

New year...

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Last year we said goodbye to Ian Whittle whom we thank for all his hard work and welcome Peter Warnke from Liverpool as our new Associate Editor for Neurosurgery. We also say goodbye to many members of the editorial board and welcome new faces. The vitality of the journal rests with its reviewers and authors. We listed our reviewers in the December issue and reiterate our thanks to them. With over two thousand submissions a year the burden on unpaid reviewers forever increases. In order to reduce the

burden we have tried to make an early decision on priority for the journal with the result that over a third of papers do not go out to review. This will include many papers that are well conducted and worthy of publication but which we consider are not best suited to the *JNNP*, usually because they are too specialised. In order to assist authors with the decision of whether to submit to the journal we have revised the website guidelines. In summary we wish to attract papers of general interest to the multi-disciplinary readership of

Neurologists, Psychiatrists, and Neurosurgeons. Papers should be of direct clinical relevance and so we will not generally publish papers on normal brain function nor on animal studies. We hope that these changes will provide a quick decision for our authors whilst reducing the burden on reviewers. Nevertheless prioritising between good papers remains very difficult and to assist this we have established a weekly editorial meeting.

As we enter 2005 we reiterate our thanks to reviewers and authors and hope to continue to attract similar high quality manuscripts to those we have handled over the last year.

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EDITORIAL

Migraine—anxiety related dizziness (MARD): a new disorder?

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Dizziness is a common complaint that can result from abnormalities of the vestibular apparatus of the inner ear and of those portions of the central nervous system (CNS) that process information from the peripheral vestibular system and other senses, particularly vision and somatosensation. Recently, two CNS disorders, migraine and anxiety, have been recognised as being commonly associated with dizziness.^{1,2} These associations may be an expression of an aetiological relationship, for example, dizziness caused by migraine, or dizziness caused by anxiety; alternatively, migraine or anxiety may influence the presentation of a balance disorder. For example, chronic dizziness may become more disabling during the added stress of a migraine headache or panic attack. In addition, dizziness occurs comorbidly with both migraine headache and anxiety disorders.^{3,4} Finally, there is increased comorbidity between anxiety and migraine.⁵

Thus, it is not surprising that some patients with dizziness may suffer from a combination of a balance disorder, migraine, and an anxiety disorder, a symptom complex that we propose to name migraine—anxiety related dizziness (MARD) (fig 1). The general recognition of MARD may be limited because of the fragmented nature of our healthcare system, where specialists in one field, such as psychiatry or neurology, fail to recognise phenomena known to specialists in other fields, such as otoneurology.

This editorial will focus on the pathophysiology and clinical issues relating to MARD, including the interfaces among balance disorders, migraine, and anxiety. We use current epidemiological data and studies of pathogenesis to develop comorbidity models. These models serve as hypotheses that may lead to possible treatment options for many patients with dizziness, including those with MARD.

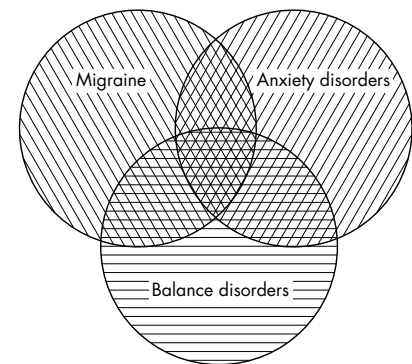


Figure 1 Venn diagram of the interfaces among migraine, anxiety, and balance disorders. The central sector, which denotes the three way interface, represents an hypothesised new ailment, migraine—anxiety related dizziness (MARD).

DEFINITIONS: DISORDER, SYNDROME, DEFINING SYMPTOMS, AND ASSOCIATED SYMPTOMS

Medical conditions are diagnosed by a variety of signs and symptoms. Specific constellations of signs and symptoms are usually called syndromes, whereas a disorder is ideally identified by specific pathophysiological mechanisms. Some diagnostic systems distinguish between symptoms necessary for the diagnosis of the disorder (defining symptoms),⁶ and those that are associated but not defining (associated symptoms). Although associated symptoms occur with increased prevalence in a disorder, they

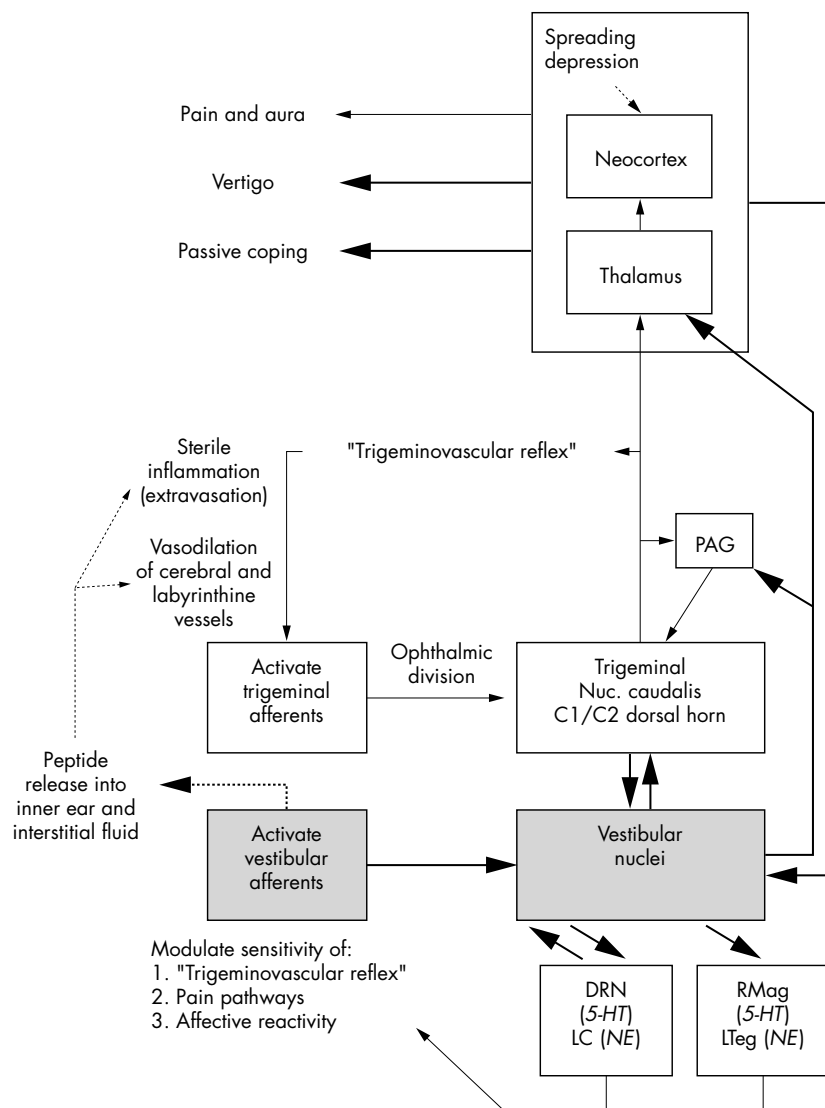


Figure 2 Pathogenetic model for migraine related dizziness. The core of the diagram represents pathogenetic mechanisms in migraine related pain, shown as unshaded boxes. The vestibular linkages to migraine mechanisms are shaded. Adapted from Furman *et al.*⁴ 5-HT, 5-hydroxytryptamine (serotonin); DRN, dorsal raphe nucleus; LC, locus ceruleus; LTeg, lateral tegmental noradrenergic neurones; NE, norepinephrine; PAG, periaqueductal grey; RMag, nucleus raphe magnus.

do not in themselves identify the disorder. For example, dizziness occurs as an integral or defining symptom in Meniere's disease⁷ and panic disorder—that is, dizziness during a panic attack.⁸ Dizziness can also be considered an associated symptom for migraine⁹ or generalised anxiety disorder.⁶

MIGRAINE RELATED DIZZINESS

The term "migraine" refers to both a syndrome and a disorder. The diagnosis of migraine syndrome requires the presence of a neurological aura associated with headache or a mixture of symptoms including unilateral, disabling, throbbing pain associated with sensitivity to noise and light or with nausea.¹⁰ In addition, migraine is characterised by interictal alterations in neurochemicals

(including serotonin, norepinephrine (noradrenaline), and dopamine) and cutaneous allodynia, representing aberrant neurophysiology during migraine.¹¹ In addition to these defining features of migraine, patients often describe a variety of additional migraine associated symptoms. One of the most common migraine accompaniments is dizziness or balance disturbance. Dizziness occurs in 28–30% and vertigo in 25–26% of patients with a primary complaint of migraine.^{9, 12} The association tends to be specific to migraine, rather than headache in general. Dizziness or vertigo occur in 54.5% of patients with migraine, compared with 30.2% of patients with tension-type headache.⁹ In addition, abnormal posturography testing is seen in patients with migraine

but not in patients with tension-type headache.¹³ Conversely, migraine was reported by 38% of 200 consecutive patients with the primary complaint of dizziness, compared with 24% in a comparison group of orthopaedic patients.¹ A similar study evaluating migraine in patients with isolated vertigo ($n = 72$) compared with orthopaedic controls identified migraine in 61% of the vertigo patients but only 10% of orthopaedic patients.¹⁴ Clinical laboratory vestibular tests in migraineurs unselected for the presence or absence of dizziness show a variety of abnormalities, including both peripheral and central abnormalities;^{12, 13, 15} however, these vestibular abnormalities are more prominent in patients with migraine associated with dizziness.^{9, 13, 16–20}

The link between vestibular symptoms and migrainous symptoms and the increased prevalence of vestibular test abnormalities in migraineurs suggests that migraine related dizziness is based on a specific pathophysiology—that is, that migraine related dizziness is a bona fide disorder. In fact, Neuhauser, *et al* have established specific diagnostic criteria for migraine related dizziness, which they term "migrainous vertigo".¹ A validated structured diagnostic interview for migrainous vertigo using these criteria may help to identify this condition.²¹ Using the Neuhauser criteria, migrainous vertigo was diagnosed in 9% of migraine headache patients. In 45% of these patients, migraine headache episodes were regularly accompanied by vestibular symptoms, and in another 48%, vestibular symptoms co-occurred irregularly.¹ The influence, if any, of migraine aura on the link between migraine and vestibular symptoms is unknown. We speculate that some episodes of vertigo in patients with MARD represent migraine aura without headache.

Pathophysiology of migraine related dizziness

Reflecting the uncertainty regarding the pathophysiology of migraine headache, the pathophysiology of migraine related dizziness is largely unknown. In fig 2, we provide a framework that integrates the possible neuroanatomical pathways with the clinical manifestations of migrainous vertigo. Fundamental to the pathophysiology of migraine is the trigeminovascular reflex. This is a parasympathetic reflex that can produce vasodilation of large cranial vessels. The vasodilation of large cranial vessels is a consequence of activation mediated by the trigeminal nucleus caudalis (Vc) and C1-C2 dorsal horn neurones.^{22, 23} In addition to the parasympathetic effects of the trigeminovascular reflex,

vasodilation may be induced or augmented by direct vasodilator effects of neurokinin A (NKA), calcitonin gene related peptide (CGRP), and substance P (SP) release from trigeminal sensory terminals.²²

Vestibular pathways can contribute to both central and peripheral migraine mechanisms.⁴ The reciprocal connections between the inferior, medial, and lateral vestibular nuclei and trigeminal nucleus caudalis suggest that vestibular and trigeminal information processing may be altered concurrently during migraine attacks, and that vestibular signals may directly influence trigemino-vascular reflex pathways. In addition, central vestibular activation can affect activity in monoaminergic pathways through direct connections from the vestibular nuclei to the dorsal raphe nucleus, nucleus raphe magnus, locus coeruleus, and lateral tegmental region. These changes in monoaminergic activity due to vestibular activation may both trigger migraine related symptoms and modulate activity in both pain related and anxiety related pathways. Conversely, regionally specialised noradrenergic²⁴ and serotonergic²⁵ inputs are potential substrates for altering central vestibular information processing during and between²⁶ migrainous episodes. Finally, two possible mechanisms may be related to vertigo as a migraine aura. Short duration vertigo symptoms have been suggested to be a "brainstem aura" that may be accompanied by changes in blood flow.¹⁹ Alternatively, direct connections from the posterior parietal cortex to the vestibular nuclei may provide a direct access for cortical mechanisms underlying migraine aura to reach areas important for vestibular information processing and reflex performance.

The vestibular periphery may also influence migraine pathways. Vass *et al*²⁷ have demonstrated that there is a significant trigeminal sensory innervation of the stria vascularis, spiral modiolar blood vessels, and dark cell region of the cristae ampullaris. They have shown also that electrical stimulation of the trigeminal ganglion produces extravasation from the basilar, anterior inferior cerebellar, and cochlear arteries of albino guinea pigs, and that round window application of capsaicin produces extravasation in the former two sites.²⁸ The powerful vasodilators SP and NKA are present in the eighth nerve afferent terminals in the organ of Corti and vestibular sensory epithelia.²⁹ SP and NKA may be released during nerve activation in the same manner as vasodilatory peptides are released by peripheral trigeminal nerve terminals as a neurogenic mechanism in

migraine. As CGRP is present in efferent projections to cochlear and vestibular epithelia,^{30,31} release is expected during efferent activation. Thus, it is possible that released SP, NKA, and CGRP from trigeminal and eighth nerve fibres could contribute to migraine related dizziness via hormone-like actions on neural and vascular elements.

ANXIETY RELATED DIZZINESS

Numerous studies have confirmed that anxiety and dizziness are interrelated.^{6,32} For example, among 268 patients recruited from a tertiary otolaryngology clinic, panic disorder was identified in 17.2% and major depressive disorder in 11.2%.³³ Furthermore, patients recruited in an anxiety clinic setting, particularly those with agoraphobia, have an increased rate of balance dysfunction.³⁴⁻³⁷ Consequently, recent studies have moved away from the previously held assumption that the presence of anxiety automatically implies a "psychogenic" cause for dizziness.³⁸ In a study by Eckhardt-Henn *et al*,³⁹ patients with dizziness recruited at a neurological clinic underwent both psychiatric and otoneurological evaluations. Based on the findings, the 189 patients were divided into the following groups: (a) organic (27%), (b) mixed "psycho-organic" (16%), (c) psychiatric (52%), and (d) idiopathic (5%). The most common psychiatric diagnosis was an anxiety disorder, followed by somatisation and depressive disorders. There were no differences between the psychiatric and psycho-organic groups with respect to the distribution of psychiatric diagnoses, suggesting that the presence of a particular diagnosis does not rule out a vestibular disorder. Based on a retrospective chart review of 132 (77%) of 172 patients at a tertiary dizziness clinic who had been referred for psychiatric evaluation, Staab *et al*⁴⁰ classified patients into three groups: (a) psychiatric disorder causing dizziness, (b) primary otoneurological disorder with secondary anxiety, and (c) pre-existing anxiety or prodromes escalating as a result of the neurotological disorder. Patients were nearly equally divided among the three categories. A diagnosis of panic disorder predicted membership in the psychiatric dizziness group, whereas membership in the primary neurotological group was associated with an elevated prevalence of spatial phobias. The fact that panic disorder appeared preferentially in the psychiatric group⁴⁰ is consistent with a definition of "psychiatric dizziness" previously proposed by our group.² These criteria include: (a) the dizziness is a defining or associated symptom of a psychiatric disorder, and (b) the

dizziness is not correlated with vestibular function test abnormalities. The only psychiatric disorder for which dizziness is a defining symptom is panic disorder. Furthermore, we have found that dizziness that occurs only during panic attacks is not correlated with vestibular dysfunction,³⁶ whereas dizziness as an isolated symptom occurring between panic attacks is correlated.^{35,36}

Anxiety seems to be a particular problem in patients with acute vestibular disorders. In a recent study,⁴¹ 17 (57%) of 30 patients with acute vertigo reported that anxiety symptoms seemed disproportionate to the seriousness of the disorder. Only 23% had no anxiety. The increase in anxiety was not just a general reaction to having an acute illness, because the comparison group of patients with other acute neurological conditions without dizziness reported significantly less anxiety (17%). In patients with chronic dizziness, anxiety is present but less pronounced. In a study of 112 patients with Menière's disease who remained symptomatic despite treatment, clinically significant anxiety was found in only 17%.⁴²

Pathophysiology of anxiety related dizziness

Three partially overlapping modes of interaction between anxiety and vestibular dysfunction have been proposed: somatopsychic, psychosomatic, and linkage.⁴³ A somatopsychic explanation would be that the perception of vestibular dysfunction, for example, dizziness or vertigo, causes anxiety. The initial high anxiety reactions to a vestibular disorder is an example of somatopsychic effects. Psychosomatic effects imply that anxiety causes dizziness. The psychiatric dizziness of panic is an example. Anxiety or hyperventilation may also reactivate a vestibular disorder by interfering with central compensation⁴⁴ or by altering somatosensory input.⁴⁵ The linkage model suggests a common underlying disorder that manifests as both anxiety and balance problems. The underlying neural circuitry includes the parabrachial nucleus, the vestibulothalamocortical and ceruleo-vestibular pathways, and serotonergic neurotransmission. In addition, the periaqueductal grey (PAG) is an area involved in dizziness, pain, and anxiety, and will be discussed in the next section. The pathophysiology of anxiety related dizziness is outlined in fig 3, which provides a framework for the three modes of pathogenesis of this condition, and incorporates information concerning both anatomical pathways and clinical manifestations.

The parabrachial nucleus (PBN) provides a key interface between anxiety

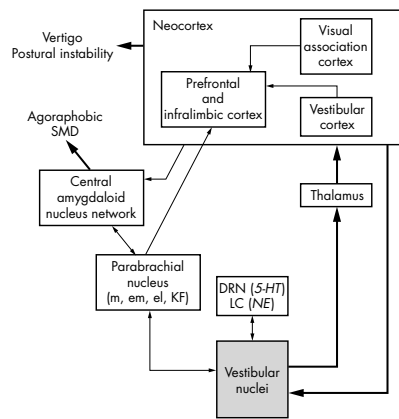


Figure 3 Pathogenetic model for anxiety related dizziness. This simplified representation of the neuroanatomical bases of the balance-anxiety interface is updated from recent reviews.^{67–102} These balance-anxiety linkages appear to involve integrated activity of at least four neural circuits: (a) a vestibuloparabrachial nucleus (PBN) network, (b) a vestibulothalamocortical network, (c) a ceruleo-vestibular network, and (d) a raphe nuclear-vestibular network. 5-HT, 5-hydroxytryptamine (serotonin); DRN, dorsal raphe nucleus; LC, locus ceruleus; NE, norepinephrine; m, em, el, KF, medial, external medial, external lateral, and Kölliker-Fuse nucleus subdivisions; SMD, space and motion discomfort.

related circuitry and central vestibular pathways. The discovery of the vestibulo-PBN pathway emerged from neuroanatomical tracer studies of vestibuloautonomic pathways. These studies indicated sparse direct vestibular nucleus connections to the ventrolateral medulla, nucleus of the solitary tract, nucleus ambiguus lateral tegmental area,^{46–49} and the anteromedian/Edinger-Westphal nuclei,⁵⁰ and robust projections from the vestibular nuclei to the medial, external medial, and external lateral subnuclei of the PBN and the Kölliker-Fuse nucleus.^{48–49–51} The neurones in this vestibulorecipient PBN region respond to whole body rotation in alert primates,⁵¹ and some PBN cells project to a wide region in the vestibular nuclei.⁵² Reciprocal connections between the PBN and the central amygdaloid nucleus, the hypothalamus, and the infralimbic cortex are consistent with the role of the PBN as an integral component of circuitry that mediates formation of conditioned fear and anxiety responses.^{53–55} Thus, the PBN appears to be an important node for linking vestibular information with the neural substrates for panic disorders and anxiety.

The vestibulothalamocortical pathway links the vestibular nuclei with discrete fields within the neocortex (including portions of parietoinsular cortex, areas 3a, 7, and 2v, and the posterior sylvian

cortex) containing neurones that respond to vestibular stimulation.^{56–57} These responses are mediated by projections from thalamic regions⁵⁸ that receive direct projections from the vestibular nuclei^{59–63} and show activation in functional imaging studies.⁶⁴ This cortical pathway is regarded as an important substrate for perceptions of vertigo, imbalance, and instability in patients and might be a pathway for somato-psychic effects.

The ceruleo-vestibular pathway arises from the caudal pole of the locus ceruleus (LC) and the adjacent nucleus subceruleus.^{24–65} There are four quantitatively distinct density levels of noradrenergic fibres in the vestibular nuclei, with the highest innervation densities in regions that probably increase postural sway and alter vestibular evoked eye movements during anxiety and changes in alertness.²⁴ The caudal locus ceruleus/nucleus subceruleus complex also contains cells that are known to project by collaterals to: (a) the hypothalamus, hippocampus, neocortex, and cerebellum; (b) the spinal cord, cerebellum, neocortex, and hypothalamus; or (c) the spinal cord and cerebellum.⁶⁶ As locus ceruleus projections are also highly collateralised, we have proposed^{24–67} that the ceruleo-vestibular pathway may be one branch of fibres that co-activate (or co-modulate) neurones in the vestibular nucleus and other motor pathways, contributing to the known effects of the state of arousal on vestibular reflex performance.^{68–71}

The actions of selective serotonin reuptake inhibitors (SSRIs) have provided compelling evidence for a role of serotonergic transmission in vestibular function. Recent evidence indicates that SSRIs are efficacious in the treatment of vertigo;^{18–32–72} furthermore, the beneficial effect of benzodiazepines such as clonazepam on both dizziness and anxiety may be mediated by their serotonergic effects.^{73–75} In addition, the vestibular manifestations of the SSRI discontinuation syndrome (acute onset of dizziness, vertigo, and uncoordination) are exacerbated by head and eye movements,^{76–77} which is consistent with direct effects on vestibular information processing. Serotonergic projections to the vestibular nuclei originate from both the dorsal raphe nucleus and a caudal region spanning the nucleus raphe obscurus and nucleus raphe pallidus.²⁵ These pathways also contain a significant non-serotonergic component. As individual raphe neurones often project to multiple sites via axon collaterals,^{78–81} we have suggested⁶⁷ that collateralised raphe-vestibular projections may co-modulate activity in the vestibular nuclei and sites such as the parabrachial

nucleus, neocortex, and central amygdaloid nucleus.^{79–82–83}

MIGRAINE—ANXIETY RELATED DIZZINESS

The link between migraine and balance disorders and the link between anxiety and balance disorders suggests that a subgroup of such patients will manifest migraine, anxiety, and a balance disorder. MARD is unlikely to be simply the chance combination of a balance disorder, migraine headache, and anxiety. This notion is supported by the increased prevalence of panic disorder in migraine patients with and without aura. In a recent study, the lifetime prevalence of panic disorder was 19.6% in migraine patients with aura and 14.3% in migraine patients without aura.⁸⁴ In addition, the presence of anxiety in patients with migraine suggests a worse prognosis.⁸⁵ In an 8 year follow up study, Guidetti *et al* found that anxiety disorders were predictive of headache persistence 8 years later. Specifically, among patients with migraine and anxiety, 75% had enduring migraines and anxiety 8 years later, 19% changed to tension headaches, and only 6% were headache free. By comparison, among migraine patients without anxiety, only 30% had enduring migraines, 42% changed to tension headaches, and 27% were headache free.

Pathophysiology of MARD

In fig 4, we present a schematic diagram of the pathophysiology of MARD that draws from material regarding migraine related dizziness, illustrated in fig 2, and anxiety related dizziness, illustrated in fig 3. In fig 4, we highlight particularly the role of the PAG. Note that the superior vestibular nucleus projects to the ventrolateral and ventral columns of the PAG. These PAG regions receive projections from the medial, dorsolateral, and ventrolateral orbital cortex and from the posterior and dorsal agranular insular cortex.⁸⁶ The ventrolateral and ventral PAG are also connected reciprocally with the central amygdaloid nucleus.^{87–88} Therefore, the ventrolateral and ventral PAG appear to be at the nexus of loops linking vestibular, migraine, and anxiety related pathways. This PAG related network appears to constitute a linkage between the affective and behavioural responses to balance disorders and migraine. Both ventral and ventrolateral PAG are components of “emotional motor” pathways that mediate passive emotional coping in response to deep or chronic pain or traumatic injury.⁸⁹ The activation of pathways linking the vestibular system with anxiety and migraine mechanisms

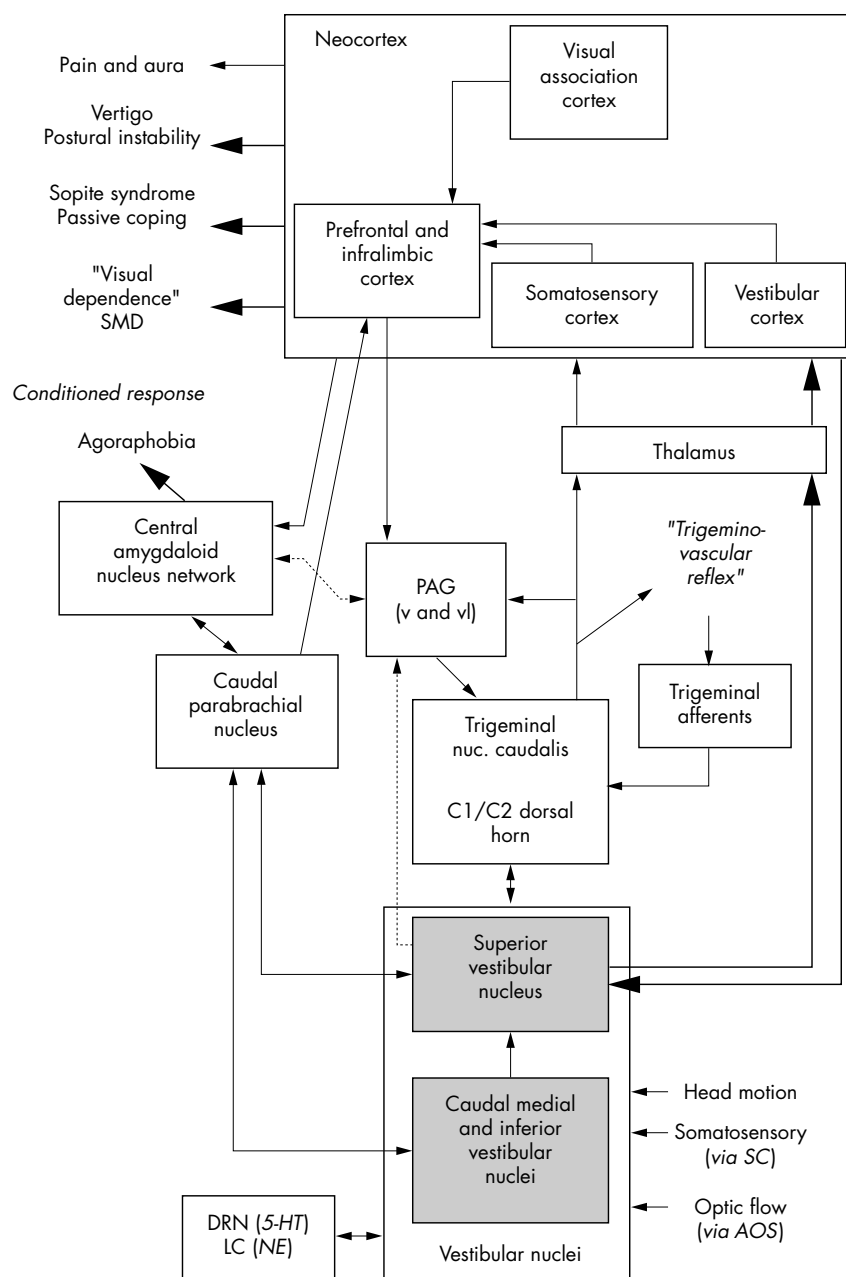
Unconditioned perceptions

Figure 4 Pathogenetic model for migraine-anxiety related dizziness (MARD) showing the three way interface among migraine, anxiety, and dizziness. The interactions between the balance-migraine and the balance-anxiety interfaces are shown schematically as a fusion of figs 2 and 3. Neuronal activity in the vestibular nuclei, particularly the superior vestibular nucleus, is a first major integrative site for the balance-migraine-anxiety linkage. As this activity is a function of (a) afferent input regarding head motion from the inner ear, somatosensation from the spinal cord (SC) and optic flow information from the accessory optic system (AOS); (b) trigeminal sensory inputs; and (c) descending inputs from the neocortex, it has the potential to participate in the triggering, buildup, and perseverance of episodic dysfunction. The effects of noradrenergic and serotonergic modulation of vestibular, anxiety, and migraine pathways may be viewed as parallel operations of the mechanisms described in figs 2 and 3. 5-HT, 5-hydroxytryptamine (serotonin); AOS, accessory optic system; DRN, dorsal raphe nucleus; LC, locus ceruleus; NE, norepinephrine; PAG (v and vl), periaqueductal grey (ventral and ventrolateral columns); SC, superior colliculus; SMD, space and motion discomfort.

may produce additive effects in terms of perceptions, affective changes, and coping strategies. Because these perceptions and affective changes are not easily attributed by a patient to a specific

physical cause, they may serve as unconditioned stimuli for development of phobic avoidance. Further, it is important to note that the additive central effects of migraine, vestibular,

and anxiety related circuits on perceptions of pain, vertigo, postural instability, passive coping, visual dependence, and space and motion discomfort (SMD) are subject to considerable individual variations. These variations may be an important factor in understanding individual differences in susceptibility to the development of avoidance behaviour, including agoraphobia.

Clinical implications of MARD

The clinical implications of the overlap between migraine, anxiety, and balance disorders in MARD relate to diagnosis, clinical course, and treatment. Because the care of these patients tends to be distributed among primary care physicians, neurologists, otolaryngologists, and psychiatrists, the initial diagnosis may reflect the background of the examining doctor in addition to the symptoms of the patient. Furthermore, patients may self select to a particular specialist depending on which component predominates. Patients with MARD may be misdiagnosed if one or more components go unrecognised. In our experience, balance symptoms in patients with a clinically significant anxiety disorder are most likely to be overlooked, as their symptoms are often attributed entirely to anxiety. An awareness of the existence of MARD will enable physicians not only to appreciate the predominant complaint but also stimulate them to look for the other components.

A common feature in MARD is visual dependence—that is, an excessive reliance on visual cues for balance. Visual dependence and its symptomatic expression, SMD, affect many patients with migraine, anxiety, or a balance disorder. Patients with SMD often have discomfort in visual environments that are overly complex or devoid of visual orientation cues. Migraine patients are also known to be sensitive to certain visual aspects of the environment, perhaps independent of vestibular mechanisms. In certain anxiety disorders, particularly in height phobia, patients have an increased tendency to manifest discomfort in certain visual environments. As noted in figs 2–4, visual dependence and SMD may be seen in patients with migraine related or anxiety related dizziness, and in MARD.

Despite our knowledge concerning CNS pathways that are important for MARD (see fig 4), the relative importance of the different components of MARD is unknown. The effect of treatments may shed light on the nature of MARD, including the inter-relationships among its components. For example, if MARD represents a disorder in which the three manifestations constitute

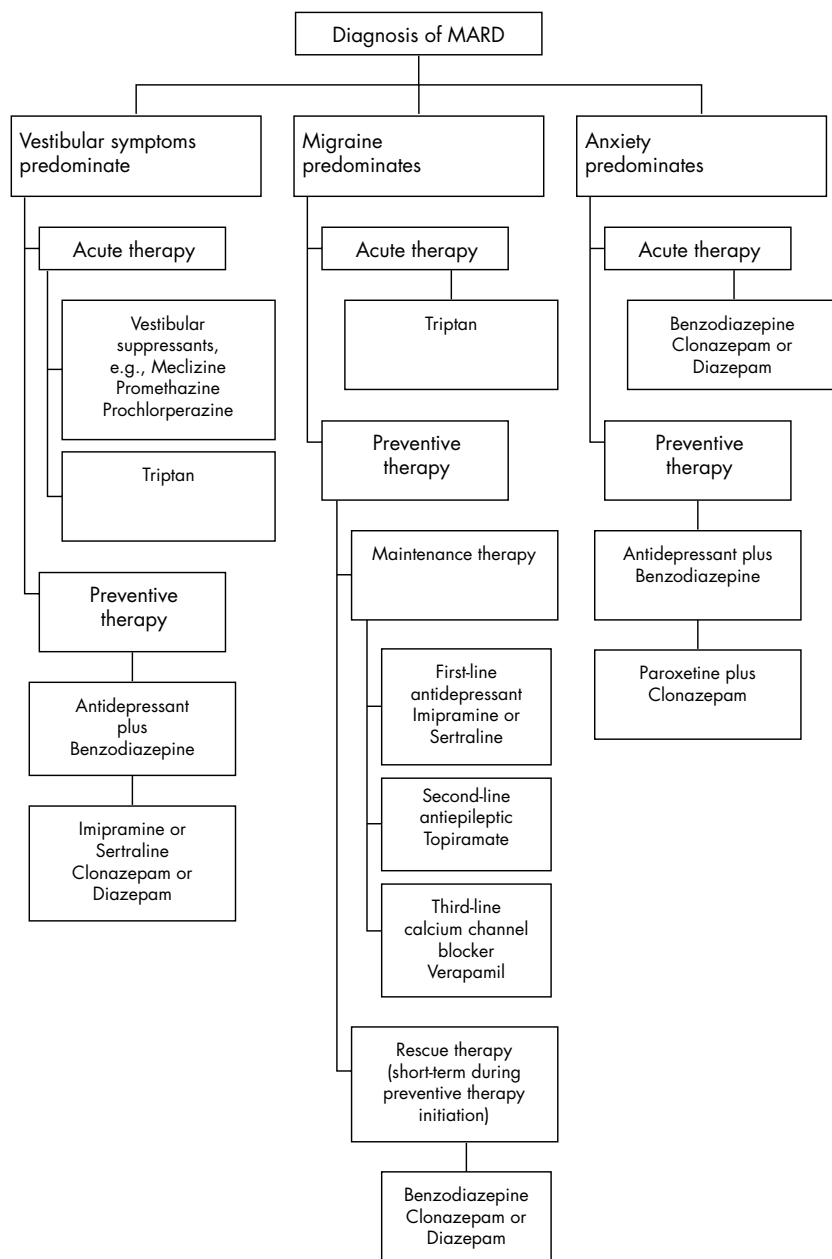


Figure 5 Flowchart for the treatment of migraine-anxiety related dizziness (MARD).

different symptomatic expressions of the same pathological substrate, a treatment directed at that underlying common pathological substrate should result in improvement of all three components. However, treatment directed at a component that constitutes a superficial manifestation of the condition (symptomatic treatment) should result in improvement of that component but not the others.

Although empirical information on the simultaneous effects of treatment on the three components of MARD is lacking, studies that focus on two of the three components have been conducted. With respect to the combination of dizziness and anxiety, several drugs, including antidepressants and

benzodiazepines, are used to treat both conditions. Treatment with SSRIs may reduce both dizziness⁹⁰ and posturographic abnormalities in agoraphobia.⁹¹ Dizziness limited to panic attacks in panic disorder (psychiatric dizziness)⁹² resolves as panic frequency is reduced with treatment of this condition. In our laboratory, we have found that vestibular rehabilitation therapy can be of value for patients with agoraphobia with vestibular dysfunction who did not respond to behaviourally oriented therapy.⁹³ With respect to the combination of dizziness and migraine, both abortive and prophylactic migraine medications effectively control headache and balance symptoms in patients with both migraine and balance complaints.⁹⁴

Reploeg and Goebel found a reduction of at least 75% in the frequency of attacks of dizziness in 72% of patients with migraine related dizziness who were treated with either a tyramine restrictive diet alone or diet in combination with nortriptyline or atenolol.⁹⁵ The calcium channel blocker dotarizine has also been reported to be effective in relieving both migraine and peripheral vertigo.⁹⁶ With respect to the combination of migraine and anxiety, no study has specifically addressed the simultaneous treatment of these components. However, migraine preventive medications such as antidepressants and antiepileptics are also effective for the management of anxiety disorders.⁷²⁻⁹⁷

At this time, the clinical treatment for MARD is largely speculative (fig 5). However, in our opinion, each component of the disorder should be considered when making treatment decisions. The choice of treatment or treatments should be influenced by clinical impressions regarding cause and effect relationships, if any, and by the relative severity of the various comorbidities.

In our experience, patients with MARD in whom balance symptoms predominate should be treated with a combination of an antidepressant, such as imipramine, and a benzodiazepine, such as clonazepam. Sertraline and diazepam are alternates. For patients in whom vertigo is considered a migraine aura or migraine equivalent, a triptan may be beneficial⁹⁴ for acute attacks. Patients with MARD in whom migraine predominates may also benefit from treatment with an antidepressant. Our preferred medication is imipramine. This type of patient may also benefit from treatment with an anticonvulsant such as topiramate or a calcium channel blocker such as verapamil. Note that in our experience, beta blocking agents do not appear to be helpful for patients with MARD. Rescue therapy includes short term benzodiazepines. For patients with MARD in whom anxiety symptoms predominate, an SSRI such as paroxetine⁹⁸⁻⁹⁹ or sertraline⁹⁰ is preferred. Benzodiazepines such as clonazepam are valuable, particularly for those patients with both prominent anxiety and pronounced balance symptoms or SMD, and may be used chronically. As vestibular rehabilitation therapy has been shown to be efficacious for balance disorders,¹⁰⁰ migraine related dizziness,¹⁰¹ and anxiety related dizziness,⁹³ all patients with MARD, especially those with SMD, may benefit from vestibular rehabilitation therapy.

CONCLUSION

Migraine and anxiety are two conditions that are frequently associated

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with dizziness and balance disorders. Moreover, migraine and anxiety are comorbid, occurring concomitantly more frequently than would be expected by chance alone. Thus, it is not surprising that a subgroup of dizzy patients presents with both migraine and anxiety. MARD is a newly defined condition wherein a patient presents with a combination of a balance disorder, migraine, and anxiety. The relative severity of each component and the functional relationships between each component may differ from one patient to another and may change over time. The pathophysiology of MARD probably relates primarily to monoaminergic pathways important for migraine, anxiety, the central vestibular system, and their interconnections. Recognising MARD is important, as management requires amelioration of each of the underlying conditions, preferably by implementing treatments that benefit more than one component of the disorder.

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