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Sensorintegrative dysfunction underlying vestibular disorders after traumatic brain injury: A review

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Abstract—Vestibular symptoms are persistent and problematic sequelae of blast exposure. Several lines of evidence suggest that these symptoms often stem from injury to the central nervous system. Current methods of assessing the vestibular system have described vestibular deficits that follow traumatic brain injury and differentiate blunt and blast trauma but have not examined the full range of vestibular functions that depend on the cerebral structures above the midbrain. Damage to the central vestibular circuits can lead to deficits in vital processes of spatial perception and navigation, in addition to dizziness and disequilibrium, and may also affect emotional functioning, particularly noradrenergically modulated states of anxiety. Perceptual functions can be assessed to determine the extent of central nervous system involvement in vestibular symptoms and to provide greater confidence when vestibular dysfunction is to be excluded. The ability to detect central vestibular dysfunction will significantly enhance our response to the dizziness and balance symptoms that are a common source of distress for Veterans.

Key words: Afghanistan, anxiety, balance, blast injuries, brain injuries, central nervous system, Iraq, nonblast injuries, posttraumatic stress disorder, spatial perception, vestibular cortex, vestibular system.

INTRODUCTION

Active Duty servicemembers and Veterans who have been deployed in war zones and exposed to blasts have reported high rates of vestibular symptoms, such as dizziness, clumsiness (15%–40%) [1–3], imbalance (7%) [4], and vertigo (24%) [2]. Balance symptoms have also been found to persist for months to years following the injury [5–7] and have been associated with poor prognosis after traumatic brain injury (TBI) [8]. In addition to vestibular complaints, impairment in multiple sensory modalities is very common in U.S. military combatants in Iraq, Afghanistan, and other regions of the Middle East (Operations Iraqi

Abbreviations: BPPV = benign paroxysmal positional vertigo, CDP = computerized dynamic posturography, CNS = central nervous system, DSI = dual sensory impairment, MSI = multisensory impairment, mTBI = mild traumatic brain injury, PIVC = parieto-insular vestibular cortex, PTSD = posttraumatic stress disorder, SVV = subjective visual vertical, TBI = traumatic brain injury, VOR = vestibulo-ocular reflex.

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Freedom, Enduring Freedom, and New Dawn) [3,9]. Of subjects in large samples of servicemembers postdeployment, 32 percent reported dual sensory impairment (DSI) to the auditory and visual systems [9] and 13.9 percent reported multisensory impairment (MSI), with deficits in three domains (auditory, vestibular, and visual) [3]. Furthermore, the norm for vestibular symptoms may be coexistence with symptoms in other modalities; for example, dizziness is more often endorsed in concert with auditory and visual symptoms than alone [3], and factor analyses of postconcussive symptoms in Veterans suggest that dizziness symptoms stem from the same source as vision problems, hearing problems, or both [10–11]. Although the mechanism for such co-occurrence of deficits in multiple modalities could be simultaneous injury to the separate sensory organs, empirical evidence supports a TBI mechanistic role, at least in part. In two recent studies, mild TBI (mTBI) history, either blast or nonblast, was significantly associated with the presence of DSI and/or MSI [3,9].

Deployed servicemembers frequently sustain mTBI (also known as concussion) from blast or other causes [4]. Head trauma sometimes leads to injury of the primary vestibular organs, generating conditions such as benign paroxysmal positional vertigo (BPPV) [12]. However, TBI's effects on multiple sensory systems may be in large part centrally mediated, occurring by damage to multimodal gray matter and by disconnection from diffuse axonal injury [13] that impairs coordination between anatomically remote brain areas [14–15]. The vestibular and balance system is especially vulnerable to central injury, because its function relies on the precise coordination of multisensory inputs at all levels of the central nervous system (CNS). Because peripheral vestibular organs can only transmit information about the acceleration and deceleration vectors of the head and gravity, additional visual, auditory, somatosensory, and proprioceptive information must be integrated with vestibular input to represent the full picture of the self in space. Reflecting this need for multisensory integration, the vestibular and balance system is multimodal even at the level of vestibular nuclei. For example, neurons of the vestibular nucleus respond to optokinetic rotation stimulation as well as to bodily rotation [16], and the vestibulo-spinal reflexes are modulated by inputs from other sensory modalities [17]. At the cortical level, it has been known for some time that, unlike the classic auditory and visual primary cortices, the primary vestibular cortex is not modality specific [18]. Together, the functional anatomy of the vestibular system, the high rate of TBI after blast, and the potentially low incidence of vestibular deficits unaccompanied by deficits in other modalities strongly implicate central mechanisms in the vestibular consequences of blast.

METHODS

Articles were assembled through PubMed and Google Scholar searches with combinations of the following terms: "mild traumatic brain injury", "blast injury," "vestibular," "balance," "dizziness," "vestibulo-ocular reflex" (VOR), "posturography," "subjective visual vertical" (SVV), "central nervous system," "cortex," "vestibular cortex," "lesions," and "neuroimaging." Only articles with human participants published in the English language were included. Case-studies were not included. Relevant articles cited in those returned by the searches were also reviewed.

SPECIFIC EFFECTS OF BLAST ON VESTIBULAR FUNCTION

Much of the evidence for high rates of vestibular dysfunction after mTBI comes from large cohort studies using questionnaire-type symptom reports, indices that are generally nonspecific and prone to misclassification. Typically, the respondent is asked whether the general symptom (dizziness, imbalance, etc.) is present or absent [1,19], and in some cases [3,9], to rate the severity of the symptom on an instrument such as the Neurobehavioral Symptom Inventory [20]. While this approach gives a useful estimate of the extent of disability in the population, it does not enable differentiation between etiologies of dizziness and imbalance or confirmation of physiological abnormality.

Studies using objective measures of vestibular function after blast TBI provide more specific information about the true prevalence and nature of vestibular dysfunction. To date, these studies support the presence of abnormalities and indicate that both peripheral and central vestibular systems are affected. Hoffer et al. objectively verified that dizziness and imbalance are common following blast exposure [7]. In that study, nearly all of the patients presenting for balance problems after blast exposure exhibited a profile of vestibular impairment on

computerized dynamic posturography (CDP), sway, and gait tests. Further, Hoffer et al. observed that blunt trauma and blast trauma were associated with different profiles, with blast-induced imbalance tending to be constant rather than intermittent, sensitive to the onset of exercise, and less characterized by BPPV. Additional evidence of a distinction between vestibular effects of blast versus blunt-head trauma is seen with multiple reports of horizontal canal dysfunction (caloric test asymmetry). Across reports, abnormal caloric testing is more common (14%–71%) in blunt trauma patients with dizziness [21–23] than in blast trauma patients with dizziness (0%–22%) [6,24–26].

Differentiating blast from nonblast trauma using other measures of the VOR has yielded inconsistent results. In a study of 31 blast-exposed patients with mTBI, only 1 had spontaneous nystagmus and no patients had failure of fixation suppression [26]. Eye movement abnormalities in phase, gain, and asymmetry were relatively low among those with blast injury during rotary chair testing, with 18 percent demonstrating abnormality in one study [26] and 24 percent in another [27]. In the latter study, two-thirds of those having abnormal results showed patterns consistent with peripheral injury, whereas the results of the other third, or 8 percent overall, were consistent with central injury. Furthermore, abnormal nystagmus, mostly of central origin and equally distributed across etiology of trauma, was found during videonystagmography in 25 percent of patients in this study [27]. However, abnormal nystagmus was not present in another blast-exposed cohort [6]. Scherer et al. describes a greater variability in VOR gains for patients with TBI who are symptomatic for balance disorders compared with asymptomatic patients [28]. However, the relationship between blast-related dizziness and VOR function has not been directly tested.

Reports of other tests of vestibular function after blast exposure are also inconsistent. In one report, static SVV was abnormal in only 11 percent of subjects [27], while in another study, SVV was abnormal in nearly all subjects (96%) [26]. In this latter study, however, it was not specified whether the abnormality was on the static or rotational test, and these are differentially sensitive to a peripheral versus a central locus of damage. Inconsistent results for cervical vestibular-evoked myogenic potentials are also described. Just 14 percent of subjects tested abnormal in Scherer et al.'s sample [27], but 53 percent tested abnormal in Akin and Murnane's investigation [26]. Differences in proportion of blast versus nonblast TBI may partly explain the large difference in results between these two studies; Akin and Murnane's sample contained about one-third nonblast mTBIs, whereas Scherer et al.'s sample all had blast-related mTBIs.

Unlike VOR, postural stability appears to be consistently impaired for blast-exposed individuals with or without TBI. Akin and Murnane found 64 percent of patients to be impaired on posturography testing [26], and Cohen et al. found 46 percent to be abnormal on CDP testing [6], with all of these individuals having dizziness at time of testing and 83 percent still symptomatic 6 months later. Scherer et al. found that 63 percent of symptomatic and 74 percent of asymptomatic patients had abnormal CDP results, although the symptomatic subjects performed more poorly on conditions targeting the vestibular modality and exhibited an increased reliance on visual and proprioceptive information [27]. In a recent report, Walker et al. examined kinematics during standing and found that a small sample of Veterans with blast mTBI, dizziness, and imbalance symptoms exhibited significantly more sway than noninjured controls during all conditions (eyes closed and open and standing on floor or on a soft surface).* Impairments during both eyes open and closed conditions suggest a multilevel deficit involving integration of vestibular, somatosensory, and visual information (i.e., the entire balance system).

Overall, it does not appear that blast TBI can be characterized by a specific pattern of vestibular test results, but it instead generates a pattern consistent with diffuse damage to multiple levels of the vestibular and balance system. Balance and postural deficits are common findings across reports, while abnormal VOR is less reproducible from study to study. Across study methods, evidence for both peripheral and central dysfunction exists. However, limitations within the published literature leave many questions for future research. While the findings do suggest greater impairments in the symptomatic compared with asymptomatic groups, the lack of a noninjured control group in most studies prevents firm conclusions about the vestibular effects of blast-induced brain injury. Further, the small sample sizes, use of patients with mixed injury mechanisms, and recruitment from balance clinics precludes accurate measures of the

*Walker MF, Liao K, Pan T, Roenigk K, Daly J. Postural instability in blast-exposed Veterans. NATO RTO Human Factors and Medicine Panel (HFM) Symposium; 2001 Oct 3–5; Halifax, Canada.

prevalence of vestibular dysfunction in the entire cohort of individuals with blast-related TBI. The specificity of the tests used to perform assessments is another ongoing challenge and would benefit from the establishment of a standardized battery of tests with universally accepted thresholds for normal. For example, tests such as CDP or the Romberg test assess balance behavior, which involves many integrative processes. Impairment on these tests confirms a balance deficit but lends limited insight into the source of the abnormality. Further, abnormalities on VOR or SVV tests may occur following lesions of central or peripheral vestibular pathways, because the VOR is a complex function involving integration of information at the brain stem, cerebellar, and cortical levels. Finally and critically, the test batteries only assess a portion of the vestibular system. Although centrally mediated processes are likely to be affected by blast on a number of grounds (presence of TBI, high incidence of MSI, and potentially high rates of balance problems relative to peripheral dysfunction), these processes have not been adequately assessed in this population. Future efforts should examine the effects of blast on the full range of vestibular system functions, including central processes.

HIGHER-ORDER CENTRAL VESTIBULAR FUNCTIONS

Much of the testing used in clinical assessment of the vestibular system examines the integrity of the VOR. However, vestibular input is communicated to many areas of the brain stem, cerebellum, and cortex subserving other complex functions not measured by the VOR. These CNS contributions to vestibular processing are usually not evaluated, and standardized tests of these processes are not available. Several functional anatomic studies indicate that a core region of vestibular information processing known as the parieto-insular vestibular cortex (PIVC) exists. Stimulation of this region was found to generate the sensation of dizziness by Penfield [29], and this same region is active during caloric stimulation in humans [30–31]. In addition to the PIVC, projection targets of the vestibular nuclei also include the ventral and posterolateral thalamus, cerebellar nuclei (these also receive direct input from the vestibular organs), the superior temporal gyrus, the precuneus and inferior parietal lobule, the amygdala, the anterior cingulate cortex, and the locus coeruleus (**Figure**) (see Dieterich and Brandt [32]). Activity during vestibular stimulation has also been observed in the hippocampus [33]. Evidence to date suggests that this central vestibular network critically supports spatial analysis and memory. Specific processes attributed to this network include perception of self in vertical space, perception of self-motion, and navigation. Notably, these dysfunctions are perceptual and can occur without VOR or postural abnormalities.

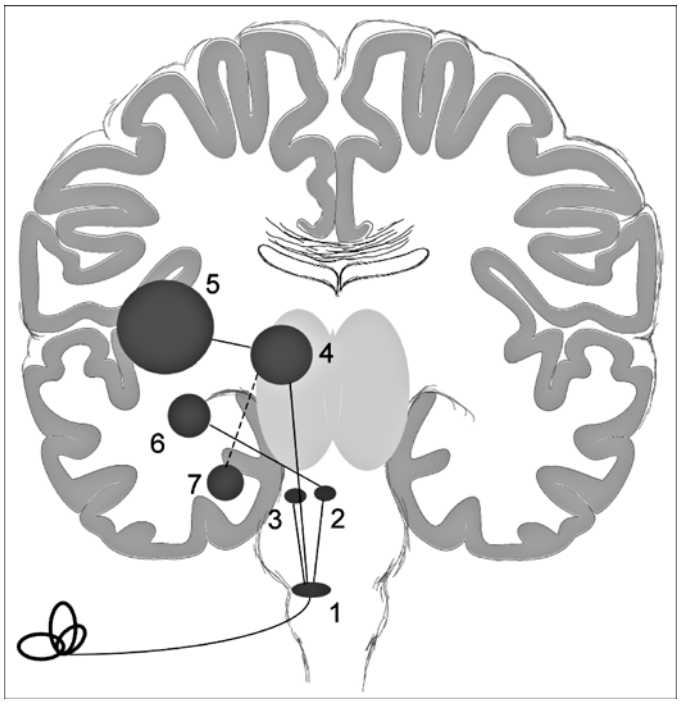

Figure.
Posterior central nervous system projections of vestibular nuclei subserving spatial and emotional processing. Solid lines indicate known projections and dashed line indicates hypothesized projection. (1) Vestibular nuclei, (2) locus coeruleus, (3) parabrachial nucleus, (4) posterolateral thalamus, (5) parieto-insular vestibular cortex, (6) amygdala, and (7) hippocampus. Projections are stronger to nondominant hemisphere (typically right side).

Perception of Verticality

Computations within structures rostral to the midbrain contribute to the perception of verticality. In order to perceive oneself as upright in space, both the environment and the self must be perceived as aligned with gravity. Subcortical and cortical lesions can impair these perceptions. Brandt et al. found that posterior insular lesions were

accompanied by aberrant tilt perceptions in 69 percent of patients, while lesions to other brain areas did not predict SVV abnormalities [34]. In addition to the orientation of the visual world, the central vestibular system subserves the perception of the body relative to gravity. Karnath et al. describe disturbed perceptions of postural uprightness in patients with lesions to the posterolateral thalamus, where patients perceive themselves as upright only when tilted toward the side of the lesion [35]. Lesions to posterolateral thalamus do not affect oculomotor function, but can result in abnormal SVV, gait abnormalities, and falls [36], as well as disturbed perceptions of environmental tilt [37]. Somatosensory loss from spinal cord injury or cerebral stroke also impairs the SVV and its adaptation to vestibular stimulation [38]. Thus, computations within the thalamus and posterior insula are required for accurate perception of verticality. Presently, the exact contributions of the CNS to verticality perception are not clear but appear to involve integration of vestibular input with somatosensory and visual information to bind environmental and postural representations of verticality.

Perception of Self-Motion

Disturbed perceptions of movement are sometimes experienced after head trauma. Vertigo is an aberrant perception of rotation of self or spatial milieu, and several neuroimaging studies show that regions of the PIVC are active during the perception of vertigo resulting from caloric [30] and galvanic [39] stimulation. Further, lesions to the inferior parieto-temporal area can eliminate the perception of vertigo during caloric stimulation while the nystagmus response is preserved [40]. The perception of self-motion can also be induced by auditory or visual cues without vestibular stimulation, such as in cases of rest and constant velocity [41–42]. For example, a sense of self-movement can be induced by seeing an object move away from the viewer, which sometimes occurs at traffic lights and train stations when an adjacent car or train pulls away. The PIVC is involved in the sense of self-motion derived from purely visual stimulation. This perception of self-motion is thought to emanate from inhibitory reciprocal connections between the PIVC and visual cortex [43], the coordination of which may be damaged by TBI. Precise and dynamic sensorintegrative visual and vestibular interactions have been demonstrated in kinematic analyses of stepping [44]. Such interactions depend on the integrity of the PIVC; strokes in this area do not affect quiet standing but lead to impaired standing when somatosensory and visual information are removed [45]. Based on neuroimaging research, some investigators have proposed that the key function of the PIVC-visual interactions is the shifting of sensorial weight as conditions require [32,46], emphasizing a highly flexible and dynamic central network. Small alterations in timing of inputs and interactions within this network could be damaged by TBI, resulting in abnormal motion perception and control of movement, especially under conditions demanding fast adaptation.

Navigation

Self-motion perception and action control depend on a self-referenced representation of space. Navigation, or updating information about that self-referenced space as one moves, is a critical ability. This ability is known to depend on the hippocampus [47]. The vestibular system contributes to spatial navigation, even in the absence of acceleration. Brandt et al. found that subjects with bilateral vestibular loss exhibited both a reduction in hippocampal volume and impaired navigation based on spatial memory [48]. Note that the navigation task stimuli were entirely visual and the subject remained seated throughout; thus, there was no stimulation of the vestibular organs. This result suggests that navigation using even visually derived spatial memory engages the vestibular system. In an animal model, temporary pharmacological inactivation of the vestibular periphery disrupted the normal encoding of self in space by the hippocampus without any disturbances in gait or other motor function [49].

Together, these results indicate that integration of activity between structures, including the PIVC, thalamus, higher-order visual areas, and hippocampus, subserves the perception of self-referent space and motion in a manner distinct from the oculomotor or other motor responses. Within this system, dynamic flexibility and precise timing of neural transmission are paramount. Damage to this central system could affect a myriad of spatial computations and most of these deficits would not be detectable by current vestibular evaluative methods. Such deficits could imaginably lead to distress even in the absence of substantial behavioral abnormalities.

SENSORINTEGRATIVE VESTIBULAR DYSFUNCTION AND EMOTION

In addition to its role in spatial analysis, the vestibular system is also highly integrated with arousal, autonomic functions, and emotional modulation. Vestibular nuclei project to and receive projections from multiple rostral

structures implicated in arousal, autonomic function, emotional decisions, fear, and anxiety. These structures are the locus coeruleus (the main source of cortical norepinephrine) and, via the parabrachial nucleus, the amygdala, infralimbic cortex, and hypothalamus (see Balaban and Thayer [50]). Additionally, the PIVC includes regions in the posterior insula that are associated with the experience of pain [51]. Because of the close alignment between the vestibular system and the noradrenergic and limbic systems, vestibular signals have the capacity to generate strong negative emotions, from disgust to fear [50]. Thus, vestibular dysfunction can result in negative emotions and avoidance behavior, which has been observed for those with nontraumatic vertigo. When vestibular dysfunction is chronic and continuous, which is characteristic of blast trauma [7], it may generate anxiety rather than phobia, and the link between anxiety and vestibular symptoms may not be apparent to the patient.

Indeed, recent studies have demonstrated a link between sensorintegrative balance dysfunction and anxiety. Deficits in sensorintegrative control of balance in the absence of peripheral vestibular dysfunction are specifically associated with a form of space and motion anxiety but not anxiety disorders in general [52]. Similarly, dizziness from blast injuries is also correlated with an enhanced dependence on somatosensory and visual cues for balance [28]. Further, premorbid deficits in spatial analysis functions, like those described earlier, have been identified as risk factors for posttraumatic stress disorder (PTSD) [53]. Together, these findings suggest that blast-related damage to central vestibular sensorintegration networks also carries a risk for spatial anxieties (see Jacob et al. [54] for more detail about these disorders) and may also relate to the development of PTSD. Given these risks, it is critical to accurately identify higher-order vestibular deficits following combat-related blast injury.

Dizziness can occur in the absence of a recognized vestibular disorder, in which case the diagnosis of psychogenic dizziness is traditionally applied. Psychogenic dizziness is thought to originate from psychological conflicts and therefore is a psychiatric rather than a vestibular disorder [55]. Because this diagnosis is employed when dizziness is present but no known vestibular disorder is found, it may be overused in cases of central dysfunction where objective injury cannot be confirmed. Given the neuroanatomical links between the vestibular and the emotional systems, it is likely that anxiety and vestibular symptoms will co-occur. Further, as described earlier, central vestibular dysfunction is not comprehensively assessed, so at this time, it is difficult to rule out CNS sources of dizziness symptoms. Thus, especially in cases of TBI, caution should be used in attributing dizziness to psychogenic causes.

CONCLUSIONS

The precise rates and nature of vestibular consequences of blast exposure remain largely unknown. Central mechanisms are likely involved, supported by the high incidence of TBI and multimodal deficits. But larger controlled studies of objective vestibular dysfunction are needed to corroborate these largely self-report findings. To date, examinations of the effects of blast TBI on vestibular function have been limited to VOR measures and nonspecific measures of balance and postural control. However, the vestibular system is also involved in sophisticated multimodal computations of self in space, processes that can be affected by TBI pathophysiology. To understand the effects of blast TBI on the vestibular system, assessments of vestibular deficits should include tests of the full range of vestibular functions. Sway tests and caloric testing are useful in differentiating blast TBI from blunt injury and controls, but normal results do not exclude vestibular dysfunction. Additional tests would assess the extent of cerebral involvement in vestibular symptoms. Perception of verticality is a sensitive test of vestibular dysfunction, but current tests (SVV) are nonspecific regarding the location of damage. Future efforts could build on emerging research in the central contributions to verticality perception to develop more specific tests. More immediately, tests aimed at assessing central contributions to vestibular dysfunction might target the following functions: navigation and spatial memory (e.g., virtual Morris water maze [56]), self-motion perception from visual stimulation, or functional neuroimaging measures of stimulation of the vestibular system or visual cortical inhibition during self-motion perception. Although nonspecific, CDP is sensitive to visual-vestibular interactions and so will likely prove useful in the assessment of the central vestibular system in concert with other tests. Objective confirmation of coincident deficits in central visual and auditory function would further inform the extent of the vestibular abnormality. Research is necessary to determine the variability in these responses and the threshold for normal, which is also lacking in many standard tests.

The multimodal nature of the vestibular system also offers innovative possibilities for rehabilitation of TBI.

Stimulation of vestibular periphery has been shown to have therapeutic benefits for cognition (see Smith et al. [57]) and persistent pain [58]. Although untested as of yet, additional possibilities exist for intermodal benefits from peripheral stimulation, such as hearing and vision improvements or anxiety reduction from vestibular training. Because of its position at the intersection of higher-level sensory computations and emotions, the central vestibular system is an intriguing access point to better understand the multisensory effects of TBI.

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