# **American Journal of Aerospace Engineering**

2021; 8(1): 14-26

http://www.sciencepublishinggroup.com/j/ajae

doi: 10.11648/j.ajae.20210801.13

ISSN: 2376-4813 (Print); ISSN: 2376-4821 (Online)



# Improving Psychological Resilience with Cognitive Retraining Methods Using EEG Brain Network Biomarkers: Example from UND/NASA Lunar/Martian Habitat

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#### To cite this article:

Curtis Cripe, Rebecca Cooper, Sonnee Weedn. Improving Psychological Resilience with Cognitive Retraining Methods Using EEG Brain Network Biomarkers: Example from UND/NASA Lunar/Martian Habitat. *American Journal of Aerospace Engineering*. Vol. 8, No. 1, 2021, pp. 14-26. doi: 10.11648/j.ajae.20210801.13

Received: May 17, 2021; Accepted: June 15, 2021; Published: June 28, 2021

Abstract: The brain is the only organ that does not heal itself once injured, but it does adapt and relearn quickly once injured. Whether the brain is cognitively optimized or is dysfunctional, the same brain networks and brain systems are at play to optimize or regulate and repair. That is why studying brain function of optimized brains from astronaut candidates, or individuals within TBI and depression populations can help both ends of the cognitive spectrum to achieve repair for dysfunctional populations or maintain optimal performance. Opportunities to increase coping capabilities neurophysiologically that impact psychological resilience are appealing both clinically and when applied to space travel. The subject of this paper is reporting the results of one such method that is currently being employed in an ongoing UND/NASA Inflatable Lunar Mars Analog Habitat (ILMAH) simulator study. Our Habitat study's primary goals are many fold: 1) to develop a predictive profile, based on real-time measurable neurophysiological metrics that model cognitive health and resulting task/behavioral health performance; 2) demonstrate the viability of developing a wearable dry sensor device that produces a profile that can be used in extreme environments such as long duration space missions; 3) demonstrate the viability to provide crew countermeasures that mediate negative reduced resilient stress effects on an on-going and as needed basis. Our study method employs the NeuroCoach® Training System that focuses on developing targeted resilient flexible adaptability neural circuit responses through the application of brain training exercises to support psychological resilience. The training program assumption is that if key neural circuits and network systems that support resilient, adaptive behaviors are coupled with proper problem-solving skills, resilient adaptive behaviors emerge. The NeuroCoach® program is based on modern Restorative Cognitive Rehabilitation Training Methods (rCRT). The program provides in-the-moment neural network performance metrics to monitor and adjust the training difficulty level using a Brain Computer Interface. Experimental and clinical results demonstrate the program success at increasing and maintaining optimal cognitive and brain performance quantitatively (by the numbers) and qualitatively (social reintegration). We have found that by studying astronaut crew needs to remain at optimized performance during long duration space travel as well as our studies with various clinical populations with acquired brain dysfunctions presents us with a unique opportunity to compare. They are opposite ends of the spectrum, but both are instructive in what a damaged brain can potentially achieve vs what an optimized brain might suffer during deep space travel.

Keywords: Psychological Resilience, Cognitive Retraining, Spaceflight Astronaut Monitoring

# 1. Introduction

This paper establishes the research plans for a repeated measure, cognitive study utilizing practical space mission tasks performed by astronaut-like subjects in an Isolation, Confined and Extreme (ICE) analogous environment. The

origin for this investigation is the anticipation that Long-Duration Spaceflight (LDSF) crews must operate independently. [1-10] This increased cognitive demand for expertise creates critical learning and forgetting dilemmas for spaceflight crew. With adequate pre- and during-mission training systems, many of the other LDSF stressors can be mitigated. However, detecting changes in how resilient and responsive the brain is and distinguishing when training is most needed to ensure continued fitness for duty is vital for sustained and safe spaceflight [1-10]. Living and working in outer space introduces unique physiological, psychological, and psychosocial stressors to the human body. Many stressors are known and documented, LDSF crews will travel well beyond Earth's protective lower orbits, which will create additional and more troublesome stressors. More research is needed into how these stressors affect the natural brains resilience and how they can be adequately mitigated. LDSF is known to alter brain structure and function and leading to an imbalance in the neuronal and glial networks' function and the neurovascular unit [6].

Resilience - In a constantly changing world, our brain has evolved to fine-tune its behavior under changing environmental conditions, needed to help appropriate responses essential to attain goals, interact socially, avoid danger and sustain proper mental health. The evolution of our natural abilities has progressed neurophysiologically and is reflected in many skills sets that include our professional and interpersonal domains. These biological advancements have resulted in many abilities that allow humans to learn, develop skills, and adapt to new conditions. All are required for effective functioning in social and professional environments. For our astronauts, it may be even more important that these abilities remain resilient and be preserved at the highest level throughout a mission and upon their return from space. Equally important, these same needs exist on earth and become more obvious for those in many clinical settings.

The paper is structured in the following format: Introduction, Problem at Hand, Habitat and Clinical Results report, followed by a more detailed description regarding the rationale behind neural circuit and metrics choices.

# 2. Problem at Hand

#### 2.1. Astronaut Needs

Long-duration space missions will generate neurophysiological and psychological challenges never before experienced due to extended periods of microgravity and radiation exposure. Both are proven to modify Central Nervous System (CNS) performance, comprising the brain's natural ability to self-regulate, process information, maintain cognitive control and neurogenesis [1-10]. Relevant to longterm space missions, the hippocampus, thalamus, cerebellum and amygdala (the brain's cognitive control system mediators) are vulnerable to radiation and microgravity effects [8-24]. space have demonstrated Past experiments neuroadaptations (structural and neuro-network connectivity changes) occur in space due to space related environmental effects that affect cognitive performance (3D spatial perceptions, reaction times, moods, etc.) [1-9]. Equally important to note, the entire interwoven set of brain networks participate in neuro-adaptive processes altering basic neural

network performance throughout the brain. Thus, neuroadaptations to a space environment may potentially not only affect other primary brain networks that contribute to task performance, but also to behavioral health and wellbeing. In other words, monitoring the effect of the neuroadaptive process is necessary to keep an astronaut at peak optimal brain function before, during and after a mission is a top priority.

#### 2.2. Clinical Population Needs

Likewise, recent and on-going mental health literature evidence indicates consistent observations of cognitive dysfunctions as fundamental mental health factors, regardless of the diagnostic condition [21-23]. Cognitive dysfunction complaints are cited as a major reason for elevated exploitation of health-care resources and have been found to be principal factors in the influence of health-care outcomes [21-23]. As such, cognitive dysfunctions can be considered transdiagnostic abnormalities with dissimilar yet intersecting phenotypic traits; their use as primary therapeutic targets is recommended. What this means in the field of Psychology and treatment, is that effects related to cognitive function are being recommended to be added to treatment plans for many diagnostic conditions [22-28]. Underpinning complaints and a target for treatment is a reduction in one's ability to implement resilient vigilant and flexible adaptable behavior – both essential for recovery and reintegration back into society. This means the individual's ability to learn, develop skills, and adapt to new conditions is compromised from a brain circuitry and neural network perspective and these abilities are natural remediation targets.

# 3. Background

#### 3.1. Improving Psychological Resilience

Based upon recent mission reports, the need to reduce and/or avoid neuroadaptive space travel effects during long duration space missions is necessary [1-10]. Similarly, this same need exists in clinical settings as an adjunctive clinical intervention for many clinical cases [28-30]. In support of the possibility of increasing one's coping abilities and resilience, several authors are demonstrating supportive evidence through behavioral interventions and targeted neuro-physical exercises in various treatment settings [30-47]. Neurophysical improvements are seen by fMRI and other observable and quantified behavior means. At the neurophysiological level, improvements appear to be achievable by increasing either gray or white matter density within and between key nodes in the neural circuity that results in improved neural function [41-47]. The results of our data, while working with crew both pre and during habitat missions, further strengthens this hypothesis as a possibility. More importantly, our results are adding to the identification of key behavioral health neurophysiological monitoring targets.

In the cognitive neuroscience literature several authors are

reporting important relationships as they relate to resilience. For example, Santarnecchi et. al. (2015, 2018) note resiliency at the neurophysiological and psychological levels appear to vary based upon key circuits that support IQ performance that include language, memory, the salience, and default mode networks. Additionally, authors are also suggesting other important neural network circuit properties that include efficient neural network hubs that correlate with intelligence, cognitive control, and vigilance [48-53].

#### 3.2. Neural Circuit and Metrics Choice Rationale

#### 3.2.1. Psychological Resilience

Resilience is defined as a multi-dimension construct representing an individual's ability to positively adapt and respond to stress and adversity while maintaining proper mental health and well-being [47, 65, 66]. The construct includes interacting factors such as genetics, epigenetics, psychosocial factors, childhood developmental environment, cognitive abilities profile, and functional neural circuitry integrity (65-66). Implied in the construct definition, are two stances for consideration: 1) physical (i.e. physiology, neurophysiology and state of health); and 2) skills (i.e. natural/learned expressions - abilities-talents).

Regardless of the domain in life (space travel, athletics, academics, careers, leadership, social, etc.) it is commonly accepted that the expression of a person's natural abilities are modulated by four interrelated but conjoining features: 1) *current* physical abilities (strength/health); 2) learned skills (knowledge and ability to adapt); 3) motivational intent; 4) environmental conditions (opportunities/stressors).

One major key that defines success is how resilient we are to adapt to these four modulating factors -- i.e., the ability to resourcefully adapt to any and all unplanned situations that may impact one's goals and to adapt and remain resilient under many/any forms of stress. (In particular with deep space travel, the unplanned and unknown will always be a factor). However, when too much stress and/or adversity enters one's life, one's ability to respond in a resilient manner is often impacted, either because of the lack of skills to cope, and/or the neurophysiological strength to remain resilient. In other words, to be successful it is important to be psychologically strong, skillful, present in the moment to respond, and to have access to our inner resources to make it happen... i.e., to Problem Solve or Cope.

The need to remain neurophysiologically resilient under stressful unknown conditions, is the key training driver and focus that underpins the NeuroCoach® program in general, but specifically regarding our Habitat crew experiments. The NeuroCoach® monitoring/training program focuses on key neural circuits that support resilient adaptive behaviors to allow the brain to remain or become more resilient and open to coping strategies, thereby allowing one's natural Fluid Intelligence to take place and continue to be expressed under stressful conditions. Hence through the BCI interface measurements, neurophysiologically, allowing for a more robust state of mindfulness that can provide access to proper problem-solving skills, and resilient adaptive behaviors.

#### 3.2.2. Coping Styles

Coping styles are an important element of psychological resilience [47, 65, 66]. Positive adaptive problem-oriented coping skills are interconnected with well-being and a higher quality of life. Adaptive problem-oriented coping skills are considered coupled with psychological factors encompassing positive and negative affect, positive emotion regulation, self-esteem, emotional flexibility, inhibitory control, and more [67-69]. In contrast, avoidance coping styles have been linked to a predisposition to psychiatric disorders such as PTSD, anxiety, and major depression.

#### 3.2.3. Increasing Coping Abilities – Behaviorally

Notably, many behavioral interventions effectively aid in transferring proper coping skills (strategies) which can be seen in neuroimaging as changes between brain regions that support proper neural function, including mindfulness training, controlled stress exposure, stress inoculation training, and behavioral training targeting psycho-social risk factors [70-72]. However, by their behavioral nature these interventions do not explicitly target the brain circuitry responsible for individual differences in coping/resilience. What is missing is supporting interventions that focus on strengthening and developing the neuro-physiological mechanisms, and thereby provide structural support for neural circuit performance and can easily and effectively be implemented alongside existing behavioral intervention programs. In other words, both behavioral intervention and brain circuit strengthening will work better in tandem, than each as a standalone.

## 3.2.4. Neurophysiology of Coping Styles

Addressing if neurophysiological differences in each coping style even exists, Santarnecchi et al. (2018) used fMRI scans to study 102 healthy adults' brains as they relate to coping styles. In the study, the authors successfully identified significant associations between neural network "functional connectivities" (connectivity strength between brain regions) between different neural circuits in the brain. Significant correlations for three out of five major coping styles were found (avoidance-oriented, problem-oriented, and social-support-oriented) with the Salience Network (SN) and the Default Mode Network (DMN) [47].

The SN and DMN networks, especially the DMN, are correlated with problem-oriented (left angular gyrus - BA39) and social support-oriented coping (left frontopolar cortex - BA10), whereas the avoidance-oriented (ACC) coping also explains individual variability in this coping style by means of its negative correlation with medial structures of the DMN [47]. These finding linked coping styles with the SN and DMN networks to emotional processing, viscero-somatic perception, the integration of somatic signals for interoceptive awareness, the determination of stimulus salience and attentional focus, as well as imagination of past and future scenarios, mind wandering, and auto-biographical memory [73, 74]. The authors further noted that the tendency to express one style over another was linked to spontaneous brain patterns that guided automatic selection of one stress-

related response instead of another. In this context, the authors introduced the reasonableness of linking coping style relationships to the two resting-state networks. Moreover, the possibility of increasing one's ability to cope by addressing the neuro-physical underpinnings of coping styles was introduced by the authors.

#### 3.2.5. Fluid Intelligence and Resilience

Fluid intelligence (gf) characterizes the ability to solve problems unrelated to previously learned knowledge an essential element in resilient behavior [75]. This ability underwrites encoding of new information and its efficient manipulation, representing a critical component of human cognition and has been shown to have a strong predictive power over both educational and professional success [76], making the neural networks that support these operations obvious training targets.

To explore the resilience relationship aspect of these networks, Santarnecchi et al. [29] documented the association between individual intelligence quotients (IQ) and brain resilience as it responded to targeted simulated (specific network nodes) and random attacks, using resting-state fMRI and graph analysis methods (n= 102 healthy individuals). Enhanced brain resilience to targeted attacks (TA) was correlated with higher IQs in networks belonging to language and memory processing regions, whereas regions related to emotional processing are mostly supported by lower IQ individuals. These results suggest that pre- and post-changes in IQ scores may be both useful training targets as well as predictors of astronaut performance and for clinical recovery.

#### 3.2.6. Fluid Intelligence and White Matter

Other authors have investigated white matter (WM) substructures, level of efficient hub connections and their relationship with gf [76-82]. Network nodal efficiency, a graph analysis metric, has been shown to be significantly related to intelligence in three brain regions. Higher gf scores showed higher nodal efficiency in right anterior insula (AI) and dorsal anterior cingulate cortex (dACC), two hub regions the salience network, with both regions shown to be vulnerable to space flight environmental effects [1-6] and implicated in various mental health conditions [21-27]. Likewise, higher gf was linked with lower nodal efficiency in the left temporo-parietal junction area (TPJ). This relationship was found to be similar between younger and older participants [82]. Further, other gF components findings including cognitive measures of information processing speed and reasoning ability, but not memory performance, were significantly related.

In line with these findings, neuroimaging studies of gF are commonly supportive of the parieto-frontal integration theory (P-FIT) of intelligence [84-86]. The P-FIT model postulates a theoretical framework for how the assimilation of cortical structures relates to individual intellectual abilities [84]. Equally the theory points the way to how performance on tests of intelligence requires processing of modality specific sensory inputs, integration of multimodal sensory

information, and then cataloging and blending of those in frontal cognitive control areas. Notably, these finding further focus on both the monitoring NeuroCoach® function and provide individualized brain regions training targets when needed.

#### 3.2.7. Working Memory and Resilience

Several emerging theories of consciousness that include the Global Workspace, Neural Blackboard Architectures and IDOYP [87, 88] link the function of the working memory network as the "workspace" in which all forms of information are integrated. The WMN serves as a primary network supporting reasoning, expanded thought, and awareness by providing the mind a conscious workspace for information to reside in [78, 87, 88]. Several theories describe working memory as the "desktop of our conscious awareness", is utilized to hold thoughts in our mind, gives rise to awareness and task execution limitations that vary under different cognitive load and stress conditions [79, 87, 88]. Recent research has identified brain networks that contribute to distinctive aspects of cognitive control and how they operate with the working memory network [78, 80]. Putative WMN structural and functional mechanisms are often found impaired in several conditions including aging, learning impairment, addiction, as well as a number of psychopathological diseases, such as schizophrenia, depression, and obsessive-compulsive disorder [60, 61], making working memory and cognitive control areas critical to monitor. Recent electrophysiological studies note that increases or decreases in task- related activation, predominantly within the theta or alpha band produced by cognitive control/working memory networks, is associated with schizophrenia, inhibitory and sustained attention, lapses of attention, working memory dysfunction, deficits in emotional engagement and reward processing (depression), error processing and conflict monitoring (obsessive-compulsive disorder) [89-95].

#### 3.2.8. Cognitive Control Networks (CC) and Resilience

Recent findings suggest the existences of a set of brain networks contemplated as the cognitive control network system. This network system involves of a set of welldefined brain structures that consist of flexible hubs that regulates a distributed set of brain systems (e.g., visual, limbic, motor) according to current task goals [96-102]. More importantly, an increasing number of studies report alterations to this system are found throughout a noticeable range of mental diseases. Equally important, many acquired mental health disorders (due to health, injury, or poor lifestyle choice such as substance abuse) have been shown to disturb this system via neuroadaptations and are considered the root of poor mental health. These reports, indirectly, suggest that the CC networks may play a critical role for promoting and maintaining mental health as well as indirectly imply a relationship to resilience.

# 4. Method

#### 4.1. Study Purpose

The ILMAH study is an ongoing experiment that aims at examining and characterizing the impact of different simulated spaceflight environmental situations on the temporal changes in five large-scale brain networks that support neurocognitive functions critical performance and behavioral health maintenance during extended long duration space expeditions. We chose to examine the changes in the neural functional connectivity EEG metrics during resting and cognitive task, based upon the need to obtain an evidence-based biomarker that would be predictive of possible reduction in task performance and/or behavioral health disturbances. The study procedures are demonstrating the feasibility of using dry sensors to wirelessly collect continuous real-time temporally integrated brain performance data experienced during simulated space mission events. Various mission events are included linking experimental conditions such as real time data collection during simulated EVA scenarios within spacesuits in combination with previous night sleep profiles, physical exercise routines, and operational workload scenarios.

## 4.2. Inflatable Lunar Mars Analog Habitat (ILMAH)

The ILMAH is a surface planetary analog facility located in Grand Forks, North Dakota. The interior consists of a galley, bathroom, lab space, and private sleeping quarters for up to 4 crewmembers. The ILMAH is about 12.2 meters (40 feet) long, 3 meters (10 feet) wide, and 2.4 meters (8 feet) in height, although the living space is a little less. Crewmembers enter their simulation through the "airlock" in the front. As you walk through the habitat, there is a small port on the other end that leads to a tunnel. This crawlspace leads to a rover that allows crewmembers to drive around on the "planetary surface" and find a spot to explore using the simulated spacesuits attached to the back of the rover. Throughout this process, the crewmembers are never exposed to the conditions outside, however, the habitat relies on the water and air supplied from the mission support team.

Since its completion, the ILMAH has been used for seven different "missions" from 10-30 days, simulating various phases of surface Mars operations. In all missions, only three crewmembers were selected at a time, in order to leave some space available for experimentation. The studies have mostly involved human psycho-social response to isolation and confinement. Construction techniques and operations during Extra Vehicular Activities (EVAs) were also explored during two missions. Studies about microbial growth and plant production in small, closed spaces has also occurred [55, 56]. We have successfully conducted and collected neurocognitive data during Mission V, VI and VII and are currently participating in Mission VIII, in which we continue to refine our procedures to be less invasive.

#### 4.3. Habitat Sample Size Limitation

Each habitat mission is limited to a crew of three, which limits our sample size. To date we have been involved in 3 missions, plus one currently on going. To help support the viability of our approach of improving psychological resilience, we report also on recent findings from clinical studies using the NeuroCoach<sub>®</sub> method where larger samples sizes are available.

# 4.4. Monitoring/Training Networks for Resilient Flexible Adaptability Responses

We selected five key networks considered to fine-tune behavior under variable environmental conditions. These networks are implicated in maintaining proper task performance and mental health preservation [56-59]. The networks include: Working Memory - the primary network that supports reasoning, expanded thought, and awareness by providing the mind a conscious workspace for information to reside in [60, 61]; Cognitive Control Networks (CCN) Cognitive control incorporates processes involved in producing and preserving appropriate task goals, including suppressing irrelevant mental and physical activities that distract from achieving the desired set of task goals [60, 61] – CCN Subdivisions - (60, 61) The Frontal-Parietal network (FPN) provides active online control allowing it to adaptively initiate and adjust control [59-60]; (2) the Cingulate-Opercular Network (CON) provides stable 'set-maintenance' (state maintenance) over the entire task epoch or behavioral strategy [60, 61]; (3) the Salience Network (SN) (Attention Networks plus Insula Network) is involved in rapid detection of goal-relevant events and facilitation of access to appropriate cognitive resources by interacting with multiple functional systems and thereby supporting a wide range of cognitive processes [60, 61]. Default Mode Network (DMN) is implicated in the brain's default resting state conditions and in its ability to sustain task performance. The DMN is composed of functionally specialized subsystems, with the anterior DMN (i.e. medial Prefrontal Cortex (PFC)) associated in identifying stimuli as self-salient, whereas the posterior DMN region jointly with the parahippocampal gyrus are involved in autobiographical search and memory retrieval. Mechanisms within the DMN are implicated in regulating emotional reactivity and may take a key role in the empathic process by establishing a distinction between other and self- related feelings [60, 61]. Further, regarding congruent cognitive/behavioral health performance a close relationship between empathy and executive regulatory mechanisms exist. Sluggish and/or poor (dis) engagement of the DMN is a noted biomarker within several mental health conditions including depression and attention deficit disorders [60-64]. The opposed relationship between DMN and cognitive control networks may influence the ability to exert cognitive control [61-64] and play an important role in the regulation of mind-wandering and rumination that impacts task performance [64].

# 4.5. NeuroCoach® Training Methods

The NeuroCoach® system employs the use of the most current rCRT methods that incorporates a BCI that provides neural network performance integrity metrics (nPIMs) to the training activity. The program supports non-verbal cognitive enhancement/ repair treatment programs by providing a set of cognitive remediation applications (training programs) that monitors and evaluates a user's defined neural networks system performance status in real-time. Based on a NeuroCodex<sup>®</sup> evaluation and brain map that measures cognitive abilities while the individual is undergoing cognitive activities measures everyone's brain performance. These metrics (nPIMs) are derived from the neural network system that supports the cognitive function being trained. The CRT methodology is implemented as a set of computer activities to engage the desired training cognitive functions based on classic neuroscience experiments found in the literature. The BCI interface informs the trainer, the user, and CRT activity in real time, regarding current neural network performance integrity status based on the user's present nPIMs state.

The CRT activity incorporates a performance leveling algorithm (PLA) to adjust the intensity of the activity by rendering the pursuit to be either more or less intense. Unique in our method is that the PLA encompasses both nPIMs and behavioral responses (response times, accuracy) to adjust the level of intensity play of the activity. This is based upon the current real-time performance ability of the user that is required to properly engage the long-term potentiation (LTP) and long-term depreciation (LTD) network learning rules [102-107]. The intention of the performance leveling algorithm adjustment is to adjust the level of activity play to a comfortable level, thus allowing the user to progress through the activity successfully while at the same time focusing on developing and/or strengthening the performance integrity of the neural system being trained. The BCI interface informs the trainer, the user, and CRT activity in real time, current neural network performance integrity status based on the user's present nPIMs state. Incorporated within the device is an FDA registered EEG brain-computer interface (BCI) that integrates with a previously FDA registered neurometric database to identify and then enhance/strengthen/repair neuro-circuit performance needed to promote clear, resilient and stable cognitive function.

4.6 rCRT Example and Description: The Split-Attention application is an adaptive process-based, nonverbal training technique designed to aid in "resetting/enhancing" the attention (ANT), working memory (WM), frontal parietal network (FPN) and salience network (SN). Split-Attention uses a relaxation and restorative framework that allows the trained networks to regain or obtain natural homeostatic balance needed to maintain a desired level of performance. The application focuses on training the useful field of view (visual attention), working memory, cognitive speed, task switching, and multiple attention abilities all in one application.

The application has been used to promote a relaxed sustained attentional focus in professional athletes and clinically as a restorative cognitive enhancement tool in brain injured and learning-disabled populations clinically the last 10 years. The Split Attention exercises was built based on the neuroscience literature that satisfies The Institute of Medicine's Checklist criteria for brain training.

The application uses an adaptive training procedure to adjust difficulty level of the cognitive training exercises. As accuracy of performance is achieved at a specified level (e.g., of 75% for a combined neural network performance level – selected nPIMs, response successes, response times) the exercise difficulty is increased (or decreased) incrementally based on performance criteria. Increasing evidence demonstrates that adaptive training promotes neural network transfer between functional brain system, that are reflected in everyday function. The level of difficulty of the program adjusts based upon the current responses with the goal of proper ratio of neurocircuit engagement as opposed to level of correct responses.

# 5. Habitat and Clinical Results

#### 5.1. Preliminary Study Results

To date we have conducted three 14-day mission studies during Mission V, VI and VII (and currently are in the habitat for Mission VIII) within the Inflatable Lunar/Martian Analog Habitat located at the University of North Dakota. All experimental Mission occurrences offer a continued opportunity to determine the feasibility and quality of using a rapid-application wearable dry EEG sensor system and self-administered cognitive task battery by crewmembers to gain insights into NASA's Human Research Program (HRP) questions of whether functional changes in the brain can be effectively monitored and could be predictive of cognitive performance during a mission.

We analyzed data quality and temporal changes in sleep, and task-related EEG (ERP, ERSP, and brain connectivity) and behavioral measures from seven male and two female crew members, through the multiple missions. EEG, ECG, and EMG data were obtained from crewmembers during extravehicular activities in planetary spacesuits, while sleeping, and while performing a cognitive task battery. Significance tests or temporal changes in measures were computed using ANOVA.

Resting connectivity analysis and normative database comparisons were performed. A comprehensive analysis of data quality during cognitive tasks and sleep, as well as questionnaire data obtained from crewmembers, revealed suitable data quality, ease of use, and comfort of the EEG systems.

Figure 1 highlights changes in functional connectivity of the Supplementary Motor Area (SMA) with 88 regions of the brain throughout mission duration. Note, the reallocation of the neural network functional connectivity during the mission, indicating possible ICE mission effects that affect the SMA interactions the left and right hemispheres, including hypo and hyper connectivity reallocation of resources.

Supplementary Motor Area (BA6) resting state functional connectivity changes with respect to 88 Brain Areas using sLORETA and coherence analysis

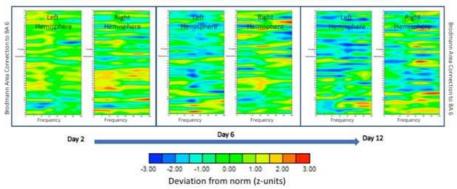


Figure 1. Resting state functional connectivity changes in crew member S3 during ILMAH Mission 5. Note resource reallocations between 88 brain regions and SMA (BA6) during mission phases. Z-scores obtained with respect to an age normed FDA registered database using BrainDx Light blue colors indicate an reduced connectivity requiring the brain to exert more effort in achieving a particular performance level on a behavioral task/activity. This same trend was observed on all subsequent missions.

Figure 2 shows significant reduction in sensory (auditory) evoked potential (AEP) amplitude in 2 of 3 crew members, throughout the mission in response to passive auditory stimuli.

Equally important, exploratory results shown in Figure 3, suggests the feasibility of possible predictive task performance results. Taken together, our preliminary results support the feasibility and practicability of crewadministered dry EEG data collection procedures within an ICE as proposed below. We are currently repeating the study during Mission VIII.

On Mission VII we included the NeuroCoach<sub>®</sub> Split

Attention training application module as a crew countermeasure, to determine both viability and impact on neural network measured changes. The *Split-Attention* application is an adaptive process-based, nonverbal training technique designed to aid in "resetting/enhancing" the attention (ANT), working memory (WM), frontal parietal network (FPN) and salience network (SN). The crew member assigned to that activity reported it was an easy task to perform. More importantly, we did not observe the changes in the working memory/attentional drifts that we observed in other crew members. Suggesting a potential positive effect.

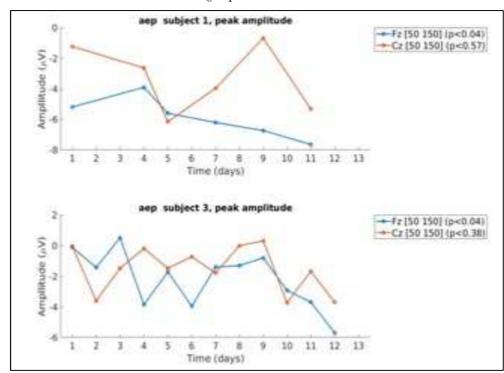


Figure 2. Significant reductions in sensory (auditory) evoked potential amplitude throughout mission.

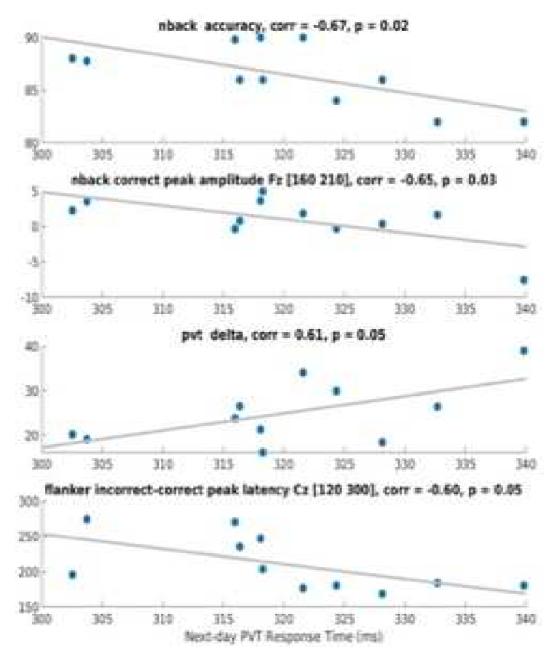


Figure 3. EEG metrics may predict task performance Significant correlation observed between neural metrics related to working memory, cognitive control, an vigilant attention system measured on a given day an psychomotor vigilance task (PVT) reaction time on the following day.

#### 5.2. Clinical Results Substance Abuse Augmented Treatment

A retrospective chart review was performed on 200 participants (100 males and 100 females) who completed a BCI/CRT augmented treatment program. Participant records were structured using a pre-test and post-test profile analysis quasi-experimental design to explore treatment effects over 48 training sessions. Participants' records were organized into treatment group (n=200) and non-treatment comparison group (n=120). The treatment group was composed of 200 participant records (n=100: 100 males and 100 females); the non-treatment comparison group included 121 records (n=121: 61 males and 60 females). The following exclusion

criteria were used for all groups: (1) <60 days of sobriety; (2) a history of severe traumatic brain injury with a loss of consciousness of >30 minutes; and (3) histories of schizophrenia, bipolar disorder, or obsessive-compulsive disorder. Each group received the same pretest and posttest. Experimental Pre- and Post-Test Measures: Table 1 depicts the ten dependent (i.e., treatment) measures chosen from the Woodcock Johnson Cognitive Abilities III Assessment Battery (WJIII) (64). The WJIII is a set of cognitive ability sub-tests based on the Cattell-Horn-Carroll (CHC) theory of cognitive abilities. The CHC theory provides a comprehensive framework for understanding the structure of cognitive information processing abilities.

The pre- and post-treatment results established a contributing inferential response towards treatment as

increasing cognitive control abilities. The 18-month follow-up assessment indicated over 80% of treated participants-maintained sobriety in contrast to 44% of non-treated. A profile analysis was conducted to investigate the effect that treatment status (No Treatment, Treatment) had on 10 subtests of the Woodcock Johnson Test of Cognitive Abilities III (WJIII). The grouping Group means were used for data screening. All participants had complete data sets (i.e. no missing data). No univariate or multivariate outliers were detected, with p =.001, assumptions regarding normality of sampling distributions, homogeneity of variance—covariance matrices, linearity, and multicollinearity were met.

#### 5.3. Effects on Cognitive Abilities

Table 1 displays mean scores, standard deviations and number of participants for each between subjects' group (Treatment, No Treatment) for all ten subtests of the WJIII. A significant multivariate effect was found after testing the difference for all variables across time between test groups. Results from the test revealed that the profiles of the two groups (Treatment, No Treatment) deviated significantly from parallelism and there was a significant multivariate affect for all variables (see Table 1). Thus, results imply that participant's measured cognitive abilities in the treatment group increased significantly more across tests administration compared to participants measured cognitive abilities in the no treatment group. In Table 1, the eta-squared coefficients are displayed revealing that between 22% to 53% of the reasons why the variables varied across time was due to treatment group status. Figure 1 displays the estimated marginal means scores for each group across test administration.

#### 5.4 Conclusion

Consistent with addiction neurobehavioral imbalance models, current results suggest traditional treatment programs augmented with BCI/CRT training focused on improving cognitive control abilities, may help strengthen self-control abilities, which may in turn improve sobriety rates.

Table 1. Cognitive results vs. no treatment.

	Wilk's Lambda			
Variable	(λ) (1,319)	F	p	$\eta^2$
GIA (Fluid Intelligence)	0.463	370.14	<.001	0.537
Thinking Efficiency	0.651	171.04	<.001	0.349
Concept Formation	0.774	93.03	<.001	0.226
Working Memory	0.689	144.13	<.001	0.311
Numbers Reversed	0.700	136.91	<.001	0.300
Visual Auditory Learning	0.688	144.66	<.001	0.312
Vis/Auditory Learning Delayed	0.677	152.51	<.001	0.323
Verbal Ability	0.726	120.59	<.001	0.274
Verbal Comprehension	0.752	105.23	<.001	0.248

# 6. Conclusion

Both experimental and clinical results have demonstrated

that the by using a rCRT program such as the NeuroCoach® program to increase and maintaining optimal cognitive and brain performance, both quantitatively (by the numbers) and qualitatively (social reintegration) can be achieved. We have found that by studying astronaut crew needs to remain at optimized performance during long duration space travel as well as our studies with various clinical populations with acquired brain dysfunctions presents us with a unique opportunity to compare and contrast both ends of the cognitive performance spectrum. These individuals represent opposite ends of the spectrum, both are instructive in what a damaged brain can potentially achieve vs what an optimized brain might suffer during deep space travel and needs to be guarded against. Equally important, exploring both ends of the cognitive performance spectrum allows us to observer how we might develop common solutions that might solve both problems.

# References

- [1] Vessel E., Russo S., (2015) Effects of Reduced Sensory Stimulation and Assessment of Countermeasures for Sensory Stimulation Augmentation A Report for NASA Behavioral Health and Performance Research: Sensory Stimulation Augmentation Tools for Long Duration Spaceflight.
- [2] Roberts, D. R., Albrecht, M. H., Collins, H. R., Asemani, D., Chatterjee, A. R., Spampinato, M. V.,... Antonucci, M. U. (2017). Effects of Spaceflight on Astronaut Brain Structure as Indicated on MRI. *New England Journal of Medicine*, 377 (18), 1746–1753. https://doi.org/10.1056/NEJMoa1705129.
- [3] Marušič, U., Meeusen, R., Pišot, R., & Kavcic, V. (2014). The brain in micro- and hypergravity: The effects of changing gravity on the brain electrocortical activity. *European Journal of Sport Science*, 14 (8), 813–822. https://doi.org/10.1080/17461391.2014.908959.
- [4] Koppelmans, V., Bloomberg, J. J., Mulavara, A. P., & Seidler, R. D. (2016). Brain structural plasticity with spaceflight. *Npj Microgravity*, 2 (1). https://doi.org/10.1038/s41526-016-0001-9.
- [5] Demertzi, A., Van Ombergen, A., Tomilovskaya, E., Jeurissen, B., Pechenkova, E., Di Perri, C.,... Wuyts, F. L. (2016). Cortical reorganization in an astronaut's brain after long-duration spaceflight. *Brain Structure and Function*.
- [6] Cassady, K., Koppelmans, V., Reuter-Lorenz, P., De Dios, Y., Gadd, N., Wood, S.,... Seidler, R. (2016). Effects of a spaceflight analog environment on brain connectivity and behavior. *NeuroImage*, 141, 18–30. https://doi.org/10.1016/j.neuroimage.2016.07.029.
- [7] Pyne, S. J. (2007). The extraterrestrial Earth: Antarctica as analogue for space exploration. *Space Policy*, 23 (3), 147–149. https://doi.org/10.1016/j.spacepol.2007.06.00.
- [8] Garrett-Bakelman, F. E. (2019). The NASA Twins Study: A multidimensional analysis of a year-long human spaceflight. HUMAN PHYSIOLOGY, 24.
- [9] J. R. Ball, Safe Passage: Astronaut Care for Exploration Missions, Institute of Medicine, National Academy of Sciences, Washington, DC, 2001.

- [10] N. Kanas, D. Manzey, Space Psychology and Psychiatry, second ed., Microcosm Press, El Segundo, CA, and Springer, Dordrecht, The Netherlands, 2008.
- [11] D. A. Shayler, Disasters and Accidents in Manned Spaceflight, Springer/Praxis, Chichester, UK, 2000.
- [12] P. Suedfeld, Canadian space psychology: the future may be almost here, Canadian Psychology 44 (2) (2003) 85–92.
- [13] P. Suedfeld, Invulnerability, coping, salutogenesis, integration: four phases of space psychology, Aviation, Space and Environmental Medicine 76 (2005) B61–B66.
- [14] Sweet, T, Panda, N., Hein, A, Das, S, Hurley, S, Olschowka, J., Williams, J., & O'Banion, (2014) M, Central Nervous System Effects of Whole-Body Proton Irradiation, Radiation Research 182, 18–34.
- [15] Denisova, N., Shukitt-Hale, Rabin & Joseph (2002) Brain Signaling and Behavioral Responses Induced by Exposure to Fe-Particle Radiation Radiation Research 158 725-734.
- [16] Heuer, H.; Manzey, D.; Lorenz, B.; Sangals, J. Impairments of manual tracking performance during spaceflight are associated with specific effects of microgravity on visuomotor transformations. Ergonomics 2003, 46, 920–934.
- [17] Johannes, B.; Salnitski, V. P.; Polyakov, V. V.; Kirsch, K. A. Changes in the autonomic reactivity pattern to psychological load under long-term microgravity—twelve men during 6month spaceflights. Aviakosmicheskaia i Ekologicheskaia Meditsina 2003, 37, 6–16.
- [18] Manzey, D.; Lorenz, B. Poljakov, V. Mental performance in extreme environments: Results from a performance monitoring study during a 438-day spaceflight. Ergonomics 1998, 41, 537–559.
- [19] Manzey, D.; Lorenz, B.; Heuers, H.; Sangals, J. Impairments of manual tracking performance during spaceflight: More converging evidence from a 20-day space mission. Ergonomics 2000, 43, 589–609.
- [20] Whitmore, M.; McQuilkin, M. L.; Woolford, B. J. Habitability and performance issues for long duration space flights. Hum. Perferm. Extrem. Environ. 1998, 3, 64–74.
- [21] Sha, Z., Wager, T. D., Mechelli, A., & He, Y. (2019). Common Dysfunction of Large-Scale Neurocognitive Networks Across Psychiatric Disorders. *Biological Psychiatry*, 85 (5), 379–388. https://doi.org/10.1016/j.biopsych.2018.11.011
- [22] Redish, A. D., & Gordon, J. A. (Eds.). (2016). Computational psychiatry: new perspectives on mental illness. Cambridge, Massachusetts: The MIT Press.
- [23] da Silva, A. G., Malloy-Diniz, L. F., Garcia, M. S., Figueiredo, C. G. S., Figueiredo, R. N., Diaz, A. P., & Palha, A. P. (2018). Cognition As a Therapeutic Target in the Suicidal Patient Approach. Frontiers in Psychiatry, 9. https://doi.org/10.3389/fpsyt.2018.00031
- [24] Kesler, S., Hadi Hosseini, S. M., Heckler, C., Janelsins, M., Palesh, O., Mustian, K., & Morrow, G. (2013). Cognitive Training for Improving Executive Function in Chemotherapy-Treated Breast Cancer Survivors. *Clinical Breast Cancer*, 13 (4), 299–306. https://doi.org/10.1016/j.clbc.2013.02.004
- [25] Copersino, M. L. (2017). Cognitive mechanisms and

- therapeutic targets of addiction. *Current Opinion in Behavioral Sciences*, 13, 91–98. https://doi.org/10.1016/j.cobeha.2016.11.005.
- [26] Vinogradov, S., Fisher, M., & de Villers-Sidani, E. (2012). Cognitive Training for Impaired Neural Systems in Neuropsychiatric Illness. *Neuropsychopharmacology*, 37 (1), 43–76. https://doi.org/10.1038/npp.2011.251.
- [27] Motter, J. N., Pimontel, M. A., Rindskopf, D., Devanand, D. P., Doraiswamy, P. M., & Sneed, J. R. (2016). Computerized cognitive training and functional recovery in major depressive disorder: A meta-analysis. *Journal of Affective Disorders*, 189, 184–191. https://doi.org/10.1016/j.jad.2015.09.022.
- [28] Santarnecchi, E., Bossini, L., Vatti, G., Fagiolini, A., La Porta, P., Di Lorenzo, G.,... Rossi, A. (2019). Psychological and Brain Connectivity Changes Following Trauma-Focused CBT and EMDR Treatment in Single-Episode PTSD Patients. Frontiers in Psychology, 10. https://doi.org/10.3389/fpsyg.2019.00129.
- [29] Santarnecchi, E., Brem, A.-K., Levenbaum, E., Thompson, T., Kadosh, R. C., & Pascual-Leone, A. (2015). Enhancing cognition using transcranial electrical stimulation. *Current Opinion in Behavioral Sciences*, 4, 171–178. https://doi.org/10.1016/j.cobeha.2015.06.003.
- [30] Brem, A.-K., Almquist, J. N.-F., Mansfield, K., Plessow, F., Sella, F., Santarnecchi, E.,... Myers, E. (2018). Modulating fluid intelligence performance through combined cognitive training and brain stimulation. *Neuropsychologia*, 118, 107– 114. https://doi.org/10.1016/j.neuropsychologia.2018.04.008.
- [31] Novakovic-Agopian, T., Chen, A. J.-W., Rome, S., Abrams, G., Castelli, H., Rossi, A.,... D'Esposito, M. (2011). Rehabilitation of Executive Functioning With Training in Attention Regulation Applied to Individually Defined Goals: A Pilot Study Bridging Theory, Assessment, and Treatment. *Journal of Head Trauma Rehabilitation*, 26 (5), 325–338. https://doi.org/10.1097/HTR.0b013e3181f1ead2.
- [32] Kong, F., Ma, X., You, X., & Xiang, Y. (2018). The resilient brain: psychological resilience mediates the effect of amplitude of low-frequency fluctuations in orbitofrontal cortex on subjective well-being in young healthy adults. *Social Cognitive and Affective Neuroscience*, 13 (7), 755–763. https://doi.org/10.1093/scan/nsy045.
- [33] Kong, F., Wang, X., Hu, S., & Liu, J. (2015). Neural correlates of psychological resilience and their relation to life satisfaction in a sample of healthy young adults. *NeuroImage*, 123, 165–172. https://doi.org/10.1016/j.neuroimage.2015.08.020.
- [34] Paban, V., Modolo, J., Mheich, A., & Hassan, M. (2018). Psychological resilience correlates with EEG source-space brain network flexibility. *Network Neuroscience*, (Just Accepted), 1–25.
- [35] Van der Werff, S. J., van den Berg, S. M., Pannekoek, J. N., Elzinga, B. M., and Van Der Wee, N. J. (2013). Neuroimaging resilience to stress: a review. Frontiers in behavioral neuroscience 7, 39.
- [36] Vidaurre, D., Hunt, L. T., Quinn, A. J., Hunt, B. A., Brookes, M. J., Nobre, A. C., and Woolrich, M. W. (2018). Spontaneous cortical activity transiently organizes into frequency specific phase-coupling networks. Nature communications 9, 2987.

- [37] Waugh, C. E., and Koster, E. H. (2015). A resilience framework for promoting stable remission from depression. Clinical Psychology Review 41, 49-60.
- [38] Kalisch, R, Muller, M., & Tuscher, O. (2015). A conceptual framework for neurobiological study of resilience. *Behavioral* and *Brain Sciences*, 38, E92. Doi: 10.1017/S0140525X1400082X.
- [39] Sari, Berna A., Koster, Ernst H. W., Pourtois, Gilles, Derakshan, Nazanin, Training working memory to improve attentional control in anxiety: A proof-of-principle study using behavioral and electrophysiological measures. Biological Psychology http://dx.doi.org/10.1016/j.biopsycho.2015.09.008.
- [40] Posner, M. I., Rothbart, M. K., & Tang, Y.-Y. (2015). Enhancing attention through training. *Current Opinion in Behavioral Sciences*, 4, 1–5. https://doi.org/10.1016/j.cobeha.2014.12.008.
- [41] Wang, H., Hua, C., Wang, Q., Fu, Q., & Fetlework, T. (2019). Training state and performance evaluation of working memory based on task-related EEG. *Biomedical Signal Processing and Control*, 51, 296–308. https://doi.org/10.1016/j.bspc.2019.03.002.
- [42] Larsen, S. E., Lotfi, S., Bennett, K. P., Larson, C. L., Dean-Bernhoft, C., & Lee, H.-J. (2019). A pilot randomized trial of a dual n-back emotional working memory training program for veterans with elevated PTSD symptoms. *Psychiatry Research*, 275, 261–268. https://doi.org/10.1016/j.psychres.2019.02.015.
- [43] Leszkowicz, E. (n. d.). Effects of cognitive training in aging in MRI/fMRI studies. 11.
- [44] Han, K., Chapman, S. B., & Krawczyk, D. C. (2018). Neuroplasticity of cognitive control networks following cognitive training for chronic traumatic brain injury. *NeuroImage: Clinical*, 18, 262–278. https://doi.org/10.1016/j.nicl.2018.01.030.
- [45] Zatorre, R. J., Fields, R. D., & Johansen-Berg, H. (2012). Plasticity in gray and white: neuroimaging changes in brain structure during learning. *Nature Neuroscience*, *15* (4), 528–536. https://doi.org/10.1038/nn.3045.
- [46] Hosseini, S. M. H., Pritchard-Berman, M., Sosa, N., Ceja, A., & Kesler, S. R. (2016). Task-based neurofeedback training: A novel approach toward training executive functions. NeuroImage, 134, 153–159. https://doi.org/10.1016/j.neuroimage.2016.03.035.
- [47] Belleville, S., Clement, F., Mellah, S., Gilbert, B., Fontaine, F., & Gauthier, S. (2011). Training-related brain plasticity in subjects at risk of developing Alzheimer's disease. *Brain*, 134 (6), 1623–1634. https://doi.org/10.1093/brain/awr037.
- [48] Karbach, J., & Schubert, T. (2013). Training-induced cognitive and neural plasticity. *Frontiers in Human Neuroscience*, 7. https://doi.org/10.3389/fnhum.2013.00048.
- [49] Gonzalez-Escamilla, G., Muthuraman, M., Chirumamilla, V. C., Vogt, J., & Groppa, S. (2018). Brain Networks Reorganization During Maturation and Healthy Aging-Emphases for Resilience. Frontiers in Psychiatry, 9. https://doi.org/10.3389/fpsyt.2018.00601.
- [50] Iadipaolo, A. S., Marusak, H. A., Paulisin, S. M., Sala-Hamrick, K., Crespo, L. M., Elrahal, F.,... Rabinak, C. A. (2018). Distinct neural correlates of trait resilience within core

- neurocognitive networks in at-risk children and adolescents. *NeuroImage: Clinical*, 20, 24–34. https://doi.org/10.1016/j.nicl.2018.06.026.
- [51] Kong, Feng, Xiaosi Ma, Xuqun You, and Yanhui Xiang. "The Resilient Brain: Psychological Resilience Mediates the Effect of Amplitude of Low-Frequency Fluctuations in Orbitofrontal Cortex on Subjective Well-Being in Young Healthy Adults." Social Cognitive and Affective Neuroscience 13, no. 7 (September 4, 2018): 755–63.
- [52] Ibrahim, G. M., Cassel, D., Morgan, B. R., Smith, M. L., Otsubo, H., Ochi, A.,... Doesburg, S. (2014). Resilience of developing brain networks to interictal epileptiform discharges is associated with cognitive outcome. *Brain*, 137 (10), 2690–2702. https://doi.org/10.1093/brain/awu214.
- [53] Joyce, K. E., Hayasaka, S., & Laurienti, P. J. (2013). The Human Functional Brain Network Demonstrates Structural and Dynamical Resilience to Targeted Attack. *PLoS Computational Biology*, 9 (1), e1002885. https://doi.org/10.1371/journal.pcbi.1002885.
- [54] De León, P., Harris, G. L., & Wargetz, A. M. (2013, July). Design construction and implementation of an inflatable lunar habitat base with pressurized rover and suit ports. In 43rd International Conference on Environmental Systems (pp. 14-18).
- [55] Mayer, T., Blachowicz, A., Probst, A. J., Vaishampayan, P., Checinska, A., Swarmer, T.,... & Venkateswaran, K. (2016). Microbial succession in an inflated lunar/Mars analog habitat during a 30-day human occupation. Microbiome, 4 (1), 22.
- [56] Sheffield, J. M., Kandala, S., Tamminga, C. A., Pearlson, G. D., Keshavan, M. S., Sweeney, J. A.,... Barch, D. M. (2017). Transdiagnostic Associations Between Functional Brain Network Integrity and Cognition. *JAMA Psychiatry*, 74 (6), 605. https://doi.org/10.1001/jamapsychiatry.2017.0669.
- [57] Donar, J., Blumberger, D. M., & Daskalakis, Z. J. (2016). The Neural Crossroads of Psychiatric Illness: An Emerging Target for Brain Stimulation. *Trends in Cognitive Sc* Prichep, L. S., & John, E. R. (1992). QEEG profiles of psychiatric disorders. *Brain Topography*, 4 (4), 249–257. Siences, 20 (2), 107–120. https://doi.org/10.1016/j.tics.2015.10.007.
- [58] Prichep, L. S., & John, E. R. (1992). QEEG profiles of psychiatric disorders. *Brain Topography*, 4 (4), 249–257.
- [59] Cole, M., Repovs, G., & Anticevic, A. (2014). The frontoparietal control system: A central role in mental health. *The Neuroscientist*, 1–13.
- [60] Gratton, G. (2018). Brain reflections: A circuit-based framework for understanding information processing and cognitive control. Psychophysiology, 55 (3), e13038. https://doi.org/10.1111/psyp.13038.
- [61] Cai, W., Chen, T., Ryali, S., Kochalka, J., Li, C.-S. R., & Menon, V. (2016). Causal Interactions Within a Frontal-Cingulate-Parietal Network During Cognitive Control: Convergent Evidence from a Multisite–Multitask Investigation. *Cerebral Cortex*, 26 (5), 2140–2153. https://doi.org/10.1093/cercor/bhv046.
- [62] Sternberg, S. (1965). High Speed Scanning in Human Memory. J. Comp. Physiol. Psychol, 59, 439.
- [63] Siemann, J., Herrmann, M., & Galashan, D. (2018). The effect of feature-based attention on flanker interference processing: An fMRI-constrained source analysis. *Scientific Reports*, 8 (1). https://doi.org/10.1038/s41598-018-20049-1.

- [64] Braboszcz, C., & Delorme, A. (2011). Lost in thoughts: Neural markers of low alertness during mind wandering. *NeuroImage*, 54 (4), 3040–3047. https://doi.org/10.1016/j.neuroimage.2010.10.008.
- [65] WJII referencevan der Werff, S. J., van den Berg, S. M., Pannekoek, J. N., Elzinga, B. M., and Van Der Wee, N.J. (2013). Neuroimaging resilience to stress: a review. Frontiers in behavioral neuroscience 7, 39.
- [66] Southwick, S. M., & Charney, D. S. (2012). The science of resilience: Implications for the prevention and treatment of depression. Science, 338, 79–82.
- [67] Burns, R. A., Anstey, K. J., & Windsor, T. D. (2011). Subjective Well-Being Mediates the Effects of Resilience and Mastery on Depression and Anxiety in a Large Community Sample of Young and Middle-Aged Adults. *Australian & New Zealand Journal of Psychiatry*, 45 (3), 240–248. https://doi.org/10.3109/00048674.2010.529604.
- [68] Curtis, W. J., & Cicchetti, D. (2007). Emotion and resilience: A multilevel investigation of hemispheric electroencephalogram asymmetry and emotion regulation in maltreated and nonmaltreated children. *Development and Psychopathology*, 19 (03), 811. https://doi.org/10.1017/S0954579407000405.
- [69] Zhang, Y., Xie, B., Chen, H., Li, M., Guo, X., & Chen, H. (2016). Disrupted resting-state insular subregions functional connectivity in post-traumatic stress disorder: *Medicine*, 95 (27), e4083. https://doi.org/10.1097/MD.00000000000004083.
- [70] Thompson, R. W., Arnkoff, D. B., & Glass, C. R. (2011). Conceptualizing Mindfulness and Acceptance as Components of Psychological Resilience to Trauma. *Trauma, Violence, & Abuse*, 12 (4), 220–235. https://doi.org/10.1177/1524838011416375.
- [71] Craske, M. G., Kircanski, K., Zelikowsky, M., Mystkowski, J., Chowdhury, N., & Baker, A. (2008). Optimizing inhibitory learning during exposure therapy. *Behaviour Research and Therapy*, 46 (1), 5–27. https://doi.org/10.1016/j.brat.2007.10.003.
- [72] Karatsoreos, I. N., & McEwen, B. S. (2011). Psychobiological allostasis: resistance, resilience and vulnerability. *Trends in Cognitive Sciences*, 15 (12), 576–584. https://doi.org/10.1016/j.tics.2011.10.005.
- [73] Chiong, W., Wilson, S. M., D'Esposito, M., Kayser, A. S., Grossman, S. N., Poorzand, P.,... Rankin, K. P. (2013). The salience network causally influences default mode network activity during moral reasoning. *Brain*, 136 (6), 1929–1941. https://doi.org/10.1093/brain/awt066.
- [74] Raichle, M. E. (2015). The Brain's Default Mode Network. Annual Review of Neuroscience, 38 (1), 433–447. https://doi.org/10.1146/annurev-neuro-071013-014030.
- [75] Cattell, R. B., & Cattell, R. B. (1987). *Intelligence: its structure, growth, and action*. Amsterdam; New York: New York: North-Holland; Sole distributors for the U.S.A. and Canada, Elsevier Science Pub. Co.
- [76] Deary, I. (2008). Why do intelligent people live longer? Nature, 456 (7219), 175–176. doi: 10.1038/456175a.
- [77] Li, Yonghui, Yong Liu, Jun Li, Wen Qin, Kuncheng Li, Chunshui Yu, and Tianzi Jiang. "Brain Anatomical Network and Intelligence." Edited by Olaf Sporns. PLoS

- Computational Biology 5, no. 5 (May 29, 2009): e1000395. https://doi.org/10.1371/journal.pcbi.1000395.
- [78] Santarnecchi, Emiliano, Alexandra Emmendorfer, and Alvaro Pascual-Leone. "Dissecting the Parieto-Frontal Correlates of Fluid Intelligence: A Comprehensive ALE Meta-Analysis Study." *Intelligence* 63 (July 2017): 9–28. https://doi.org/10.1016/j.intell.2017.04.008.
- [79] Marsman, Anouk, René C. W. Mandl, Dennis W. J. Klomp, Wiepke Cahn, René S. Kahn, Peter R. Luijten, and Hilleke E. Hulshoff Pol. "Intelligence and Brain Efficiency: Investigating the Association between Working Memory Performance, Glutamate, and GABA." Frontiers in Psychiatry 8 (September 15, 2017). https://doi.org/10.3389/fpsyt.2017.00154.
- [80] Bathelt, J., G. Scerif, A. C. Nobre, and D. E. Astle. "Whole-Brain White Matter Organization, Intelligence, and Educational Attainment." *Trends in Neuroscience and Education* 15 (June 2019): 38–47. https://doi.org/10.1016/j.tine.2019.02.004.
- [81] Santarnecchi, Emiliano, Alexandra Emmendorfer, Sayedhedayatollah Tadayon, Simone Rossi, Alessandro Rossi, and Alvaro Pascual-Leone. "Network Connectivity Correlates of Variability in Fluid Intelligence Performance." *Intelligence* 65 (November 2017): 35–47. https://doi.org/10.1016/j.intell.2017.10.002.
- [82] Cattell, Raymond B., and Raymond B. Cattell. *Intelligence: Its Structure, Growth, and Action*. Advances in Psychology 35. Amsterdam; New York: New York: North-Holland; Sole distributors for the U.S.A. and Canada, Elsevier Science Pub. Co, 1987.
- [83] Hilger, Kirsten, Matthias Ekman, Christian J. Fiebach, and Ulrike Basten. "Efficient Hubs in the Intelligent Brain: Nodal Efficiency of Hub Regions in the Salience Network Is Associated with General Intelligence." *Intelligence* 60 (January 2017): 10–25. https://doi.org/10.1016/j.intell.2016.11.001.
- [84] Jung, Rex E., and Richard J. Haier. "The Parieto-Frontal Integration Theory (P-FIT) of Intelligence: Converging Neuroimaging Evidence." *Behavioral and Brain Sciences* 30, no. 2 (April 2007): 135–54. https://doi.org/10.1017/S0140525X07001185.
- [85] Barbey, A. K., R. Colom, J. Solomon, F. Krueger, C. Forbes, and J. Grafman. "An Integrative Architecture for General Intelligence and Executive Function Revealed by Lesion Mapping." *Brain* 135, no. 4 (April 1, 2012): 1154–64. https://doi.org/10.1093/brain/aws021.
- [86] Glascher, J., D. Rudrauf, R. Colom, L. K. Paul, D. Tranel, H. Damasio, and R. Adolphs. "Distributed Neural System for General Intelligence Revealed by Lesion Mapping." Proceedings of the National Academy of Sciences 107, no. 10 (March 9, 2010): 4705–9. https://doi.org/10.1073/pnas.0910397107.
- [87] Dehaene, Stanislas, Jean-Pierre Changeux, and Lionel Naccache. "The Global Neuronal Workspace Model of Conscious Access: From Neuronal Architectures to Clinical Applications." In *Characterizing Consciousness: From Cognition to the Clinic?*, edited by Stanislas Dehaene and Yves Christen, 55–84. Berlin, Heidelberg: Springer Berlin Heidelberg, 2011. https://doi.org/10.1007/978-3-642-18015-6\_4.

- [88] Baars, Bernard J., Stan Franklin, and Thomas Zoega Ramsoy. "Global Workspace Dynamics: Cortical 'Binding and Propagation' Enables Conscious Contents." *Frontiers in Psychology* 4 (2013). https://doi.org/10.3389/fpsyg.2013.00200.
- [89] Burns, Richard A., Kaarin J. Anstey, and Timothy D. Windsor. "Subjective Well-Being Mediates the Effects of Resilience and Mastery on Depression and Anxiety in a Large Community Sample of Young and Middle-Aged Adults." *Australian & New Zealand Journal of Psychiatry* 45, no. 3 (March 2011): 240–48. https://doi.org/10.3109/00048674.2010.529604.
- [90] Ren, Ping, Benjamin Chapman, Zhengwu Zhang, Giovanni Schifitto, and Feng Lin. "Functional and Structural Connectivity of the Amygdala Underpins Locus of Control in Mild Cognitive Impairment." NeuroImage: Clinical 20 (2018): 297–304. https://doi.org/10.1016/j.nicl.2018.07.021.
- [91] Wang, Shui-Hua, Khan Muhammad, Yiding Lv, Yuxiu Sui, Liangxiu Han, and Yu-Dong Zhang. "Identification of Alcoholism Based on Wavelet Renyi Entropy and Three-Segment Encoded Jaya Algorithm." *Complexity* 2018 (2018): 1–13. https://doi.org/10.1155/2018/3198184.
- [92] Luo, Lizhu, Kunhua Wu, Yi Lu, Shan Gao, Xiangchao Kong, Fengmei Lu, Fengchun Wu, Huawang Wu, and Jiaojian Wang. "Increased Functional Connectivity Between Medulla and Inferior Parietal Cortex in Medication-Free Major Depressive Disorder." Frontiers in Neuroscience 12 (December 10, 2018). https://doi.org/10.3389/fnins.2018.00926.
- [93] Spray, Amy, Anton L. Beer, Richard P. Bentall, Vanessa Sluming, and Georg Meyer. "Microstructure of the Superior Temporal Gyrus and Hallucination Proneness a Multi-Compartment Diffusion Imaging Study." NeuroImage: Clinical 20 (2018): 1–6. https://doi.org/10.1016/j.nicl.2018.06.027.
- [94] Troche, Stefan J., Felicitas L. Wagner, Annik E. Voelke, Claudia M. Roebers, and Thomas H. Rammsayer. "Individual Differences in Working Memory Capacity Explain the Relationship between General Discrimination Ability and Psychometric Intelligence." *Intelligence* 44 (May 2014): 40–50. https://doi.org/10.1016/j.intell.2014.02.009.
- [95] Buzzell, George A., John E. Richards, Lauren K. White, Tyson V. Barker, Daniel S. Pine, and Nathan A. Fox. "Development of the Error-Monitoring System from Ages 9– 35: Unique Insight Provided by MRI-Constrained Source Localization of EEG." *NeuroImage* 157 (August 2017): 13–26. https://doi.org/10.1016/j.neuroimage.2017.05.045.
- [96] Badre, David, and Derek Evan Nee. "Frontal Cortex and the Hierarchical Control of Behavior." *Trends in Cognitive Sciences* 22, no. 2 (February 2018): 170–88. https://doi.org/10.1016/j.tics.2017.11.005.

- [97] Jiang, Jiefeng, Jeffrey Beck, Katherine Heller, and Tobias Egner. "An Insula-Frontostriatal Network Mediates Flexible Cognitive Control by Adaptively Predicting Changing Control Demands." *Nature Communications* 6, no. 1 (December 2015). https://doi.org/10.1038/ncomms9165.
- [98] Tops, Mattie, and Maarten A. S. Boksem. "A Potential Role of the Inferior Frontal Gyrus and Anterior Insula in Cognitive Control, Brain Rhythms, and Event-Related Potentials." Frontiers in Psychology 2 (2011). https://doi.org/10.3389/fpsyg.2011.00330.
- [99] Pourtois, Gilles, and Wim Ntebaert Wim Notebaert, eds. Cognitive and Affective Control. Frontiers Research Topics. Frontiers Media SA, 2013. https://doi.org/10.3389/978-2-88919-092-8.
- [100] Cole, Michael W., and Walter Schneider. "The Cognitive Control Network: Integrated Cortical Regions with Dissociable Functions." *NeuroImage* 37, no. 1 (August 2007): 343–60. https://doi.org/10.1016/j.neuroimage.2007.03.071.
- [101] McTeague, Lisa M., Madeleine S. Goodkind, and Amit Etkin. "Transdiagnostic Impairment of Cognitive Control in Mental Illness." *Journal of Psychiatric Research* 83 (December 2016): 37–46. https://doi.org/10.1016/j.jpsychires.2016.08.001.
- [102] He, Kaiwen, Marco Huertas, Su Z. Hong, XiaoXiu Tie, Johannes W. Hell, Harel Shouval, and Alfredo Kirkwood. "Distinct Eligibility Traces for LTP and LTD in Cortical Synapses." *Neuron* 88, no. 3 (November 2015): 528–38. https://doi.org/10.1016/j.neuron.2015.09.037.
- [103] Sha, Zhiqiang, Tor D. Wager, Andrea Mechelli, and Yong He. "Common Dysfunction of Large-Scale Neurocognitive Networks Across Psychiatric Disorders." *Biological Psychiatry* 85, no. 5 (March 2019): 379–88. https://doi.org/10.1016/j.biopsych.2018.11.011.
- [104] Gerstner, Wulfram, Marco Lehmann, Vasiliki Liakoni, Dane Corneil, and Johanni Brea. "Eligibility Traces and Plasticity on Behavioral Time Scales: Experimental Support of NeoHebbian Three-Factor Learning Rules." Frontiers in Neural Circuits 12 (July 31, 2018).
- [105] Suvrathan, Aparna. "Beyond STDP towards Diverse and Functionally Relevant Plasticity Rules." *Current Opinion in Neurobiology* 54 (February 2019): 12–19. https://doi.org/10.1016/j.conb.2018.06.011.
- [106] Lisman, John, and Nelson Spruston. "Postsynaptic Depolarization Requirements for LTP and LTD: A Critique of Spike Timing-Dependent Plasticity." *Nature Neuroscience* 8, no. 7 (2005): 839.
- [107] Suvrathan, Aparna, Hannah L. Payne, and Jennifer L. Raymond. "Timing Rules for Synaptic Plasticity Matched to Behavioral Function." *Neuron* 92, no. 5 (December 2016): 959–67. https://doi.org/10.1016/j.neuron.2016.10.022.