Association Between Joint Hypermobility Syndrome and Panic Disorder: A Case–Control Study

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Background: *A significant association between joint hypermobility syndrome (JHS) and panic disorder was observed in a sample of rheumatology outpatients.* **Objective:** *The aim of this study was to assess whether JHS is more frequent in panic-disorder than in control subjects.* **Method:** *The authors conducted a case–control study comparing 55 untreated patients with panic disorder and three matched-control groups: psychiatric patients, fibromyalgia patients, and healthy persons.* **Results:** *JHS was more frequent among panic-disorder than among psychiatric patients, the healthy group, or the fibromyalgia group. In the panic-disorder group, there was a significant correlation between severity of JHS and anxiety.* **Conclusion:** *The strong association between JHS and panic disorder points to a genetic association. There is also a possibility that JHS and mitral valve prolapse, another condition frequently associated with panic disorder, share a common pathophysiological mechanism.* (Psychosomatics 2010; 51:55–61)

Joint hypermobility syndrome (JHS) is a highly hereditary clinical condition characterized by increased distensibility of joints in passive movements and hypermobility in active movements.[1] Its prevalence in the general population appears to range between 10% and 15%, and it is more common in women than in men.[1] Although JHS often goes unnoticed, affected individuals may suffer from repeated injuries of the musculoskeletal system,[2] so its early diagnosis is recommended to avoid these complications. A significant association between JHS and panic disorder was observed in a sample of rheumatology outpatients.[3,4] There is also a report on the high association of panic disorder and/or agoraphobia with JHS (the odds ratio [OR] compared with psychiatric control subjects was 18.6, and the OR compared with medical control subjects was 14.7).[5] Also, another study relates JHS to both state and trait anxiety (the former with less intensity) in the general population.[6]

The magnitude of the JHS and panic disorder association, uncommon in medical research, points to a causal connection between these two conditions. Gratacós et al.[7] identified an interstitial duplication of the human chromosome 15q24–26 (named DUP25), which was significantly associated with panic/agoraphobia/social phobia/joint laxity in families, and with panic disorder in nonfamilial cases. Mosaicism, different forms of DUP25 within the same family, and absence of segregation of 15q24–26 markers with DUP25, and the associated psychiatric phenotypes, suggest a non-Mendelian mechanism of disease-causing mutation. These authors[7] proposed that DUP25, which is present in 7% of the control subjects, is a susceptibility factor for a clinical phenotype that includes

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panic and phobic disorders and joint laxity. However, this genetic finding was not confirmed by two other research groups, who achieved different results.[8,9]

To date, most of the research papers published on the association between JHS and panic disorders/agoraphobia[3–7] have been developed by the same team of researchers. To our knowledge, three replication studies have been carried out, with inconclusive results: two[10,11] failed to confirm this association; the first, probably owing to the unbelievably high JHS percentage (52.6%) found in the control group; and the second, probably resulting from methodological limitations,[11] such as the kind of instruments used. The third study, the only one to confirm the association between panic disorder and JHS,[12] has only been published in Turkish. The present study was designed to replicate the research of the Barcelona group and, more specifically, to answer the following questions: 1) Is JHS more common in patients with panic disorder than among appropriate comparison subjects (psychiatric controls, medical controls, and healthy people)? and 2) Does severity of panic/anxiety symptoms correlate with JHS severity in these groups?

METHOD

A Case–Control Study

Setting The study was carried out in the Torrero, Casablanca, and Arrabal primary-care health centers, in the city of Zaragoza, Spain.

Patients Four groups of patients were included: a Case group of patients diagnosed with panic disorder, and three other Control groups (psychiatric, medical, and healthy) that were selected on the basis of the two previous papers published on the subject[5,6] and matched one-to-one by sex, age (plus-or-minus 2 years), and ethnic group, to the group of panic-disorder patients. The following is a description of each sample group:

Patients diagnosed with panic disorder: All consecutive, newly diagnosed, and untreated patients attending the aforementioned primary-care health centers over an 18-month period (from January 2005 to June 2006) who fulfilled inclusion criteria were included. We applied the following criteria: 1) DSM–IV criteria for panic disorder (with or without agoraphobia); 2) age 18–65 years; 3) ability to understand and read Spanish. Exclusion criteria: 1) Any other DSM–IV Axis I psychiatric disorder, such as psychosis, drug abuse, cognitive disorder; 2) severe medical disorders that hamper physical (including joint) examination.

The psychiatric control group: These patients were recruited from the same primary-care health centers and included consecutive, newly diagnosed psychiatric patients who did not suffer from DSM–IV panic disorder and who had never met criteria for any anxiety disorder. This selection criterion was also used by the original authors.[5] Inclusion criteria: 1) any DSM–IV psychiatric diagnosis except those described in the exclusion section; 2) age: 18–65 years; and 3) untreated patients, or patients able to discontinue the treatment at least 2 weeks before the JHS assessment. Exclusion criteria: 1) lifetime diagnosis of any anxiety disorder; 2) any psychiatric diagnosis that, from the point of view of the clinician, would not allow the study to be completed (e.g., severe psychosis or personality disorder, cognitive deterioration, drug abuse); and 3) severe medical disorders that hamper physical (including joint) examination. Many of these patients were getting pharmacological treatment and were not able to discontinue them before the assessment.

The medical control (fibromyalgia) group: The original authors[5] recruited this second control group from four medical outpatient clinics (dermatology, gastroenterology, general surgery, and internal medicine) at the same hospital. We preferred to include in this group only patients with a specific rheumatologic disorder, fibromyalgia, which has been reported to show a high association with JHS. In the Spanish population, this association has been calculated to be 27.3%.[13] All consecutive, newly diagnosed patients with fibromyalgia attending the aforementioned primary-care health centers were invited to participate in the study. Inclusion criteria: 1) diagnosis of primary fibromyalgia by a rheumatologist according to the American College of Rheumatology criteria;[14] and 2) age: 18–65. Exclusion criteria: 1) any psychiatric diagnosis that, from the point of view of the clinician, would not allow the study to be completed (e.g., severe psychosis or personality disorder, cognitive deterioration, or drug abuse); and 2) severe medical disorders that hamper physical (including joint) examination. Every effort was made to recruit only untreated patients; however, most of these patients were taking various kinds of analgesics and/or antidepressants. They were asked to discontinue the treatment at least 2 weeks before the JHS assessment.

The healthy-control group: These were persons accompanying patients with panic disorder, or other psychiatric disorders, who were visiting the previously mentioned primary-care health centers and who, according to the Standardized Polyvalent Psychiatric Interview (the SPPI), did not suffer from any psychiatric disorders. A sample group of this type was also assessed by the original authors[6] to evaluate JHS's association with anxiety in