Neurobehavioral Conditions Checklist:  
A Literature Review and Operational Assessment

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Executive Summary / Recommendations

The following recommendations outline steps to improve the understanding of neurobehavioral signs and symptoms in long-duration space missions. The recommendations have been developed through a systematic literature review and an operational assessment that included semi-structured interviews with subject matter experts from NASA, the U.S. Army, the U.S. Air Force, the Department of Defense, and from private industry. The recommendations are organized to make suggestions in three broad areas: Developing a taxonomy of neurobehavioral signs and symptoms; Measuring neurobehavioral signs and symptoms; and Understanding the sources of neurobehavioral signs and symptoms.

A Taxonomy of Neurobehavioral Signs and Symptoms

Recommendation 1: A comprehensive approach to understanding neurobehavioral decrements is needed.

The Exploration Medical Condition List (EMCL) serves to guide medical efforts to ensure the safety and effectiveness of crews who will embark on asteroid redirect and Mars missions. In the most recent iteration of this living document, NASA has identified anxiety, depression, and insomnia as the neurobehavioral symptoms of interest for an exploration class mission. The EMCL also lists “behavioral emergency” as a medical condition of interest. These medical conditions have been identified as potential threats to the health and performance of crews on exploration missions. Absent from the EMCL are a number of cognitive and affective disorders that have the potential to affect crew health and performance on long-duration missions.

To develop a comprehensive checklist of neurobehavioral signs and symptoms likely to develop in long-duration space exploration (LDSE), the U.S. Department of Defense Neurobehavioral Symptoms Inventory (NSI) serves as a useful starting point. The NSI is a 22 item inventory of cognitive, emotional, somatic/sensory, and vestibular symptoms thought to be indicative of brain injury. While developed to assess neurobehavioral decrements among service members with suspected brain injuries, the NSI provides sufficient coverage of the neurobehavioral symptoms expected to impact astronauts on a LDSE. It is recommended that NASA and BHP draw on the cognitive and emotional variables assessed by the NSI in the development of a neurobehavioral conditions checklist.

As part of the current effort, an operational assessment consisting of interviews with subject matter experts from both NASA and various branches of the U.S. military was conducted. The results of the operational assessment suggest that symptoms such as attentional biases, irritability/anger, and boredom may also be critical to assess during the course of a mission. Each of these factors has the potential to negatively impact the performance of individuals and crews. Furthermore, the development of attentional biases may also negatively impact the
uptake and use of psychological countermeasures, particularly those that rely upon cognitive behavioral therapies to mitigate the presence of psychological decrements.

Thus, in addition to the core set of neurobehavioral conditions assessed by the NSI, these conditions should also be incorporated into the development of a checklist. Table 1 below presents a checklist of neurobehavioral symptoms that have the potential to develop during LDSE. The symptoms in the column labeled NSI Symptoms are those derived from the NSI. The symptoms listed in the Additional Symptoms column are those that were identified through the literature review and operational assessment that are included as part of this report.

| Table 1. Checklist of Neurobehavioral Conditions in Long-Duration Space Exploration |
|-----------------------------|-------------------------------|-----------------------------|
| Factor                     | NSI Symptoms                  | Additional Symptoms         |
| Cognitive                  | Cannot get organized/finish things | Attention/Threat Biases    |
| Cognitive                  | Forgetfulness (memory)        |                             |
| Cognitive                  | Making decisions              |                             |
| Cognitive                  | Poor concentration            |                             |
| Emotional                  | Anxiety/tension               | Anger                       |
| Emotional                  | Depressed/sad                 | Boredom                     |
| Emotional                  | Fall/stay asleep              |                             |
| Emotional                  | Fatigue                       |                             |
| Emotional                  | Irritable                     |                             |
| Emotional                  | Low frustration tolerance     |                             |

It is likely that most of these symptoms will not reach clinical levels. That is, some symptoms may exist, but likely not at debilitating levels. Nonetheless, it will be important for NASA and the broader scientific community to develop effective methods to: 1) identify the presence of such symptoms among crewmembers, and 2) examine correlational evidence between these symptoms and crewmember health and performance. Consequently, additional research on this set of symptoms in spaceflight and analog settings may be needed.

**Measuring Neurobehavioral Conditions**

**Recommendation 2**: A suite of neurocognitive tests, psychological questionnaires, and clinical assessments should be developed to assess the neurobehavioral symptoms likely to develop in long-duration space missions.

Subject Matter Experts (SMEs) interviewed as part of the operational assessment made it clear that a comprehensive suite of tools to assess neurobehavioral symptoms will be critical to ensuring the health and performance of crews on LDSE. Consistent with this view, Cowings et al. (2007) advocated a multi-indicator approach to assessing individual differences in adaptation to spaceflight. Toward the development of such a multi-indicator approach, it is important to take a critical look at existing instruments to determine whether such instruments provide adequate coverage of potential neurobehavioral symptoms that might impact health and performance in LDSE.
Existing neurobehavioral assessments such as the Windows Spaceflight Cognitive Assessment Tool (WinSCAT), and next generation neurocognitive assessments such as Cognition (NASA Techport, 2015) focus heavily on the cognitive aspects of neurobehavioral functioning. While such tools adequately assess cognitive impairments, they do little to detect the presence of emotional symptoms such as anxiety and depression.

Therefore, neurobehavioral assessment platforms must be developed so that emotional symptoms are assessed alongside cognitive impairments. Ideally, emotional disorders would be assessed clinically, through a thorough assessment by a flight surgeon. However, in a long-duration spaceflight context, clinical assessments by flight surgeons will be impractical due to communication delays and the lack of real-time communication with ground crews (unless, of course, there is a flight surgeon on board). Therefore, the use of non-invasive assessment strategies may be necessary. For example, anxiety disorders may be assessed through the use of eye tracking technologies that are able to detect attentional threat bias, a common indicator of anxiety in high stress populations (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van Ijzendoorn, 2007). Further, the use of lexical or text analysis may assist in the detection of depressive symptoms (P. Lieberman, Morey, Hochstadt, Larson, & Mather, 2005).

**Recommendation 3: A multi-method approach should be taken in the development of a neurobehavioral assessment tool.**

A number of SMEs expressed concern that current neurocognitive tools such as the Automated Neuropsychological Assessment Metric (ANAM), the WinSCAT, and Cognition all rely exclusively upon an electronic delivery system. In the view of at least one of the SMEs, overreliance on cognitive assessment delivered through the electronic format may bias results in favor of individuals high in cognition and that are more comfortable completing tasks using electronic formats. SMEs indicated that electronically-delivered cognitive assessments should be supplemented with psychological questionnaires. While it is commonly believed that crewmembers do not enjoy self-report psychological questionnaires, the use of such tools may need to be considered in order to vary the methodology with which neurobehavioral assessments are delivered. Adopting such an approach may more evenly distribute the measurement error associated with delivery mode.

Furthermore, to the extent that electronic assessments are used (e.g., in the measurement of reaction times and similar metrics), these should include both visual and audio cues to prompt users. The exclusive use of visual cues—as is the case in most neurocognitive tools—may bias results toward individuals who are predisposed to favor this particular methodology. Incorporating the use of audio cues in addition to visual cues may help provide a more balanced assessment tool. The use of audio cues may also allow researchers to assess the presence of somatic and sensory decrements that are associated with emotional and cognitive assessments. Related, the use of vibration as a cue may also prove useful given likely psychomotor and vestibular issues that will be experienced in spaceflight settings.
Recent advancements in the use of virtual reality may also hold potential for the future of neurobehavioral assessment in LDSE settings. For example versions of the Stroop Test that use virtual reality have been found to be effective at detecting decrements in executive function (Armstrong et al., 2013). Additional research suggests that this line of research holds great potential for neurobehavioral assessments (Parsons, Carlew, & Sullivan, 2015). Given the potential use of virtual reality in other aspects of long-duration spaceflight, NASA may want to leverage the existence of virtual reality platforms in space by exploring the potential application of such technologies.

**Recommendation 4: Non-invasive metrics of neurobehavioral disorders (e.g., eye tracking, facial recognition, voice recognition, text analysis) should be part of any suite of neurobehavioral assessments.**

A common criticism of current neurobehavioral assessments is the existence of learning effects (e.g., De la Torre, Navas, & Bozal, 2014). Furthermore, research has demonstrated the presence of ceiling effects on commonly used neurocognitive assessment tools in spaceflight settings (Cowings et al., 2007). This evidence is in line with Hockey and Sauer’s observation that “performance decrements are often difficult to detect in highly-motivated subjects, because of a compensatory protection of primary task requirements through increased effort” (1996, p.312).

Beyond methodological limitations to commonly-used assessment methods, anecdotal evidence provided by SMEs during the operational assessment suggests that astronauts sometimes tire of taking cognitive tests such as the WinSCAT. A practical way to address these limitations is the incorporation of non-invasive assessment techniques. The use of such methods will allow for the assessment of a wide variety of neurobehavioral decrements in a way that places minimal burden on the crew. Table 2 presents a set of suggested tests derived from the literature review and operational assessment in the present report.

As the table shows, we recommend a combination of neurocognitive tests, psychological assessments, and clinical approaches to assessing the neurobehavioral conditions likely to develop in spaceflight and other ICE settings. The assessments include both direct and non-invasive methods for assessing neurobehavioral decrements. In some cases, neurobehavioral symptoms can be assessed through both direct and non-invasive measures.
Table 2. Multi-method measurement of Neurobehavioral Symptoms in Long-Duration Space Exploration

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Direct Measurements/ Psychological Tests</th>
<th>Non-invasive Measurements/ Non-Psychological Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention/Threat Biases</td>
<td>Tests such as dot probe task; Virtual Reality Stroop Test</td>
<td>Eye tracking; functional Near Infrared Spectroscopy</td>
</tr>
<tr>
<td>Cannot get organized/finish</td>
<td>Tests such as Mathematical Processing Test</td>
<td></td>
</tr>
<tr>
<td>Forgetfulness (memory)</td>
<td>Tests such as Sternberg Memory Search</td>
<td></td>
</tr>
<tr>
<td>Making decisions</td>
<td>Tests such as Balloon Analog Risk</td>
<td></td>
</tr>
<tr>
<td>Poor concentration</td>
<td>Tests such as Visual Object Learning</td>
<td></td>
</tr>
<tr>
<td>Anger</td>
<td>Self-report assessment such as on the Deployment Stress Inventory</td>
<td>Lexical/text analysis</td>
</tr>
<tr>
<td>Anxiety/tension</td>
<td>Validated clinical instruments; Assessment from flight surgeon</td>
<td>Thyroid function; Plasma Markers</td>
</tr>
<tr>
<td>Boredom</td>
<td>Validated clinical instruments; Assessment from flight surgeon</td>
<td>Physiological measures (cortisol, heart rate, skin conductance); Eye tracking; functional Near Infrared Spectroscopy</td>
</tr>
<tr>
<td>Depressed/sad</td>
<td>Validated clinical instruments; Assessment from flight surgeon</td>
<td>Lexical/text analysis</td>
</tr>
<tr>
<td>Fall/stay asleep</td>
<td>Self-report sleep quantity/quality</td>
<td>Actigraph monitors</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Psychomotor Vigilance Test</td>
<td>Eye tracking; Facial recognition</td>
</tr>
<tr>
<td>Irritable</td>
<td></td>
<td>Facial recognition; Lexical/text analysis</td>
</tr>
<tr>
<td>Low frustration tolerance</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Recommendation 5: Self-awareness tools should be a part of any neurobehavioral assessment tool.

SMEs suggested that neurobehavioral assessments should include a self-awareness or feedback component. Such a feature serves two purposes. First, self-awareness feature allows users to see the areas of neurobehavioral performance in which they excel as well as those areas on which they may need improvement. Self-awareness may help in the application of countermeasures and interventions designed to mitigate the effects of neurobehavioral symptoms. A prime example of this is the U.S. Army’s Comprehensive Soldier and Family Fitness (CSF2) program, which utilizes the Global Assessment Tool (GAT) to track the psychological health and well-being of U.S. soldiers. Upon completion of the GAT soldiers are provided with immediate feedback. This is believed to aid in the effectiveness of psychological interventions in place in the Army by giving participants greater insight into their own cognitions and emotions as well as providing a common language to help make meaning of their experiences. Notably, instruments being developed by NASA such as Cognition provide real-time feedback to users upon completion.

Second, self-awareness tools may also help contribute to uptake among long-duration crewmembers. That is, multiple SMEs indicated that astronauts are more likely to utilize an
assessment tool if they understand its purpose and are able to incorporate information from it in their day-to-day operations.

Sources of Neurobehavioral Signs and Symptoms

**Recommendation 6: According to SMEs, radiation, microgravity, and CO\(_2\) pose the greatest threats to neurobehavioral performance and should continue to be examined.**

While these risk factors were identified by SMEs as the most important to study, these factors are also among the most difficult to study in an operational environment. Animal models that seek to study the effects of radiation and microgravity are limited in their generalizability to humans. While CO\(_2\) was identified as a major threat by a number of SMEs, others had confidence that the threat of CO\(_2\) exposure would be mitigated through the design of the spacecraft that will take humans to Mars. Current and planned year-long missions will likely be critical in contributing to the understanding of these factors upon neurobehavioral conditions.

Other environmental and habitability factors will also be important to examine. The literature suggests that temperatures may impact a variety of outcomes, including both cognitive and emotional symptoms. Research suggests that extreme cold appears may increase arousal, and therefore promote cognitive performance; extreme heat appears to have detrimental impacts upon cognitive performance. This research has important implications given the environmental conditions that will face crewmembers on the Mars surface. Noise and vibration from the spacecraft have been identified as potential risk factors for emotional and cognitive outcomes, and extant research provides some evidence that this may be the case. However, interviews with SMEs suggest that most SMEs do not view these factors as high-level risks. Light/dark cycles have important implications for circadian rhythms and ultimately sleep and fatigue. Therefore, the lighting used on the spacecraft and in the habitat on the surface of Mars will be critical in maintaining the circadian rhythms of crewmembers. However, much research on this topic has been conducted and few SMEs viewed lighting research as a crucial area of need.

**Recommendation 7: The impact of social dynamics upon cognitive outcomes needs to be more fully researched and understood.**

As indicated by the comprehensive literature review, and as discussed by multiple SMEs, there is relatively little research examining how interpersonal factors might impact cognitive outcomes. Rather, much of the research in this area has focused on the relationship between interpersonal relations and emotional symptoms. Understanding how interpersonal relationships impact cognitive outcomes may broaden our understanding of neurobehavioral signs and symptoms in the context of a long-duration space mission.

As noted by Kanas and Manzey (2008), interpersonal issues among crewmembers on a long-duration mission might include tension, withdrawal, or scapegoating. These issues, when experienced in a prolonged manner may have the potential to impact cognitive functioning as
individuals draw on cognitive resources to deal with the perceived threats that interpersonal issues might cause. Controlled laboratory studies that manipulate interpersonal issues likely to develop onboard a long-duration mission, and that subsequently assess cognitive functioning of individuals exposed to such interpersonal issues, may yield useful information about the effects of social dynamics on a Mars mission.

It is also possible that social interactions can produce contagion effects, whereby positive or negative emotions diffuse through a small group (e.g., Barsade, 2002). The diffusion of emotions can be driven by a key influencer within the group. Emotional diffusion can ultimately reach a tipping point where team performance is enhanced or degraded. To date, little is known regarding the ways in which emotional factors might spread through a small group in an ICE setting. Future research might help better understand this potentially critical source of neurobehavioral conditions.

**Recommendation 8: The development of a neurobehavioral checklist must recognize the multiphasic nature of a mission to Mars.**

A Mars mission will proceed in three distinct phases. Phase 1 will involve the transit from Earth to Mars. This phase will involve many of the space travel-related threats that have been considered in the literature. Phase 2 will take place on the surface of Mars. Here, the crew will likely undertake a high workload in a relatively unknown environment. Phase 3 will involve the return transit from Mars to Earth. Again, many of the threats related to spaceflight will be present during this phase. Between each mission phase is a transition point where crewmembers will have to adjust both physiologically and psychologically to different levels of gravity, light/dark cycles, etc. At each phase of the mission, the sources of the threats to crewmember neurobehavioral health are distinct. Therefore, the development of a neurobehavioral conditions list will need to account for the fact that particular neurobehavioral conditions will be more likely at some phases of the mission than at others.
Introduction

As NASA prepares for long-duration space exploration (LDSE), it is critical that every effort is made to understand the health and performance risks to crewmembers, as well as the factors that pose such risks. Toward this end, the Behavioral Health and Performance (BHP) element has identified through the research roadmap what is known, what is not known, or what is poorly understood with regard to health and performance risks in the LDSE context.

One area in which little evidence exists, or where there is little agreement among scholars, is with regard to the sources and manifestations of neurobehavioral signs and symptoms in spaceflight settings. To be sure, scholars have considered neurobehavioral issues in spaceflight settings (De la Torre, 2014). For example, an expert panel has recently undertaken an in-depth effort to outline neurobehavioral issues in spaceflight (De la Torre et al., 2012). The authors of that document consider the various sources of neurobehavioral decrements such environmental and psychosocial factors, as well as countermeasures to neurobehavioral and neurocognitive deficits. In the end, though, the authors conclude that it is currently unclear whether, or how, microgravity or other environmental factors lead to neurobehavioral or neurocognitive changes in crewmembers. It appears that the uncertainty expressed by de la Torre at al. is indicative of the unsettled nature of this research domain more generally.

The purpose of this report is to contribute to the understanding of neurobehavioral conditions in spaceflight by examining the neurobehavioral signs, symptoms, and diagnoses identified in spaceflight and other isolated, confined, and extreme (ICE) environments. There are five specific objectives met by this report.

Objective 1. Create a taxonomy of neurobehavioral signs and symptoms in ICE settings.

Objective 2. A systematic review of neurobehavioral signs, symptoms, and diagnoses commonly found in ICE settings.

Objective 3. Seek to identify underlying causes of neurobehavioral issues.

Objective 4. Evaluate the validity and practical efficiency of existing scales to assess neurobehavioral issues.

Objective 5. Provide recommendations for future work in this area.

This report will address each of these five objectives in the order presented here. In addition, investigators conducted an operational assessment of 12 subject matter experts. This operational assessment will be provided as a standalone section of this report below. The findings of the operational assessment are used to supplement the results of the literature review and to help inform the recommendations for future research.
Neurobehavioral as a Concept

Neurobehavioral disorders include a large group of behavioral impairments seen in association with brain disease, brain impairments, and/or brain injury (Zasler, Martelli, & Jacobs, 2013). Symptoms seen in individuals with neurobehavioral problems can include affective disorders, psychotic disorders, personality disorders, and awareness disorders. While much of the recent research on neurobehavioral disorders has been conducted in military settings among service members with traumatic brain injuries (TBI) and/or post-traumatic stress disorder (PTSD), research on various neurobehavioral symptoms has been conducted in spaceflight and analog settings.

According to Zasler et al., the assessment and management of neurobehavioral disorders in the general population are not properly addressed in the context of overall care. In the spaceflight context, though effort has certainly been made to understand neurobehavioral disorders among crewmembers, there is a similar lack of holistic understanding of the sources of neurobehavioral disorders, as well as the manifestations of such disorders. This lack of understanding is likely a direct function of the fact that extended spaceflight (such as on the International Space Station) has only recently become a standard feature of NASA operations. As a result of this, we are only now beginning to connect data with anecdotal evidence to form a better understanding of the effects of extended spaceflight on neurobehavioral functioning.

Zasler et al. recommend a biopsychosocial approach to the assessment of neurobehavioral disorders. That is, to adequately assess neurobehavioral disorders, patients’ mental health, general health, and social histories should be collected in addition to family psychiatric and general medical histories. This information should be connected to information about injury or illness onset. Of course, among the astronaut population, much of the personal and familial health information is already known to NASA. Thus, in terms of assessment, the organization is in an advantageous position regarding its knowledge of the patient. The real challenge faced by NASA is developing assessments to detect neurobehavioral decrements among crewmembers during a long-duration mission. This challenge is compounded by the fact that there is rarely a clear delineation between actual neurobehavioral impairments, the psychological reactions to neurobehavioral impairments, and the wide range of personal and genetic factors that might lead to neurobehavioral decrements (MacMillan, Hart, & Martelli, & Zasler, 2002).

Identifying Neurobehavioral Signs and Symptoms

Neurobehavioral symptoms have been assessed in a wide range of settings. Perhaps most commonly, neurobehavioral symptoms have been assessed among individuals with suspected brain injuries. These include patients with TBI or that have experienced symptoms consistent with PTSD. While some of this work has been conducted among patients in general settings, it
is not surprising that much of the recent work on the subject has been conducted in military settings among military personnel that have been deployed on oversees combat missions.

The research that has systematically examined neurobehavioral impairments in military personnel is illustrated by such efforts as the Neurocognition Deployment Health Study (NDHS; Vasterling et al., 2006a). This prospective cohort study of U.S. Army soldiers was designed to address gaps in the deployment health literature. Specifically, the study leverages access to deployed military personnel to examine the effects of deployment upon a range of health outcomes, and also examines the protective factors that assist in preventing the development of neuropsychological outcomes.

The NDHS assesses neurocognitive functioning using components of the widely used Automated Neuropsychological Assessment Metrics (ANAM). The ANAM is a battery of assessments that monitor the cognitive aspects of neurobehavioral symptoms (Kane & Reeves, 1997). Factors of cognition assessed by the ANAM include attention, concentration, decision-making, memory, processing speed, and reaction time. The specific assessments contained within the battery have been validated against other established, validated methods (Kabat, Kane, Jefferson, & DiPino, 2001). The assessments are delivered electronically using computers or other specialized devices. The ANAM can be configured such that self-administered tests such as the Profile of Mood States (POMS; e.g., Vasterling et al., 2006b) can be delivered in conjunction with the neurocognitive tests. This allows for the determination of whether neurocognitive outcomes are associated with a variety of other variables measured through psychological questionnaires.

In one prominent study using NDHS data, researchers found that deployment to Iraq did indeed have a number of impacts upon the neurocognitive functioning of soldiers (Vasterling et al., 2006b). Using a regression framework with deployment as the primary predictor, deployment was significantly related to problems with sustained attention, verbal learning, and visual-spatial memory. Deployment was also related to increases in state measures of confusion and tension. Data from the NDHS have been used in additional studies to examine neurocognition in relation to TBI and PTSD (Vasterling et al., 2012) and to examine risk and resilience factors among deployed military personnel (Vogt, Proctor, King, King, & Vasterling, 2008).

The Neurobehavioral Symptoms Inventory (NSI) is another assessment tool that is commonly used in U.S. Department of Defense (DoD) settings. Like the ANAM, the NSI is commonly used to assess neurobehavioral impairments among individuals who have experienced some insult or injury to the brain such as TBI or PTSD. Unlike the ANAM, the NSI is fully self-report with no behavioral indicators of performance. Instead, the NSI serves as a checklist of 22 symptoms where respondents are asked to self-report the severity of symptoms within the previous 30 days using a Likert scale ranging from “None” to “Very Severe.” Further, the NSI assesses affective, emotional, somatic, and vestibular symptoms, in addition to cognitive symptoms. As will be discussed in greater detail below, prior factor analytic work has suggested a number of different underlying factor structures using the NSI. Most recently, Vanderploeg et

In the spaceflight and analog contexts, research has yet to propose or identify a comprehensive list of neurobehavioral symptoms—such as the NSI—that includes both cognitive and emotional factors. Instead, research has been somewhat more fragmented whereby discrete neurobehavioral symptoms have been examined with little consideration for how various types of symptoms might relate to one another. Of course, the interplay between emotion and cognition is extremely complex. Recently, research has begun to provide more detail on the complexity of this relationship (Okon-Singer, Hendler, Pessoa, & Shackman, 2015).

In the spaceflight context a number of tools have been developed. For instance, the Advisory Group for Aerospace Research and Development (AGARD) developed a battery of tests called the Standardized Tests for Research with Environmental Stressor (STRES). The AGARD STRES battery assesses cognitive decrements such as memory and reasoning that have the potential to be impacted in extreme environments (Draycott & Kline, 1996). The MiniCog Rapid Assessment Battery was also developed for use by NASA and in other contexts where individuals are exposed to high-stress environments (Shephard & Kosslyn, 2005). The test examines various aspects of attention (vigilance, filtering, and divided attention); working memory (verbal working memory and spatial working memory); cognitive set switching (Wisconsin Card Sort task); problem solving (verbal problems and spatial problems); and perceptual reaction time.

Currently, the primary assessment tool used on the ISS is the Spaceflight Cognitive Assessment Tool for Windows (WinSCAT; Kane, Short, Sipes, & Flynn, 2005). The WinSCAT was developed specifically for use by NASA, but is heavily based on the DoD’s ANAM described above. The WinSCAT includes five tests from the ANAM: Code Substitution; Code Substitution Delayed Reaction; Delayed Matching to Sample; Mathematical Processing; and Running Memory Continuous Performance. The tool is time-limited and is completed by astronauts every 30 days before or after a periodic health status test, or when requested by crewmembers or flight surgeons (de la Torre et al., 2014). Initial evidence regarding the reliability, validity, and sensitivity of the tool in identifying neurocognitive decrements was positive (Kane et al., 2005). More recently, the WinSCAT was used in the Mars 500 study to assess neuropsychological functioning among the crew of that space simulation. Using cutoff scores designed for astronauts upon the ISS, De la Torre et al. found that the WinSCAT was able to detect reductions in reaction times, such that reaction times increased over the course of the first eight months of the Mars 500 mission. Analyses also revealed correlations between age, language, and the various neurocognitive tests employed by the WinSCAT.

A variety of other tools have been developed to assess neurobehavioral symptoms in spaceflight and ICE settings. For example, the Psychomotor Vigilance Test (PVT) is commonly used to assess neurobehavioral decrements in spaceflight and analog settings. The PVT measures
reaction time and is sensitive to sleep restriction and fatigue. Researchers have also adapted existing tools such as the ANAM for use in ICE settings (e.g., Palinkas), and have consistently made use of existing self-report scales such as the POMS in space simulations and analog settings (e.g., Basner et al., 2014).

**Sources of Neurobehavioral Symptoms in Spaceflight Settings**

In LDSE, neurobehavioral signs and symptoms are expected to come from four distinct sources according to Kanas and Manzey (2008): the physical environment, habitability factors from the spacecraft, psychological factors, and interpersonal factors. Each of these factors poses its own distinct risk to the health and performance of the crew. To better understand each of the four factors, we briefly discuss each in more detail below.

**Physical Environment**

The physical environment will play a major role in the functioning of crewmembers. Microgravity is perhaps most salient variable that will impact the behavior of individuals. Research has shown that microgravity in space settings can affect a wide range of neurobehavioral outcomes. Such outcomes include cognition and mental imagery (Grabherr & Mast, 2010), neurovestibular function (Wood, Reschke, Samiento, & Clement, 2007), posture and movement (Massion, Amblard, Assaiante, Mouchnino, & Vernazza, 1998), and visual stability (Koga, 2000). While vestibular and sensory outcomes in microgravity settings are fairly well understood, there is a relative lack of knowledge regarding how microgravity affects cognitive and affective outcomes. The impact of long-term microgravity exposure is even less understood; thus, microgravity constitutes a major risk that needs to be addressed in the lead up to LDSE.

Space radiation is currently considered the primary risk to astronaut health on a LDSE (Chancellor, Scott, & Sutton, 2014). In LSDE, it is presumed that crewmembers will be exposed to cosmic rays from which astronauts are currently protected in low Earth orbit. This exposure may impact the health, cognition, and behavior of crewmembers. However, given the ethical and practical limitations which prevent the study of radiation exposure on human health and performance, there is currently a high level of uncertainty regarding this risk and how radiation might impact humans in deep space. Recent studies have examined how radiation exposure affects the health and performance of other organisms such as mice. This research has shown that radiation exposure does appear to result in impaired cognition among mice exposed to space-like radiation (Parihar et al., 2015). Further, evidence suggests that mice exposed to radiation exhibit higher levels of anxiety-like behaviors following prolonged exposure (Olsen, Marzulla, & Raber, 2014). Given the critical nature of this risk to the successful completion of a LDSE, research continues to examine how space radiation might affect human health and performance.
Other physical factors that have the potential to impact astronaut health and performance include the lack of light/dark cycles during spaceflight, and altered light/dark cycles while on the surface of Mars. Considerable research has examined how altered light/dark cycles impact human performance in such analogs as Antarctic settings, and how circadian rhythms function in simulated spaceflight environments (e.g., Basner et al., 2013). This research has demonstrated that altered light/dark cycles have the potential to impact circadian rhythms and sleep, psychosocial outcomes such as depression, interpersonal issues, and work performance. Because of the considerable research conducted on this topic, NASA and the broader research community has developed a number of countermeasures designed to entrain individuals to a 24 hour light/dark cycle (e.g., Najjar et al., 2014).

**Habitability**

Habitability refers to the features of the spacecraft which will take crewmembers to their destination and return them to Earth upon completion of their mission. Due to the nature of the mission, the volume of the spacecraft will be necessarily small. Research has shown that the volume of a habitat can impact a number of outcomes. For example, as discussed below, isolation and confinement in small volumes can lead to stress and other related outcomes as a result of sensory deprivation (e.g., Zuckerman, 1964). The impact of isolation will be felt beyond just the limited volume of the spacecraft. The deep space mission will limit the crew’s ability to interact with ground, and communication delays of up to 20 minutes one way are expected.

The limited capacity of the spacecraft will physically limit the supplies that can be carried on board. Thus, there will be limited space for medical supplies including pharmacological interventions. Efforts are currently underway to offset these limitations with a number of countermeasures. For example, because pharmacological supplies to counteract psychiatric or neurobehavioral symptoms will be limited, non-pharmacological interventions are currently being developed. This research is exemplified by recent developments in the self-delivery of resilience interventions (Rose et al., 2013). Such resilience interventions are designed to help crewmembers prepare for, or respond to, spaceflight stressors using a self-guided set of interventions that are delivered on computer systems that are already on board the spacecraft and that will require few additional resources on board to be effective.

Toxins aboard the spacecraft have long been identified as a risk on the ISS and for LSDE (see James & Zalesak, 2012). Recently, carbon dioxide (CO₂) has emerged as the focus of toxicological factors that pose threats to health and performance in spaceflight settings. Efforts have been made to identity the various threats to health and performance that elevated CO₂ levels might have on LDSE, and work continues to identify the maximum allowable concentrations of CO₂ aboard the ISS and future spacecraft.
A variety of other habitability factors may affect health and performance outcomes on LDSE. Such factors include temperatures, vibration of the spacecraft, and various design features of the spacecraft. However, given that few of these issues have been reported as problems among the ISS, it is not expected that these factors will pose significant problems once the LSDE spacecraft has been designed and refined to reduce these potential factors.

Of course, it is important to recognize that the stay on the Mars surface will involve a habitat perhaps similar in volume and design as NASA’s Human Exploration Research Analog (HERA). Once again, the volume of the habitat will be relatively small, and it may pose many of the same challenges as the spacecraft. Specifically, the small volume may pose problems related to sensory deprivation, particularly if crewmembers are forced to spend extended periods of time in the habitat between Mars surface missions. Toxicalogical factors are likely to be a concern particularly given the fact that the Mars atmosphere contains high concentrations of CO$_2$. Crewmembers may also be exposed to other toxins originating from generators or other power sources needed to power the habitat. The temperature on the Mars surface is considerably colder than on Earth; therefore, neurobehavioral symptoms related to extended exposure to extreme cold may develop. Other design features of the habitat including sleeping quarters, lighting systems, and tight living spaces with others, which may all contribute to additional health and performance problems.

**Psychological**

Kanas and Manzey (2008) also identify psychological issues associated with spaceflight. These include isolation, confinement, danger, monotony, and workload. As discussed above, the limited volume of the spacecraft is expected to lead to have potentially detrimental impacts including perceptions of isolation (Zuckerman, 1964). Furthermore, sensory deprivation as a result of prolonged exposure to the relatively monotonous environment may have deleterious effects on psychological outcomes. Consequently, NASA has invested in research to countermeasures that may offset the detrimental impacts of sensory deprivation on neurobehavioral outcomes. Among the most visible representations of this work is the development of virtual reality systems such as ANSIBLE-A Network of Social Interactions for Bilateral Live Enhancement (Wu et al., 2015). As the name of this system implies, these virtual reality systems have been developed to counteract both the physical and social aspects of isolation in confinement in small spaces.

Again, LDSE is expected to result in greater perceived social isolation among the crew as the small group of 4-6 individuals has limited contact with the outside world. The real-time communication with ground control that crews on the ISS currently enjoy will no longer be available. Further, communications with friends and family on the ground will also involve a time lag, or will be required to take place either through video/voice messages, or through email-like systems. Together, these features of LDSE are expected to exacerbate the effects of social isolation. Therefore, systems such as ANSIBLE are designed to mitigate the negative effects of
this form of stress. This form of isolation will also require that the crew will be autonomous enough to carry out critical functions without consistent input from the ground. Consequently, team cohesion will be critical determinants of well-being and performance among the crew (see Vanhove & Herian, in press).

In general, heavy workloads are expected to increase stress (Hockey, 1997), and research in both analog and spaceflight settings has provided evidence of the psychological and physiological stress reactions to workload (e.g., Dinges et al., 2005; Leino, Leppaluoto, Ruokonen, & Kuronen, 1999; Rai & Kaur, 2012). In LDSE, workloads are likely to fluctuate widely given the phase of the mission. As explained in the following section, different phases of the mission are likely to introduce different risks to the health and performance of the crew. Specifically, workloads are likely to be relatively light during the first transit phase of the mission, and work underload may be a problem (e.g., Cochrane & Freeman, 1989). During that phase, the crew may face boredom and monotony as they travel to their destination. Prolonged periods of boredom may introduce an entirely different set of risks as individuals perhaps disengage from the mission, or as interpersonal conflicts flare up during monotonous periods (e.g., Melamed, Ben-Avi, Luz, & Green, 1995).

However, workload is likely to increase as the crew prepares to land on the Mars surface and immediately after landing. High workload is likely to be sustained as the crew carries out its surface mission and will continue up to the time that the crew prepares to disembark from the Mars surface and begin their journey back to Earth. Thus, it is possible that sustained workload will lead to prolonged stress, thus having potentially detrimental effects upon a variety of health and performance outcomes. It is important to recognize, however, that boredom and monotony may set in while on the Mars surface as the time on Mars is currently expected to be over a year. On the return transit workload is again likely to be reduced until the crew nears its return to Earth. Therefore, the same issues that accompanied the first transit phase may also accompany the second return transit phase of the mission.

The danger of the mission may have a number of effects. Most prominent among these may be hypervigilance. As noted in prominent military studies (e.g., Castro, Adler, McGurk, & Bliese, 2012) hypervigilance is an adaptive reaction to stressors faced by those in consistently dangerous settings. However, when the danger is no longer present, and the individual continues to demonstrate tendencies toward hypervigilance, then physical exhaustion and impaired social functioning may result. Furthermore, anxiety symptoms may follow exposure to potentially traumatic or especially dangerous events during the mission. As described in more detail later in the report, anxiety symptoms may result in impaired cognition such as attentional biases (Armstrong & Olatunji, 2012).

A number of efforts have been made to examine how psychological variables change over the course of missions in isolated and confined environments. As noted by De la Torre et al. (2014) time effects have been studied in polar environments looking at the mental wintering syndrome.
(Rivolier, Goldsmith, Lugg, & Taylor, 1988), the three phases model (Rorher, 1961), the winter-over syndrome (Strange & Youngman, 1971), the subsyndromal seasonal affective disorder (Rosenthal et al., 1984), the polar T3 syndrome (Palinkas, Glogower, Dember, Hansen, and Smullen, 2001), and the third quarter phenomenon (Bechtel & Berning, 1991). Each of these models of time effects examines the potential effects of time on depressive symptoms over the course of a polar expedition. These models have been applied in various other contexts to predict whether such time effects exist in other settings. It is possible that temporal effects on depressive symptoms may also occur over the course of LDSE.

**Interpersonal**

A range of interpersonal factors are expected to affect the psychological health and performance of astronauts in LDSE. As noted by Kanas and Manzey (2008), interpersonal issues can include gender issues, cultural differences, personality conflicts, crew size and composition, and leadership issues. As Kanas (1998) noted, on a long-duration space mission, these factors can lead to miscommunication among crews, role confusion, competition, and ultimately the splintering of the group. Research has examined these factors in depth among space crews (e.g., Kanas et al., 2000; 2001).

Evidence regarding each of these various factors has been found in the literature. For example, in Antarctic settings research has shown that leadership perceptions interact with gender such that perceptions of social support are significantly impacted (Schmidt, Wood, & Lugg, 2005). Evidence also suggests that while small group climate may be enhanced through the inclusion of women in small group settings, the presence of small numbers of women in a larger group of men may introduce a number of dynamics detrimental to small group performance (Rosnet, Jurion, Cazes, & Bachelard, 2004).

LDSE is likely to consist of an international crew. Notably, recent research has demonstrated that success on high risk missions can be significantly impacted by crew nationality (Anicich, Swaab, & Galinsky, 2014). Research on small groups shows that cultural identity may become stronger over an extended period of isolation and confinement (Kraft et al., 2002), a finding that has direct implications for an extended exploration class mission that may contain a crew composed of a majority nationality, with a one or two crewmembers comprising a non-majority portion of the crew.

A fairly large body of literature has examined the relationship between leadership and a range of outcomes applicable to health and performance in occupational settings. In general, effective leadership is positively associated with a range of desirable occupational outcomes among followers, though the relationship is commonly mediated by followers’ trust in the leader (e.g., Podsakoff, MacKenzie, Moorman, & Fetter, 1990). Recent research has also demonstrated that leaders in high ranking positions exhibited lower levels of stress as measured through both physiological and psychological measures (Sherman et al., 2012). In LDSE, where leadership
responsibilities may be shared, these research findings have important implications for both leaders and followers in a small group setting.

In sum, interpersonal issues can impact a number of outcomes on LDSE, including the neurobehavioral functioning of individual members. For example, in small group settings where in-group/out-group dynamics may form, symptoms of depression and anxiety may develop. Furthermore, symptoms may develop among multiple crewmembers. Together, such symptoms may impair the cognitive functioning of individual crewmembers, and ultimately affect the overall health and performance of the team.

**Phases of a Long-duration Space Mission**

A long-duration trip to Mars will involve a series of discrete phases and transition points that are important to recognize if NASA and the broader research community are to fully prepare for the mission. Figure 1 provides a simplified graphical representation of the different transitions and phases that a Mars mission will involve. As Figure 1 illustrates, there are four major transition points, and three primary phases to a Mars mission. The multiphasic nature of a long-duration mission to Mars forces us to consider the possibility that neurobehavioral signs and symptoms may be more or less prevalent at various points throughout the mission.

The first transition point of the mission will occur as the crew shifts from Earth-based environmental and social conditions to experiencing the initial stages of LDSE. Initially these conditions will be similar to those faced by crewmembers upon the International Space Station (ISS). Currently, these conditions are fairly well-understood, particularly among crewmembers that stay on the ISS for the standard six month mission. However, as the spacecraft moves beyond low Earth orbit, the crew will begin to experience the defining features of exploration-class space travel. These features will include prolonged social and physical isolation and confinement, limited communication with ground crew and social networks on Earth, lack of sensory stimulation, prolonged exposure to environmental factors (e.g., radiation, microgravity, and lack of light/dark cycles), and prolonged exposure to habitability factors (e.g., noise, vibration, elevated CO₂ levels).
In many cases, these will be experiences that humans have never before had. Thus, there is currently much uncertainty regarding the ways in which humans will cope with stressors associated with a long-duration flight. To predict how humans might react to such factors on this initial phase of the mission we are left to rely on the extant research from spaceflight and analog settings. Such research suggests, for example, that some crewmembers will experience sleep and psychosocial disturbances (Basner et al., 2014), that the prolonged microgravity may lead to alterations in visual-spatial processing of crewmembers (Clement, Skinner, & Lathan, 2013), and that prolonged exposure to radiation may lead to cognitive impairment (Parihar et al., 2015). The current year-long ISS mission (Lewin, 2015), as well as future planned year-long missions, will likely provide very valuable information regarding astronauts’ ability to adapt and function during this extended trip to Mars (NASA, 2014).

Research also suggests that individual-level adaptation to the space environment and capsule habitat may be moderated by individual-difference factors such as gender (Goel et al., 2014). Further, crew functioning and team success may be impacted by cultural issues (Anicich, Swaab, & Galinsky, 2015). These factors will also be crucial to understand given that LDSE crews will likely be mixed-gender and mixed nationality.

Upon arrival to Mars, crewmembers will again experience a transition. Here, the crew will transition from microgravity in space travel to the gravitational forces present on Mars, which is .375 that of Earth (NASA, 2015). Research has shown that gravitational transitions have the potential to impact neurobehavioral symptoms such as motion sickness (e.g., Paule et al., 2004), postural stability (Black et al., 1999), and neurovestibular function (Wood et al., 2007). Further, crewmembers will have to adjust to a slightly different circadian rhythm on Mars, as the Mars day is 24 hours and 37 minutes, as opposed to the 23 hours and 56 minutes on Earth. Crew management will have to decide whether to attempt to transition crewmembers’ circadian
rhythms to the Mars sol during transit or after landing on Mars. Together, these factors may impact crew mental health and neurobehavioral outcomes during the initial days and weeks of the Mars planetary mission. Perhaps the most dramatic changes will involve the physical dangers imposed by the Mars environment: the average temperature on Mars is much colder than Earth, the atmospheric pressure is much lower than on Earth, and the atmosphere is largely devoid of oxygen.

As the crew begins its exploration of the Mars surface, many of the same stressors will exist as during the transit phase of the mission. Specifically, the crew will have limited communications with the ground crew on Earth. As a result, the crew will be highly autonomous in its exploration of the planet, and will demand that the crew is able to effectively function on its own accord. Interpersonal and team-related issues have the potential to impact individual-level well-being (Bliese & Halverson, 2006), and consequently, the success of the surface mission. It is unclear whether environmental factors on the Mars surface—and subsequent physiological reactions to environmental conditions—will affect interpersonal relationships. However, research has shown that harsh climates may impact affective and cognitive outcomes among crewmembers (e.g., Gunderson, 1974), which may compound any interpersonal problems that exist between crewmembers.

Upon completion of the Mars surface mission, the crew will again enter transit phase which will return the crew to Earth. This will involve a gravitational transition as the crew leaves the gravity of Mars and returns to a microgravity environment. This transition has the potential to impair cognitive functioning (Paule et al., 2004), which has the potential to exacerbate any potential lingering mental health or neurobehavioral decrements that might result from time on the surface of Mars. The return trip will include many of the same threats/stressors as the initial transit phase including confinement, sensory deprivation, and the ever-present interpersonal issues. One important potential feature of the return journey to Earth is the possibility of the loss of life or serious injury to crewmembers during the Mars surface exploration. In the case that injury or death occurs to one or more crewmembers, the psychological health of individuals and the group morale may greatly impacted, thus putting the success of the return journey to Earth at risk.

As the crew nears Earth, communication lags with Earth will decrease, which may have the effect of boosting the morale of the crew as it begins to anticipate the return to the Earth surface. The end of the mission has the potential to affect individual attitudes in a number of ways. First, crewmembers may begin to experience an increase in well-being as a result of the salutogenic effects of the mission (Antonovsky, 1987; Steel, 2005). Alternatively, it is also possible that the crew may begin to experience symptoms of depression as the mission nears its end, and transition to civilian life becomes reality; research from the military context suggests this possibility (Adler, Huffman, Bliese, & Castro, 2005). Finally, as the crew returns to Earth they will again need to readapt to the Earth’s gravity and light/dark cycle.
Upon completion of the mission, NASA and other space agencies will likely need to monitor the psychological and neurobehavioral health of crewmembers. Again, crewmembers may experience depressive symptoms as a highly adventurous and extremely meaningful mission comes to a close. Similarly, the adaptation to stressors during LDSE may be difficult to “switch off” upon return home. Indeed, research in the military context has shown this to be the case among service members who return home from overseas deployments (Hotopf & Wesseley, 2006).

In general, this understanding of how different phases of the mission might differentially affect neurobehavioral outcomes suggests the need to assess and monitor different neurobehavioral symptoms depending on the particular phase of the mission. For example, while fatigue as a result of exposure to CO₂ is a major concern for astronauts who will travel in the space capsule to reach Mars, the need to monitor fatigue and related symptoms while on the Mars surface may be especially great given the potential for the CO₂ in the Mars atmosphere to build up in the astronaut habitat, vehicle, and EVA suits. Likewise, during the transit periods of the mission when sensory stimulation is expected to be quite low, the assessment of depressive symptoms may be relatively important in relation to the time spent on the mission of Mars where there is likely to be greater sensory stimulation (Vessel & Russo, 2015). Alternatively, the need to assess anxiety symptoms may be greater during the surface stay on Mars given that crewmembers may experience and/or perceive greater threats during their time on the surface than on during the transit phase inside the capsule.

The multiphasic nature of LDSE to Mars introduces additional considerations that have yet to be explored in spaceflight contexts. Specifically, it may be possible to view each phase of the LDSE as a unique mission that involves a unique environment and exposures to stress. To date, however, little research has explored the impact of multiple missions upon astronauts’ psychological or behavioral health. For example, do stressful experiences on one mission sensitize astronauts to stress in subsequent missions? Alternatively, does the stress of an initial mission inoculate astronauts to stress in subsequent missions? As of now, no systematic attempt has been made to answer such questions. Consequently, it is not known whether multiple spaceflights—particularly those that expose crews to novel stressors—will result in adverse neurobehavioral outcomes. Research from the military psychology literature (e.g., Polusny et al., 2009) certainly suggests that multiple missions will put crewmembers at risk. When we view LSDE as comprised of three discrete phases/missions we can begin to see how stressors experienced during each of the three phases of the mission might lead to downstream mental health or behavioral problems. At the same time, stressors may begin to accumulate across the phases of the mission and begin to detrimentally affect astronauts as they move through and complete each phase of the mission.
Objective 1. Create a taxonomy of neurobehavioral signs and symptoms in ICE settings.

To begin to develop a taxonomy of neurobehavioral signs and symptoms, we worked from the Behavioral Health and Performance (BHP) perspective as described in the Human Research Roadmap. As described in the roadmap, given the extended nature of current and future space missions, BHP is interested in: 1) adverse cognitive or behavioral conditions that may negatively affect crew performance, and 2) mental disorders that could develop should adverse behavioral conditions be undetected and unmitigated (NASA, 2015b). Second, given the wide range of cognitive and behavioral conditions that might fall under the conceptual umbrella of “neurobehavioral,” we sought an existing inventory of neurobehavioral disorders or an existing assessment tool that could be used as a basis for a systematic review of the academic literature.

The Neurobehavioral Symptoms Inventory (NSI)

While a number of such tools exist, we chose to utilize the Neurobehavioral Symptoms Inventory (NSI) commonly used by the U.S. Department of Defense to assess neurobehavioral symptoms among military personnel. As described above, the NSI is a self-report instrument that was originally developed to assess neurobehavioral functioning among military personnel suspected of sustaining TBI or other types of head injuries. The tool provides adequate coverage of the neurobehavioral signs and symptoms of interest to BHP and the broader NASA community. For example, the tool assesses possible sleep disorders, symptoms of depression and anxiety, and a wide range of cognitive issues. Also included are items assessing symptoms that would likely fall under the interests of the Human Health Countermeasures element and the Space Human Factors and Habitability element. Such symptoms include balance problems, headaches, hearing loss, vision, etc. Table 1 presents the neurobehavioral signs and symptoms included on the NSI.

Because of the wide-ranging nature of the symptoms included on the NSI (and the somewhat nebulous nature of the symptoms of TBI and other head-related injuries), researchers have sought to identify an underlying factor structure to the NSI. The factor structures from three separate studies of the NSI are presented in Table 3. Meterko et al. (2012) identified four factors of symptoms that can be grouped into: cognitive, affective, somatosensory, and vestibular. Caplan et al. (2010) identified a three factor solution: cognitive, affective, and somatic/sensory. More recently, Vanderploeg et al. (2015) identified a four factor solution: cognitive, emotional, somatic/sensory, and vestibular. Because Vanderploeg et al. model builds on previous validation work related to the NSI, and because of the varied nature of the samples used to conduct the analyses, we choose to use the Vanderploeg et al. factor structure as a foundation from which to taxonomize neurobehavioral symptoms and to guide the present effort.

The four factors identified by Vanderploeg et al. group neurobehavioral symptoms into an easily understood classification scheme. The cognitive factor refers to symptoms that are commonly
associated with performance in both high stress and low stress scenarios. The emotional factor includes symptoms commonly associated with psychosocial decrements among individuals and workers. Together, these two factors fall within the interests of BHP as stated in the research roadmap. The remaining two factors—somatic/sensory and vestibular—include symptoms that are less relevant to the BHP element; consequently, reduced emphasis will be placed on the symptoms that fall within these two factors. However, we will consider these factors to the extent that cognitive and emotional symptoms are implicated in the study of somatic/sensory or vestibular symptoms.

Table 3. Neurobehavioral Symptom Inventory: Symptoms and Factor Structure

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<tr>
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<tr>
<td>Cannot get organized/finish things</td>
<td>Cognitive</td>
<td>Cognitive</td>
<td>Cognitive</td>
</tr>
<tr>
<td>Forgetfulness (memory)</td>
<td>Cognitive</td>
<td>Cognitive</td>
<td>Cognitive</td>
</tr>
<tr>
<td>Making decisions</td>
<td>Cognitive</td>
<td>Cognitive</td>
<td>Cognitive</td>
</tr>
<tr>
<td>Poor concentration</td>
<td>Cognitive</td>
<td>Cognitive</td>
<td>Cognitive</td>
</tr>
<tr>
<td>Anxiety/tension</td>
<td>Affective</td>
<td>Affective</td>
<td>Emotional</td>
</tr>
<tr>
<td>Depressed/sad</td>
<td>Affective</td>
<td>Affective</td>
<td>Emotional</td>
</tr>
<tr>
<td>Fall/stay asleep</td>
<td>Affective</td>
<td>Affective</td>
<td>Emotional</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Affective</td>
<td>Affective</td>
<td>Emotional</td>
</tr>
<tr>
<td>Irritable</td>
<td>Affective</td>
<td>Affective</td>
<td>Emotional</td>
</tr>
<tr>
<td>Low frustration tolerance</td>
<td>Affective</td>
<td>Affective</td>
<td>Emotional</td>
</tr>
<tr>
<td>Appetite change</td>
<td>†</td>
<td>Somatic/sensory</td>
<td>Somatic/Sensory‡</td>
</tr>
<tr>
<td>Headache</td>
<td>Somatosensory</td>
<td>Affective</td>
<td>Somatic/Sensory</td>
</tr>
<tr>
<td>Hearing difficulties</td>
<td>†</td>
<td>Somatic/sensory</td>
<td>Somatic/Sensory‡</td>
</tr>
<tr>
<td>Light sensitivity</td>
<td>Somatosensory</td>
<td>Somatic/sensory</td>
<td>Somatic/Sensory</td>
</tr>
<tr>
<td>Nausea</td>
<td>Somatosensory</td>
<td>Somatic/sensory</td>
<td>Somatic/Sensory</td>
</tr>
<tr>
<td>Noise sensitivity</td>
<td>Somatosensory</td>
<td>Somatic/sensory</td>
<td>Somatic/Sensory</td>
</tr>
<tr>
<td>Numbness/tingling</td>
<td>Somatosensory</td>
<td>Somatic/sensory</td>
<td>Somatic/Sensory</td>
</tr>
<tr>
<td>Taste/smell</td>
<td>Somatosensory</td>
<td>Somatic/sensory</td>
<td>Somatic/Sensory</td>
</tr>
<tr>
<td>Vision problems</td>
<td>Somatosensory</td>
<td>Somatic/sensory</td>
<td>Somatic/Sensory</td>
</tr>
<tr>
<td>Balance</td>
<td>Vestibular</td>
<td>Somatic/sensory</td>
<td>Vestibular</td>
</tr>
<tr>
<td>Clumsy/poor coordination</td>
<td>Vestibular</td>
<td>Somatic/sensory</td>
<td>Vestibular</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Vestibular</td>
<td>Somatic/sensory</td>
<td>Vestibular</td>
</tr>
</tbody>
</table>

† Meterko et al (2012) did not include appetite and hearing in their final four factor solution.
‡While Vanderploeg et al. (2015) recommend a four-factor solution after dropping appetite and hearing difficulties, these two symptoms were considered symptoms of interest in the present study, and were therefore included in the literature search and related analyses.
The NSI and the Exploration Medical Condition List

To better understand how the NSI maps on to current efforts to categorize and classify neurobehavioral and other health decrements, it is useful to compare the NSI to the Exploration Medical Condition List (EMCL). The EMCL “was created to define the set of medical conditions that are most likely to occur during any one of several mission profiles, as the first step in addressing the aforementioned risk” (NASA, 2013). The document contains a list of conditions that could potentially occur on missions with an exploration profile. The conditions “could occur as a consequence of human space flight and human habitation in space, in addition to injuries that result from hardware or vehicle failure” (NASA, 2013; p. 6).

While the vast majority of conditions on the EMCL represent physical ailments, there are three conditions on the EMCL that can be classified as neurobehavioral symptoms and that are also present on the NSI. These three conditions are anxiety, depression, and insomnia. Each of these three conditions falls under the “emotional” factor of the NSI, at least according to factor analytic work on the instrument. The EMCL has not included any symptoms such as memory, decision making, or concentration that could be classified as cognitive. Thus, to the extent that current NASA efforts have tracked neurobehavioral decrements, it appears that the focus has been placed on affective or emotional neurobehavioral symptoms. The EMCL does include a condition labeled “Behavioral Emergency”, but it is not entirely clear what specific types of symptoms to which the condition refers.

The incongruence between the EMCL and the tools such as the MiniCOG and the WinSCAT suggests that neurobehavioral decrements that have the potential to put crewmember health and mission success at risk have not yet been fully considered explicit threats to crew performance. However, the lack of a presence of cognitive and emotional factors on the EMCL may simply represent a lack of research on these topics, and/or an underestimation of their potential effects in a long-duration mission.
Objective 2. A systematic review of neurobehavioral signs, symptoms, and diagnoses commonly found in ICE settings.

To review the neurobehavioral signs, symptoms, and diagnoses in ICE settings, we undertook a systematic review of the research literature using the NSI symptoms as a basis for identifying primary search terms. Terms indicative of various ICE settings were used as secondary search terms. To ensure inclusion of studies applicable to military settings/populations, a list of relevant terms were included: Afghanistan, Balkans, Bosnia, Iraq, Military, Operation Enduring Freedom, Operation Iraqi Freedom, and Vietnam. Pairing each primary search term and secondary search term, we searched PsycINFO, PubMed, the Defense Technical Information Center, the NASA Technical Reports Server, and the Johnson Technical Reports Server. Table 4 lists the search terms used.

<table>
<thead>
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<th>Table 4. Symptoms and settings used as search terms.</th>
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<tr>
<td><strong>Symptom Terms</strong></td>
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<td>Appetite</td>
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<td>Anxiety</td>
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<td>Attention</td>
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<td>Balance</td>
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<td>Boredom</td>
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<td>Clumsy</td>
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<td>Concentration</td>
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<td>Coordination</td>
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<td>Depressed</td>
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<td>Dizzy</td>
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<td>Fatigue</td>
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<td>Forgetful</td>
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<td>Frustration</td>
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<td>Headache</td>
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<td>Hearing</td>
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<td>Irritable</td>
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<td>Memory</td>
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The searches yielded over 15,000 documents, a large number that is not surprising given the wide range of search terms used. A follow up title search of documents resulted in just under 700 articles/reports being kept for inclusion in the study. Following discussion with the program officer at BHP, the scope of the review was limited to only those neurobehavioral symptoms classified as cognitive or emotional in nature. Thus, articles involving somatic/sensory and vestibular were excluded from further consideration, unless those articles implicated cognitive or emotional symptoms in some way. A subsequent abstract search of articles and reports related to cognition and emotion reduced that number further to just over 300 documents. As indicated by the bold-faced type in Table 2 above, focus was placed on those symptoms for which there was a
substantial amount of evidence in the literature. This report does not dive deep into the literature on sleep given its currently-prominent place in the research conducted by BHP, and given that extensive reviews of the topic have been provided elsewhere (a title search for the term “sleep” in the NASA technical reports server turns up 208 results). Only a small number of articles on the topic of irritability were identified, and these focused on irritability in response to sleep loss and fatigue. Due to the small number of articles on this topic, we do not provide a review. Similarly, while anger was identified by SMEs as an important neurobehavioral symptom, a follow up search yielded very little research on this topic in spaceflight and analog settings. Again, we do not provide a review of this construct due to the small number of articles on the topic. While a considerable body of military-specific literature exists on many of these subjects, studies were not included in the review of they dealt with neurobehavioral symptoms that are the direct result of combat-related injuries or illness. Given the nature of much of the military literature, this severely limited the extent to which we were able to draw on military studies in our review.

The operational assessment conducted with SMEs yielded information that led to the consideration of additional neurobehavioral symptoms: attention/threat bias and boredom. Thus, beyond the set of symptoms presented in Table 4, brief reviews of literature on these topics are provided. Where possible, the reviews of each symptom are broken out by whether the symptom is the result of environmental, habitability, psychological, or interpersonal factors.

**Cognitive Signs and Symptoms**

The NSI cognitive factor includes concentration, decision making, forgetfulness/memory, and organization. The sub-constructs attention, concentration, and memory will be considered separately before being treated with an integrated discussion below. Before discussing each of these constructs, however, it may be useful to provide a brief overview of the ways in which stressors found in LDSE settings might impact cognitive functioning.

A number of models explain how cognitive performance may be impacted under stressful conditions. First, general models of stress provide a clue of how cognitive function may be impacted by the presence of stressors. For example, the conservation of resources (COR) theory of stress states that individuals seek to gain and maintain resources in their lives (Hobfoll, 1989). Consistent with prominent theories of stress (Lazarus & Folkman, 1984), the COR perspective holds that stress occurs when a threat to resources is perceived. When a stressor is perceived and cognitive resources are dedicated to cope with the stressor, performance on tasks may suffer.

More specific models of stress and performance provide a more granular examination of the mechanisms related to cognition. Hockey (1997), for instance, outlined a cognitive-energetical framework which claims that under stressful circumstances, individuals rely upon a compensatory control model that can allocate resources according to need. Specifically, in a task
performance setting, stress represents an outside disturbance. Individuals can seek to maintain optimal cognitive performance under conditions of high stress, but at the cost of behavioral and physiological functions. Alternatively, individuals can reduce performance goals in order to maintain optimal behavioral and physiological functions. The framework provides a useful perspective for understanding the ways in which spaceflight stressors might affect neurobehavioral and cognitive performance.

In LDSE settings, sources of stress—and therefore, neurobehavioral symptoms—are many. Again, according to Manzey and Lorenz (1998), stressors in space arise from four distinct sources: the space environment (e.g., microgravity and the light-dark cycle); the space habitat (e.g., limited space and ambient noise); psychological factors (e.g., mission-specific workload and isolation); and psychosocial factors (e.g., social isolation and monotony). Each of these stressors has the potential to affect cognitive functioning of spaceflight crews, and variable amounts of research have examined the links between these sources and cognitive outcomes. Comprehensive efforts are currently underway to better understand the differential effects of these various factors upon cognitive functioning. In one notable study researchers are comparing the cognitive performance of astronauts in a microgravity environment to participants in a 70-day bed reset experiment and a group of ground-based controls (Koppelmans et al., 2013). This study follows the recently-completed Mars500 study which exposed participants to many of the habitability, psychological, and psychosocial factors that crewmembers will face on a long-duration trip to Mars (Basner et al., 2014).

**Attention**

In general, attention can be thought of as the ability to “selectively process information in the environment” (Fougnie, 2008; p. 1). According to Ballard (2001), researchers have taken a multifaceted view of attention, and have identified different neuroanatomical substrates for each. For example, Mesulum (1981) discussed spatial attention; planning and control; and arousal and vigilance. Posner and Peterson (1990) discussed an orienting circuit for selective attention; an executive control circuit to detect stimuli, coordinate subsystems of attention, and start and stop mental operations; and an alerting circuit for sustained attention and vigilance. Mirsky, Anthony, Duncan, Ahearn, and Kellam (1991) identified four elements of attention: a focus-execute element that includes the selection of stimuli for processing; a sustain element that helps maintain attentional focus; a shift element that promotes adaptive changes in focus; and an encode element that allows individuals to hold information essential to processing.

A limited amount of research has sought to specifically examine attention within environments analogous to spaceflight contexts. And that which has sought to examine the role of attention in high stress contexts have generally not taken a multifaceted view of attention. For example, (Carretta, Perry, & Ree, 1996) conceptualized a divided attention task as a subset of cognitive ability. The authors found that general cognitive ability—which included the divided attention task—was predictive of situational awareness of F-15 pilots as rated by pilot supervisors and
peers. While cognitive ability was shown to be predictive of situational awareness, the analytic approach did not allow one to see the amount of unique variance explained by the divided attention task.

The impact of sleep restriction upon attention has typically been examined in lab studies. Doran, Van Dongen, and Dinges (2001), for example, used the Psychomotor Vigilance Test (PVT) as an indicator of sustained attention. The PVT assesses sustained attention by requiring participants to press a button in response to a visual stimulus on a computer screen. The PVT measures the amount of time needed for the respondent to press the correct button in response to the visual stimulus; the PVT also measures whether the respondent errs by either pressing the button prematurely, pressing the incorrect key, or by keeping the button pressed. The results of the experiment showed that study participants in the sleep restricted condition demonstrated greater reaction times on the PVT and also exhibited a greater number of errors on the PVT than the control condition which was allowed to experience more sleep over the duration of the study. The authors conclude that sleep deprivation produces a “state instability,” where the combination of the homeostatic drive for sleep, altered circadian rhythms, and additional effort exerted by participants to perform, led to greater variability in attentional performance among participants in the sleep restricted condition.

Using a similar procedure, Jennings, Monk, and van der Molen (2003) sought to understand the effects of one night of sleep restriction upon supervisory attention. The results of that analysis showed that even a single night of sleep deprivation increased reaction times among study participants tasked with completing a choice reaction test that involved pre-task priming. The results suggest that sleep restriction may have quite nuanced impacts upon attention and related cognitive processes, and that performance decrements due to sleep restriction are mediated by a number of factors.

Research on Arctic populations has sought to uncover the potential impacts of seasonal change on attention and other cognitive indicators. Brennan et al. (1999), for example, examined attention among residents in a Norwegian community at high latitude, seeking to determine whether cognitive performance was impacted by seasonal fluctuations to the same extent that indicators of affect are impacted. Using the Stroop test, a mapping task, and a time estimation task, the authors found little evidence that circannual rhythms affect cognitive performance in the same way that affect is impacted by seasonal variations. A follow up study by Brennen (2001) demonstrated that individual difference factors such as age, gender, and nationality only slightly moderated the relationship between seasonal variation and cognition. In both studies, investigators actually found that cognitive performance on certain tasks increased during the winter, running counter to expectations that the dark and cold winter conditions would hinder cognitive performance. In a similar study, Palinkas et al. (2005) also found that attention and other indices of cognitive performance were not degraded during a polar winter. Using a matching-to-sample task and a serial addition/subtraction test to assess attention, the authors found that reaction times on tests of attention were actually reduced among participants in colder
conditions. However, accuracy on sustained attention was reduced in the colder conditions. Together this set of studies leaves open the question of whether seasonal fluctuations and temperature impact cognitive performance.

The research reviewed above provides support that sleep decrements can impact specific aspects of attention, but that environmental factors such as light/dark cycles and temperature have a negligible or mixed impact on indicators of attention. While these findings are important, it may be useful to examine attention from the perspective of stress and appraisal. Staal (2004) conducted a systematic review of the literature on stress, cognition, and performance. In that review, he provides a summary of many of the relationships relevant to the present report. With regard to stress and attention, Staal focuses on the literature related to anxiety and attention, which provides evidence that anxious individuals tend to be biased toward threatening stimuli. In sum, the research shows that individuals high in state and trait anxiety are more likely to perceive threat, and tend to spend more time processing threatening stimuli. From an operational perspective, this suggests that performance decrements may be observed among anxious individuals given their propensity to spend time processing real or perceived threats in their environments.

As noted in a recent meta-analysis that examined relationships between anxiety and attention bias (Bar-Haim et al., 2007), the relationship between trait anxiety and attentional bias has been explored more fully than has the relationship between trait anxiety and attentional bias. The small number of studies that have examined state anxiety have either attempted to experimentally manipulate state anxiety (Richards, French, Johnson, Naparstek, & Williams, 1992) or have leveraged events expected to produce stress among individuals (MacLeod & Rutherford, 1992).

**Concentration**

One of the key variables for the performance of fine-grained or high risk tasks is the mental concentration of the individual. As in any stressful occupation, mental concentration can be threatened by the stress and fatigue faced by crewmembers. According to the model proposed by Hockey (1997), concentration on complex tasks will be threatened by external stressors. In response to such stressors, individuals may increase cognitive resources to maintain concentration on a task, or will reduce concentration levels to effectively cope with the external stress. Because the term “concentration” is somewhat broad, a range of tasks have been designed to assess concentration across the studies reviewed below.

**Environmental**. Concentration has been examined in a number of analog settings that are designed to mimic the physical conditions encountered by astronauts. For example, a study of the effects of polar environments on general cognitive performance showed an increase in mental performance over the course of a 14-month Antarctic mission (Paul, Mandal, Ramachandran, & Panwar, 2010). Antarctic missions expose individuals to harsh physical conditions, such as
altered light/dark cycles, that are similar to those faced by astronauts. Paul et al. utilized the PGI Memory Scale (Pershad & Wig, 1994) to assess attention and concentration of volunteers exposed to the harsh climates of Antarctica. While no significant increases on concentration were detected, participants demonstrated stable performance over the duration of the mission suggesting that different light/cycles over the course of the mission did not adversely affect performance.

Bed rest studies are commonly used to mimic the effects of microgravity on human physiology, psychology, and performance. In one such study, investigators (Dolenc, Tusak, Dimec, & Pisot, 2008) used the Test of Concentration and Achievement (Duker & Linert, 1965) to examine whether performance on that task was negatively impacted by a 35-day bed rest. The results showed that participants’ performance improved from before to after the mission. While seemingly counterintuitive, this finding is consistent with more general tests of the effects of bed rest upon cognitive performance (e.g., DeRoshia & Greenleaf, 1993). In another study, Duker and Linert (1965) concluded that the social nature of the bed rest activity—participants in this case were able to socialize at various points of the bed rest experiment—may have increased perceptions of social support, and may have helped stave off performance decrements. It is also possible, however, that bed rest experiments simply do not yield the same level of physical adversity as would be expected from the physical environment in space.

**Habitability.** The design features in spacecraft have the potential to impact the concentration and cognitive performance of astronauts. Research from a variety of settings provides clues regarding the ways in which design and habitability factors might affect astronaut concentration. Of specific concern to NASA and the broader spaceflight community is the presence of toxins aboard the spacecraft. One such toxin is carbon dioxide (CO\textsubscript{2}), a metabolite that is formed by the breathing of the crew (see Law, Watkins, & Alexander, 2010). While life support systems (LSS) are designed to reduce the presence of CO\textsubscript{2} it is currently not possible to completely eliminate the presence of the gas; consequently, current levels of CO\textsubscript{2} are generally above those found on Earth. Recent examinations of CO\textsubscript{2} levels on astronauts upon the ISS have been based largely on anecdotal evidence and limited correlational data (Law et al., 2010). Nonetheless, there is some evidence that elevated CO\textsubscript{2} can impair cognitive functioning and other neurobehavioral outcomes.

Manzey and Lorenz (1998), for example, conducted a set of experiments to assess the impact of CO\textsubscript{2} on cognitive performance in isolated settings. In two separate studies, the investigators elevated CO\textsubscript{2} levels to 0.7% and 1.2%, respectively, well above the .03% found in the ambient atmosphere on Earth. Participants were asked to complete a series of tasks to assess performance under elevated CO\textsubscript{2} levels. The results of the study showed that cognitive performance did not suffer under 0.7% CO\textsubscript{2} levels, but that cognitive performance did suffer when participants were exposed to CO\textsubscript{2} of 1.2% for an extended period of time. In another study, Diaper et al. (2012) exposed participants to 7.5% levels of CO\textsubscript{2} finding that participants actually demonstrated an improvement on a number of psychomotor tasks, suggesting increased attention under high
levels of CO$_2$. The inconsistent results of these studies is indicative of the overall state of the literature, where the effects of elevated CO$_2$ appear to be variable across studies.

A variety of other habitability and design factors have been examined in relation to mental concentration. For example, in an experiment with naval personnel, the seating on a naval vessel was examined in relation to cognitive performance (McMorris, Myers, Dobbins, Hall, & Dyson, 2009). Participants using suspended seats demonstrated greater cognitive performance following transit in a high-speed boat in comparison to a sample using fixed seats. The authors hypothesize that the reduced vibrations of the suspended seats likely reduced the stress placed on naval personnel, which allowed them to exhibit better cognitive performance. Though seating per se may not be a critical issue for LDSE crews given in-transit microgravity, the impact of vibration on cognitive performance is an issue that may need to be studied more fully, particularly during key transition points where the spacecraft is accelerating due to launch or descent.

**Psychological.** The most general psychological factor introduced by long-duration space travel may be the sense of isolation due to the relatively small volume of the spacecraft. A LDSE will allow for a limited capsule volume, which may impact a variety of cognitive and emotional outcomes. Research by Zuckerman (1962) showed that participants who were in a confined area with perceptual isolation (i.e., lack of sensory stimulus) exhibited concentration difficulties on tasks following isolation. Zuckerman described two phases of isolation with perceptual isolation: phase one includes a stage of hyperalertness while phase two includes a loss of interest in the environment and an increased focus on internal processes. It is important to point out that Zuckerman’s research participants were in solitary isolation while LDSE will include a multi-person crew; thus, it is possible that interpersonal interactions may offset the detrimental impacts of isolation and sensory deprivation. Nevertheless, it is critical to recognize the potentially detrimental effects that isolation may have on mental concentration and other aspects of cognitive performance.

**Memory**

Closely related to the concept of mental concentration is memory. Memory is important in LDSE for a number of reasons. First and foremost, memory accuracy will ensure the correct application of training procedures during a mission. Without accurate application of training, crewmember health and wellbeing may be at risk, and the entire mission may be jeopardized. Second, in-flight memorization of mundane or emergency procedures may be needed on a long-duration mission. Notably, research has suggested that memory accuracy may be compromised in emergency situations that include traumatic or peritraumatic events (Morgan et al., 2004). Furthermore, laboratory experiments simulating a variety of stressful experiences have demonstrated that short-term memory decrements can occur as a result of stress exposure (H. R. Lieberman et al., 2006). Thus, it is critical to seek a further understanding of the factors that have the potential to affect memory accuracy in such situations.
**Environmental.** It is generally expected that the environmental stressors present during long-duration spaceflight will impact the cognition of astronauts, at least temporarily. In a review of bed rest studies that utilized cognitive experimental tasks, Lipnicki and Gunga (2009) found wide variation in the extent to which bed rest affected short term memory. Across eight studies, the authors found wide variability such that memory stabilized or improved during bed rest, or was unaffected by bed rest. The results of these controlled studies suggest that microgravity settings may not impact memory, or that there may be between-person differences in the extent to which microgravity may affect memory tasks.

Other aspects of the space physical environment have also been examined. Brennan, et al. (1999) examined verbal memory and other cognitive tasks in a polar environment. In a test of 100 individuals, the researchers drew upon the literature related to Seasonal Affective Disorder (SAD) to determine whether the lack of a dark/light cycles in extreme northern latitudes might impair cognitive performance. The research demonstrated that while the lack of sunlight during winters did impact a number of affective variables, there was little-to-no impact on the verbal memory of study participants. The research has the potential to inform expectations regarding memory processes in a spaceflight environment that lacks a natural dark/light cycle.

**Habitability.** Habitability factors have the potential to impact the cognitive performance of crewmembers. The most general habitability factors that might affect memory are the isolation and confinement associated with residing in an enclosed habitat for an extended period of time. Hockey and Sauer (1996) attempted to assess the effects of isolation and confinement on cognition by confining four individuals to a hyperbaric chamber for 60 days. While confined, subjects completed a working memory task designed to simulate the use of a contaminant management system on a spacecraft. The researchers found slight memory decrements (decision time and check time) during the second half of the mission, as well as increases in fatigue during the second half of the mission. However, some between-person differences were observed.

In a simulated experiment with Canadian astronauts, Sauer, Wastell, & Hockey (1999) used an experimental simulation known as the Cabin Air Management System (CAMS). The simulation required astronauts to take part in a seven-day mission in an isolated and confined environment, with the CAMS task comprising 30 minutes of each day. The researchers examined a number of cognitive and performance outcomes, including prospective memory. The results demonstrated slight decrements in prospective memory under high workload conditions. Sauer (2003) reviewed the extant literature in which other studies employed the CAMS experiment. The summary results were consistent with the Sauer et al. (1999) study; specifically, prospective memory appeared to be hampered under conditions of high workload.

The effects of noise and vibration on memory have also been examined in simulated environments. Smith, Baranski, Thompson, & Able (2003) for example, sought to examine the effects of noise on cognition by simulating ISS decibel levels. Study participants were randomly exposed to 70 hours of continuous ISS-level noise, 70 hours of ISS-level noise only during the
day, or 70 hours of quiet. The experiments revealed that exposure to ISS-like decibel levels did not result in memory deficits. Abel et al. (2004) reported similar effects. While the experiments do not support the link between noise and cognitive impairment, it is important to note that these time-limited studies cannot be used to understand the long-term links between noise and cognition, or the long-term links between noise, hearing impairment, and overall health. As noted above, McMorris et al. (2002) conducted an experiment to examine the effect of seating type and vibration in a high-speed boat at sea to determine whether different seating types might impact cognition differentially. The results showed that suspended seats which reduce the vibration to the rider are associated with greater success on forward number recall.

A considerable body of literature has examined the effects of temperature on memory and recall. This research has implications for habitability and design factors for any Mars spacecraft. Chia and Teo (2001) studied the effects of heat exhaustion on neurological complications among soldiers in the Singapore army forces. The results showed that soldiers with a heat exhaustion exhibited poorer performance on a short-term memory task in relation to controls. A follow up study (Chia & Teo, 2003) showed, however, that in the months following the episode, soldiers with heat exhaustion did not demonstrate lower scores, suggesting that recovery is possible. Additional research (Hocking, Silberstein, Lau, Stough, & Roberts, 2001) has also sought to examine the link between heat exposure and memory function. This research demonstrated that Australian Defense Forces exposed to tropical conditions performed slightly worse on a number of cognitive tests, including working memory. Additionally, brain imaging showed that individuals in tropical conditions expended greater amounts of energy in the completion of cognitive tasks, thereby providing evidence that extreme environmental stressors can lead individuals to utilize greater cognitive resources in the completion of tasks than under environmentally-neutral conditions. H. R. Lieberman et al. (2005a) also examined the cognitive performance of U.S. soldiers under extreme training conditions. Specifically, they studied cognitive indicators before, during, and after 53 hours of training in the heat. Using a matching-to-sample test to assess memory, the results showed that soldiers performed worse during and after training in comparison to pre-training levels. Notably, the performance decrements due to the combination of the heat and training regimen are greater than those observed among alcohol impaired individuals, and among individuals with clinical levels of hypoglycemia.

Cognitive performance has also been studied under conditions of extreme cold. For example, Hodgdon and colleagues (Hodgdon, Hesslink, Hackney, Vickers, & Hilbert, 1991) compared a group of Norwegian soldiers living in tents in the field to a group of soldiers living barracks. The two groups were compared on a variety of tasks including a memory search task. The results showed that the field group exposed to cold conditions outperformed the barracks group, as the performance of the field group was maintained while that of the barracks group decreased. Similar results were found by Paul et al. (2010) who examined cognitive performance among Indian Antarctic expeditioners that spent 14 months at Maitri, the Indian Research Base in Antarctica. The study showed that recognition memory improved over the course of the mission,
while short-term memory was unchanged. Additional evidence from Antarctic expeditions has also shown a lack of memory decrements in this environment. For example, a study of members of the Chinese National Antarctic Research Expeditions assessed memory search at four times over the course of the mission (Yan, Wu, Want, Zhang, & Saklofske, 2012). Results showed no decrements in memory over the course of the mission. A study of New Zealanders who wintered over in Antarctica also revealed no decrements in immediate memory (Taylor & Duncum, 1987).

In another study involving exposure to extreme cold, submariners participating in a survival training simulation involving a disabled submarine were given a number of cognitive tests (Slaven & Windle, 1999). During the five day simulation, the temperature in the environmental chamber dropped considerably. Cognitive tests included short-term memory assessments. Subjects did not exhibit performance decrements on short-term memory or any of the other cognitive tests administered.

Additional habitability factors and memory have been examined. For instance, research has compared various light-emitting diodes (LED) technologies to fluorescent lights upon the cognitive performance of soldiers (Hawes, Brunye, Mahoney, Sullivan, & Aall, 2012). The research showed that soldiers completing tasks in fluorescent lights exhibited slower response times on tasks measuring spatial and verbal memory. The results provide evidence that industrial lighting systems do have the potential to impact cognitive performance. Notably, respondents using fluorescent lighting systems also reported higher levels of fatigue.

**Psychological.** While a space mission is generally expected to be a stressful event, research has shown that stress associated with spaceflight might not always impact cognitive performance in the ways one would expect. Newman and Lathan (1999), for example, found no significant short-term memory decrements over the course of a mission on a mental workload and performance task. However, the prospect of spaceflight itself can be viewed as a psychological stressor that may disrupt cognitive functioning. In a study of the longest space mission to date—438 days—researchers examined a number of cognitive factors before, during, and after the mission (Manzey, Lorenz, and Poljakov, 1998). The research showed that the Russian cosmonaut exhibited slight decrements in short-term memory in the days immediately before the mission, and in the two weeks following the beginning of the mission. After that, short term memory performance returned to baseline levels observed in the months prior to the mission. Short term memory again dropped below baseline levels in the two weeks following the completion of the mission, but returned to near-baseline levels in the months following the mission.

Research on anticipatory stress may help us better understand the pre-mission decrements in short-term memory found by Manzey et al. (1998). For example, Taverniers et al. (2011) examined the cognitive performance of cadets on a first-time parachute jump. The purpose of the study was to measure the impact of excessive arousal resulting from a life-threatening event on visuo-spatial learning and memory performance. The results showed that individuals on a
first-time parachute jump exhibited extreme arousal in the form of cortisol secretion in comparison to a non-jump control group. Following the jump, only minimal differences on immediate memory were detected, though greater differences were detected as task complexity increased following the jump.

Psychological stressors in a variety of other contexts have also been examined in relation to memory and associated tasks. Among U.S. Army Rangers and U.S. Navy SEALs, working memory was assessed pre- and post-participation in highly stressful training drills (H. R. Lieberman et al., 2005b). While it was impractical to assess working memory during the training exercises, the results showed that working memory on a matching-to-sample test degraded for both populations from before to after the training. It is unclear whether and/or how long it took for working memory to return to baseline levels following the training.

In a number of other settings, indicators of memory have been found to improve following stressful missions. For instance, in a study of U.S. Army National Guard personnel deployed to Bosnia, researchers found that proficiency on a working memory task actually improved from pre- to post-mission. However, performance on a number of other neuropsychological tasks decreased (Proctor, Heaton, Dos Santos, Rosenman, & Heeren, 2009). Similarly, in a study of Mount Everest expeditioners, researchers found that hypoxia did not seem to impair recall. However, “metacognition” did appear to be affected, such that climbers exhibited a decline in their confidence regarding their ability to know the correct answers on cognitive tests (Nelson et al., 1990). This suggests that in such situations, confidence in one’s cognitive ability may be impaired.

**Summary**

Research on the cognitive aspects of neurobehavioral performance provides a varied view on signs and symptoms that might affect astronauts on a LDSE mission. With regard to attention, relatively little research has examined the factors that might affect attention in spaceflight and other ICE contexts. The research that has been conducted provides only preliminary evidence of the detrimental effects that exposure to habitability and psychological factors might have on attention. Counter to expectations, research conducted in Antarctic and polar settings has shown that extreme climates and altered light/dark cycles have little impact upon the attention of personnel. In terms of measuring attention, a wide range of tests have been used to assess attention in extreme contexts. The PVT is a well-known tool to assess attention among personnel in ICE contexts, and research has generally shown that the PVT is sensitive to fatigue and sleep loss. However, newer technologies offer the possibility of more accurately assessing attentional states among astronauts and personnel in other extreme environments. Specifically, functional Near Infrared Spectroscopy (fNIRS) holds potential for the assessment of brain activity associated with varying attentional states of individuals (Harrivel, Weissman, Noll, & Peltier, 2013). Already, NASA is investing in such technology to develop a lightweight,
efficient method with which to assess neurobehavioral functioning during exploration-class missions (NASA Techport, 2015. The further development of such technology may hold great promise for the assessment of attention deficits and other neurobehavioral symptoms in spaceflight and other extreme contexts.

Concentration is another cognitive factor that has received little attention in the literature on ICE environments. Studies that have been conducted in ICE and analog settings have generally shown that memory is not negatively impacted by environmental factors such as harsh physical environments or altered light/dark cycles. In addition, a series of bed rest studies have demonstrated that concentration is not degraded during or after extended bed rest. Research on the effects of CO$_2$ levels on concentration has been equivocal. Some studies have detected an effect of CO$_2$ while others have not. As with the measurement of attention, a range of tools have been used to assess concentration.

Of the three components of cognitive functioning considered above, the greatest amount of research has been conducted on memory. Memory is one cognitive function that is measurable through objective indices, thus it is logical that this aspect of cognitive functioning has been the focus of numerous studies. In simulated spaceflight settings, Sauer and colleagues have found that prospective memory is negatively impacted when study participants conduct complex tasks during isolation and confinement. Research has found mixed evidence regarding other habitability factors. For instance, noises that simulated the ISS did not impact memory function of study participants, while vibration during a high speed boat ride did appear to impact memory. Environmental temperature does appear to have an impact upon memory. Specifically, hotter temperatures appear to negatively impact memory, while colder temperatures seem to positively impact memory or at least have no effect.

In sum, it appears that attention may be impacted by various aspects of working in extreme environments, and recent advancements in technology appear to have the potential to greatly increase our ability to assess attention in spaceflight and analog contexts. With regard to concentration, the research is somewhat muted on the extent to which extreme and analog environments negatively impact concentration. Considerably more work has been done on memory, and it does appear that memory is negatively affected by isolation and confinement, extremely warm temperatures, vibration, and anticipatory stress of the mission.

**Emotional Signs and Symptoms**

A range of emotional variables may be impacted exposure to factors introduced by spaceflight and other extreme contexts. Again drawing on the taxonomy provided by the NSI, we focus on two variables—anxiety and depression—that have been the focus of many studies in ICE environments. We also consider boredom as an emotional variable, as it was mentioned
repeatedly by SMEs in the operational assessment (presented below) as a symptoms that needs to be addressed by any neurobehavioral assessment developed by NASA.

**Anxiety**

As noted by Bar-Haim and colleagues (2007) in their systematic review of the literature related to attentional threat bias among anxious individuals, fear is an adaptive behavior that permits individuals and organisms to detect danger in the environment and to respond accordingly. Anxiety disorders develop when such mechanisms are not properly regulated and when biases toward threat-related information occur. In spaceflight and ICE contexts where environmental conditions pose a consistent threat, the development of anxiety symptoms can disrupt cognitive performance, thus threatening the success of the mission and placing the safety of the crew at risk.

As discussed in more detail elsewhere in this report, prolonged exposure to danger may lead to attentional biases in the wake of threat exposures, and may be indicative of anxiety symptoms (e.g., Sipos, Bar-Haim, Abend, Adler, & Bliese, 2014). Furthermore, research has shown anxiety to be significantly related to various types of organizational commitment in the military context (Meyer, Kam, Goldenberg, & Bremner, 2013). Thus, the presence of anxiety may also impact individuals’ commitment to the goals and norms of the group. Anticipatory anxiety has also been shown to bias visual searches in high stress environments (Cain, Dunsmoor, LaBar, & Mitroff, 2011), suggesting that anxiety symptoms can impact the work performance of some individuals.

**Environmental.** To assess the effects of environmental factors on anxiety symptoms, Palinkas, Seufeld, and Steel (1995) studied the psychological functioning of seven polar expeditioners in the Canadian high arctic. Using the POMS to examine anxiety and a variety of other psychological variables assessed by the POMS, the researchers found that anxiety levels dropped significantly during the first three weeks of the mission. The successful adjustment of the expedition crewmembers was attributed to the use of problem solving coping strategies. However, in a later study of Antarctic expedition crewmembers, research indicated an increase in anxiety symptoms, again assessed using the POMS (Palinkas, Johnson, Boster, & Houseal, 1998). However, the trend was not linear as anxiety symptoms decreased during the second quarter of the mission, but increased during the third and fourth quarters. While the results of the 1998 study run counter to the results of the 1995 study, they perhaps paint a more realistic portrait of changes in anxiety during an ICE mission by illustrating the non-linear nature of symptoms.

In another study by Palinkas and colleagues (Palinkas et al., 2001), researchers examined the role of thyroid function in the development of anxiety symptoms during an Antarctic winter-over. The expectation is that there is a four-stage model of thyroid adjustment to cold temperature, and that polar T3 syndrome in polar settings is the result of altered thyroid function in cold
temperatures. The results of the study showed levels of T3 decreased prior to high reported levels of anxiety. The results also suggested an interactive relationship between T3 and anxiety. Simply put, the results of the study suggest the importance of assessing thyroid function in any comprehensive measure of neurobehavioral symptoms in a spaceflight setting.

Exposure to radiation is expected to pose a major threat to health and performance of crews working in and LDSE context. Research using animal models has begun to examine the ways in which radiation exposure might impact emotional symptoms such as anxiety. For instance, research on mice exposed to irradiation has provided evidence that anxiety symptoms can increase following exposure (Olsen, Marzulla, & Raber, 2014). Specifically, mice exposed to whole-body irradiation exhibited anxiety symptoms greater than mice not exposed to radiation two weeks after each group had been trained on a number of procedures. The findings may have applicability in LDSE settings, where it is expected that crewmembers will be constantly exposed to radiation during the transit phases of the mission.

Habitability. A number of studies have examined habitability factors in relation to anxiety. Tougne et al. (2008) simulated a mountain ascent by placing study participants in a hypobaric chamber and depleting oxygen levels. State and trait anxiety levels, and individual and group performance, were assessed at various simulated altitudes. The results of the study showed that state anxiety increased in step with increase in simulated altitude. Further, increases in state anxiety were associated with decreases in individual task performance. This effect did not, however, carry over to the team as group performance measures were maintained.

In another study on the effects of hypoxia on anxiety levels, researchers examined the psychological functioning of U.S. Marines who ascended to high altitude for training exercises. Within six days, a number of Marines exhibited acute anxiety symptoms. However, individuals returned to baseline levels rather quickly, thus suggesting a real, but short-lived, adjustment period for individuals exposed to low-oxygen environments. In a study of female mountain expeditioners, research showed that anxiety symptoms actually decreased from before to during and after the expedition (Petiet, Townes, Books, & Kramer, 1988).

Psychological. A considerable body of literature has examined anxiety in the military context. Given the exposure to danger and the high levels of stress that military service can place on individuals—nearly 15% of Australian Defense Forces met the criteria for an anxiety disorder (Van Hooff et al., 2014)—it is not surprising that anxiety has been studied extensively in this context. To illustrate the extent to which anxiety has been examined in military settings, a recent meta-analysis of Chinese military studies in which the Chinese version of Spielberger’s State-Trait Anxiety Inventory (STAI) yielded 45 studies that included tens of thousands of participants. While a sizable literature on the topic does exist, however, the review below focuses on those military studies that are most likely to inform the current effort.
In one demonstration of the importance of anxiety in an operational setting, researchers examined the effects of anxiety on shooting accuracy among Dutch infantry soldiers (Nibbeling, Oudejans, Ubink, & Daanen, 2014). Anxiety was manipulated in the experiment by having experimental opponents shoot non-lethal weapons at the study participants during the training exercise. Manipulation checks demonstrated that the danger of being shot successfully induced anxiety symptoms. The results of the study showed that anxiety exerted a significant influence on shooting accuracy in the high anxiety condition such that accuracy was reduced under anxious conditions. The results of the study have clear implications for understanding the effects of anxiety on performance in high-reliability settings. Other studies, however, have not demonstrated a link between anxiety and shooting accuracy. For example, Ohlson and Hammermeister (2011) found that anxiety symptoms did not exert a significant influence on simulated rifle marksmanship. Rather, the authors concluded that ability to maintain cognitive focus in the face of anxiety was found to be the key predictor of marksmanship.

Studies have examined physiological indicators of anxiety among military members. Taylor et al. (2008), for example, examined cortisol concentrations among anxious and non-anxious military members, some of whom were “free living” and some of whom were living under a military regimen. The results suggested that trait anxiety had an impact upon the diurnal cortisol patterns of free living men, but that anxiety did not predict diurnal patterns among military members who were unable to control the amounts of stress they were exposed to in a stressful military setting. In another study, researchers examined various plasma markers in relation to anxiety, depression, and fatigue (H. R. Lieberman, Kellogg, Kramer, Bathalon, & Lesher, 2012). Examining mood and various nutritional, metabolic, and hormonal plasma markers, the researchers studied 35 females enrolled in a U.S. Marine Basic Combat Training, a stressful 12 week course. The results of the study showed that anxiety decreased over the course of the training period. Notably, using an index of eight plasma markers, the researchers were able to predict 40% of the variation in self-reported anxiety (using the POMS). The research holds great potential for understanding the use of biological markers to detect the presence of anxiety symptoms among high stress populations, which may also allow NASA to select out the potential crewmembers most susceptible to stressful experiences.

Interpersonal. A number of studies have examined the effects of gender in the military context. For example Curry et al. (2014) computed gender differences on anxiety and a variety of other conditions that are comorbid with major depressive disorder. Drawing on a registry of 1,700 U.S. veterans (346 women and 1,354 men), the researchers determined that anxiety was more common among female veterans. One of the primary limitations to the study was the use of retrospective recall in the assessment of anxiety and other disorders. A separate study of Canadian forces also examined gender differences on a number of different occupational stress and mental health outcomes (Mota et al., 2012). Drawing on a representative sample of Canadian forces, the authors found that while there were no differences in generalized anxiety
disorders between men and women serving in the regular forces, there were significant differences between men and women serving in reserve forces.

In a study of Chinese military officers undergoing training, Jiang et al. (2013) examined gender differences in mental health outcomes and coping styles. The results of the study showed that female officers did exhibit higher levels of state anxiety and the use of negative coping tendencies than males. Follow up analyses demonstrated that female officers who utilized problem solving coping strategies were less likely to experience anxiety symptoms.

In another study of U.S. service members, research was unable to detect gender differences in anxiety disorders. There, researchers examined anxiety order diagnoses across the various branches of the U.S. military (Lovering, Proctor, & Heaton, 2013). Drawing on administrative data regarding diagnostic rates in the U.S. military from 2000 to 2009, the researchers found that the majority of anxiety diagnoses occurred in the Army. The authors also tested for the presence of gender differences in anxiety disorder diagnoses. The analyses revealed no significant gender differences in the diagnosis rates during this time.

In an interesting study of anxiety diagnoses among U.S. Marines who had deployed on combat missions to Iraq and Afghanistan, Booth-Kewley et al. (2013) examined the effects of gender as well as a variety of other demographic and organizational variables. Once again, results suggested that gender was a significant factor in the development of anxiety disorders. Using a regression framework, the results showed that females were more likely than males to be diagnosed with a general anxiety disorder (OR = 2.57). Notably, analyses also demonstrated that satisfaction with leadership was the strongest negative predictor of an anxiety diagnosis. This finding is consistent with other studies of the U.S. military that have examined organizational factors in relation to mental health outcomes (Joint Mental Health Advisory Team 7, 2011).

Depression

Environmental. Research has examined the potential impact of a variety of physical factors on depression and depressive symptoms. Arendt (2012), for example, reviewed evidence of circadian rhythms in Antarctic settings where light/dark cycles are altered. As part of the review, Arendt examines the relationship between light/dark cycles, circadian phase, and seasonal affective disorder (SAD). According to Arendt, some evidence exists to support the notion that altered circadian phase may be the root of SAD, though it appears that depressive symptoms in polar settings more likely occur at subsyndromal levels. For example, Harris et al. (2010) found that British Antarctic personnel reported slightly elevated depressive symptoms. Similarly, research has provided anecdotal evidence that mood and mental health problems increase, again at non-clinically significant levels (Levine, 1995). Ikegawa, Kimura, Makita, & Itokawa (1998) found no evidence of elevated depressive symptoms among a group of eight Japanese Antarctic winter-overs. Palinkas et al. (1995) actually observed decreases in depressive symptoms among nine Arctic expeditioners, as did Palinkas et al. (1998) who examined 83 individuals over the
course of an eight month Antarctic expedition. Palinkas and Houseal (2000) observed significant decreases in depressive symptoms among an Antarctic crew at the South Pole, but no significant changes in depression among crews as McMurdo and Palmer stations during the same time period. Rosen et al. (2002) found slightly elevated depression levels among U.S. Army personnel stationed in Alaska.

Bell and Garthwaite (1987) did find evidence of elevated depressive symptoms at Rothera station in Antarctica. In that study, the authors detected elevated depressive symptoms among the winter-over group in relation to a comparison group, and also found elevated depressive scores during the winter months. Notably, two individuals were diagnosed with depression and withdrew from the study. Unlike Arendt (2012) who focused her polar study on the relationship between light dark cycles and circadian rhythms, Bell and Garthwaite do not make a direct link between light/dark cycles and depression. Harris et al. (2010) examined British Antarctic personnel and found that a small percentage (8.7%) of participants indicated some or serious depressive symptoms. The primary contributors to depressive symptoms were sleep problems and tiredness.

A number of studies suggest that biological factors are linked to the development of depressive symptoms in polar settings. Palinkas et al. (2001) looked at seasonal fluctuation of hypothalamic-pituitary-thyroid (HPT) function and mood. The researchers found that mood disturbances did fluctuate over course of the year, and that fluctuations were associated with serum levels. The findings suggest that thyroid function may have role in affecting mood at high latitudes where light/dark cycles are altered. The implications for spaceflight are clear. Premkumar et al. (2014) found that depressive symptoms increased during midwinter, with 10% of subjects meeting the criteria for minor depression. Investigators examined vitamin D levels and parathyroid (PTH) levels, but were only able to hypothesize the potential role of these physiological variables as mediators between altered light schedules and depressive symptoms. Additionally, McGrath-Hanna (2003) conducted research on Arctic populations and has suggested that diet may be increasingly linked to depressive symptoms.

A lack of adaptation to other features of the physical environment may lead to depressive symptoms. For instance, research on a high altitude mountain expedition sought to examine psychological adaptation to the threatening environment (Blanchet, Noël-Jorand, & Bonaldi, 1997). Using speech analysis of expeditioners at the mountain summit, investigators found that depressive symptomatology was common among expeditioners. However, among some study participants, investigators hypothesized a correspondence between physiological maladaptation to the environment and the presence of depressive symptoms. Notably, the authors also surmised that latent depression may manifest at altitude, thus leading to physiological maladaptation. This conclusion speaks directly to the importance of selection methods in the creation of a crew.

**Habitability.** The spacecraft habitat has the potential to lead to depressive symptoms. A small, enclosed vehicle to Mars will contain many highly complex features and systems to support life
onboard the craft. While the crew will receive ample training on how to maintain and repair such systems, particularly given the relative autonomy of the crew on a Mars mission, the potential for failure or an emergency certainly exists. Research has shown that an emergency event may lead to depression or depressive symptoms among crewmembers, particularly those at greater risk for such symptoms. For example, a submarine crew who experienced flooding and a fire onboard the submarine evidenced increased levels of post-traumatic and depressive symptoms in the months following the emergency (Berg, Grieger, & Spira, 2005). Those individuals who did exhibit elevated levels of depression were those with previous and subsequent life events that placed the individual at greater risk for developing depressive symptoms in response to the submarine emergency. This finding is consistent with the expectations of Blanchet et al. (1997), and highlights the importance of selecting individuals who are not at elevated risk for developing depression, as well as to minimizing additional traumatic events in the wake of an on-board emergency.

Beyond emergency situations, it is unclear whether simply living in a confined space would induce depressive symptoms. In a 105 day pilot study leading up to the Mars500 study, investigators examined the presence of depressive symptoms among participants confined to a small space mimicking the environment expected on a vehicle for a Mars mission (Gemignani et al., 2014). The results of the simulated mission indicated no increases in depressive symptoms as a result of confinement. In the actual Mars 500 study (Basner et al., 2014), results showed that, on average, the six-person crew reported very few depressive symptoms over the course of the study. However, researchers also observed variability in reports of depressive symptoms, such that one study participant reported depressive symptoms over 90% of the reporting periods of the study. The relatively high rate of depression (one out of six individuals) speaks to the important of the selection and screening criteria that will need to be used in the composition of LDSE crews.

Social. Palinkas, Glogower, Dember, Hansen, and Smullen (2004) examined four years of Antarctic winter-over data. Results showed that just over 5% of expeditioners experienced some form of depression. The authors hypothesized that seasonal affective disorder may be the cause. However, due to the variation between McMurdo and South Pole, variation across years, and variation between Navy and civilian personnel, the authors surmise that social factors may be a more important factor than physical. Palinkas, Johnson, & Boster (2004) also found significantly-elevated levels of depression among personnel in Antarctica. The analyses demonstrated that a lack of satisfaction with social support accompanied the development of depressive symptoms, and that declines in advice-seeking behaviors among peer crewmembers was associated with depressive symptoms.
**Boredom**

Little work has been conducted that actually seeks to measure and quantify the presence of boredom among crews in spaceflight and other ICE environments. Rather, it is generally hypothesized that boredom and monotony are likely to be a fact of life among crewmembers embarking on an exploration class mission. Boredom in an exploration context presents a number of threats to health and performance. For example, boredom has been associated with risky behaviors in a number of civilian contexts (Blaszczynski, McConaghy, Franknova, 1990; Lee, Neighbors, & Woods, 2007; LePera, 2011; Mercer & Eastwood, 2010). Furthermore, research has suggested that boredom may impede the use of, or engagement in, rehabilitative programs (Seel & Kreutzer, 2003). Thus, detecting the presence of boredom may be important in not only keeping crewmembers engaged in the mission during transit periods where workloads are low, but also in keeping crewmembers from engaging in potential risky behaviors that might jeopardize the mission.

Recent work has sought to determine the psychophysiological profiles that characterize individuals in a bored state. For example, Merrifield & Danckert (2014) measured heart rate, skin conductance, and cortisol levels in an experimental setting where boredom was induced among study participants. The authors sought to determine whether boredom is characterized by a state of low or high arousal, as there is disagreement on this point in the literature. The results showed that individuals in the bored experimental condition exhibit relatively high heart rates, and relatively low skin conductance levels. While the results are somewhat difficult to interpret in the context of comparing boredom to depression and sadness, the results do provide evidence that there may be physiological indicators to help assess the presence of this affective state in crewmembers.

Recent technological advancements might also allow for an assessment of boredom in spaceflight and other settings. Again, fNIRS technologies that assesses activity in various regions of the brain may allow for the more accurate detection of boredom among individuals in and LDSE context. Recent research suggests that such technology may be used to detect the presence of “flow” among individuals engaged in a particular task (Yoshida et al., 2014). Alternatively, fNIRS may also be used to detect, boredom, or a psychological state that is the complement to flow.
Summary

The results of this review of the literature provided a nuanced view of the ways in which emotional variables are impacted by spaceflight and analog settings. First, a considerable amount of research has examined anxiety in polar settings. In general, it is presumed that operating in polar environments, where extreme temperatures are present and where personnel are isolated from broader society, will induce anxiety among individuals. The review of the literature does indicate that anxiety may increase among some individuals, but in general the evidence has been somewhat uneven in the literature.

An important aspect of anxiety that must be considered in any assessment of it, is the fact that there appears to be a biological component to the development of anxiety. In particular, Palinkas et al. (2001) found that thyroid function may be associated with the development of anxiety in polar environments. H. R. Lieberman et al. (2012) assessed eight plasma markers in relation to anxiety and other affective disorders among military members. The research team was able to explain substantial variance in self-reported indices anxiety. Together, the results suggest that it may be useful to conduct additional research in this area to identify efficient methods with which to assess biological factors in relation to neurobehavioral symptoms in the emotional domain.

A considerable amount of research has examined depressive symptoms among crews in polar environments. Much like the research on anxiety, the research is fairly equivocal regarding the effects of cold and light/dark cycles on depressive symptoms. Relatively little research has been conducted looking at the effects of habitability upon depression. In one of the few studies on the topic, Basner et al. (2014) found low mean levels of depressive symptoms among participants in the Mars 500 study. However, as noted above, one out of six crewmembers in that study exhibited high levels of depressive symptoms. It is not known whether the development of depressive symptoms was due to habitability factors, some other factor, or a combination of factors. Similarly, little research has examined the role of social factors in the development of depressive symptoms. Biological indicators of depression may hold potential for the assessment of depressive symptoms during LDSE. For example, Palinkas et al. (2001) found evidence that HPT functions were associated with mood disturbances and Premkuhar et al. (2014) found that parathyroid levels may be associated with depressive symptoms in Antarctic settings.

Boredom and monotony have been identified as major threats to LDSE, particular during the transit phases of the mission. Boredom may lead to lead to risky behaviors among crewmembers, thus it is critical to identity psychological and physiological states of boredom among crewmembers so that countermeasures can be developed and implemented. Lightweight equipment to measure cognitive activity of crewmembers is currently being developed; this equipment may yield an understanding of the physiological signature of boredom among long-duration crews.
**Objective 3. Seek to identify underlying causes of neurobehavioral issues.**

**Operational Assessment**

To better understand the sources and manifestations of neurobehavioral symptoms in spaceflight settings, an operational assessment was conducted with a number of SMEs from a variety of fields. The semi-structured interviews were conducted to gain an understanding of neurobehavioral issues from a practical standpoint. While the operational assessment is contained under the heading of Objective 3, it also helps address Objective 2 and Objective 4. The 12 SMEs included seven individuals with a specialization in spaceflight and/or analog settings (i.e., Antarctic) and five individuals with a specialization in military and military veteran populations (Army, Air Force, Department of Defense [DoD], Veterans Affairs [VA]). The spaceflight/analog SMEs included one NASA psychologist, one NASA psychiatrist, one NASA toxicologist, one retired NASA astronaut, one NASA flight surgeon, one aerospace medicine physician, and one private consulting psychologist who has worked extensively with NASA and other agencies on the study of Antarctic personnel. The DoD/VA personnel included one high ranking Army psychiatrist, one Army civilian who is very experienced researching deployment-related health issues, one DoD civilian with extensive experience studying deployment and telehealth issues, one Air Force Special Operations psychologist, and one senior psychologist from Veterans Affairs (VA). The interviews generally lasted one hour, though in the case of the astronaut and flight surgeon the interviews were 30 minutes in duration.

Questions were developed by the investigators that would have applicability across the various contexts in which SMEs work (see Appendix B for list of questions). The questions were generally divided into three sections. The first set of questions was designed to assess the types of neurobehavioral signs and symptoms experienced by personnel in the various settings of interest, the neurobehavioral symptoms that pose the greatest threat to performance and health, and the types of interventions being put in place by various agencies. We also sought to determine which neurobehavioral symptoms were best understood in terms of the research that has been done, as well as those that are least understood in the view of the SME. In all instances, we referred SMEs to the list of affective and cognitive neurobehavioral symptoms that are listed in Table 3 above.

The second set of questions was designed to better understand the sources of neurobehavioral symptoms from a spaceflight perspective. Drawing on the work of Kanas and Manzey (2008) we asked SMEs about the physical, habitability, psychological, and social/interpersonal factors that might lead to specific neurobehavioral symptoms. Once again, we asked SMEs to tell us where they thought additional research might be needed to better understand how these potential sources might relate to neurobehavioral symptoms. For those SMEs that work outside the spaceflight context, we asked them to draw on their own experiences to inform how these four factors affect neurobehavioral symptoms in other settings.
The third set of questions asked respondents to provide thoughts on the tools currently used to measure and assess neurobehavioral decrements in spaceflight and other contexts. SMEs were asked to provide their thoughts, if any, on advancements that might need to be made in the future to better identify the presence of neurobehavioral symptoms. Additional follow-up questions were asked as appropriate. The full list of questions used to conduct the interviews is included in the appendix at the end of this report.

**Types of Neurobehavioral Signs and Symptoms**

*What are the most common neurobehavioral symptoms in spaceflight contexts/among combat vets/in deployment contexts?*

Each interview began with a general question about which neurobehavioral symptom was most common among the population of interest. Among the six SMEs with spaceflight/analog experience, fatigue was identified as the most common neurobehavioral symptom in spaceflight settings. A number of SMEs pointed to a heavy workload as a common source of fatigue. For example, the flight psychologist referred to the extended periods of vigilance that are needed on the ISS. These high levels of vigilance tap crew resources to the extent that the crew has to “dig into reserves” in order to maintain concentration. Eventually, in the view of the psychologist, other important individual and crew functions such as concentration and multitasking are hampered as a result of maintaining sustained attention. Diminished performance has the potential to lead to irritability and increased frustration. Similarly, the NASA flight surgeon discussed chronic fatigue on the ISS as a result of a heavy workload. According to the flight surgeon, the tightly defined work schedule leads to fatigue among the crew, and scheduled days off may not be restorative in terms of providing rest for the crew. The astronaut also mentioned fatigue as the top problem on the ISS.

In addition to a heavy workload, circadian rhythm was identified as a potential source of fatigue among crewmembers. According to the NASA psychiatrist, desynchronization will likely lead to greater fatigue among the crew. The NASA psychologist also mentioned sleep loss as a source of diminished concentration and ability to multitask, as well as an increase in irritability and frustration among the crew. Notably, the NASA astronaut indicated that he experienced very few sleep problems while in space. As he recounted, he only recalled taking one nap during his time on the ISS. In general, the discussions related to sleep and circadian rhythms are consistent with the emphasis that NASA has placed on researching this important topic in recent years.

The NASA toxicologist identified CO₂ as another source of fatigue and irritability that has been the focus of research in recent years. While research has examined the relationship between CO₂ and cognitive functioning in ground-based studies, the relationship between CO₂ and cognitive functioning appears to be somewhat different in spaceflight settings. It was clear from this discussion—in addition to a reading of the broader literature—that more research is needed into the effects of CO₂ in spaceflight.
In the opinion of the astronaut, one important source of irritability was the inefficiency of communications between the flight crew and the ground crew. Currently, in the view of this SME, the organizational culture is such that astronauts do not have the ability to be frank with the ground crew and to let them know when mistakes were being made or when communications were not efficient. Notably, these communication problems appeared to be a source of frustration and irritability for the astronaut. This was one of the most visible examples of how interpersonal issues might affect neurobehavioral outcomes among the crew. This is a very important consideration in light of the fact that communications between the ground and crew in LDSE will lag the further the crew travels away from Earth. Thus, frustration and irritability may increase as communication delays further compound potential miscommunication between the ground and the crew.

The NASA psychiatrist provided interesting insights into factors that might moderate the presence/severity of neurobehavioral symptoms in LDSE. First, the different phases of the mission might evoke or lead to different sets of neurobehavioral symptoms. For example, during the transit phase to Mars crewmembers may exhibit excitement for the new mission and, therefore, little symptomatology. During the second phase of the mission, when the crew is on Mars, a new set of issues may lead to the presence of symptoms. Specifically, a decision will have to be made about whether to entrain crewmembers to the Martian light/dark cycle during the final portion of the transit phase, or whether to entrain the crew when they arrive on Mars. Because the Mars light/dark cycle is slightly longer than that of the Earth (24.65 hours versus 24), circadian disruption will occur, and it is expected that crew fatigue will likely set in. Notably, the ground crew will also need to entrain to the Martian day/night cycle thus adding another level of complexity to efforts to effectively deal with varying light/dark cycles. A heavy workload is also expected during the time on Mars. During the third phase of the mission—the return trip from Mars—a new set of circumstances may lead to various neurobehavioral problems. In particular, a “third quarter” effect (e.g., Bechtel & Benning, 1991) may set in. The third quarter effect has been explained in the literature as an increase in depressive symptoms during the third quarter of an exploration mission. It is theorized that this increase occurs due to crewmembers’ understanding that they are only half way through their mission, and due to the fact that monotony is high during this time. The psychiatrist believed there may be a bit of an anti-climactic feel during the return trip. Radiation exposure may begin to take its toll upon cognitive performance during the third quarter (e.g. Parihar et al., 2015), or may reach levels with critical health consequences for the crew. It is important to consider also the possibility that all crewmembers may not survive the stay on the Mars surface. If the loss of life or serious injury does occur, depression and other issues related to isolation and loneliness may ensue. Finally, during the third phase communication with ground would eventually return to near real time communication as the crew moves closer to Earth. Real time communication with the ground may serve to offset the detrimental effects of isolation that are likely to exist while the crew is in transit.
The second moderating factor in the development of neurobehavioral decrements, according to the psychiatrist, will be the experience level of the crewmembers. That is, neurobehavioral symptoms may develop differently among first time flyers than among veterans. In the view of the psychiatrist, first-time flyers will be likely to experience excitement and an “adrenaline rush” that will allow them to overcome any potential symptomatology. Veteran flyers, on the other hand, may be more likely to exhibit neurobehavioral symptoms early on a flight given that the excitement of flying a space mission may be lower. Furthermore, veterans may be more honest with ground crew regarding potential neurobehavioral issues, and may therefore be more likely than first time flyers to communicate any potential issues to flight surgeons.

Military and VA personnel provided a slightly different view on the types of neurobehavioral symptoms that they commonly see among active and retired military personnel. Not surprisingly, the insights of military personnel are shaped by the experiences of war and combat exposure that have affected thousands of U.S. troops over the past decade or so of sustained conflict. Thus, many of the neurobehavioral symptoms discussed by the DoD and VA SMEs were related to PTSD and TBI.

According to the VA psychologist, one of the key neurobehavioral decrements that seems to accompany PTSD and acute stress disorders among veterans is the lack of mental concentration. The problems with concentration among those diagnosed with stress disorders lead to a variety of other problems, with forgetfulness being one of the most salient. In the view of this SME, the problem of forgetfulness was tied to problems with the processing of information, rather than simply forgetting information once it has been processed. These insights have the potential to inform the understanding of how cognitive factors might be shaped by the experience of traumatic events during LDSE. The SME also mentioned that sleep disturbances have been found to be very common among individuals diagnosed with PTSD and/or TBI. It is important to note that the VA psychologist made it clear that her views on neurobehavioral problems among veterans are driven and shaped by the experiences of those veterans who actually seek care. The implication is that combat veterans may have other symptoms that accompany stress disorders, but such symptoms are unknown unless the veteran comes forward to seek treatment.

The Army research psychologist provided views on whether and how neurobehavioral symptoms in a combat deployed context compared to neurobehavioral symptoms in a non-deployed context such as spaceflight. Not surprisingly, the SME indicated that some of the issues faced by combat deployed soldiers map onto to issues faced by spaceflight crewmembers, while many others do not. Two of the major neurobehavioral problems that both populations are likely to see are depression and anxiety; however, the sources of these issues will be different across populations. Within the military population with which the SME deals, anger and aggression seem to be two very common neurobehavioral symptoms that are not examined with common tools such as the NSI. Once again, anger and aggression are symptoms typically seen among military personnel with PTSD and/or TBI. In addition to anger and aggression, sleep problems have been commonly reported among military personnel with stress disorders or head injuries. As noted by
spaceflight SMEs, sleep problems are commonly linked to deficits in cognitive processing. Beyond these insights, the Army psychologist had recommendations for other types of symptoms that NASA may want to assess in any effort to track neurobehavioral decrements among those exposed to stress. First, risk taking should be added to the list. In the experience of this SME, risk taking is tightly linked with other symptoms that have been observed among the population with PTSD and related stress disorders. Second, while isolation and loneliness are currently viewed as sources of neurobehavioral and other psychological symptoms, it may be worth considering these as symptoms in their own rights. That is, NASA may be well served by treating these as symptoms along with the other neurobehavioral symptoms that are assessed with current and future assessment tools.

The Army psychiatrist appeared to examine the LDSE problem set through the lens of Army operations. For example, the LDSE crew was characterized as being approximately the size of a squad. The team will experience long-term isolation and limited contact and communication. Consequently, this SME felt that an SME with expertise in special operations would be the most appropriate person for discussing military teams as an analog to an LDSE team, as special operations teams commonly serve on prolonged missions with tight-knit units. Again working from the perspective of combat deployment, the SME pointed out that deployment itself can be a traumatic event, even if not major combat experiences are had by the individual. From this perspective, it is easy to view combat deployment as similar to LDSE, as each phase of an LDSE may expose crewmembers to circumstances that may be interpreted as stressful.

In this context, sleep deprivation is likely to pose the greatest challenge to health and performance. Sleep deprivation—less than seven hours of sleep per day—will lead to decrements in concentration and decision making abilities of crewmembers. Echoing the comments made by the Army psychologist, this SME pointed to “homefront stressors” as a potential source of neurobehavioral symptoms. The SME discussed research that showed over 50% of stressors indicated by combat deployed soldiers were comprised of stressors from family and friends back in the U.S. Notably, the SME pointed to increased connectivity as a source of such issues. That is, unlike in previous conflicts where military personnel relied upon letter writing and other relatively slow means of communications, today’s military personnel have instant access to the Internet and other communication channels that allow them consistent, real-time communications with loved ones.

Two major neurobehavioral symptoms—anxiety and depression—have presented somewhat differently among deployed soldiers. The ways in which these symptoms have presented may hold lessons for crews on exploration class missions. First, symptoms of anxiety typically rise immediately after the experience of a traumatic event. Thus, drawing on the research related to state anxiety, it is possible to see how potentially traumatic experiences (mechanical failures, major injuries, or other emergencies) during LDSE might impact attention patterns and subsequent behaviors of individuals exposed to the traumatic experience. Second, depressive symptoms have generally been observed in cycles. According to the SME, soldiers experience
high levels of excitement during the first month approximately of a combat deployment (deployments typically last 12 to 15 months). After this first month the excitement of the mission dissipates and depressive symptoms may develop as the individual begins to settle into the combat mission. During the middle of the tour, as the individual realizes that they are at the midway point of the mission, depressive symptoms again seem to spike. Finally, toward the end of the mission, about 30 to 60 days prior to the end of the deployment, depressive symptoms have again been seen to rise. It was hypothesized that symptoms may arise as soldiers begin to worry about returning home to family and taking day-to-day household activities. Additionally, the SME surmised that some soldiers may feel a lack of closure about their deployment and may subsequently experience depressive symptoms. In general, the cyclical nature of depressive symptoms described by the SME is consistent with some of the thoughts put forth by the NASA psychiatrist. Specifically, both the Army psychiatrist and NASA psychiatrist viewed the onset of depressive symptoms to be cyclical in nature, presenting at various stages and transition points throughout the missions.

The DoD telehealth civilian indicated that sleep-related issues problems were the most prevalent neurobehavioral decrement faced by military personnel and veterans. In the view of this SME, sleep problems were simply a reality of post-deployment life for many service members. Depressive symptoms were noted as the next most common type of neurobehavioral symptoms. Finally, low frustration tolerance and anger were cited as two common symptoms, as many combat veterans express frustration and anger toward events that would be considered common by many individuals.

Finally, the Air Force psychologist indicated that fatigue and attentional distraction the two most common neurobehavioral decrements among Air Force special operations personnel. In the view of this SME fatigue is caused by a number of factors including circadian rhythm disruptions and a high volume and intensity of work. Fatigue leads to attentional distraction and reduced situational awareness. These deficits have obvious implications for the effectiveness of personnel who rely on high levels of attention to detail in high stress contexts.

To summarize, the experiences of astronauts and military personnel are similar with regard to the isolation and confinement experienced by each group. However, these populations differ substantially in terms of the stressors experienced during missions: military personnel are exposed to potentially traumatic and violent combat experiences, while astronauts are much less likely to be exposed to such traumatic stressors. With this important caveat in mind, we can see how the neurobehavioral symptoms of military and non-military personnel compare and contrast. In general, fatigue was the most commonly mentioned neurobehavioral decrement across the two populations. For SMEs from NASA and the Air Force, fatigue was typically viewed as occurring as a result of circadian disruption, sleep deficits, and/or heavy workloads. For military personnel, fatigue was also seen as a result of a heavy workload. However, sleep-related problems were much more often associated with PTSD and TBI symptomology. Similarly, the symptoms of low frustration tolerance and anger were cited multiple times by SMEs as potential...
problems in spaceflight and military contexts. But again, the sources of such issues differed between SMEs from the NASA/Air Force communities and those from other DoD organizations that are more likely to deal with service members exposed to traumatic combat experiences.

*What are some efforts that NASA/the DoD has used to deal with these issues? What are additional resources that could be made available?*

SMEs were next asked about the programs and interventions that have been used to prevent the onset of neurobehavioral symptoms, or that are designed to help individuals cope with such symptoms. The diverse background of SMEs resulted in the discussion of a wide range of programs and interventions. Once again, the programs largely differed between spaceflight and non-spaceflight contexts.

Within the spaceflight context, the NASA psychologist discussed the effectiveness of cognitive sleep training among astronauts. This program involves astronauts training 1-to-1 with medical specialists from NASA. Anecdotally, astronauts have reported high levels of effectiveness with the program. To date, the cognitive sleep training program is voluntary, though the SME believed that mandating the program may lead to fewer sleep-related issues among astronauts. Consequently, the SME expected to see fewer fatigue induced behavioral problems among astronauts who participate in the program.

The NASA flight surgeon focused his discussion on the need for rules to allay fatigue-related problems during spaceflight. Once again, heavy workloads are seen as the major source of fatigue for astronauts on the ISS. In the view of this SME, the heavy workload stems directly from the scheduling protocol which is composed by the ground crew. Astronauts’ days are scheduled in five minute increments; this high level of specificity leads to a steady workload that may lead to fatigue. In the view of the SME, the scheduling protocol is not designed to provide an adequate amount of rest for astronauts. The SME recommended that NASA adopt a set of rules and regulations that ensures astronauts do receive the proper amount of rest during each work period. Furthermore, the SME indicated that it was important to make sure that astronauts have access to the necessary diversions during their time off. For example, on an ISS mission, delivering care packages to the astronauts might help address problems related to isolation and confinement. Additionally, having amenities such as large screen televisions for movies and teleconferences will help provide diversions to crewmembers. In LDSE, diversions will also be needed. However, in addition to amenities such as televisions, crew-specific diversions will likely be necessary. For example, if members of the crew have an interest in music, then it may be wise to bring musical instruments on the mission as payload limits allow. Notably, this perspective was shared by the private consulting psychologist who discussed the presence of novel stimuli during Antarctic winter overs. The SME noted that many of the individuals best able to cope with the winters in Antarctica are those who pack novel stimuli such as games, and begin to use those stimuli once the depths of the Antarctic winter set in.
As noted, the astronaut viewed communications between the flight crew and the ground crew as a source of frustration and irritability. Specifically, the organizational culture does not fully allow astronauts to be honest with the ground crew when miscommunication may be occurring. One important way in which frustration and irritability issues might be alleviated, then, would be to foster more effective communication channels between astronauts and the ground crew. In order for this to occur, however, a new organizational culture would have to be established and take hold.

Once again, there was a significant distinction between the comments offered by NASA personnel and those offered by military personnel. In terms of the types of programs to prevent or alleviate neurobehavioral symptoms among service members and veterans, military SMEs were able to discuss a wide range of current and emerging programs that have been used in the DoD context.

The Army psychiatrist referred to the Army’s CSF2 program as one of the most salient and cogent efforts to enhance the psychological resilience and readiness of soldiers. The CSF2 program takes a holistic approach to enhancing resilience by promoting both the physical and psychological health of soldiers. Recent evaluations have shown some evidence of effectiveness (Harms, Herian, Krasikova, Vanhove, & Lester, 2013). In addition to CSF2, SMEs identified a number of other programs. The Air Force psychologist, for example, discussed the Tactical Human Optimization, Rapid Rehabilitation and Reconditioning Program (THOR3). THOR3 is a program used by U.S. Special Operations Command to enhance the physical and mental capacities of special operations units. Much like CSF2, THOR3 is designed to be a holistic program that focuses on both physical and mental aspects of well-being and fitness. Unlike CSF2 which relies upon a train the trainer model and which only tracks physical fitness but does not actively promote it, THOR3 training is delivered by psychologists, trainers, and coaches who specialize in their respective fields. A recent evaluation of the program demonstrated some effectiveness (Kelly, Masi, Walker, Knapp, & Leuschner, 2013). Another program mentioned by the Air Force psychologist is the U.S. Special Operations Command Preservation of the Force and Family (POTFF). In the words of the SME, this program is designed to enhance resilience and hardiness by promoting spiritual and psychological guidance to service members and their families.

One of the most wide-reaching efforts to identify potential neurobehavioral and other symptoms across the DoD has been the Deployment Health Assessment program. Spurred in part by the experiences of Vietnam and the 1991 Gulf War, the DoD implemented this systematic screening program for service members deployed to various locations throughout the globe. The screening program consists of the Pre-Deployment Health Assessment, the Post-Deployment Health Assessment, and the Post-Deployment Health Reassessment. Together, these three components are designed to provide systematic surveillance of deployed military personnel. To date, millions of records have been collected on military personnel deployed to Iraq, Afghanistan, and various other locations throughout the world. While the effort represents a comprehensive policy
approach to understanding health and neurobehavioral problems among service members, reports have suggested that the surveillance may be falling short of providing a comprehensive look at service member health due to gaps in coverage and a variety of process-related issues (Kean, 2012).

As is likely the case with astronauts, many military personnel are reluctant to fully disclose potential health impairments to officials. Stigma has been identified as one of the primary reason for lack of disclosure among military personnel (Hoge et al., 2004). Other potential reasons for a lack of disclosure may be concerns over how mental health conditions might impact job responsibilities, or may stem from concerns about post-deployment delays in returning home as a result of disclosing mental health problems. Because of these issues, the DoD has invested resources into exploring telehealth options. The DoD telehealth civilian indicated that he and his office recognize that DoD personnel rarely ask for help when it comes to mental health and neurobehavioral problems. Recognizing this important fact, his office develops tools to deliver health care to people even when they do not actively seek it. These tools are designed to be “provider-like” in terms of resources, and many of them rely upon a cognitive behavioral therapy (CBT) framework. The tools being developed by the SME in his office—or at the very least the lessons learned by the SME in developing telehealth resources—have the potential to inform efforts by NASA to deliver telehealth solutions to astronauts on a LDSE.

Beyond these existing programs/policies, military SMEs identified a number of other changes that might be made to DoD policy as it relates to identifying and treating neurobehavioral symptoms. The Army psychiatrist noted a number of things that might improve accessibility to mental health services among deployed soldiers. Such changes might involve placing mental health providers on the front lines with soldiers in combat settings. The reasoning behind this suggestion is that soldiers may be more likely to report symptoms to experts if they know the health care provider. Consistent with the telehealth SME, the Army psychiatrist also mentioned the potential for telehealth capabilities for soldiers serving on front lines. Such tools could deliver coaching with primary care providers in environments where it is not practical for health providers to work. Both of these changes would allow for quick treatment of mental health and neurobehavioral symptoms that result from combat stressors, and would facilitate the rapid return of soldiers to normal duty. This is in contrast to treatment solutions that keep affected soldiers out of combat duty and that may lead to soldiers believing they are not fit for duty once mental health or neurobehavioral symptoms emerge. Other approaches to treating mental health and neurobehavioral symptoms in combat settings included the use of pharmacological solutions, which are much less risky than in the past, and screening programs consistent with the DoD Deployment Health Assessment program.

The Army psychologist had a range of policy recommendations for ensuring the mental and behavioral health of soldiers, with a specific focus on deployed contexts. First, proactive assessment of neurobehavioral symptoms is critical. However, as noted in other SME interviews stigma may be an issue; thus, assessment may need to be done in such a way that is not
documented in order to promote the honesty of soldiers. As noted above, resilience training programs such as CSF2 have been a key feature of Army efforts to prevent or counteract mental health and neurobehavioral symptoms. Evidence continues to emerge that such efforts are effective (Cacciopo et al., 2015; Vanhove et al., 2015). The Army psychologist offered a somewhat novel idea that has been found to be effective in the military context. Specifically, drawing on the “battle buddy” concept used in the military, the psychologist referred to the effectiveness of “sleep leaders” (Gunia, Sipos, Lopresti, & Adler, 2015). As the name implies, sleep leadership refers to the ability of leaders to foster effective sleep among his or her peers. Research shows that followers who indicated their leaders promoted sleep among his or her subordinates were more likely to experience more and higher quality sleep. The concept of a “sleep leader” may be applied to other areas such as nutrition, psychological health, etc.

In your view, what is the neurobehavioral symptom that poses the most serious threat to performance and health in long-duration spaceflight settings/of active service members?

SMEs offered a wide range of responses to this question. The NASA psychologist indicated that symptoms that impact cognition are the most serious threats to performance. The SME noted that human error will result from inattention; for example, prior to Extravehicular Activity (EVA), it is critical that the astronaut has sufficient levels of attention and concentration. Errors of omission can result from a lack of concentration. Related, two other SMEs identified sleep and fatigue as two sets of neurobehavioral problems likely to put health and performance at risk. The flight surgeon indicated specifically that sleep and fatigue are the greatest threats. Fatigue and sleep restriction are dangerous in that they both are likely to detrimentally impact performance. Notably, the flight surgeon mentioned elevated CO₂ levels as a potential source of fatigue. The NASA aerospace physician noted that the length of the mission is likely to determine which neurobehavioral symptom is likely to pose the greatest threat. On short duration missions chronic sleep problems are expected to be the cause of neurobehavioral problems such as anxiety and other emotional problems. On longer duration missions, boredom is likely to be the source of psychological problems.

This sentiment was echoed by the NASA astronaut. The astronaut indicated that the top three threats to performance and health were fatigue, boredom, and depression. While fatigue is typically conceptualized as the result of a heavy workload, the astronaut noted that fatigue may also result from boredom and tedium during the mission. Of course, sleep will be a concern, but will not be the only source of fatigue. Of note, the astronaut mentioned that sleep problems were very rare during his ISS mission, and that he took only one nap during his mission. One interesting aspect of the astronaut’s thoughts on long-duration spaceflight was his views on the role of culture during the mission. As noted, the astronaut views depression as one of the three major threats to health and performance during a mission. However, during his mission if he had experienced depressive symptoms he felt he would have been unable to communicate such issues to his Russian counterparts. Due to cultural differences, he felt that the Russian cosmonauts may have viewed him as weak if he came forward to discuss his problems.
Two other NASA SMEs pointed to interpersonal issues when discussing this topic. First, the NASA psychiatrist pointed to the irritability of crewmembers as the most important issue. In his view, the irritability of individuals will be the result of social issues and incompatibility among crewmembers. Ultimately, compatibility issues may have a sort of multiplication effect, or what may be described as a contagion effect where interpersonal problems spread through the team and introduce threats to group cohesion and team functioning. Second, the NASA aerospace physician indicated that the personalities of crewmembers may pose threats to crew cohesion and may introduce psychological issues for crewmembers. In the view of both of these SMEs, crew selection methods will be of utmost importance in order to mitigate the presence of these problems.

Military SMEs indicated many of the same threats to health and performance. For example, the VA psychologist identified sleep disturbances as a major threat to the health and performance of combat veterans. Similarly, the Air Force psychologist identified fatigue and sleep loss as two concerns of interest. For Air Force special operations, fatigue and sleep loss can be the result of both a heavy workload, but may also be the result of the routine and monotony. In this way, the views of the Air Force psychologist are consistent with the views of the NASA astronaut. The DoD telehealth professional indicated that depression was the clearest neurobehavioral symptom among combat veterans. However, sleep, frustration, and anger were all mentioned as threats to the effective functioning of combat veterans.

The primary reason for sleep disturbances in the view of the VA psychologist is hyperarousal. In a combat setting, arousal and resulting hypervigilance are adaptive strategies that allow service members to effectively identify and cope with threats. However, as the combat mission ends and the individual moves from a combat to a non-combat context, it is sometimes difficult to immediately reduce tendencies toward hypervigilance. This view is consistent with the comments of the Army psychologist who indicated attentional threat bias as a major problem among combat veterans. Attentional threat bias typically occurs among individuals with high levels of state or trait anxiety. Such individuals disproportionately focus on real or perceived threats. In the military context, where individuals may experience prolonged exposure to minor threats, or may experience a small number of more acute threats, attentional bias may occur following a mission lasting 12 to 15 months. In the long-duration spaceflight context, such research may prove very valuable as attentional biases may lead to decrements in the health and performance of crews. Thus, it is recommended that NASA conduct further research on the ways in which attentional biases may develop among long-duration crews, including understanding the sources and manifestations of such biases. Understanding such biases is particularly important given the multiphasic nature of the mission. Again, the mission is viewed to consist of three distinct phases: an initial transit to Mars, a Mars planetary mission, and a return transit to Earth. The development of threat perceptions and attentional biases during the first or second phase of a mission may jeopardize the success of subsequent phases of the mission.
Which neurobehavioral symptom do you feel that NASA/DoD has done the best job of studying and understanding? In other words, which neurobehavioral symptom do you feel is best understood?

The purpose of this question was to gain an understanding of the areas in which SMEs felt that there was sufficient research coverage of neurobehavioral signs and symptoms. Three of the NASA SMEs pointed to sleep and fatigue as the areas in which they felt there was currently a great amount of research or a firm understanding of the issues. For example, the NASA psychiatrist indicated that the volume of research on circadian rhythms and sleep/wake cycles has led to a firm understanding of the symptoms related to those issues. The SME indicated that researchers probably have the best understanding of sleep as it serves as the cornerstone for the health and performance of space crews. The NASA psychologist also indicated that sleep and fatigue were well-researched topics, and the NASA flight surgeon pointed to fatigue as the most researched topic, again due to the fact that it is, perhaps, the most important topic to understand.

The NASA astronaut pointed to vestibular and environmental issues as those that are most well-understood in spaceflight settings. The astronaut also noted that habitability issues are fairly well understood in spaceflight contexts. The aerospace physician noted that emotional and familial support is currently very good on ISS missions. Specifically, the physician lauded the use of care packages and similar methods of connecting astronauts to people on Earth. When pressed to discuss which methods would be feasible in LDSE, the physician discussed the potential use of virtual reality and time-controlled care packages (e.g., “Don’t open until your birthday”) as potential alternatives.

Among military SMEs, researchers provided a range of responses. The VA psychologist, not surprisingly, indicated that the clusters of symptoms associated with PTSD and TBI had probably been the most studied in military contexts. The Army psychologist provided a similar response when asked. Two DoD SMEs indicated that sleep-related issues were the best understood in DoD contests. First, the Army psychiatrist indicated that the study of sleep had gained traction in recent years. Interestingly, the SME noted that funding and resources aimed at the study of sleep-related issues likely increased recently because of the emerging evidence suggesting the importance of sleep, as well as the fact that it is an easily understood topic and is able to be measured objectively unlike many other problems associated with psychological and physiological health issues. The DoD telehealth expert also noted that sleep was perhaps the most well-researched topic.

Once again, the Air Force psychologist’s perspective were consistent with the views of the astronaut. Here, the Air Force psychologist perceived research to have the firmest handle on physical environmental issues. In particular, the psychologist felt that the Air Force firmly understands the various ways in which the physical environment impacts the stress experienced by airmen in the Air Force.
Which neurobehavioral symptom do you feel needs the most research? In other words, which neurobehavioral symptom do you feel is the least understood?

Once again, SMEs offered a variety of responses to this particular question. The flight psychiatrist indicated irritability and frustration tolerance as areas of need in the study of neurobehavioral symptoms. It is the view of this SME that NASA and the broader research community currently do not fully understand the idiosyncrasies of these problems. Similarly, the NASA psychologist indicated that irritability was an area of need. The psychologist also noted that decision making and concentration impairments are topics that need greater research attention.

Two NASA SMEs once again referenced the importance of interpersonal dynamics, team effectiveness, and selection issues in response to this question. The flight surgeon noted that interpersonal relations will be especially important on long-duration missions. Further complicating interpersonal issues will be the likely presence of a multi-national crew, as cultural differences have the potential to exacerbate potential interpersonal issues. The aerospace physician also mentioned the importance of crew composition on a long-duration flight. The physician emphasized the importance of getting the right people together to serve on the crew.

SMEs with a military background also offered a variety of responses. First, the VA psychologist discussed the need to understand emotion-based factors such as depression and anxiety as outcomes rather than as mediating variables. This SME also discussed the importance of better understanding how cognitive impairments might impact the effectiveness of interventions. For example, the effectiveness of CBT treatments—which rely upon the effective cognitive functioning of the individual exposed to the intervention—may be diminished among populations that are experiencing cognitive impairment as a result of physical, psychological, or interpersonal factors. While the SME answered this particular question in the context of DoD research, the lessons from this response can certainly be applied in the spaceflight context.

The Army psychiatrist pointed to anxiety and cognitive issues associated with TBI as the symptom(s) most in need of study in the DoD context. The SME noted the difficulties of how to measure associated symptoms, as well as the challenges in getting people to be forthright in their responses to various assessments. Once again, this response is directly applicable to the challenges facing NASA in its assessment of neurobehavioral signs and symptoms.

The Air Force psychologist referred to the study of interpersonal issues as an area of need, but noted the difficulty of conceptualizing and quantifying how interpersonal issues can affect neurobehavioral symptoms. The DoD telehealth specialist indicated frustration and anger as two areas of study that are needed given the sparse nature of the literature on those topics. The Army psychologist noted aggression and depressive symptoms as areas in which more research is needed.
Sources of Neurobehavioral Signs and Symptoms

SMEs were next asked about the sources of neurobehavioral symptoms in spaceflight and DoD contexts. The questions were designed to assess the neurobehavioral symptoms that might result from exposure to the various threats faced by astronauts, service members, and other personnel working in isolated and confined environments. Once again, the Kanas and Manzey (2008) classification of environmental factors, habitability factors, psychological factors, and interpersonal factors were used as a heuristic in the administration of these questions. During the interviews, respondents were provided a list of examples for each of the four general sources of neurobehavioral symptoms.

What do you see as the greatest health risk as a result of physical factors? Where is research most/least needed in this area?

Most of the NASA SMEs indicated that radiation and microgravity are the two physical factors that pose the greatest threat to crewmember health. For example, both the flight surgeon and the NASA psychiatrist noted that radiation provided the primary threat and that microgravity posed the second greatest threat. While little research has been able to discern the effects of radiation on human health and cognition over the long term, the psychiatrist expanded on the fact that very little is known about the effects of long-term microgravity. In the words of the psychiatrist, blindness could actually result from extended microgravity given how little is known at this point. The aerospace physician also noted the unknown effects of long-duration microgravity and indicated that this feature of long-duration spaceflight is probably the most important factor to understand at this point. The physician also pointed to the importance of the current one year ISS mission in informing this particular aspect of a long-duration flight. The astronaut took the view that radiation poses the greatest threat during LDSE.

The NASA psychologist also indicated radiation and microgravity but offered a bit more nuance in responding to the question. In a short-duration mission such as an ISS mission, the primary threats to health and performance are microgravity and associated vestibular issues. For example, it is believed that there will be about two weeks of adaptation, with the first two to seven days involving physiological adaptation to microgravity, vestibular issues, and adaptation to “three dimensional thinking.” After the initial four to six weeks of an ISS mission, there is a plateau in performance where many of the adaptations to space are mastered. On a long-duration mission, however, the effects of radiation are likely to pose the greatest threat. In the view of the SME there is likely to be a gradual development of neuropsychological problems that are subclinical at first, but that may gradually develop into serious neurobehavioral problems.

Not surprisingly, military SMEs were reluctant to speak to this particular question. However, a number of military SMEs did indicate that there was research being conducted on these topics in military settings.

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What do you see as the greatest health risk as a result of habitability factors? Where is research most/least needed in this area?

NASA SMEs were generally in agreement that CO$_2$ concentrations pose greatest threat to crewmember health on a LDSE. The NASA toxicologist provided critical insight into this topic by outlining the processes used by NASA and the broader research community to determine spacecraft maximum allowable concentrations (SMACs) of CO$_2$ and other toxins on board the ISS and on future exploration-class vehicles. This SME also expanded on the fact that CO$_2$ has really been at the forefront of habitability issues for the past three to five years. The flight surgeon, psychiatrist, and psychologist each also mentioned CO$_2$ as the critical habitability issue that needs to be addressed on the ISS and in the design of the spacecraft for a Mars mission. The psychologist cited the potential effects of elevated CO$_2$ on headaches and irritability, and also mentioned the potential long-term effects of CO$_2$ exposure on the health of astronauts. Importantly, the psychiatrist and the aerospace physician both communicated their confidence that the issues related to elevated CO$_2$ exposure will be solved by the time an exploration class mission vehicle is developed.

A number of other habitability issues were discussed. For example, both the astronaut and the psychologist pointed to cabin temperature as an important factor that needs to be addressed in an exploration class mission. In addition, the psychologist and psychiatrist both mentioned noise and vibration aboard the spacecraft as potential sources of neurobehavioral problems that need to be studied and addressed. As discussed in the literature review above, each of these factors has been explored to some extent in spaceflight and other analog contexts.

What do you see as the greatest health risk as a result of psychological factors? Where is research most/least needed in this area?

Two of the NASA SMEs indicated that monotony and boredom are likely to present the biggest health and performance risks. The astronaut indicated that monotony and a relatively low workload will be key threats to the health and morale of the crew. Further, the isolation of the crew and crewmembers may interact with a low workload to pose significant health and performance issues. The NASA psychiatrist indicated that monotony as a result of a lack of meaningful work may pose problems for crewmembers. Interventions to offset the detrimental effects of underwork and lack of meaningful work will need to be tailored to individual personalities. Interestingly, the SME suggested that the selection of crewmembers for this particular mission may be different from selection processes on regular ISS missions. In particular, the SME indicated that the selection of individuals who are not as driven and that are more mindful than typical astronauts may be needed. In the view of the SME, these individuals may be better equipped to handle underwork and the potential ambiguity that may stem from a lower workload.

The psychological consultant with experience in Antarctica was able to provide some interesting and applicable insight based on the observation of Antarctic crews over the years. According to
the SME, Antarctic crews, when they are involved in team-dependent work during the spring and fall months, are typically able to focus on “macro” issues such as the successful completion of tasks and the overall success of the mission. However, during winter months where the small crews are more or less isolated to living quarters, the SME indicated that crewmembers can begin to focus on micro issues such as the individual quirks of other crewmembers. Focus on such micro issues can lead to interpersonal conflict and ultimately be disruptive to the team. In exploration class missions where the transit phases are likely to involve extended periods of downtime and work underload, it may be useful to examine whether such micro issues rise to the surface and threaten to disrupt team cohesion.

In contrast to the views of the astronaut and psychiatrist, the NASA psychologist indicated that a high workload is likely to pose threats to the health and performance of crews. Consistent with other thoughts and with a substantial body of research, the SME expressed concern that a heavy workload will lead to fatigue and sleep loss. Nonetheless, the SME did recognize the potential for crews to be underutilized during the transit portion of the phase. In the view of the SME, a lack of meaningful work may decrease morale and increase apathy among the crew. The aerospace physician echoed this perspective, discussing the ways in which workload and danger will vary from being quite low during the transit missions to being quite high during the Mars surface mission.

**What do you see as the greatest health risk as a result of interpersonal factors? Where is research most/least needed in this area?**

In response to this question the psychiatrist, psychologist, astronaut, and physician all pointed to selection issues, personality differences, and leadership as the critical factors. The psychiatrist discussed the role of gender culture. However, this SME tended to focus on structural aspects of interpersonal issues such as the size of the crew and how leadership would be determined. In the opinion of this SME, NASA should look to Navy SEALs and Special Forces to develop the organizational structure for the small team. In particular, the SME feels that a hierarchical structure needs to be developed and recognized, but that redundancies need to be put in place so that the crew will be prepared to function in the case that a leader is incapacitated.

The NASA psychologist first discussed the importance of personality differences in the context of cultural and gender differences among crewmembers. The SME does not believe gender composition will be a threat, but does feel that intercultural issues will be a threat to team performance. These differences will interact with individual differences—particularly with regard to the ways in which individuals treat one another. The second primary point discussed by the psychologist is the role of leadership. Currently on ISS missions the ground crew takes much of the responsibility for leadership, but this will change during LDSE.

The astronaut first discussed the importance of leadership among the crew. The SME noted that while a commander would be good for emergencies, a leader with strong management capabilities would be needed. In addition, the astronaut was consistent with other SMEs in
saying that gender composition will likely not be a problem, but that cultural issues do have the potential to pose a problem to group cohesion and effectiveness.

The physician focused on the proper selection of personality types to produce a workable mix of individuals. Notably, the SME focused on personality traits with a specific focus on leadership. That is, might the selection of certain types of personality types produce too many leaders? Therefore, the question becomes what is the right mix of personalities? Further, how do you train leaders? Does leadership rotate? These are all questions of critical importance.

**Measures of Neurobehavioral Signs and Symptoms**

The final set of questions was designed to assess SME’s thoughts on current measures of neurobehavioral symptoms and to determine how current or future measures might be improved in terms of methodology and symptom coverage. Due to the variability in SME knowledge of the neurobehavioral assessments currently in use, some SMEs felt very comfortable discussing these issues while others did not. Therefore, we present the results of the interviews with SMEs who were comfortable responding to these questions and who elected to share their thoughts on the assessment of neurobehavioral symptoms. While a series of questions was administered, SMEs generally responded to this set of questions in the context of one broader response to the issue of measurement. Therefore, we present below the entire set of questions put forth to SMEs and then summarize the responses of each SME who chose to respond to this set of questions.

*In the spaceflight/military setting, what measure/tool is most useful or efficient in detecting neurobehavioral decrements? In your view, what are the strengths of the tool? What are the weaknesses of the tool? What methodological advances need to be made for future versions of neurobehavioral assessments? What type of tool/product would be most beneficial in documenting and assessing neurobehavioral problems in spaceflight/military settings?*

The NASA flight surgeon based the discussion around the WinSCAT, the current neurocognitive assessment tool used onboard the ISS. In the view of the SME some crewmembers don’t mind completing the WinSCAT while other crewmembers have noted that they do not like using the tool. The flight surgeon noted that if a behavioral tool is not transparent—meaning that if astronauts do not understand the purpose and rationale of the tool—then it will not be embraced by the crew. Any neurobehavioral or neurocognitive tool needs to be “quick, easy, and fun.” Another aspect of a neurobehavioral assessment is the distinction between passive versus active measures of neurobehavioral symptoms. The SME is unconvinced that passive indicators of neurobehavioral symptoms are effective. Moreover, the SME indicated that tools such as the WinSCAT have never “saved their bacon,” meaning that the WinSCAT has never been the deciding factor in whether to intervene when it appears an astronaut may be experiencing severe neurobehavioral decrements. In the end, the SME pointed to the importance of selection in the prevention of neurobehavioral symptoms: good selection techniques will eliminate the need to assess and prevent the onset of neurobehavioral symptoms.
The NASA psychologist also mentioned the WinSCAT diagnostic instrument. As it is currently configured, the WinSCAT lacks the precision to detect sub-clinical levels of neurobehavioral symptoms. In the opinion of this SME, cognitive tests need to be developed to develop clinical and sub-clinical deficits, such as when a crewmember is “running on fumes” or not performing at peak.

The NASA psychiatrist first pointed out the importance of the interaction between the therapist and the crewmember in identifying neurobehavioral and other health decrements. In the opinion of this SME, person-to-person interaction is better in this regard than a computerized tool or assessment instrument. However, the SME followed up that comment with the view that any computerized assessment must be available, quick, and easy. The tool must be easy to use for the crewmember and must provide valid, real-time assessments of neurobehavioral problems. With regard to current assessment tools, the SME indicated concern that tools do not tell them why someone may be “off.” In discussing the development of future assessment tools, the SME made clear that another game-like assessment tool is not desirable. The SME also mentioned that astronauts may stop using such assessments if they continue to be viewed as annoying, and relayed an example of an astronaut that stopped using an actiwatch due to a perceived invasion of privacy.

The NASA aerospace physician noted that peer observation may be the most effective tool in the detection of neurobehavioral problems. For example, if an individual notices a slight change in the behavior of a fellow crewmember, then that may be the most accurate way to detect neurobehavioral decrements. The SME noted the importance of a personal relationship between the crewmember and the flight surgeon so that a frank and honest discussion about crewmember health might be had. In discussing the development of new neurobehavioral tools the SME did note that crewmembers have largely been receptive to new tools and methodologies. The SME pointed to passive monitoring as a possibility for future assessments. Any advancement must be evidence based. In the end, the SME returned to the view that the personal relationship between the crewmember and the flight surgeon is critical. In the SMEs experiences as a physician, having time to spend with the patient is the most important predictor of effectively assessing potential health problems. The SME did also note that a doctor may be aboard the LDSE given that physician level care is to be provided to all crewmembers on a long-duration mission.

The astronaut with flight experience provided a number of thoughts on current and prospective tools. The SME referred to the WinSCAT and indicated that current astronauts may be unhappy with using the tool given the interface and other issues. The SME did mention the psychomotor vigilance tool (PVT) and indicated some satisfaction with that tool. In the end, the astronaut encouraged creativity in the development of any tool and recommended an assessment that makes use of a video-game like interface. In particular, a 20 minute video game that was able to assess the various neurobehavioral symptoms of interest would be very intriguing. In support of person-to-person assessment methods, the astronaut did mention that medical consultations were very helpful and beneficial during spaceflight.
Military SMEs provided a variety of perspectives on the development of neurobehavioral assessments. The VA psychologist began the discussion by emphasizing the importance of construct selection when developing a battery of neurocognitive or psychological tools. Using the ANAM as an illustration, the SME noted that its electronic delivery method is very efficient and convenient. However, the sole reliance on a computerized modality may introduce bias in the results of the assessment. In particular, by relying exclusively on tests that use psychomotor skills, the results of the assessment may result in one “psychomotor factor” to use the language of factor analysis. Alternatively, the SME recommended using a multi-method approach to assessing neurobehavioral symptoms, as doing so may more evenly spread the error due to measurement method across individuals. Similarly, the presentation of stimuli in neurobehavioral assessments should be multi-modal such that audio cues are used in conjunction with visual cues, which are currently the primary method in which stimuli are presented.

The Army psychologist responded to this set of questions by first discussing the importance of tapping into a variety of constructs in the development of a neurobehavioral assessment tool. The SME noted that it would be impossible for one battery to cover every possible neurobehavioral symptom. While the SME was reluctant to discuss the ANAM and the DANA, it was noted that both tools were developed with brain injuries in mind, so that there may be limited utility in applying these tools in a spaceflight context.

The Air Force psychologist provided a number of thoughts on the development of a neurobehavioral tool. First, the ANAM and similar tools were designed to assess symptoms of TBI, and are therefore not useful in the spaceflight context. However, the SME did concede that such tools may be useful in the assessment of radiation exposure symptoms. Alternatively, the SME suggested that peer ratings may be the best way to assess neurobehavioral changes in astronauts. Of course, peer ratings would require that individuals need to be trained on the signs and symptoms that might indicate the presence of neurobehavioral problems.

Summary

The wide range of SMEs and the opinions offered by them do not contribute to a simple summary of responses to the interview questions. Often, though the perspectives of NASA and DoD SMEs were similar, the rationale behind responses was slightly different. Not surprisingly, DoD SMEs discussed research conducted in the context of military combat experiences, where acute stressors are highly salient and where TBI and PTSD are common afflictions. Alternatively, NASA SMEs focused on the sources of stress commonly seen on ISS missions, or that are expected to occur during LDSE. In such contexts, acute stressors are less likely to occur, whereas more mundane stressors are likely to impact neurobehavioral performance.
In general, the information offered by SMEs was consistent with much of the research on neurobehavioral functioning in extreme environments. Specifically, sleep loss, fatigue, and interpersonal issues were viewed as threats to healthy functioning across contexts. Each SME brought a unique perspective on ways in which to identify and measure neurobehavioral outcomes, as well as countermeasures to prevent or mitigate the presence of them. The recommendations of the SMEs have been thoughtfully considered and, where our team feels applicable, have been included in the recommendations put forth at the outset and at the conclusion of this report.
Objective 4. Evaluate the validity and practical efficiency of existing scales to assess neurobehavioral issues.

An excellent review of the cognitive measures used in spaceflight and analog settings was recently provided by Strangman, Sipes, and Bevin (2014). The diversity of measures reviewed precluded the authors from formally meta-analyzing the cognitive effects of working in spaceflight and analog contexts. Further, the authors did not put forth critical reviews of the various cognitive measures used in such settings. The review did demonstrate, however, the wide variability in the apparent effects of spaceflight and ICE settings on cognitive functioning. This variability seems to be consistent with the heterogeneity of findings presented in the literature reviewed in this report.

In Appendix A below, a list of commonly-used batteries, questionnaires, and methods used in spaceflight, military, and ICE research is presented. The tools presented include many of those discussed throughout this report. Other tools presented include those used in one or a few studies, but that may have the potential to be utilized as part of a broader set of tools to assess neurobehavioral signs and symptoms during long-duration spaceflight. Basic features of each instrument are provided, along with a general comment on each, and relevant citations in the literature. The list is not intended to be comprehensive. Rather, we chose to focus on batteries that have been used widely in the literature, or those tools that we felt might provide useful methods with which to assess neurobehavioral symptoms in spaceflight.

One of the overriding features of neurobehavioral assessment is the lack of standardization in the tools to assess neurobehavioral outcomes in various settings. Indeed, in previous analyses we have noted the wide heterogeneity in the tools used in ICE settings, as well as the outcomes examined in studies in ICE settings (Vanhove, Herian, Harms, Luthans, & DeSimone, 2014). While some tools such as the ANAM have been used in a wide range of contexts, and serve as the basis for systematic efforts to track neuropsychological problems among service members and veterans (Vasterling et al., 2006a), the development of a singular tool to measure symptoms has been hampered by the varied ways in which the tool has been employed (Friedl, Grate, & Proctor, 2007). For example, Short, Cernich, Wilken, & Kane (2007) noted that, “While the ANAM system is composed of over 30 tests, only a few have been used on a routine basis” (p. S66). The non-systematic use of the instrument precludes a comprehensive understanding of the battery and its utility in military and other extreme contexts.

With newer tools such as the DANA and Cognition, the evidence base is relatively low at this point. The DANA has been employed in a number of contexts that are applicable to LDSE missions. For example, the tool has been use to assess cognitive function in high altitudes (Subudhi et al., 2014). That research provided evidence that the tool is sensitive enough to detect changes in cognitive function among expeditioners at high altitude. With regard to cognition, even less evidence exists. However, it is likely that the tool will also prove sensitive as its constituent parts are similar in nature to the cognitive tests employed in the ANAM and the
DANA. At this point, though, it is difficult to make an assessment of the predictive validity of the tool.

Other tools such as the POMS have been used widely in the literature on ICE environments, and a fairly wide evidence base exists. Further, the dimensions of symptoms covered by the POMS align fairly well with the neurobehavioral symptoms that are the focus of this report. However, the self-report nature of the tools limits its utility given the known problems with self-report measures among high-achieving individuals, as well as the anecdotal reports from SMEs that self-report measures are not likely to be embraced by astronauts.

Below, we provide a list of tests to assess neurobehavioral outcomes. This list identifies potential tests that may be used in spaceflight settings for specific outcomes. Some of the tests are included in broader test batteries described throughout this report. For example, the Balloon Analog Risk Test is included in the Cognition battery. Other tests have been used sporadically in ICE and spaceflight settings. To the right of the table, we draw on the Oxford Centre for Evidence-Based Medicine Levels of Evidence so that readers might better understand the extent to which these tests have been used in the literature. The levels of evidence range from 1-5, with Level 1 indicating the highest level of evidence and Level 5 indicating the lowest level of evidence. As the table shows, the tests range from an evidence Level of 2 to 4. It is important to note that only a few of these tests have actually been used in ICE or spaceflight environments; thus, the evidence levels are primarily based on research conducted in non-ICE and non-spaceflight settings.

<table>
<thead>
<tr>
<th>Test</th>
<th>Potential Outcome(s) Assessed</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balloon Analog Risk</td>
<td>Making decisions</td>
<td>3</td>
</tr>
<tr>
<td>Deployment Stress Inventory</td>
<td>Anger</td>
<td>4</td>
</tr>
<tr>
<td>Dot Probe Task</td>
<td>Attention/Threat Biases</td>
<td>2</td>
</tr>
<tr>
<td>Eye tracking</td>
<td>Attention/Threat Biases; Boredom; Fatigue</td>
<td>2</td>
</tr>
<tr>
<td>Facial recognition</td>
<td>Fatigue; Irritable; Frustration tolerance</td>
<td>4</td>
</tr>
<tr>
<td>functional Near Infrared Spectroscopy</td>
<td>Attention/Threat Biases; Boredom</td>
<td>2</td>
</tr>
<tr>
<td>Lexical/text analysis</td>
<td>Anger; Depressed/sad; Frustration tolerance</td>
<td>4</td>
</tr>
<tr>
<td>Mathematical Processing Test</td>
<td>Cannot get organized/finish things</td>
<td>3</td>
</tr>
<tr>
<td>Physiological measures (cortisol, heart rate, skin conductance)</td>
<td>Boredom</td>
<td>3</td>
</tr>
<tr>
<td>Psychomotor Vigilance Test</td>
<td>Fatigue</td>
<td>3</td>
</tr>
<tr>
<td>Self-report sleep quantity/quality</td>
<td>Fall/stay asleep</td>
<td>3</td>
</tr>
<tr>
<td>Sternberg Memory Search</td>
<td>Forgetfulness (memory)</td>
<td>4</td>
</tr>
<tr>
<td>Thyroid function; Plasma Markers</td>
<td>Anxiety/tension</td>
<td>4</td>
</tr>
<tr>
<td>Virtual Reality Stroop Test</td>
<td>Attention/Threat Biases</td>
<td>4</td>
</tr>
</tbody>
</table>
Objective 5: Provide recommendations for future work in this area.

A Taxonomy of Neurobehavioral Signs and Symptoms

Recommendation 1: A comprehensive approach to understanding neurobehavioral decrements is needed.

The Exploration Medical Condition List (EMCL) serves to guide medical efforts to ensure the safety and effectiveness of crews who will embark on asteroid redirect and Mars missions. In the most recent iteration of this living document, NASA has identified anxiety, depression, and insomnia as the neurobehavioral symptoms of interest for an exploration class mission. The EMCL also lists “behavioral emergency” as a medical condition of interest. These medical conditions have been identified as potential threats to the health and performance of crews on exploration missions. Absent from the EMCL are a number of cognitive and affective disorders that have the potential to affect crew health and performance on long-duration missions.

To develop a comprehensive checklist of neurobehavioral signs and symptoms likely to develop in long-duration space exploration (LDSE), the U.S. Department of Defense Neurobehavioral Symptoms Inventory (NSI) serves as a useful starting point. The NSI is a 22 item inventory of cognitive, emotional, somatic/sensory, and vestibular symptoms thought to be indicative of brain injury. While developed to assess neurobehavioral decrements among service members with suspected brain injuries, the NSI provides sufficient coverage of the neurobehavioral symptoms expected to impact astronauts on a LDSE. It is recommended that NASA and BHP draw on the cognitive and emotional variables assessed by the NSI in the development of a neurobehavioral conditions checklist.

As part of the current effort, an operational assessment consisting of interviews with subject matter experts from both NASA and various branches of the U.S. military was conducted. The results of the operational assessment suggest that symptoms such as attentional biases, irritability/anger, and boredom may also be critical to assess during the course of a mission. Each of these factors has the potential to negatively impact the performance of individuals and crews. Furthermore, the development of attentional biases may also negatively impact the uptake and use of psychological countermeasures, particularly those that rely upon cognitive behavioral therapies to mitigate the presence of psychological decrements.

Thus, in addition to the core set of neurobehavioral conditions assessed by the NSI, these conditions should also be incorporated into the development of a checklist. Table 5 below presents a checklist of neurobehavioral symptoms that have the potential to develop during LDSE. The symptoms in the column labeled NSI Symptoms are those derived from the NSI. The symptoms listed in the Additional Symptoms column are those that were identified through the literature review and operational assessment that are included as part of this report.
### Table 6. Checklist of Neurobehavioral Conditions in Long-Duration Space Exploration

<table>
<thead>
<tr>
<th>Factor</th>
<th>NSI Symptoms</th>
<th>Additional Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive</td>
<td>Cannot get organized/finish things</td>
<td>Attention/Threat Biases</td>
</tr>
<tr>
<td>Cognitive</td>
<td>Forgetfulness (memory)</td>
<td></td>
</tr>
<tr>
<td>Cognitive</td>
<td>Making decisions</td>
<td></td>
</tr>
<tr>
<td>Cognitive</td>
<td>Poor concentration</td>
<td></td>
</tr>
<tr>
<td>Emotional</td>
<td>Anxiety/tension</td>
<td>Anger</td>
</tr>
<tr>
<td>Emotional</td>
<td>Depressed/sad</td>
<td>Boredom</td>
</tr>
<tr>
<td>Emotional</td>
<td>Fall/stay asleep</td>
<td></td>
</tr>
<tr>
<td>Emotional</td>
<td>Fatigue</td>
<td></td>
</tr>
<tr>
<td>Emotional</td>
<td>Irritable</td>
<td></td>
</tr>
<tr>
<td>Emotional</td>
<td>Low frustration tolerance</td>
<td></td>
</tr>
</tbody>
</table>

It is likely that most of these symptoms will not reach clinical levels. That is, some symptoms may exist, but likely not at debilitating levels. Nonetheless, it will be important for NASA and the broader scientific community to develop effective methods to: 1) identify the presence of such symptoms among crewmembers, and 2) examine correlational evidence between these symptoms and crewmember health and performance. Consequently, additional research on this set of symptoms in spaceflight and analog settings may need to be carried out.

**Measuring Neurobehavioral Conditions**

**Recommendation 2:** A suite of neurocognitive tests, psychological questionnaires, and clinical assessments should be developed to assess the neurobehavioral symptoms likely to develop in long-duration space missions.

Subject Matter Experts (SMEs) interviewed as part of the operational assessment made it clear that a comprehensive suite of tools to assess neurobehavioral symptoms will be critical to ensuring the health and performance of crews on LDSE. Consistent with this view, Cowings et al. (2007) advocated a multi-indicator approach to assessing individual differences in adaptation to spaceflight. Toward the development of such a multi-indicator approach, it is important to take a critical look at existing instruments to determine whether such instruments provide adequate coverage of potential neurobehavioral symptoms that might impact health and performance in LDSE.

Existing neurobehavioral assessments such as the Windows Spaceflight Cognitive Assessment Tool (WinSCAT), and next generation neurocognitive assessments such as Cognition (NASA Techport, 2015) focus heavily on the cognitive aspects of neurobehavioral functioning. While such tools adequately assess cognitive impairments, they do little to detect the presence of emotional symptoms such as anxiety and depression.
Therefore, neurobehavioral assessment platforms must be developed so that emotional symptoms are assessed alongside cognitive impairments. Ideally, emotional disorders would be assessed clinically, through a thorough assessment by a flight surgeon. However, in a long-duration spaceflight context, clinical assessments by flight surgeons will be impractical due to communication delays and the lack of real-time communication with ground crews (unless, of course, there is one on board). Therefore, the use of non-invasive assessment strategies may be necessary. For example, anxiety disorders may be assessed through the use of eye tracking technologies that are able to detect attentional threat bias, a common indicator of anxiety in high stress populations (Bar-Haim et al., 2007). Further, the use of lexical or text analysis may assist in the detection of depressive symptoms (P. Lieberman et al., 2005).

**Recommendation 3: A multi-method approach should be taken in the development of a neurobehavioral assessment tool.**

A number of SMEs expressed concern that current neurocognitive tools such as the Automated Neuropsychological Assessment Metric (ANAM), the WinSCAT, and Cognition all rely exclusively upon an electronic delivery system. In the view of at least one of the SMEs, overreliance on cognitive assessment delivered through the electronic format may bias results in favor of individuals high in cognition and that are more comfortable completing tasks using electronic formats. SMEs indicated that electronically-delivered cognitive assessments should be supplemented with psychological questionnaires. While it is commonly believed that crewmembers do not enjoy self-report psychological questionnaires, the use of such tools may need to be considered in order to vary the methodology with which neurobehavioral assessments are delivered. Adopting such an approach may more evenly distribute the measurement error associated with delivery mode.

Furthermore, to the extent that electronic assessments are used (e.g., in the measurement of reaction times and similar metrics), these should include both visual and audio cues to prompt users. The exclusive use of visual cues—as is the case in most neurocognitive tools—may bias results toward individuals who are predisposed to favor this particular methodology. Incorporating the use of audio cues in addition to visual cues may help provide a more balanced assessment tool. The use of audio cues may also allow researchers to assess the presence of somatic and sensory decrements that are associated with emotional and cognitive assessments. Related, the use of vibration as a cue may also prove useful given likely psychomotor and vestibular issues that will be experienced in spaceflight settings.

Recent advancements in the use of virtual reality may also hold potential for the future of neurobehavioral assessment in LDSE settings. For example versions of the Stroop Test that use virtual reality have been found to be effective at detecting decrements in executive function (Armstrong et al., 2013). Additional research suggests that this line of research holds great potential for neurobehavioral assessments (Parsons, Carlew, & Sullivan, 2015). Given the potential use of virtual reality in other aspects of long-duration spaceflight, NASA may want to
leverage the existence of virtual reality platforms in space by exploring the potential application of such technologies.

**Recommendation 4: Non-invasive metrics of neurobehavioral disorders (e.g., eye tracking, facial recognition, voice recognition, text analysis) should be part of any suite of neurobehavioral assessments.**

A common criticism of current neurobehavioral assessments is the existence of learning effects (e.g., De la Torre et al., 2014). Furthermore, research has demonstrated the presence of ceiling effects on commonly used neurocognitive assessment tools in spaceflight settings (Cowings et al., 2007). This evidence is in line with Hockey and Sauer’s observation that “performance decrements are often difficult to detect in highly-motivated subjects, because of a compensatory protection of primary task requirements through increased effort” (1996, p.312).

Beyond methodological limitations to commonly-used assessment methods, anecdotal evidence provided by SMEs during the operational assessment suggests that astronauts sometimes tire of taking cognitive tests such as the WinSCAT. A practical way to address these limitations is the incorporation of non-invasive assessment techniques. The use of such methods will allow for the assessment of a wide variety of neurobehavioral decrements in a way that places minimal burden on the crew. Table 6 presents a set of suggested tests derived from the literature review and operational assessment in the present report.

As the table shows, we recommend a combination of neurocognitive tests, psychological assessments, and clinical approaches to assessing the neurobehavioral conditions likely to develop in spaceflight and other ICE settings. The assessments include both direct and non-invasive methods for assessing neurobehavioral decrements. In some cases, neurobehavioral symptoms can be assessed through both direct and non-invasive measures.
### Table 7. Multi-method measurement of Neurobehavioral Symptoms in Long-Duration Space Exploration

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Direct Measurements/ Psychological Tests</th>
<th>Non-invasive Measurements/ Non-Psychological Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention/Threat Biases</td>
<td>Tests such as dot probe task; Virtual Reality Stroop Test</td>
<td>Eye tracking; functional Near Infrared Spectroscopy</td>
</tr>
<tr>
<td>Cannot get organized/finish</td>
<td>Tests such as Mathematical Processing Test</td>
<td></td>
</tr>
<tr>
<td>Forgetfulness (memory)</td>
<td>Tests such as Sternberg Memory Search</td>
<td></td>
</tr>
<tr>
<td>Making decisions</td>
<td>Tests such as Balloon Analog Risk</td>
<td></td>
</tr>
<tr>
<td>Poor concentration</td>
<td>Tests such as Visual Object Learning</td>
<td></td>
</tr>
<tr>
<td>Anger</td>
<td>Self-report assessment such as on the Deployment Stress Inventory</td>
<td>Lexical/text analysis</td>
</tr>
<tr>
<td>Anxiety/tension</td>
<td>Validated clinical instruments; Assessment from flight surgeon</td>
<td>Thyroid function; Plasma Markers</td>
</tr>
<tr>
<td>Boredom</td>
<td></td>
<td>Physiological measures (cortisol, heart rate, skin conductance); Eye tracking; functional Near Infrared Spectroscopy</td>
</tr>
<tr>
<td>Depressed/sad</td>
<td>Validated clinical instruments; Assessment from flight surgeon</td>
<td>Lexical/text analysis</td>
</tr>
<tr>
<td>Fall/stay asleep</td>
<td>Self-report sleep quantity/quality</td>
<td>Actigraph monitors</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Psychomotor Vigilance Test</td>
<td>Eye tracking; Facial recognition</td>
</tr>
<tr>
<td>Irritable</td>
<td></td>
<td>Facial recognition; Lexical/text analysis</td>
</tr>
<tr>
<td>Low frustration tolerance</td>
<td></td>
<td>Facial recognition; Lexical/text analysis</td>
</tr>
</tbody>
</table>

**Recommendation 5: Self-awareness tools should be a part of any neurobehavioral assessment tool.**

SMEs suggested that neurobehavioral assessments should include a self-awareness or feedback component. Such a feature serves two purposes. First, a self-awareness feature allows users to see the areas of neurobehavioral performance in which they excel as well as those areas on which they may need improvement. Self-awareness may help in the application of countermeasures and interventions designed to mitigate the effects of neurobehavioral symptoms. A prime example of this is the U.S. Army’s Comprehensive Soldier and Family Fitness (CSF2) program, which utilizes the Global Assessment Tool (GAT) to track the psychological health and well-being of U.S. soldiers. Upon completion of the GAT soldiers are provided with immediate feedback. This is believed to aid in the effectiveness of psychological interventions in place in the Army by giving participants greater insight into their own cognitions and emotions as well as providing a common language to help make meaning of their experiences. Notably, instruments being developed by NASA such as Cognition provide real-time feedback to users upon completion.

Second, self-awareness tools may also help contribute to uptake among long-duration crewmembers. That is, multiple SMEs indicated that astronauts are more likely to utilize an assessment tool if they understand its purpose and are able to incorporate information from it in their day-to-day operations.
Sources of Neurobehavioral Signs and Symptoms

Recommendation 6: According to SMEs, radiation, microgravity, and CO₂ pose the greatest threats to neurobehavioral performance and should continue to be examined.

While these risk factors were identified by SMEs as the most important to study, these factors are also among the most difficult to study in an operational environment. Animal models that seek to study the effects of radiation and microgravity are limited in their generalizability to humans. While CO₂ was identified as a major threat by a number of SMEs, others had confidence that the threat of CO₂ exposure would be mitigated through the design of the spacecraft that will take humans to Mars. Current and planned year-long missions will likely be critical in contributing to the understanding of these factors upon neurobehavioral conditions.

Other environmental and habitability factors will also be important to examine. The literature suggests that temperatures may impact a variety of outcomes, including both cognitive and emotional symptoms. Research suggests that extreme cold appears may increase arousal, and therefore promote cognitive performance; extreme heat appears to have detrimental impacts upon cognitive performance. This research has important implications given the environmental conditions that will face crewmembers on the Mars surface. Noise and vibration from the spacecraft have been identified as potential risk factors for emotional and cognitive outcomes, and extant research provides some evidence that this may be the case. However, interviews with SMEs suggest that most SMEs do not view these factors as high-level risks. Light/dark cycles have important implications for circadian rhythms and ultimately sleep and fatigue. Therefore, the lighting used on the spacecraft and in the habitat on the surface of Mars will be critical in maintaining the circadian rhythms of crewmembers. However, much research on this topic has been conducted and few SMEs viewed lighting research as a crucial area of need.

Recommendation 7: The impact of social dynamics upon cognitive outcomes needs to be more fully researched and understood.

As indicated by the comprehensive literature review, and as discussed by multiple SMEs, there is relatively little research examining how interpersonal factors might impact cognitive outcomes. Rather, much of the research in this area has focused on the relationship between interpersonal relations and emotional symptoms. Understanding how interpersonal relationships impact cognitive outcomes may broaden our understanding of neurobehavioral signs and symptoms in the context of a long-duration space mission.

As noted by Kanas and Manzey (2008), interpersonal issues among crewmembers on a long-duration mission might include tension, withdrawal, or scapegoating. These issues, when experienced in a prolonged manner may have the potential to impact cognitive functioning as individuals draw on cognitive resources to deal with the perceived threats that interpersonal issues might cause. Controlled laboratory studies that manipulate interpersonal issues likely to develop onboard a long-duration mission, and that subsequently assess cognitive functioning of
individuals exposed to such interpersonal issues, may yield useful information about the effects of social dynamics on a Mars mission.

It is also possible that social interactions can produce contagion effects, whereby positive or negative emotions diffuse through a small group (e.g., Barsade, 2002). The diffusion of emotions can be driven by a key influencer within the group. Emotional diffusion can ultimately reach a tipping point where team performance is enhanced or degraded. To date, little is known regarding the ways in which emotional factors might spread through a small group in an ICE setting. Future research might help better understand this potentially critical source of neurobehavioral conditions.

**Recommendation 8: The development of a neurobehavioral checklist must recognize the multiphasic nature of a mission to Mars.**

A Mars mission will proceed in three distinct phases. Phase 1 will involve the transit from Earth to Mars. This phase will involve many of the space travel-related threats that have been considered in the literature. Phase 2 will take place on the surface of Mars. Here, the crew will likely undertake a high workload in a relatively unknown environment. Phase 3 will involve the return transit from Mars to Earth. Again, many of the threats related to spaceflight will be present during this phase. Between each mission phase is a transition point where crewmembers will have to adjust both physiologically and psychologically to different levels of gravity, light/dark cycles, etc. At each phase of the mission, the sources of the threats to crewmember neurobehavioral health are distinct. Therefore, the development of a neurobehavioral conditions list will need to account for the fact that particular neurobehavioral conditions will be more likely at some phases of the mission than at others.
References


Koga, K. (2000). Gravity cue has implicit effects on human behavior. Aviation, Space, & Environmental Medicine, 71 (9S), A78-86.


Appendix A. Brief Review of Cognitive Batteries and Psychological Tests

Test Batteries

Name of Battery: Windows Spaceflight Cognitive Assessment Tool (WinSCAT)

Description: The WinSCAT is the primary neurocognitive assessment tool used onboard the ISS. According to Kane et al. (2005), the instrument was designed to be sensitive to changes in neurocognitive status resulting from environmental stressors; was designed to take no longer than 15 minutes to complete; had to be available; had to be interpretable by flight surgeons and crews; needed to measure performance efficiency, including speed and accuracy; and had to meet ISS requirements.

What is measured: The tool utilizes: a mathematical processing test; a running memory continuous performance test; a delayed matching to sample test; a code substitution test; and a code substitution delayed recognition test.

Comments: The battery is based on the ANAM, a tool which has been used and validated in a variety of DoD settings. The operational assessment conducted as part of the present study revealed that astronauts may not enjoy the test. It is unclear whether the dissatisfaction is due to the test itself, or the procedures that dictate its use.

Sources:


Name of Battery: Automated Neurocognitive Assessment Metrics (ANAM)

**Description**: Battery of tests designed to assess cognitive decrements in various populations. Originally designed to assess changes in healthy individuals undergoing environmental challenges (Kane, Roebuck-Spencer, Short, Kabat, & Wilken, 2007), the tool has increasingly been used to assess cognitive changes in a variety of populations. Of particular relevance to the present work, the ANAM has been used to assess TBI symptoms in military populations, and served as the basis for WinSCAT, the primarily neurocognitive assessment instrument used on the ISS. The ANAM is delivered electronically.

**What is measured**: The ANAM measures cognitive performance along five dimensions: attention, concentration, decision-making, memory, processing speed, and reaction time.

**Comments**: Provides an efficient method for delivering an assessment of neurocognitive performance. Appears to be much variation in the extent to which the ANAM predicts outcomes of interest to the DoD. SMEs with knowledge of the battery indicated in the operational assessment that an initial lack of validity evidence may have undercut the legitimacy of the measure. Further, it has never been assessed in a clinical setting.

**Sources**:


Special issue of *Archives of Clinical Neuropsychology*, Vol.22 (supplement 1), contains a number of articles on the use of the ANAM in a wide variety of settings.
Name of Battery: Defense Automated Neurobehavioral Assessment (DANA)

**Description:** The DANA is among the newest DoD assessments for neurobehavioral and neuropsychological symptoms (see Lathan, Spira, Bleiberg, Vice, & Tsao, 2013). The DANA consists of three test batteries: the DANA Rapid (5 minutes), the DANA brief (15 minutes), and the DANA standard (45 minutes). The tests consist of a combination of neurocognitive and psychological tests that are delivered electronically using an Android operating system. In all, eight cognitive tests and seven psychological questionnaires were selected for use in the DANA.

**What is measured:** Cognitive Tests include Simple Reaction Time; Procedural Reaction Time; Go/No-Go/ Code Substitution Simultaneous; Spatial Discrimination; Code Substitution Delayed; Matching to Sample; and Sternberg Memory Search. Psychological tests include Patient Health Questionnaire; Primary Care PTSD Screen; Insomnia Screening Index; Combat Exposure Scale; Pittsburg Sleep Quality Index; PTSD Checklist-Military Version; and Deployment Stress Inventory. More detailed information on each test is presented by Lathan et al. (2013).

**Comments:** Preliminary evidence from Lathan et al. (2013) suggests that the DANA has acceptable test-retest and external validity and also shows convergent validity with the ANAM. More recent evidence provides evidence that the DANA can detect neurocognitive decrements among those with recent concussions (Spira, Lathan, Bleiberg, & Tsao, 2014) and among individuals who experience rapid ascent to high altitudes (Subudhi et al., 2014). Test assesses anger through self-report methods. There exists relatively little validity evidence to date.

**Sources:**


Name of Battery: Individualized Real-Time Neurocognitive Assessment Toolkit for Space Flight Fatigue (Cognition)

Description: The battery of tests is designed to provide real-time neurocognitive assessment and feedback in a spaceflight setting. The tool seeks to provide a more comprehensive and sensitive assessment tool than is currently available upon the ISS. The battery takes 20-30 minutes to complete.

What is measured: Motor Praxis (sensory-motor ability); Visual Object Learning (visual object learning and memory); Fractal 2-Back (Attention and working memory); Abstract Matching Task (Abstraction); Line Orientation (Spatial orientation); Emotion Recognition (Emotion recognition); Matrix Reasoning (Abstract reasoning); Digital Symbol Substitution (Complex scanning, visual tracking, attention); Balloon Analog Risk (Risk decision making); Psychomotor Vigilance (Vigilant attention and psychomotor speed).

Comments: This measure is under development but holds great promise to serve as an important component of any suite of neurobehavioral assessments. The focus on risk is a novel addition that aligns with the suggestions of DoD SMEs that suggested risk taking be assessed through neurobehavioral instruments.

Sources: http://www.nasa.gov/mission_pages/station/research/experiments/1256.html
Name of Battery: MiniCog Rapid Assessment Battery

Description: The MiniCog is a software system that presents simple cognitive tests to individuals, such as astronauts, at risk for cognitive impairments due to environmental or occupational hazards. Originally developed to be implemented through the use of a personal digital assistant (PDA), the test is now delivered on machines with Windows operating systems.

What is measured: Attention (divided attention, selective attention: vigilance, selective attention: filtering); Memory (verbal working memory, spatial working memory); Reasoning (visualization, logic, information ordering).

Comments: According to Criteriacorp, the holders of the license, the tool has been utilized in a variety of settings and has proven to be predictive of performance in those settings. There appears to be a general lack of validity evidence with regard to the MinCog Rapid Assessment Battery.

Sources:

Name of Battery: Advisory Group for Aerospace Research and Development Standardized Tests for Research with Environmental Stressors (AGARD STRES)

Description: The AGARD STRES battery is a collection of standardized performance tasks designed to assess psychomotor and cognitive performance in spaceflight settings. Using the AGARD STRES, research has shown that short-term memory and logical reasoning were not impacted by spaceflight, but that tracking performance was negatively impacted by spaceflight. The results suggest that the AGARD STRES can detect decrements in psychomotor functioning as a result of spaceflight.

What is measured: Single Reaction Task (attention and vigilance); Memory Search Task (working memory and short term memory); Grammatical Reasoning Task (processing of complex mental procedures); Unstable Tracking Task (coordination, sensorimotor function); Dual Task (reserve capacity under pressure).

Comments: AGARD STRES has been used to detect stress in operational settings. Research has generally shown that psychomotor and cognitive performance is degraded during the very early and latter stages of the mission.


Name of Battery: World Health Organization Neurobehavioral Core Test Battery (WHO NCTB)

Description: The WHO NCTB was designed to assess neurotoxicity in occupational settings. As noted by Anger (2003), “The WHO group selected seven of the most widely used tests in human behavioral neurotoxicity research that were judged to be sensitive to marker neurotoxic chemicals—lead, mercury, and carbon disulfide.”

What is measured: Digit symbol (psychomotor performance); digit span (attention); Benton visual retention (perception and memory); pursuit aiming (psychomotor); simple reaction time; Santa Ana (dexterity); and the POMS.

Comments: Some tests are difficult to score reliably. Test was originally administered on separate machines rather than as a suite of tests on a computer system.

Sources:

Name of Battery: Naval Medical Research Institute Performance Assessment Battery (NMRI PAB)

Description: The NMRI PAB was designed to measure the impact of military stressors upon the cognition and performance of service members. Recognizing that military personnel encounter extreme environments, are exposed to dangerous toxins and other elements, and are required to wear protective gear that is restrictive, researchers sought to develop a test that could detect the detrimental effects of each of these factors.

What is measured: Matching-to-sample test; Stroop test; Simple reaction time; Serial Addition/Subtraction Task; Grammatical Reasoning Task; the Manikin test; the Pattern Comparison tests; the Repeated Acquisition of Response Sequences Task; and the Visual Scanning Test.

Comments: Very little information about this battery exists in the literature.

Sources:

Individual Scales/Tools/Methods

Name of Scale/Tool: Neurobehavioral Symptoms Inventory (NSI)

Description: The NSI is a 22 item self-report inventory used to detect the presence of neurobehavioral symptoms in individuals suspected of suffering TBI. Developed for use by the U.S. DoD., the tool has been used extensively in defense settings. Considerable factor analytic work has been conducted, with most research demonstrating a three or factor solution.

What is measured: According to Vanderploeg et al. (2015) the NSI measures the following four factors of neurobehavioral health: Cognitive (organization and finishing tasks, forgetfulness, decision making, concentration); Emotional (anxiety/tension, depression/sadness, sleep, fatigue, irritability, frustration tolerance); Somatic/Sensory (appetite, headache, hearing, light sensitivity, nausea, noise sensitivity, numbness/tingling, taste/smell, vision); and Vestibular (balance, coordination, dizziness).

Comments: The NSI provides adequate coverage of the neurobehavioral symptoms likely to face LDSE astronauts. Thus, it was selected to serve as the basis of the taxonomy used in the present report.

Sources:


Name of Scale/Tool: Brunel Mood Scale (BRUMS)

Description: The NSI is a 22 item self-report inventory used to detect the presence of neurobehavioral symptoms in individuals suspected of suffering TBI. Developed for use by the U.S. DoD., the tool has been used extensively in defense settings. Considerable factor analytic work has been conducted, with most research demonstrating a three or factor solution.

What is measured: The self-report BRUMS measures anger, confusion, depression, fatigue, tension, and vigor. Items are rated on a five-point scale that ranges from 0-4.

Comments: The BRUMS is an adapted version of the Profile of Mood States (POMS) questionnaire that is commonly used in analog settings. Results of an analysis by Pedlar et al. (2007) demonstrated that the BRUMS can be used to detect changes in mood in relation to sleep loss and a variety of operational variables.

Sources:

Name of Scale/Tool: Discursive Analysis

**Description:** Objective of the study by Blanchet, Noel-Jorand, & Bonaldi (1997) was to examine whether linguistic markers were capable of indicating the psychological state of individuals in an extreme environment (Mt. Sajama). Using established methods to analyze speech, results showed that speech patterns revealed depressive symptoms among mountaineers. The findings could indicate a lack of adaptation by mountaineers, or could simply point to latent depressive states among the mountaineers.

**What is measured:** Structured and semi-structured interviews with participants were used to elicit verbal responses to a set of probes. Verbal responses were coded using propositional discourse analysis.

**Comments:** Study provides a non-invasive method for detecting affective states among individuals in extreme environments. Lack of real time analysis of verbal data limits applicability in LDSE context.

**Sources:**

Name of Scale/Tool: Speech Monitoring of Cognitive Deficits and Stress

Description: Study by P. Lieberman et al. (2005) examined vowel duration and speech motor sequencing errors in response to cognitive fatigue in a group of study participants on Mount Everest. Results of the study showed that metric was reliable indicator of fatigue and basal ganglia impairment in mountain climbers.

What is measured: Voice recordings were used to assess speech patterns.

Comments: Non-invasive measure of fatigue and basal ganglia impairment. While the P. Lieberman et al. (2005) study relied upon analysis of voice recordings, real-time measures will be needed for practical use on LDSE. Such an application has great potential to serve as an additional measure of depression or fatigue in LDSE crewmembers.

Sources:

Name of Scale/Tool: Virtual Reality Stroop Test

Description: Virtual Reality Stroop Test presents test stimuli during a virtual reality military convoy with simulated combat threats.

What is measured: Test examines the impact of environmental stimuli on cognitive performance/executive function.

Comments: Initial tests demonstrate convergent validity with existing metrics including the ANAM. Method holds great potential for the assessment of neurobehavioral conditions given the likely availability of virtual reality systems onboard a long-duration spacecraft.

Sources:

Name of Scale/Tool: Assessment of Daily Group Photos

Description: Examined the feasibility of using photographs of small group members to determine patterns in mood and behaviors.

What is measured: Group photos were taken daily over the life of the mission. Pictures were coded for individuals’ facial expressions and other nonverbal indicators of mood such as clothing and posture. Independent raters scored facial expressions and other behavioral indicators. From the photos, investigators were able to determine changes in mood, and correlations with other self-reported indicators of psychological health demonstrated that the method could help measure mood over time.

Comments: Method may provide a very simple way to track individual and team performance in a non-invasive way.

Sources:

Appendix B. Operational Assessment Questions

Operational Assessment Questions for SMEs

The purpose of this interview is to obtain your view of the causes and outcomes of neurobehavioral signs and symptoms in a spaceflight setting. By neurobehavioral, we are referring to the study of behavior that stresses the importance of nerve and brain function. While neurobehavioral symptoms can include psychomotor function such as posture, accuracy of aimed movements, and timekeeping, we are primarily interested in neurobehavioral issues of interest to the Behavioral Health and Performance working group. We have highlighted these as the Cognitive and Emotional symptoms below.

<table>
<thead>
<tr>
<th>Neurobehavioral Symptoms</th>
<th>Vanderploeg et al 2013 Factors</th>
<th>Neurobehavioral Symptoms</th>
<th>Vanderploeg et al 2013 Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor concentration</td>
<td>Cognitive</td>
<td>Dizzy</td>
<td>Vestibular</td>
</tr>
<tr>
<td>Forgetfulness</td>
<td>Cognitive</td>
<td>Loss of Balance</td>
<td>Vestibular</td>
</tr>
<tr>
<td>Making decisions</td>
<td>Cognitive</td>
<td>Clumsy/poor coordination</td>
<td>Vestibular</td>
</tr>
<tr>
<td>Cannot get organized/finish things</td>
<td>Cognitive</td>
<td>Headache</td>
<td>Somatic/Sensory</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Emotional</td>
<td>Nausea</td>
<td>Somatic/Sensory</td>
</tr>
<tr>
<td>Fall/stay asleep</td>
<td>Emotional</td>
<td>Vision problems</td>
<td>Somatic/Sensory</td>
</tr>
<tr>
<td>Anxiety/tension</td>
<td>Emotional</td>
<td>Light sensitivity</td>
<td>Somatic/Sensory</td>
</tr>
<tr>
<td>Depressed/sad</td>
<td>Emotional</td>
<td>Hearing difficulties</td>
<td>Somatic/Sensory</td>
</tr>
<tr>
<td>Irritable</td>
<td>Emotional</td>
<td>Noise sensitivity</td>
<td>Somatic/Sensory</td>
</tr>
<tr>
<td>Low frustration tolerance</td>
<td>Emotional</td>
<td>Numbness/tingling</td>
<td>Somatic/Sensory</td>
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<td></td>
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<td>Taste/smell</td>
<td>Somatic/Sensory</td>
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<td></td>
<td></td>
<td>Appetite change</td>
<td>Somatic/Sensory</td>
</tr>
</tbody>
</table>

Types of Neurobehavioral Signs and Symptoms

1. Based on your knowledge, what is/are the most common neurobehavioral (NB) symptom(s) in spaceflight settings? (symptom does not have to come from this list).
   a. What are some efforts that BHP has used to deal with these issues?
   b. Are there additional resources that could be made available to minimize these symptoms?

2. In your view, what is the NB symptom that poses the most serious threat to crew performance and health in long-duration spaceflight settings? (symptom does not have to come from this list).
   a. What organizational resources could be made available to minimize these symptoms?
3. Which NB symptom do you feel NASA and the broader spaceflight community have done the best job of studying and understanding? In other words, which NB symptom do you feel is the best understood?

4. Which NB symptom do you feel needs the most research? In other words, which NB symptom do you feel is the least understood?

Sources of neurobehavioral signs and symptoms

Researchers (e.g. Kanas & Manzey, 2008) have identified four general sources of NB signs and symptoms:

   - **Physical factors** (radiation, microgravity, light/dark cycles, acceleration)
   - **Habitability factors** (air quality [CO2], lighting, temperature, noise, vibration)
   - **Psychological factors** (danger, isolation, monotony, workload)
   - **Social/interpersonal factors** (crew size, culture, gender, leadership, personality)

5. What do you see as the greatest health risk as a result of **physical factors**?
   a. Where is research most/least needed in this area (of course recognizing the ethical and practical limitations of radiation exposure and microgravity)?

6. What do you see as the greatest health risk as a result of **habitability factors**?
   a. Where is research most/least needed in this area?

7. What do you see as the greatest health risk as a result of **psychological factors**?
   a. Where is research most/least needed in this area?

8. What do you see as the greatest health risk as a result of **social/interpersonal factors**?
   a. Where is research most/least needed in this area?
Measures of neurobehavioral signs and symptoms

There are a number of measures of NB signs and symptoms currently in use.

9. In the spaceflight setting, what measure/tool is most useful or efficient in detecting NB decrements?

10. In your view, what are the strengths of the _____?

11. What are the weaknesses of the _____?

12. What methodological advances need to be made for future versions of NB assessments?
   a.  e.g., More or fewer self-report measures?
   b.  e.g., Continue or slow the move toward “gamification”?

13. What type of tool/product would be most beneficial in documenting and assessing NB problems in spaceflight settings?

Additional Questions

Physiological Measures

- Imagine, for instance, that we were designing a study to examine neurobehavioral decrements in ICE settings. If we were to validate—or triangulate—psychological or neurobehavioral data with physiological data, what would be the most important physiological measure to include in a pilot study?

Protective Factors

- Previously we have examined indicators of psychological well-being and resilience in spaceflight and ICE settings. In general, we have referred to various factors such as hope, optimism, and social support as protective factors against the detrimental impacts of spaceflight. Which protective factors are most important in reducing the presence or impact of NB signs and symptoms?
**11. SUPPLEMENTARY NOTES**

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**13. ABSTRACT (Maximum 200 words)**
The purpose of this report is to contribute to the understanding of neurobehavioral conditions in spaceflight by examining the neurobehavioral signs, symptoms, and diagnoses identified in spaceflight and other isolated, confined, and extreme (ICE) environments. There are five specific objectives met by this report. Objective 1. Create a taxonomy of neurobehavioral signs and symptoms in ICE settings. Objective 2. A systematic review of neurobehavioral signs, symptoms, and diagnoses commonly found in ICE settings. Objective 3. Seek to identify underlying causes of neurobehavioral issues. Objective 4. Evaluate the validity and practical efficiency of existing scales to assess neurobehavioral issues. Objective 5. Provide recommendations for future work in this area. This report will address each of these five objectives in the order presented. Investigators conducted an operational assessment of 12 subject matter experts. This operational assessment helps address Objective 3. However, the findings of the operational assessment are used to supplement the results of the literature review and to help inform the recommendations for future research.

**14. SUBJECT TERMS**
neurobehavioral, neurocognitive, cognitive, affective, emotional, anxiety, attention, concentration, depression, memory

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