Aerospace Implications of Key Neurological Conditions

Vini G. Khurana; Rondhir Jithoo; Michael Barnett

INTRODUCTION: The neurological impact (or lack thereof) of certain medical histories and imaging findings is important to understand in the context of air and spaceflight. There are a number of neurological conditions that, if present in pilots and astronauts, carry variable (and sometimes adverse) functional implications for safety and overall mission success. In this systematic overview, the authors will refer to the relevant clinical and radiological features of brain tumors and vascular anomalies, cerebral edema and intracranial hypertension, concussion and the traumatic brain injury (TBI) spectrum, hematomas, cerebrospinal fluid circulation anomalies including hydrocephalus and sequestrations, spinal degenerative changes, and cerebral ischemia and demyelination. It is notable that these last two conditions have recently been reported to be a complication in some people with coronavirus disease 2019 (COVID-19). A paradigm for practical neurological workup of symptomatic pilots and astronauts will be discussed, as will the controversial notion of pre-emptive radiological screening (vs. not screening) in asymptomatic or clinically occult situations. The concepts of medical surveillance in the setting of known or diagnosed pathologies, and expert panel review and simulator and flight checks in complex neurological cases, are also elaborated on in this paper. We believe this overview will contribute toward the enhancement of a broad understanding of neurological conditions, their clinical workup, and their precautionary management in the setting of aviation and aerospace.

KEYWORDS: aerospace medicine, neurological conditions, clinical management.

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Aerospace environments present unique and mission-specific challenges to their human crews. They are typically mentally and physically challenging,[7,21] often dangerous, and in the foreseeable future will become more remote[18,40] and isolated.[29,38] Pilots of such missions carry the ultimate responsibility for the welfare and survival of their crews and human and material payload. Pilot incapacitation is an infrequent but well recognized phenomenon in general and commercial aviation.[5,13] In spaceflight, nearly 2000 single medical events occurred during manned missions between 1981 and 1998 alone.[7] The crew's biomedical data telemetry[27] and direct communication with mission control specialists[27,31] may viably help in the setting of a medical emergency arising during a near-Earth mission only.[38] Hence, steps taken toward preventing aerospace medical emergencies arising in the first place are paramount. The paradigm described below may assist in this regard, from a neurological perspective, with the aim being to optimize flight and mission safety.[22,26]

METHODS

Relevant literature was identified using keyword searches via PubMed and Google Scholar search engines. Keywords included the following: aerospace medicine; air travel; clinical management; emergency treatment; medical assessment; neurological conditions; pilot screening; spaceflight. Germane publications from the Aerospace Medical Association (AsMA), Civil Aviation Safety Authority (CASA), Federal Aviation Administration (FAA), International Civil Aviation Organization (ICAO), and National Aeronautics and Space Administration (NASA) were also sought. Clinical input from the three authors of this paper, together amounting to almost 100 years of experience in medicine (including approximately 60 yr in clinical neurology and operative neurosurgery), and the additional piloting experience of the lead author, was also drawn upon for the purposes of this article. A combination of organizational publications, review articles, and scientific papers was selected, based on their perceived clarity, interest, quality, and relevance, to match this comprehensive yet succinct topic review.

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Table I. Neurological Symptom and Sign Inventory Clusters.

SYMPTOMS AND SIGNS
Intracranial pressure (ICP): Headache, unexplained nausea or vomiting, ± other
Brainstem: Diplopia, dysarthria, dysphagia, vertigo, tinnitus, deafness
Cerebellar: Imbalance, incoordination
Cognitive: Concussion, confusion, impaired memory and concentration, word finding difficulty, multitasking errors, personality change
Motor: Weakness, hyperreflexia, fasciculations, slurring, facial droop
Sensory: Numbness, paresthesia, pain, dysesthesia
Spells: Seizure, pre/syncope, visual (blurring, loss of vision, scintillation)
Systemic: Fever with neck stiffness, night sweats, bowel or bladder dysfunction, lethargy, malaise

Table II. Practical Neurological Workup.

WORKUP CATEGORIES
Blood: Comprehensive metabolic panel (CMP), complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP); serum vitamin levels including B12 and D; endocrine panel (including morning fasting cortisol, thyroid function tests, prolactin, fasting glucose, HbA1c)
Basic imaging: CT brain, CT spine
More advanced imaging: MRI brain, MRI spine, ± contrast; MRI arteriography or venography
Nuclear medicine: Regional bone scan with CT single photon emission computed tomography (SPECT); positron emission tomography (PET) scan
Physiology: Nerve conduction study, electromyography (EMG); electroencephalography (EEG); formal neuropsychological testing
Special: Lumbar puncture with cerebrospinal fluid (CSF) studies; catheter angiogram; CT myelogram; urine assay; MR tractography, functional MRI, MR spectroscopy, MR perfusion, cine MRI; bone mineral density - dual energy X-ray absorptiometry (BMD - DXA); carotid ultrasound, cardiac testing (echo, stress); genomic & proteomic analyses

Neurological History: 'Clusters' and 'Red Flags'

Of the various types of medical conditions encountered in an aerospace setting, a neurological etiology[6,20,34] features highly in terms of both frequency[15] and consequence.[24,30] In such environments, the most common neurological symptoms appear to be 'pain' (headache/migraine, neck or back pain, and/or limb pain, numbness, and paresthesia)[20,21] and some form of cognition-impairing 'spell' (confusion, lightheadedness, or loss of consciousness with or without seizure).[6,24] For the aerospace medical officer, obtaining a detailed medical history, with a focus on the biological system involved, in this case neurological, is

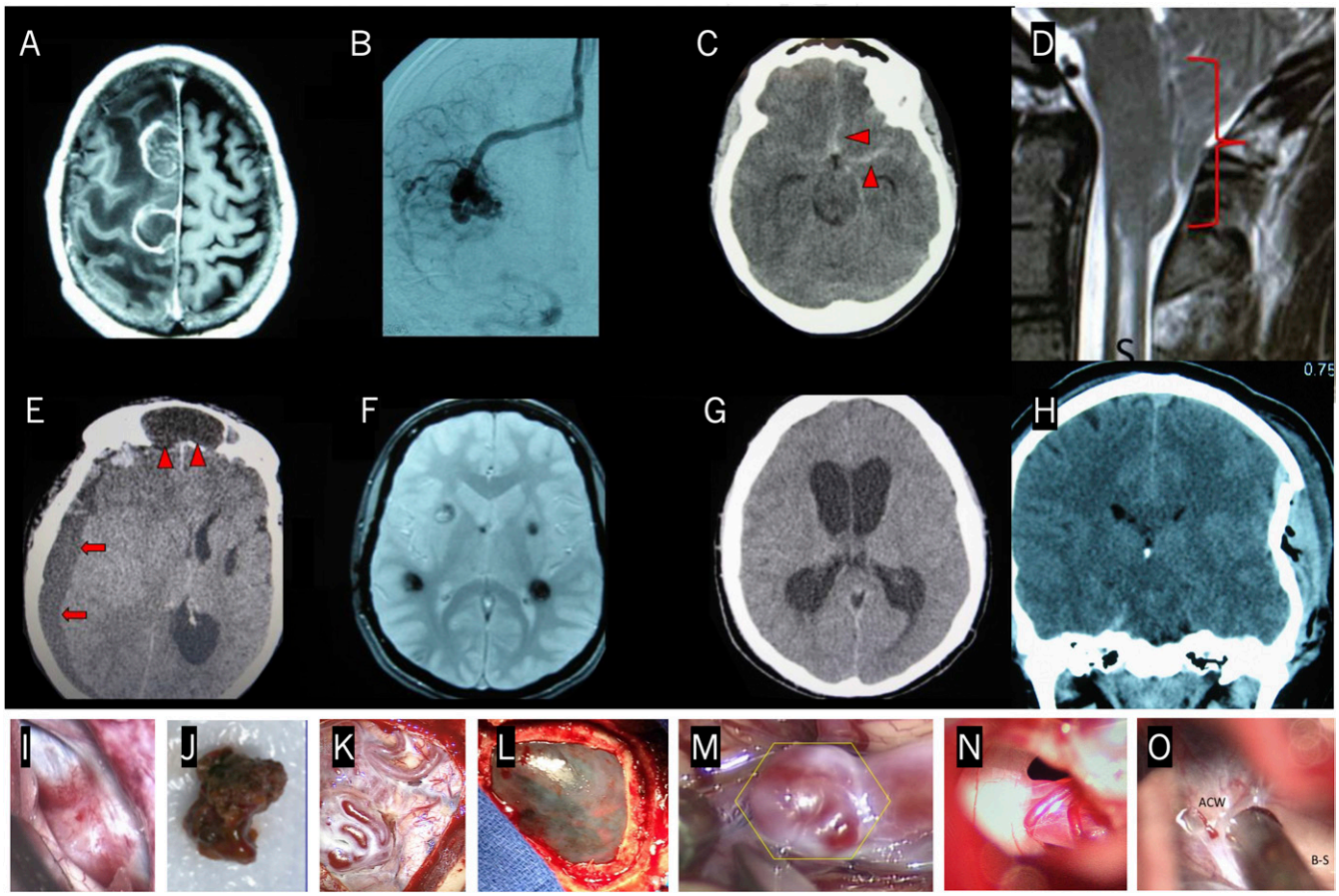

Fig. 1. Some structural intracranial pathologies. A) MRI T1 axial postcontrast; multifocal brain cancer (glioblastoma multiforme; GBM) with unilateral cerebral edema. B) Catheter angiogram; arteriovenous malformation (AVM). C) CT axial noncontrast; ruptured intracranial aneurysm with subarachnoid hemorrhage (SAH). D) MRI T2 sagittal; Chiari I malformation with established cervical syrinx (s). E) CT axial postcontrast; subdural empyema (abscess) from chronic untreated sinusitis. F) MRI gradient echo axial; multiple cavernous malformations. G) CT axial; hydrocephalus; H) CT coronal; posttraumatic extradural hematoma (EDH) and open (compound) depressed skull fracture prior to evacuation and reconstruction. I) Skull base meningioma prior to excision. J) Excised brainstem cavernous malformation. K) AVM prior to excision. L) Posttraumatic subdural hematoma with glistening outer membrane on view prior to incision and evacuation. M) Intracranial aneurysm with 'daughter sacs' prior to surgical clipping. N) Trigeminal nerve compressed and deviated by superior cerebellar artery branch in a trigeminal neuralgia patient during microvascular decompression surgery. O) Arachnoid cyst membrane fenestrated in cyst decompression surgery. See the online version of this article (https://doi.org/10.3357/AMHP.5744.2021) for color.

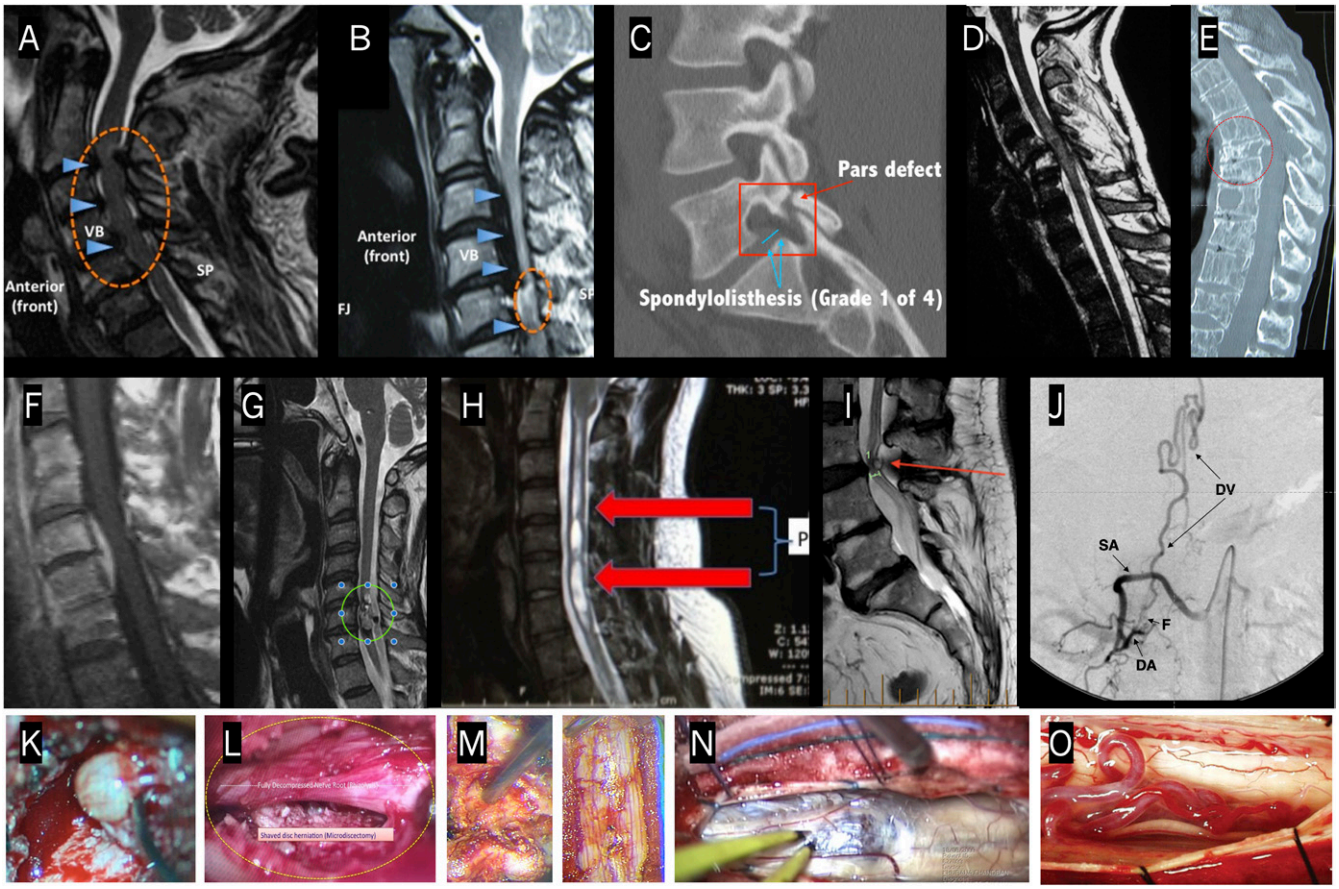

Fig. 2. Some structural spinal pathologies. A) MRI T2 sagittal; severe cervical stenosis in a patient presenting with quadriparesis following a fall. B) MRI T2 sagittal; severe cervical stenosis in a patient with ossification of the posterior longitudinal ligament. C) CT sagittal; congenital pars interarticularis defect resulting in a spinal 'slip' or spondylolisthesis prior to surgical reconstruction. D) MRI T2 sagittal; traumatic cervical spinal cord injury prior to surgical intervention. E) CT sagittal; pathological spinal fracture in a 'moth-eaten' spine infiltrated with multiple myeloma in a paraplegic patient. F) MRI T1 sagittal postcontrast; extradural abscess (differential was a meningioma). G) MRI T2 sagittal; cervical spinal cord cavernous malformation (differential was a glioma). H) MRI T2 sagittal; syringomyelia from untreated Chiari I malformation. I) MRI T2 sagittal; lumbar spinal stenosis from degenerative facet cyst prior to surgical decompression. J) Catheter angiogram; spinal dural arteriovenous fistula (SDAVF) prior to being shut down surgically. K) Intraoperative view of a 'pearly' lumbar facet cyst being excised. L) Surgically decompressed spinal nerve during lumbar microdiscectomy. M) Cervical spinal stenosis pre- (left panel) and post- (right panel) surgical decompression, with the right panel showing the dural covering of the posterior cervical spinal cord. N) Cavernous malformation of the cervico-medullary junction at the time of incision of the posterior midline spinal cord prior to excision of the lesion (dark discolored area). O) SDAVF with engorged tortuous draining vein on view at the time of its surgical disconnection (spinal dura opened and retracted with thin black sutures at bottom of photograph). See the online version of this article (https://doi.org/10.3357/AMHP.5744.2021) for color.

key. Familiarity with a neurological inventory of symptom and sign clusters is therefore useful (**Table I**). Certain neurological 'red flags' are worth noting. First, raised intracranial pressure from a skull-bound space-occupying lesion (SOL) will often present with the triad of headache (especially in the morning hours owing to cerebral venous dilatation stretching the nerve-rich dura), nausea, and vomiting (medulla-mediated emetic response). There may be other symptoms associated with SOLs, including some form of visual disturbance (diplopia, blurred vision, peripheral loss of vision), limb weakness, and seizure. Second, the symptom itself may be profoundly alarming, such as a frank 'blackout' or the experience of a sudden and most severe headache (as can occur in an aneurysmal subarachnoid hemorrhage or a brain parenchymal hemorrhage). Third, the symptom's trend may be a giveaway in alerting a clinician to an underlying pathology. For example, increasing frequency or severity of the symptom, or the development of new additional symptoms. Finally, some neurological symptoms help to localize pathology to a particular site in the central nervous system (CNS). For example, a 'cape distribution' of sensory symptoms could indicate the presence of a cervico-thoracic syrinx or tumor ('cape' dysesthesia), or a SOL or mechanical instability at the cervico-medullary junction (resulting in Lhermitte's phenomenon; that is, jolts of truncal electrical dysesthesia). A 'saddle area' distribution of symptoms (perineal or perianal numbness and bowel or bladder dysfunction) often occurs in cauda equina compression from local spinal neoplasms, cysts, or herniated discs. On the other hand, one or more of double vision, vertigo, slurring of speech, and dysphagia can be associated with brainstem ('bulbar') pathologies.

Practical Neurological Workup

There are common tests and certain special tests that can be ordered in the evaluation of an aircrew member experiencing

Table III. Main Neurological Differential Diagnosis.

DIFFERENTIALS
CSF circulation anomalies: hydrocephalus, arachnoid cyst, syringomyelia; Chiari I malformation
Degenerative: Parkinson's disease, dementia; cervical and lumbar spondylosis with neurological compression
Demyelinating conditions: multiple sclerosis, Guillain-Barré syndrome, COVID-19
Intracranial hypertension: venous sinus thrombosis; cerebral edema or papilledema from any cause
Ischemia: transient ischemic attack, stroke
Trauma: concussion, diffuse axonal injury (DAI) and contusions; subdural or extradural hematoma
Tumors: glioma (including Schwannoma), meningioma, metastatic disease, pituitary adenoma
Vascular anomalies: aneurysm, arteriovenous (AV) malformation (AVM) or AV fistula, cavernous malformation; trigeminal neuralgia
Miscellaneous: infective or inflammatory conditions affecting the central nervous system (CNS; quite rare, but now also include COVID-19); iatrogenic (e.g., pharmacologic side-effects); idiopathic (e.g., migraine)

Table IV. Individual and Mission Adversity/Risk by diagnosis.

Higher risk
Poorly controlled migraine disorder
Seizure disorder from whatever cause
Traumatic brain injury that is radiologically evident (e.g., contusion, subdural hematoma, brain-penetrating), and/or associated with prolonged amnesia or postconcussion syndrome
Syncope if primarily cardiogenic (arrhythmia) or neurogenic (rare, e.g., colloid cyst-related acute obstructive hydrocephalus)
Psychological impairment from whatever cause
Infiltrative brain or spinal cord glioma
Ruptured brain aneurysm or arteriovenous malformation
Cervical or thoracic myelopathy
Trigeminal neuralgia
Encephalitis, demyelination, or stroke from any cause (including COVID-19 infection)
Hydrocephalus and intracranial hypertension requiring cerebral spinal fluid shunting
Lower risk
Syncope if simply 'vasovagal' (e.g., heat, dehydration, pharmacological/medication)
Conservatively managed concussion without significant radiological brain injury including no significant diffuse axonal injury
Surgically treated spondylosis (e.g., disc herniation, stenosis, synovial cyst; spondylolisthesis) including by disc replacement/arthroplasty or instrumented fusion
Medically and/or surgically resolved infection
Surgically evacuated extradural hematoma without evidence of recurrence
Endovascularly treated unruptured brain aneurysm or arteriovenous malformation/arteriovenous fistula
Resected noncomplex cavernous malformation if low seizure risk
Surgery and/or radiation-treated skull base or spinal meningioma or Schwannoma
Successfully decompressed Chiari malformation (with absent or resolving syrinx)
COVID-19 exposure without significant systemic (e.g., pulmonary, neurological) sequelae
Decompressed symptomatic arachnoid cyst

neurological symptoms (**Table II**). Each of these tests has particular utilities and limitations beyond the scope of this paper. The authors recommend a measured approach to investigations, i.e., one that usually is akin to 'least expensive to most expensive' in its order. However, magnetic resonance imaging (MRI) should be considered early on in the workup if there are new, unusual, or persistent headache(s) or other neurological symptoms localizing to the brain and spinal cord or craniospinal nerves.[32] This should provide an anatomically useful radiological baseline because a regular brain or spine computed tomography (CT) scan, while a handy pathology-screening tool, is of insufficient spatial resolution compared with an MRI. In addition, CT scans are associated with ionizing radiation exposure to the brain, no matter how quick the scan time. Finally, early referral to a neurologist and/or neurosurgeon for their opinion should be undertaken in brain and spinal clinical scenarios in the aerospace sector, regardless of complexity, given the aircrews' responsibilities and inherent implications. The expectation should be that the neurologist and neurosurgeon will provide helpful recommendations for surveillance and management, and not necessarily any cause for concern or invasive intervention, but this is context dependent.[6,24]

The Neurological Differential

There is a wide variety of conditions that can affect the brain and spine, and each of these can affect anyone at any time (**Fig. 1** and **Fig. 2**). Such conditions present with symptoms mentioned in the neurological inventory (Table I) and in the figure legends and can be diagnosed based on suitable imaging studies (Table II). It is well recognized that the CNS can be affected secondarily from the effects of situations involving pilot fatigue,[8] intoxication, hypoxia,[16,35] dehydration, trauma,[25] anemia, hypoglycemia, cardiogenic syncope, and systemic illness.[21,30] In the present pandemic, neurological complications of COVID-19 are also being recognized, including anosmia, ageusia, and hypoxic encephalopathy, as well as thrombosis/cerebral ischemia and encephalitis.[14] Given that headaches/migraines, spinal pain, seizures, and bleeds are seen relatively commonly in neurological practices, the causative/etiological differential of many of the primary CNS structural afflictions is important to note (**Table III**).

Key Implications of Diagnosis, Surveillance and Treatment

Following the establishment of the neurological diagnosis, the essential question in all cases is this: "will the disease or its treatment interfere with the safe execution of the flying task?".[24] The implications of the diagnosis may or may not be anything substantial, but can be expected to be mission role-specific. The risk assessment[12,22,24] needs to be considered on a case-by-case basis.[6] For example, a crewmember's history of a (posttraumatic) cerebral contusion, surgically evacuated subdural hematoma, or prolonged amnesia would itself advocate against return to operational duties; this would be in no doubt if posttraumatic epilepsy arose.[3,9,24] For the individual concerned, there are potential effects on personal aspirations, employability and livelihood, career trajectory,

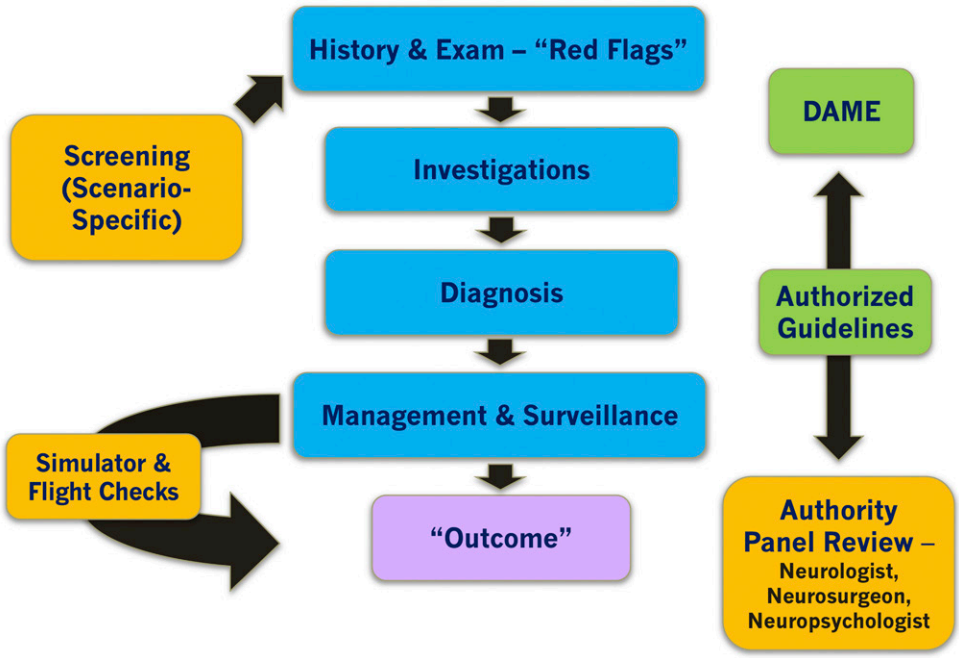

Fig. 3. Aerospace neurological clinical paradigm. The expected is that the process of medical review starts with the "History & Exam" (top middle box) and, through a systematic process (middle boxes), ends with the "Outcome" box. At least one designated aerospace medical examiner (DAME) is involved, practicing according to accepted authorized guidelines/protocols (right boxes). The 'Screening', 'Simulator', and 'Panel Review' boxes represent additional important steps for clinical consideration; one of more of these can be used in the paradigm on a case-by-case/scenario-specific basis. See the online version of this article (https://doi.org/10.3357/AMHP.5744.2021) for color.

and psyche. Any surveillance and treatment recommendations may interfere with their mission participation, rostering, and specific capabilities and responsibilities. For the mission itself, there is the possibility of its alteration or compromise. For the aerospace sector, viable policies and protocols regarding the evaluation of an aircrew member's neurological condition need to be in place, reflecting 'best practice'. The process needs to be comprehensive, but also fair and with a justifiable conclusion. Some neurological diagnoses will carry a higher risk of adversity for the individual and mission (**Table IV**). Other diagnoses, however, may not be of much future consequence following initial definitive management, but, again, a case-by-case consideration needs to be made (Table IV).

A Role for Pre-Emptive Screening?

Aerospace environments can be anticipated to pose certain physiological stresses, constraints, and risks on crew (and passengers). Such factors can include hypoxia,[35,36] acceleration forces, pressure/volume changes,[23] low gravity,[21] circadian rhythm, radiation,[28] fatigue, multitask stress, ergonomics, exercise and nutrition, as well as interpersonal, isolation, and separation stressors.[7,21,31] There are certain helpful guidelines provided by organizations such as AsMA,[1,2,19] FAA,[4,17] CASA,[10] NASA,[11] and ICAO[22] regarding personnel (and passenger) medical assessment and screening. However, these need to be applied in a rather specific manner to individuals depending on their roles and the complexity of the mission, including its distance from Earth and duration. While screening is prudent for space missions, the need to apply any screening to Earth-based pilots and crew is more controversial and may not be necessary beyond the required medical and questionnaire evaluations for medical risk factors. Questionnaire-based screening could include questions relating to present or past head or body pains, seizure, cranial or spinal trauma, illness and/or hospitalization with COVID-19,[14] cerebral ischemia events or other similar events, pain conditions, medications, and surgical or radiation history. Screening techniques or technologies might be radiological (biomedical imaging;[32] Table II), neuropsychological testing,[25] or tissue fluid (e.g., blood, urine) testing for genomic/proteomic[33,37,39] (predictive biomarker) and biochemical/toxicological analyses, or a (multimodality) combination. Unexpected results of screening should be anticipated to occur and to be managed in a comprehensive but fair manner with specialist consultation as appropriate.

Neurological Diagnostic and Management Paradigm

The expected clinical paradigm for aircrew with medical complaints, including neurological, begins with the generic elements of comprehensive history (with attention to 'red flags'; Table I) and physical examination. These are followed by the ordering and interpretation of appropriate investigations (Table II), the consideration of a diagnostic differential (Table III), and finally the establishment of the actual diagnosis. Thereafter usually comes the institution of evidence-based management and surveillance steps, as required (**Fig. 3**). However, particularly in more complex neurological cases involving pilots and space mission crew, special consideration should be made by the aerospace medical officer and/or relevant air safety authority to the utilization of: 1) scenario-specific screening; 2) simulator and flight checks; and 3) a 'neuro-panel' review (i.e., neurologist, neurosurgeon, and neuropsychologist; Fig. 3).

Conclusion

Neurological conditions can be expected to arise in air and space crew, whose missions are physiologically challenging and often physically and psychologically demanding. When such circumstances do occur, a paradigm should be in place aiming to

accurately diagnose, manage, and prognosticate, given the broad implications involved. We recommend appropriate multimodality screening measures in space mission crews, but for air crews questionnaire-based screening should suffice. If a substantial neurological diagnosis is established, or if uncertainty remains, we recommend involvement of a multidisciplinary 'neuro-panel' to aid in the workup and decision-making process. This is particularly important given that certain neurological diagnoses are associated with more adverse prognostication than others.

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