central nervous system stimulant treatments for ADHD in patients with FM and CFS [5] [6] [7], there have been no reports on the treatment effects of non-central nervous system stimulant treatments for ADHD in such patients.

In the present study, patients with chronic pain whose symptoms were considered to be largely a result of psycho-social factors were recruited from a specialized pain clinic. All of these patients had been referred to a psychiatrist. The following were investigated: 1) The rate of patients with an ADHD diagnosis; 2) the effect of a screening measure for ADHD among patients with chronic pain; and 3) the effects of ADHD medications (central nervous system stimulants and non-central nervous system stimulants) on pain symptoms, as well as ADHD symptoms in individuals with both chronic pain and ADHD.

2. Methods

2.1. Patients

We retrospectively surveyed 110 patients (37 male, 73 female) with chronic pain who had been referred to a psychiatrist (S.K.) by an attending physician at the Anesthesiology and Pain Relief Center, University of Tokyo Hospital, Japan, between April 2012 and July 2015. All patients provided written informed consent, and their anonymity was preserved. The study was approved by the appropriate ethics committee of the University of Tokyo Hospital, Japan (application/ approval number 3678).

2.2. Measures

To assess treatment outcome, we used mean recorded pain intensity measured

via the Numerical Rating Scale (NRS) [14]. The diagnosis of ADHD was made during an interview by a psychiatrist (S.K.) based on DSM-IV-TR criteria [15]. In addition, patients completed a self-assessment screening measure, the Wender Utah Rating Scale (WURS) [16]. The WURS evaluates ADHD symptoms experienced by patients in childhood and during their school years. It is scored on a 5-point scale and comprises 25 items that can effectively discriminate adults with ADHD from healthy controls [16]. A score exceeding the cutoff value of 46 indicates a high likelihood of the patient having adult ADHD.

Comorbidity with pervasive developmental disorder was assessed by a psychiatrist (S.K.) based on DSM-IV-TR criteria [15]. Retrospective assessment of clinical responses was made by a psychiatrist (S.K.) using the Clinical Global Impression Severity (CGI-S) subscale for ADHD severity and the Clinical Global Impression Improvement (CGI-I) subscale for treatment response [17]. The CGI-S rates severity of ADHD from 1 - 7, where 1 = normal, 2 = borderline mentally ill, 3 = mildly ill, 4 = moderately ill, 5 = markedly ill, 6 = severely ill, and 7 = extremely ill. The CGI-I assesses ADHD symptoms relative to baseline, where 1 = very much improved, 2 = much improved, 3 = minimally improved, 4 = no change, 5 = minimally worse, 6 = much worse, and 7 = very much worse. Patients with chronic pain and concomitant ADHD received psychiatric treatment (pharmaceutical and cognitive-behavioral therapies) for ADHD symptoms, and improvement was assessed via the above-mentioned assessment measures.

2.3. Statistical Analysis

Initially, we used descriptive statistics to represent the frequency of ADHD diagnosis in patients with chronic pain. Next, we assessed the effects of pharmaceutical treatments on ADHD symptoms, as well as on chronic pain. We used the Jonckheere-Terpstra test to identify possible trends in improvement of ADHD symptoms and chronic pain. We analyzed relationships between improvement in NRS and gender and age (divided into 10-year strata) using Student's *t*-test and the Jonckheere-Terpstra test, respectively. Lastly, we investigated age differences between groups with and without 100% improvement in the NRS, via Student's t-test. Values of $P < 0.05$ were considered significant. All statistical analyses except the Jonckheere-Terpstra test were performed with JMP pro, version 11 (SAS Institute of Japan, Tokyo, Japan). The Jonckheere-Terpstra test was performed with SPSS version 23 (IBM Japan, Tokyo, Japan).

3. Results

3.1. Patient Characteristics

Of 110 patients with chronic pain who were referred to a psychiatrist, 35 (31.8%) were diagnosed with ADHD and their characteristics are shown in Table 1. None of these patients had a previous diagnosis of ADHD. Among the patients with ADHD, 25 were female (mean age 46.9 ± 16.8 years) and 10 were male

Table 1. Characteristics and treatment effects of the patients.

No.	Sex	Age	Main complaint	Pain region	Duration (months)	WURS	IQ	Subtype	PDD	Before CGI-S	After CGI-S	CGI-I	Before NRS	After NRS	Improvement in NRS (%)	Meth	Atom
1	F	17	widespread pain	more than three major sites	96	NA	67	inattentive	–	4	3	3	9	9		36 mg	
2	F	25	back pain	lower back, lumbar spine, sacrum, coccyx	14	26	89	inattentive	–	4	2	1	8	0	100.0	18 mg	
3	F	30	head and cervical pain	head, face, mouth	12	82	95	inattentive	–	4			9	9		72 mg	
4	F	31	left hand, cervical, left upper extremity pain	more than three major sites	132	56	103	inattentive	–	5	4	3	8	8		36 mg	
5	F	32	widespread pain	more than three major sites	8	21	81	combined	–	5			9				
6	F	32	sternum, back, lower back pain	more than three major sites	24	69	77	combined	–	4			8				
7	F	33	widespread pain	more than three major sites	12	81	46	inattentive	–	4	2	2	10	8	20.0	72 mg	
8	F	37	numbness and pain in the right arm	upper shoulder, upper limbs	6	NA	104	inattentive	–	4			6				
9	F	39	right lower extremity pain	lower limbs	48	NA	81	combined	–	4			8				
10	F	41	pain deep inside the clavicle	thoracic region	15	13	91	inattentive	–	3			10	2	80.0	CBT	CBT
11	F	42	cervical, shoulder, elbow pain	more than three major sites	276	49	94	inattentive	–	4	2	1	7	0	100.0	72 mg	120 mg
12	F	42	lower back pain	lower back, lumbar spine, sacrum, coccyx	94	NA	113	inattentive	–	4	2	2	1	0	100.0	36 mg	
13	F	42	pain within the ear	head, face, mouth	9	17	64	combined	–	4			10			AE	
14	F	42	widespread pain	more than three major sites	36	40	104	inattentive	–	4			7				

Continued

15	F	47	cervical, chest, knee pain	more than three major sites	444	10	65	combined	–	6	5	3	10	10		54 mg	
16	F	47	pain around the eyes	head, face, mouth	24	NA	106	inattentive	–	4	3	3	10	10		36 mg	
17	F	52	pain in both shoulders	upper shoulder, upper limbs	24	40	104	combined	–	5	3	1	8	0	100.0	AE	80 mg
18	F	55	lower back and lower extremity pain	lower back, lumbar spine, sacrum, coccyx	120	54	76	inattentive	–	6	3	1	8	3	62.5	72 mg	120 mg
19	F	60	lower back pain	lower back, lumbar spine, sacrum, coccyx	60	47	95	inattentive	–	4	2	1	7	4	42.8	72 mg	
20	F	66	face, cervical pain	head, face, mouth	84	3	123	combined	–	5	3	2	5	1	80.0	54 mg	
21	F	67	buttocks, lower extremity pain	lower limbs	4	24	127	inattentive	–	4			7	3	57.1	CBT	CBT
22	F	69	non-standard toothache	head, face, mouth	180	46	103	combined	–	6	4	2	6	6		18 mg	80 mg
23	F	72	both hands, right lower extremity pain	more than three major sites	24	25	126	inattentive	–	3	2	2	8	6	25.0	36 mg	
24	F	76	lower back and lower extremity pain	lower back, lumbar spine, sacrum, coccyx	180	NA	102	combined	–	4			10				
25	F	77	thoracic pain	thoracic region	192	NA	96	inattentive	–	3			8	8		AE	AE
26	M	27	anterior chest pain	thoracic region	96	NA	78	combined	–	4			7				
27	M	34	back and neck pain	lower back, lumbar spine, sacrum, coccyx	300	24	91	inattentive	+	6	5	3	6	6		36 mg	
28	M	35	headache	head, face, mouth	72	NA	112	inattentive	–	3			6	0	100.0	CBT	CBT
29	M	39	widespread pain	more than three major sites	72	26	100	inattentive	–	4	2	1	7	4	42.8	72 mg	120 mg

Continued

30	M	40	widespread pain	more than three major sites	27	54	104	combined	–	4	2	1	10	2	80.0		18 mg
31	M	44	lower back pain	lower back, lumbar spine, sacrum, coccyx	120	41	130	inattentive	+	4	3		7			AE	
32	M	47	lower back pain	lower back, lumbar spine, sacrum, coccyx	72	13	116	combined	–	4	3	3	9	5	44.4	AE	80 mg
33	M	57	lower back and lower extremity pain	lower back, lumbar spine, sacrum, coccyx	12	70	85	combined	–	4	2	2	6	4	30.0		18 mg
34	M	71	lower back pain	lower back, lumbar spine, sacrum, coccyx	48	NA	100	combined	–	5			8			AE	AE
35	M	79	lower back pain	lower back, lumbar spine, sacrum, coccyx	300	39	130	inattentive	–	4	2	1	9	2	77.7	AE	120 mg

WURS, Wender Utah Rating Scale; PDD, pervasive developmental disorder; CGI-S, Clinical Global Impression Severity; CGI-I, Clinical Global Impression Improvement; NRS, Numerical Rating Scale; Meth, methylphenidate; CBT, cognitive-behavioral therapy; AE, adverse effect, NA: not available. CGI-S key: 1 = normal, 2 = borderline mentally ill, 3 = mildly ill, 4 = moderately ill, 5 = markedly ill, 6 = severely ill, and 7 = extremely ill. CGI-I key: 1 = very much improved, 2 = much improved, 3 = minimally improved, 4 = no change, 5 = minimally worse, 6 = much worse, 7 = very much worse

(mean age 47.3 ± 16.8 years). As determined via the Wechsler Adult Intelligence Scale-III (WAIS-III) [18], the 35 patients had a mean IQ of 96.5 ± 19.9.

Completed WURS forms were received from 25 patients, and the mean score was 39.0 ± 22.1. With regard to ADHD subcategories, 21 patients were classified as the predominantly inattentive subtype and 14 as the combined subtype. Comorbid pervasive developmental disorder was only diagnosed in 2 patients. No patients met the DSM-IV-TR criteria for major depressive disorder.

Patients identified their primary sites of pain based on the International Association for the Study of Pain (IASP) classification [19], with 11 (31.4%) answering "more than three major sites", 11 (31.4%) answering "lower back, lumbar spine, sacrum, and coccyx", and 6 (17.1%) answering "head, face, and mouth." These answers comprised 80.0% of the total. The mean pain intensity measured with the NRS was 7.8 ± 1.8. The mean duration of pain symptoms was 92.5 ± 103.7 months (7.7 ± 8.6 years).

3.2. Treatment Effects on ADHD Symptoms and Chronic Pain

Figure 1 shows the drug administration algorithm for the 35 patients diagnosed with ADHD. In this algorithm, in principle, a central nervous system stimulant is the first-choice treatment. If after subsequent evaluation the effect of the stimulant is deemed insufficient, the algorithm approves either switching to a non-central nervous system stimulant, or co-administration of one drug from each class.

Twenty-six patients agreed to initiate pharmaceutical treatment with a central nervous system stimulant and/or a non-central nervous system stimulant. Following the withdrawal of 5 patients from pharmaceutical treatment due to adverse events or cancellation, dosage adjustment was completed in 21 patients. We assessed ADHD symptoms in these 21 patients via the CGI-I, and observed improvements in 20 (95.0%). Improvements in pain symptoms as determined via the NRS were observed in 14/20 (66.6%).

Twenty patients with improved CGI-I for ADHD symptoms were divided into three subgroups according to their degree of improvement. Eight (40%) were considered "very much improved", 6 (30%) "much improved", and 6 (30%) "minimally improved". Among 14 patients showing improvements in both ADHD symptoms and chronic pain, there was a mean reduction in pain NRS score of 64.7% ± 30.1%.

The mean dosages (mg/day) of administered drugs and mean improvement rates (%) were 40.5 ± 23.0 mg/day and 59.7% ± 33.8% for methylphenidate alone
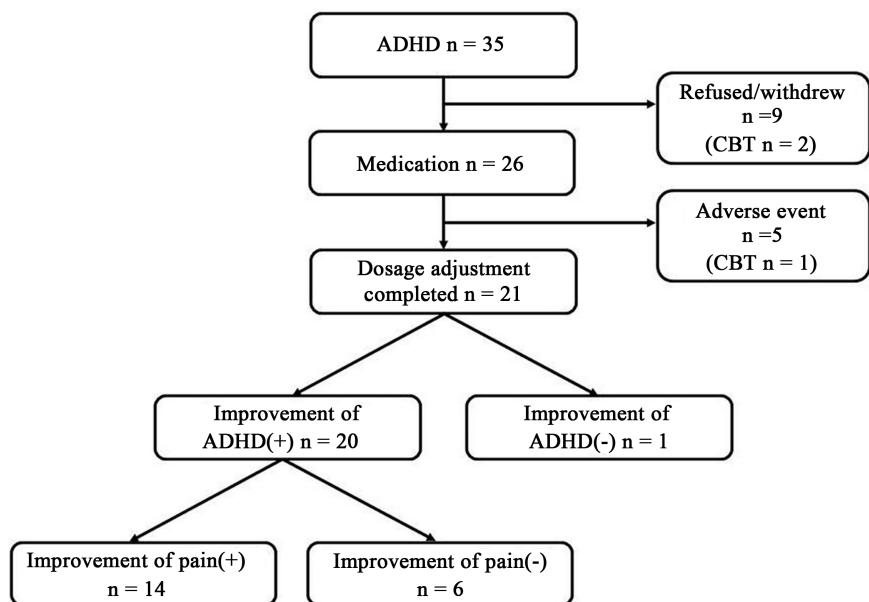

Figure 1. Flowchart of treatment selection in patients with chronic pain presenting with ADHD. Among 110 patients, 35 (31.8%) were diagnosed with ADHD. Of these 35 patients, 21 completed drug adjustment. Of these 21 patients, ADHD symptoms improved in 20 (95%). Pain symptoms also improved in most patients who completed dosage adjustment. ADHD, attention-deficit hyperactivity disorder; CBT, cognitive-behavioral therapy.

(n = 8); 93.3 ± 23.0 mg/day and 74.0% ± 27.9% for atomoxetine alone (n = 3); and for concurrent administration of methylphenidate and atomoxetine (n = 3) they were 72.0 ± 0 mg/day for methylphenidate, 120 ± 0 mg/day for atomoxetine, and 68.4% ± 29.0%. Among 14 patients who rejected pharmaceutical treatment or dropped out due to adverse events, 3 agreed to receive cognitive-behavioral therapy (CBT), and they responded well to CBT with a mean improvement rate of 79.0% ± 21.4%.

There were improvements in chronic pain in 17 patients (14 with pharmacotherapy and 3 with CBT). Improvement rates as determined via the NRS were 68.3% ± 38.8% in patients with "mild" ADHD (n = 3), 63.2% ± 29.6% in patients with "moderate" ADHD (n = 11), and 80.8% ± 18.8% in patients with worse than "marked" ADHD (n = 3). When we examined the relationship between ADHD severity and NRS-determined pain improvement using the Jonckheere-Terpstra test, there was no significant trend ($P = 0.58$). However, it was notable that the NRS-determined pain improvement rate exceeded 80% in patients with worse than "marked" ADHD severity.

The NRS improvement rate for men (n = 6) was 62.5% ± 27.3%, and for women (n = 11) it was 69.8% ± 30.5%, with no significant difference between the sexes (*t*-test, $P = 0.63$). We also assessed NRS improvement rates according to age group. Those aged ≤ 40 years (n = 9) had a rate of 74.1% ± 30.7%; those aged 50 - 59 years (n = 3) had a rate of 64.2% ± 35.0%; those aged 60 - 69 years (n = 3) had a rate of 60.0% ± 18.8%; and those aged 70 or more years (n = 2) had a rate of 51.3% ± 37.3%. Analysis of the relationship between age group and NRS improvement rate showed that improvement rate tended to decline as age increased, albeit non-significantly (Jonckheere-Terpstra test, $P = 0.19$). The average age of the patients who showed 100% NRS improvement (n = 5) was 39.2 ± 10.0 years, and the average age of patients who did not show 100% improvement (n = 12) was 54.7 ± 14.7. The difference between these two groups was statistically significant (*t*-test, $P = 0.05$).

4. Discussion

In the present study, a psychiatrist (S.K.) at our pain clinic with extensive experience in the treatment of chronic pain was responsible for providing psychiatric diagnoses according to the DSM-IV-TR diagnostic criteria [15]. In the current study, 31.8% of patients were diagnosed with ADHD, and none of these patients had been diagnosed with ADHD in the past. Although this figure is lower than the rate of comorbid ADHD (80%) previously reported in a clinic specializing in FM [7], it is similar to the figure of 25% reported in patients with FM by Derksen *et al.* [8]. A recent meta-analysis estimated that the global prevalence of adult ADHD was 2.5% [20], while it has been estimated to be 1.7% in Japan [21]. The rate in the current study was 12.7 times that of the estimated global rate, and 19.3 times that of the estimated rate in Japan. ADHD prevalence among patients with refractory chronic pain at pain clinics is considered to be markedly high.

Previous studies have reported a similar prevalence of ADHD among male and female adults [21] [22]. In the present study, there were more than twice as many female patients as male patients (25 vs. 10). This is consistent with previous reports that the frequency of pain is higher, the duration of pain is longer, and the tendency to seek treatment is higher in women [23]. It has also been reported that there are more female patients with FM or CFS who have comorbid ADHD than there are males [5]. A potential relationship with sex hormones has been suggested as the cause of these sex differences. Notably, it has been reported that in some women ADHD symptoms worsen during periods when the female hormone estrogen is reduced (for example before a menstrual period, after childbirth, and during menopause), which may aggravate inattention, a tendency to get upset, and emotional instability [24]. In the current study, there were 25 women with an average age of 46.9 ± 16.8 years, therefore female hormonal factors associated with menopause may have had an impact on the results.

Among 35 patients diagnosed with ADHD in the present study, the average WURS score for the 25 patients who completed the assessment was 39.0 ± 22.1. Only 36% of these exceeded the cutoff value, thus 64% of patients with ADHD were not identified by screening with the WURS. Subsections of the WURS do not directly relate to attention deficit symptoms, but use "academic underachievement" as a result of attention deficit as a proxy. In the current study, the mean IQ of patients with ADHD was 96.5 ± 19.9, and as they had not generally underachieved in school, their attention deficit symptoms may not have been reflected in their WURS score. Furthermore, a factor analysis of the Japanese version of the WURS did not reveal factors related to "attention deficit" [25]. Therefore, it has been suggested that while the WURS is a useful assessment tool to use to identify hyperactivity, it may not be appropriate for identifying cases of predominantly inattentive ADHD [26]. In particular, careful interpretation is required when the WURS is used to screen patients with chronic pain as well as attention deficit [7].

In the present study, of the patients who showed improvements in pain as well as ADHD symptoms, 8 received methylphenidate alone, 3 received atomoxetine alone, and 3 received concurrent administration of both drugs. This suggests the existence of subgroups among patients with ADHD and concurrent chronic pain, who differ in their neurological conditions. As mentioned above, FM and CFS can reportedly be improved by central nervous system stimulants [5] [6] [7], and administration of atomoxetine and central nervous system stimulants has been considered an appropriate treatment strategy to alleviate executive dysfunction in FM [27]. There has been speculation about the potential mechanisms underlying these changes. Patients with ADHD who exhibit inattention symptoms are highly sensitive to the environment, and have difficulty "filtering out" unpleasant stimuli and showing intolerance to mild tactile stimuli [28]. They are prone to overreacting in stressful environments, and it has been suggested that they are prone to developing chronic pain because their cognitive

impairments make it difficult for them to filter out physical stimuli (including pain and tinnitus) throughout their bodies [6]. Central nervous system stimulants are considered to effectively enhance the filtering function by increasing the signal-to-noise ratio, allowing patients to properly discriminate various irritating stimuli and improving pain symptoms [29].

In the present study, the average improvement rates in NRS scores for the different categories of the CGI-I were 75.7% ± 24.3% for "very much improved" (n = 8), 51.0% ± 36.5% for "much improved" (n = 5), and 44.4% for "minimally improved" (n = 1). This suggests that patients achieving greater improvement in ADHD symptoms may exhibit greater improvements in pain, too. Nine patients (25.7%) either declined or discontinued with drug treatment for a variety of reasons, including "I do not accept a diagnosis of ADHD", "I do not want to receive drug treatment", and "I could not wait until the treatment took effect", among others. In some cases, pain symptoms were not improved but the drug treatment was effective for ADHD symptoms. This situation may have resulted from the dosage not being adjusted adequately, which may in turn have been due to inadequate dosing management or a lack of patience with regard to waiting to determine the effects of gradual dose increments. It is possible that devising better ways of informing patients about their diagnosis and the management of drug regimens may facilitate further improvements.

Notably, in 3 cases where drug treatment was ineffective in the current study, CBT (assertive training and operant conditioning) was conducted and improvements in pain symptoms were achieved. This suggests that psychological intervention alone may be able to improve a patient's condition even if they have concurrent chronic pain and ADHD. Thus, the optimal treatment modality should be considered on a case-by-case basis.

Two main subtypes of ADHD were diagnosed in the patients in the current study, including 21 patients (60%) with the predominantly inattentive subtype, and 14 (40%) with the combined subtype. This is consistent with a previous report that most patients with FM or CFS who have comorbid ADHD have either the predominantly inattentive or the combined subtype [6] [7]. However, epidemiological studies of the prevalence of adult ADHD suggest that 78.5% of patients have the predominantly inattentive subtype, [21], so this could also be considered consistent with general trends in adult ADHD cases. No patients in the current study had previously been diagnosed with ADHD. This may be because patients with the predominantly inattentive subtype do not exhibit noticeable symptoms, and patients with the combined subtype who have hyperactivity also tend to exhibit reduced hyperactive-impulsive symptoms as they grow older [30]. This makes such symptoms difficult to observe. Furthermore, patients often state that they cannot keep still because of pain, making it all the more difficult to recognize that ADHD is the cause of their hyperactivity. In addition, because pain clinicians are generally not experienced in the diagnosis of ADHD, in many patients symptoms of ADHD may go unnoticed during assessments.

Many patients with chronic pain pay excessive attention to pain stimuli, which in turn increases the feeling of pain [31]. According to the gate control theory [32], this is due to the fact that attention to pain inhibits the descending pain inhibitory system, thereby increasing information that reaches the brain. For this reason, a technique called "distraction" which diverts attention from a pain stimulus is recommended in CBT for chronic pain [31]. Patients with ADHD are easily distracted by matters that in ordinary circumstances would be outside their interest. Conversely, they also devote excessive attention to matters that interest them. We suspect that accordingly, when excessive attention is paid to an unpleasant pain stimulus, the effect of the descending pain inhibitory system diminishes and the feeling of pain increases.

In our experience, patients with chronic pain can be broadly classified into two types depending on activity patterns. One type tends to reduce their amount of activity for fear of pain exacerbation, and the other type desires to continue their activities without taking breaks [31]. The former tend to engage in catastrophic thinking about pain and fear associated with performing various physical activities. When patients with ADHD are exposed to stressors such as pain, it induces excess norepinephrine and dopamine release in their prefrontal cortices, which often makes them anxious due to hyper-arousal [27], and causes them to fear pain. In our clinical experience, patients with the predominantly inattentive subtype of ADHD tend to exhibit activity reduction. The other kind of patient is known to engage in an overly active behavioral pattern, undertaking too much exercise rather than gradually increasing exercise intensity. As a result, pain is aggravated and subsequently they must stop activities. This has been dubbed the "yo-yo pattern" [31]. Given these considerations, "pacing" is recommended as a technique to gradually increase exercise intensity in accordance with a plan during CBT for patients with chronic pain [31]. When this type of patient is asked why they engage in too much exercise all at once, they will usually assert that they do not have the patience to gradually increase the amount of exercise they engage in, and that they cannot keep still in order to promptly alleviate pain. This represents the presence of strong impulsiveness and hyperactivity. In our clinical experience, combined ADHD patients tend to exhibit this hyperactivity type.

Some patients with chronic pain often express stronger anger towards their family members, doctors, employers, and even themselves than individuals without chronic pain do, and their feelings of anger are reportedly strongly correlated with the intensity of their chronic pain, self-conscious impairments, and the frequency of their pain behaviors [33]. The brain circuit related to anger expression reportedly overlaps with the circuit related to pain [34]. As a result of this overlap, previous episodes associated with anger experienced by patients with ADHD may recur vividly, and they often talk about a feeling of strong anger as if they have just experienced the emotion even several years after the preceding episode. It may be that such irrepressible feelings of anger induce physical pain.

5. Conclusion

In summary, characteristics of patients with ADHD such as over-attentiveness to pain and being overly active may facilitate a vulnerability to developing chronic pain. "Excessive attention," "hyperactivity," and "anger" are observed in many patients with chronic pain, particularly those with ADHD. To our knowledge, this is the first study to report on the comorbidity of ADHD and chronic pain at a pain clinic. However, further research is required to replicate our results with regard to ADHD prevalence among patients with chronic pain who visit pain clinics.

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Disclosure Statement

The authors declare that there are no conflicts of interest.

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