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Neurological Manifestations Among US Government Personnel Reporting Directional Audible and Sensory Phenomena in Havana, Cuba

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IMPORTANCE From late 2016 through August 2017, US government personnel serving on diplomatic assignment in Havana, Cuba, reported neurological symptoms associated with exposure to auditory and sensory phenomena.

OBJECTIVE To describe the neurological manifestations that followed exposure to an unknown energy source associated with auditory and sensory phenomena.

DESIGN, SETTING, AND PARTICIPANTS Preliminary results from a retrospective case series of US government personnel in Havana, Cuba. Following reported exposure to auditory and sensory phenomena in their homes or hotel rooms, the individuals reported a similar constellation of neurological symptoms resembling brain injury. These individuals were referred to an academic brain injury center for multidisciplinary evaluation and treatment.

EXPOSURES Report of experiencing audible and sensory phenomena emanating from a distinct direction (directional phenomena) associated with an undetermined source, while serving on US government assignments in Havana, Cuba, since 2016.

MAIN OUTCOMES AND MEASURES Descriptions of the exposures and symptoms were obtained from medical record review of multidisciplinary clinical interviews and examinations. Additional objective assessments included clinical tests of vestibular (dynamic and static balance, vestibulo-ocular reflex testing, caloric testing), oculomotor (measurement of convergence, saccadic, and smooth pursuit eye movements), cognitive (comprehensive neuropsychological battery), and audiometric (pure tone and speech audiometry) functioning. Neuroimaging was also obtained.

RESULTS Of 24 individuals with suspected exposure identified by the US Department of State, 21 completed multidisciplinary evaluation an average of 203 days after exposure. Persistent symptoms (>3 months after exposure) were reported by these individuals including cognitive (n = 17, 81%), balance (n = 15, 71%), visual (n = 18, 86%), and auditory (n = 15, 68%) dysfunction, sleep impairment (n = 18, 86%), and headaches (n = 16, 76%). Objective findings included cognitive (n = 16, 76%), vestibular (n = 17, 81%), and oculomotor (n = 15, 71%) abnormalities. Moderate to severe sensorineural hearing loss was identified in 3 individuals. Pharmacologic intervention was required for persistent sleep dysfunction (n = 15, 71%) and headache (n = 12, 57%). Fourteen individuals (67%) were held from work at the time of multidisciplinary evaluation. Of those, 7 began graduated return to work with restrictions in place, home exercise programs, and higher-level work-focused cognitive rehabilitation.

CONCLUSIONS AND RELEVANCE In this preliminary report of a retrospective case series, persistent cognitive, vestibular, and oculomotor dysfunction, as well as sleep impairment and headaches, were observed among US government personnel in Havana, Cuba, associated with reports of directional audible and/or sensory phenomena of unclear origin. These individuals appeared to have sustained injury to widespread brain networks without an associated history of head trauma.

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Editorial page 1098
Author Audio Interview
Related article page 1079
Supplemental content

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In late 2016, US government personnel serving in Havana, Cuba, began presenting to their embassy medical unit after experiencing unusual auditory and/or sensory stimuli of variable intensity and character, with associated onset of varied neurological manifestations. Initial signs and symptoms pointed toward injury of the auditory system, leading to the establishment of a triage program at the University of Miami centered around otolaryngology evaluation. Eighty embassy community members underwent initial evaluation between February and April 2017, and 16 individuals were identified with similar exposure history and a constellation of neurological signs and symptoms commonly seen following mild traumatic brain injury, also referred to as concussion.[1] Exposures continued with time and 8 additional individuals were identified who had similar findings. The US Department of State, Bureau of Medical Services, subsequently convened an expert panel in July 2017, which came to consensus that the triage findings were most likely related to neurotrauma from a nonnatural source and recommended that further investigation into this novel cluster of findings was necessary.

The University of Pennsylvania's Center for Brain Injury and Repair was subsequently selected to coordinate multidisciplinary clinical evaluation, treatment, and rehabilitation of individuals identified during initial triage and additional patients with exposure. The purpose of this preliminary communication is to describe preliminary findings from 21 patients who were exposed to the same nonnatural source.[1]

Key Points

Question Are there neurological manifestations associated with reports of audible and sensory phenomena among US government personnel in Havana, Cuba?

Findings In this case series of 21 individuals exposed to directional audible and sensory phenomena, a constellation of acute and persistent signs and symptoms were identified, in the absence of an associated history of blunt head trauma. Following exposure, patients experienced cognitive, vestibular, and oculomotor dysfunction, along with auditory symptoms, sleep abnormalities, and headache.

Meaning The unique circumstances of these patients and the consistency of the clinical manifestations raised concern for a novel mechanism of a possible acquired brain injury from a directional exposure of undetermined etiology.

Methods

Design

This retrospective study was approved by the institutional review board of the University of Pennsylvania's Perelman School of Medicine, which waived the need for informed consent. The participants signed general consent forms for treatment permitting use of their data in research. Because of security and confidentiality considerations, individual-level demographic data cannot be reported.

Clinical Approach

The US Department of State directly referred individuals with suspected exposure to the University of Pennsylvania for comprehensive evaluation and treatment. A multidisciplinary team was convened consisting of physical medicine and rehabilitation, occupational medicine, neurology, neuroradiology, and neurosurgery. Each specialist independently obtained clinical histories and conducted comprehensive assessments. Reported signs and symptoms were extracted from these interviews.

Based on individual clinical indication, additional referrals were made to vestibular physical therapy, neuro-optometry, neuropsychology, occupational therapy, speech therapy, audiology, otorhinolaryngology, and sleep medicine for focused evaluation and treatment. Patients were referred to the University of Pennsylvania for clinical care, as opposed to enrollment in a structured research study. The **Box** shows an abbreviated list of objective measures used during clinical assessments and supplements for additional information.[2-29]

Cognitive, Neurobehavioral, and Mood Evaluations

When clinically indicated, comprehensive neuropsychological assessments were conducted by experienced neuropsychologists, who were not blinded to patient status. Neuropsychological test batteries included assessment of the following domains: (1) auditory attention, (2) auditory and visual working memory, (3) auditory and visual memory, (4) visual-spatial perception, (5) visual-motor construction, (6) motor function, (7) language function, (8) executive function, (9) processing speed, (10) academic achievement, (11) reasoning, (12) mood functioning, and (13) effort (Box and eAppendix in the Supplement). Following neuropsychological testing, individuals with cognitive deficits were referred for cognitive rehabilitation with occupational therapy, speech therapy, or both, depending on the individual clinical indication. Cognitive rehabilitation was intentionally not started prior to completion of neuropsychological testing to avoid affecting results.

Balance and Vestibular Evaluations

Clinical evaluations identifying balance abnormalities prompted referral to vestibular physical therapy. Focused vestibular evaluation included expert clinical assessment and the use of validated measures of static and dynamic balance (Box).[15-21] Also per clinical indications, patients were referred to audiology for comprehensive evaluation of the peripheral vestibular system, including caloric reflex testing.[23,24] Individuals confirmed to have a unilateral peripheral vestibulopathy (ie, relative vestibular reduction of ≥25% on caloric reflex testing) underwent magnetic resonance imaging (MRI) of the head with and without gadolinium contrast, with focus on the internal auditory canals in addition to the MRI sequences detailed.

Oculomotor Evaluations

Individuals found on clinical evaluation to have abnormalities of oculomotor function were referred to neuro-optometry for further evaluation and treatment. Oculomotor function was quantified using the following standard optometric clinical measures (Box).[25,26] Vergence testing included step vergence with prism bar, vergence facility with prisms, and near point of convergence. Accommodative testing in nonpresbyopic patients included amplitude of accommodation, accommodative facility with plus and minus lenses, and accommodative lag. Pursuit and saccadic testing was done qualitatively to assess accuracy of tracking eye movements and whether symptoms were provoked as with Vestibular/Ocular Motor Screening.[29] Saccadic speed and accuracy were quantified using the Developmental Eye Movement test,[26,28] a timed visual-verbal test. Diagnoses of accommodative, vergence, and/or saccadic/pursuit dysfunction were made using standardized criteria, in conjunction with symptomatic reporting,[26] which were quantified using the Convergence Insufficiency Symptoms Survey.[27]

Auditory Evaluations

Audiometry evaluations were performed prior to referral for care at the University of Pennsylvania. However, when patients had balance function testing as described here, comprehensive audiology evaluation included both pure tone and speech audiometry.

Imaging Evaluations

Initial conventional MRI sequences were acquired at 3T on a Siemens Magnetom Prisma[fit] scanner, and included high-resolution sagittal 3-dimensional MP-RAGE, T2 SPACE and FLAIR SPACE, coronal 2-dimensional T2-weighted imaging, axial 2-dimensional diffusion-weighted imaging, and axial T2* gradient echo. Resulting images were clinically interpreted by neuroradiology clinicians.

Box. Examples of Standardized Measures Used in Clinical Assessments[a]

Cognitive
- Boston Diagnostic Aphasia Examination[2]
- California Verbal Learning Test–2nd Edition[3]
- Grooved Pegboard[4]
- Test of Memory Malingering[5]
- Trail Making Test, Parts A and B[6]
- Wechsler Adult Intelligence Scale–IV[7]
- Wechsler Memory Scale–IV[8]

Mood
- Beck Depression Inventory (2nd edition)[9]
- Beck Anxiety Inventory[10,11]
- Frontal Systems Behavior Scale[12]
- Post-Traumatic Stress Disorder Checklist[13,14]

Balance and vestibular
- Functional Gait Assessment[15]
- Activities-Specific Balance Confidence[16]
- Balance Error Scoring System[17]
- Clinical Test of Sensory Organization and Balance[18,19]
- Dizziness Handicap Index[20]
- Computerized Dynamic Posturography[21,22]
- Caloric reflex test[23,24]

Vision and oculomotor
- Formal Evaluation of Vergence and Accommodation[25,26]
- Convergence Insufficiency Symptoms Survey[27]
- Developmental Eye Movement Test[26,28]
- Vestibular/Ocular Motor Screening[29]

[a] Measures were used based on clinical indications; therefore, every patient did not complete all measures in this abbreviated list.

Results

There were 21 individuals evaluated (11 women and 10 men, with a mean age of 43 years). Multidisciplinary evaluations began an average of 203 days (range, 3-331 days; median, 189 days; interquartile range, 125 days) following exposure (**Table 1**).

Exposure

For 18 of the 21 individuals (86%), there were reports of hearing a novel, localized sound at the onset of symptoms in their homes and hotel rooms (**Table 2**). Affected individuals described the sounds as directional, intensely loud, and with pure and sustained tonality. Of the patients, high-pitched sound was reported by 16 (76%), although 2 (10%) noted a low-pitched sound. Words used to describe the sound include “buzzing,” “grinding metal,” “piercing squeals,” and “humming.”

The sounds were often associated with pressurelike (n = 9, 43%) or vibratory (n = 3, 14%) sensory stimuli, which were also experienced by 2 of the 3 patients who did not hear a sound. The sensory stimuli were likened to air “baffling” inside a moving car with the windows partially rolled down.

Both the sound and sensory stimuli were often described as directional in that the individuals perceived a distinct direction from which the sensation emanated (hereafter referred to as *directional phenomena*). Further, the directional phenomena appeared to be localized to a precise area, as individuals (n = 12, 57%) noted that after changing location, the sensation disappeared and the associated symptoms reduced. Five individuals (24%) reported covering their head and/or ears, although doing so did not result in attenuation of the directional phenomena.

Accurately determining the dose and duration of exposure has been difficult because of the limitations of patient recall. Some patients were awakened by sounds and were unsure of the start of the event. The shortest reported event involved two 10-second pulses reported as a single exposure episode, whereas other patients reported that they perceived sound continuously for longer than 30 minutes. Owing to security concerns, further details of potential dosage cannot be provided.

Of the affected individuals, 20 (95%) reported immediate onset of neurological symptoms associated with directional phenomena (eTable 1 in the Supplement). One individual awoke from sleep with acute symptoms (including headache, unilateral ear pain, and hearing changes) but did not perceive directional phenomena. From days to weeks after exposure, individuals reported that they experienced the onset

Table 1. Demographics of Patients Evaluated at the University of Pennsylvania[a]

	Men (n = 10)	Women (n = 11)	Total (N = 21)
Age, mean (SD), y	39 (7)	47 (8)	43 (8)
Time from exposure to evaluation, mean (SD), d	229 (98)	180 (85)	203 (93)

[a] Potentially identifying information intentionally omitted for security and privacy concerns.

Table 2. Exposure Descriptions of the Directional Phenomena

Patient No.	Associated Sound			Associated Sensory Stimuli			Movement Attenuation[a]	Duration >3 mo		
	Reported	High Pitch	Low Pitch	Reported	Pressure	Vibration		Persistent Symptoms	Objective Findings	Required Treatment
1	X	X					X	X	X	X
2	X	X					X	X	X	X
3	X	X					X			
4	X		X	X		X		X	X	X
5	X	X		X	X			X	X	X
6	X		X	X	X		X	X	X	X
7				X	X		X	X		
8	X	X					X	X	X	X
9	X	X		X		X		X	X	X
10	X	X		X		X		X	X	X
11	X	X		X	X			X	X	X
12	X	X		X	X			X	X	X
13	X	X					X	X	X	X
14	X	X					X	X	X	X
15	X	X		X	X		X	X	X	X
16	X	X					X	X	X	X
17	X	X		X	X		X	X	X	X
18								X	X	X
19	X	X		X	X			X		
20				X	X		X	X	X	X
21	X	X						X	X	X
No. (%)	18 (86)	16 (76)	2 (10)	12 (57)	9 (43)	3 (14)	12 (57)	20 (95)	18 (86)	18 (86)

[a] Patients reported attenuation of sound, pressure, or vibration when moving to a different location.

of additional cognitive, neurobehavioral/mood, and physical symptoms. Twenty individuals (95%) reported that they experienced persistent (>3 months) symptoms, and 18 individuals (86%) exhibited objective clinical manifestations in 6 predominant domains (**Table 3**).

Cognitive, Neurobehavioral, and Mood Findings

Persistent cognitive manifestations were reported by 17 individuals (81%). Subjective symptoms included memory problems (n = 16, 76%), feeling mentally foggy (n = 16, 76%), impaired concentration (n = 15, 71%), and feeling cognitively slowed (n = 14, 67%) (Table 3). In addition, they reported neurobehavioral difficulties including irritability (n = 14, 67%), nervousness (n = 12, 57%), feeling more emotional (n = 11, 52%), and sadness (n = 5, 24%). For at least 6 individuals (29%), a clear change in work performance was noted by supervisors and colleagues (eTable 1 in the Supplement). Individuals also reported a "good day-bad day" pattern where significant cognitive or physical exertion would be followed by exacerbation of their symptoms for several days. Cognitive symptoms, as well as disequilibrium and headache, reportedly were also frequently exacerbated by cardiovascular exercise.

Multidisciplinary evaluations raised concern for cognitive impairment in 16 individuals (76%). Prior to referral, 4 of these individuals underwent neuropsychological evaluation (data not shown as generated outside of the University of Pennsylvania). Repetition of comprehensive neuropsychological testing is precluded within 1 year due of practice effects when material is presented within this timeframe. With previous exposure to material, the individual may score higher on a repeated neuropsychological evaluation within 1 year. Neuropsychological assessments were performed on 10 individuals after referral. Of those, interpretation was ongoing in 4 at the time of this publication. Per their preference, 2 individuals did not complete neuropsychological testing.

For the 6 individuals with complete neuropsychological testing data and analysis at the University of Pennsylvania, all had significant areas of cognitive weakness and/or impairment (eTables 2, 3, and 4 in the Supplement). Impairments were found in executive function (n = 6), motor function (n = 5), auditory and visual memory (n = 4), visual-spatial perception and visual-motor construction (n = 4), auditory attention and working memory (n = 3), language (n = 3), processing speed (n = 4), and reasoning (n = 1). All individuals

Table 3. Prevalence of Persistent Symptoms and Objective Findings[a]

	Subjective		Objective	
Domain	Symptom	No. (%)	Finding	No. (%)
Cognitive and behavioral	Combined	17 (81)	Neuropsychological testing indicated	16 (76)[b]
	Difficulty remembering	16 (76)	Neuropsychological testing performed at Penn	10 (48)
	Mental fog	16 (76)	Neuropsychological testing outside Penn	4 (19)
	Difficulty concentrating	15 (71)	Neuropsychological testing not yet performed	2 (10)
	Feeling slowed	14 (67)	Cognitive rehabilitation	13 (62)[b]
	Irritability	14 (67)		
	Feeling more emotional	11 (52)		
Balance and vestibular	Combined	15 (71)	Vestibular physical therapy referral	17 (81)
	Balance problems	14 (67)	Static postural stability	16 (76)
	Dizziness	13 (62)	Dynamic balance	16 (76)
	Nausea	7 (33)	VOR dysfunction	15 (71)
			Unilateral caloric impairment	4 (31)[c]
			Vestibular rehabilitation	17 (81)
Vision and oculomotor	Combined	18 (86)	Neuro-optometry referral	15 (71)
	Visual problems	16 (76)	Convergence insufficiency	11 (52)
	Light sensitivity	13 (62)	Smooth pursuit dysfunction	11 (52)
	Difficulty reading	12 (57)	Saccadic dysfunction	10 (47)
	Eye strain	11 (52)	Neuro-optometric rehabilitation	14 (67)
Auditory	Combined	15 (68)	Audiology referral	13 (62)
	Sound sensitivity	14 (67)	Moderate to severe SNHL	3 (23)[c]
	Tinnitus	12 (57)	Hearing aid provided	3 (14)
	Hearing reduction	9 (43)		
	Ear pressure	8 (38)		
Sleep	Combined	18 (86)	Pharmacological intervention	15 (71)
	Drowsiness or fatigue	16 (76)		
	Decreased sleep duration	15 (71)		
	Trouble falling asleep	14 (67)		
Headache	Combined	16 (76)	Pharmacological intervention	12 (57)
	With cognitive tasks	13 (62)		
	With therapy	11 (52)		
	Due to photophobia	9 (43)		
	Due to phonophobia	6 (29)		
Overall	Combined subjective	20 (95)	Combined objective	18 (86)

Abbreviations: Penn, University of Pennsylvania; SNHL, sensorineural hearing loss; VOR, vestibulo-ocular reflex.

[a] Persistent defined as presence more than 3 months after exposure.

[b] Neuropsychological characterization ongoing. Start of cognitive rehabilitation held until neuropsychological testing performed.

[c] Of 13 patients tested thus far during persistent symptom evaluation.

demonstrated a high level of effort during testing and had intact cognitive domains including visual working memory and academic achievement.

Neurobehavioral function was evaluated using the Frontal System Behavior Scale, a self-report measure of frontal lobe dysfunction. Specifically, comparing before and after exposure retrospectively via patient recall and self-report, individuals noted apathy (n = 5), executive dysfunction (n = 4), and disinhibition (n = 2). Two individuals met criteria for posttraumatic stress disorder and endorsed severe levels of anger on the Brief Mood Survey, 1 of whom also endorsed moderate to severe levels of depression and anxiety.

Balance and Vestibular Findings

Individuals described acute nausea (n = 7, 33%) and dizziness (n = 5, 24%) during exposure, which continued to progress in the subacute and persistent stages (acute stage = during or hours following exposure; subacute stage = days to weeks after exposure patient recall]; and persistent stage = more than 3 months after exposure). Specifically, more than 3 months after exposure, individuals reported a higher prevalence of dizziness (n = 13, 62%) and nausea (n = 7, 33%), in addition to general balance problems (n = 14, 67%) (Table 3). These symptoms were exacerbated by walking quickly, tasks involving head movements, complex visual environments, or in some cases while simply standing still. Balance symptoms were also worsened with eyes closed or in low light conditions.

Clinical examinations raised concern for balance impairment in 17 patients (81%), prompting referral to vestibular physical therapy. Focused vestibular evaluations demonstrated impairments in static postural stability (n = 16, 76%), dynamic balance (n = 16, 76%), and the vestibulo-ocular reflex (n = 15, 71%) (eTables 5, 6, and 7 in the Supplement). Patients with the most severe balance impairments on clinical evaluation underwent caloric reflex testing, which demonstrated peripheral vestibular dysfunction in 4 of 13 patients evaluated. MRI findings focusing on the internal auditory canals on these 4 patients were normal. Taken together, these balance symptoms and evaluation findings are consistent with central and, in some cases, peripheral vestibular abnormalities.

Oculomotor Findings

Of the individuals with persistent symptoms, 16 (76%) reported visual problems (Table 3). Light sensitivity (n = 13, 62%) and difficulty reading (n = 12, 57%) were also frequently reported. Eye strain (n = 11, 52%) was experienced particularly with reading and was associated with headaches, disequilibrium, and nausea.

Clinical examinations raised concern for oculomotor dysfunction in 15 individuals (71%), prompting referral to neuro-optometry. The most common findings confirmed on focused oculomotor evaluation were convergence insufficiency (n = 11, 52%), abnormal smooth pursuits (n = 11, 52%), and saccadic dysfunction (n = 10, 47%) (eTables 8 and 9 in the Supplement). Similar to vestibular testing that provoked symptoms, oculomotor examination elicited headache and disequilibrium.

Auditory Findings

At the onset of the directional phenomena, affected individuals reported hearing a loud sound (n = 18, 86%), associated with ear pain (n = 7,33%) and tinnitus (n = 6, 29%). Within days to weeks following exposure, individuals continued to report tinnitus (n = 12, 57%) and ear pain (n = 5, 24%), with the addition of a change in hearing (n = 7, 33%) and sensitivity to noise (n = 5, 24%). More than 3 months after exposure, sound sensitivity was the most common auditory concern (n = 14, 67%), followed by tinnitus (n = 12, 57%) and ear pressure (n = 8, 38%).

While 9 individuals (43%) reported persistent hearing reduction, pure tone audiometry, including pure tone average and word identification, revealed moderate to severe sensorineural hearing loss in 3 individuals (23%) (eTable 10 in the Supplement), who were fitted with hearing aids. For 2 individuals, the moderate to severe sensorineural hearing loss was unilateral and corresponded with the side of peripheral vestibular dysfunction on caloric testing. Otoscopy and tympanometry findings were unremarkable.

Sleep

Individuals commonly reported issues with sleep (n = 18, 86%), including reduced sleep duration (n = 15, 71%) and difficulty falling asleep (n = 14, 67%). In addition, individuals experienced significant daytime fatigue (n = 16, 76%). Most individuals required pharmacological intervention to improve subjective report of sleep architecture (n = 15, 71%) (eTable 11 in the Supplement).

Headaches

At the initiation of directional phenomena exposure, 8 individuals (38%) reported immediate onset of headache, while 5 (24%) reported intense head pressure. In the days to weeks following exposure, 17 individuals (81%) developed headaches, with 16 (76%) experiencing persistent headaches longer than 3 months after exposure (Table 3).

In the persistent stage, headaches were reported to be exacerbated or associated with cognitive tasks (n = 13, 62%), rehabilitative therapies (n = 11, 52%), photophobia (n = 9, 43%), and phonophobia (n = 6, 29%). Patients with antecedent headaches were able to differentiate the character of these headaches from that of their standard headaches. Headaches were generally reported to improve with medications (n = 12, 57%) and appropriate therapies for oculomotor and vestibular impairments (eTable 11 in the Supplement).

Imaging

MRI neuroimaging was obtained in all 21 patients. Most patients had conventional imaging findings, which were within normal limits, at most showing a few small nonspecific T2-bright foci in the white matter (n =9, 43%). There were 3 patients with multiple T2-bright white matter foci, which were more than expected for age, 2 mild in degree, and 1 with moderate changes. The pattern of conventional imaging findings in these cases was nonspecific with regard to the exposure/insult experienced, and the findings could perhaps be attributed to other preexisting disease processes or risk factors. Advanced structural and functional neuroimaging studies are ongoing.

Rehabilitation and Return to Work

Individualized rehabilitation programs were developed, which included combinations of neuro-optometric rehabilitation (n = 14, 67%), vestibular physical therapy (n = 17, 81%), and cognitive rehabilitation with speech pathology and/or occupational therapy (n = 13, 62%). The most symptomatic patients (n = 14, 67%) requiring multiple therapies did not return to work.

Vestibular physical therapy sessions focused on balance retraining, static and dynamic posture control with substitution via visual and somatosensory systems, gaze stabilization exercises, habituation, smooth pursuits, and saccadic eye movement exercises. Patients treated with vestibular rehabilitation have demonstrated a positive response with improved balance and reduction of disequilibrium.

Formal neuro-optometric rehabilitation, including manipulation of disparity vergence and accommodative amplitude and latency, has been used to treat ocular motor deficits. Rehabilitation for abnormal smooth pursuit and saccadic dysfunction was coordinated between neuro-optometric rehabilitation, vestibular physical therapy, and occupational therapy. Vestibular physical therapy focused on oculomotor function with the body in motion and occupational therapy emphasized functional tasks such as visual scanning in a simulated work environment.

Following comprehensive neuropsychological testing, a formal cognitive rehabilitation program was initiated in the form of occupational therapy and/or speech therapy.

Early return to work with intensive cognitive loading led to an exacerbation of neurocognitive, vestibular, and visual symptoms in 7 individuals (33%). Individualized return to work plans were designed to reintegrate individuals using a stepwise process and appropriate work modifications.

Discussion

Preliminary findings are described of a case series of individuals stationed in Havana, Cuba, nearly all of whom reported directional audible and/or sensory phenomena that was followed by the development of a consistent cluster of neurological signs and symptoms. The clinical manifestations may represent a novel clinical entity, which appears to have resulted from a widespread brain network dysfunction (ie, cognitive, oculomotor, and central vestibular) as seen in mild traumatic brain injury, or concussion,[30] as well as injury to the peripheral vestibular system in some cases. It is currently unclear if or how the noise is related to the reported symptoms. In particular, sound in the audible range (20 Hz-20 000 Hz) is not known to cause persistent injury to the central nervous system and therefore the described sounds may have been associated with another form of exposure.

Cognitive symptoms, including difficulty remembering (n=16, 76%) and feeling cognitively slowed (n=14, 67%) were the most problematic for individuals in this series more than 3 months after exposure, with neuropsychological testing identifying impairments in at least 1 cognitive domain in all 6 patients who completed neuropsychological evaluation to date (eTables 2, 3, and 4 in the Supplement). Cognitive difficulties interfered with these patients' ability to multitask, process information quickly with accurate recall, solve problems, and perform rapid decision making. Compared with vestibular and oculomotor impairments, cognitive impairments are often the slowest to improve following acquired brain injury, which was observed in this series. Therefore, extended cognitive rehabilitation with emphasis on return to work was used. In addition, it is not uncommon for patients with neurological injury resulting in cognitive impairment to have mood disturbances such as depression, anxiety, and/or posttraumatic stress disorder. Mood dysfunction can directly result from acquired brain injury or develop in response to the precipitating event and novel deficits.[31-33]

The presence of subjective neurological symptoms presenting in a cohesive community has raised concerns for collective delusional disorders, including mass psychogenic illness. However, neurological examination and cognitive screens did not reveal evidence of malingering, and objective testing and behavioral observations during cognitive testing indicated high levels of effort and motivation. Several of the objective manifestations consistently found in this cohort (such as oculomotor and vestibular testing abnormalities) could not have been consciously or unconsciously manipulated. Furthermore, mass psychogenic illness is often associated with transient, benign symptoms with rapid onset and recovery often beginning with older individuals.[34,35] In contrast, the Havana cohort experienced persisting disability of a significant nature and are broadly distributed in age. Rather than seeking time away from the workplace, the patients were largely determined to continue to work or return to full duty, even when encouraged by health care professionals to take sick leave.

While not systematically excluded, viral etiologies, chemical etiologies, or both associated with acute onset of persistent neurological impairment and peripheral vestibulopathy with the directional nature of exposure descriptions are not readily apparent. No other manifestations of viral illness, such as preceding fever, were identified. It is unlikely a chemical agent could produce these neurological manifestations in the absence of other organ involvement, particularly given that some individuals developed symptoms within 24 hours of arriving in Havana.

There are important considerations in this investigation. In particular, the anatomic substrates causing the symptoms have not yet been identified. This may represent a significant challenge because even the designation of "concussion," is not yet a true diagnosis, as no definitions include the underlying cause. Nonetheless, there is an emerging consensus that concussion, or mild traumatic brain injury, is a type of brain network disorder, based on classic symptoms (eg, slowed processing speed and memory dysfunction) as well as changes in the white matter tracts and consecutive connectivity, as detected with advanced neuroimaging studies.[30,36]

Beyond the absence of blunt head trauma, there were additional notable differences between the manifestations observed in the Havana cohort and characteristic acute and persistent symptoms of concussion. For example, individuals experienced unilateral ear pain and tinnitus after exposure, and some were later detected to have a unilateral peripheral vestibulopathy (along with central vestibular dysfunction), a finding uncommon in concussion. Further, studies have reported that while most individuals following concussion have a relatively rapid full recovery, at least 15% are thought to experience characteristic persisting symptoms.[37,38] In contrast to classic concussions, most patients referred following suspected exposure in Havana exhibited significant impairment that persisted for months with no significant improvement in multiple cases until rehabilitation was initiated.

For practicing clinicians, if a patient presents reporting a similar potential exposure and symptoms similar to those observed in mild traumatic brain injury, in addition to a thorough history, objective evaluation should include screening assessments of vestibular, oculomotor, and cognitive functioning. Based on findings of this assessment, appropriate referrals to subspecialists should be considered including neurorehabilitation physiatry, vestibular physical therapy, neuro-optometry, neuropsychology, and audiology.

Limitations

This study has several limitations. First, due to the sensitive nature of this publication, certain details typically reported in a case series of exposure were omitted, including specifics about geography, relationships between individuals, and individual demographics. Second, because these patients' first evaluation was elsewhere, each patient did not undergo each of the tests described. In particular, neuropsychological characterization was incomplete at the time of publication.

Preliminary results were presented given the importance and strong public interest in this case series. Third, the rehabilitative course of this Havana cohort may not be representative because this represents a referral population. There may be additional individuals exposed while in Havana, Cuba, who have not been identified due to subtler manifestations that either resolved spontaneously or did not prompt presentation for medical treatment. Therefore, the actual number of individuals exposed is unknown, and the relative "dose" of exposure that causes acute and chronic symptoms remains unclear.

Conclusions

In this preliminary report of a retrospective case series, persistent cognitive, vestibular, and oculomotor dysfunction, as well as sleep impairment and headaches, were observed among US government personnel in Havana, Cuba, associated with reports of directional audible and/or sensory phenomena of unclear origin. These individuals appeared to have sustained injury to widespread brain networks without an associated history of head trauma.

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