Etiology and Onset of Agoraphobia: A Critical Review

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ABSTRACT

Research on the etiology and onset of agoraphobia is reviewed. Evidence indicates that it is the most prevalent clinical phobic disorder with age of onset in the mid- to late-twenties. It primarily affects women with no particular socioeconomic distinctions. A number of claims have been made linking various family, childhood, and premorbid personality characteristics to onset, however, strong empirical support for these has yet to be demonstrated. Increased attention is being devoted to the role of biological factors in the development of this disorder and some findings have suggested that spontaneous panic attacks may be biologically linked. Studies have shown that the onset of agoraphobia usually occurs following a period of stress or an identifiable precipitant. Interpersonal difficulties have frequently been reported as stressors, but the range of traumata associated with onset is quite extensive. Suggestions for future research are presented.

ETIOLOGY AND ONSET OF AGORAPHOBIA: A CRITICAL REVIEW

AGORAPHOBIA has received considerable attention in the last decade with a growing body of empirical evidence attesting to the efficacy of both behavioral and pharmacological approaches in alleviating phobic symptomology.[1] Furthermore, longterm follow-up studies have shown that lasting changes are possible.[2] Unfortunately, research aimed at understanding the etiology and onset of agoraphobia has lagged far behind treatment advances. Although recent efforts have shed light on possible predisposing risk factors, these investigations have been plagued by the absence of adequate controls, by ill-defined measures, and by a host of other problems.[3] This review attempts to critically examine the relevant literature and propose several directions for future research.

The term *agoraphobia* was first coined by Westphal[4] in his description of three males who experienced intense anxiety when walking across open spaces or through empty streets. In this classic paper, Westphal also noted the physiological symptoms of anxiety and the anticipatory fear that typifies present-day agoraphobia, the most disabling of phobias and the most difficult to treat.[1] Although agoraphobia is often defined as a fear of open spaces, this definition is inaccurate since agoraphobics typically exhibit a wide range of avoidance behaviors including an inability to enter closed and open spaces, to travel, to interact socially, and to be alone. According to Marks,[5] the most common clinical feature of the syndrome is a fear of entering public places. Other defining characteristics are physiological changes associated with accompanying panic attacks. These can include palpitations, lightness in the head, weakness, atypical chest pain, and dyspnea. Most agoraphobics also express fears of losing control, going insane, embarrassing themselves and others, dying, and fainting. This central cluster of symptoms has been observed in several studies.[6,7]

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Demographics

A survey taken in Vermont reported the incidence in the general population to be 6.3 per 1000.[8] Nearly identical figures of 6.0 per 1000 were reported by the Phobic Society in Manchester, England.[9] In psychiatric practice, the prevalence of phobias as a primary complaint is approximately 2% to 3% in America and England[10,11] with approximately half of these being agoraphobic.[8] Most agoraphobics referred for treatment are women, with figures ranging from 82% to 88%.[12,13] The majority are married and tend to marry at ages comparable to normal populations.[14] Several studies have shown no differences in intelligence, occupation, or educational history between agoraphobics and controls.[10,15–17] Similarly, Buglass and his colleagues[18] found no differences in employment history, social activities, or family of origin between agoraphobics and age-matched controls.

Age at Onset

Agoraphobia usually begins in young adults between the ages of 18 and 35 with a mean age in the mid- to late-twenties.[16–21] While the disorder is rare in children,[5] Solyom et al[17] found 21% of his sample had experienced phobic symtoms during childhood. According to Marks and Gelder,[22] the disorder has peak onsets at ages 20 and 30 which correspond to the onset of anxiety states. Mendel and Klein[21] also found a similar bimodal distribution. Recently, Sheehan et al[20] examined a large, carefully screened sample of agoraphobics and found a uniform distribution of onset age peaking in the mid-twenties. They criticized previous studies on the basis of small sample size and showed that if the findings of these past reports[22,21] were combined with theirs ($N = 209$) a unimodal distribution resulted.

The age patients usually seek treatment is in the mid-thirties, although the time from onset to professional contact varies considerably.[5] A survey of 2000 members of an agoraphobia correspondence club revealed the average duration prior to members seeking help was 17 months for general practitioners, 34 months for psychiatrists, and 57 months for religious and spiritual healers.[16] Bowen and Kohout[12] found 31% of agoraphobics surveyed had experienced symtoms for less than 6 months, 12% had symptoms 6 months to 2 years, 27% reported symptoms for 2 to 5 years, and 20% of the sample had symptoms longer than 5 years. Other studies reported the average duration ranged from 6.5 to 8 years.[18,19] Differences in knowledge concerning agoraphobia, availability, and accessibility of treatment may all contribute to the reported discrepancies in the length of time from onset to contact. It is likely that the recent upsurge in interest in agoraphobia will result in patients seeking help earlier than they have in the past.

Psychosocial Predisposing Factors

Interesting yet elusive questions have been raised concerning the types of childhood experiences and personality characteristics that may contribute to the development of agoraphobia. While considerable research has been devoted to this area, there is yet no persuasive evidence pointing to any specific psychosocial risk factors. Marks[5] has noted, "On this subject little systematic work can be quoted: figures of different workers depend on varying criteria and are not equivalent, nor are they easily compared with control populations" (p. 540). Studies published since Marks' observations continue to suffer many of the same inadaquacies.

Family Characteristics

Parental overprotection has been put forth as a possible etiological factor in the development of agoraphobia. Several workers have shown support for this hypothesis by noting a significant incidence of maternal overprotection among agoraphobics.[10,23,24] Bowlby[25] suggested that agoraphobic families frequently lack sufficient maternal affection and are dominated by an overprotective mother. Maternal overprotection was also noted more frequently in a mixed phobic group comprised of 91.3% agoraphobics compared to controls, although the difference was not quite significant.[17]

More recent reports have found little support for the increased incidence of maternal overprotection in the background of agoraphobics. In one of the more well-controlled studies comparing the childhood experiences of 30 agoraphobic housewives with age-matched controls, Buglass et al[18] found no significant differences between groups in frequency or type of contact with parents. Parker[26] examined differences in overprotection between social phobics, agoraphobics, and controls. In this study overprotection was defined as controlling, intrusive, infantilization and encouragement of dependency. Generally, both neurotic groups scored their parents as less caring and more overprotective than controls. However, separate analyses revealed important differences between the two groups. Social phobics rated both parents as low on care and high on overprotection, while agoraphobics scored their parents low on maternal care but were identical to controls on ratings of overprotection. Parker argues that failure to confirm earlier findings of maternal overprotection was due to a lack of appropriate controls and combining other phobic disorders in the same sample.

Parker's findings of low maternal care support the general consensus, with the exception of Buglass,[18] that agoraphobics have a history of poor relationships with their parents.[27] According to Chambless and Goldstein,[28] the deficiency of the parental relationship is such that children by being punished, criticized, or denied the opportunity to practice independent behaviors grow up viewing themselves as basically incompetent and unable to cope with many situations. They argue that these early experiences serve as significant predisposing factors in the development of agoraphobia. Although, this hypothesis has yet to be tested by controlled investigations.

Another observation regarding agoraphobic families is that the prevalence of psychiatric disorders has been found to be higher than in the families of normal controls. Studies by Roth[29] and Roberts,[30] reported the prevalence of other psychiatric disturbances to be 21% and 40%, respectively. The incidence of neuroses in the families of phobics was found to be significantly higher than a control group of temporal lobe epileptics.[31] Additionally, Solyom et al[17] reported a greater number of psychiatric problems (i.e., neurosis, alcoholism, and depressive illness) in the families of mixed phobics when compared with the families of matched controls. Evaluating these reports is difficult due to the lack of consistency in how psychiatric disorders were measured; a variety of assessment techniques were used to determine diagnostic and classification criteria.

Several studies have indicated that the fears of phobics are transmitted in families and are especially associated in mothers and daughters. In one of the first reports, Hagman[32] found a correlation of .67 between the number of fears reported by

phobic mothers and their children. Marks and Herst[16] reported that 19% of agoraphobics in Britian indicated a close relative with the same phobia. Another study comparing mixed phobics to normal controls, found that there was a significantly greater number of mothers with phobias in the experimental group.[17] The authors suggested that there seemed to be evidence for modeling in the acquisition of phobias. However, the incidence of fears between agoraphobics and their mothers could be due to genetic inheritability not modeling.

Parental loss has also been postulated as a possible etiological factor in the onset of agoraphobia. This assumption is popular among clinicians who suggest that loss can promote anxious attachment in the child and predispose him to develop anxiety attacks with future losses or threat of loss.[25] However, this hypothesis has not been empirically confirmed. Controlled studies have shown no differences in permanent separation from either parent before age 15 and no increase in parental death between agoraphobics and controls.[18,17] Even if a history of separation experiences had been found to be more prevalent in the background of agoraphobics, recent reports have found no clear-cut relationship between these early experiences and adult anxiety states.[33,34] Instead, the results have shown that childhood separations due to parental illness, childhood illness, parental marital discord, and wartime evacuation were more highly correlated with adult depression than anxiety symptoms.[33]

Studies examining the stability of agoraphobic families have provided conflicting results. Several investigations have suggested that agoraphobics come from stable families.[14,29,10] On the other hand, Webster[23] reported that the fathers of agoraphobics were absent with unusual frequency and Snaith[35] found agoraphobic families to be more unstable when compared to other phobic types. The lack of agreement may stem from how *stable* was defined and measured. Divorce, separation, and the temporary absence of either parent have all been used as dependent measures. Unfortunately, there have been no consistently used criteria across studies.

Childhood Background

Childhood fears have been studied and related to the development of agoraphobia. The incidence of childhood fears and night terrors has been shown to be more frequent in phobic subjects than normals.[10,14] Harper and Roth[31] found that 60% of their sample of agoraphobics had phobias as a child. Similar findings were obtained by Solyom et al[17] in their sample of mixed phobics. These authors speculated that agoraphobia may be a reactivation of childhood fears precipitated by some stressful experience.

Several reports have indicated that one of the most frequent childhood fears of agoraphobics is separation anxiety. Furthermore, it has been suggested that these childhood fears may lead to the development of future panic attacks.[28,36] This assumption was discussed earlier in the context of early parental loss. To date, empirical support for this hypothesis is lacking. Similarly, there are no controlled studies which clearly demonstrate a greater incidence of childhood separation fears in agoraphobics. Liebowitz and Klein[36] reported that 20% of outpatients and 50% of inpatient adult agoraphobics had a history of separation anxiety usually manifested as difficulty attending school. However, problems in school attendance hardly qualify as definitive confirmation of separation anxiety. Buglass et al[18] attempted

to answer this question more directly by eliciting a childhood history of separation anxiety symtoms during brief separations from mother, difficulties in school, and individual freedom to choose own clothes after age 18. No differences were found between agoraphobics and controls.

In other findings pertaining to the childhood background of the agoraphobic, Shafar[19] reported that over one-third of her agoraphobics and social phobics surveyed recalled a very unhappy childhood and in 12% this was mentioned as the most significant factor at onset. She also found that bereavement was involved in 11 of the 33 agoraphobics with unhappy childhoods.

Premorbid Personality

The premorbid personality of the agoraphobic has often been described as soft, infantile, passive, anxious, dependent, obsessive, introverted, emotionally immature, retiring, and highly neurotic.[5] There are several reports substantiating these descriptors, both controlled and uncontrolled.[37,30] The difficulty is determining what problems stemmed from the onset of agoraphobia and those that existed premorbidly. As Marks pointed out,[5] some agoraphobics were active, sociable, and outgoing before their symptoms began. With the onset of panic attacks, they become increasingly anxious, afraid of venturing outside, dependent on others for support, withdrawn, retiring, and so on. By the time they are evaluated, they evidence many traits mistakenly assumed to have existed premorbidly.

Biological Predisposing Factors

The contribution of genetic factors in the development of agoraphobia remains inconclusive. Most studies have shown support for genetic influences either by noting a high incidence of target symptoms in first and second degree relatives[38-42] or by observing a significantly higher correlation of anxiety symptoms between monozygotic twins compared to dizygotic twins.[43-45] However, early studies were hampered by methodological inadequacies in proband selection, small sample size, varying diagnostic criteria and an over reliance on history information obtained solely from probands. While recent reports have corrected most of these shortcomings, one problem remains. Subject selection has been based on criteria for anxiety neurosis and panic disorder, not agoraphobia. Studies using selection criteria appropriate to agoraphobia question the significance of genetic factors in the development of the disorder. For example, one well-controlled study found no significant differences in phobia prevalence among the parents of agoraphobics compared to age matched controls.[18] Clearly, further studies are needed that include accepted diagnostic criteria for agoraphobia.

According to Mathews et al,[1] the evidence for direct genetic transmission of agoraphobia is weak, but certain individuals may inherit general personality traits (e.g., introversion) that increases their susceptibility to developing agoraphobia. As they point out, these traits may represent a general vulnerability factor. Support for this hypothesis comes from several reports that have shown neuroticism scores are higher in MZ than in DZ twins.[43]

Constitutional and physiological factors (many of which may be genetically transmitted) may play a part in the development of agoraphobia. The early studies of Lader and Wing[44] and others[46] centered on the abnormal *arousal* of agoraphobics.

These researchers contended that excess arousal is controlled in normal individuals by a physiological habituation mechanism. They postulated that in some individuals there is no dampening of arousal. Thus, positive feedback can occur causing arousal to increase until the individual experiences a panic attack which may be the core stimulus for future avoidant behavior.[47] Lader and Wing[44] showed that agoraphobics displayed more spontaneous fluctuations in skin resistance and habituated more slowly to auditory stimuli than normal controls. These physiological differences were not found with simple phobics. While these findings seem to suggest a physiological malfunction in the arousal habituation mechanism among agoraphobics, an alternative explanation exists. Since the feared objects of simple phobics are more easily avoided, their basal level of arousal may remain unaffected. By contrast, agoraphobics are not as successful in avoiding what they fear because the phobic stimuli are more diffuse. As such, their tonic level of arousal may remain elevated producing a physiological oversensitivity to a variety of stimulus inputs.

Recent reports have linked agoraphobia and panic to cardiovascular disorders[48–52] and in particular, to mitral valve prolapse (MVP). MVP is a generally benign cardiac abnormality occurring in 5% to 10% of the general adult population. It has an autosomal dominant genetic transmission[53] and is especially prevalent in young women.[54] Although most persons with MVP are asymptomatic, symptomatic patients have a syndrome of tachycardia, palpitations, syncope, fatigue, dyspnea, and atypical chest pain.[54] Palpitations may be related to cardiac arrhythmias.[54] Kantor and colleagues[52] compared 25 agoraphobic women who had been selected for prominent cardiovascular symptoms to a group of normal female controls and, using echocardiography, found MVP in 44% of the agoraphobics and 9% of the controls. However, the two groups differed significantly by echocardiographic, but not clinical criteria for MVP (i.e., midsystolic click). This was also true in the only other controlled study by Venkatesh.[50] Echocardiographic evaluation of panic disorder patients showed a significant prevalence of MVP in the psychiatric patients versus the controls, but again, clinical auscultation of their hearts for midsystolic clicks showed no significant difference between the groups. This discrepancy suggests that the form of MVP found in psychiatric patients is either the uncommon silent MVP or the studies suffer from biases of undersensitive ausculatation and/or over sensitive echocardiographic criteria.[54] However, it is possible that cardiac arrhythmias, causing and perpetuated by anxiety, can lead to panic and agoraphobia in psychologically predisposed individuals. It could also be postulated that MVP reflects an organic defect also underlying agoraphobia, a notion supported by research showing autonomic dysregulation in MVP patients.[55]

Panic has also been induced pharmacologically in patients with hyperdynamic β-adrenergic states by infusion of the β-adrenergic agonist isoproteronol.[56,57] Its effects were reversed by an infusion of propranolol, a beta-blocker. These findings suggest an increased β-adrenergic sensitivity in some panic patients.

Pitts and McClure demonstrated that infusions of sodium lactate reliably produced panic in a majority of anxiety neurotics, but not in normals.[58] These results have been replicated by others[59–61] and have led to speculation regarding a common biochemical basis for panic attacks. Pitts[62] postulated that lactate induced panic attacks involve the chelation of calcium by lactate, thus interfering with normal nerve transmission. This was based on the observation that adding calcium mitigated

the effects of the lactate infusion.[58] The lactate theory of anxiety, however, has been seriously questioned.[63,64] It has been argued that lactate infusions are a nonspecific stressor in patients conditioned to overreact to altered bodily sensations,[64] rather than a specific biochemical trigger.

Further evidence pointing to the role of biochemical factors in the development of agoraphobia comes from findings that tricyclic antidepressants and monoamine oxidase inhibitors are effective in suppressing panic but not in reducing anticipatory anxiety.[47] These results suggest that separate pathophysiological mechanisms may be involved in each type of anxiety.[65] These drugs also block lactate-induced panic although there is preliminary evidence that active placebos such as methscopolamine, which produces anticholinergic side effects, have been shown to perpetuate this panic-blocking effect after the active drug has been discontinued.[55] This suggests the role of cognitive factors in the conditioning of responses to bodily sensations and biochemical interventions and attests to the complexity of methodological factors involved in such studies.

Yohimbine, an α-adrenergic antagonist, has been shown to cause panic[66] that may be mediated by unopposed, relatively accentuated beta adrenergic receptor stimulation. There is some controversy over the efficacy of β-adrenergic blockers in panic, with some authors suggesting that they only block the peripheral manifestations of anxiety[47] and not lactate-induced panic,[55] while others maintain that there is some evidence for effects on both somatic and subjective anxiety if the beta-blockers are taken continuously for 3 to 6 weeks.[61]

Other medical disorders such as hyperthyroidism, hypoglycemia, pheochromocytoma, and acute labyrinthitis can produce symptoms of nervousness, dizziness, and palpitations and have been associated with panic attacks. For most individuals the physiological symptoms are distressing but self-limited. But for some, the interaction of physical illness and premorbid personality characteristics (e.g., neuroticism) may contribute to the development of agoraphobia.

Overall, biological factors, particularly those operating through the emergence of spontaneous panic attacks, seem to merit inclusion in a conceptual model of the etiology of agoraphobia. Their synergy and reciprocal interaction with cognitive processes[67] should form the basis for future research in this area.

Onset

The majority of agoraphobic symptoms seem to occur following a period of background stress or an identifiable precipitant. Shafar[19] reported 83% of her sample of phobics (74% agoraphobics) could identify precipitating causes and Sheehan et al[20] found 91% of a large sample of agoraphobics could identify life changes that appeared to be related to the onset of their symptoms. Similar findings have been reported by others.[12,17,68] Buglass et al[18] also showed that 25 of 30 agoraphobics could identify a clear relation of events to onset of their symptoms. However, only seven cases were able to identify a discrete event at the time of onset and only two of these were specific.

Interpersonal problems are a commonly reported precipitating event. Bowen and Kahout[12] found 76% of those agoraphobics identifying a precipitating source said rejection or loss in an interpersonal relationship was associated with the onset of their panic attacks. It has been shown that a substantial number of phobics (56 of

81) reported that interpersonal difficulties were associated temporally with the onset or aggravation of the phobic disorder; in 43 phobics this problem was found to be the primary precipitant.[19] Chambless and Goldstein[28] offered anecdotal support by stating that a majority of their patients reported they experienced panic attacks following an unpleasant interpersonal interaction in which they had not asserted themselves appropriately. They indicated that many of these interactions involved marital conflicts. This claim is supported by several studies in which patients identified an increase in marital quarrels prior to the onset of phobic symptoms.[69-71] Hafner[71] described one woman who experienced anxiety attacks whenever she asserted herself with her husband who would threaten separation. Interestingly, there is evidence that the onset of panic attacks is often accompanied by a reduction in quarreling[69] suggesting that the distressed marriage may be negatively reinforcing phobic symptomology.

Another precipitant often reported is separation or threat of separation. In a sample of phobic patients, 32.6% stated the death of a relative or friend was associated with the onset of symptoms.[17] The loss of a loved one was related to onset for 13 of 80 phobics in another study[13] while Shafar[19] found that 21% of her sample lost a figure very close to them within 5 years of onset.

In several cases, panic attacks began after physiological upheaval. Shafar[19] found 38% of her sample linked onset to serious illness. Similar findings have been reported by other investigators.[17,20] In one study, 16% of onsets were related to childbirth and 6% to surgical operations.[13] Similar causes for onset include problems discussed earlier in the context of physical predisposition. According to Liebowitz and Klein,[36] a large proportion of individuals develop panic attacks after experiencing endocrinological changes such as hypothyroidism.

Other factors identified with onset include fright and acute danger, psychiatric illness, change of abode, accident or assault, guilt regarding abortion, and pharmacological factors.[19] In fact the range of precipitating factors related to onset is quite extensive and appears to include nearly any stressful experience.

DISCUSSION

A host of intriguing hypotheses concerning psychosocial and physiological factors related to the etiology and onset of agoraphobia have been put forth by workers in the field. Unfortunately, well-controlled studies appear to be more the exception than the rule. Many of the investigations failed to compare their phobic group to a psychiatrically normal or diagnostically dissimilar group, thus rendering most of the findings tenuous and largely uninterpretable.

The criteria used to define predisposing factors warrants further attention. The vagueness of the measures employed in the etiological literature to date precludes a systematic comparison across studies. For example, in the majority of studies it was unclear how each was defining maternal overprotection. This lack of specificity and clarity of definition may account for the inconsistencies in previous reports. Measures need to be operationally defined to insure a more reliable and valid assessment.

The etiological literature has relied almost entirely on patient self-reports as the mode of assessment. While self-report provides a convenient avenue for data collection, certain drawbacks exist, namely social demand, recall distortion, and mem-

ory loss. Rather than relying exclusively on this method, other sources of information need to be considered. For example, useful information could be collected from significant others as well as archival records. The latter might include school records, psychological testing and municipal and county documents. Although both options suffer some of the same disadvantages as patient self-report, they can be used as ancillary measures to corroborate and enhance already available information.

The reliability of measurement was neglected for all the studies reviewed. Providing reliability coefficients for the different measures employed is of utmost importance since they provide an estimate of the degree of error fluctuation due to uncontrolled sources of variation such as mood, health, and setting. The test-retest procedure in which subjects are retested two to three weeks after the first administration using an identical or equivalent questionnaire is one method frequently used. Patients' responses on the two different testing occasions are subjected to correlational analyses to determine the stability of the responses across time.

A final issue that deserves mention has been the varied and often loosely defined criteria for defining agoraphobia. At the very minimum, subjects should be screened for the presence and frequency of spontaneous panic attacks, presence and magnitude of anticipatory anxiety, and avoidance behavior, as well as level of depressed mood. Combining some patients who manifest marked spontaneous panic, anticipatory anxiety, and avoidance with other patients who exhibit only one of the above symptoms (e.g., as in the case of panic disorder with no avoidance), is unjustified since the predisposing risk factors for the different symptoms may be quite different. Moreover, in a number of studies agoraphobics and other phobic types were included as one sample. The inclusion of different phobic types within the same study has certain advantages so long as separate analyses are conducted for each subgroup.

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