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Research

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Adult Attention-Deficit and Hyperactivity Disorder and Fibromyalgia: A Case-Control Study

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ABSTRACT

Introduction: Fibromyalgia syndrome (FMS) is a disorder characterized by widespread musculoskeletal pain accompanied by fatigue, sleep, memory and mood issues. An association between attention deficit and fibromyalgia was reported. However, to our knowledge, there are few articles reporting an association between adult Attention Deficit Hyperactivity Disorder (ADHD) and FMS.
We hypothesized that ADHD should be frequently associated with FMS. To confirm this hypothesis we conducted this study.
Methods: Patients with Cognitive Complaint (CC) recruited from the membership of the Italian Hospital Medical Care Program in Argentina from 2009 to 2013 were classified as ADHD or without ADHD, and compared with Normal Controls (NC) about the presence of FMS. Adapted DSM-IV criteria for adult ADHD and validated to Spanish Wender Utah Rating Scale were used to identify individuals with adult ADHD. FMS was diagnosed according to Criteria Classification of Fibromyalgia of American College of Rheumatology of 1990. Analysis of categorical variables was carried out using chi-square. Mann-Whitney test was used for continuous variables. Statistical significance was $P<0.05$.
Results: We identified 154 patients with ADHD, 71 NC, and 262 with CC without ADHD. Amongst ADHD cases, 37.7% were men, the median age was 72.5 years, in NC group, 40.8% were men with a mean age of 71.9, and in CC group, and 40% were men with a median age of 71.4 years. No significant differences in these variables between groups or in the years of education were found.
Frequency of FMS was 24.7% in ADHD cases, 4.6% in CC group and 0% in NC. Prevalence of FMS in ADHD patients was significantly higher compared with other control groups ($P<0.00001$, 95% confidence interval extends from 0.0786 to 0.1330).
Conclusion: In our sample, FMS is more prevalent in adult ADHD cases than in NC and CC patients as we expected. It should be done future studies to characterize the association of this disorders.

KEYWORDS: ADHD; Fibromyalgia; Adult attention-deficit and hyperactivity disorder; FMS.

ABBREVIATIONS: FMS: Fibromyalgia syndrome; ADHD: Attention Deficit Hyperactivity Disorder; CC: Cognitive Complaint; NC: Normal Controls; IHMCP: Italian Hospital Medical Care Program; WURS: Wender Utah Rating Scale.

INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) affects 5-12% of children in the United States[1] being the most prevalent cause of childhood learning disabilities.[2,3] The only epidemiological report of our country (Argentina) shows similar finding, with a prevalence of 9% of this disorder in children.[4]

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This disorder is characterized by symptoms of inattention, hyperactivity, and impulsivity. These characteristics persist into adulthood.[5,6] Unfortunately, there are very few epidemiological studies in adulthood and this disorder is usually underdiagnosed.[7] However, in recent years, there are some reports about this disorder comorbidities.[8]

Fibromyalgia syndrome (FMS) is the second most common disorder, after osteoarthritis, observed by rheumatologists. It's a chronic, and debilitating disorder that impair the quality of life of 2-4% of the population, with 9:1 female-to-male incidence ratio.[9] The defining symptoms of FMS include chronic widespread pain, intense pain in response to tactile pressure (allodynia), prolonged muscle spasms, weakness in the limbs, nerve pain, muscle twitching, palpitations and diffuse tenderness, along with fatigue, sleep disturbance and cognitive impairments. These impairments affect short and long- term memory, short-term memory consolidation, speed of information processing, and include reduced attention span and limited multi-tasking performance as well.[10-12]

The profile of cognitive symptoms in FMS and ADHD is very similar, and ADHD is commonly mistaken with anxiety, depression and other behavioral disorders[13] which are comorbidities of FMS.[14,15] FMS and ADHD are part of a family of related disorders known as affective spectrum disorders.[16] These disorders share physiologic abnormalities and genetic risk factors that may be central to their etiology.[17] One previous report showed an association between fibromyalgia and a polymorphism of the dopamine D4 receptor and its relationship to novelty seeking personality traits, which symptoms are very similar to ADHD.[18] Furthermore, the polymorphism of the dopamine D4 receptor has been associated to ADHD in children and adulthood.[19] Considering these investigations, in both disorders (FMS and ADHD), an overlap in clinical features and neurobiologic substrate was found. However, to our knowledge, there are few articles reporting an association between adult ADHD and FMS.[20-22] Moreover, there is no case-control study of the association.

We hypothesized that both syndromes are associated. Since the cognitive deficit has been described in both entities, to confirm the hypothesis, we conducted this study, comparing a more elderly group with ADHD with another group of cognitive impairment from other causes, assuming that there may be even more cases of FMS than usual, in this kind of control group.

METHODS

Participants

This study was conducted at the Italian Hospital Medical Care Program (IHMCP) in Buenos Aires, Argentina with approval from the institutional Review a Board of the IHMCP research committee. Patients and controls were analyzed after informed consent was signed (a general approval for the release for medical records and data for use in this study). Patients with ADHD and controls were recruited from the membership of the IHMCP, a large prepaid health maintenance organization model. IHMCP provides comprehensive medical and health services through two medical center hospitals and 24 medical office buildings to over 140,000 members primarily located in the urban areas around the Autonomous City of Buenos Aires, Argentina. Approximately, 5-7% of the population in this geographic area is affiliated to the IHMCP. The IHMCP population characteristics are closely representative of the metropolitan population of the Autonomous City of Buenos Aires, as demonstrated by 2001 census data in a series of socioeconomic categories (Table 1).

	City of Buenos Aires (%)	IHMCP (%)
Socioeconomic level		
Upper	10	5
Upper middle	16	19.4
Middle	30	37.5
Lower middle	21	25.6
Lower	17	12.5
Total	100	100
Ethnic origin		
Caucasian	92	95.5
Asian	4	2
African American	1	0.5
Mestizos(²)	3	2
Total	100	100

(*)IHMCP: Italian Hospital Medical Care Program
(²)Mestizos: Spanish term used to designate people of mixed European and Amerindian ancestry living in the region of Latin America.

Table 1: Socioeconomic level and ethnic origin of inhabitants of the Autonomous City of Buenos Aires and IHMCP* affiliates, based on the 2001 Argentinean census.

The period of the study was conducted from 2009 through 2013. The sample included two groups of subjects: Each participant was classified as adult ADHD on the basis of the DSM-IV criteria adapted for the identification of adult patients with ADHD and the validated to Spanish Wender Utah Rating Scale (WURS) were used as an instrument for retrospective diagnosis of childhood ADHD[23,24] to identify patients and controls with preceding ADHD during their adult life.

DSM-IV criteria and the Wender Utah Rating Scale have been successfully adapted for the identification of adult patients with ADHD and have been used in numerous studies in the past.[24,25] To obtain a full diagnosis of adult ADHD, subjects were required to have the following criteria: (i) fully met the DSM-IV criteria for diagnosis of ADHD within the past years; (ii) described a chronic course of ADHD symptoms from adolescence to adulthood; and (iii) endorsed a mild to severe level of impairment attributed to those symptoms.

Participants were also provided with the validated to Spanish Wender Utah Rating Scale for retrospective diagnosis

of ADHD in childhood.[26]

The validated to Spanish version scale comprises 25 items which are rated on a 5-point scale (0-4).[26] The total score ranges from 0 to 100. For the retrospective diagnosis of ADHD in childhood, the authors recommended a cutoff score of 32 or higher to obtain a sensibility of 91.5% and specificity of 90.8%, with a positive and negative predictive value of 81% and 96%, respectively, and a Cronbach co-efficient of 0.94. This cut-off score was used because it demonstrated the best behavior (ROC curve) of the validated scale.[23] Whenever possible, diagnosis was obtained from the patient and a direct informant who had known the patient for at least 10 years and had information obtained from a close relative who knew the patient in childhood.

To avoid other overlapped disorders, we considered as adult ADHD symptoms only those patients who presented symptoms that fully met the DSM-IV criteria for diagnosis of ADHD and who fulfilled the cutoff score of the Spanish Wender Utah Rating Scale of 32 points or higher during their infancy. For example, if a patient had ADHD symptoms in adult life but he/she did not remember if those symptoms were present during childhood, the patient was not considered as a positive case of ADHD symptoms.

Fibromyalgia was diagnosed according to the American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia.[27] As these criteria don´t consider cognitive symptoms to diagnose FMS, they are suitable to search an association with ADHD.

Patients with ADHD and controls were matched as groups on a range of demographic variables to ensure comparability. All patients were evaluated and diagnosed by a trained neurologist. Routine clinical investigations were conducted to exclude other causes of cognitive impairment.

Patients were excluded if formal examination showed evidence of any other brain disorder or physical and/or mental illness sufficient to contribute considerably to the clinical picture. In all cases, we exclude those in which the consumption of psychotropic drugs or alcohol could be a potential confounder. Patient selection was strictly consecutive and included all the prevalent cases in the center who met previous criteria.

Controls

We included 2 groups of controls, one of them composed from those subjects volunteers of our database, living in the geographic area of residence of patients, with the same age and years of education range, subjects with cognitive complaints or impairment were excluded from this group. The same exclusion criteria that we applied in subjects were considered in controls as well. In another group, we included patients with cognitive complaints that didn't meet criteria for ADHD after underwent procedures to ascertainment of this disorder, previously described.

Controls were never duplicated. Records of potential controls were reviewed by a neurologist to exclude those controls in which the presence of any type of neurological disease was suspected before the year of inclusion in database. The list of the entire population from which potential controls were randomly drawn was provided by the record database system of the epidemiological center of the IHMCP, and control subjects were selected for cases using a statistical program.

Procedure and Data Analysis

The evaluation of cases and controls regarding the identification of ADHD using the DSM-IV criteria and the Wender Utah Rating Scale was performed by a trained neurologist unaware of the objective of the study. Only cases and controls fulfilling ADHD criteria by this kind of evaluation, were considered as positive exposure.

Raters who collected the information about ADHD symptom status were blind to the presence of FMS and control status. When the evaluation was completed, data were analyzed by an unblended neurologist aware of the objective of the study.

The presence of FMS was retrieved by a neurologist from the medical records. In all cases the diagnosis was made by a rheumatologist or an expert clinician in this field. Analysis was performed using Stata 8.0 version.

Analysis of differences in the frequency of categorical variables was carried out using the chi-square test. The Mann-Whitney test for independent samples was used for continuous variables. Statistical significance was set up at $P<0.05$.

RESULTS

We identified 154 patients fulfilling criteria for adult ADHD, 71 normal controls (NC), and 262 with cognitive complaint (CC) but without ADHD criteria. All patients authorized the use of their medical records for research. Age, sex and years of education of all groups were in Table 2.

	ADHD	Cognitive complaint (CC)	Normal controls (NC)
N (patients)	154	262	71
Gender, men (%)	58(37.7)	105(40)	29(40.8)
Age, mean (years)	72.5 (range 60-83)	71.4 (range 60-86)	71.9 (range 60-83 years)
Education, mean (years)	10.7 (range 3-18)	11.2 (range 3-18)	11.8 (range 3-18)

Table 2: Demographic and clinical data ADHD *vs.* cognitive complaint and normal controls.

There were no significant differences in these variables evaluated between the three groups.

The frequency of FMS was 24.7% in ADHD cases (n=38), 4.6% (n=12) in the CC group and 0% (n=0) in the NC group. The prevalence of FMS in ADHD cases was significantly higher when compared with the other control groups. The chi-square statistic is 52.0227 and P-Value is <0.00001. The 95% confidence interval extends from 0.0786 to 0.1330 (Table 3). As expected, all the patients with FMS were females, except only one subject belonged to ADHD group.

	ADHD N=154	CC N=262	NC N=71
FMS (%)	38(25)	12(4,5)	0
No FMS (%)	116(75)	250(95,5)	71(100%)

The chi-square statistic is 52.0227. The P-value is <0.00001. The result is significant at p<0.05.
ADHD: Adult Attention-Deficit and Hyperactivity Disorder, CC: cognitive complaint, NC: Normal Controls, FMS: Fibromyalgia Syndrome

Table 3: Statistical findings in each group.

DISCUSSION

In this case-control study, we identified a higher prevalence of FMS, amongst patients with ADHD than in the normal control group and CC groups. To our knowledge, this is the first study that examined the frequency of FMS in adult ADHD in a case-control study. Furthermore, this study has considered only older adults with ADHD, allowing to determine a true association between FMS and ADHD without confusion with the cognitive disorders of FMS.

There are many previous reports about the features of cognitive disorders in FMS.[28-34] Most of these studies suggested that people with FMS have cognitive dysfunction and are mainly affected more than one domain as attention, working memory and episodic memory.

Despite these findings, it seems that deficits in working memory and attentional tasks are more frequent than in other domains. The fact that these domains are affected in ADHD, showed the need to determine the true source of cognitive symptoms in FMS. The question is whether patients with FMS have cognitive disorders related to FMS itself, or this is secondary to ADHD, which seems to be a common comorbidity of FMS. Our study seemed to answer this question, because our results would show an association between both entities, and we didn't find this association with the CC group. Another interesting fact that supports an overlap between ADHD and FMS, is dysfunction in neurotransmitters in the central nervous system. It has found in FMS, a deficit in serotonin, noradrenaline and especially dopamine.[35-37] Thus, an attenuation of dopamine synthesis and release might contribute to the cognitive dysfunction that is increasingly recognized as a critical aspect of the disorder.[37] This latter dysfunction, coincidentally, have been linked to attention deficit in ADHD and it was reported previously that comorbidity between ADHD and FMS could be explained by both entities sharing a dopamine disorder, proposed as underlying pathophysiology.[18,19] However, there are still few reports describing the characteristics of these dysfunctions, and future studies focused on different subtypes of pre- and postsynaptic receptors, in brain areas associated with cognition, are required. It has been proposed that these alterations in the neurotransmitters may be related to an impaired stress response due to dysfunction of the hypothalamic pituitary axis[38] and may be triggered, according to emerging evidence, by adverse reactions to foods or food components.[39] An understanding of the interactive responses involved in the neuroendocrine-immunological network seems essential for a comprehension of the pathophysiology of ADHD and FM, and has been suggested to study in the future, the role of allergies as an important triggering event in each of the disorders.[39]

The strength of this study was that we examined thoroughly a large group of patients and controls, including only older people. A weakness of our study was that we didn´t control these variables with other potential comorbidities such as depression, anxiety or personality disorders, that could be confounding factors.

Unfortunately, reliable biological tests to examine this hypothesis are lacking. Future studies should focus on the search for biomarkers that allow dopaminergic dysfunction be compared in these populations. Our findings should be confirmed by similar studies. If this confirmation will be achieved, treatments that have already been effective in ADHD could be used in clinical trials for FMS symptoms.

CONFLICTS OF INTEREST

Authors has nothing to disclose.

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