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Agoraphobia between panic and phobias: clinical epidemiology from the Sesto Fiorentino Study

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Abstract

In the last few decades, there has been a long debate on the existence of agoraphobia (AG) without a history of panic attacks (PAs). In the present study, the problem of the relationships between AG and PAs is addressed trough a reevaluation of the cases who had been diagnosed with AG in the community survey of Sesto Fiorentino. Forty-one of the 75 subjects who met the criterion of AG in the Sesto Fiorentino Study were reinterviewed by experienced clinical psychiatrists. The Structured Clinical Interview for *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (*DSM-IV*) and the Composite International Diagnostic Interview were used to make the diagnoses. The Mobility Inventory for Agoraphobia (MIA) and a specific adjunctive question, "why do/did you avoid?," were used to compare AG subjects with or without PD. Of the 41 subjects with a lifetime history of AG, 12 cases had original diagnosis of AG without PAs and the remaining 29 had PD with AG. After the reassessment, in 10 cases, the criteria for the diagnosis of AG without PAs were confirmed, totaling a lifetime prevalence of 0.4% (confidence interval, 0.2-0.8). Agoraphobia subjects with and without PAs were comparable as regard to sex, age, age of onset, duration of illness, family history for anxiety or mood disorders, MIA scores, number, and type of situations avoided. Thus, AG seems to exist also in absence of a history of PAs, and the one-way relationship between the occurrence of PAs and a following development of AG, postulated by *DSM-IV*, should be reconsidered for the future classifications.

1. Introduction

Since the publication of the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition* (*DSM-III*) [1], the relationship between agoraphobia (AG) and panic attacks (PAs) has always been controversial. Two positions have given rise to a long lasting debate. On one hand, most North American psychiatrists consider PAs as the central feature of the disorder, and its association with AG is interpreted as a derived phenomenon, both from etiopathogenetic and chronological points of view [2]. Because AG is considered solely as a consequence of PAs, this position denies its existence without panic. Most studies carried out on clinical samples agreed that AG constantly begins after the first PA and that the presence of AG without nonsituational PAs is extremely rare, thus supporting this position [3-14].

On the other hand, the so-called European position maintains that a phobic attitude precedes the development of panic disorder (PD) and that specific temperamental features are necessary for the occurrence of PD. Such features would be the primary aspect of the disorder. Consistently with this position, most of the community surveys reported the existence of substantial prevalence rates of AG without preexisting PAs [15-32], also signaling the presence of AG before the onset of PD [17,33].

It may be objected that the epidemiological studies that use structured diagnostic interviews, administered by lay interviewers, may miss the presence of PAs in the history of patients with AG [34]. When cases originally diagnosed as AG without PAs in community studies were reevaluated by clinical psychiatrists, the rate of such diagnoses decreased to a considerable extent [19,23]. On the other hand, it may be objected that clinicians may overemphasize minor signs of distress in their search of preceding PAs in those patients presenting with AG. The discrepancy between clinical and

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epidemiologic studies might also be because of other reasons. Epidemiologists have hypothesized that subjects with more severe diseases and high degree of comorbidity are more common in clinical than in community settings [35,36], and this may explain the lower prevalence of AG without PAs observed in clinical studies. Thus, the higher prevalence of AG without PAs in community samples may be explained that these subjects are less likely to seek treatment than those with PD with AG [23,26].

This historical background of the dispute is largely reflected in the current classification systems. The *International Classification of Diseases, 10th Revision* (*ICD-10*) [37], in line with the "European" position, includes AG without PAs in the chapter of phobias, whereas *DSM-IV* considers the association PAs-AG as a form of PD and specifies that AG without PAs is a consequence of limited panic symptoms (ie, dizziness, depersonalization, cardiac distress) or of an isolated full-blown PA [38]. Furthermore, whereas in *DSM-III* there was a single definition of AG, defined as fear/avoidance..."in case of sudden incapacitation," *DSM III-R* [39] introduced different definitions, according to whether AG was in association with PAs (fear/avoidance of situations...in the event of a PA) or not (here, the fear in case of sudden incapacitation was maintained). The *DSM-IV* returned to the single definition of AG, but the version initially tailored to PD with AG (fear of panic) was also applied for AG without history of PAs. This tautological solution that was aimed at solving the problem of AG without a history of PAs failed to get rid of this inconvenient problem. In fact, recent studies, even using *DSM-IV*, found a certain number of subjects with AG without not situational PAs, although to a lesser extent than using *DSM-III-R* [23,26-29,32,40] and, in a recent national community survey, carried out in adults more than 55 years, the correlation between AG and PD was found low and not significant [41].

Thus, the classification of AG without previous unexpected PAs, as well as the definition of AG still remain an open problem, and the existence of a "continuum," ranging between AG without any experience or fear of PAs and PD without AG, has been hypothesized [26]. Unfortunately, the picture is even more complex; some authors underlined that the boundaries of AG are weak not only toward PD but also toward other anxiety disorders. Even in the above quoted studies, where the original diagnoses of AG without PAs were not confirmed by the psychiatric reappraisal, they shifted to simple phobia, separation anxiety disorder, social phobia, anxiety due to medical condition, but the fact that these subjects avoided public places remained [19,23,42]. The definition itself of AG, with its reference to "embarrassment," opens the door to AG as a possible manifestation of social phobia.

In the light of the need of further field studies needed for *DSM-V*, the present report attempts to address the problem of AG again, using clinical interviewers in a community sample; the people who had a lifetime history of AG, irrespective of whether with or without PAs, in the Sesto Fiorentino Study [43,44] were reinterviewed and reevaluated by means of specific instruments.

2. Methods

Background and methods of the Sesto Fiorentino Study have been described in detail elsewhere [43]. Briefly, this is a 3-phase 2-wave design where a representative sample of 2500 people aged more than 14 years living in the municipality of Sesto Fiorentino (close to Florence, central Italy) and registered in the lists of the National Health System (NHS) (99.7% of the Italian population is registered with the NHS), was randomly selected to be interviewed. Two thousand three hundred sixty-three subjects (94%) were interviewed by their own general practitioners (GPs) (irrespective of whether they had consulted the GP), who used the Mini International Neuropsychiatric Interview [45] plus 6 additional questions. Six hundred thirteen resulted positive at the GP screening. Six hundred nine of 613 screen positives and 123 of 130 randomly selected screen negatives were reassessed by interviewers with clinical experience (qualified psychiatrists or fourth-year residents) that used the Florence Psychiatric Interview (FPI) [46]. This is a typical clinical semistructured instrument that resembles the structure of a clinical research record. Briefly, the FPI is a combination of several modules, each representing already established and validated research procedure.

As a first step, the occurrence and timing of psychopathologic episodes, defined as any interruption of normal well-being, are recorded. For each episode, 121 symptoms, including most of those listed in the *DSM-IV*, are explored independently of their diagnostic value. Each symptom is scored on a 5-point severity scale (0 = absent, 1 = dubious, 2 = mild, 3 = moderate, and 4 = severe). Other relevant information such as life events, treatments, consequences of the episode is also registered. On the basis of this information, *DSM-IV* diagnoses are generated by computerized diagnostic algorithms. The ability of the FPI to produce *DSM-IV* diagnoses was compared with the Structured Clinical Interview for *DSM-IV* (SCID) I, and an almost perfect concordance was found. As the FPI is a typical bottom-up procedure, where symptoms are explored regardless of any predefined diagnostic system, it is well suited to the study of the natural relationship of symptoms and/or sets of symptoms.

Family history is studied by interviewing the patients and their treating GPs (who are usually the physicians of the entire family) for the presence of psychiatric disorders and/or any kind of treatments in their first-degree relatives.

On the basis of the FPI, 75 (16 male and 59 female) subjects met the criterion of AG, defined as follows: "Marked fear and avoidance being in places or situations from which escape might be difficult or help not promptly available in case of occurrence of any of the previously listed