Evidence Report:

Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders

Human Research Program

Behavioral Health and Performance

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I. PRD RISK TITLE: RISK OF ADVERSE COGNITIVE OR BEHAVIORAL CONDITIONS AND PSYCHIATRIC DISORDERS

A. Risk statement

Taken verbatim from the Human Research Program Roadmap, the risk statement for Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders ("Risk", 2015) states:

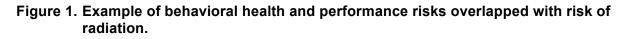
Given the extended duration of current and future missions and the isolated, confined and extreme environments, there is a possibility that (a) adverse cognitive or behavioral conditions will occur affecting crew health and performance; and (b) mental disorders could develop should adverse behavioral conditions be undetected and unmitigated.

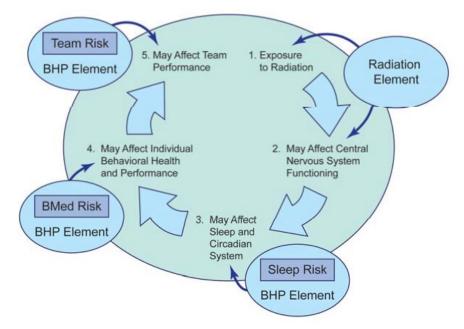
B. Context

The NASA Human Research Program (HRP) is organized into six topical areas called Elements^{*} and the Behavioral Health and Performance (BHP) Element is tasked with the responsibility of managing three risks: (1) Risk of Performance Decrements and Adverse Health Outcomes Resulting from Sleep Loss, Circadian Desynchronization, and Work Overload; (2) Risk of Performance and Behavioral Health Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team; and (3) Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders. While each of these risks is addressed in a separate evidence report, they should not be construed to exist independently of one another but, rather, should be evaluated in conjunction with one another. Furthermore, BHP risks overlap with risks in other HRP Elements (e.g., radiation, immunology, sensorimotor, human factors, nutrition) and, as such, must also be considered in conjunction with one another. Refer to figure 1 for one example of these overlaps.

The risk to behavioral health can be conceptualized as a continuum. On one end is the possibility of adverse cognitive and behavioral conditions arising as a result of factors associated with human space exploration; on the other end, a mental disorder can develop if adverse cognitive or behavioral conditions are not detected or mitigated. The operations side of NASA Behavioral Health and Performance (BHP) defines an adverse behavioral condition as any decrement in mood, cognition, morale or interpersonal interaction that adversely affects operational readiness or performance. If an adverse cognitive or behavioral condition, whether acute or chronic, appears during space flight, crewmembers might be at an increased risk of developing a mental disorder, defined in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) as "a syndrome characterized by clinically significant disturbance in an individual's cognition, emotion regulation, or behavior that reflects a dysfunction in the psychological, biological, or developmental processes underlying mental functioning" (APA, 2013, pp. 20).

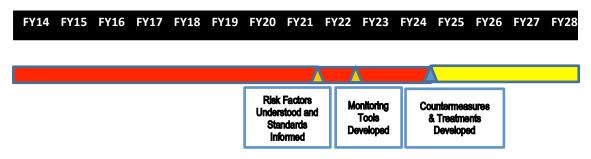
^{*} The six elements include: Behavioral Health and Performance, Exploration Medical Capability, Human Health and Countermeasures, Space Human Factors and Habitability, Space Radiation, and ISS Medical Projects.





The relationships and integration of the BHP Element with other HRP Elements are further outlined in the HRP Integrated Research Plan $(IRP)^{\dagger}$ and delineated in the Behavioral Medicine Path to Risk Reduction (see figure 2). The nature of the IRP requires that the BHP Element continually review and update integration points with other elements. While research is designed to address identified gaps, updating and revising each of the BHP evidence reports and the IRP is necessary as existing element gaps are closed and new gaps emerge.

Figure 2. Path to risk reduction for the risk of adverse cognitive and behavioral conditions and psychiatric disorders.



[†]See <u>http://humanresearch.jsc.nasa.gov/about.asp</u>.

C. Operational Relevance

The BHP element follows NASA's Human Research Program's operationally driven framework "from Evidence to Products." This ensures the BHP element develops and maintains an "operationally driven" research program consistent with "human health and performance standards" that are aligned with major "Exploration Program" objectives and milestones. Thus, BHP operational needs help guide BHP research needs in order to identify and better understand human health and performance standards for spaceflight exploration mission and design, identify and develop effective countermeasures in three key areas to prevent or reduce risks, determine how to leverage technologies to monitor and assess risk, and guide BHP research. In turn, BHP research seeks to characterize and mitigate operational risks while addressing those needs that might arise under different mission parameters. BHP research is focused on risk mitigation for exploration missions, defined as missions that go beyond low Earth orbit (LEO). Some BHP research is focused on utilizing ISS as a platform to better understand spaceflight factors important for exploration missions, particularly with regard to the new ISS one-year mission that considerably extends duration in an isolated, confined and extreme environment.

The process of addressing the risk of adverse cognitive or behavioral conditions and psychiatric disorders developing during or following a long duration mission begins with research and mitigation strategies to detect, quantify, mitigate or monitor the risk. Developing methods for monitoring behavioral health during exploration missions allows BHP to detect signs of stress or other risk factors before behavioral or psychiatric conditions arise. This early detection allows for addressing those risk factors before behavioral health is negatively affected. Countermeasures aimed at preventing or mitigating risk are then refined and arrayed to further safeguard behavioral health and performance during long duration isolated, confined, and highly autonomous missions. BHP research findings also provide recommendations regarding space medicine best practices and updates for behavioral health and performance standards.

II. EXECUTIVE SUMMARY

In April 2010, President Obama declared a space pioneering goal for the United States in general and NASA in particular. "Fifty years after the creation of NASA, our goal is no longer just a destination to reach. Our goal is the capacity for people to work and learn and operate and live safely beyond the Earth for extended periods of time, ultimately in ways that are more sustainable and even indefinite." Thus NASA's Strategic Objective 1.1 emerged as "expand human presence into the solar system and to the surface of Mars to advance exploration, science, innovation, benefits to humanity, and international collaboration" (NASA 2015b).

Any space flight, be it of long or short duration, occurs in an extreme environment that has unique stressors. Even with excellent selection methods, the potential for behavioral problems among space flight crews remain a threat to mission success. Assessment of factors that are related to behavioral health can help minimize the chances of distress and, thus, reduce the likelihood of adverse cognitive or behavioral conditions and psychiatric disorders arising within a crew. Similarly, countermeasures that focus on prevention and treatment can mitigate the cognitive or behavioral conditions that, should they arise, would impact mission success. Given the general consensus that longer duration, isolation, and confined missions have a greater risk for behavioral health ensuring crew behavioral health over the long term is essential.

Risk, which within the context of this report is assessed with respect to behavioral health and performance, is addressed to deter development of cognitive and behavioral degradations or psychiatric conditions in space flight and analog populations, and to monitor, detect, and treat early risk factors, predictors and other contributing factors. Based on space flight and analog evidence, the average incidence rate of an adverse behavioral health event occurring during a space mission is relatively low for the current conditions. While mood and anxiety disturbances have occurred, no behavioral emergencies have been reported to date in space flight. Anecdotal[‡] and empirical evidence indicate that the likelihood of an adverse cognitive or behavioral condition or psychiatric disorder occurring greatly increases with the length of a mission. Further, while cognitive, behavioral, or psychiatric conditions might not immediately and directly threaten mission success, such conditions can, and do, adversely impact individual and crew health, welfare, and performance.

Identification of predictors and other factors that can contribute to the risk of behavioral and psychiatric conditions at all stages of a mission increases the efficacy of prevention and the treatment of those conditions. Additionally, identification of these factors can help predict psychosocial adaptation. Predictors and contributing factors discussed for this risk can be roughly dichotomized into internal or external. More internally focused predictors and contributing factors include: personality (including how it relates to adjustment), resiliency (hardiness), physiological changes that occur when adapting to microgravity and isolation, and emotional reactions (especially negative emotions). Factors external to the individual include those that might be beyond the control of the individual such as: radiation exposure, habitability and environmental design, job design (autonomy and meaningful work), monotony and boredom, daily hassles and major life events, cultural factors, ground support/mission support, family and social support, world events, and lighting and sleep shifting (with the resulting disruptions to circadian rhythms). Not all of these factors have a negative effect on behavioral health and performance. Positive or salutary aspects of space flight (such as viewing the Earth) also contribute to behavioral health outcomes. Other factors can have both detrimental and salutary aspects; teamwork, giving and receiving social support, and leadership responsibilities are a few examples.

The current approaches to prevent adverse cognitive or behavioral conditions and psychiatric disorders begin during selection and continue post-flight. The goal of the behavioral health component of the astronaut selection system is to identify individuals who, at the time of application, have diagnoses that are incompatible with the demands of space flight, and also to identify those who are believed to be best suited psychologically to be astronauts. Current BHP research efforts involving biomarkers may serve to inform the selection process for future exploration missions, as well as further enable a personalized approach to flight medicine. NASA-funded research is currently assessing the predictive value of specific biomarkers, including catecholamines (such as dopamine), as potential biomarkers for sensitivity to central nervous system effects resulting from radiation exposure (Goel et al. 2015; St. Hilare et al. 2015); metabolomics, as potential biomarkers (e.g., Rokutan et al. 2005), such as single nucleotide polymorphisms of certain clock genes (e.g. PER3), as biomarkers for vulnerabilities to sleep loss (Goel 2015; Goel and Dinges 2011). These investigations seek to build off of laboratory research and assess the predictive value of more established biomarkers in the context of a long duration mission.

Once selected, BHP's focus for the astronaut corps is prevention, mitigation, and treatment. We do this by implementing a system of countermeasures. Countermeasures are a second line of defense (after selection) to prevent adverse cognitive or behavioral conditions from occurring preflight, during flight, and post-flight. Many countermeasures, such as the support provided by the BHP operational psychology section with ISS crew care packages and psychological conferences, are aimed at promoting crewmember well-being and preventing adverse behavioral health symptoms. If behavioral signs and symptoms do occur, then early detection of behavioral symptoms allows for early intervention. BHP is currently investigating less obtrusive ways of monitoring the crew so that changes in behavioral health and performance are identified earlier and without requiring verbalization by the crewmember. These approaches are less dependent on the linkage to earth-based support and therefore offer greater support for the autonomous operations of an exploration mission. Approaches that prevent or mitigate adverse cognitive or behavioral conditions often can be used to treat the occurrence of behavioral or psychiatric problems should they occur. Private psychological conferences, for example, can provide both prevention and treatment. The clinical appraisal of the crew psychiatrists and clinical psychologists is that current psychological support countermeasures are adequate for six-month missions on the ISS (Beven, 2014). However, the NASA Office of Inspector General Report released in October 2015 noted that "as of August 2015, NASA does not have a validated mitigation strategy for any of the behavioral risks for a Mars mission." (NASA Office of Inspector General, 2015d).

In anticipation of deeper exploration beyond LEO and space pioneering missions, BHP continues to work with subject matter experts to improve or develop countermeasures to more effectively prevent, mitigate, and treat adverse cognitive or behavioral conditions and psychiatric disorders to support current and future operations.

III. INTRODUCTION

The NASA commitment to human space flight includes continuing to fly astronauts on the ISS until it is decommissioned as well as possibly returning astronauts to the moon or having astronauts venture to an asteroid or Mars. As missions leave low Earth orbit and explore deeper space, BHP supports and conducts research to develop capabilities, necessary countermeasures, and technologies to develop acceptable risk mitigation of adverse cognitive or behavioral conditions and psychiatric disorders for pre-, in, and post-flight.

The Human System Risk Board (HSRB) determines the risk of various mission scenarios using a *likelihood* (per person per year) *by consequences* matrix examining those risks across two categories—in mission health and performance, and long-term health. Colors from a stoplight signal are used by HSRB and quickly provide a means of assessing overall perceived risk for a particular mission scenario. These risk ratings serve as only one of several inputs to determine research priorities, management decisions, and program resourcing. Risk associated with the current six month missions on the ISS are classified as "yellow" (moderate), where the risk is accepted with monitoring, while planetary missions, such as a mission to Mars, are recognized to be a "red" (high) risk that requires mitigation to ensure mission success.

Currently, the HSRB deems that the risk of adverse cognitive or behavioral conditions and psychiatric outcomes requires mitigation for planetary missions owing to long duration isolation and radiation exposure (see Table 1). While limited research evidence exists from spaceflight, it is well known anecdotally[§] that the shift from the two-week shuttle missions to the six-month ISS missions renders the psychological stressors of space as more salient over longer duration missions. Shuttle astronauts were expected just to tolerate any stressors that arose during their mission and were successful at doing so (Whitmire et al 2013). While it is possible to deal with stressors such as social isolation and to live with incompatible crewmembers for two weeks on shuttle, "ignoring it" is much less likely to be a successful coping mechanism on station. For the longer missions of the ISS, astronauts require a larger, more robust set of coping skills and more psychological support. Evidence of this are the large number of BHP's Operational Psychology (Op Psy) staff who have been awarded Silver Snoopys by ISS astronauts^{**}, in the statements of praise for the Op Psy and Family Support Office teams, and in the written and oral statements from flown astronauts regarding difficulty of longer missions and how much Op Psy helped.

Extrapolating beyond the shift from shuttle to the ISS, it is not unreasonable to assume that the shift from ISS to exploration missions will be just as challenging, if not more so. Not only might

[§] Anecdotal reports, similar to case reports in medicine, offer preliminary results that serve an important role in alerting us to "possibly relevant" information but cannot be relied on as valid evidence since it is limited to self-reports or observations. However, while not providing compelling evidence, these anecdotal reports can alert us to "what might be there" and therefore at times helps bridge the gap between retrospective, uncontrolled observations (subject to all forms of bias and dependent on memory) and eventual research validation. Contemporary psychologists recognize the value anecdotal reports as a form of narrative accounts, which have been described as the "central human means of making sense of the world" (Murray 2003).

^{**} Awardees are chosen by astronauts and "must have significantly contributed to the human space flight program to ensure flight safety and mission success." This is the highest award an astronaut can give. Source: Silver Snoopy Award criteria (https://www.nasa.gov/directorates/heo/sfa/aac/silver-snoopy-award).

the missions be longer, but given their unprecedented distance from earth, there will also be other stressors not experienced on the Station. For example, depending upon the specific destination, exploration missions will be characterized by confinement in decreased habitable volume, decreased privacy, an inability to see Earth, a lack of resupply and care packages, anticipated periods of increased monotony and routine, limited medical care, no evacuation options, less social, physical, and sensory stimulation, danger from radiation exposure, and a delay in communication of up to 20 minutes one-way. These in turn are anticipated to affect both mission operations and crewmembers' perceptions of isolation and their limited ability to stay in touch with mission control and family and friends on the ground. Further, exploration missions will be marked with greater uncertainty as we move away from the known (the ISS) toward the unknown (e.g., deeper space, new destinations, new spacecraft).

Table 1.Risk of adverse cognitive or behavioral conditions and psychiatric
disorders for operations and long-term health—Determined as likelihood
by consequences for various design reference missions

DRM Categories	Mission Duration	L×C OPS	Risk Disposition	L×C LTH	Risk Disposition
Low Earth Orbit	6 Months	3 × 2	Accepted With Monitoring	3 × 2	Accepted With Monitoring
	1 Year	3 × 3	Requires Mitigation	3 × 2	Accepted With Monitoring
Deep Space Sortie	1 Month	2 × 3	Accepted With Monitoring	2 × 2	Accepted With Monitoring
Lunar Visit/ Habitation	1 Year	3 × 3	Requires Mitigation	3 × 2	Accepted With Monitoring
Deep Space Journey/Hab	1 Year	3 × 3	Requires Mitigation	3 × 2	Accepted With Monitoring
Planetary 3 Years		3 × 4	Requires Mitigation	3 × 4	Requires Mitigation

Source: Presentation to the Human Risk Board Decisional, June 2015. The risk matrix designated above uses the "likelihood" (L) X "consequences" (C) for both "Operations" (OPS) and "Long-term Health" (LTH) with the "Risk Likelihood Criteria" ranging from 1 = "Low" (≤ 0.1 %) to 3 = "High" (≥ 1.0 % person per year) and "Risk Consequence Criteria" looking at Mission Health and Performance (OPS) and Long Term Health (post mission) (LTH) with each factor rating from 1-4 anchored with descriptive criteria. For example, the "OPS" Consequence ranges from "1" = "Temporary discomfort or Insignificant impact to performance and operations - <u>no</u> additional resources required" to "4" = "Death or permanently disabling injury to one or more crew (LOC) or Severe reduction of performance that results in loss of most mission objectives (LOM)".

We do not know whether the relationship between parameters (e.g., duration, distance from Earth) and psychosocial adaptation to space is linear, if it will accelerate or at what point it may achieve asymptote. For example, do the effects of stressors level off after an astronaut becomes adapted to space? To what extent will psychosocial adaptation to space depend on the length and other characteristics of the mission, which are as varied as habitability issues such as the size and

number of windows within a spacecraft to distance from Earth? Likewise, the shape of the relationship between mission characteristics and increased risk of a cognitive or behavioral event occurring is unknown. Experts in analog and space environments state that they expect the risk of a psychological event to increase in direct proportion to the length of the mission (Ball and Evans 2001; Otto 2007; Stuster 2008) (Category IV^{††}), although some evidence may indicate "red flags" emerging earlier in the mission and then leveling across the duration (Basner et al. 2014) (Category IV) while others posit risk peak fluctuations in the early stages which then re-emerge at the final phase of the mission (Vanhove et al. 2014).

Although anecdotal evidence indicates that psychological adaptation is more difficult on longer duration missions, there has been no incidence of reported psychiatric disorders on either shuttle missions (Billica 2000) (Category III) or ISS missions (Integrated Medical Model, IMM) (Myers et al. 2015) (Category III). In other words, astronauts do report that they perceive greater stress on longer missions, but that stress has not manifested in clinically significant, mission jeopardizing mental disorders. Whether that will continue to hold true for exploration missions and whether the added challenges and stressors of exploration missions will result in greater incidence of stress, adverse cognitive or behavioral conditions, and psychiatric disorders are primary interests of BHP (and are discussed further in Section VI. *Risk in Context of Exploration Mission Operational Scenarios*). Detecting, monitoring, and mitigating behavioral health problems is, in brief, the focus and goal of research on Adverse Cognitive and Behavioral Conditions and Psychiatric Disorders risk.

^{††} For a definition of these categories, please see Appendix A of this report.

Gap Structure:

The Behavioral Medicine (Bmed) science portfolio is part of the Behavioral Health and Performance (BHP) Element of the NASA Human Research Program (HRP). The BHP element Bmed portfolio currently manages eight (8) Gaps in knowledge and technology about characterizing or mitigating the threats to behavioral medicine and psychiatric vulnerabilities related to spaceflight and long-duration space exploration.

BMed1: We need to identify and validate countermeasures that promote individual behavioral health and performance during exploration class missions.

BMed2: We need to identify and validate measures to monitor behavioral health and performance during exploration class missions to determine acceptable thresholds for these measures.

BMed3: We need to identify and quantify the key threats to and promoters of mission relevant behavioral health and performance during autonomous, long duration and/or long distance exploration missions.

BMed5: We need to identify and validate measures that can be used for the selection of individuals that are highly resilient to the key behavioral health and performance threats during autonomous, long duration and/or long distance exploration missions.

BMed6: We need to identify and validate effective treatments for adverse behavioral conditions and psychiatric disorders during exploration class missions.

BMed7: We need to identify and validate effective methods for modifying the habitat/vehicle environment to mitigate the negative psychological and behavioral effects of environmental stressors (e.g., isolation, confinement, reduced sensory stimulation) likely to be experienced in the long duration spaceflight environment.

BMed8: We need to understand how personal relations/interactions (family, friends and colleagues) affect astronauts' behavioral health and performance during exploration class missions.

BMed9: We need to understand long-term astronaut health for long duration exploration missions and find the best methods to promote long-term post-mission behavioral health. Please note: Bmed4 Gap addressed the "most effective methods for detecting and assessing cognitive performance during exploration missions" and was merged with the BMed2 Gap. The BMed Gaps, BHP Element Management Plan (April 10, 2015), Integrated Research Plan Rev F, and Human Research Roadmap structure are all focused on both the process required, and the progress in gap closure and risk mitigation. Gaps BMed 1, 2, 6, and 7 are the core gaps related to long-duration missions that focus on monitoring, mitigating risk with habitability considerations and countermeasures, and a readiness and understanding for the most efficacious treatment, if necessary. BMed Gaps 3 and 5 are related to the identification of the key threats and vulnerabilities along with a focus on selection to mitigate those risks. The remaining two gaps (BMed 8 and 9) are focused on social (family, friends, colleague's support during the mission and the best methods to ensure long-term post-mission behavioral health for astronauts.

IV. EVIDENCE

The NASA Categories of Evidence listed below are used to help characterize the kind of evidence that is provided in this report. The categories are adapted from and are comparable to more familiar versions of Levels of Evidence scales (e.g., C. Silagy and A. Haines, Evidence Based Practice in Primary Care, 2nd Ed., London: BMJ Books, 2001).

- · Category I data are based on at least one randomized controlled trial.
- · Category II data are based on at least one controlled study without randomization, including cohort, case controlled or subject operating as own control.
- · Category III data are non-experimental observations or comparative, correlation and case, or case-series studies.
- · Category IV data are expert committee reports or opinions of respected authorities that are based on clinical experiences, bench research, or "first principles."

a. Assessment of adverse cognitive or behavioral conditions and psychiatric disorders Assessment improves our understanding of the factors that contribute to the development of cognitive or behavioral conditions and psychiatric disorders, and the treatment options that are best for managing this risk. Assessments occur within a framework, a clinical approach of attending to and assessing adverse cognitive or behavioral conditions and psychiatric disorders. This clinical approach, taught by NASA BHP operational personnel to astronauts and flight surgeons, is described below. Evidence of the occurrence of adverse cognitive or behavioral conditions in space flight and space analogs follows. Predictors and other factors that contribute to the occurrence of a behavioral and psychiatric condition are then discussed. Lastly, current and possible countermeasures and treatments are described.

The majority of the evidence that is cited is Category III. Please note that from this point on, only categories other than Category III are noted within the text.

b. Clinical approach

Behavioral and psychiatric problems can be classified in various ways. While NASA medical operations is informed by The *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM–5*; American Psychiatric Association 2013),NASA psychiatrists also incorporate the *International Classification of Diseases-10* (ICD-10) (World Health Organization (WHO) 1996; 2015) standard diagnostic classification system when teaching behavioral medicine to astronauts. The *ICD-10*, which is global, multidisciplinary, and multilingual, also offers a more comprehensive system than the *DSM*. For example, it is used to classify physical and mental diseases as well as conditions for all general epidemiological and many health management purposes. That is, "Mental and Behavioural Disorders" is only one chapter in this much broader scope of ICD-10. In contrast, the *DSM* combines all mental and personality disorders, intellectual disabilities, as well as other medical diagnoses (with psychosocial and contextual factors and other medical conditions that contribute to or exacerbate psychiatric conditions represented through an expanded set of v codes^{‡‡}). A DSM diagnosis is typically given whenever there is evidence of clinically significant distress or impairment in some important area of functioning (e.g., social, occupational, interpersonal).

^{‡‡} In DSM 5, V codes are used when a patient reports significant factors that may influence their presence or future care. These conditions may either be related or unrelated to the primary diagnosis, or exist in the absence of a diagnosable mental disorder. However, at times they are significant enough so as to warrant their own diagnosis (e.g., partner relational problem associated with a Major Depressive Disorder in one of the partners).

It is important to note that a diagnosis represents an effort to use a shorthand description of complex psychological syndromes for the purpose of documenting and classifying the individual's symptoms in order to determine risk and treatment approaches (Bornstein 2015). Relatedly, assessment data (e.g., psychological testing, interviews.) of astronauts often provides valuable information about their characteristics "...to disentangle the complex array of dispositional and situational factors that interact to determine [their] subjective experiences, affects, motives, core beliefs, coping strategies and behavior patterns" providing important support to rule-in or rule-out a diagnosis (Bornstein 2015, p. 449). It is important that we continue to advance our understanding of the complex ways psychological syndromes may become manifest; remaining alert to advances in research that "integrates higher and lower order constructs from different scientific disciplines" (Sanislow et al. 2010).

The recent efforts by the National Institutes of Mental Health (NIMH 2008) to "develop, for research purposes, new ways of classifying mental disorders based on dimensions of observable behavior and neurobiological measures" (see Strategy 1.4, NIMH, 2008) offers intriguing research possibilities for translational research that links basic research to more specific problematic and possible etiological variables, biomarkers, and more effective psychosocial treatments (but is not without its critics, see e.g., Goldfried 2016). The Research Domain Criteria (RDoC) (Insel et al. 2010) implements the NIMH plan for this translational research by seeking to offers a framework for a multifaceted approach that integrates five major domains of functioning: positive valence, negative valence, cognition, social processes, and arousal/regulatory systems (Cuthbert & Kozak 2013). It proposes to consider mental disorders as falling along dimensions (e.g., cognition, mood, social interactions) with traits arrayed along a continuum ranging from normal to extreme. The RDoC offers a conceptually rich framework that views mental disorders as due to individual differences in brain function. That is, mental disorders are viewed as "disorders of development" that manifest in adulthood as a result of an accumulation of or inability to handle a new stress along with a relative ineffectiveness of compensatory mechanisms, resulting from periods of developmental vulnerability (Sanislow et al. 2010). The translational research approach of RDoC, its emphasis on the "individual risk factors" and biomarkers, the linkage of cognition, affect, and social behavior to an individual's risk and opportunities, combine to make this an intriguing area to monitor as we move forward in identifying individual variability and vulnerability with regard to both the psychological and physiological stresses of long-term space exploration.

Of the three approaches described above, the DSM and the ICD employ a categorical approach that helps determine either the "presence" or "absence" of the symptoms related to the diagnosis of a mental disorder. Behavioral medicine training for the International Space Station (ISS) teaches NASA flight surgeons, crew medical officers (CMOs), and astronauts that there are three main types of significant mental disorders that might be encountered in a long-duration mission (NASA 2008a): (1) *delirium*,^{§§} which is a syndrome characterized by cognitive impairment and attention

^{§§} Delirium is of particular interest both because it is commonly associated with acute illnesses, with urinary tract infections one of most frequent triggers in older people and Foley catheters have already been used in space (see e.g., Stepaniak, Ramchandani, & Jones 2007). Longer duration missions may increase the risk for UTIs since urinary retention is a frequent concern in current space flight (both due to privacy and in some cases believed related to the use of promethazine for space motion sickness, see e.g., Law et al. 2013). Other known risk factors include: potential hypoxia/anoxia, toxic gas/smoke inhalation, or head injury. A severe presentation of delirium would be dangerous for both the individual and have a potentially very negative impact on crew. As a neuropsychiatric syndrome, delirium creates strain of those around the victim (see e.g., Detroyer, et. al. 2016; Teodorczuk, Reynish, & Milisen 2012) with

deficits that can occur in response to acute illness, exposure to high levels of CO2, trauma, surgery, or drugs (Cunningham & MacLullich, 2013) (2) *adjustment disorder*, which is a severe and negative emotional response to a tragedy or significant change in one's situation; and (3) *neurasthenia*,^{***} which is a progressive negative psychological response to the isolation and rigors of a long-duration mission. The Russian Space Agency, even more so than NASA, recognizes asthenia as a condition that occurs during long-duration missions (Kanas, 1991; Myasnikov et al. 1996, 2000). NASA behavioral medical training also instructs astronauts to be vigilant for other possible adverse cognitive or behavioral conditions or psychiatric disorders. These other conditions fall under the rubric of *any other psychiatric disorders*, which is the first indication of a preexisting or latent mental disorder that is, perhaps, worsened or triggered by the stress of long-duration space flight.

A. Space Flight Evidence

NASA differentiates between an adverse behavioral condition and a psychiatric disorder in the following manner: a behavioral condition is any decrement in mood, cognition, morale, or interpersonal interaction that adversely affects operational readiness or performance; whereas a psychiatric disorder is one that meets the *DSM* criteria for diagnosis of a disorder. In the movie depiction of Apollo 13, the crew is shown spontaneously and emotionally ripping off their biomedical monitors. In the biographical book *Lost Moon* (later renamed *Apollo 13*) (Kluger and Lovell 1994; see also Lovell and Kluger 2006), Lovell is described as having made a deliberate choice to remove his monitors, basing his decision on comfort (the glue was irritating to skin), saving battery power, and a desire for privacy. Regardless, the more emotional movie version resonates because we, as humans, believe that an emotional behavioral reaction to the stress of a life-threatening situation is reasonable. As all space flight is extreme, and by definition potentially life-threatening, the possibility of psychological reactions to the stressors of space flight is not unreasonable. In truth, space flight has had less of an effect on psychological behavior than might otherwise be expected.

1. Sources of evidence

Evidence of psychological well-being during space flight is accumulated from several sources. Perhaps the most common, at least here at Johnson Space Center, is the stories that one hears directly from astronauts and from those with whom they interact. However, as noted earlier, without other supporting evidence, anecdotal evidence is only useful for directing lines of investigations or providing examples to help bring out the more personal characterization offered by situation. Published histories and biographies offer one source of anecdotes. Since they are

the clinical presentation of symptoms including a significant risk of altered alertness, agitation and hyperactivity, altered sleep-wake cycle and psychosis. Research is only beginning to determine both susceptibility and the triggers for delirium, with animal models demonstrating both inflammation, side-effect of an infection and/or stress-related mechanisms (see e.g., Cunningham & MacLullich 2013); which given potential radiation-induced inflammatory processes or even potential for mild-traumatic brain injury, makes this a condition worthy of our attention.

^{****} Asthenia is considered an important psychiatric condition by Russian space psychologists (e.g., Myasnikov et al. 2000) and is defined as a syndrome marked by "fatigue, irritability and emotional lability, attention and concentration difficulties, restlessness, heightened perceptual sensitivities, palpitations and blood pressure instability, physical weakness, and sleep and appetite problems" (Kanas, 2009, p. 19).

published, they provide, perhaps, a more accountable and therefore credible source of evidence than do oral anecdotes or second-hand reports.

A valuable source of available evidence is the Lifetime Surveillance of Astronaut Health (LSAH) (NASA, 2015c). The LSAH captures information from Flight Surgeon or Crew Surgeon (FS/CS) notes taken during weekly Private Medical Conferences (PMC). While crewmembers do have regular Private Psychological Conferences (PPC) with a psychiatrist or clinical psychologist, any notes taken by these doctors remain private and are not available for release for research purposes. While behavioral health and performance vulnerabilities or concerns may exist within the PMC records, these data are considered an extension of the PPC and therefore not available for release. This operational necessity protects the confidentiality of the crew and does not jeopardize the confidential relationship between the crew and their PMC care providers. Currently, LSAH and BHP are exploring appropriate methods and policy for the selected release of some of these types of data.

Data from the LSAH *are* periodically provided to the Integrated Medical Model (IMM). The IMM was designed to be a statistically-based tool for forecasting risk to crew health (Myers et al 2015). As part of its medical checklist, the IMM has included three behavioral medical conditions: behavioral emergency, depression, and anxiety (NASA 2013). A fourth medical condition, adjustment disorder, is under consideration for future inclusion in the model (E. Kerstman, personal communication, November 12, 2014). The IMM uses the higher threshold of diagnosis rather than the lower threshold of occurrence of symptoms or signs used by the LSAH. Because of the higher threshold, no cases of the three behavioral medical conditions captured by IMM have met diagnostic criteria. However, since the IMM recognizes that the risk of incidence of one of these behavioral events is unlikely to be zero, the model uses incidence rates taken from terrestrial studies (in particular the Stirling County Study, see e.g., Murphy 1980; Murphy et al. 2000).

One of the richest sources of data that does help identify potential adjustment reactions and other psychological factors comes from Jack Stuster's (2008; 2010b) ongoing journals research study. Astronauts who agree to participate record their experiences in journals during their missions. Stuster later conducts content analysis on the journals, aggregating the data that permits commonalities across astronauts to emerge. For example, Stuster (2010b) reported that 10 categories with behavioral health and performance implications accounted for 88% of all journal entries: Work, Outside Communications, Adjustment (physical & mental fatigue as well as adaptation), Group Interaction, Recreation/Leisure, Equipment, Events, Organization/Management, Sleep, and Food (emphasis added). It is important to note that many of these entries highlighted the "saluatogenic" experience of living and working aboard the ISS.

2. Occurrences of behavioral signs and symptoms

a. Occurrences of behavioral signs and symptoms in general

During the Shuttle program, thirty-four behavioral signs and symptoms were reported among the 208 crew members who flew on 89 shuttle missions between 1981 and 1989, spending a total of 4,442.8 person-days in space. This is an incidence rate of 0.11 for a 14-day mission; in other words, behavioral signs and symptoms, regardless of the type of sign or symptom, occurred at the rate of approximately one per every 2.87 person-year (see Table 2). The behavioral symptoms

that were most commonly reported in these 89 missions were anxiety and annoyance (Billica 2000).

As well as tracking occurrences of behavioral signs and symptoms, events of the type that could reasonably be expected to trigger a behavioral reaction, and thus impact mission success, can also be tracked. Over 41 ISS expeditions and the 45 NASA astronauts who have flown those missions, only one is thought to have possibly affected the mission. This was the unexpected death of a parent of one of the astronauts. The resulting incidence rate of such an event occurring is 2.5 (Beven 2014).

Reactions to space flight, be they physiological or psychological, can be categorized by type. The more common types of behavioral symptoms and conditions are discussed below.

Table 2. In-flight medical events for U.S. astronauts during the Space ShuttleProgram (STS-1 through STS-89, Apr 1981 to Jan 1998)

Medical Event or System by ICD-9ª Category	Number of Events	Percent	Incidence/ 14 days	Incidence/ year
Space adaptation syndrome	788	42.2	2.48	64.66
Nervous system and sense organs	318	17.0	1.00	26.07
Digestive system	163	8.7	0.52	13.56
Skin and subcutaneous tissue	151	8.1	0.48	12.51
Injuries or trauma	141	7.6	0.44	11.47
Musculoskeletal system and connective tissue	132	7.1	0.42	10.95
Respiratory system	83	4.4	0.26	6.78
Behavioral signs and symptoms	34	1.8	0.11	2.87
Infectious disease	26	1.4	0.08	2.09
Genitourinary system	23	1.2	0.07	1.83
Circulatory system	6	0.3	0.02	0.52
Endocrine, nutritional, metabolic, and immunity disorders	2	0.1	0.01	0.26

^a*International Statistical Classification of Diseases and Related Health Problems*, 9th edition. Source: Billica (2000)

b. Psychosocial adaptation

Psychosocial adaptation is the psychological and social process of adjusting or conforming to new conditions. The majority of astronauts adapt well to life in orbit as is evident from their journals (Stuster 2010b). As missions become longer and leave Earth's orbit, however, many of the psychological countermeasures (such as real-time video conferences with family) will not be available. At present, we know little about whether the inability to provide the type and level of psychological support and countermeasures currently available on the ISS will affect the speed and quality of astronaut psychosocial adaptation. Successful psychosocial adaptation is essential since unsuccessful psychosocial adaptation can lead to adjustment disorders characterized by decrements in performance (APA 2000).

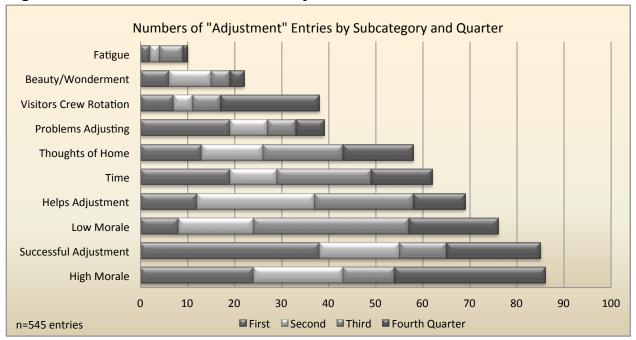
Anecdotal evidence from crew members provides insight into the adaptation that occurs during long-duration space flight missions. In-flight diaries, cosmonauts and astronauts recount periods of both psychological distress and wellbeing experienced during extended periods in space (Ball and Evans 2001; Stuster 2008; 2010b) and even crew members with otherwise cheerful dispositions may demonstrate changes in temperament when meeting the challenges of space flight adaptation. Lebedev wrote in his journal, "[M]y nerves were always on edge, I get jumpy at any minor irritation" (Lebedev 1988, p. 291). From ISS astronaut journals, Stuster (2010) identified 545 entries related to psychosocial adaptation. The entries encompassed a range of emotions from the negative (e.g., "just feeling grumpy today" and "feel a little lost today") to the very positive (e.g., "today was a great day" and "I am 'riding high' today". Over the course of an expedition, morale on the ISS tends to dip during the third quarter and then rise during the final quarter (Stuster 2010b). More entries classified as low morale were made during the third quarter of expeditions providing some evidence for the much discussed, but somewhat statistically inconsistent third quarter phenomenon (cf., Bechtel and Berning 1991). During the fourth quarter, the situation flips with journal entries involving high morale disproportionately occurring, perhaps as they start to reflect on a job well done and to look forward to returning home.

But, adapting is not without its challenges and training cannot entirely eliminate those challenges. Linenger (2000, p. 151) described his inability to prepare fully for long-duration space flight challenges, "I was astounded at how much I had underestimated the strain of living cut off from the world in an otherworldly environment". Familiarity with the environment may play a role. Astronauts who return for a second ISS expedition may have an easier time adjusting, as evidenced by journal entries such as this "adjusting to life here on ISS has been really easy; it is like coming home for me." (Stuster, 2010b, p. 18). If this is the case, then this argues for sending astronauts who have flown in low Earth orbit on missions that leave Earth's orbit.

Ineffective adjustment to life in space can take many forms, such as withdrawal from fellow crew members or ground support crew or discord or tense relations with fellow crew. A third form of ineffective adjustment is deviant behavior. One expert of isolated and confined environments has identified two categories of deviant behavior in U.S. Antarctic winter-over crews: (1) individuals who fail to conform to group norms/expectations; and (2) individuals who act as the station class jester, whose behavior is outside of the mainstream yet not outrageously disruptive or threatening (Palinkas, 1989, 1992). Deviant types of behavior in space may fall into these same two categories. For example, Lebedev admitted that he disregarded safety procedures when he became frustrated. In his haste to access new letters from home, he did not wear safety goggles because "they fogged up, but if metal dust had entered my eye the flight would have ended" (Lebedev, 1988, p. 304). Illustrating the second category of deviant behavior is Linenger's coping behavior: "I also made my own diversions ... Playing the space version of 'sneaking up' ... Flying silently down the length of a module, I would approach one of my crewmates and, still undetected by him, move very close. I would then hover patiently until he turned around. I knew that I had gotten him whenever he would gasp and flail his arms backward" (Linenger, 2000, p. 159). Anecdotal evidence from space flight suggests that astronauts and cosmonauts at times engage in disruptive coping behaviors that could presage larger behavioral issues.

Crew size may be another factor contributing to different behavioral outcomes. In examining rates of deviance in seven polar and three space flight missions (Salyut 7; Apollo 11; and Apollo 13), Nolan and Dudley-Rowley (2005) determined that deviance rates were highest for crews of three. These researchers classified deviant behavior into three general categories: (1) bizarre or puzzling behavior, such as withdrawal; (2) acts of violence, verbal or physical; and (3) acts of deliberation, such as hoarding resources. They found that when crew size increases to four, there is an apparent significant decrease in the amount of deviant behavior exhibited. This study was based on a small sample size. Stuster, in his journal project, has collected data from members of two and three person crews and is now collecting data from astronauts who are part of six person crews. Further investigation is required before a conclusion can be reached regarding optimal crew size for minimal conflict.

While adjusting to life in space can be difficult, there are some factors that make the process of adaptation easier. This is evidenced by the categories involving psychosocial adjustment that emerged during the astronaut journals project. Out of the 10 categories identified, four directly include aspects of life in flight that had a positive effect on adjustment. These include in descending order of frequency: *high morale* (which Stuster differentiates from low morale), *successful adjustment, helps adjustment*, and *beauty/wonderment*. The *helps adjustment* category is described by Stuster as relating to those activities and factors that contribute to overall behavioral adjustment (e.g., exercising, viewing earth, meaningful work, eating together, helpful crew mates, etc.). Together, these four categories of adjustment are ambiguous (Stuster 2010b), meaning that the journals entries could be positive or negative in tone. One such category is Visitors/Crew Rotation. Typically, events such as crew rotations might be anticipated yet stressful. Figure 3 summarizes Stuster's findings regarding the prevalence of journal entries that discussed factors related to psychosocial adaptation to life on the ISS.





Source: Stuster (2010)

c. Behavioral and psychiatric emergencies

NASA considers any behavioral or psychiatric condition that causes serious behavioral or cognitive symptoms leading to incapacitation and severe mission impact as a behavioral emergency. As noted earlier, examples include the development of delirium due to a head injury, hypoxia/anoxia, toxic gas/smoke inhalation or a brief psychotic episode following a tragic event such as the death of a family member or an international catastrophe. To date, no behavioral emergencies have occurred before or during any U.S. space flight. As previously mentioned however, as the length of space missions increases, the probability of a behavioral and psychiatric emergency occurring also increases (Ball and Evans 2001; Stuster 2008) (Category IV).

Not a lot of data are available from which to assess the many types of behavioral and psychiatric conditions that could occur during a long-duration mission. This is due, in part, to the relatively few numbers of long-duration flyers, the comparatively short mission length, and other ameliorative factors such as an ability to see Earth. Based on the IMM, one estimate of the possible rate of a behavioral or a psychiatric emergency occurring in flight as the result of depression or anxiety ranged from 0.000087 to 0.000324 cases per person-year (NASA 2007b). The likelihood of such an emergency occurring would further increase as mission length exceeded 1 year. Calculation of this estimate is discussed more fully in the "Mood and mood disorders" section below.

Some Russian space flight missions in the 1970s and 1980s were terminated early due to psychological factors (Cooper 1976). In 1976, during the Soyuz- 21 mission to the Salyut-5 space station, the crew was brought home early after the cosmonauts complained of a pungent odor. No source for this odor was ever found, nor did other crews smell it. Since the crew had not been getting along, a shared delusion (cf., Folie a' quatre) may offer a possible explanation (see e.g., Ohnuma and Arai, 2015 for an explanation of how strong beliefs and environmental factors such as social isolation, can combine to create strong psychological "sympathy" for shared beliefs leading to the vulnerability for group suggestibility). The Soyuz TM-2 mission in 1987 was similarly cut short because of some apparent psychosocial factors (Clark 2007). The early termination of these missions may have prevented escalation of behavioral and psychiatric occurrences. Not all incidents have resulted in an earlier than planned return to Earth. Point in case, a NASA psychiatrist interviewed for a review of sensory stimulation brought up rage in early Mir crews. The rage was attributed to sensory-poor environment and inadequate ability to communicate (Vessel and Russo 2015).

1) Payload specialists

While no astronaut has had a behavioral emergency during a mission, it cannot strictly be said that no behavioral emergencies have occurred. A special class of individuals who flew during the Shuttle program is payload specialists. These are individuals who had specialized duties onboard, most often related to a particular payload or experiment. As they are not part of the Astronaut Candidate Program, they did not go through the same selection or training processes as do astronauts. They were, however, required to have education and training appropriate to their required onboard duties. Additionally, all payload specialists were required to meet certain physical requirements and pass NASA space physical examinations.

Payload specialists selected by NASA are not anticipated to be a part of exploration missions. Regardless, as a group of individuals who flew yet did not go through the same selection and training process as NASA astronauts, payload specialists offer a unique comparison group to astronauts.

Taylor Wang was a payload specialist on STS-51B, which launched April 29, 1985. Back in the 1970's he had proposed studying fluid physics in space to NASA. When he was selected as a payload specialist, he spent two years training for his experiment. On the second day of the mission, his experiment failed. In his own words, he panicked. Not only had his experiment failed, but he was the first Chinese descendant to fly on the shuttle. Because of the collectivist nature of the Chinese culture, he viewed his experiment's failure as a reflection on the Chinese community. When he asked mission control for time to repair his experiment and was denied due to schedule constraints, he threatened that he was "not going back" to Earth (Reichhardt 2002, p. 233). His crewmembers offered to take on some of his tasks, freeing up the schedule and providing mission control with the opportunity to allow Wang time to repair his experiment.

The experience with Wang might have contributed to both an increased emphasis on crew safety when flying payload specialists and the use of locks on shuttle hatches. Another factor that likely contributed was recalled by Hank Hartsfield: "Early on when we were flying payload specialists, we had one payload specialist that became obsessed with the hatch. 'You mean all I got to do is turn that handle and the hatch opens and all the air goes out?' It was kind of scary. Why did he

keep asking about that? It turned out it was innocent, but at the time you don't know. We had some discussions, so we began to lock the hatch." (Butler and Hartsfield 2001).

While it is difficult to determine when locking devices were first used on an outward opening hatch, transcripts of the *NASA Johnson Space Center Oral History Project* reveal that locks were used on more than one shuttle mission. On STS-61B, CDR Brewster Shaw locked the hatch on the side of the Orbiter when Mexican payload specialist Rodolfo Neri Vela flew in November of 1985. Shaw stated that it was the first time he had flown with someone he did not know well. As Shaw recalled, "I didn't know what he was going to do on orbit. So I remember I got this padlock, and when we got on orbit, I went down to the hatch on the side of the Orbiter on orbit you can go down there and you just flip this little thing and you crank that handle once [demonstrates], the hatch opens and all the air goes out and everybody goes out with it, just like that. And I thought to myself, "Jeez, I don't know this guy very well. He might flip out or something." So I padlocked the hatch shut right after we got on orbit, and I didn't take the padlock off until we were in de-orbit prep. I don't know if I was supposed to do that or not, but that's a decision I made as being responsible for my crew and I just did it." Shaw went on to acknowledge that Vela was a "great guy" (Rusnak and Shaw 2002).

Astronaut Bryan O'Connor in April 2006 told of requesting and using a combination lock on the June 1991 flight STS-40, six years after Shaw's STS-61B flight. O'Connor cited concern that the two payload specialists on the flight were not career aviators and had not gone through the same training and experiences as astronauts. O'Connor laughed when recalling telling each payload specialist that "It's because we [astronauts] don't know you guys [payload specialists] all that well." He felt a lack of trust even after having spent two years training with the payload specialists (Johnson and O'Connor 2006).

Payload specialists did not go through the same level of psychological scrutiny during selection and had less training than astronauts. Regardless, a question is raised regarding whether the lock on the hatch was a necessary safety measure or whether it served more as a psychological management tool employed by astronauts to control payload specialists. It is unknown to what extent an crew member's extra precautions taken that were attributed to perceived risk and relative lack of rigor in selection and training of payload specialists may also have increased the pressure and tension on these payload specialists. Certainly, there are proportionally more reports of payload specialists having psychological difficulties during flight. These difficulties could be due to the aforementioned less rigorous selection and training of payload specialists, which would then provide evidence that NASA's more demanding selection and training of astronauts was effective. Alternatively, payload specialists rarely flew more than once suggesting that payload specialists might have been more likely to be open about any psychological struggles experienced during flight since such disclosure would not affect their future flight status. From reading transcripts of the Oral History Project, there does seem to have been an "us versus them" mentality held by astronauts. This was perhaps reinforced by payload specialists often flying "before" NASA astronauts, bypassing those who had completed the more demanding training and were waiting in the queue for spaceflight.

d. Mood and mood disorders

Astronauts must adapt to complex and demanding training, danger, isolation, confinement and many of major stressors of spaceflight (Harrison, 2005). It is anticipated that everyone's mood states may vary from time to time and be either positive or negative (Watson and Tellegen 1985). Positive moods have been linked to increased helping behavior toward others (e.g., Fisher 2002; George 1991; Isen and Levin, 1972) and may result in better performance through interpersonal processes such as helping others (Tsai et al. 2007). Further, employees in positive moods may perform better through a motivational process such as higher self-efficacy and task persistence (Tsai et al. 2007). George and Brief (1996) found that people who were in positive moods were more likely to view their progress toward task goals positively and were more likely to engage in increased task diligence. The effects of positive mood are discussed in later sections of this chapter that address salutogenesis in space flight and analogs, respectively.

Like positive moods, negative moods can be functional. They can cause individuals to better identify problems by focusing on their current situation rather than on their underlying assumptions, attending to shortfalls in the status quo, identifying opportunities, and exerting high levels of effort to improve a situation (George and Zhou, 2002; 2007; Kaufmann, 2003; Martin and Stoner, 1996; Schwarz, 2002; Schwarz and Skurnik, 2003). Additionally, negative moods promote creativity under certain conditions (e.g., Gasper, 2003; George and Zhou, 2002; Kaufmann, 2003; Kaufmann and Vosburg, 1997), which can facilitate problem-solving.

Obviously, individuals will vary in their tendency to form negative inferences from life events. This variability, according to Abramson et al.'s (1989) formulation, can create vulnerabilities for depression and hopelessness in the presence of negative events or the absence of positive ones. However, individual variability may exist between his/her tendency to form negative inferences across either interpersonal or achievement domains. According to this conceptualization, it is only when, for example, an interpersonal vulnerability (negative thoughts about one's ability to be truly loved) matches the experienced negative life event (loss of relationship on a long-duration flight), that the interaction of the two then places the individual at increased risk for developing a negative mood state that could lead to depression (Liu et al. 2015).

While our temporary moods and affective reactions do not always influence our behavior (Clore & Schnall, 2005), there is a complex and dynamic interaction that links behavior to mood (see e.g., Albarracin & Hart, 2011). It is this complexity that helps explain why negative moods may at times increase performance but at what cost (Glasman and Albarracin, 2006)? For example, at times, negative moods can increase more negative interpersonal interactions or increase actions that may be harmful to ourselves or others (e.g., overeating, ignoring normal procedures, choosing to not respond to the interpersonal needs of others). Taken to the extreme, it is well known that negative mood states that meet the criteria for diagnosis of a mood disorder can have a deleterious effect on performance, morale, health (Bardwell et al. 2005), and often increase behaviors aimed at harming oneself or others (see e.g., Marquart et al. 2009).

NASA's astronaut selection process removes from further consideration those applicants who have been identified with any psychiatric disorder. However, important aspects of an individual's mental health history, e.g., exposure to a traumatic event, family history of mental health struggles such as depression or schizophrenia – are not always discoverable during the selection process.

Not only may potential astronauts be hesitant to share information that would prohibit selection, but also, some current astronauts have demonstrated a reluctance to share information if they perceive such information could jeopardize their flight status, limiting the utility of countermeasures available to them.

Clinically significant negative mood states are characterized within the DSM as major depressive disorders which is a highly prevalent clinical condition in the general population with lifetime prevalent rates ranging from 13% to 16% (Hasin et al., 2005). Disorders such as anxiety, post-traumatic stress, sleep loss/insomnia, adjustment, and depression can develop unexpectedly in otherwise healthy individuals. A study by Tozzi et al. (2008) indicates that the average age of onset of depression for persons who have no family history of depression is 41 years (sd=13.67). For the astronaut classes of 1990 through 2013, the average age of individuals who were selected as astronaut candidates was 34.9 years old, ranging between 26 to 46 years (NASA, 2008b). Over those same astronaut classes, the average age of those selected has slightly increased (r = .20, p < .01). Behavioral health is a concern in highly educated and high functioning populations such as physicians (Frank & Dingle, 1999; Ruitenburg, Frings-Dresen, & Sluiter, 2012) suggesting that astronauts might be at risk as well. This suggests that astronauts who have no history of depression are not immune from its development.

Data collected through the LSAH reveals that symptoms of anxiety and depression have occurred during space flight (although there are no reports any diagnoses for either have been give). Over 28.84 person-years of NASA space flight, flight and crew surgeons have documented 24 instances of anxiety related symptoms presented in space flight for an incidence rate of 0.832 cases per person-year (NASA 2007a). Over the same 28.84 person-years, four astronauts experienced signs and symptoms of depression during space flight for an incidence rate of 0.139 per person-year (NASA, 2007a). In other words, signs and symptoms of anxiety during space flight occurred once every 1.2 years, and signs and symptoms of depression occurred once every 7.2 years. These data are from the Shuttle program only. Examination of LSAH data collected from the ISS could very well reveal higher prevalence of symptoms than were reported during the Shuttle era^{†††}. This supposition is supported by the journals project in that several astronauts have reported in their journals avoiding scrutiny by not informing their flight surgeons of every problem (Stuster, personal communication, June 2, 2015). This suggests that symptoms of mood disorders are likely much more prevalent than officially reported.

The IMM only includes cases from space flight that meet certain diagnostic criteria. For mood disorders, the criteria are as specified in the DSM. To date, no astronaut has been officially diagnosed as having anxiety or depression during flight. The modelers of the IMM recognize that the risk of mood disorders is not zero so they include estimated incidence rates based on published terrestrial studies, specifically the Stirling County Study with its repeated surveys and follow-up cohort investigations. The rates in the IMM are based on the incidence of anxiety or depression in otherwise healthy individuals aged 40-49, a cohort that as noted earlier, is congruent with the majority of current astronauts. For anxiety, the IMM incidence rate is 0.0071 per person-year for females and 0.0019 per person-year for males. The incidence rate included in the IMM for depression is 0.0036 per person-year for females and 0.0029 per person-year for males.

^{†††} BHP has been unable to update the table for this revision of the Bmed Evidence Report.

NASA astronauts have accumulated approximately 120 person-years of space flight. Extrapolated IMM incidence rates over that period are detailed in Table 3. Based on the extrapolated rates, there is an 85.2% chance that a case meeting DSM criteria of anxiety has occurred in the population of female astronauts contrasted with a 22.8% chance for males. Regarding diagnosed instances of depression, the extrapolated rates estimate a 43.2% chance for females and 34.8% for males.

Diagnosis	Incidence Rate (Per Person-Year)	Probability Over Life of Space Flight*
Anxiety		
Female	0.0071	57%
Male	0.0019	20%
Depression		
Female	0.0036	35%
Male	0.0029	29%

Table 3. Projected probability of meeting DSM diagnostic criteria during space flight for anxiety and depression

* Based on 120 person-years of accumulated space flight over the life of NASA's manned programs. Source: IMM.

One criticism of the IMM with regards to mood disorders is that the incidence rates are based on terrestrial studies of the general population. While selected cohorts of the general population can match certain demographic factors (e.g., age, education), they are not an accurate representation of the astronaut population overall. This is in part due to the rigorous assessment and selection system used in selecting the astronaut corps. This helps to ensure that the astronaut corps is stronger (i.e., less vulnerable) in behavioral health than is the general population.^{‡‡‡} This suggests that the incidence rates used by the IMM are likely overstated. Further, while the IMM distinguishes based on gender, experience with selecting multiple classes indicates that the incidence rates is little psychological difference in astronauts due to gender. Thus, it is possible that the incidence rates in the general population.

Examining the history of the space program reveals that decrements in mood, and in particular at least reports of depressive symptoms, have been seen throughout human space flight and across space agencies. Anecdotal reporting suggests it is most likely to be seen in missions lasting months rather than days. For example, on Skylab, a precursor to the ISS, the crew of Skylab 4 was described derogatively with terms such as hostile, irritable, and grumpy when the crew conducted a daylong work stoppage (Harrison & Fiedler 2012). The Skylab 4 mission in 1973 was 84 days

^{‡‡‡} Two USAF studies assessed Aviator depression and anxiety prevalence, respectively, finding similarly lower rates of both when compared to the general population (Lollis et al. 2009; Marsh et al. 2010).

and 1 hour long. In Russia, depression may have contributed to early termination of the Soyuz T14 – Salyut 7 in 1985. The crew returned after 56 days, 160 days early) (Buckey 2006).

Between March 1995 and June 1998, seven NASA astronauts flew on the Russian space station *Mir*; during this time, two (29%) astronauts reported depressive symptoms for an incidence rate for astronauts of 0.77 per person-year (see Table 4) (Marshburn 2000). The actual incidence rate for both shuttle and Mir is likely to be understated, however, because of astronaut reluctance to report such symptoms (Ball and Evans 2001; Shepanek 2005). This reluctance to report symptoms out of concern doing so may potentially jeopardize future flight status is a recurring theme seen throughout the history of both military aviation and space flight (Lollis et al. 2009; Marsh et al. 2010).

Event	Number of Events	Incidence/100 days	Incidence/year
Musculoskeletal	7	0.74	2.70
Skin	6	0.63	2.30
Nasal congestion, irritation	4	0.42	1.53
Bruise	2	0.21	0.77
Eyes	2	0.21	0.77
Gastrointestinal	2	0.21	0.77
Psychiatric	2	0.21	0.77
Hemorrhoids	1	0.11	0.40
Headaches	1	0.11	0.40
Sleep disorders	1	0.11	0.40

Table 4. Medical events among seven NASA astronauts on Mir, Mar 14, 1995through Jun 12, 1998

Note: Data from the Russian Space Agency report that there were 304 in-flight medical events on board the *Mir* from Feb 7, 1987 through Feb 28, 1998. The numbers of astronauts at risk or the incidence per 100 days was not reported.

Source: Marshburn (2000)

More recently on the ISS, evidence of symptoms of depression and anxiety have been either self-reported or reported anecdotally. Based on his examination of 10 journals from the original phase of his project, Stuster stated "a few of the ten astronauts who participated in the study self-reported mild depression, as illustrated by some of the example entries included in the report, and others suffered more acutely" (personal communication, November 5, 2014). Vessel and Russo (2015), who interviewed LDM ISS and Mir astronauts, found that mood changes were mentioned a number of times and that interviewees felt mood changes during exploration missions were likely to occur. They also reported that psychiatrists interviewed by them confirmed the potential for mood changes in astronauts and reporting an increase in crew dysphoria during the second half of expeditions (Vessel and Russo 2005).

In sum, despite careful selection, a depression-free past does not guarantee a depression-free future.^{§§§} The data that were collected in the general population as well as in NASA populations are not definitive enough at this time to accurately predict the likelihood of an astronaut becoming depressed or suffering from a mood disorder while in flight. Rather, it emphasizes that the risk is real and should not be ignored. Therefore, NASA is continuing to gather the data needed to define and mitigate the risk of an astronaut developing an anxiety or a depressive disorder.

e. Neurasthenia

Neurasthenia appears in the ICD-10 (WHO 2015) and Russian medical personnel view neurasthenia as one of the largest problems affecting the emotional well-being of cosmonauts (Kanas 1991). This syndrome, which is sometimes called asthenia, asthenization, and psychasthenia^{*****}, has been defined as "a nervous or mental weakness manifesting itself in tiredness…and quick loss of strength, low sensation threshold, extremely unstable moods, and sleep disturbance" (Kanas and Manzey, 2003, p. 115). It can be caused by excessive mental or physical strain, prolonged negative emotional experience or conflict, as well as somatic disease (Petrosvsky and Yaroshevsky, 1987). The diagnostic criteria for neurasthenia are listed in the ICD-10 (WHO 2015). Neurasthenia is characterized by at least 3 months of persistent and distress feeling of exhaustion or fatigue after minor physical or mental effort with no recovery after rest or relaxation along with the presence of at least one of the following: muscular aches, sleep disturbances or irritability in the absence of depression or anxiety.

There is some evidence that the concept of neurasthenia does offer insight into the relationship between the more commonly (and socially acceptable) reports of "fatigue" related to psychiatric disorders (Harvey et al. 2009). Sandoval and colleagues (2011) compared ICD-10 criteria for neurasthenia to the DSM-IV-TR criteria for depression, general anxiety, dysthymia, and chronic fatigue syndrome and determined that while there are similarities in symptoms, neurasthenia fails to meet all criteria necessary for a diagnosis of depression, general anxiety, and dysthymia. They viewed the secondary symptoms (e.g., memory disorder, weakness, anxiety symptoms, excessive mental strain, excessive physical strain, headache, etc., as symptoms developed, as part of an adaptive reaction (Sandoval et al., 2011). Molina et al. (2012) examined prevalence rates for neurasthenia and comorbidities with DSM-IV diagnoses across both racial and ethic groups in two nationally representative samples (ages 18 years and older) in the United States. They report the adjusted prevalence rates of 4.89 and 2.80% with lifetime neurasthenia increasing the odds of also meeting diagnostic criteria for any depressive, anxiety, or substance abuse disorder.

Given the ambiguities, subjective nature, and lack of consensus on neurasthenia symptoms as being distinguishable from psychiatric disorders (Goldberg and Bridges 1991), a separate neurasthenia diagnosis has never been recognized in the DSM (APA 2013). Perhaps due to this

^{§§§} NASA has an increased interest in a "personalized medicine", aka, using an omic approach with regard to both the identification of biomarkers for prevention and for individualized countermeasures. Recent investigations linking respiratory sinus arrhythmia as a biological predictor of later depression is but one example (see e.g., Yaptangco et al. 2015) for how a genomic biomarker may help to identify long-duration spaceflight vulnerabilities.

^{****} The ICD-10 differentiates asthenia NOS (R53.1: general symptoms and signs – malaise and fatigue – weakness) and psychasthenia (F48.8: other specified neurotic disorders) from neurasthenia (F48.0: other neurotic disorders). Asthenia NOS appears to involve physiological impairment without the corresponding psychological component that defines neurasthenia. Psychasthenia is reported as having a strong association with locally held cultural beliefs and behaviors.

lack of recognition in the DSM or possibly other reasons such as differences in national culture, NASA flight surgeons have not reported observing multiple symptoms of asthenia presenting together in any one NASA astronaut. However, an examination of cosmonauts suggests that neurasthenia is unlikely to occur when space flights last less than 4 months (Myasnikov and Zamaletdinov 1996). In addition, while an official diagnosis was never made, there are anecdotal reports that U.S. astronauts who flew during Mir and Skylab experienced signs and symptoms consistent with neurasthenia (Burrough 1998; Freeman 2000; Harris 1996). That said, we still lack empirical support for the occurrence of neurasthenia during Mir missions Kanas et al. (2001).

In summary, although reports of fatigue are often vague or subjective, they do represent one of the most commonly reported symptoms encountered in astronauts (Barger et al. 2014) and in medical consultations (Kroenke et al. 1988). Given the common overlap of both psychological and physiological symptoms that can present as fatigue, and the uncertainty as to whether major life events mediate or moderate prolonged fatigue (see e.g., Zhang et al. 2007), we need to maintain diligent monitoring, along with a robust and effective psychological support system so as to apply effective countermeasures when symptoms (regardless of what the syndrome is called) first appear (Myasnikov et al. 2000, as cited in Kanas et al., 2001). Longer-duration missions may also demonstrate a need for more systematic collection of signs and symptoms of neurasthenia especially since long duration space exploration will no doubt continue as a multi-national endeavor. It is important that we remain alert to the importance of neurasthenia for different cultural groups (see e.g., Paralikar et al. 2011; Schwartz 2002) and their space programs (e.g., cosmonauts in the Russian Space Program).

f. Psychosomatic reactions

Psychosomatic reactions, occurring prior to the ISS missions, have occasionally been reported during space flight. Psychosomatic refers to a physical manifestation of distress caused by or substantively influenced by emotional factors. These health struggles are not imaginary; in fact, more than half of all individuals in the general population who are seeking medical attention are suffering from psychosomatically induced or exacerbated illnesses (Goldensen 1970; Birley 1977; Fava and Sonino 2000). An example from space exploration is provided by a report of an otherwise healthy cosmonaut who experienced a cardiac arrhythmia that required medication after being exposed to sustained stressors related to on-board equipment failure (Carpenter, 1997; Cowings et al., 2000; Kornilova et al., 1998, 2000).

There also are direct self-reports of somatizing by cosmonauts with other psychosomatic reactions including complaints of toothaches after dreams of tooth infections (Chaikin 1985) and fears of impotence due to perceived prostatitis (Harris, 1996). In 1985, the crew of the Soyuz T-14 mission to Salyut-7 was brought home after 65 days after a cosmonaut complained that he had a prostate infection (Clark 2007). Doctors later believed that the problem was partly psychological.

The crew of Soyuz T10 – Salyut-7 reported hallucinations. While these hallucinations were believed to have been due to a toxic gas, and not psychologically induced, they still enforce the knowledge that psychological reactions can result from physical ailment, be it an infection or due to a toxic environment (Troitsyna 2011). Although reports of hallucinations associated with spaceflight may legitimately raise concern, there is a reported linkage between sustained "motion" or "space sickness" and reports of disorientation, or inversion of images, and what are described as

"formed hallucinations" (e.g., distorted images) or "unformed hallucinations" (e.g., flashes of light, see e.g., Fazio et al. 1970). These types of reactions relate to the vestibular symptoms of dizziness and may be caused by vascular insufficiency to the posterior cerebral artery with spasms of this vessel impacting the area of the temporoparieto-occipital cortex (i.e., the occipital for the "flashes of light" and the midtemporal for the "distorted images", Schneider 1978; Schneider and Crosby, 1980).

g. Salutogenesis

Hans Selye's conceptualization of psychophysiological stress reactions recognized both positive (eustress) and negative (distress) stress is associated with any challenge (Selve 1974). Astronauts readily seek out the opportunity for spaceflight and both their communications, and accounts of their experiences reflect far more positive emotions and thoughts than negative (Suefeld 2005). By extension, is it very unlikely that astronauts will view the opportunity and anticipated experience of long-duration space exploration missions as negative. Over twenty ago, Antonovsky, in 1979 (Category IV), coined "salutogenesis" as the opposite of pathogenesis. Salutogenic experiences are those that promote a sense of health. The key factor of salutogenesis, according to Antonovsky (1979), is a person's sense of coherence. He defined this sense of coherence as "a global orientation that expresses the extent to which one has a pervasive, enduring though dynamic feeling of confidence that one's internal and external environments are predictable and that there is a high probability that things will work out as well as can reasonably be expected" (p. 10). Kobasa et al. (1979) described individuals who stay healthy, even when they find themselves in challenging circumstances, as having the following characteristics: believing that they exert control over their environment; embracing life as meaningful; and experiencing changes in life as normal and beneficial. Factors contributing to salutogenesis are comprehensibility, manageability, meaningfulness, social support, spirituality, happiness, humor, and love (Kent 2002; Smith 2002). Smith (2002) commented that "an organism with a salutogenic brain would experience the world as manageable and coherent ... with a self-perpetuating cycle for enhancing self-confidence and well-being" (p.325).

Suedfeld (2005) differentiated between positive environmental aspects and the positive personal and social aspects of space flight. Environmental aspects concern the external environment (e.g., mystery; beauty of space; views of Earth) and the capsule environment (e.g., safe haven; familiarity; free time). The positive personal and social aspects of space flight were likewise dichotomized into astronaut group dynamics (e.g., membership in an elite group; superordinate goals) and post-mission consequences (e.g., self-confidence; respect; new skills and values).

Preliminary results suggest that a salutogenic response to space flight is common across astronauts and endures for some time post-flight. Astronauts and cosmonauts have reported experiencing transcendental, religious experiences or a sense of the unity of humankind while in space (Connors et al. 1985; Ihle et al. 2006; Kanas 1990). Analysis of the memoirs of four astronauts reveals that all four reported post-flight feelings of increased spirituality, defined as "meaning and inner harmony through transcendence" (Suedfeld and Weiszbeck 2004, p. C7). Ihle et al. (2006) examined the positive psychological outcomes of space flight. All 39 astronauts and cosmonauts who responded to the survey reported a positive reaction to being in space. Likewise, as was noted earlier (see Figure 3), Stuster's (2010) journals study identified the two largest categories of journal entries as related to psychosocial adaptation and both were both positive: "successful adjustment" and "high morale." This provides further evidence of positive benefits associated with space flight.

A frequently endorsed benefit of space flight is related to the perception of the Earth; i.e., its beauty and fragility. Analysis of photographic images taken from ISS during Expeditions 4 through 11 indicates that most images taken by crew members were self-initiated (84.5% of 144,180 photographs) and that photography was considered a leisure activity (Robinson et al.2011). During missions to Mars, however, the Earth will not always be visible. The effects of not being able to see Earth could have a detrimental effect on the psychological well-being of crew members (Kanas and Manzey 2003; 2008). Astronaut Mike Lopez-Alegria emphasized the importance of seeing Earth in an interview with NPR (National Public Radio), "Looking out the window and seeing the Earth below, and seeing places you recognize and where you grew up and places you visited has a lot to do with keeping sane, so to speak" (Greenfieldboyce 2010).

Vessel and Russo (2015) suggest a biological basis for salutogenic experiences. They link aesthetically inspiring experiences, part of the class of emotions associated with novelty and understanding, with other inspirational (or salutogenic) experiences. These inspirational experiences are associated with activation of the Default Mode Network, a network of brain regions active when individuals are at wakeful rest and not focused on the external environment (Buckner et al. 2008).

h. Cognitive Functioning

Evidence of the effects of space flight on cognitive functioning is at best equivocal. Strangman (2010; Strangman et al. 2014) examined attention, memory, learning, executive or higher order functioning, emotion processing, and social processing in his extensive review of cognition in space flight and other isolated, confined, extreme (ICE) environments. He concluded that there is a mismatch between research findings and anecdotal reports. While the empirical results he reviewed failed to find significant decrements in cognitive functioning during space flight, the prevalence of anecdotal reports of difficulties attending to tasks, complaints of cognitive slowing, and memory problems while on orbit makes it difficult to conclude that there is no significant cognitive decrement occurring. For example, crew members do report that their cognitive functioning is impaired (Schroeder & Tuttle, 1991) even though this impairment is not manifested "objectively" as impaired performance. Successful performance of tasks, however, is not a particularly precise measurement of cognitive functioning since many other factors can affect task performance. Alternatively, significant findings of cognitive impairment may not have been found due to small sample sizes and inadequate statistical power.

Ambient air quality could also affect cognitive functioning. The increased levels of carbon dioxide CO_2 concentration on the ISS averages 0.3-0.5% (with 0.5% = 3-4 mmHg), exposing its crew to levels of CO_2 that are 10-fold higher than levels on earth (Norsk et al.2015). Evidence is mixed regarding the effects of CO_2 on cognitive functioning although this could be in part a function of the varying levels of CO_2 investigated (Stankovic et al. 2015).

Chancelor, Scott and Sutton (2014) have identified space radiation as the number one risk astronauts face as they venture beyond low earth orbit. Although radiation risk models focus primarily on the health of crewmembers, there also is increasing awareness for how radiation

exposure could also significantly degrade cognitive performance to such an extent that it could compromise the mission. For example, Chancelor et al., note that ionizing radiation damages the central nervous system (Schultheiss et al. 1995) which leads to fatigue, negative mood, as well as difficulty sustaining attention (Davis et al. 2015). In addition, there is evidence of synaptic structural changes, reduced neurogenesis, neuroinflammation, and acceleration of the pathophysiology of any neurodegenerative disease (e.g., Alzheimer's disease; see e.g., National Council on Radiation Protection and Measurements, 2014). In short, there is compelling clinical outcome results that serve as an "exposure analog," as well as animal data, that have helped NASA increasingly recognize that deep space exploration will likely result in astronaut exposure to galactic cosmic radiation, consisting of high-energy, high-charged (HZE) particles, that are known to pose a significant threat to the brain and cognitive abilities (Cherry et al., 2012).

Another possible explanation for the discrepancies between self-reported and measured cognitive deficits relates to the notion of "reserve capacity." Higher functioning individuals are postulated to possess a reserve factor that moderates the expression of impairments in cognitive functioning in the face of brain pathology or depletion (Jones et al., 2011). Reserve capacity is further conceptualized in terms of two models: brain and cognitive reserve. Brain reserve refers to structural aspects of the brain (e.g., size, number of neurons, synapses), whereas cognitive reserve involves aspects of complex cognitive processes (efficiency, capacity or flexibility; Barulli & Stern, 2013).

Reserve capacity is inferred in the discrepancy between observed and expected performance for a given degree of brain depletion or pathology. It has been operationalized in terms of proxy measures such as educational attainment and IQ. Thus more intelligent or better educated individuals are thought to possess a greater degree of cognitive reserve and at any given degree of brain pathology will manifest lower amounts of cognitive impairment than those with lower amounts of cognitive reserve (lower educated or IQ individuals). There is robust literature demonstrating the moderating effects of both brain and cognitive reserve in the expression of impairment in a variety of neurological disorders (Snowdon et al. 1996; Stern, 2002; Valenzula and Sachdev, 2006).

By virtue of selection on various proxy indicators of reserve capacity (e.g., intelligence, education), astronauts as a group can be considered to manifest a high degree of brain or cognitive reserve capacity. As such, it is not surprising that they show the ability to compensate for the performance depleting effects of such conditions as stress, fatigue, and other environmental conditions (e.g., higher levels of CO_2).

Preliminary findings suggest that attention might be negatively affected for at least some types of tasks (Heuer, et al., 2003; Manzey et al., 1995; Manzey et al., 2000), although whether it is a change in motor control in microgravity or other stressors present in an ICE environment that is the cause of attention deficit is unclear. Efforts to study the influence of gravity on learning, memory, and cognitive processing have increasingly recognized the need to discriminate between the contributing factors of the role gravity, radiation, and other physiological and psychological dysregulations (see e.g., Porte & Morel, 2012). In addition, the effects of space flight on other aspects of cognitive functioning including learning, executive function, and social processing are being explored (Porte & Morel, 2012). However, it is difficult to parse out the effects of

microgravity on memory proper versus identifying how stress associated with being in a microgravity environment (Ishii et al., 2004). The importance of this is evident when considering the exposure to radiation and multiple stressors associated with the isolation and confinement that is anticipated with an exploration mission, along with the fact that the hippocampus (the key to the consolidation and retrieval of long term memories), is particularly sensitive to both stress and radiation (Lupien et al., 2005; Monje, 2008; Obenaus et al, 2008). The Spaceflight Cognitive Assessment Tool for Windows (WinSCAT) is currently used on the ISS to test cognitive processes of attention and memory (Kane, Short, Sipes & Flynn, 2005).

Assessments of cognition throughout the mission, if sensitive enough to reliably and validly detect early changes, may serve as an important sentinel for subtle but sustained decreases in cognitive functioning due to radiation exposure.^{††††} The long-term exposure of our astronauts to galactic cosmic rays (GCR) during exploration missions poses overall health risks and introduces uncertainties pertaining to specific additional risks for the central nervous system (CNS) (Cucinotta et al. 2013) and the associated cognitive processes. The GCR exposure is comprised of high-energy (H) and high-charge (Z) protons and energy (E) along with a variety of different elements such as ⁵⁶Fe particles (Nelson 2003) and the low and medium energy protons referred to as solar particle events (SPE) (Cucinotta, et al. 2013). Exposure to cranial radiation can have progressive and debilitating effects on cognition (Barani et al. 2007), causing diverse and disruptive changes in important areas of cognitive functioning (e.g., learning, memory, processing speed, attention, and executive functioning) (Meyers, 2000). Other CNS effects are well known in medical patients exposed to radiation treatment with the resulting putative agents changes to the neuronal structure, plasticity, and architecture of the hippocampus (Chakraborti et al., 2012; Parihar et al., 2015). The dentate gyrus (DG) has been shown to be particularly sensitive and susceptible to the adverse effects of even low doses of radiation (Mizumatzu et al., 2003; Monje, 2008) with changes particularly noted in the dendritic and spine morphology, areas associative with several neurodegenerative disorders (Kaufman & Moser, 2000; Tronel et al., 2010), to include recurrent depressive disorder (Bremner et al., 1995). Radiation induces oxidative stress, neuroinflammation, as well as disruption and alteration of the complex neuroprotective system known as the blood brain barrier (BBB) as well as damage to the cerebral microvascular (see e.g., Warrington et al., 2011), both of which increase vulnerability for neurodegenerative diseases. Given the constellation of areas effected and the demonstrated impacts of radiation on cognition, it reinforces the importance of better understanding the long-term effects of radiation exposure and how these effects appear mediated by the dopaminergic system (see e.g., Kennedy, 2014; Davis, DeCicco-Skinner, Hienz, 2015).

There is recognition of the need for a more robust, comprehensive and validated assessment measures for cognition and memory with research ongoing in both analogues and ISS to meet the need for assessment and monitoring of cognitive functioning. This is an important area that will allow BHP to work closely with Space Radiation, Exploration Medicine Capability (ExMC) along with nutrition in the Health and Human Countermeasures elements for both monitoring and countermeasure opportunities.

^{††††} Of interest are animal studies that demonstrate that a diet rich in polyphenolic compounds (blueberry or strawberry extract) given to rats 8 weeks prior to radiation exposure enhanced their ability to perform behavioral tasks; putatively helping to counter the effects on cognition of high doses of ⁵⁶Fe ions (Rabin et al., 2005).

i. Post-expedition cognitive and behavioral health

The stress of flight does not end at landing. Returning astronauts must transition from an environment somewhat insulated from outside happenings where they have one primary focus (the success of their mission) back to a world with multiple pulls on their time and attention.

In order to make that transition successfully, they must shift their focus from the mission. To help make that transition, one astronaut relied on advice from a previously flown astronaut who said, "At this particular time, you just have to start letting go. It's time to move on, and you can't hold onto the role that you had, so don't even try. Instead take comfort in knowing that you did a good job and that it's time to come home" (Stuster, 2010, p. 19). Another succinctly stated that "as the end of the mission approaches, I will no doubt start to think of all the things I could have and should have done" (Stuster, 2010, p. 18), illustrating one difficulty that arises as roles change.

Once they return, astronauts must reintegrate into their lives on Earth. Anecdotal evidence, gathered largely from biographies, suggests that returning to routine work assignments and daily family life is not without its stressors. In a study of retired cosmonauts, confrontations, defined here as use of aggressive or assertive interaction in an attempt to resolve a situation, increased during post-flight but were not commonly mentioned by cosmonauts during flight (Suedfeld, Brcic, Johnson, & Gushin, 2015).

As concluded in a review by Collins (1985), behavioral problems that occur during space flight often do not terminate when the mission ends, but can linger with notable aftereffects (Category IV) making reintegration that much more difficult. If behavioral or psychiatric symptoms do emerge post-flight, space flight is not necessarily the sole or even a primary cause. Other stressors in life, such as marital distress (Aldrin, 1973; Kanas, 1987; Koppel, 2013) or the death of a family member (Clark, 2007), also may contribute to any behavioral and psychiatric symptoms. Nevertheless, space flight and its associated factors – e.g., isolation, confinement, workload – can become significant triggers or sources of stress. These space flight stressors, when they are paired with traditional life stressors, will likely have an exponential impact on behavioral health for long-duration astronauts (Kanas and Manzey, 2008). Minor stressors and daily hassles along with accumulated exposure to radiation is a likely contributor to post-expedition behavioral health. Objective measures are preferred to self-report measures of post-mission behavioral health and well-being (Bryan, 2015) (Category IV).

3. Predictors and contributing factors

The factors discussed here are believed to be predictors and contributing factors to post-mission behavioral health of astronauts. In many cases, a lack of empirical evidence necessitates that we rely on expert opinions to help synthesize the quality of research and to lend their scientific acumen and recommendations to our risk reduction efforts (Coulter, Elfenbaum, Jain, & Jonas, 2016).

Precursors of behavioral health distress serve as warning signals with many factors contributing to an individual's well-being and their behavioral health. Monitoring the presence of predictors and contributing factors will allow for the development of better screening methods to prevent behavioral and psychiatric conditions from emerging and the implementation of countermeasures more quickly and, thus, more effectively.

As noted previously, numerous factors contribute to an individual's behavioral health status. Certain factors such as crew member personality together with the quality and quantity of sleep predict the likelihood that behavioral and psychiatric distress will develop. These factors, which can be viewed as "stressors," are discussed in the following section. Note that not all "stressors" are negative in terms of their impact on the behavioral health of an individual.

The Space Studies Board of the U.S. National Academy of Sciences differentiates between physical and psychosocial environmental stressors (National Research Council, NRC, 2000) as factors that contribute to changes in behavioral health. Physical environmental stressors include microgravity and the inherent hazards of space flight (e.g., radiation, high CO2 levels). Psychosocial environmental stressors on exploration missions are likely to include the isolation, confinement, and at times, monotony of life in space.

a. Personality

The results of personality tests have been used to predict job performance for many years. As mission length and distances from Earth increase, selecting astronauts and, later, composing compatible crews/space flight teams based on personality traits becomes increasingly important. As an added challenge, personality characteristics required could very well vary depending on mission length (Ursin, Comet, Soulez-Larivière, 1992).

Some personality evidence that is specific to astronauts exists (Musson& Helmreich, 2005; Rose, Fogg, Helmreich, & McFadden, 1994; Rose, Helmreich, Fogg, & McFadden, 1993). Generally speaking, the following types of personality comparisons are found: (1) astronauts or astronaut applicants to a normative group; (2) astronauts to another occupational group; and (3) astronauts to peer/supervisor performance ratings or selection decision. No research has been undertaken that examines the relationship between personality and objective job performance, perhaps due to the difficulty in finding objective performance data that is not confounded by factors beyond the control of the astronaut. This lack of objective job performance limits any true attempt to identify the "right stuff (Santy, 1994). Further, no known research has examined astronaut personality with respect to successful reintegration post-flight.

To date, the published research that is related to space flight has primarily focused on two approaches of personality. One uses what is referred to as the Personal Characteristics Inventory and based on early work by Helmreich, Spence & Beane et al. 1980 and then applied to pilot personality (Chidester, Helmreich Gregorich, & Geis, 1991). This measure was designed to assess the both the positive and negative aspects of the two broad constructs of Instrumentality and Expressivity (Musson & Helmreich, 2005), while the other delineates personality in terms of the "Big Five" factors (i.e., neuroticism, extroversion, openness, agreeableness, and conscientiousness). The findings of each approach are discussed below.

1) Instrumentality and Expressivity

Instrumentality provides an indication of the degree of goal-seeking and achievement orientation. Expressivity assesses social competence or how an individual behaves in interpersonal relationships with those high in expressivity typically seen as kind and warm in their interactions with others. In contrast, those low in expressivity demonstrate negative communion (e.g., submissiveness, servility, gullibility) and are verbally aggressive (Kanas and Manzey, 2008).

The two factors of instrumentality and expressivity and their positive and negative levels has led some to identify what they refer as "trait characteristics" that reveal the "right stuff," the "wrong stuff," and "no stuff" (Gregorich et al., 1989, see also, Musson and Helmreich, 2005). The right stuff, which is characterized as *high positive instrumentality* and expressivity along with *low negative instrumentality*, is related to higher peer evaluations of job and interpersonal competence (McFadden et al., 1994). Having the right stuff in settings that involve complex group interaction is related to superior performance (Musson and Helmreich, 2005). In contrast, those who have the "wrong stuff" display high positive instrumentality, high negative instrumentality, along with high work orientation, mastery and verbal aggressiveness. Individuals who are low on both instrumentality and expressivity with low work orientation, are considered to have "no stuff."

2) The Big Five

As stated earlier, neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness comprise the Big Five factors of personality. Individuals who are highly neurotic are more likely described as impulsive, self-conscious, and are more prone to psychological distress. Those who are highly extroverted tend to experience more positive emotions and are likely to be more outgoing and energetic in their dealings with others. Persons who are highly open to experience actively seek that which is new and more likely to embrace more unconventional ways of getting things done. Agreeable individuals will tend to be more trusting and helpful, preferring interactions that are compassionate rather than competitive or tough-minded. Those who are highly conscientious show a level of goal-directed behavior that is organized, dutiful, organized, motivated, controlled, and persistent (Costa and McCrae, 1992). While agreeableness is closely related to aspects of positive expressivity, the other four factors (i.e., neuroticism, extraversion, openness to experience, and conscientiousness) do not easily map onto the instrumentality/expressivity approach (Musson et al. 2004).

Musson (2003), in his examination of human performance data that were collected by the Human Factors Research Project at the University of Texas, found that males who made it to the final round of astronaut selection were high on agreeableness and conscientiousness and low on neuroticism. As with males, female applicants were high on agreeableness and conscientiousness and low on neuroticism. Female applicants were also high on extraversion.

Regarding astronauts rather than astronaut applicants, Musson (2003) found that male astronauts follow the same pattern as male astronaut applicants; i.e., they are high on agreeableness and conscientiousness and low on neuroticism. Female astronauts, on the other hand, appeared much different from their female applicant counterparts. This may be an artifact of the small sample size for female astronauts (N = 10); therefore great caution is needed in generalizing these findings.

Tying personality to performance, Rose et al. (1994) found that agreeableness is positively related to four ratings of performance (i.e., peer-rated interpersonal, technical, and leadership competence as well as supervisor-rated job performance) for U.S. astronauts. Openness to experience was negatively related to peer-rated technical and leadership competencies and to supervisor-rated job performance. No other significant correlations were found between these performance ratings and

the Big Five. This is a surprising finding given that conscientiousness is considered one of most valid personality predictors of job performance (see e.g., Mount & Barrick, 1998). For example, conscientiousness, along with extraversion and low levels of neuroticism, were found, along with military service, to serve as positive, independent predictors of performance in ICE environments (Palinkas et al., 2000). The absence of significant relationships may reflect methodological approaches (e.g., use of subjective vs objective job performance ratings). It also may reflect the fact that certain environments "pull differentially" on the way certain, more narrow expressions of our traits may help us adapt. For example, a study by Hough (1992) helped identify two separate narrow traits of extraversions; affiliation and potency, that differentially predicted technical proficiency and overall job performance, respectively. In similar fashion, ICE environments may differentially pull for higher levels overall facets of conscientiousness (e.g., "order" or "dependability") but with lower needs for achievement strivings (i.e., increased need for getting along and "fitting in"). In another study looking at a variety of space and simulation environments (e.g., polar expeditions, space missions, submarine missions, etc.), Sandal (1998) identified that individuals with strong achievement motivation (i.e., a facet of conscientiousness) combined with interpersonal sensitivity (i.e., agreeableness), seemed to adapt more effectively than others. Ursin and colleagues found moderate aggressiveness to be appropriate for short space flight missions, such as Shuttle, but not, they proffered, for longer duration missions (Ursin et al, 1992)

These findings point to the importance of continuing to determine the appropriate contributions of personality for job performance, interpersonal, and psychosocial adjustment to help set the conditions for behavioral health risk reduction and optimal performance required by exploration missions.

b. Resiliency and hardiness

Resiliency can be defined as "a class of phenomena characterized by patterns of positive adaptation in the context of significant adversity or risk" (Masten & Reed, 2001, p. 75). Resiliency traces its roots to research on children who overcame adversity (e.g., alcoholic parents, disadvantaged economic conditions) and displayed healthy functioning. Resilience can mean many things to many people and at times it might be described as a trait, a process, or as an outcome. Indeed, Meredith et al (2011) captured 104 definitions resilience and note that most of these definition come down to two characterics: position adaptation in the presence of an adversity. That is very similar to how Space flight experts define resilience during space flight as having two facets. One involves endurance or an ability to sustain when faced with unremitting stressors (e.g., low light, ambient low, monotonous tasks). The second is focused more on recovering, or bouncing back, from acute stressors, such as an unscheduled EVA (spacewalk) (Vanhove et al. 2014).

A resilient individual is one who is cognitively high functioning, has internal locus of control, notoverly-reactive emotional style, and strong social support (Miller 2008). Miller's list of characteristics suggests that resiliency has both innate components (e.g., emotional style) and components that can be enhanced through training (e.g., development of a social support network). Indeed, resilience-building training programs have been effective in non-analog environments (Vanhove et al. 2014) suggesting that similar training in ICE environments, including space flight, might also be effective. Ensuring crewmember resilience is not simply an issue for the individual crewmember. Others can behave in ways to bolster crewmember resilience. Organizational processes and resources offer an important dimension enhancing resilience of its members. When interviewed, experts indicated that mission controllers, for example, can support crewmember resilience with honest and efficient communication, and also by demonstrating understanding of stressors in space flight (Vanhove et al. 2014) (Category IV). Individually, crewmembers may act to support another's resilience.

Resiliency has also been posited to be a team level phenomenon. Teams are particularly important for enhancing resilience in high-risk occupations (Adler 2013). Team resilience has been conceptualized to be a psychosocial process that adapts as necessary to protect a group from negative effects of stressors group members encounter together (Morgan et al. 2013). For more on resiliency in teams refer to the evidence book on the *Risk of Performance and Behavioral Health Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team.*

A construct closely related to resilience is hardiness. It was first characterized by Kobasa (1979) as a collection of related personality qualities or traits separating healthy executives under stress from unhealthy ones. Hardiness is conceptualized in terms of three related attitudes: commitment, control, and challenge. High-hardy individuals have a strong commitment to their values, goals, and capabilities, a greater sense of control or influence over what happens in their lives, and a perception of stressors as challenges to be mastered (Maddi and Kobasa 1984).

Bartone (2006) has expanded this conceptualization and sees individuals high in hardiness as incorporating a strong future orientation, while at the same time learning from the past, and possessing a sense of humor. Hardiness is traditionally thought of as a trait and sometimes referred to as "dispositional resilience" (Bartone 2006), reflecting a generalized tendency to display resilient responses. Dolan and Alder (2006) view hardiness as a trait marker for resilience within the military. Britt et al. (2001) found that hardiness was associated with an increase perception of meaningfulness along with viewing the military deployment as more beneficial. However, hardiness may also be somewhat amenable to influence through leadership in organizations and training (Bartone and Hystad 2010). That is, hardiness has been shown to increase with more effective leadership within the organization (see e.g., Bartone 2006), can be enhanced via training programs (Maddi 2007; Maddi et al. 1998), and is linked to performance outcomes (see e.g., Bartone et al. 2008; Eid and Morgan 2006; Westman 1990).

Studies have found that hardiness does play a role in keeping people healthy under stress. Although the mechanisms are not clear, studies show that hardiness is related to baseline HDL cholesterol levels (Bartone et al. 2009) and reduced blood pressure responses to stress (Contrada 1989). More recently high hardiness (with a balanced profile) has been linked to more moderate and healthy immune and neuroendocrine responses to stress (Sandvik et al. 2013).

Hardiness has been shown to be particularly protective with regard to the effects of military-related stressors on psychological health outcomes and performance under stressful circumstances. Bartone (1999) found that hardiness moderated the effects of combat exposure on subsequent psychological well-being in U.S. Gulf War veterans. Hardiness has also been shown to be negatively related to posttraumatic stress in studies of Vietnam veterans (King et al. 1998), and to

veterans returning from Operations Enduring Freedom and Iraqi Freedom (OEF/OIF; Pietrzak, Johnson, Goldstein, Malley, & Southwick, 2010). Hardiness has been found to be a predictor of success in rigorous selection programs including those for U.S. military Special Forces (Bartone, Roland, Picano, & Williams, 2008), Norwegian border patrol military personnel (Johnsen, Bartone, Sandvik, Gjeldnes, Morken, Hystad, & Stornaes, 2013), and Norwegian military officers (Hystad, Eid, Laberg, & Bartone, 2011).

c. Emotional Reactions

Emotional reactions, according to the National Research Council (NRC) report by the Committee on Space Biology and Medicine (1998), have three primary response systems: language, behavioral acts, and the physiological response of alterations to the hypothalamic-pituitaryadrenal (HPA) axis. Language can be used to voice reactions to stress through reports of feelings. Behavioral reactions to emotions are more physical in nature, however, and include acts of avoidance or attack. Negative emotions are associated with: decreased performance and motivation; disruptions to short-term memory, attention, and other cognitive processes; increased interpersonal conflict; isolation from others; various psychosomatic and psychophysiological symptoms (NRC 1998); and greater perceived stress. HPA activation can be affected by, or cause inadequately regulated emotions, thereby suppressing the immune system and leaving the individual at greater risk for disease (Charles and Mavandadi 2004). HPA is a major component of the stress system that regulates the secretion of corticosteroids. Activation of the HPA during depression is common, although whether HPA activation causes or results from depressed mood is not known (NRC 1998). Alterations of the HPA axis are known to be associated with negative emotion and affect in ICE environments (Connors et al. 1986; Palinkas, 1991; Palinkas et al. 1989). Thus, during long-duration missions, it is possible that changes may take place in the HPA axis that might also affect mood, affect, memory, and the immune system (Baum et al. 1982; NRC 1998; Otto 2007). These areas of research bring to light the important and complex interactions of the HPA axis and how its responses set the physiological and psychological conditions through which we adapt to physical, emotional, and environmental demands of our social world (Whitaker-Azmita 2016). As we venture forth into the isolation, confinement and extremes of long-term exploration, a better understanding of the biological basis of social support provides important insights and potential strategies to help strengthen the social bonds that serve adaptive functions and develop countermeasures to sustain those bonds during the long mission and with reintegration upon their return.

d. Sleep and the Circadian Rhythm

While it is difficult to predict who will or will not develop depression, sleep disruption is one early warning sign. Sleep disturbances are common diagnostic criteria for many psychiatric disorders (Colton and Altevogt 2006). Comorbidity of a sleep disorder with a psychiatric disorder is also common; e.g., 40% of individuals who are diagnosed with insomnia also have a psychiatric disorder. This comorbidity is higher for hypersomnia, where 46.5% of individuals also have a psychiatric disorder (Ford and Kamerow 1989). Insomnia is both a risk factor for and a manifestation of major depression (Livingston et al. 1993; Ohayon and Roth 2003; Cole and Dendukuri 2003). Research indicates that 15% to 20% of individuals who are diagnosed with insomnia also suffer from major depression (Ford and Kamerow 1989; Breslau et al. 1996).

There is great inter-individual, systematic differences in how sleep deprivation impacts various neurobehavioral responses and vulnerabilities (Van Dongen et al. 2004) and these seem to be associated with individual circadian differences (see e.g., Sletten et al. 2015). The circadian rhythm of the human body is linked to patterns of biological activities such as brain wave activity, hormone production, and cell regeneration. Circadian rhythms can be affected by environmental factors; e.g., the amount and timing of ambient light (Czeisler et al. 1986) (Category I). Humans require 2,500 lux to entrain their circadian cycles, however the illumination available on ISS at this time is limited between 108 and 538 lux. Slated to begin in the autumn of 2016, a much brighter and more flexible LED-based lighting system will be installed on ISS that is intended to mimic a day-earth night cycle and will include alertness, phase shifting, and sleep promoting capabilities.

Sleep is a large component of the daily circadian cycle and, as such, is affected by changes that influence the underlying circadian rhythm (NCR 1998). Changes in work schedule also can adversely affect a crew member's circadian rhythm. During the Russian Soyuz program, sleep schedules were occasionally set counter to the local time of the launch site. This change in sleep schedules was associated with decreased quantities of sleep and decrements in performance among the cosmonaut crews (NASA 1991). Indeed, the Space Studies Board states that a lack of sleep leads to increased stress and decreased cognitive and psychomotor functioning (Lim and Dinges, 2010; NRC 1998).

A recent well-controlled randomized cross-over study of 70 submariners demonstrated that humans can live in an isolated environment for more than two months by following an organized regular shift with controlled light and temperature, and social isolation (to avoid external cues)(Trousselard et al. 2015). In a study designed to assess how human performance and sleep were affected while adhering to a Martian sol schedule for 37 days, they found improvements in subjective (but not objective measures) reports of sleep and alertness with no apparent cognitive decline (Griofa et al. 2011). This research, while preliminary, offers intriguing findings that help us better understand the potential impact of light/dark cycles and opportunity to exercise some control over them in a long-duration journey to Mars.

Barger and colleagues (Barger et al. 2014) collected data from ISS and Shuttle astronauts confirm the findings of previous assessments of sleep quantity and quality on orbit; i.e., sleep duration in flight on average six hours and appears to be reduced in comparison to terrestrial sleep. The reasons for reduced sleep in space are varied and range from temperature, noise, carbon dioxide levels, voids, rumination, high tempo workload, to possibility that microgravity affects sleep architecture via fluid shifts. Current ISS operations still require schedule shifting, including times of slam shifting (i.e., sudden shifts in sleep/wake schedule), which can result in sleep loss and fatigue for the astronauts. Such schedule changes force critical mission operations to occur against the natural circadian rhythm of the body. The commander of Expedition 3, Frank L. Culbertson, Jr., did not consider slam shifting to be a problem for the flight crew as long as they had "adequate recovery time following the sleep shift and ensuing activities. He advised that sleep/slam shifting did have some physiological effects on the crew with respect to insufficient rest time" (Safety Review Panel 2002) (Category IV). Slam shifting also impacts the ground teams that support the ISS during critical operations as well as the ground teams that work overnight against the homeostatic drive to sleep (Barger et al. 2014). For detailed information on the performance risk that is associated with sleep loss and circadian rhythm disturbances, refer to the evidence book on the

Risk of Performance and Health Decrements Due to Sleep Loss, Circadian Desynchronization, and Work Overload.

e. Habitability and environmental design

Depending on the destination, exploration missions could have delayed communication, no view of Earth, and tight quarters. All of these result in reduced sensory stimulation. Humans require varied sensory input. Sensory stimulation meets our needs, including foraging for information, restorative relaxation, therapeutic release of emotion, and maintaining homeostasis (Vessel and Russo 2015). As such, creating an environment that is as sensory rich as possible and appropriate is paramount.

Space flight offers many unique challenges to designing an environment that provides sensory stimulation. For one, in an environment in which an individual floats freely, distinctions between up and down are no longer meaningful. Environmental design, or habitability, is thus no longer confined to the Earthly distinctions among floors, walls, and ceilings; this is an asset when the size of the ship or the station is limited. How readily a crew member adapts to this truly three-dimensional world varies by individual (Connors et al. 1986).

Lack of privacy, which has been associated with impaired individual well-being in analog studies, is a major psychosocial stressor in space flight (Connors et al. 1985). At the 2015 Human Research Program Investigators' Workshop, veteran astronaut Peggy Whitson, when asked by a member of the audience what she felt the single most important habitability factor to be, stated a private space, such as individual sleeping areas, to be most critical (Category IV). Research supports Whitson. Individuals who are in confined spaces tend to withdraw from one another during leisure time (Basner et al. 2014). Further, the leisure time is characteristically spent in more passive activities (Seeman et al., 1971). Having private crew quarters in which a crew member can be alone thus becomes extremely important on long-duration missions (Santy 1983; Kanas and Manzey 2008; Simon et al. 2011; Whitmire et al. 2015).

Evidence suggests that interior décor of spacecraft can affect well-being (Kearney 2013; Stuster 1996). Use of many different colors and the wide use of darker colors are contraindicated (Kanas and Manzey 2008). Colors can also be used to orient crew members since gravitational cues, which are missing in space, no longer provide navigational aids (Raybeck 1991). Windows promote well-being in ICE environments by decreasing the sense of confinement and monotony of the environment (Haines 1991). Anecdotal evidence from the earliest space flights supports the importance of being able to look outside (Haines 1991; Lebedev 1988). Kelly and Kanas (1992) provide empirical evidence that "watching" activities became more important.

Exposure to natural environments (i.e., nature) can be restorative and thus will be important on exploration missions (Kearney 2013; Simon et al. 2011). Time spent in natural, rather than urban, setting can reduce stress and increase recovery from health issues. It can also improve attention and mood (Vessel and Russo 2015). Limitations of the space vehicle, however, may preclude much in the way of nature. Ideally, plants will be included in the environment both as a food source and as a way of increasing sensory input and reducing stress (Simon et al 2011). A simulated nature experiences could be utilized as an effective countermeasure (Kearney 2013).

For greater detail, refer to Risk of an Incompatible Vehicle/Habitat Design evidence report.

f. Job design—Autonomy and meaningful work

How a job is designed can affect an employee's well-being. In the research literature, well-being is considered to be one of two forms. Either well-being is a hedonic form focused more on attaining pleasure (positive affect) and avoiding pain or it is considered to be eudaimonic and focused on meaning and striving toward a purpose deeper and more noble than simply self-gratification (Ryan and Deci 2001). Autonomy and meaningful work, long touted as important to astronauts, are both deemed indicators of this second form of well-being (Vanhove et al. 2014).

Eudaimonic well-being is associated with various health outcomes. Evidence from non-astronaut populations of the relationship between eudaimonic well-being and depressive symptoms is mixed. With other outcomes (anxiety, poor quality of life, and maladaptive coping strategies), the relationship with eudaimonic well-being has been moderate and negative (Vanhove et al. 2014).

While the ISS was designed to be flown from the ground, exploration missions that leave low Earth orbit will necessarily require crew to keep the spacecraft flying although much of it may be automated. This necessity will in part offset the increased stressors associated with the longer missions because it will force space agencies to put more control into the hands of the crew, to give the crew more autonomy. In long-duration exploration missions, asynchronous communication will create the opportunity for, and necessitate, providing greater autonomy and latitude for the crew to make decisions once reserved for mission control. Simulation studies suggest that crew autonomy might improve performance and sustain, if not augment, psychosocial adaptation to space and behavioral health (Roma, et al., 2009). In a ground-based study, Bassi and colleagues (2013) found that those employees with higher levels of eudaimonic well-being were also more likely to be autonomous. Thus the very nature of exploration missions will necessitate increased crew autonomy and thereby bolstering eudaimonic well-being.

Autonomy has been an issue since the beginning of the space program. Striking the right balance between crew autonomy and interdependence is dependent on understanding both the crew and the intraorganizational, social control of risk weighed against the technical design and the risk management procedures (Vaughan 1990). Crew autonomy benefits may differ by personality and by their culture. For example, in the Mars500 program, European crewmembers reported higher dysphoric mood in low autonomy compared to high while Russians reported generally the same mood. With regard to personality influences on autonomy, Ng, Ang and Chan (2008) found that a leader's self-efficacy was rated as more effective and better able to increase motivation in those they led, in high autonomy versus low autonomy situations. In a survey of 54 astronauts, Kanas (2005) identified increased crew autonomy, more dependence on onboard technical resources (in contrast to Mission Control), and communication delays with earth as potential interpersonal stressors than need additional research.

Mercury astronauts lobbied to be able to pilot spacecraft rather than simply being passengers in a craft controlled from ground (Wolfe 2008). A need for autonomy manifests in other ways besides just a desire to fly the craft. The crew of Skylab 4 stopped work as to protest a lack of control over their work schedule (Cooper 1976). Time demands control over time, as well as being overscheduled, continues to be an issue on the ISS even today. Entries in journals kept by ISS

crew provide multiple examples of the stress of maintaining a rigorous work schedule. The crew is continually pressured to perform (Stuster 2010b). Providing crewmembers with greater autonomy to set their own schedules might help prevent overworking, thereby reducing performance errors that occur as physical and mental exhaustion sets in (Nechaev 2001). ISS journal entries also talk about the value of setting one's own schedule: "Happy it is the holiday and we get to drive our own schedule. That feels a little like we have some control over our lives. I think that is why it feels good." (Stuster 2010b, p. 19). Space psychology researchers Kanas and Manzey (2008) concluded that crew members should have autonomy in planning their work schedules, managing their workloads, and deciding when to perform nonessential tasks to the extent possible (Kanas and Manzey 2008). As one astronaut summed it up, "It does help to have control of your own environment if you're going to be isolated." (Stuster 2010b, p. 19).

The amount of control granted to the crew will almost certainly vary depending on the phase of the mission. Closer proximity to Earth will allow ground crew to provide more direct support in all aspects of the mission. So, autonomy afforded to the crew will increase for the crew and decrease for ground support as the spacecraft travels away from Earth with the crew having the most autonomy when physically farthest from Earth. Later in the mission as the spacecraft returns toward Earth, the balance of autonomy will follow the same path, flowing from the crew back toward ground support. Both crew and ground support will need to learn to cede autonomy as the other assumes it. This shift in autonomy is anticipated to be challenging.

Control in the form of autonomy is not the only aspect of designing the job that will affect eudaimonic well-being on exploration missions. Astronauts have often reported about the importance of meaningful work (Britt, Jennings, Goguen, and Sytine, n.d.). Having sufficient meaningful work to conduct is more than just an important component of a successful exploration mission; it will be a critical one. Quoting the first U.S. astronaut on Mir, Norman E. Thagard, "[T]he single most important psychological factor on a long-duration flight is to be meaningfully busy. And, if you are, a lot of the other things sort of take care of themselves" (Herring 1997, p. 44). A lack of sufficient meaningful work can adversely affect mental well-being. Again, ISS astronauts' journal entries provide insight into the importance of meaningful work. ISS astronauts, like others before them, express frustration with tedious and repetitive tasks (Stuster 2010b). They dislike doing tasks without a purpose. In other words, astronauts do not like busy work. "Busy work," wrote one astronaut, "also causes me to miss home more. I think I feel less of a sense of purpose if I don't believe in the tasks that I am doing" (Stuster 2010, p. 11). Meaningful work likely varies across individual. Vehicle maintenance, for example, might be deemed meaningful by one crewmember while another views such work as necessary but not personally meaningful. The type of work that is considered meaningful could very well differ during the mission. During an outbound phase of a mission, crew is more likely to be focused on training tasks. In contrast, on the return phase, training might be less meaningful while analyses of samples would be more meaningful.

g. Monotony and boredom

Monotony is a frequent complaint of individuals in ICE environments such as space flight (Kanas 1998; Otto 2007). Among other contributing factors, monotony and boredom are closely tied to design of the environment and meaningful work, which were discussed in the two immediately preceding sections. A lack of variety in social interaction, leisure activities, and the physical

environment can contribute to perceptions of monotony and lead to boredom, interpersonal conflict, loss of energy and concentration, and a decrease in physical activity and social interaction (Basner et al. 2014; Otto 2007; NRC 1998).

Life in onboard a spacecraft such as the ISS is often characterized as a combination of monotonous work with requirements for high degrees of alertness and penalties for errors. This combination of monotony with high-risk consequences for errors is especially stressful (Thackray 1981). Even in the face of monotony, however, performance remains high enough for mission success, provided that the motivation is high (Kanas and Fedderson 1971).

Chronic boredom, well documented in environments with limited sensory stimulation, could lead to more serious mood disturbances (Vessel and Russo, 2015). As missions become longer, the focus on the amount of work that humans can safely perform changes from how much to how little (Weiner, 1977).

h. Daily hassles and major life events

Although some stressors that are found in space are a result of the fact that space is an ICE (isolated, confined, extreme) environment, other stressors are unique to space itself. The number and extent of daily hassles of life, i.e., those "irritating, frustrating demands that occur during everyday transactions with the environment" (Holm and Holroyd 1992, p. 465), are significant predictors of health (DeLongis et al. 1982; Lazarus and DeLongis 1983; Rowlison and Felner 1988) since increased stress can lead to diminished health. Daily hassles that are associated with the physical environment that is unique to space include: a growing accumulation of garbage, limited facilities for sanitation, the need for constant vigilance, and a relative lack of privacy. The noise and vibration of ISS are acoustic stressors that can affect sleep quality and quantity, the low level of illumination on ISS is a photic stressor (NCR 1998). Astronaut journals provide direct evidence of hassles associated with life and work on the ISS. One astronaut stated it succinctly, "Today was a hard day. Small things are getting to me." (Stuster 2010b, p. 10). These seemingly small hassles can aggregate into larger psychological issues (Nicoletti & Garrido n.d.).

Psychometrically, measuring the impact hassles have on a crewmember's well-being can be very challenging. An inherent dislike of psychological testing is one impediment to measuring psychological constructs in general. One NASA BHP researcher has related that more than one astronaut has informed him that they respond to psychological tests in such a way as to confuse or mislead the researcher. Further increasing the difficulty in measuring the relationship between hassles and well-being or mood is the transient nature of hassles. A disconnect between occurrence of hassles and measurement means that the impact of hassles can be missed. Fortunately, Stuster's ongoing astronaut journal project provides some insight into the effect hassles have on mood and well-being. For example, "Thanks journal. Venting complete. I feel much better now... It is funny. A bunch of hours later and I am completely over this issue. Not a care in the world about it. Glad I could vent to the journal and not via email because that could be catastrophic to my career" (Stuster, current research).

Life on Earth continues even as the crew is isolated on the ISS. The result is a crewmember occasionally experiencing a major life event while on the ISS. Daniel Tani's mother was killed in

a vehicular accident while he was on board the ISS. His loss had ripple effects on the entire crew. Fortunately, not all major life events are negative. Michael Fincke's son, for example, was born during his first expedition to the space station. While the inability to be present for the birth of his son might not have been stressful, even desired major life events can result in stress due to the changes such an event has on one's life.

i. Cultural factors

Culture is a broad term that can encompass national culture at a macro level as well as organizational culture or even intra-organizational subcultures, such as a distinction between civilian scientists and military pilots, at a more micro level. The crew can be impacted by all of these cultural factors. In an extensive review of ICE environments literature, Palinkas found crew homogeneity to be related to social compatibility in both space and ground analog environments (Palinkas, 2010). Yet, because the ISS is international, crews must contend with a fair amount of heterogeneity amongst its members. Both organizational and national cultural differences between the five national space agencies involved in the ISS influence crew dynamics (NRC, 1998), potentially hindering crew cohesion and resulting in increased perceptions of stress. Factors associated with national and other types of culture are covered in greater detail in the evidence book on the *Risk of Performance and Behavioral Health Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team*.

j. Ground support / Mission support

Research on the theory of minimal group paradigm tells us that even arbitrary and apparently meaningless differences between groups of people will result in feelings of in-group versus outgroup (Tajfel et al. 1971). Not surprisingly, then, an "us vs. them" attitude can develop between the crew and its off-site support, as well as feelings of animosity toward the same off-site support. This dynamic is sometimes termed "displacement" because the team is displacing the intra-group tension onto safer, more remote individuals (Kanas and Feddersen, 1971). Although displacement is not an uncommon occurrence between remote teams and their support centers, it nevertheless becomes more critical for space flight as the missions grow longer and the conditions of isolation expand.

While crew members' feelings of lack of control, such as a lack of autonomy, can exacerbate the perceived distance between these two groups, there is more to the phenomenon of "us versus them" than is created only by ground control setting the crew's schedule. Still, examples of ground having control over the crew's schedule do provide powerful illustrations of feelings of injustice that arise. In 1974, friction between crew members and Mission Control during a Skylab mission resulted in a work stoppage in which crew members insisted on taking a scheduled day off after weeks of work without a day of rest.

Ground support can have a positive or negative impact on the crew. One journal entry captured the profound effect that ground-crew interactions can have on the crew: "Interesting, how you can be on top of the world one moment (literally) and then be completely demoralized the next, because of what is said on the ground" (Stuster, 2010, p. 15). Knowing that communications with ground can negatively impact crew morale and performance, communications between mission control and crew frequently involve praise inflation (profuse compliments and avoidance of criticism). Instead of

improving relationships between ground and crew, praise inflation can be a source of annoyance and may even undermine trust.

The tension between organizational management and autonomy addressed earlier often is revealed in the journals of astronauts as they express their feelings about the interactions they have with "the management" on the ground. For example, Stuster, upon review of his astronaut journals project, concluded that actions taken by NASA support or management have resulted in serious declines in morale on the ISS (2014, personal communication). Management decisions have seriously upset ISS astronauts and these often take the form of feeling irritated with actions being taken ("amazed by the degree to which the ground has gotten into the habit of taking action and not informing the crew," opportunities denied (e.g., no PAO event after a spacewalk), or a sense of being micromanaged ("safety folks seem to concentrate on minutia while neglecting big things" (Stuster, 2010, p. 31). Regardless, astronauts continued to perform well (Stuster, 2014, personal communication).

Perhaps not surprisingly then, crews sometimes choose to deal with conflict with the ground by choosing to ignore the ground for a period of time or by censoring the information shared with the ground. The crew of one Salyut space station shut down communications with Mission Control for 24 hours. Lebedev (1988) and crew members failed to report a fire to the ground because "it would have just caused more panic" (p. 309). In addition, this phenomenon extends beyond just space flight. Antarctic winter-over crews report having avoided communicating with their administrative support or deliberately misleading their administrative support (Otto, 2007). In a review of the ICE literature, Vanhove and colleagues (2014) concluded that such avoidant behaviors offer an effective coping strategy for maintaining good psychosocial functioning.

k. Family and Social Support

According to a former NASA Family Support Officer, astronauts have reported feeling more relaxed and able to concentrate on tasks at hand when they believe that someone is taking care of their families (Category IV). Worrying about family and family events that might occur at home while the crew member is away can be stressful. Psychiatric intervention was required post-flight for an Apollo 11 astronaut due to his marital distress and depression (Aldrin, 1973; Kanas, 1987). For example, after the death of one cosmonaut's mother, he psychologically withdraw for 1 week during his mission (Clark, 2007).

A fuel gauge problem required that a shuttle mission be postponed for 2 months resulting in astronaut Daniel Tani's duties as a space station flight engineer being extended by 4 months. It was during this extension period that Tani's mother died. At his return home ceremony, which was held in Houston on February 21, 2008, Tani commented on the importance of psychological support: "We so rightfully thank every technical trainer we have, but when you go and live on the station, there is a whole aspect of living that we have to think about and anticipate." He expressed his gratitude for flight surgeons and psychologists as well as the implication for future missions: "That was invaluable to me. This is something we will have to learn how to really support and develop for long-duration flights to the moon and Mars" (Carreau, 2008). Tragedies such as the death of Tani's mother affect all crew members, including those who are on the ground crews, and they can be especially challenging for mission commanders who seek to lend support to a grieving crew member.

The benefits of social support are well documented (Ertel, Glymour, & Berkman, 2009; House, Landis, & Umberson, 1988; Robles & Kiecolt-Glaser, 2003; Umberson & Montez, 2010). Seeking social support in an ICE environment as a coping mechanism, however, is negatively related to resilience (Vanhove, et al, 2014). So, having social support and knowing one has social support is beneficial (Miller, 2015), but seeking social support as a coping mechanism could be an indicator of a deeper issue.

I. World Events

"The world changed today," ISS Commander of Expedition 3, Frank Culbertson stated in a September 12, 2001 letter reflecting on the events of the past day. In addition to family events, world events viewed from space, can be stressful. In 1991, the Mir space station crew launched as Soviet Union cosmonauts yet later returned to Earth as members of a different space agency from a different country (the Russian Federation) (Russian Spaceweb, 2008). A decade later on board the ISS, Astronaut Frank L. Culbertson, Jr., used video and still cameras to document the aftermath of the Twin Towers attack on September 11, 2001. On being told of the attacks, he writes that he found a window that would give him a view of New York City, "It was pretty difficult to think about work after that, though we had some to do, but on the next orbit we crossed the US farther south. All three of us were working one or two cameras to try to get views of New York or Washington" (Culbertson 2001). Although far from home, astronauts and cosmonauts are not untouched by turbulent events on Earth.

4. Prevention and monitoring countermeasures

Seyle's model of the General Adaptation Syndrome states that as a stressor appears and continues, an individual's coping resources are first mobilized, deployed, and depleted if not resolved. Seyle (1978) termed these stages alarm, resistance, and exhaustion. One of the goals of prevention is to avoid distress by providing crew members with the wherewithal to minimize or negate a stressor. One type of countermeasure attempts to do exactly that by seeking to prevent occurrence of the risk or mitigate the potential severity of the risk. A second type seeks to monitor or treat the risk if it does occur (Strangman 2008).

According to Kearney (2013), countermeasures can act to reduce risk by (1) reducing environmental stressors (due to habitability and mission) by modifying the environment, (2) increasing capacity of crew to cope with and respond to stressors (through selection, training), or (3) providing crew with mechanisms and strategies for coping with and recovering from environmental stressors (e.g., stimulate the brain; promote the recovery of directed attention and reduction of overall stress; provide social support and social interaction; foster group cohesion and positive group dynamics).

The psychological support provided to spaceflight crews uses both types of countermeasures (prevention/mitigation and monitoring). If conditions do arise, a psychological support system allows for early detection of the condition and timely application of countermeasures. If necessary, more intensive treatment methods can be applied. The goal for exploration missions will be similar: To provide the means for early detection and countermeasure application, followed by treatment methods as needed. The difference is that for exploration missions, communication delays will require crewmembers to monitor their behavioral health status via key indicators and autonomously implement countermeasures.

The current practices and services that are offered by the BHP Operational Psychology Group at NASA are comprehensive, beginning pre-flight and continuing through post-flight (Sipes and Vander Ark 2005). These services are shaped in part by a crew member's personal preferences, family requests, and specific events during the missions, as well as by programmatic requirements and other lessons learned.

The lack of behavioral and psychiatric emergencies during spaceflight provides indirect evidence of the efficacy of current countermeasures for current mission lengths of approximately 6 months.

a. Selection

The first opportunity to prevent behavioral symptoms and/or psychiatric conditions occurs when selecting new astronauts. Since 1959, selecting astronauts at NASA has included screening for mental illness that could jeopardize mission success, with the process of psychiatrically qualifying or disqualifying astronaut applicants being standardized in 1989 (Santy 1994). In response to the unique demands of missions extending past the average two weeks of a shuttle mission, Galarza and Holland (1999) conducted a preliminary job analysis distinguishing between the relative importance of skills required for long-duration mission success. These skills, or competencies, identified as necessary for successfully living and working in space for months at a time have been incorporated into the selection process. As we move from space missions on the ISS to exploratory missions that will leave near Earth orbit, BHP undertook another job analysis (Vessey et al. 2014). This time the focus is on those competencies required to be successful during missions that will explore deeper space, where crews will necessarily be more autonomous from ground support owing to communication delays and no evacuation options, and within a confined habitat of a small volume vehicle for up to 30 months.

Expectations are that the present structure of the selection process will be maintained, adapting the tests and interview content, as required, to reflect any identified changed competencies. Currently the selection system seeks both to screen out those applicants with a pre-existing illness and to identify those applicants best suited to life as an astronaut (Cox et al. 2013). The former reduces the likelihood of psychiatric conditions and the latter reduces the incidence of psychiatric conditions as well as adverse cognitive or behavioral symptoms. For screening out those with pre-existing illnesses, clinical judgments are based on a standardized psychiatric interview augmented with personality measures as a secondary source of information. Identifying applicants most suited to being astronauts likewise involves a standardized interview, with a focus on psychological factors identified as critical for success in long duration spaceflight (Galarza & Holland, 1999) leveraging both psychological testing and assessments based on observations during field exercises (Slack, Sipes, & Holland, 2014).

Prevention begins with selection. Those individuals identified as most likely to have a behavioral and psychiatric emergency in flight are eliminated during the selection process; i.e., they never become astronauts. This facet of the selection process is commonly called "select-out". The NASA select-out system is thorough, but the predictive ability (and validity) of all selection systems diminishes over time. Individuals and circumstances change as time passes so that a test that was administered during selection 10 years before an individual is assigned to a mission, has a limited ability to predict in-flight and post-flight behavior.

Not only are the individuals who are most likely to have a behavioral and psychiatric emergency selected-out, individuals best suited to being astronauts are identified. This aspect of selection is typically termed "select-in." Because this aspect of the current NASA selection system occurs under Medical Operations, the use of the term "select-in" is technically inaccurate. Instead, this aspect of selection is more accurately described as a "suitability" determination.

A suitability score, which is given to each interviewee, is derived using both clinical judgment and actuarial measures to make a determination of the degree to which that interviewee meets the criteria for what is determined to represent a good astronaut. Factors that are considered when determining suitability include: personality, emotional stability, interviews, assessed performance in the field exercises, and family demands. Again, as with select-out tests, suitability scores are less predictive over time. To counteract the deterioration of the selection data, annual psychological assessments were recommended in the "NASA astronaut health care system review committee: Report to the administrator (February - June, 2007)" (Bachmann et al., 2007). Annual BHP assessment interviews, which are performed by an experienced crew flight surgeon, also boardcertified in psychiatry, started in October 2008. This assessment is comprised of a 30-minute interview in the Johnson Space Center (JSC) Flight Medicine Clinic and covers broad areas of occupational relevance, including space flight experience, workload, fatigue, sleep, peer relationships, family, challenges, goals, and future plans. These annual assessments, however, are not intended to be comprehensive psychological screenings for mental disorders or psychiatric illness. Such an assessment would be very time-consuming and produce an extremely low yield of any useful data. Of greater importance operationally are the ISS pre-flight assessments that begin 1 year prior to an astronaut being given a backup assignment. These interviews are longer (90 minutes) and far more intensive in terms of content.

b. Pre-flight

Despite the annual and pre-flight BHP assessments, there is a risk of unpredicted in-flight behavioral degradation due to unforeseen circumstances such as a mishap, personal tragedy, interpersonal conflict, or the development of symptoms of a mental disorder that was latent before flight. In this regard, there remains a risk of mission-impacting mental distress and performance degradation that cannot be ignored, one that requires further review, improved assessment techniques, and autonomous intervention methods. BHP is beginning to explore, via research with computer adaptive testing assessment batteries, an effort to identify an optimal balance between the assessment validity of the various measures used, while reducing the respondent burden on the astronauts.

The Operational Psychology (Op Psy) component of BHP provides psychological support to ISS crew members (Sipes & Vander Ark, 2005) (Category IV). While the majority of Op Psy support occurs in flight, preparations begin pre-flight as astronauts express their preferences for support options such as crew member website content, movies, games, and food. These decisions allow crew members to take some of the familiarity and comfort of home with them.

"Lessons learned" are shared both formally and informally among astronauts and family members. Formal Astronaut Office briefings are scheduled following each mission as well as between the assigned crew members of adjacent missions. These lessons learned are documented and distributed among astronauts and their families. Formal briefings and training sessions are also scheduled with crew and family members before each mission. Informal briefings occur between experienced and inexperienced astronauts, as well as between their spouses or significant others. Other opportunities to share information are provided by the Astronaut Spouses Group (ASG) during social and educational events. General advice that is not targeted to a specific individual or family is available from a variety of resources such as the ASG newsletter, Astronaut Office documents, and Flight Medicine Clinic handouts.

The JSC Family Support Office (FSO) acts for astronauts and their family members by liaising with the Astronaut Office, the ASG, BHP, JSC security, the Flight Medicine Clinic, the Military Liaison Office, the Public Affairs Office, and others. An organizational FSO is needed when employee tasks include lengthy deployments or hazardous duties that affect employee families. Personnel in the FSO assist with all issues or concerns in a confidential manner. They also connect and communicate with families so that these families are informed and ready in the event of an emergency. To support families in their readiness preparations, the FSO provides publications, newsletters, email notices, training and educational classes, and specialized seminars. The FSO was created to address the unique challenges that face astronauts and their families during astronaut training cycles and flight assignments (Sipes & Vander Ark, 2005). As several astronauts have noted, the FSO provides the support that enables them to more easily concentrate on their work in space because they believed that their family needs are being met by FSO personnel in their absence.

1) Behavioral Health and Performance Training as a Countermeasure

One method for providing crew members with additional coping mechanisms is to teach them specific coping skills. BHP Op Psy provides initial trainings to astronaut candidates (ASCANs) and further training to astronauts, and in some cases their families, once a flight has been assigned.

Upon their arrival at NASA—JSC, ASCANs attend a set of BHP sponsored trainings. Descriptions of these initial classes are provided below.

Behavioral Health and Performance Overview is an ASCAN's first introduction to the services BHP provides to astronauts. Included is a description of clinical services, preparation for flight, and support while in flight. The overview also provides a quick introduction to all the training astronauts will receive once they are assigned to a flight.

Conflict Management is a discussion-oriented training lesson that introduces a three-point cycle that drives, escalates, and de-escalates conflict. The course reviews methods for breaking the cycle at each of the three points so that conflicts are resolved in ways that preserve relationships with colleagues, friends, and family. Techniques include "rules" for fair fighting, checking the accuracy of interpreted meanings, and recognizing and managing emotions that can perpetuate conflict.

Stress Management as a class has morphed over the years from its original focus on traditional stress management techniques. The training now essentially covers the fundamentals and methods of psychosocial adaptation—becoming accustomed to the stressors inherent in living and working in the spaceflight environment for months on end. As part of this, self-care/self-management,

which refers to keeping oneself satisfied and productive under demanding circumstances and managing one's own stress, is covered. This class teaches ASCANs to apply strategies of self-care/self-management as they encounter the stressors that are common to being astronauts, both on the ground and during an expedition.

Cross-cultural Training exposes U.S. astronauts to special circumstances that can arise from working with crew members and ground control personnel from the International Partners of NASA. The course addresses cultural factors, communication and negotiation styles, and work and social factors. Potential positive and negative effects of cultural differences are identified. Methods, strategies, and resources that can be used to handle cross-cultural challenges are described and practiced within the context of case-situations that occurred previously. This course was devised in answer to the interview requests of astronauts who flew on the ISS and Mir for more and better cross-cultural training.

Expeditionary Workshop occurs periodically throughout the ASCAN training flow. The workshop covers the primary BHP competencies (e.g., teamwork and self-care/self-management) used during selection. The workshop, facilitated by BHP operational psychologists, is taught by experienced LDM flyers. The ASCANs hear stories and lessons learned from astronauts who have already been through the rigors of life on the ISS and review ISS critical incidents, experiences, and effective behaviors and coping strategies for living on the ISS.

National Outdoor Leadership School (NOLS) is time in the wilderness practicing those skills covered in the expeditionary workshop. NOLS allows teams to practice managing risk while they conduct scientific field campaigns in remote, stressful, and harsh environments. The curriculum is designed to develop leadership skills in particular and also provides opportunities to practice teamwork and self-care skills.

Once an astronaut has been assigned to a flight, mission specific BHP training begins. Descriptions of these classes follow.

At 28 months prior to launch, *In-flight Resource Plan Introduction* is taught. This course provides astronauts with an overview of the support that BHP provides to ISS astronauts. At launch minus 12 months and launch minus three months, *In-flight Resource Plans 1 and 2* go into further depth. These follow-on courses further familiarize astronauts with BHP and its functions, and provide them with a first look at some of the coping mechanisms that are available.

Psychological Factors 1 exposes crew members to the psychological effects of long-duration space flight. The manifestations of various psychological factors are discussed, as well as the procedures that are used to manage any contingencies.

Psychological Factors 2 continues the discussion of the support resources that are available during a mission for the crews and their families. It also identifies the principle environmental, interpersonal, and programmatic factors that can impair psychological health and performance during extended confinement.

Psychological Support Planning 1, Psychological Support Planning 2, and ISS Crew/Family Psychological Support Familiarization classes brief crew members on the psychological support program that was established to assist crew members and their families during the pre-flight, inflight, and post-flight phases of the mission. Each crew member begins to identify his or her desired in-flight support resources, based on the options that are currently available. At the crew member's discretion, family and/or primary support individuals will be invited to the meeting.

Practical Planning for Long-duration Missions encourages crews and family members to consider important personal arrangements before long-duration missions. This class stresses critical actions (e.g., wills, emergency contact information), reviews "lessons learned", and provides tools and checklists to help simplify the personal preparation process. The FSO offers this class in conjunction with BHP and the Astronaut Office. Spouses, significant others, and other key family members may attend this event at crew member discretion.

ISS Behavioral Medicine Training is provided to crew medical officers and flight surgeons. This training provides an overview of the psychiatric symptoms and disorders that might be seen during a mission. Discussion includes the therapeutic clinical response and resources available that are available on the ISS should a crew member exhibit seriously disordered behavior. The focus of this training is on serious psychiatric symptoms or illness as opposed to behaviors that fall within the norm for persons who are living in stressful circumstances.

2) Behavioral Health and Performance Behavioral Medicine Interview and WinSCAT

Behavioral medicine psychiatric interviews begin 12 months before launch and end at 30 days post-return. These interviews are the mainstay of pre-flight detection and prevention of in-flight psychological or psychiatric problems (NASA 2008). Interviews focus on mission training issues, crew-crew interaction, family issues, sleep and fatigue, workload, crew-ground communication, mood, cognition, ground re-adaptation, and family reintegration.

Another behavioral medicine requirement on the ISS is the WinSCAT (Space flight Cognitive Assessment Tool for Windows), which is an 11- to 15-minute computer-based cognitive screening test. Baseline testing begins 6 months before launch, and the astronaut is requested to take it once a month while in orbit. WinSCAT is an operational medical requirement that will be used after an astronaut has suffered any unexpected medical event (e.g., head trauma, decompression sickness, exposure to toxic gases, medication side effects); it will serve as a data point for crew surgeon medical assessment/disposition (Kane et al. 2005). Off-nominal WinSCAT scores are evaluated in context before considering whether to adjust the work-rest schedule or take another course of action.

These extensive ISS pre-flight behavioral medicine interviews along with the BHP training classes help to prepare crews and their families for long-duration space flight and act as another behavioral health-screening aid.

3) Future directions and current research associated with pre-flight

One possible area of future training involves resilience building, which has been shown to be effective for a variety of at-risk populations. Training that focuses on perceived social support,

positive cognitive reframing, and problem-focused coping results in increased resilience (Vanhove, et al, 2014). In order to maximize effectiveness of resilience-building training, Vanhove and colleagues (2014) recommend that ground control and family members also receive support training. As its name suggests, Rose and colleagues' (2013) SMART-OP, or Stress Management and Resilience Training for Optimal Performance, is designed as a stress resilience training countermeasure for both pre-flight and inflight.

Selection of a crew and associated teambuilding of that crew has merit for promoting psychological health of crewmembers. Crew selection based on psychosocial factors is largely constrained by logistical and planning issues (e.g., availability, training or flight queue status). Still, NASA recognizes the importance of doing what is possible to ensure that a crew gets along and can work well together. Two themes emerged when Vanhove and colleagues (2014) interviewed experts at NASA regarding ways resilience might be enhanced (Category IV). The first involved the need to consider crew compatibility and characteristics detrimental to crew compatibility when selecting a crew. The second theme emphasized the importance of affording crew members with opportunities to familiarize themselves with one another prior to mission commencement so that less adjusting to each other's foibles occurred during missions.

The military has conducted decades of research on all aspects of the psychological aspects associated with the stressors of daily life in the military and occasional deployments to ICE environments (see e.g., Sinclair and Britt 2013). Vasterling, at the Boston VA, is examining pre-flight social support using the military as a model. Focusing on all phases of a mission (pre, during, and post flight), William Brim at the Uniformed Services University of Health Sciences— Center for Deployment Psychology is reviewing military research associated with the role families play in promoting and maintaining behavioral health of members of the military.

c. In flight

Currently, provision of psychological support is at its most intensive when the astronauts are in flight as opposed to during the pre- or post-flight periods. This support system, which is provided to each crewmember and family is comprised of four to five personnel from by BHP Op Psy and includes items such as crew care packages, contact with family and friends, communication technologies, and leisure/recreation activities. Specific inflight psychological support currently offered is discussed below.

1) Private psychological conferences

Regular private psychological conferences begin once an astronaut is in flight and continue throughout the duration of the mission. Private psychological conferences, which are held between a psychologist or psychiatrist and a crew member, are normally conducted every 2 weeks for at least 15 minutes. These conferences enable the psychologist or psychiatrist to assess the behavioral health of the astronaut, and provide the astronaut a venue for venting and voicing concerns.

2) Social interaction and support

Social interaction offers a sense of connection and support. Humans are inherently social beings and severely restricting opportunities for staying connected can have deleterious effects. Currently on the ISS, crewmembers have the ability to contact friends and family on Earth almost at will which provides a significant boost to crewmember well-being.

Sources of social support are not deemed interchangeable. Cohen and Wills (1985) in their review of the buffering hypotheses regarding social support and stress found that social support is most efficacious when the source of the support matches that of the stressor. In other words, a crewmember is more likely to perceive benefit from a supportive conversation about the stressors of completing a work task on time if talking to a fellow astronaut than if talking with a spouse. Likewise, a family member or close friend is more likely to provide comfort to a crewmember experiencing problems with a child left behind.

In order to ensure that an astronaut has opportunities to keep up regular contact with their families, private family conferences are conducted via video between crew member and family from within the privacy and comfort of the family home. Informally, the internet protocol (IP) telephone is an additional link between crew member and those left behind on Earth. The crew member can call friends and family or even a professor from graduate school when K_u-band coverage is available. Email is also available, deemed important, and readily used. The IP phone, however, appears to provide the greatest benefit to crewmembers. The phone is repeatedly mentioned in journals with entries such as "Loving the phone we have. It makes me feel closer to home" and "And the most rewarding tool here—the IP phone! What a treat to talk to family and friends!" (Stuster 2010b, p. 14).

Other social contact with the ground that is not necessarily family-specific also helps to broaden the social support networks of crew members and acts to lessen crew member feelings of being objectified and separated. These additional social contacts can be direct, such as discretionary events, or indirect, such as receiving a Christmas stocking handmade for that crew member. Discretionary events might include talking with an actor, politician, author, or other person of particular interest to that astronaut. While the majority of these events are, and remain, private, occasionally a more public appearance is made, such as Mark Kelly's virtual appearance at a 2011 U2 concert.

More recently, astronauts have been taking advantage of social media, which provides a means of connecting with a large audience. Twitter has become almost *de rigueur* for astronauts these days. Chris Hadfield became a sensation on YouTube with his rendition of David Bowie's Space Oddity. Reid Wiseman was the first to post a video on Vine. Don Pettit preferred educational outreach with his Saturday Morning Science experiments on the ISS. Social media is broad enough that it can afford astronauts with such a variety of methods for staying connected that can meet almost anyone's needs.

Providing information to the crew rather than having the crewmember initiates the social exchange is a standard countermeasure. The crew webpage, for one, can help crew members feel more connected to events on Earth. The webpage, which is updated twice weekly for each crew member, is specifically tailored to a crew member and thus provides that crewmember with a gateway to personal news selections, videos, MP3s, and photographs.

Support can be demonstrated in tangible ways as well. Crew care packages, sent by BHP, are either sent with the crew to be opened later or via resupply to ISS. They consist of items that are selected by crew members and their families and friends, such as favorite foods.

3) Cognitive functioning

A cognitive battery administered once ASCANs first begin their training provides baseline cognitive ability information. As mentioned under pre-flight countermeasures, WinSCAT also assesses cognitive functioning and is scheduled to be taken once a month by crew members while they are in orbit. WinSCAT scores that are recorded after an astronaut has sustained any unexpected medical event are compared to baseline and other pre-insult scores. WinSCAT, along with other data, would then allow the crew surgeon to make an evaluation regarding the severity of the event (Kane et al. 2005). A more sensitive tool to assess a broader range of cognitive functioning associated with exploration missions is considered important. As such, BHP Research is working on developing a tool that would be more comprehensive and yet acceptable to the astronauts. By definition, a screening tool should have accuracy in its predictions (see e.g., Meehl and Rosen 1995); achieved in part by its sensitivity (i.e., accurate prediction of likely problem) and its specificity (i.e., accurate avoidance of mistaken prediction); both of which are strongly influenced by the determination of cutoff or threshold scores (Treat and Viken 2012). Astronauts naturally are not happy when told that their performance, cognitive or otherwise, was measured as inadequate; thus a tool that is sufficiently sensitive, specific and accepted by astronauts is essential.

4) Group cohesion and positive dynamics

The benefits of solid group cohesion are myriad. A close-knit group can help relieve social monotony by providing desirable others for conversing and opportunities for intellectual engagement. It also offers a safe environment for venting frustrations while being able to avoid more serious conflicts.

Communal eating is perhaps that most commonly mentioned method of promoting crew cohesion on the ISS. While it is the commander of an ISS expedition's discretion, most choose to enforce a regular time in which all work stops and a meal is shared. Astronauts talk of the role this shared meal time played in creating and maintaining crew cohesion. Other shared activities are possible and can also promote cohesion. These can be as mundane as a haircut or a movie night or more celebratory such as the traditional party to celebrate a crew's 100th day on the ISS. Additionally, milestone events such as the 100 day party and other special events such as Christmas, birthdays, and arrival of crew care packages help crew mark the passage of time.

At times, group cohesion is better served by venting frustrations outside of the group. Writing in a private journal or communicating with friends and family or coworkers on the ground can provide such an outlet without damaging group cohesion.

The evidence book on the *Risk of Performance and Behavioral Health Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team* provides a more in depth discussion.

5) Views outside the space craft

Astronauts repeatedly mention the views from the ISS, especially those of Earth. The everchanging view outside of the space craft provides sensory stimulation that might otherwise be lacking. Sitting in the cupola watching the Earth is mentally restorative and reduces perceived stress. It affords a connection to something greater than one's own self. Astronaut Chris Hadfield and Canadian singer Ed Robertson of the band Barenaked Ladies sing of just that connection in the chorus "If you could see our Nation / from the International Space Station / you'd know why I want to get back soon." One astronaut wrote in his/her journal that "It's become a ritual for me...to stare out the window before I go to bed. The view is awe-inspiring and beyond comprehension" (Stuster 2010b, p. 24).

The sheer number of photographs voluntarily taken of Earth also provides evidence of the importance of being able to view Earth (Robinson et al. 2011). In part this desire, or need, to gaze at Earth might be explained as a way of reminding crewmembers' of the greater purpose for their sacrifices, that their work provides meaning to one's life (Jahoda 1982).

6) Habitability, Capsule Design and Layout

The crew of the ISS is fortunate when it comes to the size of their space craft. The ISS is likened to a five bedroom house and with its 13,696 cubic feet of habitable volume (NASA 2015d) is significantly larger than any previous space craft. Such a large vehicle allows for the crew to move around freely. They are not forced to work, eat, and sleep in the same capsule. Indeed, the ISS has individual sleeping compartments, which afford the crew a degree of privacy and a place where they can have respite from social interaction if desired. All of these features promote crew behavioral health.

Still even with its size, various pieces of equipment can get in the way of each other causing a bottleneck of sorts and potential scheduling issues. For example, the location of the waste collection system (WCS; toilet) is blocked by the treadmill while it is being used for exercise impeding both access to the WCS and the preferred amount of privacy. Stowage is a significant problem as is evident from journal entries such as "Spent the entire morning unpacking. I am starting to get irritated at the stowage plan...I'm not sure where the ISS designers figured we were going to put all this stuff." (Stuster 2010b, p. 37). The ISS is notoriously cluttered which has had a negative impact on timely completion of work tasks. Before being able to complete a procedure, a crew member might be required to locate a specific tool. Said tool might be located behind multiple bags of trash or supplies that must be moved and anchored again before the procedure can even begin. One astronaut reported a "big victory" when they "finally located a [piece of equipment] that has been lost for over a year. It's the size of a home water heater, so it's hard to imagine how it got lost" (Stuster 2010b, p. 38).

Any exploration space craft will necessarily be significantly smaller than the ISS. To use Orion as an example, the net habitable volume of its crew capsule is 316 cubic feet (NASA 2011), approximately 2.3 percent of the habitable volume on the ISS. Using the NASA Mars Design Reference Architecture 5.0 (Drake 2009), a panel of subject matter experts determined that the minimum net habitable volume required for crew to perform tasks and maintain behavioral health to be 883 cubic feet per person. For a six person crew, this equates to a total space craft net habitable volume of 5298 cubic feet, approximately 38.7 percent the habitable volume of the ISS (Whitmire et al. 2015).

The *Risk of an Incompatible Vehicle/Habitat Design* evidence report focuses on all aspects of capsule design and layout.

7) Interior design

A rich sensory environment will counteract some of the negative aspects associated with ICE environments and provide protection against attention fatigue and a reduction in overall stress (Vessel and Russo 2015). The interior of the ISS is predominantly monochromatic, varying from a dull white to metallic grey. Crews over the years have added some color in the form of personal items such as a flag from an alma mater or other mementos that are left behind when they leave but in general, the interior décor of the ISS is not what provides the greatest variety in sensory input. Instead, it is the ever-changing view from the windows.

Sensory stimulation can be viewed as more than just the color of the walls and number of windows. Sensory countermeasures have been categorized into (1) information foraging (designed for active learning and exploration), (2) restorative (support emotional coping, reduce stress, and restore ability to attend), and (3) active or therapeutic (provide a release of tension and stress) (Vessel and Russo 2015). Aspects of the ISS allow for each of these types of countermeasures. The science conducted on the station meets the human need for information foraging by providing meaningful work and an opportunity to learn and discover. Several aspects of the ISS, such as the private sleeping compartments, the cupola, and the musical instruments on board act as restorative countermeasures. Exercise, along with celebratory meals, provides therapeutic relief.

Greater detail is available in the Risk of an Incompatible Vehicle/Habitat Design evidence report.

8) Leisure activities

Providing choices of leisure activities for crew members is another tool that can prevent behavioral health distress. Before flight, crew members request movies, music, and electronic books that will be uploaded to them. Even equipment can be requested; for example, in response to the request of various ISS crew members, several musical instruments are now on board the station. Looking at Earth is a favorite leisure activity.

Astronauts have stated that they use movies and music to accompany their required daily exercise regimes. In addition to its physical benefits, exercise also is an effective countermeasure for maintaining positive mood. Astronauts report that they look forward to having down time or time off (Stuster, 2010).

9) Summary of currently available in-flight countermeasures

On the ISS, astronauts have access to variety of countermeasures. Having such a portfolio addresses a range of environmental and personal stressors. Individual crewmembers are allowed to choose those countermeasures best suited to them.

d. Post-flight

In addition to providing the best measures and tools to monitor and assess mood management of behavioral and psychiatric conditions before and during space flight, BHP is required to continue this provision after an astronaut's return from space flight (NASA 2007). Prevention and treatment of post-flight behavioral and psychiatric conditions relies primarily on behavioral medicine interviews after a crew member returns to Earth. These post-flight interviews may not be of sufficient length to be of benefit, since time is required to allow astronauts to feel comfortable and open up. Before astronauts will speak candidly, they must also trust the individual who is

conducting the interview and believe that the contents of the interview will not adversely affect their future flight status.

Other post-flight prevention and treatment methods could be incorporated. For instance, the annual psychological exams for current astronauts that are recommended in the Bachmann report (2007) would provide post-flight support for flown astronauts. A similar psychological exam could be implemented for retired astronauts. As all of the effects of flight and return might not be present immediately, continuing the behavioral medicine interviews for a longer period of time would provide astronauts with opportunities to discuss issues that might arise post-flight. If necessary, pharmacological aids can be prescribed.

When astronauts return to Earth, reintegration back into the family is not easy. It takes time and requires adjustment from all family members, not just the returning astronaut. A class for astronauts and their families that specifically targets the challenges of reintegration could be developed or an existing class could be modified. Education of astronauts and their families regarding reintegration is especially important for those who have no deployment experience.

5. Monitoring and treatment countermeasures

a. Pre-flight

Astronauts and their families have pre-flight access to counseling. There might be some hesitancy to use these services, however, given the NASA culture and astronaut concern that flight status might be negatively impacted (Shepanek, 2005).

b. In flight

Medical kits that are currently or have been aboard NASA spacecraft contain supplies to help crew members cope with a variety of possible medical emergencies. These kits include medications that can be used in the treatment of space motion sickness, sleep problems, illnesses, injuries, and behavioral health problems. For example, space shuttle medical kits included medications that could help to counter anxiety, pain, insomnia, fatigue (Caldwell et al., 2003), depression, psychosis, and space motion sickness (Graybiel and Lackner, 1987; Savin et al. 1997; Bagian and Ward 1994; Davis et al. 1993; Harm et al. 1999; Hughes and Forney 1964; Parrott and Wesnes 1987; Cowings et al. 2000; Rice and Synder 1993; Wood et al. 1985, 1992).

Putcha et al. (1999) evaluated the in-flight use of medications from astronaut debriefings that were conducted after 79 U.S. shuttle missions. The results show that 94% of the records indicated that medication was used during flight. Space motion sickness accounted for 47% of the medications that were used, while sleep disturbances accounted for 45%. The remainder of the medications were reportedly taken for headache, backache, and sinus congestion. These findings indicate a higher usage rate compared to the findings of Santy (1990), who reported that 78% of crew members took medications in space, primarily for space motion sickness (30%), headache (20%), insomnia (15%), and back pain (10%). Barger et al (2014) found that three-quarters of shuttle crew members reported taking sleep-promoting drugs in-flight.

Currently, the ISS medicine kit contains two anxiolytics, two antidepressants, and two antipsychotics. While the use of these medicines would be unexpected and unlikely, their inclusion

is necessary in the event of an actual emergency; just as flying a defibrillator is a medical requirement, although no cardiac arrests have occurred to date. For extreme situations, a physical restraint system is available. Sedatives are also included in the medical kit if a crew member requires sedation to ensure the crew member's or fellow crew members' safety.

Two factors are important when considering the use of either psychostimulant or antidepressant medications in spaceflight. First, there is very little sound scientific data regarding the pharmacokinetics and pharmacodynamics of antidepressants, anxiolytics, or antipsychotics in a microgravity environment. The pharmacokinetics relate to the absorption, distribution, and metabolism of the medication *within* the body and then the excretion *from* the body (Wotring 2015). An important consideration is future research on potential genetic biomarkers that will "personalize" the approach to help predict antidepressant and anxiety disorder treatment responses since both have effects on the serotonergic neurotransmitter system (Helton and Lohoff 2015).

Related to the more "personalized" approach medication dispensing on exploration missions is BHP's need to work closely with ExMC on medical labeling and dispensing of medications. There are multiple reasons for this consideration: cognitive functioning, metabolic changes due to microgravity, lighting effects on dispensing dose or type of medication, are but a few considerations. In one review of over 60 studies investigating dispensing errors in five countries, the most frequent problems were with the wrong drug, wrong time, strength, form or quantity, or not following the directions (James et al. 2008). The objective is to ensure optimized medication therapy when indicated with reduced risk of dispensing errors to minimize drug use misadventures.

An important consideration for the use of any antidepressants, such as selective serotonin reuptake inhibitors (SSRIs) by astronauts, if necessary, is the need to remain acutely aware of the potential risk such use has for increased risk of bone fracture (Davidge-Pitts and Kearns 2011). Davidge-Pitts and Kearns report on a prospective cohort study involving over 5000 adults older than 50 years taking SSRIs daily finding lower bone mineral density and that they had 2.35 times the risk of a nonvertebral fracture compared to those not on SSRIs. These results point to serotonin serving an important function outside the CNS and indicates that by inhibiting the serotonin transporter (which is the role of the SSRIs), it also detrimentally impacts on the body's ability to regulate BMD (Warden et al. 2005). BHP views this an important area to work closely with Human Health and Countermeasures Element in the risk areas of "Accelerated Osteoporosis, with Exercise (for both the positive benefits to mental health and BMD), with Nutrition (for the nutritional components linked with stress management since high stress contributes to the loss of calcium), and with ExMC for monitoring of this risk and multi-disciplinary contributions to ensure appropriate countermeasures are in place to reduce this overall risk.

As described above, several non-pharmacological tools are available to monitor behavioral issues on U.S. spacecraft. The first, and perhaps most important, is the private psychological conference that is held biweekly between a psychologist or psychiatrist and a crew member. Private psychological conferences are useful both as a monitoring tool and in cases in which an intervention is required. They also can be used to counsel or treat astronauts. Initial statistical data that were compiled by BHP experts representing European, Russian, and U.S. space agencies indicate that private psychological conferences are accepted by crew members (Manzey et al. 2007). During private psychological conference debriefings, astronauts have praised the pre-flight briefings as well as the psychological services that are provided by operational psychology during flight (e.g., private

family conferences, crew discretionary events, crew care packages, recreational items) and the behavioral medicine support (pre-flight briefings and private psychological conferences). NASA flight psychiatrists and psychologists have reported that in debriefings astronauts relate that they did not realize how important "that psyc stuff" was until after they were on the ISS.

The crew surgeon is also an important line of defense for reducing the likelihood of a behavioral or psychiatric condition occurring or developing. The role of the flight surgeon is to monitor the physical health and well-being of the astronaut. To ensure this, the flight surgeon conducts a 15-minute private medical conference once a week with the astronaut. As with the psychologist or psychiatrist, the flight surgeon, although focused more on physical health, may be able to recognize early signs of behavioral health distress in an on-orbit crew member. Currently, flight surgeons must rely on their training to glean information about a crewmember's behavioral health unless the topic is directly addressed by the crewmember. A standard list of signs and symptoms to look for is being developed by BHP Research. Lebedev describes the value of his crew doctor intervening during his Salyut 7 flight: "I kept myself under control but I was irritated. Our crew doctor, Eugeny Kobzeb, sensed it, and during the evening period of communication said, 'Wait a minute.' Suddenly I heard a very familiar Ukrainian melody. I couldn't understand where it came from. Finally it dawned on me: it was my son playing the piano. It was so wonderful and unexpected that tears ran from my eyes" (Lebedev 1988, p. 77).

c. Post-flight

Several of the methods that are used to prevent the occurrence of post-flight behavioral and psychiatric conditions can also be used to treat these conditions if they occur post-flight. Annual psychological exams for current and retired astronauts can be used as a springboard for targeting treatment options; e.g., continued counseling or pharmacological aids. As not all effects of space flight and reintegration are immediately present at the time at which an astronaut returns, post-flight behavioral medicine interviews could be continued at additional intervals beyond those intervals that currently occur post-flight. To the extent that a family is experiencing difficulty with an astronaut reintegrating, family counseling is another treatment option that is available post-flight.

A few studies have been conducted examining astronauts and cosmonauts post-flight. In a 2006 review of astronaut memoirs, Suedfeld found that reflecting on their lives, female astronauts were more likely to label transcendence (a combination of spiritual harmony and universalism or seeing the world as a place of beauty) as most important post-flight. Achievement, which was the value rated the highest while they were active astronauts, sank substantively post-flight. Perhaps the female astronauts shifted their focus to other facets of their lives once they achieved their goal of space flight. Changes post-flight occur cross-culturally. In a study of cosmonauts, Suedfeld (2012) concluded that cosmonauts experience personal growth after their space flights. A finding supported in part by his later finding that cosmonauts who have been retired longer were more likely to score higher on Accept Responsibility (Suedfeld et al. 2015) although the reason for the difference is unclear.

6. Evolution of countermeasures

The countermeasures currently available to prevent and monitor adverse cognitive and behavioral conditions and treat psychiatric disorders are focused on stressors of low Earth orbit space flight.

Exploration missions will be an entirely different beast owing to the unprecedented distance and duration. Current practices such as selection and periodic PPCs will likely remain, but differences between low Earth orbit space flight and exploration space flight will necessarily change the efficacy of some current countermeasures. For example, although PPCs are unlikely to be dropped as a countermeasure, the communication delay of exploration missions will potentially render them less relevant to the crew.

B. Ground-based Evidence

Ground-based analogs, such as those in the Arctic and Antarctica or undersea habitats, are frequently used as a comparison to space flight because they are more numerous and therefore more accessible than space flight and provide an Earth environment in which to test and validate the feasibility of BHP countermeasures, tools, and procedures. Analogs, however, are also frequently criticized. It has been suggested that their fidelity, especially in laboratory simulation studies, is not always high. Natural analogs, such as those found in Antarctic and on submarines, frequently depart from actual space flight conditions. Most frequently, there are more individuals in analog settings than the two to six crew members that are common to current, and expected in future, long-duration space flight operations. Regardless of their limitations, however, some of the higher-fidelity mission analogs are the best, and often the only method, that is available for gathering the data necessary to successfully prepare for exploration missions. Presenting data from his Antarctic mission, Astronaut Donald Pettit succinctly summed up the value of analogs when he stated that "analog physics might be wrong, but the mindset is right" (Pettit 2007).

The research arm of BHP has developed a statistical model that can be used to assess relative strengths of different analog environments (Keeton et al. 2011). Its purpose is to aid researchers in identifying the best analog for their particular research project. By using the model, BHP can assure that the aspects of the analog most critical to the research question at hand best matches the characteristics of exploration space flight.

1. Sources of evidence

Analogs are essential to accomplishing BHP's Pathway to Risk Reduction research strategy. Fidelity of analogs varies depending on the type of analog environment. Typically, a new line of BHP research begins in a lab which affords the greatest control yet the least realistic (lowest fidelity) setting. As the research progresses, so too the fidelity of the analog used increases. High fidelity ICE environment replicates conditions of space flight (e.g., danger, isolation, environmental factors, psychological stressors). These high fidelity ICE analog environments help to quantify likelihood and consequences of adverse behavioral health conditions and psychiatric outcomes. Countermeasures and treatment options can be tested and validated in the analogs. Research results obtained from analogs can be used to establish and inform NASA crew health and safety standards and thresholds for exploration (Musson and Helmreich 2005; Nicholas and Foushee 1990; Palinkas 1990; Ploutz-Snyder 2015; Schneiderman and Landon 2015).

There are numerous analog environments around the world. Antarctica is perhaps the best known and most commonly studied analog environment (Lugg 2005). Different stations on Antarctica provide a contrast in the number of people who winter-over and the level of remoteness. NEEMO, or NASA Extreme Environment Mission Operations, is a facility 63 feet under the Atlantic Ocean on the Aquarius Reef off the Florida Keys. Aquanauts live and work underwater for the length of

the mission. A third analog in a remote location is the Haughton Mars Project located on Devon Island in the High Arctic region. Like Haughton Mars, NASA's Desert Research and Technology Studies (DRATS, or more commonly called Desert RATS) is located near Flagstaff in Arizona in an area that approximates the terrain of Mars. CAVES, a European Space Agency analog, is short for Cooperative Adventure for Valuing and Exercising human behaviour [sic] and performance Skills. It is a two-week expedition living in and exploring Sa Grutta caves in Sardinia, Italy. Other analog environments for space exploration include Mount Everest, submarines, the Pavilion Lake Research Project in British Columbia, and PISCES (Pacific International Space Center for Exploration Systems). The Russian led Mars500 involved a crew staying in a chamber facility for 520 days, closer to the anticipated length of a Mars mission.

Beginning in 2014, two additional analogs to space flight were added. Human Exploration Research Analog (HERA), at Johnson Space Center, is a two-story, four-port habitat designed along a vertical axis with a simulated airlock. HI-SEAS, short for Hawai'i Space Exploration Analog and Simulation, was designed on an abandoned quarry on Mauna Loa's northern slope and is an analog for Mars missions. These two chamber facilities allow for research in environments with a level of isolation more closely resembling that of space flight to be conducted.

Relevant behavioral health data are not available for each of these analog environments. Those data that are available are discussed below.

2. Occurrences of behavioral signs and symptoms

a. Behavioral and psychiatric emergencies

Extreme cases of psychiatric emergencies are rare in space flight and isolated, confined, extreme environments. A disruptive schizophrenic was part of the 1957-1958 International Geophysical Year on Antarctica (Stuster 1996). Decades later, an evacuation from Antarctica occurred due to probable depression (Buckey 2006). Fortunately, occurrences that reach the point of becoming an emergency requiring evacuation are not common in ICE environments. At times, incidents occur that could be classified as behavioral emergencies if not psychiatric. In 2007, for example, two men were evacuated, one with a broken jaw, after a physical fight between the two men. In this instance, alcohol was involved.

Examining actual occurrences in Antarctica between 1994 and 1997, Palinkas et al. (2004) found that 12.5% of the crew members at two Antarctic stations, McMurdo and South Pole, presented to the clinic with symptoms that met the DSM-IV-TR criteria for one or more disorders. This translates to an overall incidence rate of 5.2% over an 8.5-month austral winter. Age, gender, year, level of education, and prior winter experience were not statistically correlated to the DSM-IV-TR diagnoses. Although unknown, the incidence rates for presentation of symptoms that failed to meet diagnostic criteria naturally would be higher.

Another analog environment for space flight is submarines, with their typical mission lengths of 3 months. As with space missions, submarine missions occur in a physically confined, socially and physically isolated, and extreme environment. For submariners, the incidence of psychiatric disorders severe enough to result in either the loss of a workday or the need to be medically

evacuated ranged between 0.44 and 2.8 per person-year (Wilken 1969; Tansey et al. 1979; Dlugos et al. 1995; Thomas et al. 2000).

b. Mood and mood disorders

Subclinical levels of mood disturbance is commonly reported in ICE environments (Vessel and Russo 2015). Indeed, Palinkas et al. (2004) found that the most common category of disorders for individuals who were wintering-over in Antarctica was mood disorders; these accounted for 30.2% of all diagnoses. Depressive symptoms were significantly related to gender (females were at greater risk), military occupation (rather than civilian), station (all diagnosed individuals were stationed at McMurdo; none were stationed at South Pole), year of expedition, and having a DSM-IV diagnosis.

Cushman and Parazynski (2014) examined all medical encounters, teasing out those deemed to be psychiatric in nature. Over the course of three years at McMurdo Station on Antarctica, medical providers had 15,048 encounters with patients. Of these a low percentage (1.8%; n=276) were deemed to be psychiatric in nature. Sleep disturbances (n=124) together with fatigue (n=27) accounted for the majority of the psychiatric encounters. While sleep disturbances and fatigue arguably could be due to reasons other than psychiatric, these outside influences were unlikely to have caused all presentations of sleep disturbances and fatigue. Along with sleep disturbances and fatigue, patients presented with symptoms of depression (n=27), anxiety (n=23), and, much less commonly, substance abuse (n=4). The average number of presentations per week did not appear to vary significantly across seasons (winter 1.4/week; winfly^{‡‡‡‡} 1.0/week; summer 1.3/week). However, when adjusting for the seasonal variation in population size, winter (4.6 patient encounters per person week) saw many more psychiatric encounters than did the short winfly or summer seasons (1.3 and .44 patient encounters per person week, respectively) (Cushman & Parazynski 2014).

Otto (2007) reviewed 12 years of data from another Antarctic station, the South Pole, and found that between 1994 and 2005, the overall incidence rate for depression that required pharmacological intervention was 2.03%. This means that one case of depression can be expected every 1.1 winter seasons at the South Pole station.

The incidence rate for diagnoses of overall mental disorders, including depression, was 4.5% at the three Australian Stations according to the Australian National Antarctic Research Expeditions (ANARE) and 6.4% at McMurdo Station (Otto, 2007). These incidence rates appear to be lower than those for the general public, which average 9.5% (Kessler, et al., 2005). Antarctic incidence rates could be artificially lower, however, due to a selection process that disqualifies individuals with existing diagnoses from wintering-over. Alternatively, the lower rate in Antarctica could be a result of self-selection, whereby individuals who apply to winter-over tend to have better behavioral health than the general population.

Table 5 summarizes both behavioral and psychiatric emergencies and manifestation of psychiatric disorders in Antarctica.

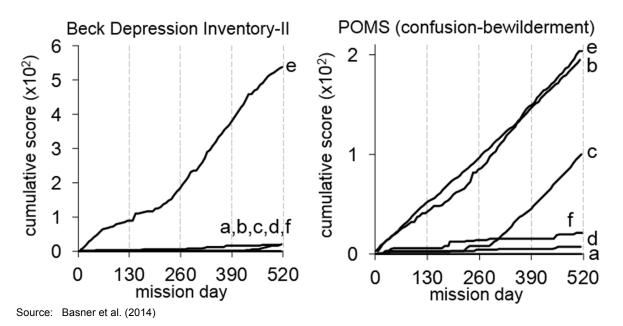
^{‡‡‡‡‡} Winfly is a shortened version of "Winter Fly-in" that heralds the six-weeks long period in Antarctica that commences in August during which supplies and personnel are brought in to prepare for the surge of research scientists who typically arrive in early October, the beginning of the main summer field season.

Table 5. Behavioral health problems in Antarctic over-winterers

1 Long-term confinement and evacuation due to psychosis (out of ~40 people)	IGY 1958 Antarctica	Buckey (2006), Stuster (2011)
1 Evacuation due to probable depression (out of 12 people)	IBEA Antarctica (1981)	Buckey (2006), Stuster (2011)
12.5% met the diagnostic criteria for one or more disorders	McMurdo and South Pole Stations	Palinkas et al. (2004)
4.6 psychiatric patient encounters per person week over winter compared to 1.3 for the short winfly and .44 during summer session	McMurdo Station	Cushman & Parazynski (2014)
4.5% diagnoses of overall mental disorders	Three Australian stations	Otto (2007)
6.4% diagnoses of overall mental disorders	McMurdo Station	Otto (2007)

Moving away from the Antarctic, Lieberman and colleagues (2005, 2006, 2009), in their studies of Army Rangers and serving members of the military, consistently found a stressful environment was related to impaired mood states compared to baseline mood states. The Russian Mars chamber studies provide additional insight into mood in ICE environments other than Antarctica. Of the six member crew in the 520 day study, one (20 percent) developed depressive symptoms. Three of the six (50%) developed symptoms of confusion – bewilderment. See Figure 4.





When discussing mood, depression is more commonly the focus, reflecting more negative thoughts and self-depreciation, with affective disengagement and negative attitudes toward both the past and the future. On the other hand, anxiety often reflects a theme of danger with an apprehensiveness and uncertainty about future events (Tellegen 1985). Anxiety is less common than depression in ICE environments and that may be one reason it is not as frequently studied. There are a few cases of extreme anxiety seen in ICE environments although the incidence level is higher in less extreme environments (Vessel and Russo 2015).

Selection procedures are frequently touted as a primary reason more mood disturbances are not seen in ICE environments. Another factor that can impact the occurrence of depressive symptoms is the coping strategies employed. Coping strategies, rather than personality characteristics, appear to be predictive of susceptibility to depression in ICE settings (Vessel and Russo 2015). Still another factor is that high stress conditions tend to show relatively more individual variability than in low stress conditions (Htaik et al. 2012).

c. Winter-over syndrome

Winter-over syndrome consists of a cluster of symptoms that includes interpersonal tension and conflict, cognitive impairment, sleep disturbance, and negative affect (Palinkas and Suedfeld, 2008; Strange and Youngman, 1971). This syndrome usually is not severe enough to warrant a DSM-IV diagnosis. Rather, it might more accurately be considered a subclinical condition (Judd et al. 2002). Some research has shown that symptoms peak shortly after the mid-point of an expedition (Palinkas and Suedfeld, 2008). This effect, which is called the third-quarter effect, is independent of the length of the expedition. It is believed to occur as a result of individuals realizing that their expedition is only half over. Evidence regarding this third-quarter effect is inconsistent and researchers continue to evaluate its existence in different environments (e.g., Kanas and Manzey 2008; Stuster 2008).

Winter-over syndrome shares many similarities with asthenia (Otto 2007; Palinkas and Suedfeld, 2008; Sandoval et al. 2011). Perhaps the most telling similarity is that they both reflect deadaptation to a stressful situation (Myasnikov et al. 2000, as cited in Kanas and Manzey, 2008).

d. Salutogenesis

Palinkas and Suedfeld (2008) (Category IV) dichotomize the salutary effects of polar expeditions as being: (1) the enjoyable characteristics inherent in the situation, and (2) the positive reactions that come from having successfully met and overcome the challenges of the environment. The former are positive effects that are felt during the mission. These effects can require coping and resilience. The latter are positive effects that are more long-term in nature, and they are met through post-return growth (Palinkas and Suedfeld 2008) (Category IV).

The isolated, confined, and extreme (ICE) environment for some individuals, provides personally rewarding experiences (Palinkas et al. 1995). For example, the number of people requesting repeated winter-over assignments in Antarctica is evidence of the positive benefits that are associated with the ICE experience (Steel 2000; Wood et al. 2000).

These kinds of effects are also seen in simulation studies. For example, three crew members were isolated in the Mir space station simulator for 135 days. They reported more expressiveness and self-discovery and less tension than during their pre-isolation training session (Kanas et al. 1996).

e. Cognitive functioning

Some evidence from Antarctic research suggests that clinical cognitive changes may occur in individuals who are exposed to ICE environments for long periods of time. Investigators studying animal research have further speculated that behavioral changes in such environments may even be attributable to the effects of chronic stress on the hippocampus (Otto 2007). In one study of 109 days, chronic stress resulting from multiple sources, including limited sleep, intense physical activity, and low calorie diet, was associated with impaired cognitive function and mood. Vigilance and mood were further weakened when acute cold weather was involved. Recovery was rather quick with cognitive functioning improving within about 3 days once stressors were removed (Lieberman et al. 2009).

Comparing declines in cognitive functioning with those in physical performance revealed that, in a lab-based sustained operations scenario, cognitive functioning declined faster and more extensively than physical performance when soldiers were faced with sleep loss, continuous physical activity, and food deprivation. Mood states also deteriorated significantly from baseline. Soldiers in the study were healthy males with a mean tenure of 1 year and a mean age of 23 (Lieberman et al. 2006).

The BHP sleep risk research has recently explored the impact of sleep inertia and the operational readiness/effectiveness once aroused from various stages of sleep. This is addressed in the BHP Sleep Evidence report. Other research has focused on medications to sustain alertness and vigilance during periods of inadequate sleep but have found not all aspects of cognition are improved equally. For example, Killgore et al. (2009) found that deliberation, speed of completion of tasks, indices of preservative responding, and preservative errors produced, all differed as a function of type of stimulant medication (comparing modafnil, caffeine, and dextroamphetamine).

Decrements in cognitive performance due to stress were not limited to one area of cognition. Instead, in exercises designed to simulate stress of combat, every aspect of cognitive functioning tested was impaired compared to baseline, including rather simple functions such as reaction time and vigilance. These findings were true for officers of USA Rangers with a mean tenure of 9 years as well as for those training for Navy Seals who were mostly enlisted and with a mean tenure of 3 years. Further, these decrements in cognitive functioning were not negligible. The magnitude of cognitive decrement due to environmental stress was greater than that due to clinical hypoglycemia, treatment with sedating drugs, and alcohol intoxication (Lieberman 2005).

Other physical aspects of the environment can also produce cognitive changes. Exposure to high levels of radiation, for example, can damage the subcortical basal ganglia and hippocampus that are critical to cognitive functioning (Madsen et al. 2003; Vasquez et al. 2003, as cited in Lieberman et al. 2005). Rats exposed to radiation equivalent to that of deep-space resulted in long-term cognitive deficits (Davis et al. 2014; Hienz et al. 2008). For specifics regarding the risks of space radiation please refer to the associated risks of NASA's human research roadmap.

f. Analog Mission Duration of 2 or More Years

Available evidence from assignments in any analog lasting 2 or more years, as could occur for a Mars mission, is scant. In Biosphere 2, an eight-member team was isolated on a 3.15-acre artificial, closed ecological system in Arizona for 2 years (Sep 1991 to Sep 1993). Although they were in a relatively lush and diverse environment – with access to television and radio, and daily contact via an observation window - the inhabitants of Biosphere 2 nevertheless experienced psychological stress (MacCallum and Poynter, 1995). The team split into two factions within 6 months; stolen food was hoarded; and daily tasks were reported as monotonous. One month after the midpoint, some crew members reported experiencing depression that was severe enough to interfere with their ability to complete daily tasks (Poynter 2006). The severity of these behavioral and psychiatric responses was most likely due, in part, to a need for more rigorous psychological evaluation when selecting those who were best suited for this study. Problems that were experienced with Biosphere 2, in comparison to those of space flight, include poor selection of participants and lack of adequate preparation and training. Extensive publicity also may have influenced the experiences of the Biosphere 2 team by sensationalizing them. Although the reader is cautioned about over-interpreting data as well as misapplication of the study to space flight, the Biosphere 2 experience is included in this report because it is one of the few examples of very long-duration isolation and confinement

Two-year assignments, which are common at the Russian Antarctic Station of Vostok, provide additional evidence that lengthier periods spent in isolation and confinement increase behavioral and psychiatric problems (Otto 2007). Alcohol consumption contributed to the main power-generating building burning down, as well as, to the death of a station physician due to alcoholic liver failure. The depth of psychological stress that was experienced by some at the Vostok station is vividly illustrated by the unsubstantiated legend of a wintering-over Russian male, who after losing a game of chess, murdered his opponent with an axe (Anthony, 2006; Wheeler, 1999).

These examples most likely do not generalize to astronauts and space travel due to the differences between analog and astronaut populations as well as the differences in mission characteristics. However, these examples have been included to emphasize the increased risk of behavioral health and psychiatric problems that are associated with extended stays in highly isolated, confined, and extreme environments; such long durations are clearly at the outside boundary of our experience and evidence base.

g. Post-expedition cognitive and behavioral health

The majority of reintegration research involves returning service men and women. Because of the potential confound of combat experience, this body of evidence was not considered for inclusion here. Still there are diary accounts and similar reports of difficulties by individuals returning home from expeditions. One such event occurred in the last decade of the 1800s when renowned Antarctic explorer Amundsen sent one of his men, Johansen, home early for insubordination. Johansen later shot himself (Lugg 2005).

In a recent case study of one 29 year old man who circumnavigated the globe solo in a sailboat, significant differences manifested in two factors of personality. Compared to pre-trip measures, agreeableness was significantly lower at 180 days post-trip and remained stable at the level when

measured 360 days post-trip. Conscientiousness also changed, though in the opposite direction. Post-trip levels of conscientiousness were higher than the pre-trip level. Unlike agreeableness though, conscientiousness at 360 days post-trip was lower than that at 180 days, although still significantly higher than the pre-trip measure (Kjaergaard et al. 2015) suggesting that conscientiousness might eventually return to pre-trip levels. This seems a reasonable assumption given that a lapse of conscientious is less likely to have life threatening consequences on *terra firma* than it would while traversing the world's oceans alone. The individual's level of disinhibition or tendency to lack of impulse control (Patrick et al. 2009), increased significantly from pre-trip levels when measured at 180 days post-trip, and was even higher at 360 days post-trip (Kjaergaard et al. 2015).

2. Predictors and contributing factors to behavioral health

a. Personality

1) Instrumentality and Expressivity

Viewing personality in terms of instrumentality and expressivity has been found to be predictive in flight crews as well as in other aviation and space populations (Chidester and Foushee 1991; Chidester et al. 1991; McFadden et al. 1994; Musson et al. 2004; Musson and Helmreich 2005) and in the analog environments of submarines, hyperbaric chambers, polar expeditions, and the military (Sandal et al. 1996, 1998, 1999).

2) The Big Five

A 1991 meta-analysis suggests that conscientiousness is positively related to job performance (defined as job proficiency, training proficiency, and personnel data) across occupations as varied as professionals, managers, sales, police, and skilled/semi-skilled (Mount and Barrick 1991). Whether this holds true in Antarctica and possibly other ICE environments such as space flight is uncertain. Palinkas et al. (2000) found the opposite to be true in Antarctica, namely that better job performance was related to lower conscientiousness. These results could be artifacts of the sample or a function of how job performance was operationalized, however.

Research with individuals who seek expeditions to Antarctica suggests that ideal candidates for wintering-over in such an isolated and confined environment are relatively low in neuroticism, need for orderand achievement motivation, as well as low in extraversion and conscientiousness (Palinkas et al. 2000). This corresponds with Biersner and Hogan's (1984) findings that narrow interests and a low need for stimulation also is associated with good adjustment with those who winter-over in Antarctic. Rosnet et al. (2000) confirm that ideal individuals would be low on extraversion. In a third study, polar workers were found to place more highly than the normative group in all factors except neuroticism. Breaking these findings down by occupation reveals that scientists are lower than military personnel on extraversion and lower than technical/support staff on both agreeableness and conscientiousness. The next section addresses the how personality traits may differentially contribute to adjustment differences between South versus North Pole winter-over crew members.

b. Personality as a predictor of adjustment

Antarctic workers are higher than those in the Arctic in terms of extraversion, agreeableness, and conscientiousness (Steel et al. 1997). However, interpersonal conflict and tension is reportedly the greatest source of stress for individuals who are wintering-over in Antarctica (Natani and Shurley 1974; Stuster et al. 2000). This likely explains the tendency to adapt better when these individuals are low in extroversion and assertiveness (i.e., they keep to themselves more and avoid confrontation) (Rosnet et al. 2000). Three individual characteristics that are related to adaptation in isolated and confined conditions in Antarctica are: high social compatibility, high emotional stability, and high task motivation (Gunderson 1966; Stuster 1996). Gunderson (1966a) also found that "achievement needs, needs for activity, needs for social relationships and affection, aesthetic needs, needs for dominance or leadership, a sense of usefulness in one's job, and control of aggressive impulses [are] particularly important for adjustment in Antarctic small groups" (p. 4).

Polar explorers with positive personality traits, including absorption and positive expressivity, demonstrated higher well-being (Atlis et al. 2004). Examination of psychological capital provides another way to examine the relationship between personality and well-being. Psychological capital (PsyCap) is viewed as a higher-order construct such that individuals with positive psychological capital are those characterized by hope, resiliency, optimism, and self-efficacy (Luthans 2002; Luthans et al. 2007). PsyCap is predictive of lower perceived stress (Avey et al. 2009), improved psychological adjustment (Lamp 2013 as cited in Vanhove et al. 2014), and higher psychological well-being (Avey et al. 2010).

c. Monotony, boredom, and meaningful work

Members of Biosphere 2 reported that finding sources of stress relief was a major part of working in the Biosphere (MacCallum and Poyntner 1995). Likewise, of major concern during long-duration missions is the possibility of too much monotonous free time. Boredom has long been known to be the worst enemy of Polar explorers (Stuster 1996). Meaningful work counteracts the negative effects of monotony and boredom. Meaningful work contributed to health and performance in polar expeditions (Britt, Jennings, Goguen, & Sytine, n.d.; Leon et al. 2002; Leon et al. 2004, 2011; Palinkas and Browner 1995) and submarine missions (Kimhi 2011; Sandal et al. 1999).

3. Prevention and treatment countermeasures`

a. Selection

1) Biomarkers

BHP Research is currently investigating the efficacy of using biomarkers to predict biological likelihoods of reactions to the stressors of space. There is a question as to whether biomarkers, if found to be sufficiently efficacious, would be best utilized during selection or as something that should be monitored and used to prescribe countermeasures during expeditions.

BHP Research's initial foray into biomarkers as predictors began with mood, specifically depression. Strangman (2012, Category II) completed an investigation of neural biomarkers for the detection of the presence and severity of depression. In both lab and field (Kilimanjaro)

studies, his team found more than one putative brain biomarker that detected the presence or absence of depression as well as severity of depression.

Three other investigations of biomarkers involve sleep and are in the beginning stages. Identification of biomarkers indicating a susceptibility to neurobehavioral decrements to sleep loss in space flight will be the goal of both retrospective and prospective laboratory studies (Dinges 2015, Category II). While the Dinges study focuses on the effects of fatigue on neurobehavioral functions, another study examines biomarkers that distinguish resilience and susceptibility to the adverse neurobehavioral effects of high performance demands and sleep loss stressors. Investigations will occur in HERA and another ICE environment (Goel 2015, Category II) with the goal of identifying a set of diverse biomarkers for distinguishing neurobehavioral differences. Out of Lockley's lab (2015) is anticipated a core set of biomarkers to predict neurocognitive and psychological responses to behavioral health disruptions. Lockley and colleagues are taking a broader approach to biomarkers and testing the predictive value of a range of behavioral, performance, sleep and circadian biomarkers on neurocognitive impairment. In particular, they are interested in sleep deprivation and circadian misalignment that is a feature of life on the ISS. Lockley's investigations will occur first in a lab (Category II) and then through the use of archival Antarctic data (Category III). For additional information refer to the evidence book for the Risk of Performance Decrements and Adverse Health Outcomes Resulting from Sleep Loss, Circadian Desynchronization, and Work Overload.

b. Prevention

1) Traditional prevention countermeasures

Many of the same types of countermeasures used in space are used in ground-based ICE environments. These include, among others, providing opportunities to stay connected through electronic media, a variety of leisure activities, and food. In a Mir simulator study, crew anxiety, total mood disturbance, and overall crew tension was significantly lower after the simulator received additional supplies (Stuster 1996) (Category II).

Additional means of preventing adverse behavioral conditions and psychiatric disorders that might one day be of use during space flight will be first investigated in ground-based analogs. These are discussed below.

2) Unobtrusive monitoring

Developing unobtrusive monitoring that does not require input from an astronaut nor any astronaut time is part of the focus of BHP research strategy. Valid, feasible, and acceptable tools involving unobtrusive monitoring should provide real-time, meaningful feedback regarding key indicators of behavioral health to the crewmember in the context of the long duration space exploration environment and be used to implement countermeasures autonomously. Facial expressions and voice (speech and tone) are possible targets for such unobtrusive technologies.

Some work has been done via Dinges' lab at University of Pennsylvania regarding a facial recognition technology. The optical computer recognition (OCR) system uses cue integration-based tracking to capture both rigid and non-rigid parts of the face. The concept is that such a facial tracking can identify phenomenon such as eyelid closures, positive, neutral, and negative

emotional expressions which could then be extrapolated to determine when astronauts are experiencing levels of stress, fatigue, and emotion that could disrupt effective performance. If proven, such a system could provide meaningful feedback to astronauts and crew surgeons, allowing the implementation of countermeasures as deemed necessary (Dinges 2008, 2012, 2015). While the OCR system has been under development and undergone some initial testing in space analogs (the 105 and 520 day Russian Mars chamber studies conducted 2009 through 2011), the results have not yet validated the tool's reliability, sensitivity, and specificity. Part of the challenge for OCR as an unobtrusive measure is that we don't just use facial expressions as emotional cues to interpret our social surroundings; we also use perceptual and contextual factors to remove ambiguities and delineate our understanding (Carroll and Russell 1996). In order to fully capitalize on this area, we will need to fully understand this potent emotional context, parsing out the emotional biases to identify valid and reliable ways to understand attributions of affect within the social-emotional context (Marian and Shimamura 2012).

Lexical monitoring, being investigated by Salas (2015) will use lexical indicators as a means of predicting performance decrements by identifying changes in cognitive, emotional, and social functioning. Data were collected in HERA (Category II) and NEEMO 18 (Category III). Findings along with the empirically-validated assessment tool for non-obtrusive detection of stress and anxiety at both individual and team levels are expected at project completion in 2016. The evidence book on the *Risk of Performance and Behavioral Health Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team* discusses results from Miller and Wu investigator team that used automated analysis technology of speech to detect psychosocial states, including positive and negative valence, but from a team perspective.

3) Delays in communication

In anticipation of the delays in communication that will occur during exploration missions (up to 22 minutes one way for Mars), BHP Research has begun examining the effects of such a delay through a series of spaceflight and spaceflight analog studies. An initial study was conducted in which included tasks that varied in their levels of novelty and criticality along with variations in the length of communication delays. An initial feasibility study was conducted using the underwater NEEMO facility using 5 and 10 minute communication delays (Palinkas, 2014). During this initial study, significant impacts were seen in the ability of the crew to coordinate on emergency scenarios with a remote mission control group. However, the quality and team performances remained relatively steady for any one-way delays at or longer than 5 minutes. Another study was recently conducted for four weeks and involved the astronauts on the ISS Increment 39/40 as well as CAPCOMs^{§§§§} and Flight Directors on duty (Palinkas 2015). Initial analyses indicate negative impacts on both individual well-being, due to increased stress and frustration, and on team performance resulting from even relatively short communication delays due to reduced efficiency (Kintz & Palinkas, 2016). In particular, tasks involving a high level of interdependence between crew and ground exacerbated these negative impacts. Along similar lines, another recently completed study focused on the development and testing of protocols for asynchronous communication during spaceflight operations, including testing in the NEEMO and

^{\$\$\$\$} CAPCOM refers to Capsule Communicator that is traditionally another astronaut in mission control who communicates information, directions to other astronauts in the spacecraft in the belief that they can pass information in the clearest manner for other astronauts to understand.

HERA analog environments (Mosier & Fischer, 2016). Crews not trained in the asynchronous communication protocols reported less communication and less effective communication than trained crews, citing loss of shared perspective on communications and insensitivity to the timing of communications as the primary factors. For this risk, communication delays are of focus only when considering how best to deliver and/or provide behavioral health countermeasures or treatments for crewmembers. Other investigations are being conducted into the effect of delays in communication at a team level (see evidence book on the *Risk of Performance and Behavioral Health Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team.*

4) Virtual environments and virtual agents

As virtual technology continues to evolve, the possibility of using it as a preventative or treatment countermeasure likewise increases. Development of and testing the efficacy of using such technology is the focus of a couple of BHP research efforts.

ANSIBLE, short for A Network of Social Interactions for Bilateral Life Enhancement, uses socially intelligent virtual agents (avatars) to alleviate environmental stressors through social interactions in a virtual environment. ANSIBLE is being designed to facilitate asynchronous communications with Earth as well as to provide increased social interaction necessary to human well-being. ANSIBLE provides the crew with the ability to watch and interact with avatars in the virtual environment similarly to watching a video. The avatars provide simulated social interactions typical to those they would experience on Earth (Wu et al. 2015). Such a tool offers great potential to mitigate the effects of social isolation, sensory deprivation, and monotony through the introduction of an immersive, social-sensory rich virtual environment.

Exercise while in space is essential to maintain muscle and aerobic fitness. Exercise has also been found to be an effective countermeasure. Task groups (dyads in particular) have been associated with gains in motivation. As many factors limit the ability and availability for astronauts to serve as each other's exercise partner, cyber (or virtual agent) exercise partners are being investigated as a means of increasing motivation to exercise. Feltz (2015) is currently developing Software Generated (SG) exercise partners and will test those partners within designed exercise video games over a 24-week time period to determine whether use of an SG exercise partner leads to increase muscle strength, aerobic capacity, adherence to the exercise program. Additionally, more psychological factors will be assessed, including perceived self-efficacy, enhanced enjoyment in exercise, and a sense of social connectedness.

5) Self-management

Methods of providing astronauts with information on their own well-being are currently being investigated. Such tools will both inform astronauts about their current behavioral health status and could provide countermeasures to be used in prevention and/or treatment of adverse cognitive or behavioral symptoms.

An increasingly popular approach and fast becoming one of most widely used psychological interventions is mindfulness-based stress reduction. Mindfulness is an introspective process that focuses on increasing "awareness" with "clear comprehension" to reduce "mind wandering" and increase "sustained attention" (Bishop, Lau, Shapiro et al. 2004). It stems from eastern spiritual

practices, primarily Buddhism (Barinaga, 2003). Systematic reviews of mindfulness based stress reduction training have found it moderately effective. Khoury, Sharma, Rush and Fournier (2015) systematically reviewed 29 studies involving over 2600 health adults to evaluate the efficacy, mechanisms of actions and moderating variables for non-clinical populations. They found mindfulness based stress reduction is has large effects on stress reduction, and is moderately effective in anxiety, depression, and distress as well as in improving the quality of life and a smaller effect for reducing burn-out. There are methodological concerns with how mindfulness interventions are delivered, with calls for standardizing and validating the approaches. There is some evidence that "state" and "practice" of mindfulness enhances cognitive appraisal and therefore may promote the ability to more effectively self-regulate emotions (Garland, Hanley, Farb, & Froeliger, 2015; see also Garland, Froeliger, & Howard, 2014 for an appraisal of the neurocognitive processes targeted by mindfulnessness based interventions). Bishop (2002) reports that randomized clinical trials have confirmed the positive effect of the meditative component to decrease stress and increase one's sense of emotional well-being. Mindfulness is of particular interest for BHP not only for its positive stress reduction component, but also for its putative ability to influence interpersonal emotional reactions (Grecucci et al., 2015). However, mindfulness-based approaches have not been without those who question its methodological soundness (see e.g., Caspi & Burleson, 2005; Davidson & Kaszniak, 2015), while others have identified dispositional variations in mindfulness, questioning whether it may exist as a distinct trait (Anicha, Ode, Moeller, & Robinson, 2012).

Mollicone (2011; 2012) spearheaded an effort to develop a prototype individualized behavioral health monitoring tool (informally known as a Dashboard). This dashboard integrated all behavioral health indicators. It included physiological signals such as heart rate and heart rate variability) and behavioral signals such as sleep wake patterns. The combined data will provide an overview of well-being and allowed for tracking over time. Additional behavioral health signals can be added to the dashboard as they are developed (Mollicone, 2011, 2012). A prototype of the behavioral health stress module for the dashboard has been delivered. The future of the dashboard with respect to behavioral health usage is uncertain at this time because most behavioral health needs for the dashboard are currently being met by electronic medical records, from a research perspective, BHP is working the ExMC element to ensure behavioral data, collected via BHP standard measures will be integrated into the medical systems for future spaceflight missions. At present, use of the dashboard is focused on the sleep risk (refer to the evidence book on the *Risk of Performance and Health Decrements Due to Sleep Loss, Circadian Desynchronization, and Work Overload*.

A second behavioral health self-management tool is SMART-OP, or Stress Management and Resilience Training for Optimal Performance (Rose et al, 2013) (Category I). The tool is a computer-based program that is designed for use primarily during pre-flight training to boost resilience and reduce stress experienced by astronauts. It is also projected to be available during flight to augment prior training or to be used as a treatment method. SMART-OP is discussed more fully in the Treatment section following this section on Prevention.

6) Cognitive functioning

Various alternatives to WinSCAT are being investigated to determine if a quicker, more comprehensive, more sensitive measure of cognitive functioning (that also is acceptable for crew)

can be developed. In addition to offering immediate feedback to the astronaut, desirable features would also recommend one or more countermeasures if functioning falls below a threshold. A tool named simply *Cognition* is being developed by Basner's lab and has been tested in the lab and several analogs (Categories II and III). Its feasibility is being demonstrated with a small sample of mission controllers and astronauts, including on the ISS (Basner, 2015a, Category III). *Cognition* continues to be further tested in various analogs (e.g., with crews wintering over in Antarctic stations, CO2, head-down bedrest, medication use) (Basner, 2015b, Category III). The goal for *Cognition* is to have a comprehensive, software-based, neurocognitive toolkit. *Cognition* builds on existing brief (1 to 5 minute) neuropsychological tests to permit evaluation of a full range of cognitive functions. Going beyond WinSCAT as the current screening tool for cognitive functioning, the *Cognition* battery also provide the capability to assess social-emotional and sensorimotor functioning.

c. Treatment

1) In-flight

In-flight treatment of adverse cognitive and behavioral conditions and psychiatric disorders, if any occur during long-duration spaceflight, will be very different than what can currently be provided to ISS crews. On the ISS, astronauts and crews have real-time audio and video capabilities. Thus, any psychological intervention, were it ever required, could be performed essentially as it is on Earth albeit with the two parties physically separated (cf., telemedicine). On long duration exploration missions, however, delays in communication will make real-time therapy between crewmember and psychologist or psychiatrist impossible. To address the possible need for psychological therapy when communication delays exist, two researchers, Rose (n.d.) (Category I) and Gonzalez (n.d.) (Category I), are conducting laboratory studies. These lab studies will build on current empirical findings regarding the efficacy of periodic face-to-face sessions with a psychologist combined with working a computer based cognitive-behavioral therapy plan on a more frequent basis. The goal is to determine under what means asynchronous cognitive behavioral therapy can most effectively be administered.

Other tools, which can be used as a stand-alone or as part of an overall therapy plan, are also being investigated. As mentioned under *Prevention* above, SMART-OP is being designed as a self-directed interactive computer program that uses cognitive-behavioral principles in training astronauts about detecting, preventing, and managing stress during space flight. While primary use is anticipated to be during pre-flight training, SMART-OP will remain available for additional training or interventions during flight. In a randomized controlled trial with a stressed but otherwise healthy sample, the SMART-OP group demonstrated less stress and more perceived control over stress than the control group (Rose et al, 2013) (Category I). Further trials will be compared to a wait-list control group. SMART-OP will further be examined against biomarkers for stress (i.e., cortisol and a-amylase) along with cognitive and behavioral performance in this sample of flight controllers.

The Virtual Space Station (VSS) is another computer-based system designed to assist astronauts in detecting, preventing, and treating psychological and social problems that might arise during long duration space flight. It is a compilation of self-guided, self-help modules. The conflict resolution module has been designed to use cognitive-behavioral therapy to help manage real conflicts.

Other modules are focused on depression and stress management. As well as informing astronauts on detecting and preventing depression, it will utilize Problem-Solving Treatment as a means of treating depression (Cartreine, 2009, 2014). Additional conflict resolution content, along with a behavioral health assessment and an immersive virtual reality to enhance psychosocial well-being, is also being added (Buckey, 2015). Evaluation of the acceptance of the VSS is planned with the Canadian military (Buckey, 2015).

2) Post-flight

The effects of an ICE environment can persist long after individuals return from that environment. At times, an ICE environment can induce physiological changes such as neuro-structural changes. BHP Research is currently examining the impact of such environments on both humans and rats.

Bed rest with its 6-degree head-down tilt mimics the physiological changes that occur during space flight and affords a unique controlled environment for conducting experiments. Seidler (2015a, Category II) used structural and functional MR brain imaging with bed rest subjects to determine whether post-bed rest brain structure, function, and network integrity differs from pre-bed rest baselines. They hypothesize that changes found will be associated with changes in cognitive, sensory, and motor function. Continuing on from the bed rest studies, functional MRI data are being collected pre- and post-flight from astronauts (Seidler, 2015b). At Concordia station in Antarctica, Basner (2015b, Category I) also used functional (fMRI) to examine a variety of anticipated changes over a winter-over. Specifically, neuro-structural, cognitive, behavioral, physiologic, and psychosocial changes will be assessed, with Antarctic crewmembers being compared with controls. Their aim is a better understanding of the changes that occur and the length of time for which those changes might persist.

Rats are frequently used in research that investigates the effects of radiation. Hienz (2012, 2015) and his lab (Davis, 2015a) are particularly interested in the behavioral changes that occur post radiation. Using a rodent version of the Psychomotor Vigilance Test used on the ISS (rPVT), they have demonstrated that head-only radiation significantly impairs neurobehavioral function and slows motor function. They are continuing with behavioral pharmacology studies and neurotransmitter protein level studies to examine both how individuals differ in their susceptibility to radiation and the degree to which changes are restricted to certain brain regions. In another attempt to counter the effects of radiation, Davis (2015b) is examining the extent to which dietary flaxseed provides protection and/or recovery from radiation. The BHP will continue exploring the connection between diet and protection from ionizing radiation (Kennedy, 2014), remaining vigilant for cross-discipline collaborations (e.g., a recent study demonstrated that dietary supplementation with dried plums offered prevention from skeletal effects of radiation, see e.g., Schreurs et al., 2016).

C. Summary

Based on our past experiences with space flight, various types of behavioral and psychiatric conditions are expected to be a risk for future exploration missions (Table 6). While current selection and countermeasure strategies have prevented the occurrence of any behavioral health emergencies during space flight to date that could have jeopardized mission success, the uniquely long durations and distances of future exploration missions necessitates comparisons with analog environments that might indicate the other types of occurrences that could be expected.

	Occurred During Space Flight			
Condition	YES	NO		
Behavioral/Psychiatric Emergency		\checkmark		
Anxiety – Diagnosed		\checkmark		
Anxiety – Signs and Symptoms	\checkmark			
Depression – Diagnosed		\checkmark		
Depression – Signs and Symptoms	\checkmark			
Asthenia – Signs and Symptoms	\checkmark			
Psychosomatic Reactions	\checkmark			
Salutogenic Responses	\checkmark			
Successful Psychosocial Adaptation	\checkmark			
Poor Psychosocial Adaptation and Disorders				

Table 6. Behavioral and Psychiatric Conditions Occurring DuringSpace Flight

BHP Research is directing research focused on identifying and minimizing any potential risk of behavioral conditions or psychiatric disorders that could occur during an exploration mission. These endeavors, along with other investigations in analog environments not instigated by NASA, have been discussed in parts A and B of this section.

V. COMPUTER-BASED MODELING AND SIMULATION

N/A

VI. RISK IN CONTEXT OF EXPLORATION MISSION OPERATIONAL SCENARIOS

Exploration and pioneering missions will go beyond any space missions to date. Humans might return to the moon or venture much further, to an asteroid or even Mars. In this section, any assumptions that must be made to define mission constraints are discussed. We consider new stressors that such a mission could add. Finally, based on the accumulated evidence presented in earlier sections of this report, we proffer our best guess of the likelihood of a behavioral emergency or psychiatric condition occurring on such an exploration mission.

A. Constraints for exploration missions

Some of these constraints are known while some will vary depending on the destination chosen. Still other constraints are unknown and require that we make assumptions.

Based on current prototypes for manned exploration of space, the size of the crew will likely be four or six. Extrapolating from the ISS, current political climate, and expected costs of exploration missions, an international crew is anticipated. Not only are partnerships with other countries expected to continue, but NASA also has begun to partner with commercial space companies. Exactly how commercial companies might figure into an exploration mission is unknown. The most recent class of astronauts selected was half male and half female. That fact along with the frequently mixed gender on the ISS provides evidence that an exploration mission would also be of mixed gender.

Compared with the ISS, any exploration vehicle will be much more limited that the 13,696 cubic feet of habitability volume of the ISS compared to the 316 cubic feet of habitable volume for the Orion crew module.^{*****} Some have argued that the ISS is actually a poor analog for a mission that leaves low earth orbit because of its variety of leisure activities, communication capabilities with the ground, and the physical space of the station. The exploration habitat itself will be small with limited privacy and even more limited personal space. The limited capacity of the habitat will also necessitate fewer exercise options. Indeed, *limited* is a key word when discussing exploration missions. A lack of widely varied entertainment will limit leisure options. Communications delay with Earth will limit access to ground-based mission support and support from friends and family. Limited space will likely result in a substitution of food bars for some meals.

B. Additional stressors for exploration missions

Added to general stressors of space flight, stressors specific to exploration missions are also expected. For one, the nature of exploration missions will require the crew to become more autonomous. The ISS was never developed to serve as an autonomous space platform, but rather to be controlled from Earth. Longer flights also mean that crew members will be required to take greater responsibility for training, need to remember technical information for longer periods, and potentially will need to complete just in time training while *en route*. Other challenges to be addressed in selection and training include the constraints for exploration missions mentioned above. Future challenges regarding selection will be impacted by decisions that have yet to be

^{*****} http://www.nasa.gov/sites/default/files/fs-2014-08-004-jsc-orion_quickfacts-web.pdf

made and include issues like crew composition, single or multinational explorers, commercial explorers, multi-space agency involvement. Possible ways of mitigating some of the increased or new stressors are discussed below.

Views and interaction with nature, virtual nature, and other virtual environments

As space travel moves past the moon, one of the strongest countermeasures we have, the ability to view and photograph Earth, will be lost. Adding virtual windows to actual windows to replace the lost view of Earth is recommended. Immersive virtual environments, especially of natural settings, along with actual plants are possible countermeasures. Benefits of such environments include mental restoration, stress reduction, connection with home (seeing Earth), and increased resiliency. Actual windows will allow crew to feel connected to something greater than self as their changing view of stars will remind them of what their mission gives to humanity. Plants, as well as being a potential food source, will provide tactile sensory stimulation and allow crewmember to care for living objects separate from themselves,

Capsule design and layout

Factors such as net habitable volume, layout, color, private personal space, crowding, traffic flow, windows, lighting, noise levels, and virtual reality can affect emotional well-being, performance, and individual and crew behavioral health. In ICE environment, these effects can be far more pronounced (Suedfeld & Steel, 2000). Designing a capsule with private quarters for crewmembers, efficient workspace, and possibly even flexible or reconfigurable spaces can promote social engagement as well as relief from social interaction. Both private quarters and reconfigurable spaces will allow crewmembers to feel a sense of control as they personalize their own spaces.

Crew selection and management

To the extent possible, a crew would be selected with consideration given to individual traits and group compatibility. Cohesion among the crewmembers will allow them to better cope with stressors as a group. In-flight training and increased crew autonomy will provide intellectual engagement and meaningful work, keys to preventing boredom.

Leisure activities

The plethora of the leisure activities available on the ISS will be limited on an exploration mission due to the size of the capsule and delayed communication. Movies, electronic books, and music will still be available, but with fewer choices and a decreased ability to receive additions. A virtual environment, as discussed above, would allow crewmembers to virtually immerse themselves in nature, look at Earth, or care for their virtual pet or plants.

C. Likelihood of a behavioral emergency or psychiatric condition

The different constraints and stressors of an exploration mission will affect the likelihood that a behavioral emergency or psychiatric condition will occur. Stuster (2008) predicted that the incidence rate of behavioral problems that could be expected on long-duration exploration missions is based on known incidence rates in analog environments. Behavioral problems here are defined as symptoms that normally would warrant hospitalization. Stuster's analyses show that as the length of a mission increases, so will the incidences of psychiatric disorders (see Table 7). Stuster's (2008) assumptions are as follows:

The figures in the row labeled *Behavioral Problem* assume a 6% per year incidence rate of serious behavioral problems throughout the duration of the two mission options considered (i.e., Mars Long Stay, 905 days total; and Mars Short Stay, 661 days total). This predicted incidence rate is based on incidence rates of behavioral problems reported from Antarctic experience (i.e., Matusov, 1968; Gunderson, 1968; Lugg, 1977; Rivolier and Bachelard, 1988; Otto, 2007). The row labeled Differential assumes a 6% incidence rate per person-year during the interplanetary transit phases and a 2% rate per person-year while on the surface of Mars, when confinement would probably be less of a factor and other stressors might be offset by the novelty and fulfillment of task performance. The expected occurrence of a behavioral problem serious enough to require hospitalization on Earth in a crew of six is estimated to be .534 for the long stay option and .626 for the short stay option. Using the differential values, these translate to a 53.4% probability that a serious behavioral problem will occur during the long stay option and a 62.6% probability during the short stay option. Stuster (2010a) asserts the probability of a serious problem occurring to be greater for the short stay [on Mars] option, due to the substantially longer time that must be spent by the crew confined to the spacecraft than in the long stay option. However, the long stay option will always generate a higher probability if the incidence rate remains constant throughout the mission. A uniform 6% incidence rate per person-year would increase the estimated probability of a serious behavioral problem to 65.2% for the short stay option and 89.3% for the long stay option.

	incluence and Probabilities in Analog Environments									
			Long Stay Option							
	Incidence Per 365 Days	Outbound	Surface	Return	Total Long- Stay Risk	Expected in a Crew of Six				
		180 days	545 days	180 days	905 days					

0.090

0.030

0.030

0.030

0.149

0.089

Table 7. Calculation of Expedition Risk of a Behavioral Problem Occurring Based onIncidence and Probabilities in Analog Environments

Source: Jack Stuster, Ph.D., CPE, Anacapa Sciences, Inc., used with permission.

0.030

0.030

0.060

0.020

Behavioral

Differential

Problem

Using data collected from astronauts (N=16) on the ISS provides a different look at predicted behavioral health for the length of a mission to Mars (Dinges, 2014). As part of a larger study, astronauts were asked to rate their current feelings of stress every four days while in-flight. Perceptions of stress tended to change over time and susceptibility to stress varied across individuals. For most astronauts (50%), stress increased over the duration of their six-month missions. Another 25 percent reported no significant change in stress over the mission, while the remaining 25 percent reported a decrease in perceived stress. Astronauts who reported increasing stress with time in mission tended to also report less total sleep time and increased physical exhaustion. Increased physical exhaustion was in turn associated with increased tiredness and decreased sleep quality. Of particular interest to long duration exploration missions, the aggregated data revealed that stress over the length of a mission does not increase in a linear

0.893

0.534

fashion. Instead, perceptions of stress accelerate as more days are spent in-flight. Extrapolating the increase in stress to the length of a mission to Mars results in levels of stress that would be difficult to sustain without resulting in adverse cognitive, behavioral, and physical conditions. There is a cost associated with longer missions. At some point, perceptions of stress might asymptote but with only data from six-month missions along with small numbers of longer missions, it is difficult to project at which point this might happen.

While differing approaches to estimating the incidence rate of behavioral and psychiatric conditions will yield different predictions, the general consensus seems to be that the longer the exploration mission, the more likely a psychiatric disorder (not just an increase in symptoms) will occur.

VII. GAPS

At time of writing, BHP has identified eight research knowledge gaps directly related to the risk of behavioral and psychiatric conditions associated with human space exploration. These are summarized in the Human Research Program Roadmap ("Risk", 2015) and are:

- BMed1: We need to identify and validate countermeasures that promote individual behavioral health and performance during exploration class missions.
- BMed2: We need to identify and validate measures to monitor behavioral health and performance during exploration class missions to determine acceptable thresholds for these measures.
- BMed3: We need to identify and quantify the key threats to and promoters of mission relevant behavioral health and performance during autonomous, long duration and/or long distance exploration missions.
- BMed4: [Gap content has been merged with BMed2. Formerly was: What are the most effective methods for detecting and assessing cognitive performance during exploration missions?]
- BMed5: We need to identify and validate measures that can be used for the selection of individuals that are highly resilient to the key behavioral health and performance threats during autonomous, long duration and/or long distance exploration missions.
- BMed6: We need to identify and validate effective treatments for adverse behavioral conditions and psychiatric disorders during exploration class missions.
- BMed7: We need to identify and validate effective methods for modifying the habitat/vehicle environment to mitigate the negative psychological and behavioral effects of environmental stressors (e.g., isolation, confinement, reduced sensory stimulation) likely to be experienced in the long duration spaceflight environment.
- BMed8: We need to understand how personal relations/interactions (family, friends and colleagues) affect astronauts' behavioral health and performance during exploration class missions.
- BMed9: We need to understand long term astronaut health for long duration exploration missions and find the best methods to promote long term post-mission behavioral health.

Please note: BMED4 Gap addressed the "most effective methods for detecting and assessing cognitive performance during exploration missions" and was merged with the BMed2 Gap.

VIII. CONCLUSION

Evidence that was gathered from long-duration stays in ground analogs demonstrates that, despite the focus on screening and selection for suitability, behavioral and psychiatric conditions such as depression develop. Of greater relevance, anecdotal reports from the earlier long-duration space missions (i.e., Mir and Skylab) and evidence from current long-duration missions on the ISS, reveal that the signs and symptoms of depression and other behavioral disorders also have occurred in flight. The relevance of the risk of behavioral and psychiatric conditions is supported further by the implementation by NASA of the Family Support Office, as well as by the psychiatric support that is made available to the ISS crews and their families.

Exploration missions will require crews to live in isolated, confined, and extreme environments for as many as 3 years. This is a significant leap from the 6-month duration of lower Earth orbit missions. To date, only six individuals have lived and worked in space for longer than 1 year.^{†††††} The incidence of behavioral and psychiatric disorders is expected to increase as the length of the mission increases (Ball and Evans, 2001; Dinges, 2014; Otto, 2007; Stuster, 2008) (Category IV). The additional, unique stressors of radiation exposure, remote distances, and unknown dangers that will be experienced during long-term Exploration missions to the moon and Mars also may contribute to an increased likelihood of this risk.

If a behavioral or psychiatric condition should develop on an Exploration mission, the consequences could jeopardize mission objectives. Therefore, research addressing the prevention of behavioral problems, as well as the early detection and treatment of problems that do occur, is necessary.

BHP Research is following a path designed to reduce the risk of adverse cognitive and behavioral conditions or psychological disorders from occurring during long duration exploration missions prior to the anticipated earliest launch date of such a mission. To meet the goals of those objectives, BHP Research identified as highest priority the areas below for progressing along BHP's critical path for risk reduction:

- Prospective study of signs and symptoms (not just diagnoses) seen in polar analogs
- Best practices for psychotherapeutic treatment without real-time communication
- Development of treatments for the top signs and symptoms using the evidence of how to deliver therapy without real-time communication (after the first two goals are met)
- Standardized common set of measures to be used in research conducted ground-based space analogs and spaceflight
- Environmental effects on cognitive and behavior (e.g., CO₂ and radiation)
- Evaluation of commercial, off-the-shelf monitoring technologies

^{†††††}Four Russian cosmonauts (Sergei Krikalev, Sergei Avdeyev, Alexander Kaleri and Valeri Polyakov) and three U.S. astronauts (C. Michael Foale, E. Michael Finke) have spent more than 1 year in space. Two others, astronaut Scott Kelly and cosmonaut Mikhail Kornienko are scheduled to complete their one year mission on the ISS in March 2016.

A methodological goal for future BHP Research includes improving the level of evidence. This can be achieved through controlled clinical trials, meta-analysis, and systematic reviews rather than anecdotal or expert opinion.

This review of the evidence to date reveals that much work has been done to identify, prevent, and treat the behavioral and psychiatric conditions that might affect astronauts and their performance during all phases of a mission. Given the relative lack of behavioral and psychiatric conditions that have occurred within the astronaut population, the lack of behavioral and psychiatric emergencies in flight, and the number of long-duration mission successes, the current system for mitigating the risk of behavioral and psychiatric conditions appears to be effective. However, characteristics of exploration missions will greatly differ from the challenges, demands, duration, and characteristics of current space flight; and, we do not know how effective our current system of monitoring technologies and countermeasures will be under these changed conditions. As missions return to the moon or look toward Mars, changes to behavioral medicine will be required. Our view of the "right stuff" will need to be adjusted. Factors such as personality might play a greater role, while other factors, such as pilot experience, might play a lesser role than they do at present. The selection system will therefore need to reflect any necessary changes. Countermeasures will need to evolve. Some current countermeasures will not be relevant for longer flights, while other, new ones will need to be developed (e.g., alternative to seeing Earth). Effective countermeasures will help to protect and ensure astronaut behavioral health and performance, and, in turn, help NASA achieve mission success on future missions that leave low Earth orbit to explore deeper space.

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XI. LIST OF ACRONYMS

ANARE	Australian National Antarctic Research Expeditions
ANSIBLE	A Network of Social Interactions for Bilateral Life Enhancement
ASCAN	Astronaut candidates
ASG	Astronaut Spouses Group
BHP	Behavioral Health and Performance
BMed	Behavioral medicine
CAPCOMs	Capsule communicator (the individual in mission control who traditionally talks
	with the space craft)
CAVES	Cooperative Adventure for Valuing and Exercising human behaviour and
	performance Skills
СМО	Crew Medical Officer
CO_2	Carbon dioxide
CS	Crew Surgeon
DRATS	Desert Research and Technology Studies (AKA Desert RATS)
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text
	Revision
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
FS	Flight Surgeon
HDL	High-density lipoprotein
HERA	Human Exploration Research Analog
HI-SEAS	Hawai'i Space Exploration Analog and Simulation
HPA	Hypothalamic-pituitary-adrenal
HRP	Human Research Program
HSRB	Human System Risk Board
IBEA	International Biomedical Expedition to Antarctica
ICE	Isolated, confined, extreme
ICD-10	International Statistical Classification of Diseases and Related Health Problems-
	10 th Revision
IGY	International Geophysical Year

IMM	Integrated Medical Model
IP	Internet protocol
IRP	Integrated Research Plan
IQ	Intelligence quotient
ISS	International Space Station
JSC	Johnson Space Center
K _u -band	Band directly under the K band (originally German: Kurz-unter)
LED	Light-emitting diode
LSAH	Lifetime Surveillance of Astronaut Health
LTH	Long Term Health
L×C	Likelihood by Consequence
NASA	National Aeronautics and Space Administration
NEEMO	NASA Extreme Environment Mission Operations
NIMH	National Institute of Mental Health
NOLS	National Outdoor Leadership School
NRC	National Research Council
OCR	Optical computer recognition
Op Psy	Operational psychology group that supports crew on the ISS
OPS	Operational Health
PISCES	Pacific International Space Center for Exploration Systems
PPC	Private Psychological Conference
PRD	Programmatic Risk Document
Psyc	Psychology
PsyCap	Psychological capital
rPVT	Psychomotor Vigilance Test (rodent version)
SG	Software generated
SMART-OP	Stress Management and Resilience Training for Optimal Performance
U.S.	United States
WCS	Waste Collection System
WHO	World Health Organization
WinSCAT	Space flight Cognitive Assessment Tool for Windows