

Chapter 2

Long Duration Flight Data

Astronaut's bodies suffer in microgravity. Without effective countermeasures, muscles atrophy, bones shed calcium, and eyesight deteriorates. We've known about this for some time, but the problem has only been put under the spotlight recently with several astronauts experiencing severe eyesight deficiencies [1]. Until crewmembers began complaining of eyesight-related symptoms researchers had thought the problem to be transient.

However, thanks to anecdotal reports by astronauts and a comparison of pre- and post-flight ocular measures, microgravity-induced visual acuity impairments have now been recognized as a significant risk. And this problem doesn't affect a minority of crewmembers. Retrospective analysis of medical records has revealed that 29 percent of 300 shuttle astronauts and 60 percent of space station astronauts have suffered some form of visual degradation [1]. That's a serious problem for an agency planning on sending its astronauts to asteroids and to Mars (Fig. 2.1).

Theories

The problem has its own acronym—this is NASA after all—and is referred to as the visual impairment/intracranial pressure (VIIP) syndrome. Since VIIP has only recently been identified, there hasn't been much research performed, so scientists are in the dark about what might cause the vision impairments. The data that is available shows that astronauts who suffer VIIP-related symptoms experience varying degrees of visual performance decrements. Some suffer cotton-wool spot formation while others may present with edema of the optic disc. Others may suffer flattening of the posterior globe while some may present with distension of the optic nerve sheath [1, 2]. In short, there is a profusion of signs and symptoms, but the reason for the vision impairment has researchers a little flummoxed.



Fig. 2.1 Canadian Space Agency astronaut, Chris Hadfield, is given an eye examination by Expedition 34/35 Flight Engineer Tom Marshburn. (Illustration courtesy of NASA)

One theory suggests that the changes in ocular structure and impairment to the optic nerve is caused by the cephalothoracic fluid shift that astronauts experience while on board the International Space Station (ISS) [3]. It is theorized that some astronauts are more sensitive to fluid shift due to genetic and anatomical factors. We'll discuss this theory some more later. In the course of conducting studies on the VIIP syndrome, researchers have focused on three systems—ocular, cardiovascular, and central nervous. These studies have revealed a variety of symptoms other than visual decrements, including increased intracranial pressure (ICP) and changes in cerebrospinal fluid (CSF) pressure [2, 3]. But, because the preflight, inflight and post-flight data is so thin on the ground, it is very difficult to define why and how these symptoms occur. Inevitably, since the impact of VIIP is an operational concern, space agencies have increased preflight, inflight, and post-flight monitoring of the syndrome to better characterize the syndrome and the risks.

To date, more than a dozen astronauts have suffered VIIP symptoms [4]. Some of these symptoms persist post-flight and some don't. Some astronauts experience quite severe symptoms, and for others it is just a mild inconvenience. Very little is known about the etiology of symptoms, but researchers believe microgravity-induced cephalothoracic fluid shift and associated physiological changes are implicated.

To better investigate the syndrome, NASA's Human Health and Performance Directorate brought together a VIIP project team in 2011 to investigate the problem using data compilation, analysis, and multi-discipline, cross-cutting collaboration.

To give you an idea of the complexity of the issue facing the VIIP project team, the following is a brief account of the first seven cases of the perplexing syndrome.

History

Case #1

The first VIIP case affecting a NASA astronaut occurred during an ISS mission. The affected crewmember first noted a reduction in his ability to see objects up close. On his return, the crewmember was subjected to fundoscopic examination, which detected choroidal folds behind the optic disc. The examination also revealed a cotton wool spot in the crewmember's right eye, although the left eye was clear. Three years after his mission the choroidal folds were still there [4].

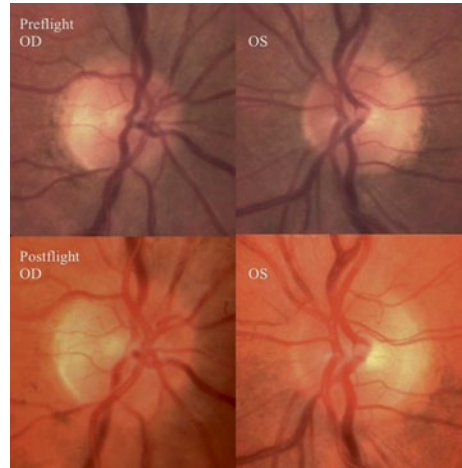
Case #2

The second case occurred three months into an ISS mission when a crewmember informed the ground that he was only able to see Earth clearly if he used his reading glasses. For the remainder of his mission there was no improvement in his condition, but neither did the symptoms get worse. After his return to Earth the astronaut noticed a gradual improvement, but his vision didn't return completely. The astronaut was subjected to fluorescein angiography that revealed choroidal folds. This was also one of the signs in the first case of VIIP. The astronaut was also subjected to magnetic resonance angiography (MRA) and magnetic resonance venogram (MRV) tests, but these were normal [4]. A more sensitive test using optical coherence tomography (OCT) was also performed. OCT is a non-invasive test that uses light waves to take images of the retina. The results of this test showed increased thickening of the astronaut's retinal nerve fiber layer (NFL). It was one more variable in the VIIP puzzle.

Case #3

The third VIIP case was a strange one because the crewmember didn't suffer any vision impairment during his mission—no headaches or diplopia. Nothing. But when he returned to Earth, ophthalmologists discovered that the astronaut had asymmetrical disc edema, which can be seen in Fig. 2.2. Unlike Cases #1 and #2, this astronaut did not have choroidal folds, but his fundoscopic examination did reveal a small hemorrhage behind the optic disc of his right eye. What was especially unusual about Case #3 was the fact that this astronaut had the most serious optic disc edema

Fig. 2.2 VIIP Case #3. The fundoscopic images of the right and left optic disc in the third case of visual impairment observed in spaceflight. Grade 3 edema can be seen in the *right* optic disc and grade 1 edema in the *left* optic disc. (Illustration courtesy of NASA, Mader and Elsevier)



of all the crewmembers tested to date, yet he had reported no visual impairment during his flight [4].

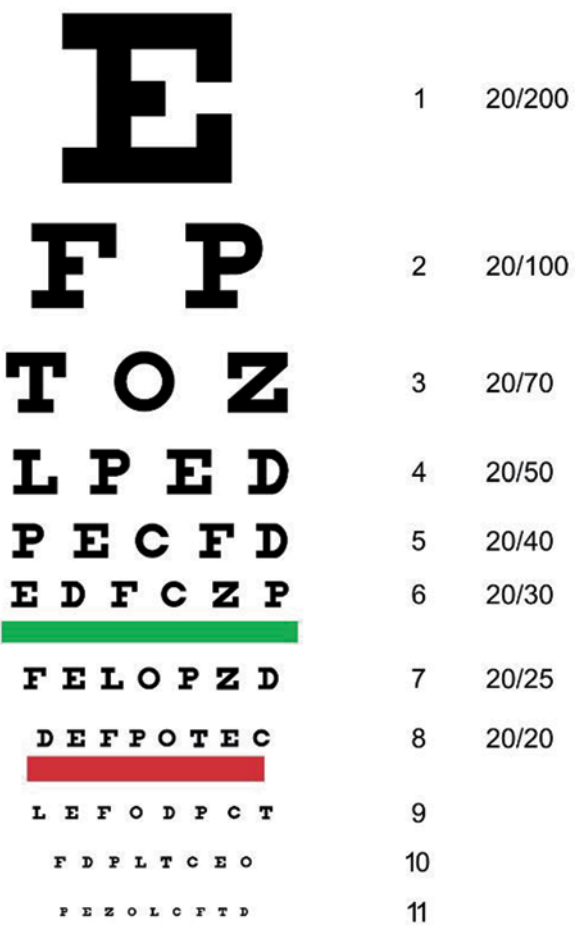
Case #4

The fourth case of VIIP was no less unusual than the first three. This astronaut noticed his vision altering after two months in orbit. His symptoms included a reduction in the near-vision of his right eye and scotoma in his right temporal field. The scotoma affected the crewmember to the extent that he was unable to read 12-point font, which is probably close to what you're reading now. What was strange was that everything about this astronaut was normal: he didn't complain of any symptoms—headache, diplopia—that might normally be associated with such vision impairment [4]. Also, the environment on board the ISS was well within nominal margins during his stay—no excess carbon dioxide concentration or toxic fumes. Furthermore, his pre- and post-flight (correctable) visual acuity were the same, although fundoscopic examination revealed choroidal folds in the astronaut's right eye.

Case #5

Another layer was added to the VIIP enigma with the fifth case, which occurred after only three weeks in orbit. This astronaut's vision was affected so badly that his glasses had to be adjusted by one to two dioptres to enable him to read procedures [4]. By this time NASA was becoming a little concerned with this VIIP issue and decided it would be prudent to perform inflight ocular ultrasound exams to observe

Fig. 2.3 A simple vision test to assess nearsightedness and farsightedness. (Illustration courtesy of NASA)



changes in the ocular health of its crew. To that end, the astronaut who represented Case #5 was subjected to ultrasound examinations, which revealed flattening of the posterior globe and dilated optic nerve sheaths. More tests were conducted after NASA had uploaded near and far acuity charts (Fig. 2.3) together with an Amsler Grid (Fig. 2.4). This case occurred back in the day when the shuttle was flying, so mission managers decided to fly up a video-ophthalmoscope, which also allowed remotely guided fundoscopic exams to be performed (Fig. 2.5) .

Once the examinations had been performed, the images were sent to neuro-ophthalmological consultants who decided that no treatment was required, but suggested that fundoscopic and visual acuity exams be conducted once a month for the remainder of the mission. The examinations served a dual purpose. They provided neuro-ophthalmologists with a baseline to compare against other vision issues and they served as a means of monitoring the ocular health of the crewmembers.

Another procedure that was added around this time was the 3-Tesla MRI examination. Before Case #4, astronauts spent three weeks recovering in Star City,

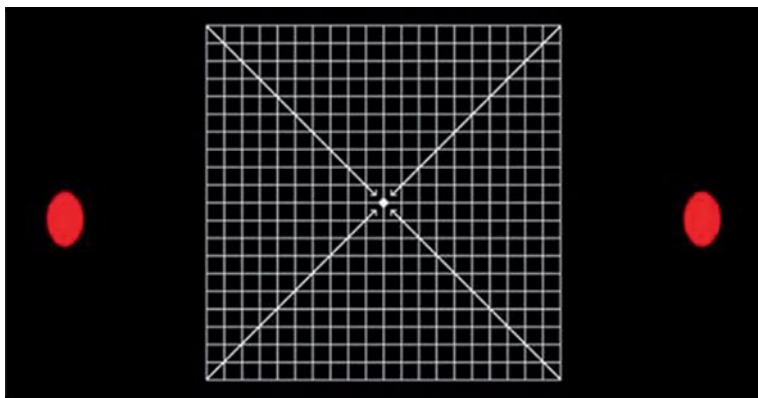


Fig. 2.4 Amsler Grid. (Illustration courtesy of NASA)

Fig. 2.5 ISS Commander Leroy Chiao performs an eye examination on Flight Engineer Salizhan Sharipov using the Advanced Diagnostic Ultrasound equipment. (Illustration courtesy of NASA)



Russia. The problem with this arrangement was that there was no 3-Tesla MRI equipment [4].

Why 3-Tesla MRI? Well, this item of equipment is extremely sensitive and can detect abnormalities that just can't be detected using other imaging equipment—all the way down to the ultra-structural level such as blood vessels just 200 to 300 microns in diameter. 1.5 Tesla MRI's had been performed on all crewmembers pre-flight, so the results of these examinations were compared against the 3-Tesla MRIs taken three days post-flight following Case #4. The comparison revealed that posterior globe flattening had not been present preflight, so researchers could rule out that pre-existing condition as a reason for VIIP—at least as far as this crewmember was concerned.

Case #5 continued to be examined following his flight. Thirty days post-flight another MRI was performed that revealed significantly dilated optic nerve sheaths, flattening of the posterior globe and thickened optic nerves [4]. At this stage the crewmember was still affected by the same vision impairment he had experienced on orbit.

Another examination—a lumbar puncture – performed 57 days post-flight revealed normal CSF pressure. This astronaut, who became aware of visual changes three weeks into his mission, reported that his vision had remained static for the remainder of his stay on board the ISS [4]. He hadn't complained of headaches, visual obscurations, or diplopia, and yet several weeks post-flight he was still suffering vision impairment. More tests were conducted, including cycloplegic refraction and fundus photos, but these were all normal; no sign of choroidal folds or disc edema. Nothing.

Case #6

VIIP Case #6 was identified after the crewmember returned from a six-month mission. This crewmember reported that his distance vision was better when he used his reading glasses. Ophthalmological tests performed three weeks post-flight revealed optic-disc edema (Fig. 2.6) in the astronaut's right eye and—in what was becoming a common sign—choroidal folds. As with Case #5, a brain MRI was conducted, which revealed flattening of the posterior globe and an enlarged optic nerve sheath in the right eye [4]. Nine weeks post-flight, ophthalmological examination—OCT—revealed disc edema and a cotton-wool spot in the crewmember's left eye.

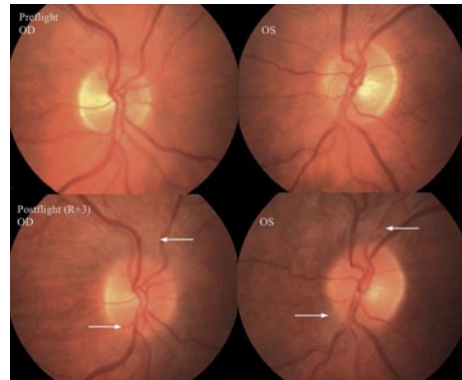
Case #7

The seventh case of VIIP was notable because this astronaut was treated post-flight. After two months in orbit, this astronaut noticed a gradual decrease in his near and distance vision in both eyes [4]. The vision impairment continued for the remainder of his mission and became so much worse that the astronaut could no longer perform close-up tasks even when using his prescription glasses. When this happened

Fig. 2.6 The sixth case of visual impairment during spaceflight. Images on the *left* are preflight images of the optic disc. Images on the *right* are post-flight images of the *right* and *left* optic disc showing grade 1 edema in the *right* optic disc. (Illustration courtesy of NASA)



Fig. 2.7 *Upper images* are preflight images of the *right* and *left* optic discs. *Lower images* show post-flight images of the optic nerve and the *superior* and *inferior* nerve fiber layers. (Illustration courtesy of NASA)



he switched to the more powerful Space Anticipation Glasses, which helped him continue his work. In common with Case #5 this crewmember did not complain of visual obscurations, headaches, or diplopia. Also in common with Case #5 the station atmospheric pressure, carbon dioxide and oxygen levels were reported to be at nominal levels during the mission.¹ Following landing a fundus assessment revealed Grade 1 bilateral optic-disc edema and choroidal folds (Fig. 2.7). Case #7, in common with several earlier cases, also had signs of an enlarged optic nerve sheath [4].

Summary

Cases 2, 4, 6, and 7 shared the common signs of disc edema, posterior globe flattening, choroidal folds, and hyperopic shift. These signs closely align with those reported by patients suffering from increased intracranial hypertension, which we will discuss shortly.

¹ As a reminder, the CO₂ levels on the ISS are between 2.3 and 5.3 mmHg, which is 10–20 times the normal terrestrial atmospheric level of 0.23 mmHg.

Table 2.1 Clinical practice guidelines classifications of 36 long-duration U. S. crewmembers [6]

CPG class	Definition	# Of affected astronauts
Non cases	<0.50 diopter cycloplegic refractive change	
	No evidence of papilledema, nerve sheath distension, choroidal folds, globe flattening, scotoma or cotton wool spots compared to baseline	2
1	(Repeat OCT and visual acuity in 6 weeks)	
	≥ 0.50 diopter cycloplegic refractive change and/or cotton wool spot	
	No evidence of papilledema, nerve sheath distension, choroidal folds, globe flattening, scotoma or cotton wool spots compared to baseline	2
	CSF opening pressure (if measured) ≤ 25 cm H ₂ O	
2	(Repeat OCT, cycloplegic refraction, fundus exam and threshold visual field every four to six weeks $\times$ six months, repeat MRI in six months)	
	≥ 0.50 diopter cycloplegic refractive change or cotton wool spot	8
	Choroidal folds and/or optic nerve sheath distension and/or globe flattening and/or scotoma	
	No evidence of papilledema	
	CSF opening pressure (if measured) ≤ 25 cm H ₂ O	
3	(repeat OCT, cycloplegic refraction, fundus exam and threshold visual field every four to six weeks $\times$ six months, repeat MRI in 6 months)	
	≥ 0.50 diopter cycloplegic refractive change or cotton wool spot	1
	Optic nerve sheath distension, and/or globe flattening and/or choroidal folds and/or scotoma	
	Papilledema of Grade 0–2	
	CSF opening pressure ≤ 25 cm H ₂ O	
4	(Institute treatment protocol as per CPG)	
	≥ 0.50 diopter cycloplegic refractive change or cotton wool spot	4
	Optic nerve sheath distension, and/or globe flattening and/or choroidal folds and/or scotoma	
	Papilledema of Grade 2 or above	
	Presenting symptoms of new headache, pulsatile tinnitus and/or transient visual obscurations	
	CSF opening pressure > 25 cm H ₂ O	
Unclassified	Too little evidence at present for definitive classification	
	Early ISS flyers with no, or limited testing	19

These cases also shared other similarities, including optic nerve sheath distension and posterior globe flattening. These observations were revealed by MRIs performed post-mission. Despite myriad tests (summarized in Tables 2.1 and 2.2) and scans, a definitive etiology for the findings in the seven crewmembers remained elusive. It was suggested that venous congestion in the eye, caused by cephalotho-

Table 2.2 Summary of ophthalmic changes from seven affected long-duration crewmembers [6]

Ophthalmic condition	Total affected
Optic nerve sheath distension	6/7 (86%)
Nerve fiber layer thickening	6/7 (86%)
Optic disc edema	5/7 (71%)
Posterior globe flattening	5/7 (71%)
Hyperopic shift in one eye or both eyes by $\geq +0.50$ dioptres	5/7 (71%)
Choroidal folds	4/7 (57%)
Elevated post-flight CSF pressure (indicative of increased ICP)	4/7 (57%)
Cotton wool spots	3/7 (43%)
Decreased intraocular pressure (IOP) post-flight	3/7 (43%)
Tortuous optic nerve	2/7 (29%)

racic fluid shift, could have been responsible for elevated choroidal volume changes. Given the commonality of that sign, it was also suggested that this could be a unifying mechanism.

A Final Note: Intracranial Hypertension

Intracranial hypertension is a disorder the primary feature of which is persistently elevated intracranial pressure (ICP) [5]. The most pertinent neurologic sign of ICP is papilledema, which is discussed in Chapter 4. Papilledema is a red flag condition because it may lead to progressive optic degeneration and ultimately blindness [5]—that’s a big problem if you’re en-route to Mars or some other far-flung destination. Typical signs and symptoms are usually related to increased ICP and papilledema and may include the following:

- headaches, often varying in type, location, and frequency
- diplopia
- pulsatile tinnitus
- pain that radiates, usually in the arms

Symptoms of papilledema may include the following:

- transient visual obscurations, often uniformly orthostatic
- gradual loss of peripheral vision in one or both eyes
- blurring and distortion of central vision
- sudden visual loss [5].

The most significant physical finding is bilateral disc edema secondary to the increased ICP. In more severe cases, edema and diminished central vision may be present. Visual function tests for diagnosing and monitoring patients with intracranial hypertension are similar to those used to assess VIIP and include:

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