



INFORMATION FOR HEALTH CARE PROFESSIONALS



Generalized Anxiety, PTSD & Migraine

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“Anxiety disorder” is a blanket term often used to describe several different forms of a mental disorder which are characterized by pathological anxiety and fear. Generalized anxiety disorder (GAD) and post-traumatic stress disorder (PTSD) are two such forms of anxiety disorders. Both are comorbid with migraine. Identifying the presence of anxiety disorders, such as GAD and PTSD, in migraine patients may impact prognosis and help guide treatment.

Generalized Anxiety Disorder (GAD)

Definition & Epidemiology: GAD is characterized by persistent worry about the events of daily life and heightened physiological arousal. In the U.S. it has been estimated that the one year period prevalence rate of GAD is almost 3%.^[1] GAD is also more prevalent in migraineurs than those without headache. In one study, 7.2% of migraineurs fulfilled DSM-IV criteria for GAD, compared to 2.3% of those without headache in a one-year period.^[2] Overall, the odds of GAD range from 2.5 to 5.7 fold greater in migraineurs as compared to those without headache.^[3] (See figure 1.) Studies have also demonstrated that individuals with GAD are 3-4 times more likely to have migraine than those without GAD. In contrast to depression, the onset of anxiety disorders typically precedes the onset of migraine. Specifically two community studies have demonstrated that anxiety precedes migraine in 80% of the cases of those with both migraine and anxiety.^[3]

Potential Mechanisms: The occurrence of anxiety disorders with migraine has been hypothesized to be related to shared pathophysiological abnormalities that can give rise to both disorders, including genetic factors and abnormalities in central monoaminergic processing.

Screening: Screening for depression is not sufficient for capturing GAD. GAD may be screened for with casual questions about being a chronic worrier, with affirmative replies meriting further evaluation. Additionally, multiple screeners for assessing anxiety exist. Two patient self-report measures that are easy to score and clinicians may consider utilizing include: The Generalized Anxiety Disorder-7 and the Patient Health Questionnaire (PHQ).

Disability & Treatment: Migraine patients with anxiety may have more headache-related disability and worse long-term outcomes than those without anxiety. Cognitive behavioral therapy has demonstrated efficacy for anxiety and headache disorders. Although selective serotonin reuptake inhibitors (SSRIs) are commonly used for initial treatment of GAD in patients without headaches SSRIs are of little benefit for migraine prevention in general. Venlafaxine is FDA approved for GAD and may be of benefit for migraine prevention, and is the drug of choice for migraine patients with anxiety. Gabapentin may also be of benefit in patients with both

migraine and GAD as it has efficacy for migraine prevention and can be utilized as an adjunctive treatment for GAD. Finally, small clinical trials have demonstrated that buspirone may be effective for migraine prevention in those migraineurs with anxiety.[4]

Post-traumatic stress disorder (PTSD)

Definition & Epidemiology: PTSD occurs as a result of a specific traumatic event arousing feelings of intense fear, helplessness, and horror. The individual's response characteristically involves emotionally re-experiencing the event, numbing of affect, avoidance of stimuli which are associated with the event, and increased arousal. The 12 month prevalence rate of PTSD is approximately 3.5% and the lifetime prevalence rate approximately 6.8%.[5]

PTSD prevalence rates have been demonstrated to be increased in those with migraine in multiple different cohorts, including tertiary pain and headache clinics, veteran cohorts, and general population cohorts.[6] In one study, the 12 month PTSD prevalence rate in migraineurs was demonstrated to be 14.3% and the lifetime PTSD prevalence rate 21.5% in migraineurs as compared to 2.1% (12-month) and 4.5% (lifetime) for those without headache.[7] (See figure 1.) Migraineurs had a 3-4 fold greater odds of PTSD than those without headache. Furthermore, the 12-month and lifetime odds ratio of PTSD in migraineurs was greater than the odds ratio for either major depression or generalized anxiety in episodic migraineurs. (See Figure 1) Male migraineurs had a 3-4 folds greater odds ratio of PTSD than female migraineurs. Similar to GAD, PTSD symptoms preceded migraine in almost 70% of those with migraine and PTSD.[7]

Migraineurs have more traumatic stressors (4.6 ± 3.6) than those without headache (2.6 ± 2.5).[7] The most common traumatic life events (TLE) reported in one headache survey included learning about a family member/close friend who was hurt or killed, sudden injury/auto accident, observing someone being hurt/killed, and violent attacks. These findings were supported by a second multi-clinic study of almost 600 migraineurs, with the most common TLE including: natural disaster, sudden violent death, combat & transportation accidents.[6]

Potential Mechanisms: There are several potential mechanisms for the association between PTSD and migraine. Potential mechanisms include dysfunction of the central monoaminergic system and the hypothalamic-pituitary-adrenal (HPA) axis.[6]

It is unknown why the PTSD-migraine association is stronger in men than women. Genetic sex differences and sex differences in the stress response of the HPA axis may play a role.[6] The age TLE occur may also be vital. Specifically when a TLE occurs <13 years of age, the risk of depression is greater than PTSD; however, when a TLE occurs ≥ 13 years of age, the risk of PTSD is greater than depression.[6] Although recent data support an association between abuse and migraine, the peak age of vulnerability for childhood sexual abuse is under 13 years of age. Thus, it may be hypothesized that sexual abuse is likely *not* the primary TLE resulting in the PTSD-migraine association or related to the male predominance of migraineurs with PTSD. In contrast, TLE such as transportation accidents and combat may be and are more commonly experienced by those ≥ 12 years of age and men. The prevalence of PTSD increased to almost 50% in a veteran cohort of migraineurs [6]

Screening: As with GAD, specific assessment tools are required to screen for PTSD. PTSD may be screened for with casual questions about continually re-living a past traumatic event, with affirmative replies meriting further evaluation. PTSD may be screened for using the Life Event checklist and the PTSD Checklist (PCL). The PCL is a validated 17 question, self-report measure. For each question, the participant is asked to indicate how much they have been bothered by each symptom on a 5-point Likert scale. Scores ≥ 44 are considered clinically significant. Finally, a shorter screener, the Primary Care PTSD Screen (PC-PTSD) may also be

utilized. It consists of four “yes”/“no” questions. A positive screen consists of ≥ 3 “yes” responses. Positive screens on either the PCL or PC-PTSD warrant further evaluation.

Disability & Treatment: Several studies have shown that PTSD has a negative impact on the disability of chronic pain patients. In addition, migraine sufferers with PTSD have significantly greater disability than those migraineurs without PTSD.[6]

No studies to date have evaluated the effect of PTSD therapy on migraine in those migraineurs with PTSD. While the largest body of evidence for efficacy for PTSD (alone) exists for SSRIs, SSRIs provide no substantial benefit for migraine prevention. Amitriptyline and venlafaxine may be the best pharmacological choices to treat those with both PTSD and migraine. Amitriptyline has been shown to be of some benefit for PTSD in at least 3 small clinical trials and is often used with success for migraine prevention. The selective noradrenergic reuptake inhibitor, venlafaxine has also been demonstrated to be effective for PTSD treatment and may likewise be of benefit for migraine prevention. Finally behavioral treatment alone can positively influence chronic pain conditions and disability in those with PTSD; thus the use of cognitive/behavioral therapy, alone or in combination with pharmacological therapy, should be considered in all migraineurs with PTSD.[6,8]

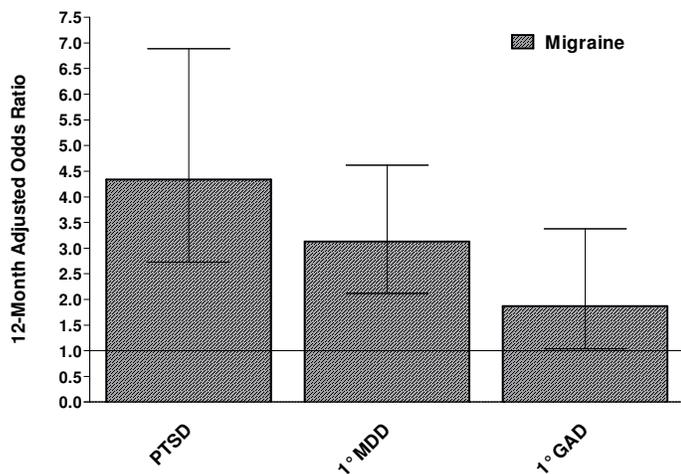


Figure 1: The 12-month adjusted odds ratio of PTSD, MDD and GAD in migraineurs as compared to those without headache.

Note: PTSD=Post Traumatic Stress Disorder; MDD=major depressive disorder; GAD=generalized anxiety.

Figure created from data from: Peterlin BL, Rosso AL, Sheftell FD, et al. Post-traumatic stress disorder, drug abuse and migraine:

new finding from the national comorbidity survey replication (NCS-R). *Cephalalgia*.

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References

1. Kessler RC, Brandenburg N, Lane M et al. Rethinking the duration requirement for generalized anxiety disorder: evidence from the National Comorbidity Survey Replication. *Psychological Medicine* 2005;35:1073-1082.
2. Saunders K, Merikangas K, Low NCP, Von Korff M, Kessler RC. Impact of comorbidity on headache-related disability. *Neurology* 2008;70:538-547

3. Merikangas KR, Low NC, Rasmussen BK. Migraine Comorbidity. In: Olesen J, Goadsby P, Ramadan NM, Tfelt-Hansen P, Welch KMA eds. The Headaches 3rd Ed. Philadelphia: Lippincott Williams & Wilkins, 2006, 243-250.
4. Griffith JL, Razavi M. Pharmacological management of mood and anxiety disorders in headache patients. *Headache* 2006;46[S3]:S133-S141
5. Bisson J. Post traumatic stress disorder. *BMJ* 2007;334:789-93
6. Peterlin BL, Nijjar SN, Tietjen GE. Post-traumatic stress disorder and migraine: Epidemiology, sex differences and potential mechanisms. *Headache* 2011;51:860-868
7. Peterlin BL, Rosso AL, Sheftell FD et al. Post-traumatic stress disorder, drug abuse and migraine: New Findings from the Natinal Comorbidity Survey Replication; *Cephalalgia* 2011;31(2):235-244
8. Ipser JC, Stein DJ. Evidence-based pharmacotherapy of post-traumatic stress disorder. *Int J Neuropsychopharmacol.* 2011;July 29:1-16