Volume 411, April, 15, 2022

CASN NeuroNotes[®] ISSN 2758-1772

The Journal of the Center for Applied Social Neuroscience (CASN)

Focusing on cognitive development and rehabilitation and the promotion and maintenance of personal well-being through the principles of <u>Applied Social Neuroscience (ASN)</u>



Proposal for Pilot Community Well-Being Center with Embedded e-AHA System for Comprehensive, Highly Integrated Elder Well-Being and Dementia Management: Final Draft

(8) 2018 by the Center for Applied Social Neuroscience (CASN), 638-2 Keyakidai, Eiheiji-cho, Yoshida-gun, Fukui 910-1223 Japan

<u>CASN NeuroNotes</u> (ISSN 2758-1772) Volume 411 April 15, 2022

Proposal for Pilot Community Well-Being Center with Embedded e-AHA System for Comprehensive, Highly Integrated Elder Well-Being and Dementia Management: Final Draft

Spencer M. Robinson, PhD Executive Director and Chief of Research and Development Center for Applied Social Neuroscience (*CASN*)

INTRODUCTION: THE PROBLEM

Background

This proposal addresses the most critical problems of the rapidly aging global society, and, as the country with the highest percentage of elders aged 65 years and older in the world, are of particular concern for Japan [see the nation-by-nation ranking of the percentage of population aged 65 years and older by the Population Reference Bureau (PRB), https://www.prb.org/countries-with-the-oldest-populations/ – the PRB statistics for Japan are based on a rounded total population of 126,180,000, as reported in *The World Population Prospects 2019* (United Nations Population Division, 2019) and in the *2019 World Population Data Sheet* (Kaneda, Greenbaum, & Patierno, 2019) – more current statistics compiled by Worldometer report the total population of Japan at 126,566,456 as of 5 April 2020 (https://www.worldometers.info/world-population/japan-population/)].

In their World Population Ageing 2013 report, the United Nations (UN) recorded an increase in the overall global population aged 60 years and older from 9.2% of the total global population in 1990 to 11.7% in 2013, and, at that escalating rate of growth, the percentage of the overall global population aged 60 years and older is expected to nearly double, reaching 21.1% of the total global population by the year 2050 (UN, 2013) – a percentage of the total population already exceeded in 2019 by Japan, with its population of people aged 65 years and older reported by PRB at 28.2% of its total population. These figures translate into a massive impact on society with a global population aged 60 years and older more than doubling from 841 million people in 2013 to over 2 billion in 2050 (UN, 2013). The UN 2013 report also projected a continual increase of the eldest of the elders (those aged 80 years and older) from 14% of those aged 65 years and older in 2013 to 19% in 2050, which would result in a global population of 392 million people aged 80 years and older – with Japan alone in 2019 already totaling a population of approximately 12,098,138 between 75 to 84 years of age and approximately 5,693,241 aged 85 years and older as reported by the PRB, for a total population of approximately 17,791,379 seventy-five years of age and older. In their 2017 follow-up report (UN, 2017), the UN reveals that the global population of those 60 years of age and older had reached 962 million in 2017, more than twice the figure of 382 million recorded in 1980, with Japan leading the world at 33% of its total population aged 60 years and older in 2017. By 2050, the global population of those aged 60 years and older is projected to more than double again, reaching nearly 2.1 billion. More concerning is the even faster rise of the population aged 80 years and older, with the UN 2017 report projecting a more than threefold increase in this population, from 137 million in 2017 to 425 million in 2050.

The massive impact of our rapidly aging society, with the disproportionate health needs and daily support requirements for basic living unique to the elder population, compounded here in Japan by a low national birth rate and an ever-shrinking percentage of able-bodied workers and tax-paying wage earners, is manifested in the extreme pressure on national and community social and economic resources and the societal infrastructure to care for and support the burgeoning elder population and to maintain both a healthy GNI/GDP (Gross National Income/Gross Domestic Product) and a viable society (see Japan Data, 2018 and 2019; Walia, 2019; The Japan Times, 2018; Bain, 2019; Tsuya, n.d.; Sobel, 2017).

The International Monetary Fund (IMF) forecasts that by 2025 Japan's dependency ratio (defined as the number of aged dependents per worker) will be the highest in the world at approximately 75%, with consequent labor shortages and a shrinking annual GDP (Bain, 2019). "Aggravating the growing labor force shortage are the rising expenses associated with aging, like caregiving needs for the ill and the fact that older people will require extra medication and hospitalization" (Walia, 2019), whereby there is an urgent need for innovative health and well-being programs "that will aim at increasing the nation's productivity" (Walia, 2019), contributing to the labor force supply by enabling more elderly people to become capable of and encouraged to play active roles in the labor force. "Healthier individuals are better able to work longer and with more energy, which suggests that protecting older individuals' health will intensify their productivity and labor force participation. In addition to savings in healthcare costs, effective health promotion programs will therefore lead to gains in productive labor hours and output. A healthy population will also lead to higher savings rates, lower medical expenses, and increased foreign direct investment" (Walia, 2019).

Cognitive decline and dementia: A major cause of elder disability

One of the single largest contributors to impaired health and disability among elders is dementia and other aging-related cognitive decline, Japan having the highest dementia prevalence amongst the OECD (Organisation for Economic Co-operation and Development) countries at 2.3% of the population in 2017, projected to reach 3.8% by 2037 (Fukawa, 2018). The Alzheimer's Association (n.d.) reports 4.6 million people living with dementia in Japan, consistent with the estimate of 4.7 million by Nakabe, Sasaki, Uematsu, Kunisawa et al. (2019), the latter projecting the number of people living with dementia in Japan to reach 7 million by the year 2025. Dementia accounts for a large proportion of Japan's elder healthcare cost, the costs related to dementia alone reaching ¥14.5 trillion for the year 2014 (The Japan Times, 2015; Sado, Ninomiya, Shikimoto, Ikeda, et al., 2018).

Dementia as well as other cognitive impairment and other mental disorders have a high incidence of comorbidity (that is, other medical conditions and physical impairment often accompany mental disorder, especially dementia and the onset of cognitive decline in elders – see Kazawa & Iwamoto et al., 2017; Nelis et al., 2019; Formiga et al., 2007; Poblador-Plou et al., 2014; Bunn et al., 2014; Callahan & Schubert, 2014; Magaki et al., 2014; Shimada, Makizako, Doi, Tsutsumimoto, et al., 2016). "The complexity of comorbidities [in dementia] calls for a patient-centered approach for care" (Callahan & Schubert, 2014 – insertion in brackets added). "Dementia is characterized by the impairment of memory and learning and at least one other cognitive domain . . . representing a highly severe functional deterioration that *interferes with the patient's daily functional abilities and independence*. Dementia is not simply a disease; it is a syndrome caused by different etiologies and it has a substantial

medical and social impact. . . individuals afflicted with dementia show a high utilization of health services and represent a significant fraction of the healthcare costs attributed to the elderly population . . . dementia currently constitutes the main cause of dependence in the elderly population . . . (Poblador-Plou et al., 2014, p. 1 – emphases added). "Approximately 15% of the world's population is estimated to have some form of disability. This rate is increasing due to an expanding aging population and increases in the prevalence of chronic health conditions such as dementia. Cognitive impairment is one factor that can be associated with disability in older adults" (Shimada, Makizako, Doi, Tsutsumimoto, et al., 2016, p. 1). "In summary, the results of this prospective cohort study indicate that cognitive impairment has a strong impact on the risk of developing disability. In particular, community-dwelling older adults with combined MCI [mild cognitive impairment] and GCI [general cognitive impairment] have an increased risk of disability incidence" (Shimada, Makizako, Doi, Tsutsumimoto, et al., 2016, p. 9 - insertions in brackets added). "The societal costs of dementia in Japan in 2014 were estimated at JPY 14.5 trillion . . . Of these, the costs for healthcare, long-term care, and informal care are JPY 1.91 trillion, JPY 6.44 trillion, and JPY 6.16 trillion, respectively. . . The total costs would reach JPY 24.3 trillion by 2060, which is 1.6 times higher than in 2014" (Sado, Ninomiya, Shikimoto, Ikeda, et al., 2018).

THE SOLUTION: COMMUNITY WELL-BEING CENTERS

Background

A meta-analysis of research results has determined that cognitive training and mental stimulation yields the following benefits for healthy older adults: 1) improvement in performance of cognitive tasks; 2) the transfer of improvements from cognitive training to untrained tasks, untrained domains, and, most critically for the elder population, *everyday functioning*; 3) up to six months duration of the positive effects of a course of cognitive training; and 4) generally greater subjective and cognitive outcomes from socially interactive group cognitive training as opposed to single-person task settings (Kelly et al., 2014). The latter a most critical point, as a new direction in the field of cognitive rehabilitation has focused on applying the research that has revealed that social interaction in conjunction with learning as the essential medium for cognitive development and the renewal of self-dependence and productive behavior, especially, as will be discussed, in the elder population and in dementia.

This new direction is the result of a synthesis of the findings of new studies and real-world feedback across different disciplines, fields and intervention/care settings from such areas as cognitive and physical rehabilitation, social neuroscience, human evolution, paleoanthropology, cognitive archaeology/neuroanthropology, cognitive psychology, social psychology, neuropsychology, developmental psychology, clinical psychology, positive psychology, and geriatrics, to hermeneutics and phenomenology and the culture change and new foci of eldercare and dementia care that has emerged from the great success of person-centered care initiatives.

The synthesis of these findings and real-world feedback has been constructed into a rigorously tight, comprehensive, breakthrough explanatory model of the antecedents of human behavior that delineates the human macroneurophysiological mechanics of response to socioenvironmental stimuli that mitigate cognition and behavior either positively or negatively, providing a critical, broad understanding of mental health through which

cognitive development and behavioral outcomes may be positively adjusted to foster wellbeing, promote physical health, both prevent and recover from cognitive and behavioral disorder, and enable a productive life well into advanced age. The application of this highly vetted model is manifested in the innovative, leading-edge, neuroscience-informed modality of Cognitive Neuroeducation (CNE).

With dementia and attendant comorbidities and general cognitive decline the most prevalent incapacitating conditions among the increasing elder population, this proposal addresses 1) what Walia (2019) describes as the urgent need for innovative health and well-being programs "that will aim at increasing the nation's productivity," and, 2) the critical need of a patient-centered approach in response to the complexity of comorbidities in dementia (Callahan & Schubert, 2014) through the development of a pilot community-oriented and community-sponsored, person-centered well-being center based on CNE for the prevention and remediation of and recovery from cognitive and behavioral disorder, with a special focus on dementia and aging-related cognitive decline.

A critical component of the center is an innovative fluidly integrated state-of-the-art e-AHA system (electronic active and healthy aging system) augmenting and supporting the CNE cognitive and physical training in fine-tuning virtual-reality exercises to each individual's base cognitive and physical functional level and the real-time monitoring of each individual's health and progress in the training sessions. The e-AHA system facilitates training administration and streamlines operation in systematizing and personalizing cognitive and physical training through tailored, graduated sessions in accordance with each individual's cognitive and physical responsiveness through on-going monitoring and recording of each individual's performance in each training session, maintaining a progress chart and basic functional profile for each individual. The e-AHA system is presented in an engaging, fun game format to foster active, motivated participation, the encouragement of continuing progress, and social orientation in teamwork, cooperation and partner interdependence in gameplay.

Understanding well-being

To understand the rationale of a well-being center, it is critical to first understand the meaning of 'well-being.' The term 'well-being' is commonly used very loosely, such that many people and many different institutions define well-being differently. Webster's unabridged *Third New International Dictionary* of the English language defines well-being as "the state or condition of being well" which is further clarified as "a condition characterized by happiness, health, or prosperity;" while a classic psychological definition of well-being is proposed to consist of a combination of 1) self-acceptance, 2) positive relationships with others, 3) environmental mastery (critical evaluation of opportunities and avoidance of inappropriate, disruptive or detrimental situations), 4) autonomy (self-dependence and a realistic appraisal of one's skills and abilities in forming one's personal goals), 5) a feeling of purpose and meaning in life, and 6) personal growth and development (self-actualization) [Ryff, 1989; Seifert, 2005], whereby psychological well-being is attained in a balance between self-restraint and the fulfillment of basic needs and realistic, positive goals through challenging and rewarding life events.

In their 2014 study, Ryff, Love, Miyamoto et al., concluded that "positive and negative emotions are construed in notably distinct ways in Japan and the U.S. Not surprisingly, such differences shape the goals and practices of clinicians seeking to promote optimal functioning." The authors state that the larger message emerging from their study as a whole is that "*cultural contexts shape ideal formulations of human well-being as well as the practices designed to promote them*" (Ryff, Love, Miyamoto et al., 2014, p. 2 – emphases added). While it is abundantly clear that cultural priorities and frames of reference shape conceptions of what defines 'well-being' and how it may be achieved, it should be equally clear that even within a particular cultural orientation, each individual's unique personality and life experience uniquely define the priorities that constitute a personal concept of 'well-being.' Well-being, then, must be understood as a highly personal construction of what defines a certain satisfaction in life that extends far beyond the boundaries of simplistic definitions of 'happiness,' 'health,' or 'prosperity,' as all of these qualities are entirely relative, taking on different meanings in the context of the unique personality and life experience of each individual. A situation where one individual finds security and 'contentment,' another may find as an intolerably repressive and suffocating, barren existence.

From the above, we can clearly recognize that 'well-being' is a purely personal concept, a relative construction defined by each individual in accordance with their situation, personality and life experience. There is no universal definition of 'well-being,' it is simply a condition in which one feels a sense of continual growth and progression, and a pervading satisfaction and a basic harmony within one's life. Health and physical vitality are certainly important components of well-being, but, like everything else in life, one's individual perception of what constitutes good health and physical vitality is relative, dependent on one's life history and particular stage in the life cycle – at 21 years of age what an individual may consider good health and vitality relative to themselves would generally be quite different from what that same individual would consider good health and vitality relative to themselves at 75 years of age. In fostering the well-being of an individual, a well-being center recognizes that 1) every individual is a unique personality with a unique set of needs; 2) an elder person is no less an unique individual than any other adult of whatever age, each with particular knowledge, expertise and abilities, and, regardless of any disability, has their own unique set of needs, emotionally, physically, intellectually, and spiritually; and 3) every adult, regardless of age or disability, has the fundamental right to satisfy their needs and maintain her/his individuality with dignity and respect.

The conception of the well-being center that we propose herein, adopting a person-centered approach through the CNE program curriculum of health-oriented, balanced, socially engaging physical, cognitive and behavioral training, is designed to meet the needs of individuals to foster their well-being in a group dynamic, by which the CNE program participants are each enabled to develop deep, meaningful connections with others; discover their hidden abilities and their very own unique core of being; restore cognitive functioning and expand cognitive potential; and refine their cognitive constructs in a more positive, personal, harmonious orientation to life that supports self-actualizing behavior and a healthier vitality toward self-dependence and a productive role in society.

THE RATIONALE OF COGNITIVE NEUROEDUCATION (CNE)

Background

As Jill Daino, on the mental health blog *Talkspace* states: "There are so many types of psychotherapy" (<u>https://www.talkspace.com/blog/different-types-therapy-psychotherapy-best/</u>). It has been variously suggested that there are anywhere from:

1) at least 365 different methods of psychotherapy (<u>http://sergeginger.net/resources/The+evolution+of+Psychoterapy+in+Europe.pdf</u>);

2) more than 400 different types of psychotherapies (https://www.psychologytoday.com/us/therapy-types/integrative-therapy);

3) hundreds of psychotherapy models and schools of thought and over a thousand different named psychotherapies (<u>https://koan-psy.com/cbt-vs-psychodynamic-psychotherapy/</u>); to

4) over a thousand different psychotherapy techniques (https://en.wikipedia.org/wiki/Psychotherapy).

So, if one or another actually works, why are there so many different psychotherapies and/or models, schools or techniques thereof? The answer is simple, just as in psychiatric treatments based on antipsychotics or other psychotropic drugs, psychotherapeutic regimens target the alleviation of a presented symptomology that falls within a particular diagnostic criterion, with some therapeutic orientations and techniques believed to be more effective than others in the remediation of a certain symptom or a certain set of symptoms or suspected causes thereof. Whichever course of treatment – whether through psychopharmacology or through psychotherapy – a prescribed intervention is absolutely critical in remediating symptomology, especially symptomology resulting in behavior that can be seriously injurious to either the symptomatic individual her/himself or any third party caught in the trajectory of such dangerous behavior. Before any real progress toward recovery from mental disorder can take place, symptoms must first be stabilized.

It must be equally understood that the alleviation or stabilization of symptoms, while a necessary first step, does not, in itself, result in well-being, as well-being, as we have dissected it, is highly personal and relative, representing a *holistic phenomenon* whereby a number of different needs both uniquely defined and uniquely important to each individual must be realized to achieve an overall balance in life that gives satisfaction, harmony, motivation, purpose and meaning to one's sense of self. Only through a person-centered, holistic approach can well-being be achieved.

In alleviating symptoms through psychopharmacology or psychotherapeutic treatment, behavior can most certainly be trained and conditioned to respond in what on the surface may appear to be a socially accepted manner; however, it is the very fundamental underpinnings of human relationships – such as a correct and perceptive understanding of the intentions, feelings and behavior of another person; a real appreciation of the concepts and implicit values of the rules of conduct that govern social situations; and the acquisition of the spontaneous ability to generate an empathetic and appropriate response that facilitates the formation and maintenance of real bonding between one human being and another – that are the faculties that define us as human and as unique personalities, and it is these very basic faculties that evidence implies are *not effectively addressed* by standard intervention approaches beyond simple mimicking and what are basically superficial adaptations (Hogarty & Flescher, 1999; Penn et al., 1997; Corrigan & Penn, 2001; Pinkham et al., 2003).

Behavioral symptoms, which certainly can be debilitating, are, in reality, rather arbitrary personality-generated manifestations of unmet psychological needs, which differ from individual to individual and largely crossover from one so-called 'diagnostic' category to another. Symptoms are not the real issue in behavioral problems, but simply the arbitrary reaction to deeper disturbances of an individual's well-being. Rather than focusing on the

alleviation of symptoms, as in psychopharmacology and psychotherapy, CNE focuses on the neurophysiological mechanisms that constitute the uniquely human social brain and the holistic core of evolutionarily constructed action patterns that drive human behavior and the personal equation that uniquely defines each individual.

Cognition, behavior, the role of learning, the uniquely human social brain, and CNE

Taking a holistic view. CNE addresses the very properties and the mechanisms thereof that both make us human and make each of us unique. These properties and the mechanisms by which they are generated are defined as *cognition*. Cognition consists of associations of data encoded in the constant instantaneously changing patterns of encephalic neuronal interconnectivity. In simple terms, cognition constitutes one's unique pattern of thinking and one's manner of understanding and interpretation of stimuli (impressions) from one's environment, directing one's actions in response to environmental stimuli from situation to situation as perceived by the individual. Cognition, then, is the process and condition of a 'knowing' or 'understanding' formed from the cumulative constructions of ideas, outlooks and conceptual orientations acquired through both incidental as well as formalized learning constituting the totality of life's experiences by which each individual uniquely interprets and assigns meaning to her or his environment in organizing interaction therewith. Since cognition consists of an individual's distinctive patterns of thinking, and distinctive responses to environmental stimuli (i.e., behavioral orientation), cognition is in fact, behavior, which is molded (i.e., *learned*) from life's experiences (Robinson, 2015; Cacioppo & Berntson, 1992; Cacioppo & Amaral et al., 2007; Cacioppo & Decety, 2011; Cacioppo, Berntson, & Decety, 2010; Cozolino, 2006; Lieberman, 2013).

Through the process of evolution, by which the human brain developed as a social brain, whereby all learning and behavior is constructed within the ongoing mechanism of socialization and all experience is internalized in a social context, behavior is a product of, and response to, social integration or lack thereof – as socialization is defined as the internalization of experience (the interpretation and registration of information; i.e., the process of learning) shaped through the social milieu and its prevailing dictates as a function of the biological predisposition forged from the evolutionary process of the formation of the social brain of the anatomically modern human (*Homo sapiens sapiens*).

Though many taxa (i.e., kinds of animals) are behaviorally oriented toward a community or social structure, with biologically hardwired, preprogramed role-specific differentiation, such as in ant and bee colonies, or by a general rudimentary cognitive tendency toward forming simple social groups, such as by chimpanzees and gorillas – some animals even eliciting such behaviors that appear as love, devotion, sympathy and even altruism – only humankind can be definitively understood as having evolved a taxonomically unique social brain inherently biologically encoded in the self-construction of the cognitive configuration and interpretation of self, individual experience and theory of mind (the ability to attribute mental states — beliefs, intents, desires, emotions, knowledge, etc. – to oneself and to others) within the framework of intricately defined social roles and the construction of complex, intertwined layers of social organization (Robinson, 2015; Cacioppo & Berntson, 1992; Cacioppo & Amaral et al., 2007; Cacioppo & Decety, 2011; Cacioppo, Berntson, & Decety, 2010; Cozolino, 2006; Lieberman, 2013; Adolphs, 2009; Bhanji & Delgado, 2014; Blakemore, 2008 and 2010; Brüne, Ribbert, & Schiefenhövel, 2003; U. Frith & Frith, 2010; Grossman & Johnson, 2007; Insel & Fernald, 2004; Kennedy & Adolphs, 2012; Saxe, 2006).

With the exception of tissue degradation from organic pathology or physical injury, all acquired psychological problems; i.e., all acquired cognitive and behavioral problems, may then be said to be social integration problems – and since socialization and human behavior are learned and not prewired, all acquired cognitive and behavioral problems, are, in effect, learning problems. The emphasis then on both the prevention of and recovery from cognitive and behavioral disorder must be on learning by broadly exercising cognitive processes and stimulating the neuroplasticity of the brain, not only to optimize deep, enduring learning outcomes, but also to effect positive, self-actualizing social integration. CNE achieves such outcomes through an enriched environment emphasizing 1) engrossing curriculum content; 2) a dialogic foundation of critical, sensitive, and constructive feedback and interpersonal bonding within a highly cohesive group dynamic; and 3) a person-centered paradigm facilitating the unique voice of the individual.

Recovery from cognitive and behavioral disorder requires more intensive positive stimulation than in normative learning in order to trigger a stronger neurophysiological response to rebuild stagnant cognitive neurocircuitry and/or rewire cognitive connections from negative (i.e., maladaptive or distorted) cognitive constructs to positive cognitive constructs, and, therefore, to override and transform negative behavioral patterns set through the previous negative experience. The design, content and application of such a more intensive positive stimulation or positive learning environment, is referred to as the 'enriched environment.'

Our brains are wired in networks of interconnected neurons (nerve cells). It is precisely the patterns of neuronal interconnections in the brain which constitute thoughts, perceptions, the recognition of particular objects of our environment; the identification of different people and their meaning in our life; the construction of self-identity; etc., by which we understand the world we live in. This cumulative understanding through experience is defined as cognition. An assemblage of associations by which we form a distinct configuration of meaning is referred to as a 'cognitive construct.' The totality of all the intricate, dynamic, ever-changing interactions between all the innumerable cognitive constructs that we formulate throughout our lives is referred to as each individual's own unique 'cognitive schema,' from which each individual's unique personality and set of behavioral characteristics arise.

Neuroplasticity, the neurophysiological process of learning, consists of the constant rewiring of neuronal interconnections in the brain in response to environmental stimuli. Learning, then, is the continuous mediator of behavior throughout life, but, dependent on environment, can either facilitate a fluid engagement of life, or deter it (Alwis & Rajan, 2014; Kleim & Jones, 2008; Kleim, 2011; Taubert, Villringer, & Ragert, 2012; Kandel, 2001; Markham & Greenough, 2004; McGaugh, 2000; Bliss & Collingridge, 1993; Bliss & Lomo, 1973; Hebb, 1949; Rioult-Pedotti, Friedman, & Donoghue, 2000). One's environment influences how one understands all phenomena – relationships, society, and the broad concepts of human experience itself – and, in all perceptions of experience, as a certain understanding may be reached, there may also be misunderstanding, and where a certain interpretation may be grasped, there may also be misinterpretation. In the accumulation of knowledge and understanding in the unfolding of life's experiences, there is also the specter of distortion and the compilation of a faulty and destructive database that may form a deleterious cognitive schema, i.e., a cognitive schema corrosive to our *evolutionarily defined core human behavior* that presents in some form of cognitive and behavioral disorder.

Our evolutionarily defined core human behavior is manifested through which we refer to herein as *pseudo-fixed action patterns*. The term 'fixed action patterns' is used in ethology to refer to the phenomenon first identified by Konrad Lorenz (1970, pp. 316-350) as the automated responses of nonhuman animals to particular stimuli inherent to an animal's habitat. In defining a range of human traits in distinction from fixed action patterns, the CNE explanatory model has adopted the term 'pseudo-fixed action patterns' to refer to strong behavioral dispositions that characterize quintessential human nature, that, rather than hardwired as in nonhuman animals, are subject in humankind to mediation by genotype and phenotype, and may even be entirely overridden by experience, stressing the flexibility of human nature, its dependence on learned response (i.e., socialization) and, consequently, its susceptibility to environmental influence. These pseudo-fixed action patterns constitute the core behavioral tendencies that uniquely define us as human.

Insufficiently equipped to compete with other animal taxa for survival on an individual basis, early protohumans evolved to rely on the competitive edge of core patterns of cooperative behavior in groups. By cooperative behavior facilitated by language, which lead to both higher-order reasoning and greater tool-making flexibility to manipulate their environment, humans were able to out-strategize, out-plan, out-maneuver, and simply out-think their taxonomic rivals for survival. Humans organized in groups such as bands or tribes also competed against each other – group against group – in a particular habitat or region, so that social cohesiveness as well as role and skill diversification and skill expertise within a group leading to more specialized supportive social structures became the keys to group survival that pushed evolutionary determinants toward the human tendency for more sophisticated, intricate and complex social organization.

So-called 'morality' evolved as a condition of group survivability. Such so-called human 'virtues' as courage, love, compassion, forgiveness, charity, mercy, consideration, honesty, honor, selflessness, steadfastness, loyalty, self-sacrifice, etc., that though became instituted in codes of behavior in the formulation of social order and sacred ideals of religious conviction, stem from *natural* tendencies embedded within the pseudo-fixed action patterns and cognitive constructions of the uniquely human social brain that are designed to solidify group cohesiveness and effectiveness in maximization of the competitiveness of a group. The greater these qualities among its members the stronger the group; conversely, the degree to which they are lacking among the members of a group (be it a mating pair, a family, a band, etc.), the less a group is able to work together effectively and benefit from the interrelationships of its members.

For basic human survival:

1) learning became the central operating principle of the uniquely human social brain;

2) curiosity or inquisitiveness in response to novelty became the driving force of learning;

3) logic and reason became the principal method of understanding;

4) and <u>affective state</u> (emotive response) became the mechanism mediating the balance between understanding and action.

Affective (emotive) qualities constitute essential components of pseudo-fixed action patterns, such as fear, anger, rage, hate, aggression and violence in the acute stress response (fight or flight response) and love, compassion, empathy, concern, and selfless, protective loyalty in the attachment/bonding response and the tend-and-befriend response, etc. While the predisposition of affect is an innate biological determinant of human behavior, the individual capacity for and/or particular nature of affective reaction is mediated by genotype and

phenotype to the extent that each individual possesses a unique basic affective profile. Individual affective reaction is highly malleable, and is learned or modified through experience such that highly indoctrinated societies can skew mass behavioral tendencies.

The regulation of affect is pivotal to the formation and maintenance of social relationships. Affect not only informs and directs reasoning, but may also block it, as even the pillars of morality can become destructive once they become extremes, such that loving kindness taken to mindless obsession can lead to both sexual depravity and lack of justice in failing to properly punish wrongdoing and thereby insufficiently protecting the innocent, and, when justice itself becomes overzealous, it can lead to unfair punishment and even to torture and the murder of innocents. With this understanding, 'emotional intelligence' – the maintenance of balance between emotion, rationality and morality – has been recognized as an integral component of social integration in the fields of psychology and psychiatry (see, for example: Mayer, Salovey, & Caruso, 2004; Mayer, Roberts, & Barsade, 2008; Mayer & Salovey, 1997; Izard, Fine, Schultz, Mostow, Ackerman, & Youngstrom, 2001; Lopes, Brackett, Nezlek, Schütz, Sellin, & Salovey, 2004; Keefer, Parker, & Saklofske, 2009; Lopes, Grewal, Kadis, Gall, & Salovey, 2006; Lam & Kirby, 2002; Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002; Emmerling, Shanwal, & Mandal, 2008; Di Fabio, 2015; Payne, 1986; Zeidner & Matthews, 2016; Schutte, Malouff, Bobik, Coston, Greeson, Jedlicka, Rhodes, & Wendorf, 2001; Sánchez-Álvarez, Extremera, & Fernández-Berrocal, 2015).

Our human core behavior is primarily a function of cognition, which includes learning ability; curiosity and inquisitiveness; logic, reason and rationality; affective reaction and social orientation. The balance between emotion, rationality and morality is critical to wellbeing and a harmonious, healthy society, as is the balanced expression of all the properties of our core human behavior as constructed within our uniquely human social brain through pseudo-fixed action patterns, however; as a result of pathology, injury or deleterious socioenvironmental conditions and circumstances, our core behavior is susceptible to suppression and even distortion, leading to cognitive and behavioral disorder, loss of well-being, and, more seriously, impairment of independent functioning in the sustainment of the instrumental activities of daily living (IADL) and even the most basic activities of daily living (ADL). Through a person-centered, enriched environment, CNE fosters the renewal of a balanced core behavior lost as a result of injury, pathology, or negative environmental conditions.

"Since the initial discovery by Hebb (1947) that environmental enrichment (EE) was able to confer improvements in cognitive behavior, EE has been investigated as a powerful form of experience-dependent plasticity" (Alwis & Rajan 2014, p. 1). ". . . neural plasticity is the mechanism by which the brain encodes experience and learns new behaviors. It is also the mechanism by which the damaged brain relearns lost behavior in response to rehabilitation" (Kleim & Jones 2008, p. S225).

The two quotes above refer to the process of recovery from cognitive and behavioral disorder by relearning in an enriched environment – relearning occurring as an inherent mechanism of neuroplasticity, by which all experience is encoded by the brain – whereby a significantly enriched environment is required to raise the reduced capacity of neuroplasticity in organic damage or to enable more powerful encoding of newer experiences in order to supersede residual deleterious cognitive constructs acquired from previous negative socioenvironmental factors. An enriched environment, is, by definition, a learning environment, as all experience is an instance of learning about our environment, the situations it imposes, and how to react thereto. But, in distinction from any incidental experience in the unfolding of everyday life, an enriched environment is an environment designed to provide more stimulation, especially, rewarding and encouraging stimulation, invoking more positive, engaged reaction than random, incidental experience. An enriched environment is also, by design, a relearning environment, either to relearn behavior lost through organic damage, or to relearn behaviors conducive to social integration that became distorted through a previously negative environment.

Over the last several decades, neuroscience research has begun to characterize the adaptive capacity of the central nervous system (plasticity). The existing data strongly suggest that neurons, among other brain cells, possess the remarkable ability to alter their structure and function in response to a variety of external and internal pressures, including behavioral training. We will go so far as to say that neural plasticity is the mechanism by which the brain encodes experience and learns new behaviors. It is also the mechanism by which the damaged brain relearns lost behavior in response to rehabilitation. (Kleim & Jones, 2008, p. S225)

Following brain injury or disease there are widespread biochemical, anatomical and physiological changes that result in what might be considered a new, very different brain. This adapted brain is forced to reacquire behaviors lost as a result of the injury or disease and relies on neural plasticity within the residual neural circuits. The same fundamental neural and behavioral signals driving plasticity during learning in the intact brain are engaged during relearning in the damaged/diseased brain. (Kleim, 2011, p. 521)

Environmental enrichment (EE) increases levels of novelty and complexity, inducing enhanced sensory, cognitive and motor stimulation. Whilst environmental enrichment is of course a relative term, dependent on the nature of control environmental conditions, epidemiological studies suggest that EE has direct clinical relevance to a range of neurological and psychiatric disorders. (Hannan, 2014, p. 13)

Because learning (i.e., neuroplasticity) actually changes brain structure in the constantly changing patterns of neuronal interconnectivity, not only are changes occurring simply in neuronal connectivity, but also in all the neurophysiological elements that support positive, learning-related connectivity, such as synaptogenesis and dendritic arborization, gliogenesis, volumetric increases (such as in increases in neuronal soma and nuclei size and glia, in capillary dimensions and dendritic density, and in astrocytic proliferation, as well as in posterior hippocampus enlargement and volume enlargement of motor and auditory areas and their anatomical connections), with changes also noted in gene expression, protein synthesis, and many other areas of brain anatomy and physiology (van Praag, Kempermann, & Gage, 2000, p. 191; Taubert, Villringer, & Ragert, 2012, p. 321; Maguire & Gadian et al., 2000; Bengtsson & Nagy et al., 2005; Gaser & Schlaug, 2003a, and 2003b; Sluming & Barrick et al., 2002; Muotri & Gage, 2006; Draganski & May, 2008, p. 140; Huttenlocher, 1990; Aimone, Wiles, & Gage, 2006; Leuner, Gould, & Shors, 2006; J. A. Kleim, Kleim, & Cramer, 2007; Markham & Greenough, 2004; Kleim & Lussnig et al., 1996; Hydén & Lange, 1983; Jin & Wang et al., 2005; McAllister, Lo, & Katz, 1995; Comery, Shah, & Greenough, 1995; Kolb, Buhrmann, McDonald, & Sutherland, 1994). These positive changes in brain anatomy and physiology (brain reserve) yield positive changes in cognition (cognitive reserve), and vice versa, constituting an intrinsically interlinked neuroprotective agency of brain and cognitive reserve (BCR).

'Brain and cognitive reserve' (BCR) refers here to the accumulated neuroprotective reserve and capacity for functional compensation induced by the chronic enhancement of mental and physical activity. BCR is thought to protect against, and compensate for, a range of different neurodegenerative diseases, as well as other neurological and psychiatric disorders. (Nithianantharajah & Hannan, 2011, p. 331)

Recent evidence suggests that the concept of BCR is not only relevant to brain aging, neurodegenerative diseases and dementia, but also to other neurological and psychiatric disorders. (Nithianantharajah & Hannan, 2009, p. 369)

Experimental evidence from the last two decades has clearly shown that learning causes distinct physiological, molecular, and structural changes in the brain. (Taubert, Villringer, & Ragert, 2012, p. 320, citing Kandel, 2001; Markham & Greenough, 2004; McGaugh, 2000)

Positive changes in the brain arising from positive structured learning have been demonstrated to induce long-lasting physiological changes in the brain, by which the brain heals itself, such that the buildup of brain and cognitive reserve (BCR) through an enriched environment can have wide-ranging benefits to overall health, even in the amelioration of such injuries and pathologies as traumatic brain injury (TBI), Parkinson's disease, stroke, multiple sclerosis, depression, epilepsy, autism spectrum disorders (ASD), schizophrenia and Alzheimer's disease and other forms of dementia, providing a powerful remediation model for intervention in aging-related cognitive decline and dementia and its frequently associated comorbidities. Even in organic damage and pathology, positive change and health benefits can be achieved through an enriched environment.

EE has also been found to ameliorate behavioural, cellular and molecular deficits in animal models of various neurological and psychiatric disorders, including Parkinson's disease, stroke, traumatic brain injury, epilepsy, multiple sclerosis, depression, schizophrenia, and autism spectrum disorders. (Hannan, 2014, p. 13)

In recent decades, the interest in behavioral interventions has been growing due to the higher prevalence of age-related cognitive impairments. Hence, behavioral interventions, such as cognitive stimulation and physical activity, and along with these, our lifestyle (education, work position, frequency of cognitive and social activities) have shown important benefits during cognitive impairment, dementia and even recovery after brain injury. (Sampedro-Piquero & Begega, 2017, p. 459)

The concept of an enriched environment, described anecdotally already by Hebb (1947), is one of the most widely used experimental paradigms for studying learninginduced plasticity. . . At the behavioral level enrichment is associated with increased learning and memory and reduction in age-related decline. (May, 2011, p. 476, citing Rampon & Jiang et al., 2000; van Praag, Kempermann, & Gage, 2000)

In their 2014 paper, Alwis and Rajan (p. 1) discuss how "The brain's life-long capacity for experience-dependent plasticity allows adaptation to new environments or to changes in the environment, and to changes in the internal brain states as occurs in brain damage" through "the demonstrated sensorimotor and cognitive benefits associated with exposure to EE" and the possible mechanisms involved therein.

As demonstrated by all of the above quotations, environmental enrichment and its ability to stimulate the brain's inherent neuroplasticity in conferring cognitive, behavioral and health benefits in promoting the alleviation of various forms of cognitive and behavioral disorder and health-related impairment in aging, is a much studied and uniformly agreed upon topic in the fields of neuroscience and neurorehabilitation. In the following it will be shown how the modality Cognitive Neuroeducation (CNE) encompasses a holistic enriched environment through a person-centered orientation. A more inclusive bibliography of the extensive body of scientific studies that validate the efficacy of the enriched environment in the remediation of cognitive and behavioral disorder and aging-related impairment is provided in the Appendix at the end of this document.

The CNE enriched environment

In CNE, the term 'enriched environment' refers to a specifically designed person-centered orientation consisting of a prevailing ambiance of respect and concern for the individual, the sanctity of selfhood and the recognition of the essential role of social integration in the wellbeing of the individual. This equal focus on both respect of the individual and on social interaction forms an encompassing milieu that facilitates the engagement of life through activities providing challenge and growth to the fullest of each individual's capacity and excites the individual's interests to promote a) a sense of accomplishment, b) bonding with others, c) joy of the moment, and d) a keen anticipation of the discoveries, camaraderie and achievements tomorrow may bring.

This enriched environment is manifest through the structure of a cohesive group dynamic predicated on perspective taking; social context appraisal; empathetic engagement in emotive connection and expression of feelings; constructive feedback in group dialog; attentive listening; support and concern for one's fellow group members; identification with the group; individual initiative; facilitation of the voice of the individual; and the confirmation of self. All of these principles of the enriched environment are maintained by the very content of the enriched environment and the group interaction therewith; therefore, both content (curriculum) and its manner of presentation are equally critical to the CNE enriched environment. With this understanding, the CNE enriched environment is at once the foundation, curriculum and presentation of a structured CNE program of well-being in the prevention of and recovery from cognitive and behavioral disorder.

Though functioning as a powerful modality for the prevention of and recovery from cognitive and behavioral disorder, effective even in profound cognitive impairment and dementia, CNE is presented as a fun, entertaining, informative program of activities conducted through a group dynamic emphasizing shared engagement through teamwork, problem solving challenges, discussion, dialog, debate, critical thinking, and personal reflection. CNE participants experience the program entirely as a recreational, social and educational curriculum promoting health and well-being for mind and body through exercise, social relations and learning activities. There are no allusions or references of any kind in the program to the stigma and negative connotations of therapy, pathology, disability, incapacitation, mental abnormality or diagnostic labels.

In the CNE group dynamic participants learn to value each other's input as well as their own; as success in learning and accomplishing tasks and engagement and enjoyment of the moment, is totally interdependent on group and individual input and effort, leading to growth of the individual and the group, to self-confirmation, bonding with others, identification with the group and the emotional anchoring of a strong sense of belonging. These interactions in

the group dynamic provide intimate rather than casual contact and constancy through structured, predictable, scheduled interaction; mutually rewarding, cooperative activities; integration within an ongoing curriculum; and the full, absorbed engagement of all participants; the latter as an inherent component of the CNE group structure and its dependence on the cooperation, constructive feedback, give and take, and planning that constitutes teamwork.

Participation within the person-centered CNE group structure through group commentary and feedback, while establishing and reinforcing group values and rules of interaction, rather than enforcing any conformity of personality and mindset, actually is a powerful vehicle of self-discovery and development of individuality. Each member comes to visualize her/himself as part of the working group, internalizing that her/his input and participation is neither distinct from the group nor judged by it or its rules, but rather an inextricable part of the group, its process, its defined protocols and its unique dynamic. Each member of the group is a living embodiment of a particular essence of the group, its values and its modes of interaction, shaped through their own individual inputs and unique contributions to the group. Each member identifies her/himself as part of the group, her/his self-identity becoming interlinked with the group identity.

Paradoxically, by observing the differences in each individual member of the group and interacting with them; sharing thoughts, opinions and experiences and developing a deeper understanding of each member, one begins to recognize not only the differences between each of the members of the group, but also between each member and oneself; such recognition informing a clearer recognition of one's own individuality, of who one is, and, in learning to appreciate the different personalities of the group and welcoming each's individual perspectives and ways of thinking, each's humor, warmth, and unique contributions to the group, one begins to better understand and appreciate one's own uniqueness and individuality and a growing sense of self and self-confidence emerges. Since we are social beings with social brains, our personalities are formed from the way each of us uniquely interacts with other people within the commonly agreed rules of social conduct.

In the CNE program individual uniqueness is celebrated, and all learning and activities are integral to the group dynamic and develop as a group process, with the experiences of the program uniquely internalized by each individual participant, being both simultaneously shared and highly personal, as each individual participant develops her/his own viewpoint of life and understanding of her/himself. Through the collective encouragement of independent growth in interactive dialog, constructive feedback and the emphasis on self-challenge, the group dynamic instills the collective sense of 'all for one and one for all.'

The CNE person-centered group dynamic stresses individual self-expression and full participation in the group as an inextricable member of the group, recognizing that each member plays a vital role without which the group loses its unique dynamic and nuance of interaction. An evolving interaction within the group parallels a growing self-confidence in each member and her/his sense of importance as an essential component of the group, leading to a growing sense of responsibility to provide input and constructive feedback to each of the other members in their participation in the activities of the group, which stimulates greater motivation to more effectively engage both the group process and learning activities in the CNE program, so that in achieving an individual's own growth toward self-realization she/he also becomes part of the growth toward the self-actualization of the other members, as they, in turn, form an integral part of her/his growth.

At the core of the CNE enriched environment and its person-centered group dynamic are the principles of perspective taking and social context appraisal. Perspective taking consists of the ability and custom to go beyond spontaneous, initial surface impressions and apply a thoughtful appraisal and a honed proficiency in recognizing and interpreting social cues that explain another person's thinking, feeling and behavior from that person's perception of her/his own situation in a particular social encounter.

Perspective taking involves the development of respect for, understanding of, and empathy with, other individuals by putting oneself in the other person's place and reflecting how one her/himself would act and feel in that place. An important component of perspective taking is social context appraisal – the balanced assessment of social contexts and circumstances which account for an individual's behavior in a particular social encounter. While the context of the individual is always essential for understanding individual behavior, in the group dynamic social context appraisal transcends individual behavior, extending to the culturally transmitted 'norms' of the group – in the group dynamic, perspective taking must equally recognize and appreciate both the personal context and the social context defined by the group 'norms' and the individual's role or position within the group.

Another essential component of perspective taking is affective (emotional) engagement. It is precisely one's own emotional state that influences the perception of another's emotional state and determines the selection and processing of individually relevant social information; either effectively picking out the essential information and its implications within the particular social encounter, or completely missing or distorting that information to one's own detriment in social interaction.

An individual's feelings are a principal determinant of behavior in any social situation, and it is imperative to understand another's feelings in order to understand that person's behavior and likely response in any social interaction as a clue to one's own appropriate behavior in a particular social encounter. However, it is impossible to understand the affective state of another unless one's own affective response is appropriately well harmonized with one's personal situation relative to the context of any particular experience. In order to correctly understand another's feelings, one has to consistently experience one's own appropriate emotional reactions. A lack of affect can be no less self-destructive and socially disruptive than uncontrolled, inappropriate emotional outbursts.

A major part of perspective taking, then, is the realization of an individual's own emotional capacity by learning to engage experiences deeply through commitment and the giving of oneself to the experience with introspection, reflection, sharing and genuine attachment. By putting oneself totally into the experience as an integral part of the experience, the individual learns involvement and concern; and learns to fully relate to the experience and to others – to feel, to empathize and to bond. In the CNE program, the participant learns to THINK AND FEEL rather than simply engaging in rote memorization, accumulating loosely connected facts or learning PURE MECHANICAL BEHAVIOR.

In the CNE program we explore together conceptualizations; beliefs; modes of social interaction and interpersonal relationships; reactions to situations; emotive contours; flights of imagination; aesthetic visions; creative artistry and the nuances of beauty; the concepts of duty, purpose, loyalty, love, and spirituality; the sense of destiny; and myriad other products of the mind in a variety of contexts through a range of media and activities by which we gain

insights on the essence of being human. We explore behavior from multiple points of view, learning how to interpret frames of meaning in understanding others and discovering ourselves in field trips, camp-outs, games, stories and through literature, music, drama, art, skits, dance, motion picture films, etc.

In answering the criticism that a large portion of such activities is recreational, creative, often fanciful, and does not reflect the day-to-day grind and responsibilities of real life, the contents of such activities however are indisputably reflections of the products of the mind – the mind being the repository of all that we experience and think about and therefore representative of our hopes, dreams, fears, longings, visions, imaginings, in short, the true essence of being human – and in our ongoing dialog and group experience in the CNE enriched environment, we learn what it is to be human and how to enjoy ourselves in connection with others and through that connection with others, discover our very own personal, unique core of being, reforming our cognitive constructs in redefining a more positive, personal, harmonious lifestyle supporting balanced, self-actualizing behavior, fluid, engaged social interaction and a real, unequivocal bonding and reengagement with oneself, with others, and with life itself. By such reengagement, we satisfy our basic psychological needs and rebuild our cognitive faculties that enable us to fortify ourselves against, while successfully navigating through, the daily grind, recognizing and fulfilling our responsibilities in real life, contributing to the maintenance of our society as productive members of the community.

We live within our mind, and the journey of life continues on in elderhood and even in infirmity of body through a healthy, active mind and an environment encouraging our innate curiosity and deep human need to share and involve ourselves with others. Even in physical decline, the restoration of cognitive function and behavioral balance in an elder can renew lost skills, knowledge and expertise previously acquired through her/his life that can be effectively utilized in a worthwhile contribution to the community, reinstilling the elder's sense of their own value and a renewed meaning and purpose in life. Even in simply recovering the facility for the execution of some of the basic activities of daily life (ADL) leads to a better understanding and cooperation between an elder under care and her/his care workers, the elder taking on more responsibility and involvement in their own care, not only greatly reducing the burden of care needed by the elder, but also giving the elder a sense of more independence and self-management of their own life.

THE PROPOSAL: THE DEVELOPMENT OF A PILOT COMMUNITY WELL-BEING CENTER

Background

As we have herein demonstrated 1) the great economic and societal burden of the rapidly aging population; 2) that cognitive decline, and especially dementia and its commonly associated comorbidities, constitute the major contributors to the economic and societal burden of the rapidly aging population; and 3) that the attainment and maintenance of well-being is essential in combating physical, cognitive and general health decline related to aging; we hereby propose the concept of community-based well-being centers as a primary solution by which to significantly ameliorate the economic and societal burden of our continually aging population in restoring elders as vital, productive members of society. And, as we have

defined well-being as a purely personal concept, a relative construction defined uniquely by each individual in accordance with their own situation, personality and life experience, we further propose that such community well-being centers are rigorously grounded in and assiduously follow a structured person-centered program of enriching activities.

Although neuroscience and physical and cognitive rehabilitation researchers have long recognized the positive benefits of environmental enrichment in the amelioration of even profound physical and cognitive disability in such conditions as traumatic brain injury, stroke, dementia, etc., these studies, especially in the case of dementia, have not been adopted by and adapted within the clinical community, which has universally declared that there is no cure and no currently effective treatment for Alzheimer's disease and other forms of dementia (https://www.mayoclinic.org/diseases-conditions/dementia/diagnosis-treatment/drc-20352019, https://www.nhs.uk/conditions/dementia/cure/, https://www.alz.org/alzheimers-dementia/treatments).

While some claims have been made for treatments that ameliorate some symptoms of dementia, such as suggested by the Mayo Clinic (<u>https://www.mayoclinic.org/diseases-conditions/dementia/diagnosis-treatment/drc-20352019</u>), such treatments are defined even by the Mayo Clinic as temporary, associated with a number of highly disturbing side effects (that themselves may require alleviation through other medications, substituting one symptom or group of symptoms for another and compounding the potential for negative effects of drug interaction) and mostly provide slight, if any real benefit to quality of life or daily functioning.

The American Psychiatric Association (APA), reiterating the universal claim of the clinical community that there is no cure for either Alzheimer's disease (the overwhelmingly predominant diagnosis of dementia) nor almost all other categories of dementia (APA, 2015, pp. 237-258), recommends two temporary treatments for Alzheimer's disease, cholinesterase inhibitors and memantine, that "may help lessen the memory symptoms for a short time" (ibid., p. 245), and suggests antidepressants to treat mood symptoms and antipsychotics for hallucinations, agitation and severe hostility, although such suggestion is in direct contradiction to the U.S. Federal Drug Administration (FDA) guidelines that antipsychotics "are not approved for the treatment of behavioural symptoms in elderly patients with dementia" (https://www.dementiacarecentral.com/aboutdementia/treating/antipsychotics#justified), reflecting the strong concerns over both the ethics and viability of off-label prescribing of antipsychotics and other psychotropic drugs such as benzodiazepine and antidepressants for elders with dementia that has shown little efficacy for that population and presents serious health risks thereto (Dudas, Malouf, McCleery, & Dening, 2018; Ray, Federspiel, & Schaffner, 1980; Stevenson, Decker, Dwyer, Huskamp, Grabowski, Metzger, & Mitchell, 2010; Rios, Perlman, Costa, Heckman, Hirdes, & Mitchell, 2017; Zagaria, 2008; Ballard & Howard, 2006; Azermai, 2015; Bullock, 2004).

From the perspective of the National Health Service (NHS) of the United Kingdom, not only is there is no cure for dementia, but it is unlikely that there will ever be such thing as a single cure for dementia (<u>https://www.nhs.uk/conditions/dementia/cure/</u>). Though the NHS is enthusiastic about experiments in new forms of highly intrusive treatments for dementia ('intrusive' in a medical sense referring to an invasive or otherwise intentionally manipulated or forced bodily response), throughout the years numerous so-called 'innovative' intrusive

experimental approaches have proven ineffective and even deleterious, and many of the newest touted intrusive experimental strategies start out on a wrong footing, such as the premise of inhibiting the activity of enzymes involved in beta-amyloid production in preventing beta-amyloid plaque buildup. It is certainly true that the buildup of beta-amyloid plaque as well as tau protein tangles have been found in a representative postmortem sampling of the brains of people that in life exhibited symptoms of dementia [and, in fact, the presence of plaque and tangles in the brain in combination with symptoms of dementia is considered a defining diagnostic marker for Alzheimer's disease - see DSM-5, the American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (APA, 2013, p. 613)]; however, postmortem examinations of the brains of individuals with no noted symptoms of dementia in life and no history of cognitive decline, behavioral anomalies or social interaction difficulties, have also found a significant number of subjects having a buildup of beta-amyloid plaque and tau protein tangles, suggesting that the buildup of plaque and tangles may not necessarily be a part of the etiological path leading to dementia but simply a sequela or by-product of some other neurophysiological process or processes that may or may not be related to dementia.

Structure and content of the proposed well-being center

Though any prospect of either an immediately available cure for dementia or that of any treatment (especially nonintrusive treatment) providing a significant period of effectiveness in the remediation from its debilitating symptoms is denied by the clinical community, more than 70 years of research (since 1947) as reported in a vast corpus of studies in the fields of physical and cognitive rehabilitation, neuroscience, and specialized areas of cognitive geriatrics and gerontology, have repeatedly documented remedial changes in the brain (BCR) in response to an enriched environment in the alleviation of cognitive and physical impairment and behavioral disorder associated with a wide range of pathology, injury and obstructive socioenvironmental conditions. Among the disorders responsive to environmental enrichment is dementia in its various diagnostic classifications. These remedial changes in the brain, through ongoing significant engagement with the enriched environment, are accumulative, providing more neuroprotective effects, greater cognitive acuity, greater fluidity of social interaction, more stabilized and effective behavior, greater resistance to the comorbidities associated with dementia and the neurodegenerative processes of aging, and improvement in overall health and physical vitality. The benefits of these changes, depending on the preexisting level of neurophysiological degeneration, severity of underlying pathology, degree of tissue damage, etc., can even be maintained throughout one's advancing years to the remainder of an individual's life.

These changes, which have long-lasting, and often even permanent effect, represent, in fact, a 'cure' insomuch as they can effect an outcome equivalent to that of a cure for a disease. Although BCR (brain and cognitive reserve) in dementia is like a cure for a disease, it is not exactly a cure in the medical sense, since dementia is not a disease, but a syndrome [World Health Organization (WHO), 2019; Zagaria, 2008; Blass, 2003; Poblador-Plou et al, 2014], a condition characterized by a set of associated symptoms of different and/or not clearly known etiologies that presents in different ways in different people and is generally considered progressive and irreversible (WHO, 2019; Blass, 2003; Zagaria, 2008). However, in spite of the denial and failure of the clinical community, the dysfunctional neurophysiology leading to dementia and its incapacitating effects can be reversed as years of studies in the efficacy of environmental enrichment clearly attest. The denial of the clinical community squarely rests on the fact that environmental enrichment and the design, development and implementation of an enriched environment lies far outside the clinical paradigm based on therapy or treatment in a clinician-patient relationship focusing on pathology or disease, or, when the etiology is unclear, on the alleviation of symptoms. Clinician-patient sessions or medications do nothing for the daily environment of the individual under treatment, i.e., the environment in which the individual is primarily immersed and which molds the individual's brain and behavior.

The brain has two principal functions, 1) to regulate the primary autonomic life-sustaining bodily functions, and 2) to direct interaction with the individual's environment through the interpretation of environmental stimuli and reactive voluntary motor control. In the second critical function, the brain acts as a repository of the input of the five senses, interpreting their sensory information, and, through the mechanisms of neuroplasticity, modifies its neurophysiology to induce a specific behavioral response to the sensory information, whereby the brain changes its neurophysiology in accordance with a specific interpretation of and reaction to the environment, this neuroplasticity constituting the elemental process of learning. These changes can be positive, in that they are appropriate to advancing the wellbeing of the individual, building up BCR, or negative, weakening BCR and impeding wellbeing by blocking or distorting the individual's natural core behavior and journey of selfactualization. Negative changes can result from either organic pathology or tissue insult due to injury that disturbs basic neurophysiological functions, and/or from deleterious socioenvironmental conditions or circumstances that predisposes or limits the interpretation of environmental stimuli, resulting in a faulty or deficient database of experience and unbalanced, misconceived or inadequate cognitive constructs.

Dementia, a product of faulty experience-driven cognitive construction deficient in or contradictory to the core behavior embedded within our uniquely human, evolutionally defined pseudo-fixed action patterns, is a result of organic damage either initiated or aggravated by deficient or deleterious socioenvironmental conditions often associated with aging and the pervasive negative societal attitudes towards aging. Regardless of what condition or conditions initiate the onset of dementia, experience, that is, environmental stimuli, has been firmly identified as the molder of cognition and behavior in the process of learning and the instrument through which cognition and behavior can be changed. Positive learning (i.e., towards self-actualizing, productive, socially integrated behavior) yields positive neuroplasticity, the mechanism for positive change in conditions of cognitive and behavioral disorder, including dementia, building BCR, whereby the brain heals itself through an enriched environment, a demonstrated process by which dementia can be reversed.

Because of a combination of deficient and/or defective cognitive constructs and neurophysiological damage in the brain in dementia, more intensive positive stimulation than that of normal incidental learning or formalized learning through life choices is required to repair the brain, restore cognitive functioning and facilitate well-being due to the reduced capacity of the brain in dementia. "... in normal incidental learning vs. relearning after brain injury or disease, the cognitive processes and neurological mechanisms don't change but the conditions of change do, often dramatically, because of the differences in both brain reserve and cognitive reserve [BCR] prior to and after brain injury, disease or psychological imbalance" (Kleim, 2011, p. 523 – insertion in brackets added). This more intensive stimulation is generated in a holistic, fun, entertaining, sustained, socially connected, motivating, encouraging, challenging and highly supportive learning environment, referred to as the enriched environment.

The key to an effective enriched environment is constancy, whereby the enriched environment is always available, a stable component of the community, readily incorporated as an integral element of an individual's lifestyle. Continued exposure to the enriched environment has been demonstrated to be essential to the maintenance and ongoing improvement of cognitive, physical and social functioning and well-being of the individual in recovery from brain damage. "... a lack or an absence of EE [environmental enrichment] is linked to cognitive decline post-injury, demonstrating the importance of continued exposure to EE in the post-discharge stages after brain injury" (Alwis & Rajan, 2014, p. 11, citing Till, Colella, Verwegen, & Green, 2008; Frasca, Tomaszczyk, McFaden, & Green, 2013 insertion in brackets added). "A reduction in enrichment in the post-acute period could be detrimental to recovery as studies have shown that functions gained during stimulation of neural pathways (such as during rehabilitation) can be lost through under-use" (Alwis & Rajan, 2014, pp. 11-12, citing Rubinov, McIntosh, Valenzuela, & Breakspear, 2009; Warraich & Kleim, 2010; Frasca, Tomaszczyk, McFaden, & Green, 2013). "Studies demonstrate continued and repeated EE exposure which provides intensive cognitive, social, and physical stimulation is necessary to induce beneficial effects (Frasca, Tomaszczyk, McFaden, & Green, 2013, p. 14, citing Blackerby, 1990; Spivack et al., 1992; De Weerdt et al., 2000; Schooler & Mulatu, 2001; Shiel et al., 2001; Zhu et al., 2001, 2007; Cifu et al., 2003; De Wit et al., 2005; Amaral et al., 2008; Willer et al., 1999; Cicerone et al., 2004).

Alwis & Rajan (2014, p. 11, citing Frasca, Tomaszczyk, McFaden, & Green, 2013) have pointed to vital factors that contribute to the provision of an appropriate level of enrichment, that include ease of access to activities and resources that are cognitively, physically and socially stimulating, as well as support that encourages participation and integration therewith; with Frasca et al. (2013) suggesting that post-discharge patients eventually need to return to remediation in an enriched environment, further emphasizing the importance of a well-being center as a readily accessible, intrinsic community resource for the provision of an ongoing, consistently structured, enriched environment leading to recovery from dementia and the promotion of self-actualization and a rich, full, active, socially engaged, independent, productive life in elderhood.

The model well-being center that is proposed herein, is one that fully understands and promotes the individual nature of true well-being through a dedicated person-centered approach fully integrated into and an inherent, principal orientation of Cognitive Neuroeducation (CNE). This model well-being center rigorously implements the CNE paradigm in an enriched environment constituting a holistic curriculum consisting of the following structural components:

____ The group dynamic

The CNE program is constructed in a group participation framework, each group consisting of 6 to 8 members by which social consciousness is internalized through learning derived from observation, discussion, reflection and continual feedback in participation in a wide

variety of activities that incorporate physical exercise, cognitive training, social interaction, cooperation, teamwork, and spiritual transcendence in forming more understanding and deeper connection with self, with others, with nature, and with the possibilities of the world which surrounds them.

The group environment provides a socializing experience in a nurturing, supportive, reassuring atmosphere in which anxiety and pressure to perform/participate and conform is minimized through a gentle orientation to the group process and a growing sense of belonging to and identifying with the group. In being included and expected to equally contribute her/his very own personal thoughts and perceptions to every part of the group process as an integral member of the group, each member begins to understand that every member of the group, including her/himself, is critical to the group, without which the group dynamic is substantively changed. Any sense of pressure or anxiety of fully participating in the group is gradually eliminated as each member visualizes her/himself a part of the working group, and her/his input and participation is not distinct from the group and not judged by it or its rules, but rather an inextricable component of the group, its process, its rules and its unique dynamic.

___ Perspective taking

Through the group process each group member practices giving support and acting empathetically in learning to understand someone else's feelings in different situations within the 'living theatre' of the group with its different members, personalities and personal problems – learning through instruction, experiences, interacting, cooperation, teamwork, feedback, discussions and exchanges of opinions and the freeing up and development of each member's own affective responsiveness and by thinking through situations and contexts; learning not by strict rules, rote memory or conditioned behavior, but by the natural learning that characterizes the learning acquired by the experiences of living a normal life in the real world without the real-world threats and chaos that overwhelm those with cognitive deficits.

_ Social context appraisal

The CNE group dynamic does not indoctrinate or impose a rigid prescription of social behavior, but sets an example of social decorum through which sensitivity to and understanding of social context, individual perspective, and an individual's affective state is formed, whereby the basic tenets of social behavior are internalized and logically applied to the myriad contexts of real-world social interaction. In the group process each member practices verbalizing and expressing clear thinking and observes and learns from the other group members who variously succeed or fail in their responses. Group members are acknowledged for their successes and supported and encouraged when struggling. The group experience provides a nonthreatening venue to acquire and strengthen basic abilities essential for fluid social integration, such as how to make and complete an intelligible statement, how to ask questions or give one's opinion appropriately and sensitively, how to agree and tactfully disagree, and how to become an active and attentive listener. All group activities are designed to 1) keep the group members focused on the tasks required by the activity; 2) instruct and reinforce how to give and receive constructive feedback; 3) emphasize cooperation and team effort; 4) recognize the value of each group member's unique input; 5) compensate for and empathize with the difficulties that a team member may be experiencing in their personal life that may be affecting their participation in a group activity; and 6) continually encourage and support individual participation and team effort.

____ Affective engagement

In order to understand either the nuance of a social context or another's emotional state in relation to a particular social context, it is necessary for one to consistently experience one's own emotional responsiveness appropriate to a particular social context and one's own individual circumstances. A lack of affect is no less self-destructive and socially disruptive than uncontrolled, inappropriate emotional outbursts. Bonding is an inherent component of a number of critical pseudo-fixed action patterns that form our basic evolutionarily defined human core behavior, but without an appropriate emotional attachment, bonding, indispensable to human social cohesiveness, is inhibited. Bonding is essential to spiritual transcendence, a basic quality that defines us as human.

In CNE, emotional responsiveness is fostered by the group dynamic, whereby, through teamwork, cooperation, interdependence and self-reflection in the sharing of successes, disappointments, failures, and accomplishments in group activities and the growing involvement in each's lives through such interdependence and closeness of association, the group members become part of each other's experience in the group dynamic, each group member evolving genuine thinking and feeling, gaining sensitivity and a true empathy with others, a deeper, more balanced understanding of her/himself and a more appropriate, self-fulfilling, affective engagement with life.

Spiritual transcendence

Spirituality is an inherent component of emotion, intellect and reason – the essential components of cognition. This may be understood from an evolutionary perspective in the recognition that spirituality evolved as the vehicle driving the uniquely human social brain's orientation towards cooperative behavior through the dual impulse of 1) commonality, community, connectedness - the basic urge of transcendence, to go beyond the confines of self to connect with others, to bond, identify with and feel part of a group and of a larger wholeness, to connect with all that there is; and 2) curiosity and reason - the striving to know and to understand, to delve into the deeper mysteries of life, to get closer to the truth of existence and the origin of all things. These dual impulses of transcendence, that combine connectedness and inquisitiveness working together in the yearning of belonging, of sharing, of purpose, of meaning – propel the quest of the intellect and reason to understand what it means to be alive, to be human. Spirituality constitutes that core of being that defines us as both human and each of us as a distinct, individual psyche that belongs to and is part of the very fabric of the world in which all life and all manifestations of nature are interwoven while simultaneously constituting our individual uniqueness and the need to define our individual, unique, special place within the universality of existence.

Spiritual transcendence is embedded in the CNE curriculum focusing on learning as the mechanism for the remediation of and recovery from dementia and aging-related cognitive decline, and sees the accumulation of learning, that is, knowledge itself, as composed of relative truths, as all things may be understood from many different starting points, frames of reference and personal perspectives. Being relative does not make these 'truths' any less real to the frames of reference in which they reside. The full recognition of this relativity leads to the undeniable, stirring realization that there are so many more, endless things to discover, so many more, endless ways by which to view all phenomena, so many more, endless ways to think about life and all its mysteries and so many more, endless contributions to knowledge waiting for eager, imaginative, curious, probing, questioning minds to reveal.

The CNE activities, related materials and group dialog explore the different realms of understanding and knowledge from the widest possible perspectives, stimulating each of the group members with the awe of the vast potentials of discovery, of endless paths on the journey through life, and the eager anticipation of the possibilities waiting beyond the bend in the road on the great adventure of being. While invisible to the CNE group members, this exploration seamlessly blends hermeneutic techniques and exegetic principles in the group dialogs and interchanges between the group members in questioning, probing and debating in the quest for understanding the various scenarios, situations and responses encountered in the group activities, thus realizing the many considerations, nuances and different sides that may reside in any question. We live within our mind and the journey of life continues on in elderhood through a healthy, active mind and an environment arousing our innate curiosity and deep human need to communicate, share experiences, exchange ideas, work through challenges and involve ourselves with others.

___ Person-centered approach

CNE, an activities-based, social-integration-oriented modality for the prevention of and recovery from dementia and associated comorbidities, signifies a major breakthrough in understanding and addressing the causes of cognitive decline and behavioral disorganization. In identifying the basic principles of brain-mind-behavior interaction, the CNE framework applies these principles to broadly stimulate and exercise the brain to rebuild BCR (brain and cognitive reserve) as a neuroprotective shield and renew or expand cognitive acuity in reclaiming or discovering one's selfhood and one's social instincts in engagement with others and one's environment.

The CNE curriculum, unique among all behavioral modalities and cognitive rehabilitation programs, focuses on a person-centered enriched environment of highly eclectic learning and bonding activities in a cohesive group dynamic that promotes high cognitive functionality with emotionally compelling social engagement that emphasizes group interaction and teamwork; individual responsibility; perspective taking; social context appraisal; empathetic, attentive listening; constructive feedback; individual initiative, facilitation of the voice of the individual, and the confirmation of self. Throughout all the CNE activities, special attention is placed on the facilitation of the voice of the individual in interaction within a mutually defined group dialog, stressing individuality and personal growth through fluid social integration.

Humankind has survived by its tendency to create and live in a social environment, a society consisting of specific cultural and social norms and structures. Due to this behavioral imperative, individual survival has become dependent on the skills to negotiate social interaction and the demands of whatever society that constitutes the environment that one must interact with to meet the basic requirements of life. Beyond pure physical survival, the human being is a psychologically complex being that requires some interaction with other human beings to meet basic psychological needs. We are defined as individuals, as unique personalities, by the psychological needs unique to each individual, and the unique manner by which each individual interacts with society (that is, with other humans within culturally determined rules and norms) to meet those needs. We are social animals and the way we interact socially defines who we are as unique individuals, that is, who each of us is as a discrete persona that is distinguished from every other person now living, that ever lived, or ever will live. Our personality, our uniqueness as an individual, is manifested through, by and within our social consciousness. We discover ourselves and become who we are though our social interactions. These essential social interactions are remolded and reconstructed after

brain damage in dementia through the CNE group dynamic, recapturing the unique voice of the individuality of the inner self though the development of connections and interrelationships with others.

___ Intergenerational programing

The CNE cohesive group dynamic provides a ready framework for intergenerational programing through its highly flexible curriculum and group structure, expanding the social network of the CNE program participants. Hamilton & Brown et al., in their 1999 study, reported that it had been demonstrated that well-designed contact between people from the broader community and senior citizens (especially those in recovery from dementia and aging-related cognitive decline) contributes to the psychological well-being and physical health of the senior citizens, citing Chamberlain, Fetterman, & Maher, 1994; Lambert, Dellmann-Jenkins, & Fruit, 1990; Newman, Lyons, & Onawola, 1985; Ward, Kamp, & Newman, 1996. "There are also potential educational and attitudinal benefits for those from the [broader] community who visit [elder centers], particularly young people. As early as 1975, the U.S. government sponsored programs that involved transporting senior citizens to schools in order that they might participate in classroom activities. Research has attempted to describe guidelines for successful intergenerational programs. These guidelines include intimate rather than casual contact (Amir, 1969); predictable, scheduled visits (Schulz, 1976): mutually rewarding, cooperative activities [emphasis added] rather than 'performances' by the children (Seefeldt, 1987); integration into the school curriculum (McCollum & Shreeve, 1994); and careful preparation of all participants (Griff, Lambert, Dellmann-Jenkins, & Fruit, 1996)" [Hamilton & Brown et al., 1999, p. 235 - insertions in brackets added].

In their 1999 paper, Hamilton & Brown et al. describe how planned, coordinated and regularly scheduled and more enduring intergenerational contact resulted in both increased health and a new "zest for life" for elder long-term care residents. While this 1999 paper and the studies it references focus on contact between young children and elders, the benefits of intergenerational interaction for elders has been well known for years and more recently great attention has been directed at sustained contact between young adults and elders, for example, in such experiments as intergenerational living where a long-term care center doubles as a student dormitory (Jansen, 2015).

While the experiments reported by Jansen have been highly successful to-date, there still remains the lack of an integrated person-centered orientation dedicated to directly addressing cognitive decline and behavioral disorder in a stable, on-going, structured program of prevention and remediation. CNE fluidly solves this problem as well as perfectly matching the general guidelines for successful, efficacious intergenerational programming as suggested in the Hamilton and Brown et al. 1999 paper. The CNE curriculum, centered on an enriched environment and engaged through a cohesive group dynamic, combines the constancy of a well-formulated structural base with an enormous flexibility in curriculum content and procedural arrangement designed for tailoring to specific circumstances. The basic CNE structure consists of placing CNE program participants in stable groups of 6-8 individuals who interact interdependently in a group dynamic in a prescribed schedule of specific activities and learning situations.

It is in this group dynamic that participants learn to value each other's input as well as their own – where success in learning and accomplishing tasks, and engagement and enjoyment of the moment are products of group and individual effort, leading to growth of the individual and the group, to self-confirmation, bonding with others, identification with the group and

sense of belonging. It is these interactions in the group dynamic in an on-going CNE program that, paraphrasing the guidelines stated in Hamilton and Brown et al. 1999, provide "intimate rather than casual contact," "predictable, scheduled interaction," "mutually rewarding, cooperative activities," "integration within an ongoing curriculum" and "careful preparation of all participants," the latter as an inherent component of the CNE group structure and its dependence on the cooperation, constructive feedback and planning that constitutes teamwork.

Taking full advantage of the flexibility built onto the CNE framework, CNE group activities can be tailored to include individuals from the surrounding community as group participants. Participants from the broader community may include a wide range of ages, with the group dynamic and activities tailored to specific situations, such as an orientation whereby the elders in a group that includes a child or children act as mentors for specific activities within the group or, in a dynamic that emphasizes bonding, the elders, both helping and needing help in paired activities, relate to the children as surrogate grandparents, or, in groups that include young adults from the broader community, mentor roles are switched between the young adults and the elders in activities that take advantage of the particular abilities and knowledge of the individual members in the respective age group. Group composition can be periodically varied in different activities to give both the elders and participants from the broader community a rich range of experience in wider opportunities for social networking and interpersonal interactions, bringing youth, elders and the community-at-large together in closer and more enduring, meaningful and mutually rewarding interaction, changing community attitudes and fostering respect and a genuine fondness in growing relationships with elders.

_ Physical exercise

Physical exercise has been demonstrated to play a major role in both cognitive and physical rehabilitation and has long been considered an instrumental component of the enriched environment as reported in a vast corpus of studies (see the Appendix at the end of this document). In particular, physical exercise has been shown to both reduce the risk of dementia and a vital aid in recovery therefrom, as well as in the restoration and maintenance of general health (Vidoni, Van Sciver, Johnson, He, Honea, Haines, Goodwin, Laubinger, Anderson, Kluding, Donnelly, Billinger, & Burns, 2012; Lange-Asschenfeldt & Kojda, 2008; Trigiani & Hamel, 2017; Pérez & Carral, 2008; Ahlskog, Geda, Graff-Radford, & Petersen, 2011; Cancela, Ayán, Varela, & Seijo, 2016; Arkin, 1999; Christofoletti, Oliani, Bucken-Gobbi, Gobbi, Beinotti, & Stella, 2011; Voss, Nagamatsu, Liu-Ambrose, & Kramer, 2011; Groot, Hooghiemstra, Raijmakers, van Berckel, Scheltens, Scherder, van der Flier, & Ossenkoppele, 2016; Hernández, Sandreschi, F. C. da Silva, Arancibia, R. da Silva, Gutierres, & Andrade, 2015; Ahlskog, 2011.

To improve the health and physical vitality of each CNE program participant, in conjunction with the physical exercise inherent in many of the CNE activities, the CNE curriculum, rigorously following geriatric exercise guidelines, incorporates a regularly scheduled routine of structured physical exercises tailored to the mobility, physical and health condition of the individual (taking into account frailty associated with age and disease); the exercises graduated in intensity, duration and range of movement in accordance with an individuals' progress in fitness (endurance and strength), balance, flexibility, and motor coordination. Vital signs, including heart rate, blood pressure, respiration rate, temperature and peripheral blood oxygen saturation level (SpO₂), are monitored before and after each scheduled exercise session and other physical activity to ensure safe physiological stability.

___Cognitive training, physical exercise and monitoring e-AHA system To provide an extra dimension to the CNE program, it is envisioned that an e-AHA system (electronic active and healthy aging system) be designed as a fluidly and seamlessly embedded adjunct and support for the basic components within the CNE curriculum, providing extrinsic feedback in knowledge of performance (KP) and knowledge of result (KR) in real-time display and as an automatic record for each individual participant. It is envisioned that this system incorporates virtual reality (VR), artificial intelligence (AI), advanced non-contact sensing (including motion sensing, environmental sensing, positioning sensing and physiological sensing) and interactive gaming technology in a fully integrated design. Physiological sensing would consist of real-time monitoring of vital signs including heart rate, blood pressure, respiration rate, temperature and blood oxygen saturation level, maintaining an automatic record of the vital signs of each participant and an automatic alarm if any vital sign exceeds a safe level.

Such a system would be based on a control and monitoring platform that contained all the basic hardware and firmware ('firmware' referring to embedded microcontroller coding and other system software) components in a single integrated unit with an open, fully supporting SDK (software development kit) for a standardized, more efficient and flexible application development environment in plug-and-play implementation. Though recently a number of 3D AI-driven VR motion sensor control units with many interesting features and supporting SDKs have become available, the Microsoft Kinect system is used herein as a model of the development platform capabilities and features conducive to the development of the proposed e-AHA system.

The Microsoft Kinect platform base has morphed over the years from Kinect for Xbox 360 (2010), Kinect for Xbox One (2013), Kinect 2 for Windows (2014), to Azure Kinect (2019). Kinect for Xbox 360 featured a range-imaging chipset in a depth-sensing system that included an infrared projector and camera and a specialized microchip that generated a grid from which the location of a nearby object can be generated in three dimensions. The depth-sensing system interacted with a microphone array running proprietary software, which provided full-body motion capture and advanced gesture recognition, facial recognition and voice recognition (English only). The embedded software automatically calibrated the depth sensor based on gameplay and the player's physical environment, accommodating for the presence of furniture or other obstacles. Kinect for Xbox 360 could simultaneously track up to six people (2 as active game players), and could extract 20 joints (pivotal points of motion) per active player in motion sensing.

The Kinect for Windows platform upgraded the hardware for better performance and featured an SDK for commercial development that included Windows 7 compatible drivers and programing in C++, C# and Visual Basic using Microsoft Visual Studio 2010. A new app, 'Kinect Studio,' allowed developers to record, playback and debug clips of users interacting with applications. Kinect for Windows also included a seated 10-joint skeletal system that would enable apps to track the head, neck and arms of a Kinect user whether they are sitting down or standing. Other new features in the Kinect for Windows platform included four new languages for speech recognition: French, Spanish, Italian and Japanese, and supported regional dialects of those languages as well as for English. The commercial SDK Kinect for Windows came with documentation and sample code. The Kinect for Xbox One platform represented a major upgrade to the Kinect system's capabilities. Incorporating a time-of-flight camera and a 2-gigabit-data-per-second steam of environmental scanning, this new Kinect had three times the fidelity of its predecessor, capable of tracking without light using an active infrared sensor with a 60% wider field of vision. Tracking up to six individuals at once, the Kinect for Xbox One platform could detect a player's heart rate, facial expression, the position and orientation of up to 25 individual joints (pivotal points of motion), including thumbs, end-of-hand and open and closed hand gestures, and could further detect the weight put on each limb and the speed of player movements, and could track gestures performed with a standard controller.

In further iterations, the Kinect 2 for Windows platform was nearly identical to the Kinect for Xbox One platform in capabilities, but designed to work with the Windows operating system rather than the Xbox game engine. It featured an updated 2.0 version of the Windows SDK. The final, currently available iteration, 'Azure Kinect,' is aimed primarily at AI applications development and is designed around the Microsoft Azure cloud service and the Microsoft Azure AI technology. The Azure Kinect platform features a 12-megapixel camera, a time-of-flight depth sensor and a seven-microphone array. It is supported by an open SDK.

Examining both the technology and the features of the Kinect system through its iterations allows a useful comparison in the search for a currently available state-of-the-art development platform offering the greatest support and the highest compatibility with the proposed e-AHA system's functional and performance requirements.

SUMMARY

This proposal lays out the critical need to systematically and most effectively address our rapidly aging society and the attendant special needs of the elder population regarding mental and physical health and daily care, that, coupled with a low birth rate that is particularly problematic in Japan, puts extreme pressure on the productivity of Japan's rapidly shrinking labor force and on the country's healthcare system, economic viability and societal infrastructure, which, without the implementation of a solution now, could all reach an absolute breaking point in twenty to thirty years. Any proposed solution that is to have any real effect must focus on the prevention of and recovery from dementia, the single most prevalent and incapacitating disorder affecting the elder population.

Though there have been many programs and clinical centers initiated through the years that have claimed to address dementia, these have all focused exclusively on symptoms using drugs and psychotherapy, the former, often prescribed off-label, have been helpful in suppressing serious symptoms for a short period up to a maximum of 6 months, but have also caused serious side effects, acute cognitive decline and a high risk of mortality, especially in long-term usage where they have been totally ineffective in symptom suppression. Psychotherapy has had almost no positive effect on dementia, and, in a number of incidences, has had a disturbing influence, exacerbating responsive behavior and BPSD (behavioral and psychological symptoms of dementia), with the individual under therapy acting out intensified frustration due to the therapy's attempt to impose behaviors that are the very basis of the individual's unmet psychological needs beyond the individual's environment to satisfy.

The failure of the approach focusing on symptoms (i.e., the medical model) is a result of the total disregard of the very basic neurophysiological mechanisms of cognitive orientation that lead to dementia onset and dementia recovery and the influence of the environment in

mediating those mechanisms, by which the brain, in the development of BCR through proper environmental stimulation, is able to naturally heal itself and the health conditions that are frequently associated with dementia.

The Dementia Policy in Japan, a component of the Japan Health Policy NOW (JHPN) created by the Health and Global Policy Institute (HGPI), critically recognizes that "there are no drugs for directly treating the primary diseases causing dementia such as Alzheimer's disease. The development of new drugs alone, however, is insufficient" (http://japanhpn.org/en/dementia/). The JHPN Dementia Policy in Japan, citing 'The Future Direction of Dementia Measures' by the Japan Ministry of Health, Labour and Welfare (MHLW), specifies the urgent need of a dramatic culture change to rebuild society "so that the rights of people with dementia are respected and so that those people can continue living in familiar spaces and communities" whereby an essential goal must be "to encourage efforts to research the promotion of such a policy" (http://www.mhlw.go.jp/stf/shingi/2r9852000002fv2e-att/2r9852000002fv5j.pdf). In January 2015, at the Global Dementia Legacy Event Japan, an evolving 10-year plan referred to as the 'New Orange Plan' was announced implementing such a policy. The New Orange Plan called for "the development of dementia-friendly communities" that improve "the living environments of people with dementia" and further calls for the establishment of 500 medical centers for dementia across the country by 2020 [Health and Global Policy Institute (HGPI), 2019].

Unfortunately, the call for 'medical' centers for dementia, especially those established in hospital and clinical settings staffed by medical doctors, directly refutes the Dementia Policy in Japan's own forthright recognition that "there are no drugs for directly treating the primary diseases causing dementia such as Alzheimer's disease. The development of new drugs alone, however, is insufficient." The promotion of medical centers for dementia totally ignores the clearly documented fact that the medical model, i.e., symptoms-based therapy (drugs and psychotherapy), is highly limited at best, and too often harmful and even fatal to the elder with dementia. The focus on medical treatment for dementia dismisses the Japan Ministry of Health, Labour and Welfare's and the Dementia Policy in Japan's own acknowledgements of the critical need for a dramatic, pervasive culture change, whereby the elder and the individual with dementia, rather than such a person being considered by medical practitioners as a pathology rather than as a unique individual with unique needs, or considered by the community as a useless castoff of society, a new frame of mind must emerge that fully recognizes the central importance of both respect for the elder and a committed community support of the autonomy, quality and improvements of the living environments of people with dementia – a culture change ushering in the dawning of a new, enlightened understanding that the quality of life and the well-being and functional level of the individual heavily depend on the degree of nurturance of the environment in which a person lives, and that the lives of elders and people with dementia very much matter. With the support of the community and the respect, concern and encouragement of the society-at-large, these lives, with their long years of varied and rich experiences and learned skills, can be saved and restored as useful, competent, responsible citizens making a vital contribution to the health, cohesion, vibrancy and productivity of the local community and the society as a whole.

What is urgently needed is not medical centers for dementia but instead person-centered wellbeing centers that foster self-healing through the renewal and growth of the elder and the individual with dementia toward self-actualization according to each's individual needs as developed within a supporting, nurturing, stimulating, enriched environment. The efficacy of the enriched environment in cognitive and physical rehabilitation has been thoroughly vetted through a vast corpus of studies in over 70 years of research from 1947 to the present (refer to the Appendix at the end of this document for a representative sampling of this extensive corpus of studies). It is time to employ the full potential of the enriched environment to meet the urgent need to combat the devastation of dementia. The goal of these proposed well-being centers is to restore a large percentage of the disabled elders to full self-sufficiency in the instrumental activities of daily life (IADL) and even employability, making a critical contribution to the labor force and productivity of the country, and a major easing of the pressure on each community's healthcare facilities and societal infrastructure. The avenue through which the efficacy of a stable, consistently structured, enriched environment can be most flexibly and powerfully implemented is within the person-centered, neuroscience-informed modality of Cognitive Neuroeducation (CNE) as previously defined above.

The first step in this direction is the proposed pilot well-being center based on the CNE principles and curriculum of activities. This pilot well-being center will provide an opportunity for rigorous assessment of the CNE well-being model's efficacy in the recovery from dementia and its attendant comorbidities, and if its efficacy is clearly demonstrated, the pilot center will constitute a successful model to follow for future centers to be established across Japan. As a successful model, the proposed well-being center will also function as a training center for CNE program facilitators, training highly qualified dementia recovery facilitators, not "dementia supporters" as labeled in the New Orange Plan along the failed lines of the medical concept of dementia viewed narrowly and wrongly as an incurable pathology, but instead focusing training on the vetted understanding that dementia, like other cognitive and behavioral disorders, is a problem of cognitive skewing, and through this new understanding, teach the basic neurophysiological mechanisms of cognitive orientation that lead to dementia onset and dementia recovery and the influence of the environment in mediating those mechanisms, by which the brain, through proper environmental stimulation, is able to naturally heal itself and the health conditions that are frequently associated with dementia. In this training, participants learn the tested and proven concepts and techniques used to create an effective enriched environment for cognitive and physical rehabilitation, turning out knowledgeable and skilled dementia educators and recovery facilitators to meet the New Orange Plan's call for a professional training program proposed in HGPI 2019, section 1.2, training, rather than 'dementia support' caregivers, a workforce of competent professionals certified in the facilitation of actual dementia recovery.

> We have the means to conquer dementia, all that is needed is the commitment to properly employ them.

_____ Spencer M. Robinson

REFERENCES

- Adolphs, R. (2009). The social brain: Neural basis of social knowledge. *Annual Review of Psychology*, *60*, 693-716. <u>https://core.ac.uk/reader/4880820</u>.
- Ahlskog, J. E. (2011). Does vigorous exercise have a neuroprotective effect in Parkinson disease? *Neurology*, 77(3), 288-294. doi: 10.1212/WNL.0b013e318225ab66.
- Ahlskog, J. E., Geda, Y. E., Graff-Radford, N. R., & Petersen, R. C. (2011). Physical exercise as a preventive or disease-modifying treatment of dementia and brain aging. *Mayo Clinic Proceedings*, 86(9), 876-884. doi: 10.4065/mcp.2011.0252.
- Aimone, J. B., Wiles, J., & Gage, F. H. (2006). Potential role for adult neurogenesis in the encoding of time in new memories. *Nature Neuroscience*, 9(6), 723-727. doi: 10.1038/nn1707.
- Alwis, D. S., & Rajan, R. (2014). Environmental enrichment and the sensory brain: The role of enrichment in remediating brain injury. *Frontiers in Systems Neuroscience*, 8 (Article 156). doi: 10.3389/fnsys.2014.00156.
- Alzheimer's Association. (n.d.). Alzheimer's and Dementia in Japan. *alz.org/japan*. Alzheimer's and Dementia Resources. https://www.alz.org/jp/dementia-alzheimers-japan.asp.
- Amaral, O. B., Vargas, R. S., Hansel, G., Izquierdo, I., & Souza, D. O. (2008). Duration of environmental enrichment influences the magnitude and persistence of its behavioral effects on mice. *Physiology and Behavior*, 93(1-2), 388-394. doi: 10.1016/j.physbeh.2007.09.009.
- American Psychiatric Association (APA). (2013). *Diagnostic and statistical manual of mental disorders, fifth edition* (DSM-5). Arlington, VA: American Psychiatric Association.
- _____. (2015). *Understanding mental disorders: Your guide to DSM-5*. Arlington, VA: American Psychiatric Publishing.
- Amir, Y. (1969). Contact hypothesis in ethnic relations. *Psychological Bulletin*, 71(5), 319-342. doi: 10.1037/h0027352.
- Arkin, S. M. (1999). Elder rehab: A student-supervised exercise program for Alzheimer's patients. *The Gerontologist*, *39*(6), 729-735. doi: 10.1093/geront/39.6.729.
- Azermai, M. (2015). Dealing with behavioral and psychological symptoms of dementia: A general overview. *Psychology Research and Behavior Management*, 8, 181–185. doi: 10.2147/PRBM.S44775.
- Bain, M. (2019). Japan's births dropped below 900,000 in 2019, a record low. *Quartz*, December 24. <u>https://qz.com/1774763/japans-births-drop-below-900000-in-2019-a-record-low/</u>.
- Ballard, C., & Howard, R. (2006). Neuroleptic drugs in dementia: Benefits and harm. *Nature Reviews Neuroscience*, 7(6), 492-500. doi: 10.1038/nrn1926.
- Bengtsson, S. L., Nagy, Z., Skare, S., Forsman, L., Forssberg, H., & Ullén, F. (2005). Extensive piano practicing has regionally specific effects on white matter development. *Nature Neuroscience*, 8(9), 1148-1150. doi: 10.1038/nn1516. <u>https://www.nature.com/articles/nn1516</u>.
- Bhanji, J. P., & Delgado, M. R. (2014). The social brain and reward: Social information processing in the human striatum. WIREs Cognitive Science, 5(1)), 61-73 (WIREs = Wiley Interdisciplinary Reviews). <u>http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.724.7182&rep=rep1&type=pdf</u>.
- Blackerby, W. F. (1990). Intensity of rehabilitation and length of stay. *Brain Injury*, *4*(2), 167-173. doi: 10.3109/02699059009026162.

- Blakemore, S-J. (2008). The social brain in adolescence. *Nature Reviews Neuroscience*, 9(4), 267-277. doi: 10.1038/nrn2353.
 - ____. (2010). The developing social brain: Implications for education. *Neuron*, 65(6), 744-747. doi: 10.1016/j.neuron.2010.03.004.
- Blass, J. P. (2003). Dementias including Alzheimer's disease. In W. R. Hazzard, J. P. Blass, J. B. Halter, J. G. Ouslander, & M. E. Tinetti (Eds.), *Principles of Geriatric Medicine* and Gerontology, 5th ed. (pp. 1391-1400). New York: McGraw-Hill.
- Bliss, T. V. P., & Collingridge, G. L. (1993). A synaptic model of memory: Long-term potentiation in the hippocampus. *Nature*, *361*(6407), 31-39. doi: 10.1038/361031a0.
- Bliss, T. V. P., & Lømo, T. (1973). Long-lasting potentiation of synaptic transmission in the dentate area of the anaesthetized rabbit following stimulation of the performant path. *The Journal of Physiology*, 232(2), 331-356. doi: 10.1113/jphysiol.1973.sp010273.
- Brüne, M., Ribbert, H., & Schiefenhövel, W. (Eds.). (2003). *The social brain: Evolution and pathology*. Chichester, West Sussex, England: Wiley.
- Bullock, R. (2005). Treatment of behavioural and psychiatric symptoms in dementia: Implications of recent safety warnings. *Current Medical Research and Opinion*, 21(1), 1-10. doi: 10.1185/030079904x16777.
- Bunn, F., Burn, A-M., Goodman, C., Rait, G., Norton, S., Robinson, L., Schoeman, J., & Brayne, C. 2014). Comorbidity and dementia: A scoping review of the literature. *BMC Medicine*, *12*, 192. https://uhra.herts.ac.uk/bitstream/handle/2299/14916/906951.pdf?sequence=2.
- Cacioppo, J. T., Amaral, D. G., Blanchard, J. J., Cameron, J. L., Carter, C. S., Crews, D.,
 Fiske, S., Heatherton, T., Johnson, M. K., Kozak, M. J., Levenson, R. W., Lord, C.,
 Miller, E. K., Ochsner, K., Raichle, M. E., Shea, M. T., Taylor, S. E., Young, L. J., &
 Quinn, K. J. (2007). Social neuroscience: Progress and implications for mental health. *Perspectives on Psychological Science*, 2(2), 99-123. doi: 10.1111/j.1745-6916.2007.00032.x.
- Cacioppo, J. T., & Berntson, G. G. (1992). Social psychological contributions to the decade of the brain: Doctrine of multilevel analysis. *American Psychologist*, 47(8), 1019-1028. doi: 10.1037/0003-066X.47.8.1019.
- Cacioppo, J. T., Berntson, G. G., & Decety, J. (2010). Social neuroscience and its relationship to social psychology. *Social Cognition*, 28(6), 675-685. https://guilfordjournals.com/doi/pdfplus/10.1521/soco.2010.28.6.675,
- Cacioppo, J. T., & Decety, J. (2011). Social neuroscience: Challenges and opportunities in the study of complex behavior. *Annals of the New York Academy of Sciences*, 1224(1), 162-173. https://doi: 10.1111/j.1749-6632.2010.05858.x.
- Callahan, C. M., & Schubert, C. C. (2014). The complexities of comorbidity in dementia. *Nature Reviews Neurology*, *10*(4), 184-186. doi: 10.1038/nrneurol.2014.46.
- Cancela, J. M., Ayán, C., Varela, S., & Seijo, M, (2016). Effects of a long-term aerobic exercise intervention on institutionalized patients with dementia. *Journal of Science and Medicine in Sport*, *19*(4), 293-298. <u>https://doi.org/10.1016/j.jsams.2015.05.007</u>.
- Chamberlain, V. M., Fetterman, E., & Maher, M. (1994). Innovation in elder and child care: An intergenerational experience. *Educational Gerontology*, 20(2), 193-204. <u>https://doi.org/10.1080/0360127940200208</u>.

- Christofoletti, G., Oliani, M. M., Bucken-Gobbi, L. T., Gobbi, S., Beinotti, F., & Stella, F. (2011). Physical activity attenuates neuropsychiatric disturbances and caregiver burden in patients with dementia. *Clinics*, 66(4), 613-618. doi: 10.1590/S1807-59322011000400015.
- Cicerone, K. D., Mott, T., Azulay, J., & Friel, J. C. (2004). Community integration and satisfaction with functioning after intensive cognitive rehabilitation for traumatic brain injury. *Archives of Physical Medicine and Rehabilitation*, 85(6), 943-950. doi: 10.1016/j.apmr.2003.07.019.
- Cifu, D. X., Kreutzer, J. S., Kolakowsky-Hayner, S. A., Marwitz, J. H., & Englander, J. (2003). The relationship between therapy intensity and rehabilitative outcomes after traumatic brain injury: A multicenter analysis. *Archives of Physical Medicine and Rehabilitation*, 84(10), 1441-1448. doi: 10.1016/S0003-9993(03)00272-7.
- Comery, T. A., Shah, R., & Greenough, W. T. (1995). Differential rearing alters spine density on medium-sized spiny neurons in the rat corpus striatum: Evidence for association of morphological plasticity with early response gene expression. *Neurobiology of Learning and Memory*, 63(3), 217-219. doi: 10.1006/nlme.1995.1025.
- Corrigan, P. W., & Penn, D. L. (Eds.) (2001). Social cognition and schizophrenia. Washington, DC: American Psychological Association. http://dx.doi.org/10.1037/10407-000.
- Cozolino, L. J. (2006). *The neuroscience of human relationships: Attachment and the developing social brain*. New York and London: W. W. Norton.
- De Weerdt, W., Selz, B., Nuyens, G., Staes, F., Swinnen, D., Van De Winckel, A., Nieuwboer, A., Lysens, R., & Feys, H. (2000). Time use of stroke patients in an intensive rehabilitation unit: A comparison between a Belgian and a Swiss setting. *Disability and Rehabilitation*, 22(4), 181-186. doi: 10.1080/096382800296872.
- De Witt, L., Putman, K., Dejaeger, E., Baert, I., Berman, P., Bogaerts, K., Brinkman, N., Connell, L., Feys, H., Jenni, W., Kaske, C., Lasaffre, E., Leys, M., Lincoln, N., Louckx, F., Schuback, B., Schupp, W., Smith, B., & De Weerdt, W. (2005). Use of time by stroke patients: A comparison of four European rehabilitation centers. *Stroke*, 36(9), 1977-1983. doi: 10.1161/01.STR.0000177871.59003.e3.
- Di Fabio, A. (2015). Beyond fluid intelligence and personality traits in social support: The role of ability based emotional intelligence. *Frontiers in Psychology*, 6(395). doi: 10.3389/fpsyg.2015.00395.

https://pdfs.semanticscholar.org/c331/ed85dfb972aae789f40f29bd28aaa8c0a6c9.pdf.

- Draganski, B., & May, A. (2008). Training-induced structural changes in the adult human brain. *Behavioural Brain Research*, *192*(1), 137-142. doi: 10.1016/j.bbr.2008.02.015.
- Dudas, R., Malouf, R., McCleery, J., & Dening, T. (2018). Antidepressants for treating depression in dementia. *Cochrane Database of Systematic Reviews*, 8 (Article CD003944). doi: 10.1002/14651858.CD003944.pub2.
- Emmerling, R. J., Shanwal, V. K., & Mandal, M. K. (2008). *Emotional intelligence: Theoretical and cultural perspectives*. New York: Nova Science Publishers.
- Formiga, F., Fort, I., Robles, M. G., Barranco, E., Espinosa, M. C., Riu, S., Grupo de Trabajo de Demencia de la Sociedad Catalana de Geriatría y Gerontología. (2007).
 Medical comorbidity in elderly patients with dementia: Differences according to age and gender. *Revista Clínica Española*, 207(10), 495-500. doi: 10.1157/13111547.
- Frasca, D., Tomaszczyk, J., McFadyen, B. J., & Green, R. E. (2013). Traumatic brain injury and post-acute decline: What role does environmental enrichment play? A scoping review. *Frontiers in Human Neuroscience*, 7 (Article 31). doi: 10.3389/fnhum.2013.00031.

- Frith, U., & Frith, C. (2010). The social brain: Allowing humans to boldly go where no other species has been. *Philosophical Transactions of the Royal Society B*, 365(1537), 165-175.
- Fukawa, T. (2018). Prevalence of dementia among the elderly population in Japan. *Health* and Primary Care, 2(4), 1-6. <u>https://www.oatext.com/pdf/HPC-2-147.pdf</u>.
- Gaser, C., & Schlaug, G. (2003a). Brain structures differ between musicians and non-musicians. *The Journal of Neuroscience*, 23(27), 9240-9245.
 <u>http://www.jneurosci.org/content/23/27/9240.short</u>.
 (2003b). Gray matter differences between musicians and nonmusicians. *Annals of the*
- New York Academy of Sciences, 999, 514-517. http://dbm.neuro.uni-jena.de/pdf-files/Gaser-AnnNYAS.pdf.
- Griff, M., Lambert, D., Dellmann-Jenkins, M., & Fruit, D. (1996). Intergenerational activity analysis with three groups of older adults: Frail, community living, and Alzheimer's. *Educational Gerontology*, 22(6), 601-612. <u>https://doi.org/10.1080/0360127960220607</u>.
- Groot, C., Hooghiemstra, A. M., Raijmakers, P. G. H. M., van Berckel, B. N. M., Scheltens, P., Scherder, E. J. A., van der Flier, W. M., & Ossenkoppele, R. (2016). The effect of physical activity on cognitive function in patients with dementia: A meta-analysis of randomized control trials. *Aging Research Reviews*, 25, 13-23. doi: 10.1016/j.arr.2015.11.005.
- Grossman, T., & Johnson, M. H. (2007). The development of the social brain in human infancy. *European Journal of Neuroscience*, 25(4), 909-919. <u>http://uvababylab.org/wp-content/uploads/2016/04/25-22-page/GrossmannJohnson-Eur-J-Neurosci-2007.pdf</u>.
- Hamilton, G., Brown, S., Alonzo, T., Glover, M., Mersereau, Y., & Wilson, P. (1999). Building community for the long term: An intergenerational commitment. *The Gerontologist*, 39(2), 235-238. doi: 10.1093/geront/39.2.235.
- Hannan, A. J. (2014). Environmental enrichment and brain repair: Harnessing the therapeutic effects of cognitive stimulation and physical activity to enhance experience-dependent plasticity. *Neuropathology and Applied Neurobiology*, 40(1), 13-25. doi: 10.1111/nan.12102.
- Health and Global Policy Institute. (2019). *Dementia policy in Japan*. Japan Health Policy NOW, Health and Global Policy Institute (HGPI). <u>http://japanhpn.org/en/dementia/#:~:text=Dementia%20Policy%20in%20Japan&text=</u> <u>Early%2Donset%20dementia%20must%20also,alone%2C%20however%2C%20is%2</u> <u>Oinsufficient.</u>
- Hebb, D. O. (1947). The effects of early experience on problem-solving at maturity. *American Psychologist*, 2, 306-307.

(1949). *The organization of behavior*. New York: Wiley & Sons.

- Hernández, S. S. S., Sandreschi, P. F., da Silva, F. C., Arancibia, B. A. V., da Silva, R., Gutierres, P. J. B., & Andrade, A. (2015). What are the benefits of exercise for Alzheimer's disease? A systematic review of the past 10 years. *Journal of Aging and Physical Activity*, 23(4), 659-668. <u>http://dx.doi.org/10.1123/japa.2014-0180</u>.
- Hogarty, G. E., & Flesher, S. (1999). Practice principles of cognitive enhancement therapy for schizophrenia. *Schizophrenia Bulletin*, 25, 693-708.
- Huttenlocher, P. R. (1991). Dendritic and synaptic pathology in mental retardation. *Pediatric Neurology*, 7(2), 79-85.
- Hydén, H., & Lange, P. W. (1983). Modification of membrane-bound proteins of the hippocampus and entorhinal cortex by change in behavior in rats. *Journal of Neuroscience Research*, *9*(1), 37-46. doi: 10.1002/jnr.490090106.

- Insel, T. R., & Fernald, R. D. (2004). How the brain processes social information: Searching for the social brain. *Annual Review of Neuroscience*, *27*, 697-722. <u>https://pdfs.semanticscholar.org/78fb/5aaeeec644790c736f1dca4d34dd582ee41a.pdf</u>.
- Izard, C. E., Fine, S., Schultz, D., Mostow, A., Ackerman, B., & Youngstrom, E. (2001). Emotion knowledge as a predictor of social behavior and academic competence in children at risk. *Psychological Science*, 12(1), 18–23.
- Jansen, T. R. (2015). The nursing home that's also a dorm. *CityLab* online. Last accessed 06/04/2020. <u>https://www.citylab.com/equity/2015/10/the-nursing-home-thats-also-a-dorm/408424/</u>.
- Japan Data. (2018). Japan spends record ¥42.2 trillion on healthcare in 2017. *Nippon.com*, November 2. <u>https://www.nippon.com/en/features/h00319/japan-spends-record-%C2%A542-2-trillion-on-healthcare-in-2017.html</u>.
- . (2019). Growing medical woes: Japan's healthcare expenditures rise to record ¥42.6 trillion. *Nippon.com*, October 23. <u>https://www.nippon.com/en/japan-data/h00561/growing-medical-woes-japan%E2%80%99s-healthcare-expenditures-rise-to-record-%C2%A542-6-trillion.html</u>.
- Jin, M., Wang, X-M., Tu, Y., Zhang, X-H., Gao, X., Guo, N., Xie, Z., Zhao, G., Jing, N., Li, B-M., & Yu, L. (2005). The negative cell cycle regulator, Tob (transducer of ErbB-2), is a multifunctional protein involved in hippocampus-dependent learning and memory. *Neuroscience*, 131(3), 647-659. doi: 10.1016/j.neuroscience.2004.10.044.
- Kandel, E. R. (2001). The molecular biology of memory storage: A dialogue between genes and synapses. *Science*, 294(5544), 1030-1038. doi: 10.1126/science.1067020.
- Kaneda, T., Greenbaum, C., & Patierno, K. (2019). 2019 world population data sheet. Washington, DC: Population Reference Bureau.
- Kazawa, K., Iwamoto, S., Rahman, M. M., & Moriyama, M. (2017). Health resource utilization and comorbidities in patients with mental disorders: Analysis based on health insurance claim data. *Health*, 9(4), 763-777. <u>https://file.scirp.org/pdf/Health_2017050514104914.pdf</u>
- Keefer, K. V., Parker, J. D. A., & Saklofske, D. H. (2009). Emotional intelligence and physical health. In C. Stough, D. H. Saklofske, & J. D. A. Parker (Eds.), Assessing emotional intelligence: Theory, research, and applications (pp. 191-218). New York: Springer.
- Kelly, M. E., Loughrey, D., Lawlor, B. A., Robertson, I. H., Walsh, C., & Brennan, S. (2014). The impact of cognitive training and mental stimulation on cognitive and everyday functioning of healthy older adults: A systematic review and meta-analysis. *Ageing Research Reviews*, 15, 28-43. https://scholar.google.com/scholar?cluster=13624855542165676016&hl=en&as_sdt=0, 5.
- Kennedy, D. P., & Adolphs, R. (2012). The social brain in psychiatric and neurological disorders. *Trends in Cognitive Sciences*, *16*(11), 559-572. https://philarchive.org/archive/KENTSBv1.
- Kiecolt-Glaser, J. K., McGuire, L., Robles, T. F., & Glaser, R. (2002). Emotions, morbidity, and mortality: New perspectives from psychoneuroimmunology. *Annual Review of Psychology*, 53(1), 83–107. http://www.uppitysciencechick.com/kiecolt-glaser pni morbid mortal.pdf.
- Kleim, J. A. (2011). Neural plasticity and neurorehabilitation: Teaching the new brain old tricks. *Journal of Communication Disorders*, 44(5), 521-528.
- Kleim, J. A., & Jones, T. A. (2008). Principles of experience-dependent neural plasticity: Implications for rehabilitation after brain damage. *Journal of Speech, Language and Hearing Research*, *51*(1), S225-S239. doi: 10.1044/1092-4388(2008/018).

- Kleim, J. A., Kleim, E. D., & Cramer, S. C. (2007). Systematic assessment of traininginduced changes in corticospinal output to hand using frameless stereotaxic transcranial magnetic stimulation. *Nature Protocols*, 2(7), 1675-1684. doi: 10.1038/nprot.2007.206.
- Kleim, J. A., Lussnig, E., Schwarz, E. R., Comery, T. A., & Greenough, W. T. (1996). Synaptogenesis and Fos expression in the motor cortex of the adult rat after motor skill learning. *The Journal of Neuroscience*, *16*(14), 4529-4535. http://www.jneurosci.org/content/16/14/4529.short.
- Kolb, B., Buhrmann, K., McDonald, R., & Sutherland, R. J. (1994). Dissociation of the medial prefrontal, posterior parietal, and posterior temporal cortex for spatial navigation and recognition memory in the rat. *Cerebral Cortex*, 4(6), 664-680. <u>https://doi.org/10.1093/cercor/4.6.664</u>.
- Lam, L. T., & Kirby, S. L. (2002). Is emotional intelligence an advantage? An exploration of the impact of emotional and general intelligence on individual performance. *The Journal of Social Psychology*, 142(1), 133-143.
- Lambert, D. J., Dellmann-Jenkins, M., & Fruit, D. (1990). Planning for contact between the generations: An effective approach. *The Gerontologist*, 30(4), 553-556. doi: 10.1093/geront/30.4.553.
- Lange-Asschenfeldt, C., & Kojda, G. (2008). Alzheimer's disease, cerebrovascular dysfunction and the benefits of exercise: From vessels to neurons. *Experimental Gerontology*, 43(6), 499-504. doi: 10.1016/j.exger.2008.04.002.
- Leuner, B., Gould, E., & Shors, T. J. (2006). Is there a link between adult neurogenesis and learning? *Hippocampus*, *16*(3), 216-224. doi: 10.1002/hipo.20153.
- Lieberman, M. D. (2013). *Social: Why our brains are wired to connect*. New York: Crown Publishers.
- Lopes, P. N., Brackett, M. A., Nezlek, J. B., Schütz, A., Sellin, I., & Salovey, P. (2004). Emotional intelligence and social interaction. *Personality and Social Psychology Bulletin*, 30(8), 1018–1034. https://pdfs.semanticscholar.org/79a1/257a260bbb16f03f042b99872e36253df650.pdf.
- Lopes, P. N., Grewal, D., Kadis, J., Gall, M., & Salovey, P. (2006). Evidence that emotional intelligence is related to job performance and affect and attitudes at work. *Psichothema*, 18(Suppl), 132–138. <u>http://www.psicothema.es/pdf/3288.pdf</u>.
- Lorenz, K. (1970). *Studies in animal and human behaviour* (Vol. 1). (R. Martin, Trans.). Cambridge, MA: Harvard University Press.
- Magaki, S., Yong, W. H., Khanlou, N., Tung, S., & Vinters, H. V. (2014). Comorbidity in dementia: Update of an ongoing autopsy study. *Journal of the American Geriatrics Society*, 62(9), 1722-1728. <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4172655/</u>.
- Maguire, E. A., Gadian, D. G., Johnsrude, I. S., Good, C. D., Ashburner, J., Frackowiak, R. S. J., & Frith, C. D. (2000). Navigation-related structural change in the hippocampi of taxi drivers. *Proceedings of the National Academy of Sciences of the United States of America*, 97(8), 4398-4403. doi: 10.1073/pnas.070039597.
- Markham, J. A., & Greenough, W. T. (2004). Experience-driven plasticity: Beyond the synapse. *Neuron Glia Biology*, 1(4), 351-363. doi: 10.1017/s1740925x05000219.
- May, A. (2011). Experience-dependent structural plasticity in the adult human brain. *Trends in Cognitive Sciences*, *15*(10), 475-482. doi: 10.1016/j.tics.2011.08.002.
- Mayer, J. D., Roberts, R. D., & Barsade, S. G. (2008). Human abilities: Emotional intelligence. Annual Review of Psychology, 59, 507-536. <u>http://dmcodyssey.org/wp-content/uploads/2013/08/Human-Abilities-Emotional-Intelligence.pdf</u>.

- Mayer, J. D., & Salovey, P. (1997). What is emotional intelligence? In P. Salovey & D. Sluyter (Eds.), *Emotional development and emotional intelligence: Educational implications* (pp. 3-31). New York: Basic Books.
- Mayer, J. D., Salovey, P., & Caruso, D. R. (2004). Emotional intelligence: Theory, findings, and implications. *Psychological Inquiry*, *15*(3), 197-215.
- McAllister, A. K., Lo, D. C., & Katz, L. C. (1995). Neurotrophins regulate dendritic growth in developing visual cortex. *Neuron*, 15(4), 791-803. https://doi.org/10.1016/0896-6273(95)90171-X.
- McCollum, S., & Shreeve, W. (1994). Young and old making a difference. *Early Child* Development and Care, 99(1), 103-112. <u>https://doi.org/10.1080/0300443940990109</u>.
- McGaugh, J. L. (2000). Memory a century of consolidation. *Science*, 287(5451), 248-251. doi: 10.1126/science.287.5451.248.
- Muotri, A. R., & Gage, F. H. (2006). Generation of neuronal variability and complexity. *Nature*, 441(7097), 1087-1093. doi: 10.1038/nature04959.
- Nakabe, T., Sasaki, N., Uematsu, H., Kunisawa, S., Wimo, A., & Imanaka, Y. (2019). Classification tree model of the personal economic burden of dementia care by related factors of both people with dementia and caregivers in Japan: A cross-sectional online survey. *BMJ Open*, 9, e026733.

https://bmjopen.bmj.com/content/bmjopen/9/7/e026733.full.pdf.

Nelis, S. M., Wu, Y-T., Matthews, F. E., Martyr, A., Quinn, C., Rippon, I., Rusted, J., Thom, J. M., Kopelman, M. D., Hindle, J. V., Jones, R. W., & Clare, L. (2019). The impact of co-morbidity on the quality of life of people with dementia: Findings from the IDEAL study. Age and Ageing 48(3), 361-367. https://ouropepme.org/backend/ntpmerender.fogi2accid=PMC6503040&blobtupe=pd

https://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC6503940&blobtype=pdf.

- Newman, S., Lyons, C. W., & Onawola, R. S. (1985). The development of an intergenerational service-learning program at a nursing home. *The Gerontologist*, 25(2), 130-133. doi: 10.1093/geront/25.2.130.
- Nithianantharajah, J., & Hannan, A. J. (2009). The neurobiology of brain and cognitive reserve: Mental and physical activity as modulators of brain disorders. *Progress in Neurobiology*, 89(4), 369-382. doi: 10.1016/j.pneurobio.2009.10.001.
- (2011). Mechanisms mediating brain and cognitive reserve: Experience-dependent neuroprotection and functional compensation in animal models of neurodegenerative diseases. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 35(2), 331-339. doi: 10.1016/j.pnpbp.2010.10.026.
- Payne, W. L. (1986). A study of emotion developing emotional intelligence: Selfintegration; relating to fear, pain and desire. (*Theory, Structure of Reality, Problem-Solving, Contraction/Expansion, Tuning In/Coming Out/Letting Go)*. (Unpublished doctoral dissertation). Union for Experimenting Colleges and Universities, Yellow Springs, Ohio.
- Penn, D. L., Corrigan, P. W., Bentall, R. P., Racenstein, J. M., & Newman, L. (1997). Social cognition in schizophrenia. *Psychological Bulletin*, *121*(1), 114-132.
- Pérez, C. A., & Carral, J. M. C. (2007). Benefits of physical exercise for older adults with Alzheimer's disease. *Geriatric Nursing*, 29(6), 384-391. doi: 10.1016/j.gerinurse.2007.12.002.
- Pinkham, A. E., Penn, D. L., Perkins, D. O., & Lieberman, J. (2003). Implications for the neural basis of social cognition for the study of schizophrenia. *American Journal of Psychiatry*, 160(5), 815-24.

- Poblador-Plou, B., Calderón-Larrañaga, A., Marta-Moreno, J., Hancco-Saavedra, J., Sicras-Mainar, A., Soljak, M., & Prados-Torres, A. (2014). Comorbidity of dementia: A cross-sectional study of primary care older patients. *BMC Psychiatry*, 14, 84. <u>https://scholar.google.com/scholar?cluster=10648686945182132313&hl=en&as_sdt=0</u>,5.
- Rampon, C., Jiang, C. H., Dong, H., Tang, Y-P., Lockhart, D. J., Schultz, P. G., Tsien. J. Z., & Hu, Y. (2000). Effects of environmental enrichment on gene expression in the brain. *Proceedings of the National Academy of Sciences of the United States of America*, 97(23), 12880-12884. doi: 10.1073/pnas.97.23.12880.
- Ray, W. A., Federspiel, C. F., & Schaffner, W. (1980). A study of antipsychotic drug use in nursing homes: Epidemiologic evidence suggesting misuse. *American Journal of Public Health*, 70(5), 485-491. doi: 10.2105/ajph.70.5.485.
- Rios, S., Perlman, C. M., Costa, A., Heckman, G., Hirdes, J. P., & Mitchell, L. (2017). Antipsychotics and dementia in Canada: A retrospective cross-sectional study of four health sectors. *BMC Geriatrics*, 17(1), 244. doi: 10.1186/s12877-017-0636-8.
- Rioult-Pedotti, M-S., Friedman, D., & Donoghue, J. P. (2000). Learning-induced LTP in neocortex. *Science*, 290(5491), 533-536. doi: 10.1126/science.290.5491.533.
- Robinson, S. M. (2015). Applied Social Neuroscience. *CASN*: *Center for Applied Social Neuroscience*. ASN. <u>https://www.brain-mind-behavior.org/asn</u>.
- Rubinov, M., McIntosh, A.R., Valenzuela, M. J., & Breakspear, M. (2009). Simulation of neuronal death and network recovery in a computational model of distributed cortical activity. *The American Journal of Geriatric Psychiatry*, 17(3), 210-217. doi: 10.1097/JGP.0b013e318187137a.
- Ryff, C. D. (1989). Happiness is everything, or is it? Explorations on the meaning of psychological well-being. *Journal of Personality and Social Psychology*, 57(6), 1069– 1081. doi: 10.1037/0022-3514.57.6.1069.
 https://pdfs.competioschological.com/psyc
 - https://pdfs.semanticscholar.org/0b7c/bc0e7b5946b39778784a2167019eebd53e52.pdf.
- Ryff, C. D., Love, G. D., Miyamoto, Y., Markus, H. R., Curhan, K. B., Kitayama, S., Park, J., Kawakami, N., Kan, C., & Karasawa, M. (2014). Culture and promotion of well-being in East and West: Understanding varieties of attunement to the surrounding context. In G. A. Fava & C. Ruini (Eds.), *Increasing psychological well-being in clinical and educational settings* (pp. 1-19). Cross-Cultural Advancements in Positive Psychology 8. Springer Science+Business Media Dordrecht. <u>https://web.stanford.edu/~hazelm/publications/2014%20Ryff%20Love%20Miyamoto %20Markus%20Culture%20and%20the%20promotion%20of%20wellbeing%20in%20East%20and%20West.pdf.</u>
- Sado, M, Ninomiya, A., Shikimoto, R., Ikeda, B., Baba, T., Yoshimura, K., & Mimura, M. (2018). The estimated cost of dementia in Japan, the most aged society in the world. *PLoS ONE*, *13*(11), e0206508.

https://pdfs.semanticscholar.org/6a6e/838d5fe5fcf042ae56a650d5027f3446151a.pdf.

- Sampedro-Piquero, P., & Begega, A. (2017). Environmental enrichment as a positive behavioral intervention across the lifespan. *Current Neuropharmacology*, 15(4), 459-470. doi: 10.2174/1570159X14666160325115909.
 https://www.researchgate.net/publication/299459148 Environmental enrichment as a positive behavioral intervention across the lifespan.
- Sánchez-Álvarez, N., Extremera, N., & Fernández-Berrocal, P. (2015). The relation between emotional intelligence and subjective well-being: A meta-analytic investigation. *The Journal of Positive Psychology*, *11*(3), 276-285.

Saxe, R. (2006). Uniquely human social cognition. *Current Opinion in Neurobiology*, *16*(2), 235-239.

https://saxelab.mit.edu/sites/default/files/publications/Saxe%2C%20R.%20%282006% 29.%20Uniquely%20Human%20Social%20Cognition%20%28Current%20Opinion%2 0in%20Neurobiology%29.pdf.

- Schooler, C., & Mulatu, M. (2001). The reciprocal effects of leisure time activities and intellectual functioning in older people: A longitudinal analysis. *Psychology and Aging*, 16(3), 466-482. doi: 10.1037//0882-7974.16.3.466.
- Schulz, R. (1976). Effects of control and predictability on the physical and psychological well-being of the institutionalized aged. *Journal of Personality and Social Psychology*, 33(5), 563-573. doi: 10.1037//0022-3514.33.5.563.
- Schutte, N. S., Malouff, J. M., Bobik, C., Coston, T. D., Greeson, C., Jedlicka, C., Rhodes, E., & Wendorf, G. (2001). Emotional intelligence and interpersonal relations. *The Journal of Social Psychology*, 141(4), 523-536.
- Seefeldt, C. (1987). The effects of preschoolers' visits to a nursing home. *The Gerontologist* 27(2), 228-232. doi: 10.1093/geront/27.2.228.
- Seifert, T. A. (2005). The Ryff scales of psychological well-being. *Center of Inquiry at Wabash College*. <u>https://centerofinquiry.org/uncategorized/ryff-scales-of-psychological-well-being/</u>.
- Shiel, A., Burn, J. P., Henry, D., Clark, J., Wilson, B. A., Burnett, M. E., & McLellan, D. L. (2001). The effects of increased rehabilitation therapy after brain injury: Results of a prospective controlled trial. *Clinical Rehabilitation*, 15(5), 501-514. doi: 10.1191/026921501680425225.
- Shimada, H., Makizako, H., Doi, T., Tsutsumimoto, K., Lee, S., & Suzuki, T. (2016). Cognitive impairment and disability in older Japanese. *PLoS ONE*, *11*(7). <u>https://pdfs.semanticscholar.org/b144/5b10bf2a23b59f7183fe3026f7de06ae5bdc.pdf</u>.
- Sluming, V., Barrick, T., Howard, M., Cezayirli, E., Mayes, A., & Roberts, N. (2002). Voxelbased morphometry reveals increased gray matter density in Broca's area in male symphony orchestra musicians. *NeuroImage*, *17*(3), 1613-1622. doi: 10.1006/nimg.2002.1288.
- Soble, J. (2017). Japan's falling birth rate posing serious problems for economy. *Independent*, June 3. News, World, Asia. <u>https://www.independent.co.uk/news/world/asia/japans-falling-birth-rate-posing-serious-problems-for-economy-a7770596.html</u>.
- Spivack, G., Spettell, C. M., Ellis, D. W., & Ross, S. E. (1992). Effects of intensity of treatment and length of stay on rehabilitation outcomes. *Brain Injury*, 6(5), 419-434. doi: 10.3109/02699059209008138.
- Stevenson, D. G., Decker, S. L., Dwyer, L. L., Huskamp, H. A., Grabowski, D. C., Metzger, E. D., & Mitchell, S. L. (2010). Antipsychotic and benzodiazepine use among nursing home residents: Findings from the 2004 National Nursing Home Survey. *The American Journal of Geriatric Psychiatry*, 18(12), 1078-1092. doi:10.1097/JGP.0b013e3181d6c0c6.
- Taubert, M., Villringer, A., & Ragert, P. (2012). Learning-related gray and white matter changes in humans: An update. *The Neuroscientist*, 18(4), 320-325. doi: 10.1177/1073858411419048.

- The Japan Times. (2015). Japan grapples with ¥14.5 trillion dementia costs. *The Japan Times*, May 29. <u>https://www.japantimes.co.jp/news/2015/05/29/national/science-health/japan-grapples-with-%C2%A514-5-trillion-dementia-costs/#.Xo7LY8gzaUk</u>.
- . (2018). Health care system could collapse if elderly people's contribution not doubled: Insurance official. *The Japan Times*, October 4. <u>https://www.japantimes.co.jp/news/2018/10/04/national/health-care-system-collapse-</u> elderly-peoples-contributions-not-doubled-insurance-official/#.Xo1w58gzaUk.
- Till, C., Colella, B., Verwegen, J., & Green, R. E. (2008). Postrecovery cognitive decline in adults with traumatic brain injury. *Archives of Physical Medicine and Rehabilitation*, 89(12, Suppl), S25-S34. doi: 10.1016/j.apmr.2008.07.004.
- Trigiani, L. J., & Hamel, E. (2017). An endothelial link between the benefits of physical exercise in dementia. *Journal of Cerebral Blood Flow and Metabolism*, 37(8), 2649-2664. doi: 10.1177/0271678X17714655.
- Tsuya, T. (n.d.). The impacts of population decline in Japan: Demographic prospects and policy implications. *Reexamining Japan in Global Context*. Suntory Foundation Research Project. Suntory Foundation: Osaka, Japan. https://www.suntory.com/sfnd/jgc/forum/005/pdf/005_tsuya.pdf.
- United Nations, Department of Economic and Social Affairs, Population Division. (2013). *World population ageing 2013*. ST/ESA/SER.A/348. <u>https://www.un.org/en/development/desa/population/publications/pdf/ageing/WorldPopulationAgeing2013.pdf</u>.
- _____. (2017). World population ageing 2017. ST/ESA/SER.A/408. <u>https://www.un.org/en/development/desa/population/publications/pdf/ageing/WPA201</u> <u>7_Report.pdf</u>.
- _____. (2019). World population prospects 2019: Data booklet. ST/ESA/SER.A/424. https://population.un.org/wpp/Publications/Files/WPP2019_DataBooklet.pdf.
- van Praag, H., Kempermann, G., & Gage, F. H. (2000). Neural consequences of environmental enrichment. *Nature Reviews Neuroscience*, 1(3), 191-198. doi: 10.1038/35044558.
- Vidoni, E. D., Van Sciver, A., Johnson, D. K., He, J., Honea, R., Haines, B., Goodwin, J., Laubinger, M. P., Anderson, H. S., Kluding, P. M., Donnelly, J. E., Billinger, S. A., & Burns, J. M. (2012). A community-based approach to trials of aerobic exercise in aging and Alzheimer's disease. *Contemporary Clinical Trials*, 33(6), 1105–1116. <u>https://doi.org/10.1016/j.cct.2012.08.002</u>.
- Voss, M. W., Nagamatsu, L. S., Liu-Ambrose, T., & Kramer, A. F. (2011). Exercise, brain and cognition across the life span. *Journal of Applied Physiology*, 111(5), 1505-1513. doi: 10.1152/japplphysiol.00210.2011.
- Walia, S. (2019). How does Japan's aging society affect its economy? *The Diplomat*, November 13. <u>https://thediplomat.com/2019/11/how-does-japans-aging-society-affect-its-economy/</u>.
- Ward, C., Kamp, L., & Newman, S. (1996). The effects of participation in an intergenerational program on the behavior of residents with dementia. Activities, Adaptation, and Aging, 20(4), 61-76. doi: 10.1300/J016v20n04_05.
- Warraich, Z., & Kleim, J. A. (2010). Neural plasticity: The biological substrate for neurorehabilitation. *PM&R* (Physical Medicine and Rehabilitation) 2(12, Suppl), S208-S219. doi: 10.1016/j.pmrj.2010.10.016.
- Willer, B., Button, J., & Rempel, R. (1999). Residential and home-based postacute rehabilitation of individuals with traumatic brain injury: A case control study. *Archives* of Physical Medicine and Rehabilitation, 80(4), 399-406. doi: 10.1016/s0003-9993(99)90276-9.

World Health Organization (WHO). (2019). *WHO factsheet on dementia*. <u>https://www.who.int/news-room/fact-sheets/detail/dementia</u>.

Zagaria, M. A. E. (2008). Antipsychotics in seniors. U.S. Pharmacist, 33(11), 20-22.

- Zeidner, M, & Matthews, G. (2016). Ability emotional intelligence and mental health: Social support as mediator. *Personality and Individual Differences*, 99, 196-199.
- Zhu, X. L., Poon, W. S., Chan, C. C. H., & Chan, S. S. H. (2001). Does intensive rehabilitation improve the functional outcome of patients with traumatic brain injury? Interim result of a randomized controlled trial. *British Journal of Neurosurgery*, 15(6), 464-473. doi: 10.1080/02688690120097688.
- (2007). Does intensive rehabilitation improve the functional outcome of patients with traumatic brain injury (TBI)? A randomized controlled trial. *Brain Injury*, 21(7), 681-690. <u>https://doi.org/10.1080/02699050701468941</u>.

APPENDIX

Select Bibliography of Studies Related to Learning/Relearning, Neuroplasticity, the Enriched Environment, and Brain and Cognitive Reserve (BCR) in Cognitive and Physical Rehabilitation

- Aimone, J. B., Wiles, J., & Gage, F. H. (2006). Potential role for adult neurogenesis in the encoding of time in new memories. *Nature Neuroscience*, 9(6), 723-727. doi: 10.1038/nn1707.
- Alwis, D. S., & Rajan, R. (2014). Environmental enrichment and the sensory brain: The role of enrichment in remediating brain injury. *Frontiers in Systems Neuroscience*, 8 (Article 156). doi: 10.3389/fnsys.2014.00156.
- Amaral, O. B., Vargas, R. S., Hansel, G., Izquierdo, I., & Souza, D. O. (2008). Duration of environmental enrichment influences the magnitude and persistence of its behavioral effects on mice. *Physiology and Behavior*, 93(1-2), 388-394. doi: 10.1016/j.physbeh.2007.09.009.
- Aronoff, E., Hillyer, R., & Leon, M. (2016). Environmental enrichment therapy for autism: Outcomes with increased access. *Neural Plasticity*, 2016 (Article ID 2734915). doi: 10.1155/2016/2734915.
- Artola, A., von Frijtag, J. C., Fermont, P. C., Gispen, W. H., Schrama, L. H., Kamal, A., & Spruijt, B. M. (2006). Long-lasting modulation of the induction of LTD and LTP in rat hippocampal CA1 by behavioural stress and environmental enrichment. *European Journal of Neuroscience*, 23(1), 261-272. doi: 10.1111/j.1460-9568.2005.04552.x.
- Barnes, S. J., & Finnerty, G. T. (2010). Sensory experience and cortical rewiring. *The Neuroscientist*, *16*(2), 186-198. doi: 10.1177/1073858409343961.
- Begré, S., Frommer, A., von Känel, R., Kiefer, C., & Federspiel, A. (2007). Relation of white matter anisotropy to visual memory in 17 healthy subjects. *Brain Research*, *1168*, 60-66. doi: 10.1016/j.brainres.2007.06.096.
- Bengtsson, S. L., Nagy, Z., Skare, S., Forsman, L., Forssberg, H., & Ullén, F. (2005). Extensive piano practicing has regionally specific effects on white matter development. *Nature Neuroscience*, 8(9), 1148-1150. doi: 10.1038/nn1516. <u>https://www.nature.com/articles/nn1516</u>.
- Bliss, T. V. P., & Collingridge, G. L. (1993). A synaptic model of memory: Long-term potentiation in the hippocampus. *Nature*, *361*(6407), 31-39. doi: 10.1038/361031a0.
- Bliss, T. V. P., & Lømo, T. (1973). Long-lasting potentiation of synaptic transmission in the dentate area of the anaesthetized rabbit following stimulation of the perforant path. *The Journal of Physiology*, 232(2), 331-356. doi: 10.1113/jphysiol.1973.sp010273.
- Boman, I-L., Lindstedt, M., Hemmingsson, H., & Bartfai, A. (2004). Cognitive training in home environment. *Brain Injury*, 18(10), 985-995. doi: 10.1080/02699050410001672396.
- Boyke, J., Driemeyer, J., Gaser, C., Büchel, C., & May, A. (2008). Training-induced brain structure changes in the elderly. *The Journal of Neuroscience*, 28(28), 7031-7035. doi: 10.1523/JNEUROSCI.0742-08.2008.
- Brothers, L. (1990). The social brain: A project for integrating primate behavior and neurophysiology in a new domain. *Concepts in Neuroscience*, 1, 27-51.

Büchel, C., Coull, J. T., & Friston, K. J. (1999). The predictive value of changes in effective connectivity for human learning. *Science*, 283(5407), 1538-1541. doi: 10.1126/science.283.5407.1538. http://science.sciencemag.org/content/283/5407/1538.full.

Chklovskii, D. B. (2004). Synaptic connectivity and neuronal morphology: Two sides of the same coin. *Neuron*, 43(5), 609-617. doi: 10.1016/j.neuron.2004.08.012.

- Chklovskii, D. B., Mel, B. W., & Svoboda, K., (2004). Cortical rewiring and information storage. *Nature*, 431(7010), 782-788. doi: 10.1038/nature03012.
- Cicerone, K. D., Mott, T., Azulay, J., & Friel, J. C. (2004). Community integration and satisfaction with functioning after intensive cognitive rehabilitation for traumatic brain injury. *Archives of Physical Medicine and Rehabilitation*, 85(6), 943-950. doi: 10.1016/j.apmr.2003.07.019.
- Cifu, D. X., Kreutzer, J. S., Kolakowsky-Hayner, S. A., Marwitz, J. H., & Englander, J. (2003). The relationship between therapy intensity and rehabilitative outcomes after traumatic brain injury: A multicenter analysis. *Archives of Physical Medicine and Rehabilitation*, 84(10), 1441-1448. doi: 10.1016/S0003-9993(03)00272-7.
- Comery, T. A., Shah, R., & Greenough, W. T. (1995). Differential rearing alters spine density on medium-sized spiny neurons in the rat corpus striatum: Evidence for association of morphological plasticity with early response gene expression. *Neurobiology of Learning and Memory*, 63(3), 217-219. doi: 10.1006/nlme.1995.1025.
- Draganski, B., Gaser, C., Busch, V., Schuierer, G., Bogdahn, U., & May, A. (2004). Neuroplasticity: Changes in gray matter induced by training. *Nature*, 427(6972), 311-312. doi: 10.1038/427311a.
- Draganski, B., Gaser, C., Kempermann, G., Kuhn, H. G., Winkler, J., Büchel, C., & May, A. (2006). Temporal and spatial dynamics of brain structure changes during extensive learning. *The Journal of Neuroscience*, 26(23), 6314-6317. doi: 10.1523/JNEUROSCI.4628-05.2006.
- Draganski, B., & May, A. (2008). Training-induced structural changes in the adult human brain. *Behavioural Brain Research*, *192*(1), 137-142. doi: 10.1016/j.bbr.2008.02.015.
- Driemeyer, J., Boyke, J., Gaser, C., Büchel, C., & May, A. (2008). Changes in gray matter induced by learning – revisited. *PLoS ONE*, *3*(7), e2669. doi: 10.1371/journal.pone.0002669.
- Eliot, L. (2000). *What's going on in there? How the brain and mind develop in the first five years of life*. New York: Bantam Books.
- Engvig, A., Fjell, A. M., Westlye, L. T., Moberget, T., Sundseth, Ø., Larsen, V. A., & Walhovd, K. B. (2010). Effects of memory training on cortical thickness in the elderly. *NeuroImage*, 52(4), 1667-1676. doi: 10.1016/j.neuroimage.2010.05.041.
- Feldman, D. E., Nicoll, R. A., & Malenka, R. C. (1999). Synaptic plasticity at thalamocortical synapses in developing rat somatosensory cortex: LTP, LTD, and silent synapses. *Journal of Neurobiology*, 41(1), 92-101. <u>https://doi.org/10.1002/(SICI)1097-</u> <u>4695(199910)41:1<92::AID-NEU12>3.0.CO;2-U</u>.
- Filippi, M., Ceccarelli, A., Pagani, E., Gatti, R., Rossi, A., Stefanelli, L., Falini. A., Comi, G., & Rocca, M. A. (2010). Motor learning in healthy humans is associated to gray matter changes: A tensor-based morphometry study. *PLoS ONE*, 5(4), e10198. doi: 10.1371/journal.pone.0010198.
- Flor, H., Elbert, T., Knecht, S., Wienbruch, C., Pantev, C., Birbaumers, N., Larbig, W., & Taub, E. (1995). Phantom-limb pain as a perceptual correlate of cortical reorganization following arm amputation. *Nature*, 375(6531), 482-484. doi: 10.1038/375482a0.

- Fox, M. D., & Raichle, M. E. (2007). Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. *Nature Reviews Neuroscience*, 8(9), 700-711. doi: 10.1038/nrn2201.
- Frasca, D., Tomaszczyk, J., McFadyen, B. J., & Green, R. E. (2013). Traumatic brain injury and post-acute decline: What role does environmental enrichment play? A scoping review. *Frontiers in Human Neuroscience*, 7 (Article 31). doi: 10.3389/fnhum.2013.00031.
- Fujiwara, Y., Chaves, P. H., Yoshida, H., Amano, H., Fukaya, T., Watanabe, N., Nishi, M., Lee, S., Uchida, H., & Shinkai, S. (2009). Intellectual activity and likelihood of subsequently improving or maintaining instrumental activities of daily living functioning in community-dwelling older Japanese: A longitudinal study. *International Journal of Geriatric Psychiatry*, 24(6), 547-555. doi: 10.1002/gps.2148.
- Gage, F. H. (2002). Neurogenesis in the adult brain. *The Journal of Neuroscience*, 22(3), 612-613. doi: 10.1523/JNEUROSCI.22-03-00612.2002.
- Gaser, C., & Schlaug, G. (2003a). Brain structures differ between musicians and nonmusicians. *The Journal of Neuroscience*, 23(27), 9240-9245. <u>http://www.jneurosci.org/content/23/27/9240.short</u>.
- (2003b). Gray matter differences between musicians and nonmusicians. *Annals of the New York Academy of Sciences*, 999, 514-517. http://dbm.neuro.uni-jena.de/pdf-files/Gaser-AnnNYAS.pdf.
- Golestani, N., & Pallier, C. (2007). Anatomical correlates of foreign speech sound production. *Cerebral Cortex*, *17*(4), 929-934. doi: 10.1093/cercor/bhl003.
- Golestani, N., Paus, T., & Zatorre, R. J. (2002). Anatomical correlates of learning novel speech sounds. *Neuron*, 35(5), 997-1010. http://www.unicog.org/publications/Golestani et al 2002.pdf.
- Golestani, N., & Zatorre, R. J. (2004). Learning new sounds of speech: Reallocation of neural substrates. *NeuroImage*, 21(2), 494-506. doi: 10.1016/j.neuroimage.2003.09.071.
- Granert, O., Peller, M., Gaser, C., Groppa, S., Hallett, M., Knutzen, A., Deuschl, G., Zeuner, K. E., & Siebner, H. R. (2011). Manual activity shapes structure and function in contralateral human motor hand area. *NeuroImage*, 54(1), 32-41. doi: 10.1016/j.neuroimage.2010.08.013.
- Hannan, A. J. (2014). Environmental enrichment and brain repair: Harnessing the therapeutic effects of cognitive stimulation and physical activity to enhance experience-dependent plasticity. *Neuropathology and Applied Neurobiology*, 40(1), 13-25. doi: 10.1111/nan.12102.
- Hayden, M. E., Plenger, P., Bison, K., Kowalske, K., Masel, B., & Qualls, D. (2013). Treatment effect versus pretreatment recovery in persons with traumatic brain injury: A study regarding the effectiveness of postacute rehabilitation. *PM&R* (Physical Medicine and Rehabilitation), 5(4), 319-327; quiz 327. doi: 10.1016/j.pmrj.2012.12.005.
- Hebb, D. O. (1947). The effects of early experience on problem-solving at maturity. *American Psychologist*, *2*, 306-307.

(1949). *The organization of behavior*. New York: Wiley & Sons.

Henderson, L. A., Gustin, S. M., Macey, P. M., Wrigley, P. J., & Siddall, P. J. (2011).
Functional reorganization of the brain in humans following spinal cord injury:
Evidence for underlying changes in cortical anatomy. *The Journal of Neuroscience*, 31(7), 2630-2637. doi: 10.1523/JNEUROSCI.2717-10.2011.

- Herdener, M., Esposito, F., di Salle, F., Boller, C., Hilti, C. C., Habermeyer, B., Scheffler, K., Wetzel, S., Seifritz, E., & Cattapan-Ludewig, K. (2010). Musical training induces functional plasticity in human hippocampus. *The Journal of Neuroscience*, 30(4), 1377-1384. doi: 10.1523/JNEUROSCI.4513-09.2010.
- Holtmaat, A., Wilbrecht, L., Knott, G. W., Welker, E., & Svoboda, K. (2006). Experiencedependent and cell-type-specific spine growth in the neocortex. *Nature*, 441(7096), 979-983. doi: 10.1038/nature04783.
- Howland, J. G., & Wang, Y. T. (2008). Synaptic plasticity in learning and memory: Stress effects in the hippocampus. *Progress in Brain Research*, 169, 145-158. doi: 10.1016/S0079-6123(07)00008-8.
- Huttenlocher, P. R. (1991). Dendritic and synaptic pathology in mental retardation. *Pediatric Neurology*, 7(2), 79-85.
- Hyde, K. L., Lerch, J., Norton, A., Forgeard, M., Winner, E., Evans, A. C., & Schlaug, G. (2009). The effects of musical training on structural brain development: A longitudinal study. *Annals of the New York Academy of Sciences*, *1169*, 182-186. doi: 10.1111/j.1749-6632.2009.04852.x.
- Hydén, H., & Lange, P. W. (1983). Modification of membrane-bound proteins of the hippocampus and entorhinal cortex by change in behavior in rats. *Journal of Neuroscience Research*, *9*(1), 37-46. doi: 10.1002/jnr.490090106.
- Ilg, R., Wohlschläger, A. M., Gaser, C., Liebau, Y., Dauner, R., Wöller, A., Zimmer, C., Zihl, J., & Mühlau, M. (2008). Gray matter increase induced by practice correlates with task-specific activation: A combined functional and morphometric magnetic resonance imaging study. *The Journal of Neuroscience*, 28(16), 4210-4215. doi: 10.1523/JNEUROSCI.5722-07.2008.
- Jacobs, B., Batal, H. A., Lynch, B., Ojemann, G., Ojemann, L. M., & Scheibel, A. B. (1993). Quantitative dendritic and spine analyses of speech cortices: A case study. *Brain and Language*, 44(3), 239-253. doi: 10.1006/brln.1993.1016.
- Jain, N., Florence, S. L., Qi, H-X., & Kaas, J. H. (2000). Growth of new brainstem connections in adult monkeys with massive sensory loss. *Proceedings of the National Academy of Sciences of the United States of America*, 97(10), 5546-5550. doi: 10.1073/pnas.090572597.
- Jäncke, L., Koeneke, S., Hoppe, A., Rominger, C., & Hänggi, J. (2009). The architecture of the golfer's brain. *PLoS ONE*, *4*(3), e4785. doi: 10.1371/journal.pone.0004785.
- Jenkins, W. M., & Merzenich, M. M. (1987). Reorganization of neocortical representations after brain injury: A neurophysiological model of the bases of recovery from stroke. *Progress in Brain Research*, 71, 249-266.

https://www.sciencedirect.com/science/article/pii/S0079612308618294.

- Jin, M., Wang, X-M., Tu, Y., Zhang, X-H., Gao, X., Guo, N., Xie, Z., Zhao, G., Jing, N., Li, B-M., & Yu, L. (2005). The negative cell cycle regulator, Tob (transducer of ErbB-2), is a multifunctional protein involved in hippocampus-dependent learning and memory. *Neuroscience*, 131(3), 647-659. doi: 10.1016/j.neuroscience.2004.10.044.
- Johansson, B. B. (2004). Brain plasticity in health and disease. *The Keio Journal of Medicine*, 53(4), 231-246. <u>https://doi.org/10.2302/kjm.53.231</u>.
- Kandel, E. R. (2001). The molecular biology of memory storage: A dialogue between genes and synapses. *Science*, 294(5544), 1030-1038. doi: 10.1126/science.1067020.
- Kempermann, G. (2006). Adult neurogenesis. In P. B. Baltes, P. A. Reuter-Lorenz, & F. Rösler (Eds.), *Lifespan development and the brain: The perspective of biocultural co-constructivism* (pp. 82-108). Cambridge, England: Cambridge University Press. <u>https://doi.org/10.1017/CBO9780511499722.006</u>.

- Kleim, J., A. (2011). Neural plasticity and neurorehabilitation: Teaching the new brain old tricks. *Journal of Communication Disorders*, 44(5), 521-528. doi: 10.1016/jcomdis.2011.04.006.
- Kleim, J. A., & Jones, T. A. (2008). Principles of experience-dependent neural plasticity: Implications for rehabilitation after brain damage. *Journal of Speech, Language, and Hearing Research*, 51(1), S225-S239. doi: 10.1044/1092-4388(2008/018).
- Kleim, J. A., Kleim, E. D., & Cramer, S. C. (2007). Systematic assessment of traininginduced changes in corticospinal output to hand using frameless stereotaxic transcranial magnetic stimulation. *Nature Protocols*, 2(7), 1675-1684. doi: 10.1038/nprot.2007.206.
- Kleim, J. A., Lussnig, E., Schwarz, E. R., Comery, T. A., & Greenough, W. T. (1996). Synaptogenesis and Fos expression in the motor cortex of the adult rat after motor skill learning. *The Journal of Neuroscience*, *16*(14), 4529-4535. http://www.jneurosci.org/content/16/14/4529.short.
- Klöppel, S., Mangin, J-F., Vongerichten, A., Frackowiak, R. S. J., & Siebner, H. R. (2010). Nurture versus nature: Long-term impact of forced right-handedness on structure of pericentral cortex and basal ganglia. *The Journal of Neuroscience*, 30(9), 3271-3275.
- Kolb, B., Buhrmann, K., McDonald, R., & Sutherland, R. J. (1994). Dissociation of the medial prefrontal, posterior parietal, and posterior temporal cortex for spatial navigation and recognition memory in the rat. *Cerebral Cortex*, 4(6), 664-680. <u>https://doi.org/10.1093/cercor/4.6.664</u>.
- Kramer, A. F., Bherer, L., Colcombe, S. J., Dong, W., & Greenough, W. T. (2004). Environmental influences on cognitive and brain plasticity during aging. *The Journals of Gerontology: Series A, Biological Sciences and Medical Sciences*, 59(9), 940-957. doi: 10.1093/Gerona/59.9.M940.
- Lee, H., Devlin, J. T., Shakeshaft, C., Stewart, L. H., Brennan, A., Glensman, J., Pitcher, K., Crinion, J., Mechelli, A., Frackowiak, R. S. J., Green, D. W., & Price, C. J. (2007). Anatomical traces of vocabulary acquisition in the adolescent brain. *The Journal of Neuroscience*, 27(5), 1184-1189. doi: 10.1523/JNEUROSCI.4442-06.2007.
- Lerch, J. P., Yiu, A. P., Martinez-Canabal, A., Pekar, T., Bohbot, V. D., Frankland, P. W., Henkelman, R. M., Josselyn, S. A., & Sled, J. G. (2011). Maze training in mice induces MRI-detectable brain shape changes specific to the type of learning. *NeuroImage*, 54(3), 2086-2095. doi: 10.1016/j.neuroimage.2010.09.086.
- Leuner, B., Gould, E., & Shors, T. J. (2006). Is there a link between adult neurogenesis and learning? *Hippocampus*, *16*(3), 216-224. doi: 10.1002/hipo.20153.
- Lüscher, C., Nicoll, R. A., Malenka, R. C., & Muller, D. (2000). Synaptic plasticity and dynamic modulation of the postsynaptic membrane. *Nature Neuroscience*, 3(6), 545-550. doi: 10.1038/75714.
- Maguire, E. A., Gadian, D. G., Johnsrude, I. S., Good, C. D., Ashburner, J., Frackowiak, R. S. J., & Frith, C. D. (2000). Navigation-related structural change in the hippocampi of taxi drivers. *Proceedings of the National Academy of Sciences of the United States of America*, 97(8), 4398-4403. doi: 10.1073/pnas.070039597.
- Markham, J. A., & Greenough, W. T. (2004). Experience-driven plasticity: Beyond the synapse. *Neuron Glia Biology*, *1*(4), 351-363. doi: 10.1017/s1740925x05000219.
- May, A. (2011). Experience-dependent structural plasticity in the adult human brain. *Trends in Cognitive Sciences*, *15*(10), 475-482. doi: 10.1016/j.tics.2011.08.002.
- McAllister, A. K., Lo, D. C., & Katz, L. C. (1995). Neurotrophins regulate dendritic growth in developing visual cortex. *Neuron*, 15(4), 791-803. <u>https://doi.org/10.1016/0896-6273(95)90171-X</u>.

- McGaugh, J. L. (2000). Memory a century of consolidation. *Science*, 287(5451), 248-251. doi: 10.1126/science.287.5451.248.
- Mechelli, A., Crinion, J. T., Noppeney, U., O'Doherty, J., Ashburner, J., Frackowiak, R. S., & Price, C. J. (2004). Neurolinguistics: Structural plasticity in the bilingual brain. *Nature*, 431(7010), 757. doi: 10.1038/431757a.
- Milgram, N. W., Siwak-Tapp, C. T., Araujo, J., & Head, E. (2006). Neuroprotective effects of cognitive enrichment. *Ageing Research Reviews*, 5(3), 354-369. doi: 10.1016/j.arr.2006.04.004.
- Muotri, A. R., & Gage, F. H. (2006). Generation of neuronal variability and complexity. *Nature*, 441(7097), 1087-1093. doi: 10.1038/nature04959.
- Newson, R. S., & Kemps, E. B. (2005). General lifetime activities as a predictor of current cognition and cognitive change in older adults: A cross-sectional and longitudinal examination. *The Journals of Gerontology: Series B, Psychological Sciences & Social Sciences*, 60(3). P113-P120. doi: 10.1093/geronb/60.3.P113.
- Nithianantharajah, J., & Hannan, A. J. (2006). Enriched environments, experience-dependent plasticity and disorders of the nervous system. *Nature Reviews Neuroscience*, 7(9), 697-709. doi: 10.1038/nrn1970.
- (2009). The neurobiology of brain and cognitive reserve: Mental and physical activity as modulators of brain disorders. *Progress in Neurobiology*, 89(4), 369-382. doi: 10.1016/j.pneurobio.2009.10.001.
- (2011). Mechanisms mediating brain and cognitive reserve: Experience-dependent neuroprotection and functional compensation in animal models of neurodegenerative diseases. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *35*(2), 331-339. doi: 10.1016/j.pnpbp.2010.10.026.
- Pang, T. Y. C., & Hannan, A. J. (2013). Enhancement of cognitive function in models of brain disease through environmental enrichment and physical activity. *Neuropharmacology*, 64, 515-528. doi: 10.1016/j.neuropharm.2012.06.029.
- Park, N. W., & Ingles, J. L. (2001). Effectiveness of attention rehabilitation after an acquired brain injury: A meta-analysis. *Neuropsychology*, 15(2), 199-210. doi: 10.1037/0894-4105.15.2.199.
- Pascual-Leone, A., Amedi, A., Fregni, F., & Merabet, L. B. (2005). The plastic human brain cortex. *Annual Review of Neuroscience*, 28, 377-401. doi: 10.1146/annurev.neuro.27.070203.144216.
- Pons, T. P., Garraghty, P. E., Ommaya, A. K., Kaas, J. H., Taub, E., & Mishkin, M. (1991). Massive cortical reorganization after sensory deafferentation in adult macaques. *Science*, 252(5014), 1857-1860. doi: 10.1126/science.1843843.
- Powell, J., Heslin, J., & Greenwood, R. (2002). Community based rehabilitation after severe traumatic brain injury: A randomised controlled trial. *Journal of Neurology, Neurosurgery, and Psychiatry*, 72(2), 193-202. doi: 10.1136/jnnp.72.2.193.
- Rampon, C., Jiang, C. H., Dong, H., Tang, Y-P., Lockhart, D. J., Schultz, P. G., Tsien. J. Z., & Hu, Y. (2000). Effects of environmental enrichment on gene expression in the brain. *Proceedings of the National Academy of Sciences of the United States of America*, 97(23), 12880-12884. doi: 10.1073/pnas.97.23.12880.
- Renner, M. J., & Rosenzweig, M. R. (2013). Enriched and impoverished environments: Effects on brain and behavior. Recent Research in Psychology. New York: Springer Science & Business Media.
- Rioult-Pedotti, M-S., Friedman, D., & Donoghue, J. P. (2000). Learning-induced LTP in neocortex. *Science*, 290(5491): 533-536. doi: 10.1126/science.290.5491.533.

- Robinson, S. M. (2015). *Applied Social Neuroscience*. Center for Applied Social Neuroscience (*CASN*), ASN. <u>https://www.brain-mind-behavior.org/asn</u>.
- . (2018). Understanding Mental Illness_Revised. *CASN NeuroNotes* 103-Rev. <u>https://www.brain-mind-behavior.org/post/2018/04/08/understanding-mental-illnessrevised</u>.
- . (2021a). CNE and Person-Centered Care vs. the Distorted Medical Model (Revised). *CASN NeuroNotes* 302. <u>https://www.brain-mind-behavior.org/post/2018/07/21/cne-and-person-centered-care-vs-the-distorted-medical-model</u>.
- . (2021b). Cognitive Neuroeducation (CNE)_Program Conductor's Instruction Manual. Center for Applied Social Neuroscience (*CASN*).
 <u>https://www.brain-mind-behavior.org/post/2013/05/01/this-is-the-title-of-your-first-blog-post</u>.
- Robinson, S. M., & The Center for Applied Social Neuroscience (*CASN*). (2021). The CNE Booklet: Cognitive Neuroeducation (CNE)_Origins and Features (Revised). *CASN NeuroNotes* 304.

https://www.brain-mind-behavior.org/post/2018/06/10/the-cne-booklet.

- Rosenzweig, M. R. (1966). Environmental complexity, cerebral change, and behavior. *American Psychologist*, 21(4), 321-332.
- Rosenzweig, M. R., & Bennett, E. L. (1996). Psychobiology of plasticity: Effects of training and experience on brain and behavior. *Behavioural Brain Research*, 78(1), 57-65.
- Rosenzweig, M. R., Krech, D., Bennett, E. L., & Diamond, M. C. (1962). Effects of environmental complexity and training on brain chemistry and anatomy: A replication and extension. *Journal of Comparative and Physiological Psychology*, 55(4), 429-437.
- Rubinov, M., McIntosh, A. R., Valenzuela, M. J., & Breakspear, M. (2009). Simulation of neuronal death and network recovery in a computational model of distributed cortical activity. *The American Journal of Geriatric Psychiatry*, *17*(3), 210-217. doi: 10.1097/JGP.0b013e318187137a.
- Sampedro-Piquero, P., & Begega, A. (2017). Environmental enrichment as a positive behavioral intervention across the lifespan. *Current Neuropharmacology*, *15*(4), 459-470. doi: 10.2174/1570159X14666160325115909.
 <u>https://www.researchgate.net/publication/299459148_Environmental_enrichment_as_a_positive_behavioral_intervention_across_the_lifespan.</u>
- Scarmeas, N., & Stern, Y. (2003). Cognitive reserve and lifestyle. *Journal of Clinical and Experimental Neuropsychology*, 25(5), 625-633. doi: 10.1076/jcen.25.5.625.14576.
- Seeman, T. E., Lusignolo, T. M., Albert, M., & Berkman, L. (2001). Social relationships, social support, and patterns of cognitive aging in healthy, high-functioning older adults: MacArthur Studies of Successful Aging. *Health Psychology*, 20(4), 243-255. doi: 10.1037/0278-6133.20.4.243.
- Shiel, A., Burn, J. P., Henry, D., Clark, J., Wilson, B. A., Burnett, M. E., & McLellan, D. L. (2001). The effects of increased rehabilitation therapy after brain injury: Results of a prospective controlled trial. *Clinical Rehabilitation*, 15(5), 501-514. doi: 10.1191/026921501680425225.
- Slade, A., Tennant, A., & Chamberlain, M. A. (2002). A randomised controlled trial to determine the effect of intensity of therapy upon length of stay in a neurological rehabilitation setting. *Journal of Rehabilitation Medicine*, 34(6), 260-266. doi: 10.1080/165019702760390347.
- Sluming, V., Barrick, T., Howard, M., Cezayirli, E., Mayes, A., & Roberts, N. (2002). Voxel-based morphometry reveals increased gray matter density in Broca's area in male symphony orchestra musicians. *NeuroImage*, 17(3), 1613-1622. doi: 10.1006/nimg.2002.1288.

- Sohlberg, M. M., McLaughlin, K. A., Pavese, A., Heidrich, A., & Posner M. I. (2000). Evaluation of attention process training and brain injury education in persons with acquired brain injury. *Journal of Clinical and Experimental Neuropsychology*, 22(5), 656-676. doi: 10.1076/1380-3395(200010)22:5;1-9;FT656.
- Spitz, R. (1983). *René A. Spitz: Dialogues from infancy*—*Selected papers*. (R. N. Emde, Ed.). New York: International Universities Press.
- Spivack, G., Spettell, C. M., Ellis, D. W., & Ross, S. E. (1992). Effects of intensity of treatment and length of stay on rehabilitation outcomes. *Brain Injury*, 6(5), 419-434. doi: 10.3109/02699059209008138.
- Sur, M., & Rubenstein, J. L. R. (2005). Patterning and plasticity of the cerebral cortex. *Science*, *310*(5749), 805-810. doi: 10.1126/science.1112070.
- Sweatt, J. D. (2016). Neural plasticity and behavior sixty years of conceptual advances. *Journal of Neurochemistry*, *139* (Suppl 2), 179-199. doi: 10.1111/jnc.13580.
- Taubert, M., Draganski, B., Anwander, A., Müller, K., Horstmann, A., Villringer, A., & Ragert, P. (2010). Dynamic properties of human brain structure: Learning-related changes in cortical areas and associated fiber connections. *The Journal of Neuroscience*, 30(35), 11670-11677. doi: 10.1523/JNEUROSCI.2567-10.2010.
- Taubert, M., Lohmann, G., Margulies, D. S., Villringer, A., & Ragert, P. (2011). Long-term effects of motor training on resting-state networks and underlying brain structure. *NeuroImage*, 57(4), 1492-1498. doi: 10.1016/j.neuroimage.2011.05.078.
- Taubert, M., Villringer, A., & Ragert, P. (2012). Learning-related gray and white matter changes in humans: An update. *The Neuroscientist*, 18(4), 320-325. doi: 10.1177/1073858411419048.
- Till, C., Colella, B., Verwegen, J., & Green, R. E. (2008). Postrecovery cognitive decline in adults with traumatic brain injury. *Archives of Physical Medicine and Rehabilitation*, 89(12, Suppl), S25-S34. doi: 10.1016/j.apmr.2008.07.004.
- Toglia, J. P. (1991). Generalization of treatment: A multicontext approach to cognitive perceptual impairment in adults with brain injury. *American Journal of Occupational Therapy*, 45(6), 505-516. doi: 10.5014/ajot.45.6.505.
- Toglia, J., Johnston, M. V., Goverover, Y., & Dain, B. (2010). A multicontext approach to promoting transfer of strategy use and self regulation after brain surgery: An exploratory study. *Brain Injury*, *24*(4), 664-677. doi: 10.3109/02699051003610474.
- Trachtenberg, J. T., Chen, B. E., Knott, G. W., Feng, G., Sanes, J. R., Welker, E., & Svoboda, K., (2002). Long-term in vivo imaging of experience-dependent synaptic plasticity in adult cortex. *Nature*, 420(6917), 788-794. doi:10.1038/nature01273.
- Tuch, D. S., Salat, D. H., Wisco, J. J., Zaleta, A. K., Hevelone, N. D., & Rosas, H. D. (2005). Choice reaction time performance correlates with diffusion anisotropy in white matter pathways supporting visuospatial attention. *Proceedings of the National Academy of Sciences of the United States of America*, 102(34), 12212-12217. doi: 10.1073/pnas.0407259102.
- van Praag, H., Kempermann, G., & Gage, F. H. (2000). Neural consequences of environmental enrichment. *Nature Reviews Neuroscience*, 1(3), 191-198. doi: 10.1038/35044558.
- Voss, M. W., Nagamatsu, L. S., Liu-Ambrose, T., & Kramer, A. F. (2011). Exercise, brain, and cognition across the life span. *Journal of Applied Physiology*, 111(5), 1505-1513. doi: 10.1152/japplphysiol.00210.2011.
- Warraich, Z., & Kleim, J. A. (2010). Neural plasticity: The biological substrate for neurorehabilitation. *PM&R* (Physical Medicine and Rehabilitation) 2(12, Suppl), S208-S219. doi: 10.1016/j.pmrj.2010.10.016.

- Willer, B., Button, J., & Rempel, R. (1999). Residential and home-based postacute rehabilitation of individuals with traumatic brain injury: A case control study. *Archives of Physical Medicine and Rehabilitation*, 80(4), 399-406. doi: 10.1016/s0003-9993(99)90276-9.
- Wilson, R., Barnes, L., & Bennett, D. (2003). Assessment of lifetime participation in cognitively stimulating activities. *Journal of Clinical and Experimental Neuropsychology*, 25(5), 634-642. doi: 10.1076/jcen.25.5.634.14572.
- Woo, C. C., Donnelly, J. H., Steinberg-Epstein, R., & Leon, M. (2015). Environmental enrichment as a therapy for autism: A clinical trial replication and extension. *Behavioral Neuroscience*, 129(4), 412-422. doi: 10.1037/bne0000068.
- Zhu, X. L., Poon, W. S., Chan, C. C. H., & Chan, S. S. H. (2001). Does intensive rehabilitation improve the functional outcome of patients with traumatic brain injury? Interim result of a randomized controlled trial. *British Journal of Neurosurgery*, 15(6), 464-473. doi: 10.1080/02688690120097688.
- (2007). Does intensive rehabilitation improve the functional outcome of patients with traumatic brain injury (TBI)? A randomized controlled trial. *Brain Injury*, 21(7), 681-690. <u>https://doi.org/10.1080/02699050701468941</u>.
- Zilles, K. (1992). Neuronal plasticity as an adaptive property of the central nervous system. *Annals of Anatomy*, 174(5), 383-391. <u>http://europepmc.org/abstract/med/1333175</u>.

CASN **NeuroNotes**[®] is an online, peer-reviewed, copyrighted journal, with free access in full accordance with the tenets of fair use, and is published by

CASN Center for Applied Social Neuroscience Cognitive Development and Rehabilitation Pioneering enrichment programs for the mind. A healthy, active mind promotes a more fulfilling life.

http://www.brain-mind-behavior.org 638-2 Keyakidai, Eiheiji-cho Ph: +81-776-0 Yoshida-gun, Fukui 910-1223 email: casn@ Japan

Ph: +81-776-63-2290 email: <u>casn@brain-mind-behavior.org</u>