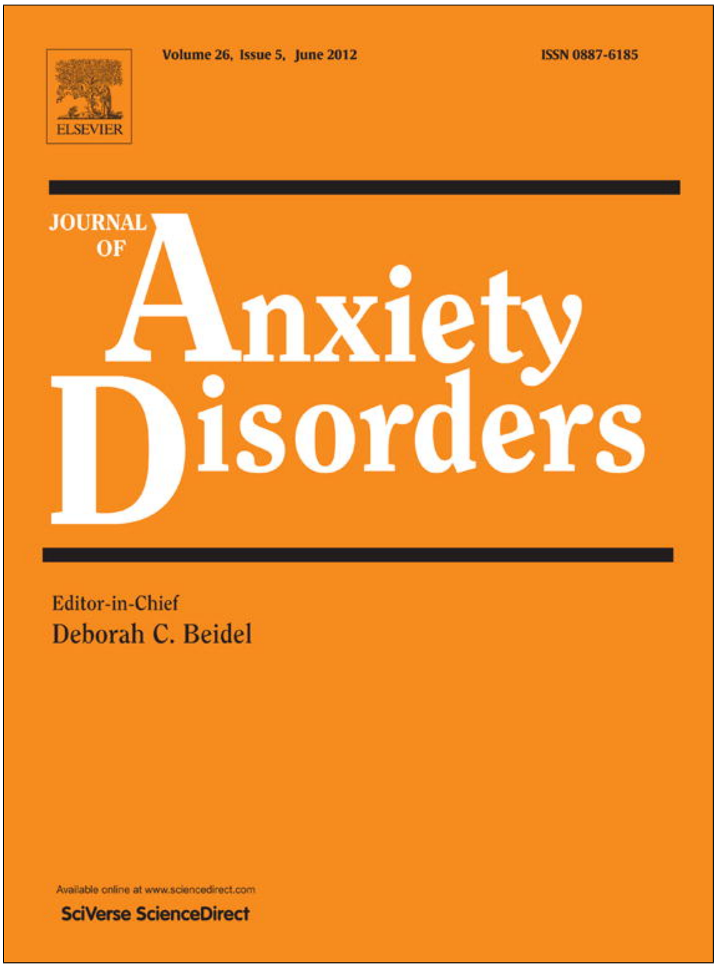

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Review

Minority inclusion in randomized clinical trials of panic disorder

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ABSTRACT

In 1993, the National Institutes of Health issued a mandate that funded research must include participation by racial and ethnic minority groups, and researchers were required to include in their proposals strategies by which they would achieve diversity in their samples. A methodological search for randomized clinical trials of panic disorder was conducted to evaluate ethnoracial differences in panic disorder symptoms, rates of minority inclusion in North American studies, and effective methods of minority recruitment. Less than half of the studies identified reported ethnic and racial data for their sample. Of the 21 studies that did report this information ($n = 2687$), 82.7% were European American/non-Hispanic White, 4.9% were African American/Black, 3.4% were Hispanic, 1.1% were Asian American, and 1.4% were another ethnicity. The remaining 6.5% was simply classified as other/non-White. The primary recruitment techniques utilized were clinical referral and advertising, but neither of these methods were correlated with improved minority participation, nor was the number of recruitment sites. As minorities are greatly underrepresented in panic disorder studies, reported treatment outcomes may not generalize to all ethnic and cultural groups. Researchers have not followed NIH guidelines regarding inclusion of special populations. Inclusion of minorities in future studies is needed to fully understand issues related to the treatment of panic disorder in non-White populations. Suggestions for improved recruitment of ethnoracial minorities are discussed.

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1. Introduction

1.1. Prevalence across ethnic groups

Panic disorder, often accompanied by agoraphobia, is a serious anxiety condition, resulting in disability and distress. The National Comorbidity Survey Replication (NCS-R) indicates that in the past year, panic disorder criteria was met by 2.7% of the population, with 44.8% of that group exhibiting serious symptoms (Kessler, Chiu, Delmer, & Walters, 2005). Lifetime prevalence for panic disorder, with or without agoraphobia, is 4.7% (Kessler, Berglund, et al., 2005). The lifetime prevalence rates among racial/ethnic groups were greatest among those who identified as Hispanic (5.4%), followed by Non-Hispanic White (4.9%), and Non-Hispanic Black (3.1%; Breslau et al., 2006). Data from the Collaborative Psychiatric Epidemiology Studies ($N = 16,711$) revealed a similar pattern of panic disorder lifetime prevalence rates among White Americans (5.1%), Hispanic Americans (4.1%), African Americans/Black (3.8%), and Asian Americans (2.1%; Asnaani, Richey, Dimaite, Hinton, & Hofmann, 2010).

The empirical literature pertaining to the epidemiology of panic disorder is further intriguing, since cultural factors are ostensibly ignored as evidenced by disparate interpretations for conclusions drawn in this area. For instance, epidemiological studies do not show a significant difference in the prevalence of panic disorder across ethnic and racial groups. However, accurate rates may be difficult to determine as North American studies of panic disorder and other anxiety disorders utilize tests and measures constructed from a predominantly European American or Western perspective, and may fail to capture culturally distinct symptoms of other ethnic groups. Research indicates that the cultural differences may manifest in the way that symptoms are described and experienced (Guarnaccia, 1997), and studies that comprise the *National Institute of Mental Health Collaborative Psychiatric Epidemiology Surveys (CPES)* mirror this sentiment. These reflect efforts to study ethnic and cultural differences in mental health and wellbeing of African Americans (NSAL), Hispanics and Asian Americans (NLAAS). Alegría, Vila, et al. (2004) note that, “The reliance on measures developed in our cultural context that do not take semantics and cultural variation into account, fosters false assumptions, attributional errors, and misleading interpretations, mostly due to the absence of a solid understanding of how to incorporate cross-cultural variation in measurement.” Others support this argument, citing America’s growing minority population as reason to investigate panic disorder and other mental health problems in non-European American groups (Alegría, Takeuchi, et al., 2004).

Currently, there are 308.7 million people in the United States, and 13.6% of these are African American, 16.3% Hispanic or Latino American, and 5.6% Asian American, alone or in combination with some other racial group (Humes, Jones, & Ramirez, 2011). With the current lifetime prevalence of panic disorder, these numbers indicate that a considerable number of people from all ethnoracial groups are suffering from this disorder, making it an important public health concern.

1.2. Panic symptomatology in African American samples

Although work with ethnic minority populations is undoubtedly burgeoning, the scope of the empirical work in this area remains relatively sparse. Though one may presume that panic symptoms generalize across cultures, some ethnoracial groups describe panic symptomatology differently than their European American counterparts. For example, African Americans report symptoms such as wooziness on the brain, swimming head, heart tremors, itching, seeing red, and blood on the breath (Horwath, Johnson, & Hornig, 1994). Moreover, many African Americans express anxiety symptomatology through somatic complaints with symptoms such as numbing and a decreased emphasis on cognitive processes, and lower levels of subjective nervousness (Barrera, Wilson, & Norton, 2010; Heurtin-Roberts, Snowden, & Miller, 1997; Smith, Friedman, & Nevid, 1999). Additionally, there is evidence that African Americans with panic disorder have more separation anxiety and social phobia than European Americans (Friedman, Hatch, & Paradis, 1994).

Much of the information we have about panic disorder in African Americans comes from the work of Friedman and Paradis (2002), who, in a single study, found a high comorbidity of panic disorder with post-traumatic stress disorder and depression in African Americans. Along these lines, the researchers suggest that there is less self-blame and more spiritual dependence as a coping measure for the disorder. Last and most significantly they noted a higher incidence of sleep paralysis in African Americans, a phenomenon where, upon waking, an individual is unable to move and often experiences frightening hallucinations. Sleep paralysis is more common in African Americans, but the rate is particularly high in those with panic disorder (59%; Paradis, Friedman, & Hatch, 1997; Paradis & Freidman, 2005), indicating a connection between these symptoms that may be unique to African Americans. Given that a single investigation of panic disorder yielded these compelling results, it is plausible to conclude that other characteristics maybe found with further, culture-centered collaboration in this area of research.

1.3. Panic symptomatology in Hispanic samples

Guarnaccia (1997) suggests that criteria and diagnostic symptoms need to be expanded to include potential factors relevant to minority groups. In examining anxiety in Hispanic Americans, Karno et al. (1989) attributed selective migration by less fearful individuals to increased rates of anxiety in Hispanics in the Los Angeles area when compared to their Mexican counterparts across the border, but the stress of migration itself and subsequent minority status in the US may also be factors. Other relevant findings surround the phenomenology of the culture-bound syndrome termed *Ataques de Nervios* (American Psychiatric Association, 2000), which is similar to panic attacks but also may include uncontrollable anger or physical outbursts, described most often in Caribbean Hispanic cultures. The most common symptoms include dissociation, suicide attempts, fainting, seizures, shouting, crying, trembling, and heat in the chest (Hinton, Lewis-Fernandez, & Pollack, 2009). These symptoms may be conceptualized as a type of stress-induced panic attack, with specific symptoms influenced by cultural expectations. This suggests that both cultural and psychosocial factors disparately influence the experience of panic in different ethnoracial groups. Initial research supports the DSM-IV distinction between panic attacks and Ataques de Nervios. However, the syndrome may occur at similar rates in both Hispanic and Non-Hispanic cultures (Keough, Timpano, & Schmidt, 2009).

1.4. Panic symptomatology in Asian American samples

Not surprisingly, research pertaining to anxiety disorders in Asian Americans is also sparse. The work that does exist, however, is promising and suggests that Asian Americans may experience anxiety at similar rates as their non-Hispanic White counterparts (Gee, 2004; Lee, Lei, & Sue, 2001; Okazaki, 2000). However, significant ambiguities continue to exist in the empirical literature pertaining to Asian Americans for many of the same reasons as other ethnic minority groups in the United States. For example, much of the literature to date has focused on social anxiety symptoms and attempts to distinguish between Western definitions of anxiety and Taijin Kyofusho (TKS), classified as a cultural bound syndrome found predominantly in individuals from Japanese decent (Kirmayer, Young, & Hayton, 1995; Kleinknecht, Dinnel, & Kleinknecht, 1997). Since TKS is based on anxiety and fear surrounding not offending others, a sociocultural factor that is endemic to Asian cultures, examining these constructs is important. However, as with other ethnic minority groups, instruments to assess social anxiety do not include specific questions to identify this culture-bound syndrome. Therefore, the potential for culturally invalid assessment continues to remain a problem when assessing anxiety in Asian American populations, which may lead to misdiagnosis (Gee, 2004; Lin & Cheung, 1999). Asian Americans have been found to report more somatic symptoms than non-Hispanic Whites (Lin & Cheung, 1999). Specifically, with respect to panic disorder, in one study Asian Americans were found to experience the symptoms of choking and terror more often than European Americans (Barrera et al., 2010). Asian patients experiencing psychological distress are more likely to report somatic symptoms to their health care providers rather than emotional symptoms, however, the literature continues to remain relatively silent as to whether there is a connection between panic disorder and somatization in Asian Americans (Lin & Cheung, 1999). Similar to the work with other ethnic minority groups, definitive conclusions are presently precluded due to the dearth of the empirical literature. Although beyond the scope of this review, it is presumed that other reasons for this ambiguity include cultural heterogeneity, differences in ethnic identity, lack of validation studies for measures of anxiety-related constructs in Asian populations, and other sociocultural factors.

1.5. Mandates for inclusion

In an effort by the National Institute of Health to ensure that ethnic and racial minorities are adequately represented in research studies, Congress passed the *NIH Revitalization Act of 1993*. This act, and the redefining of sampling regulations, ensured that minorities and women were included for in representative numbers of all studies conducted or supported by the NIH (USDHHS, 2002). The language of the Act states “there is an ethical importance of ensuring that recruitment is conducted in a manner that is fair to women, men and persons from minority populations so that no group is unduly burdened and that no group is unduly benefited” (USDHHS, 2002, p. 3). In the same guideline, it is made clear that minority samples must be included in the study if “there is no clear-cut scientific evidence to rule out significant differences of clinical or public health importance among racial or ethnic groups or subgroups in relation to the effects of study variables” (USDHHS, 2002, p. 25). By 1994, the NIH had revised its policy to require that women and minorities be included, and by 1995 the NIH refused to fund any project that did not adhere to these policies. Researchers were required to include in their grant proposals strategies by which they would achieve diversity in their samples.

1.6. Purpose of this investigation

The authors of this investigation sought to determine the rates of inclusion of minorities in randomized clinical trials by compiling a review of the literature on panic disorder. We were interested in any specific findings of particular relevance to minorities in regards to treatment issues, such as whether certain treatments were more effective for specific ethnoracial groups. Our objective was to determine if the existing data on panic disorder is adequate to represent and generalize to all portions of the population. Because of smaller numbers in many samples, this generally means that minorities would have to be oversampled to ensure enough statistical power was available for any group differences to emerge. While this sets high expectations for any study, we can hope that at the very least, the samples for studies performed in the United States mirror the composition of the population, and we include Canada as it is not uncommon for large clinical trials have collection sites in both countries. Additionally, Canada has a similar culture and ethnographic makeup to the United States in its major provinces, albeit with somewhat fewer visible minorities (Statistics Canada, 2008). If minorities are not adequately represented, it is unclear whether results from these studies are applicable to all Americans. In addition, investigation of recruitment techniques and trial locations was conducted to attempt to determine successful and unsuccessful methods for recruiting adequate samples of minorities.

2. Method

2.1. Selection of studies for inclusion

We performed a thorough and extensive search for randomized clinical trials of panic disorder. We used advanced search engines of the databases PsychINFO, MedLine, and CogNET (also known as MIT CogNET) to compile the studies. In doing so, the key terms “random,” “randomized,” “randomized control,” “panic,” “panic disorder,” and “agoraphobia,” “controlled,” and “controlled trial” were used to locate relevant articles. These key terms were searched for under the headings of title, keyword, and abstract. In addition, studies were found through the references of various meta-analyses of panic disorder and its treatment. These findings were cross-referenced with other study articles and searched for using the databases indicated. Lastly, we used the reference list of included studies as a tool to find others that might qualify for inclusion. These studies were then cross-referenced and located using the databases indicated.

Articles and research considered for this study were limited to only published works. In addition, the work had to have been conducted in North America (the United States or Canada), although it did not have to be published in a North American journal. This is because ethnicity demographics in other parts of the world are different than in North America, potentially distorting our results. Our search produced no studies from Central America or Mexico, so the regions are not represented in our data. However, the ethnic and racial demographics in these areas are very different than in the United States and Canada, and, again, would have distorted our results.

2.2. Missing data

In the event that a study met the criteria for inclusion in this analysis and did not provide the ethnic or racial information in the demographics of the paper, the corresponding author was contacted directly *via* or phone call. Several contact attempts were made, usually by (or by phone, when online contact information was not available). If no response, further attempts were made to contact the corresponding author. The last attempt was made by reaching out to another author of the study.

2.3. *Compilation of research*

The data collected from the studies selected was incorporated into one master spreadsheet. The demographic information was synchronized to compute totals, ratios and percentages of minorities in the samples. In addition, other items, such as recruitment methods and locations of the studies were collected to see if any environmental factors, such as lack of access to minority participants, were affecting the degree of minority participation.

2.4. *Statistical analyses*

Descriptive statistics were determined, based on the total N for each study, to arrive at percentages of inclusion by ethnoracial group. Data were coded based on type of recruitment method for whether advertising was utilized (1 for yes and 0 for no) and whether physician/clinic referral was utilized (1 for yes and 0 for no). The number of sites used for recruitment was tallied. Two-tailed Pearson and point biserial correlations were used to determine if there was a correlation between these variables and the percentage of minorities included in research studies.

3. Results

3.1. *Minority inclusion*

A total of 47 studies were initially selected for inclusion in this study. All were conducted in North America (the United States and Canada) between 1993 and 2010. Of these, 21 (44.7%) provided ethnic and racial information either in the study itself or by request from a contributor. Two additional trials provided some ethnic and racial information, but it was insufficient for inclusion in our data comparison. Eighteen studies failed to provide any ethnic or racial information whatsoever. (Those studies for which ethnic and racial information were not available are listed in a separate Appendix A.) While we were unsuccessful in contacting some authors, most of those authors we did contact could not provide the necessary information. Reasons given by authors for not providing the information include: the information was not collected when the trials were conducted, the authors of the study no longer had access to the data, the authors would provide the information but failed to do so, or there was no response.

There were a few studies that provided some racial and ethnic demographic information, but were not included in the final analysis. First, the corresponding author of the study done by Hicks et al. (2005) indicated that the patient sample was the same as another that was already in our analysis (Barlow, Gorman, Shear, & Woods, 2000). For that reason, we did not include this study as it would be doubly entered. Likewise, Roy-Byrne et al. (2006) used the same sample as Roy-Byrne et al. (2005), so only the 2006 study is included.

Two studies (Londborg et al., 1998; Mauret, Hofmann, & Rosenfield, 2010) did indicate that there were a majority of White participants in the study (<90%) but did not provide details as to the exact number nor the racial and ethnic makeup of the remaining sample (>10%). While it does attest to the under inclusion of minorities in panic disorder trials, these studies are not included in the tables because they lacked specific percentages. However, these articles are recognized as having provided some ethnic/racial data.

The studies can be further divided into before and after the *NIH Revitalization Act of 1993*, when researchers were mandated to include representative amounts of minorities in all studies funded by the NIH. Of the 7 studies published before the enforcement of the mandate in 1995, only 3 reported the racial and ethnic data of the population sample. Two of these studies (Black, Wesner, Bowers, & Gabel, 1993; Hoehn-Saric, McLeod, & Hiplsey, 1993) did not have any minorities participate, with 100% of the participants being non-Hispanic White.

Of the 40 studies published after the *NIH Revitalization Act of 1993* was enforced, 18 included information about ethnic and racial participation in their respective reports or provided the information upon request (including Hicks et al., 2005; Roy-Byrne et al., 2005). In addition, two of the studies, as mentioned previously, provided vague information about racial composition of their participants. Lastly, 20 studies did not provide the information at all.

Our final compilation included a total of 2687 participants from 19 studies (not counting the duplicate samples), from 1993 to 2010. Of these, 82.7% of the participants were non-Hispanic White, 4.9% were African American, 3.4% were of Hispanic origin, 1.1% were of Asian origin, and 1.4% were described as another ethnicity. Finally, 6.5% of total participants were of unknown ethnic/racial identity, as the specific makeup of this body of participants was unreported or undifferentiated. This information is detailed in Table 1. All of the studies involved participants over the age of 18, except for Pincus, May, Whitto, Mattis, and Barlow (2010), whose study was of participants between the ages of 14 and 17.

3.2. *Recruitment*

Of the 19 studies selected in our comparison, all but one were conducted in the United States, with the other conducted at sites in both the US and the Canada. Table 2 gives specific locations of testing sites. For studies with 10 or more sites only the number of sites is listed for brevity. In addition, data recruitment methods were analyzed in order to find successful outreach methods for minority recruitment. The most common recruitment method was some form of medical referral (36.8%), either by a primary care physician or mental health clinic. Advertisements in different media outlets (newspaper, television, and internet) comprised the recruitment of 15.8% of the studies, and 15.8% of the studies used a combination of the two methods. Six studies did not report a recruitment method (31.6%).

Five of the studies reported a total minority inclusion higher than 20%. Of these, three used physicians or medical caretaker referrals, one used advertisements in local media, and one did not describe methods. However, there was no correlation between the percentage of minorities included in a study and use of medical referral ($r = -.293$, $n = 13$, $p = .33$), use of advertising ($r = -.053$, $n = 13$, $p = .86$), or number of recruitment sites ($r = -.165$, $n = 19$, $p = .50$).

3.3. *Reports of differential outcomes*

When treating panic disorder, 42.1% of the studies used solely cognitive therapy or some non-pharmacological method and 36.8% analyzed the effect of pharmacological treatment alone. Of the remaining studies, 21.0% used a combination of cognitive therapy and medication to treat panic disorder.

We reviewed each article to determine if any of the studies that reported minority inclusion commented on the similarities or differences in the outcome for the different racial or ethnic groups. Only three addressed the results of minority groups. In one study, race did not have a significant contribution to the dropout rate of panic disorder treatment (White et al., 2010). Similarly, Roy-Byrne, Katon, Cowley, and Russo (2001) noted the minority group

Table 1
Ethnoracial makeup of panic disorder studies.

Study	*N*	White	Black	Hispanic	Asian	Other	Unknown
Ballenger, Wheadon, Steiner, Bushnell, and Gergel (1998)	278	240 (86.3%)	21 (7.6%)	12 (4.3%)	1 (0.4%)	15 (5.4%)	0 (0.0%)
Barlow et al. (2000) [also Hicks et al. (2005)]	312	278 (89.1%)	15 (4.8%)	13 (4.2%)	6 (1.9%)	0 (0.0%)	0 (0.0%)
Beck, Stanley, Baldwin, Deagle, and Averill (1994)	70	56 (80.0%)	5 (7.1%)	8 (11.4%)	1(1.4%)	0 (0.0%)	0 (0.0%)
Behar, McHugh, Peckham, and Otto (2010)	44	20 (45.5%)	18 (41%)	3 (7%)	2 (4.5%)	1 (2%)	0 (0.0%)
Black et al. (1993)	75	75 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Feske and Goldstein (1997)	40	34 (85.0%)	6 (15.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Goldstein, de Beurs, Chambless, and Wilson (2000)	46	43 (93.5%)	2 (4.4%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)
Hoehn-Saric et al. (1993)	50	50 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Meuret, Rosenfield, Seidel, Bhaskara, and Hofmann (2010)	41	36 (87.8%)	2 (4.9%)	2 (4.9%)	0 (0.0%)	1 (2.4%)	0 (0.0%)
Pincus et al. (2010)	26	26 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pohl, Wolkow, and Clary (1998)	166	146 (88.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	20 (12.0%)
Pollack, Otto, Wirthington, Manfro, and Wolkow (1998)	176	165 (93.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	11 (6.3%)
Roy-Byrne et al. (2001)	115	77 (67.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	38 (32.7%)
Roy-Byrne et al. (2003)	123	114 (93.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	9 (7.0%)
Roy-Byrne et al. (2006) [also Roy-Byrne et al. (2005)]	232	152 (65.5%)	32 (13.8%)	31 (13.4%)	0 (0.0%)	17 (7.3%)	0 (0.0%)
Smits, Powers, Cho, and Telch (2004)	130	106 (81.5%)	7 (5.4%)	10 (7.7%)	2 (1.5%)	0 (0.0%)	5 (3.9%)
Stahl, Gergel, and Li (2003)	351	254 (72.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	91 (27.6%)
Telch, Schmidt, Jaimez, Jacquin, and Harrington (1995)	156	128 (82.1%)	10 (6.7%)	14 (8.9%)	4 (2.2%)	0 (0.0%)	0 (0.0%)
White et al. (2010)	256	224 (87.5%)	14 (5.5%)	0 (0.0%)	14 (5.5%)	4 (1.6%)	0 (0.0%)
Total	2687	2224 (82.7%)	132(4.9%)	93 (3.4%)	31 (1.1%)	38 (1.4%)	174(6.5%)

White: European American/non-Hispanic White; Black: African American; Hispanic: Hispanic American/Latino; Asian: Asian American.

Table 2
Recruitment methods, treatment sites, and outcomes of panic disorder studies 1993–2010.

Study	Recruitment method(s)	Locations	Treatment(s)	Relevant patient outcome(s)
Ballenger et al. (1998)	Not described	20 Sites in US and Canada	Paroxetine	Paroxetine treatments with a dosage above 40 mg/day are effective in short term treatment of PD
Barlow et al. (2000)	Outpatients from anxiety clinics	Boston, MA; New York, NY; Pittsburgh, PA; New Haven, CT	Imipramine, CBT	There was "limited advantage" to using CBT and imipramine for PD short term; long term outcomes were best with combination
Beck et al. (1994)	Media advertisements	Houston, TX	CBT, relaxation therapy	Relaxation and cognitive therapy treated PD better than controls; cognitive therapy was better than relaxation for agoraphobic symptoms
Behar et al. (2010)	Newspaper ads, flyers, internet postings	Boston, MA	D-Cycloserine	D-Cycloserine significantly reduces patient bias toward threat in PD
Black et al. (1993)	Physician referral, media outlets	Iowa City, IA	Fluvoxamine, CBT	Fluvoxamine was more effecting than CBT at reducing PD symptoms
Feske and Goldstein (1997)	Not described	Philadelphia, PA	EMDR	EMDR initially was successful at alleviating panic symptoms, but advantages dissipated after 3 months
Goldstein et al. (2000)	Outpatients from anxiety clinics	Philadelphia, PA	EMDR	EMDR did not have statistically significant differences from placebo treatment
Hoehn-Saric et al. (1993)	Advertisement	Baltimore, MD	Fluvoxamine	Fluvoxamine, compared to placebo, significantly reduced panic symptoms in 3 weeks, and other anxiety and depression symptoms by 6 weeks
Meuret et al. (2010)	Outpatient clinic, community advertisements	Boston, MA; Dallas, TX	CART or CBT	Different pathways can reduce the severity of PD symptoms
Pincus et al. (2010)	Physician referral	Boston, MA	CBT	Panic CBT for adolescents (CBT-A) reduced panic rating and self anxiety levels
Pohl, Wolkow, and Clary (1998)	Not described	10 Sites in US	Sertraline	Sertraline drastically improved the rate of panic attacks *n* treated patients
Pollack, Otto, Wirthington, Manfro, and Wolkow (1998)	Not described	10 Sites in US	Sertraline	Patients with sertraline treatment showed less panic attack frequency
Roy-Byrne et al. (2001)	Physician referral	Seattle, WA	Collaborative care	Collaborative care or "PD pharmacotherapy embedded in a disease management" improved severity of PD
Roy-Byrne et al. (2003)	Advertisements, referrals	Seattle, WA; Los Angeles, CA; Dallas, TX; Charleston, NC; Denver, TX; Boston, MA	Benzodiazepines	Benzodiazepine withdrawal causes increased sensitivity to symptoms and harm avoidance of PD
Roy-Byrne et al. (2006)	Physician referral	Seattle, WA; San Diego, CA; Los Angeles, CA	CBT, pharmacotherapy	Patients below poverty line exhibited less improvement from regular treatment than those above poverty line
Smits, Powers, Cho, and Telch (2004)	Physician referral	Austin, TX	CBT	Fear of Fear is an underlying factor in PD that CBT can treat and alleviates symptoms due to the reduction of fear of fear
Stahl et al. (2003)	Not described	New York, NY	Escitalopram, citalopram	Escitalopram is a safe and effective treatment for PD
Telch et al. (1995)	Selection from prior NIMH study	Austin, TX	CBT	CBT subjects showed significant reductions in impairment, and an increase in quality of life
White et al. (2010)	Not described	Boston, MA; New Haven, CT; New York, NY; Pittsburgh, PA	CBT	Age only significant factor in predicting attrition, attrition does not strongly affect study results

CART: capnometry-assisted respiratory training; CBT: cognitive-behavioral therapy; EMDR: eye movement desensitization and reprocessing; PD: panic disorder.

in their study did not show any significant differences in treatment outcome from their non-Hispanic White counterparts in the improvement of panic disorder symptoms after treatment with collaborative care, a form of pharmacotherapy, thus proposing that their results can be generalized. However, it is not known what ethnoracial groups comprised the 38 non-Whites in the sample, limiting the usefulness of the findings.

Last, cognitive behavioral therapy was reported to be successful in treating African Americans below the poverty line with similar results to people above the poverty line, even where patients had a history of additional stressors, such as violence, financial issues, and experience of racism. However, this study suffered from a small minority sample size, and each ethnoracial group was dichotomized based on poverty status, reducing the cell sizes further, thus findings must be interpreted with caution (Roy-Byrne et al., 2006). None of the other studies in our review commented on the specific results of racial or ethnic groups in their samples. Study outcomes are summarized in Table 2.

4. Discussion

4.1. Minority inclusion

Ethnic and racial groups outside the European American population are underrepresented in randomized control trials and treatment outcome studies of panic disorder. Many studies did not even report ethnic and racial information for their study population. Of the 47 samples that were examined, 21 provided this information which accounts for less than half of the randomized clinical trials.

Of the total participants in this comparison, only 4.9% were identified as African American; Hispanics constituted 3.4% of the total amount, and persons of Asian descent were only represented by 1.1% of the total. These numbers extremely deficient when considering the proportional amounts needed to represent the population (Humes, Jones, & Ramirez, 2011). Even in comparison to the proportion of minorities in US biomedical research studies nationwide, these numbers are unacceptably low. For 2008, the NIH reported that, among its domestic, extramural clinical protocols, 13.1% of participants were Black/African American, 8.3% were Hispanic/Latino (of any race), and 7.5% were Asian (Table 10b, USDHHS, 2009). These rates are much higher than the studies compiled for this investigation. It should be noted that 5 of the studies considered for our study did not provide a breakdown of their minority sample, producing a group of people of "unknown" background, which comprised 6.5% of all participants. This is a significant number, and though it would increase the percentages of minorities in this review, it would not do so in amounts that are representative of the whole population.

It should be noted that none of the studies oversampled minorities in their samples. Given the typical *N* of clinical trials for panic disorder, if we are to suppose that the differing characteristics observed in minority populations will only emerge if those populations are oversampled, then it is even less likely that any unique results will be found.

4.2. Reasons for low rates of participation

Many factors can contribute to the low rates of minority participants in panic disorder studies, and in all mental health studies for that matter. The most common justification is a culture-wide mistrust of the field (Suite, La Bril, Primm, & Harrison-Ross, 2007). Many minorities have concerns about receiving inadequate treatment or misdiagnosis due to discrimination. For example, African Americans have a cultural memory of abuses such as the US Public Health Service Syphilis Study at Tuskegee, which continues to affect medical decision-making (Gamble, 1997), and more recent research abuses, such as the Baltimore Lead Paint Study which also disproportionality affected minorities (Spriggs, 2004).

Other reasons for low rates are not related to cultural mistrust, but are logistical in nature. These include financial and language barriers, physical accessibility, and traditional approaches in response to mental health problems (Nagayama Hall, 2001). For example, in terms of accessibility, studies may be carried out in areas that are not convenient to minority communities or in places where minorities may not feel welcome (*e.g.*, Williams, Chambless, & Steketee, 1998). Such reasons likely contribute to difficulties recruiting different ethnic and racial groups in mental health research. Minority groups are more generally disadvantaged, making it more difficult to recruit participants, as practicality dictates that inadequate compensation from the time spent in a study is outweighed by other responsibilities, such as a job or taking care of a family (Fisher et al., 2002).

Another reason may be the researcher's inability to understand certain values or expressions ethnic minorities may hold (Fisher et al., 2002). This can be as simple as a language or culture barrier between the clinician and the participant. Malgady and Costantino (1998) found that Hispanic anxiety patients were more likely to receive a more thorough and detailed diagnosis from a Hispanic clinician than from a non-Hispanic White clinician, even if the participant was bilingual. This suggests that under representation may be a cultural barrier that restricts the patient from fully expressing symptoms in a way that the clinician can understand, thus contributing to possible underdiagnosis. Among Hispanic and Asian Americans, it has been found that a culture-matched clinician is more likely to properly identify pathology and facilitate treatment than is a clinician of a different culture due to their shared understanding of psychopathological constructs (Malgady & Costantino, 1998; Sue, Fujino, Hu, Tackeuchi, & Zone, 1991). Given that cultural matching is not always possible or desirable, this underscores the importance of cross-cultural training for all clinicians. Mental health professionals must learn to make culture an integral part of each assessment as it can influence the patterns of communication between clinician and patient and subsequent diagnostic and treatment outcomes.

Hunter and Schmidt (2010) argue that rates of anxiety disorders in African Americans are misleading, proposing a model of avoidance that is driven by "awareness of racism, stigma of mental illness, and the salience of physical illness". In this model, African Americans are more likely to correlate anxiety disorder symptoms to physical or biological ailments than to mental health problems, and are thus more likely to see a primary care doctor than a mental health specialist. Friedman et al. (1994), found that, while African Americans and European Americans had no significant symptomatic differences, African American patients were more likely to go to an emergency room than to a mental health professional. Thus, African Americans are more likely to experience unnecessary hospitalization for panic disorder than European Americans, underscoring the need for empirically validated outreach strategies to treat and educate at-risk African Americans.

Finally, it is possible that minorities remain underrepresented due to apathy on the part of researchers, or even systemic exclusion due to the notion that ethnic minorities may not be good research participants in treatment studies. One large review of ethnic minorities in medical research, involving over 70,000 potential participants, found that minorities were just as willing and eligible to participate as their White counterparts (and in some cases, more willing), but were significantly less likely to be invited as study participants (Wendler et al., 2006). Likewise, Oddone et al. (2004) found that, in a survey of 83 studies conducted in VA programs, minorities were well-represented in medical studies – except in those involving an invasive treatment, where minority enrollment was significantly lower than expected. This indicates that the problem may lie not with the ethnoracial minority groups, but rather the research community itself. Researchers may be selectively excluding participants they believe would be poor candidates based on beliefs that minorities may drop out prematurely, be unable to follow directions properly, or fail to follow study rules and procedures. Thus, it could be that bias on the part of researchers against enrolling minorities in outcome studies is a contributing factor to under representation. Likewise, given that there are no consequences carried out by the NIH for failing to include minorities, it is unsurprising that researchers may lack motivation to prioritize diversity.

4.3. Recruitment and increasing participation

Although we hypothesized that certain recruitment methods might be more effective in diversifying a study sample, none of the recruitment methods reported were singularly effective in producing adequate numbers of minorities for panic disorder studies. Only two categories of recruitment methods were described, clinical referral or advertising, although some studies used both approaches. Clearly, a broader array of techniques, as discussed below, will be needed to ensure adequate inclusion of ethnoracial minorities.

Williams, Beckmann-Mendez, and Turkheimer (2012) conducted a study to determine how to improve recruitment of African Americans into anxiety disorders. Based on a qualitative analysis of responses from African American participants, mistrust of researchers and the White medical establishment emerged as dominant themes. Suggestions for increasing African American participation included assurances of confidentiality, adequate compensation, and sincere outreach into the African American community. Implementing these and other suggestions, led to a successful recruitment experience by Williams, Proetto, Casiano, and Franklin (2012), who identified and assessed 75 African Americans with OCD – a number that had not been achieved in any prior study of OCD at a single site (Williams, Powers, Yun, & Foa, 2010). This was accomplished through targeted efforts, including a wide array of advertisements that made a direct appeal to African Americans, as well as ethnoracial matching and diversification of study personnel.

Similar efforts have led to the successful recruitment of Hispanic and Asian Americans into other types of mental health studies (*e.g.*, Alegría, Takeuchi, et al., 2004; Alegría, Vila, et al. 2004; Gallagher-Thompson, Solano, Coon, & Arean, 2003), although we know of no literature that focuses specifically on the recruitment of these groups into studies of anxiety disorders. In addition to the aforementioned strategies, important elements of these efforts have included multilingual clinicians and instruments, sensitivity to idioms of distress, and a genuine commitment to diversity.

4.4. Differences in treatment outcome for minorities

Because very few studies reported findings specific to minorities, it is difficult to draw any strong conclusions as to what treatments may be most effective for specific cultural groups or how treatments may be best tailored for minorities. It was certainly encouraging that race was not predictive of study drop-out in the trial conducted by White et al. (2010), which should help to address possible concerns by researchers that ethnic minorities may not be good participants in clinical trials (*e.g.*, Wendler et al., 2006). Roy-Byrne et al. (2001) found no difference in outcomes between Whites and non-Whites treated with pharmacotherapy, but the ethnic breakup of the non-White sample is not known, limiting the usefulness of this finding. Similarly, Roy-Byrne et al. (2006) found that poverty status was not a predictor of CBT outcomes in African Americans, which is interesting and warrants replication. Regrettably, no studies examined treatment outcome by ethnoracial group.

4.5. Conclusions and future directions

Without adequate representation of minority populations in scientific studies, the mental health community cannot successfully understand or treat panic disorder cross culturally. While there is some research identifying these differences, more effort needs to be put in place to better understand how to identify and treat panic disorder. This can be done in two ways. First, more research into the different ways panic disorder is exhibited across ethnic groups would aid in diagnosis. A larger cultural understanding of the disorder would not only lead to more accurate diagnoses, but to less unnecessary use of the medical field. Second, a larger effort to include minority participants in randomized control trials studying panic disorder can help the mental health community discover treatments that would be effective across all ethnic and minority groups. In doing so, successful treatment options for different populations can potentially emerge, optimizing how panic disorder is treated across cultures. This is no simple task, as cultural, economic, and logistic barriers can deter minorities from participating in mental health research, and can also deter clinicians from including them. Only with the positive support and adequate effort from the mental health community can a truly cross-cultural understanding of panic disorder be developed.

Appendix A.

The articles listed below were considered for inclusion, but failed to provide adequate demographic information.

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