Health Neuroscience: Defining a New Field

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Complete List of Authors:	Erickson, Kirk; University of Pittsburgh, Psychology Creswell, J. David; Carnegie Mellon University, Psychology Verstynen, Timothy; Carnegie Mellon University, Psychology Gianaros, Pete; Un of Pittsburgh, Psychology
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Kirk I. Erickson

Department of Psychology and Center for the Neural Basis of Cognition, University of Pittsburgh

J. David Creswell and Timothy D. Verstynen

Department of Psychology and Center for the Neural Basis of Cognition, Carnegie Mellon University

Peter J. Gianaros

Department of Psychology and Center for the Neural Basis of Cognition, University of Pittsburgh

Author Note

Kirk I. Erickson, Department of Psychology and Center for the Neural Basis of Cognition, University of Pittsburgh; J. David Creswell and Timothy D. Verstynen, Department of Psychology and Center for the Neural Basis of Cognition, Carnegie Mellon University; Peter J. Gianaros, Department of Psychology and Center for the Neural Basis of Cognition, University of Pittsburgh.

The authors contributed equally to this work.

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Corresponding author: Kirk I. Erickson, Department of Psychology, University of Pittsburgh, 3107 Sennott Square, Pittsburgh, PA 15260 Email: kiericks@pitt.edu

Abstract

Health neuroscience is a new field that is at the interface of health psychology and neuroscience. It is concerned with the interplay between the brain and physical health over the lifespan. This review provides a conceptual introduction to health neuroscience, focusing on its major themes, representative studies, methodologies, and future directions.

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Health Neuroscience: Definition and Scope

How does the brain influence physical health? How does physical health influence the brain? We propose that these are inseparable and open questions, and a new field at the interface of health psychology and neuroscience is poised to answer them—a field called *health neuroscience*. But what is this new field and what are its conceptual themes, goals, and methods? What are its challenges and opportunities moving forward? This review addresses these questions and highlights recent studies illustrating health neuroscience approaches to understanding the dynamic interplay between the brain and physical health over the lifespan.

Here we adopt the definition of *health* as the absence of physical or mental illness, disease, pain, or discomfort. However, we would expand on this by arguing that health could be viewed as the absence, or paucity, of physiological (e.g., insulin resistance), social (e.g., loneliness), cognitive (e.g., slow processing speed), or emotional (e.g., anxiety) risk factors. Our reasoning is that these may explain the etiology, prevention, and progression of disease and specific endpoints. As discussed below, we distinguish physical health from mental health with the awareness that there are ambiguous boundaries, and significant comorbidities, between physical and mental health conditions (i.e., between cardiovascular disease (CVD) and depression) along with clear physical (i.e., biological) substrates for mental health conditions (see below). These definitions provide some clarity to what we view as the defining attributes of health neuroscience (see below).

With several ongoing international efforts to better understand brain function (e.g., Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative), we can expect that neuroscience and its methodologies will continue to play central roles in psychology. Indeed, the widespread integration of neuroscience into the fabric of psychology has been fostered over the last few decades by the rapid ascendance of neuroimaging technologies and their applications to the study of cognition, emotion, social behavior, personality, psychopathology, development, aging and other areas of inquiry. Over this same time period, we have gained a deeper and multilevel understanding of the biological, psychological, and social (biopsychosocial) determinants of *physical health*. This understanding has been enabled by the growth of health psychology and its allied areas of research and clinical practice (e.g., social epidemiology and behavioral medicine). Notwithstanding the ascendance of neuroscience and the simultaneous—but largely independent—traction of health psychology, we still lack answers to many fundamental questions about the brain and physical health. Accordingly, we believe that now is the time to formally define a new and integrative field of *health neuroscience*.

More precisely, health neuroscience can be defined as an emerging field focused on understanding how the brain *affects* and is *affected by* physical health. This definition artificially splits the brain from the other organs of the body; however, we make this conceptual separation because both research and education in neuroscience and psychology has traditionally been conducted independently from other fields of physiology and medicine. It is precisely this false distinction between the brain and body that research in health neuroscience is positioned to refute. Thus, to test hypotheses about the inter-dependent nature of the brain and body we necessarily distinguish them in our definition of health neuroscience. From this perspective, health neuroscience is thematically rooted in health psychology, while adopting neuroscience methodologies for studying brain function and structure in human and non-human animal models. It can be distinguished from the broader area of health psychology in that it has primary theoretical and empirical foci on the brain, and it differs from other areas of neuroscience in its primary focus on physical health. A chief goal of health neuroscience is to characterize bidirectional and dynamic brain-behavior and brain-physiology relationships that are determinants, markers, and consequences of physical health states across the lifespan. The motivation behind this goal is that a better understanding of these relationships will provide mechanistic insights into how the brain links multilevel genetic, biological, psychological, behavioral, social, and environmental factors with physical health—especially vulnerability to and resilience against clinical illnesses. Moreover, such mechanistic insights will also provide new cross-disciplinary platforms to develop brain-based prevention and intervention efforts to improve physical health, inform health policies, and promote successful development and aging.

Figure 1 illustrates key concepts of health neuroscience. Here, the brain is considered as the *central* organ that affects and is affected by states of health, which span a continuum from optimal well-being to clinical illness. In this regard, heath neuroscience research may conceptualize the brain as the primary or '*top-down*' determinant of downstream mediating processes that proximally influence physical health states (right side of Figure 1). Downstream mediating processes would thus be considered as emergent phenomena under the control of the brain, and could include processes related to cognition and decision-making, stress and emotion, health behaviors, and facets of peripheral physiology. Likewise, health neuroscience approaches may conceptualize the brain as a target organ that is affected by health states via '*bottom-up*' pathways. For example, health neuroscience studies may examine changes in brain structure and function that result from smoking, systemic inflammation, or other factors related to physical health (left side of Figure 1; and see below for more examples). Finally, health neuroscience approaches conceptualize these brain↔health relationships and pathways as subject to the contextually modifying influences of social, cultural, environmental, and other higher-level factors, as well as the modifying influences of life histories, genetics, and other individual-level factors (see top and bottom of Figure 1). In sum, health neuroscience studies may operationalize *direct measurements* of brain function and structure (e.g., from neuroimaging or electrophysiological recording methods) as predictor (independent) or outcome (dependent) variables, depending on the particular brain↔health relationship(s) under investigation or targeted by intervention.

There may be questions about the position of mental health (i.e., psychopathology) within the definition of health neuroscience. Indeed, research on psychopathology and mental health may be included as a part of health neuroscience to the extent that the research questions involve the examination of reciprocal associations or comorbidities between mental and physical health. For example, psychopathology (e.g., depression) is often coexistent, and may predict health outcomes (e.g., obesity) or be modified by health behaviors (e.g., physical activity and reduced risk for depression). Insofar as the neural substrates mediating these relationships are of interest, such topics would fall under the auspices of health neuroscience.

Empirical Illustrations

To illustrate applications of the above concepts we will highlight health neuroscience studies and end by considering some major methodological, computational, and conceptual challenges and opportunities in health neuroscience.

Stress, Emotion, and Social Factors

For decades, health psychologists have been interested in the connection between physical health and stress, emotion, and a vast spectrum of social factors (e.g., Adler & Matthews, 1994). Such interest has led to conceptualizations of psychological and social determinants of health that emphasize health-related *behaviors* and *peripheral biological mediators* as common downstream pathways to health endpoints (e.g., Cohen, Janicki-Deverts, & Miller, 2007). For example, anger, anxiety, and depression are thought to confer risk for cardiovascular disease by leading to disadvantageous health behaviors (e.g., smoking) and to alterations in systemic inflammation, neuroendocrine outflow, and autonomic physiology that adversely impact the heart and vasculature (Suls & Bunde, 2005). A health neuroscience approach builds on this conceptual framing in several ways. First, as indicated on the right side of Figure 1, health neuroscience studies are integrating theoretical models and empirical findings from social, cognitive, and affective neuroscience to consider the brain as the central, *top-down* regulator (i.e., determinant) of behaviors and parameters of peripheral physiology that impact physical health (e.g., B.S. McEwen & Gianaros, 2010). Second, these models and findings consider stress, emotion, and social processes as being functionally instantiated in neural circuits that also influence health behaviors and peripheral physiology (e.g., Eisenberger & Cole, 2012). Finally, as illustrated on the left side of Figure 1, health neuroscience studies are beginning to consider the *bottom-up* influences of health behaviors and peripheral physiology on brain systems and circuits that mediate stress, emotion, social, and other behavioral processes (e.g., Critchley & Harrison, 2013).

To elaborate, recent studies incorporating peripheral physiological recordings have shown that exaggerated cardiovascular reactions (e.g., large rises in heart rate and blood pressure) to acute psychological stressors (e.g., time-pressured cognitive tasks with negative feedback and social evaluative threat paradigms) are associated with concurrent alterations in stress-induced neural activity within the amygdala (Gianaros et al., 2008) and medial prefrontal cortex (Wager et al., 2009). Importantly, exaggerated cardiovascular reactions have been established by health psychologists to confer risk for cardiovascular disease (Chida & Steptoe, 2010). And both the amygdala and anatomically-networked regions of the medial prefrontal cortex participate in stress- and emotion-related processes, as well as in the regulation of peripheral physiology (Phelps & LeDoux, 2005; Roy, Shohamy, & Wager, 2012). Accordingly, health neuroscience findings are furthering our understanding of the brain systems involved in stress-related factors (cardiovascular stress reactions) important for physical health (e.g., cardiovascular disease). Moreover, such health neuroscience research has been extended to show that neural activity changes within the anterior cingulate cortex, as evoked by the cognitive regulation of negative emotions, associate with the severity of preclinical atherosclerosis in major blood vessels and that this association is mediated by systemic inflammation (Gianaros, Marsland, Kuan, et al., 2013). This work identifying a brain-body pathway to atherosclerosis complements a growing movement in health psychology toward emotion regulation interventions to improve physical health and is consistent with some models of allostatic load that describe the impact of stress on the brain, mind and body (B. S. McEwen & Gianaros,

2011) (McEwen & Gianaros, 2011). In addition to health neuroscience studies of stress and emotion, there is emerging work on social factors and interpersonal processes known to predict wide ranging health outcomes, including work on socioeconomic status (Gianaros, Marsland, Sheu, Erickson, & Verstynen, 2013), social ties and support (Eisenberger, 2013), and social discrimination (Akdeniz et al., 2014). Collectively, the work highlighted above promises to increase our brain-based understanding of how stress, emotion, and social factors "*get under our skin*" to influence our physical health (Miller, Chen, & Cole, 2009).

Health Behaviors

Health psychology holds a longstanding interest in health behaviors that increase (e.g., smoking) or decrease (e.g., mammography screening) health risks. Emerging health neuroscience studies extend this interest to conceptualize the brain as both a determinant and target of behaviors linked to physical health. For example, greater brain activity evoked by rewarding food cues *predicts* subsequent weight gain over six months (Demos, Heatherton, & Kelley, 2012). Moreover, weight gain may subsequently alter the function of brain systems that are responsive to food-related reward cues: women who gained weight over a six-month period had reduced striatal reward responses when consuming a milkshake (Stice, Yokum, Blum, & Bohon, 2010). Moreover, recent work suggests that weight gain negatively affects the structure of gray (Raji et al., 2010) and white matter tissue (Verstynen et al., 2013; Verstynen et al., 2012), illustrating *bottom-up* influences of physical health states on the brain.

Emerging neuroscience research is also informing psychological models of health behavior *change*. For example, increased neural activity in brain regions important for inhibitory-control processes predict smoking cessation among smokers attempting to quit (Berkman, Falk, & Lieberman, 2011). The brain may also mediate the efficacy of targeted health messages for health behavior change. For example, greater activity in the medial prefrontal cortex predicts subsequent sunscreen use (Falk, Berkman, Mann, Harrison, & Lieberman, 2010), healthy food choices (Hare, Malmaud, & Rangel, 2011), and smoking cessation (Chua et al., 2011).

Moreover, some of this work suggests that brain activity may predict broader success of national public health ad campaigns (Falk, Berkman, & Lieberman, 2012).

Interventions

Recent studies are also characterizing the role of the brain in determining how behavioral interventions (e.g., aerobic exercise, mindfulness meditation training) improve health. For example, randomized controlled trials (RCTs) of aerobic exercise training may increase hippocampal volumes ((Erickson et al., 2011) Figure 2), functional correlations in the activity within brain networks (Voss et al., 2010) and task-related functional activity in regions involved in executive functions, memory, and attention (Colcombe et al., 2004). Importantly, these changes to the brain account for exercise-related improvements in cognitive performance (Erickson et al., 2009; Erickson et al., 2011), which have implications for understanding how health behaviors associate with dementia and memory problems in adulthood via brain-body pathways (Erickson et al., 2010). Recent RCTs also suggest that mindfulness meditation interventions can reduce pain and stress reactivity, possibly via functional alterations in cortical and limbic brain circuits important for stress and emotion regulation (Creswell, 2014). These are only some of many other examples (i.e., pain management; (Hong et al., 2013)) that illustrate how health neuroscience approaches are extending the study of major topics in health psychology, particularly by conceptualizing and considering the bidirectional relationships between the brain and health behaviors.

Methodological and Computational Considerations

The conceptual and empirical goals of health neuroscience engender multilevel and often expansive methodological approaches—which, in a single study, may span genetic, molecular, organ systems, psychological, behavioral, social, and environmental levels of analysis. Accordingly, the computational challenges posed by health neuroscience may be expanded in size and complexity relative to other fields of psychology and neuroscience. This is particularly true when employing popular neuroimaging tools and analysis pipelines for studying brain↔health relationships. Most “off-the-shelf” analytical tools for neuroimaging data are tasked with estimating functional responses or morphological (structural) features of volumetric parcels of space resulting in up to several hundreds of thousands of correlated observations per subject. This not only results in challenges to control for the possibility of reporting chance findings and other quantitative issues affecting study inferences, but also forces health neuroscientists to confront so-called “Big Data” problems. Thus, in size alone, typical neuroimaging data sets can easily run into several gigabytes of data per person. When scaled to larger sample sizes typical of health psychology studies (e.g., hundreds of subjects), this can easily mushroom into terabytes or more of data per study. Indeed, the challenge of scaling to population-level neuroscience studies is an immensely complex topic that has been detailed elsewhere (Falk et al., 2013). Computational challenges may be further compounded by the use of analytic approaches that examine both individual brain areas and neural network dynamics across hundreds or thousands of connected brain areas. Furthermore, many questions in health neuroscience are often mediational in nature (e.g., Does the brain *mediate* the relationship between a health behavior intervention and improvements in physical health?). This means applying computationally demanding techniques often used in health psychology, like mediation analysis and structural equation modeling, to neuroimaging data, which could result in estimating hundreds of thousands of hierarchical or mediational models across the brain. In fact, such techniques have already been used to elucidate complex relationships like the influence of psychosocial factors on the neural representation of pain (Atlas, Bolger, Lindquist, & Wager, 2010) or the influence of social and physiological systems on global myelin integrity (Verstynen et al., 2013). These analytical approaches, along with machine learning techniques designed to refine hypothesis generation on neuroimaging data sets (Voytek & Voytek, 2012; Yarkoni, Poldrack, Nichols, Van Essen, & Wager, 2011) can dramatically expand the utility of assessing complex brain-health relationships.

Opportunities and Future Directions

As health neuroscience continues to grow, we anticipate an expansion of our knowledge about the role(s) of the brain in physical health and the reciprocal relationships between physical and mental health via brain pathways. Such knowledge will be driven in large part by questions that are cross-fertilized by interdisciplinary perspectives. For example, common questions asked in cognitive neuroscience (e.g., What are the neural correlates of response inhibition?) can be extended as health neuroscience questions (e.g., Do the neural correlates of response inhibition relate to health behaviors, such as smoking cessation? (Berkman et al., 2011)). Likewise, traditional social-affective neuroscience questions on the neural correlates of emotion regulation can be extended to questions about how the neural systems supporting emotion regulation also relate to health relevant aspects of hypothalamic-pituitary-adrenal axis functioning (Urry et al., 2006) or behavioral treatment efficacy (Lieberman et al., 2004). Hence, what will define creative future health neuroscience approaches and questions is whether there is a brain-based focus on physical health mediators and outcomes.

As this field grows, we also anticipate the continued refinement of conceptual and analytical perspectives with respect to the parent disciplines of health psychology and neuroscience and allied fields of study. We maintain that in health neuroscience, the brain can be thought of as an outcome, or dependent, variable—but in a unique interpretive framework. Thus, some studies noted above have examined the extent to which health behaviors (e.g., engagement in exercise) influence brain morphology, function, or integrity (Figure 2). However, in addition to conceptualizing the brain as an outcome, health neuroscience also views the brain as a potential mediator of health outcomes or as a predictor of health behaviors (Figure 1). Thus, health neuroscience envisions the brain as an important node that could be positioned either as a predictor, mediator, or outcome depending on the particular framework of the research question being studied. And, we expect that work on the horizon will fill in the details of this general conceptual framework.

We acknowledge that we selectively reviewed only a manageable subsample of possible studies illustrative of health neuroscience approaches and that there are other avenues and directions by which to incorporate neuroscience methods, theories, and models into topics of health psychology. We fully recognize the importance of integrative questions, methods, and findings from other disciplines relevant to health neuroscience and also recognize the importance of circumspect interpretations of studies that are correlational in nature and the need for methodological rigor when designing and interpreting the results from health neuroscience studies.

Over a decade ago, Sung and colleagues (Sung et al., 2003) argued that the most exciting science in the 21st century is likely to evolve *among*, not within, traditional disciplines. As a field situated *among* the traditional disciplines of health psychology and neuroscience, our hope is that our initial description of health neuroscience results in the growth of this exciting interdisciplinary area. As this new field is defined and shaped, we face important questions about how to fund this research, how to effectively train individuals in both neuroscience and health, and to build programs of research that can offer mechanistic and translational impacts. Nonetheless, health neuroscience investigations are poised to address longstanding questions in both health psychology and neuroscience—by helping the field develop new mechanistic models, and in understanding factors that confer risk and protection for physical health outcomes. In doing so, health neuroscience can have a significant impact on improving and transforming public health.

Recommended Reading

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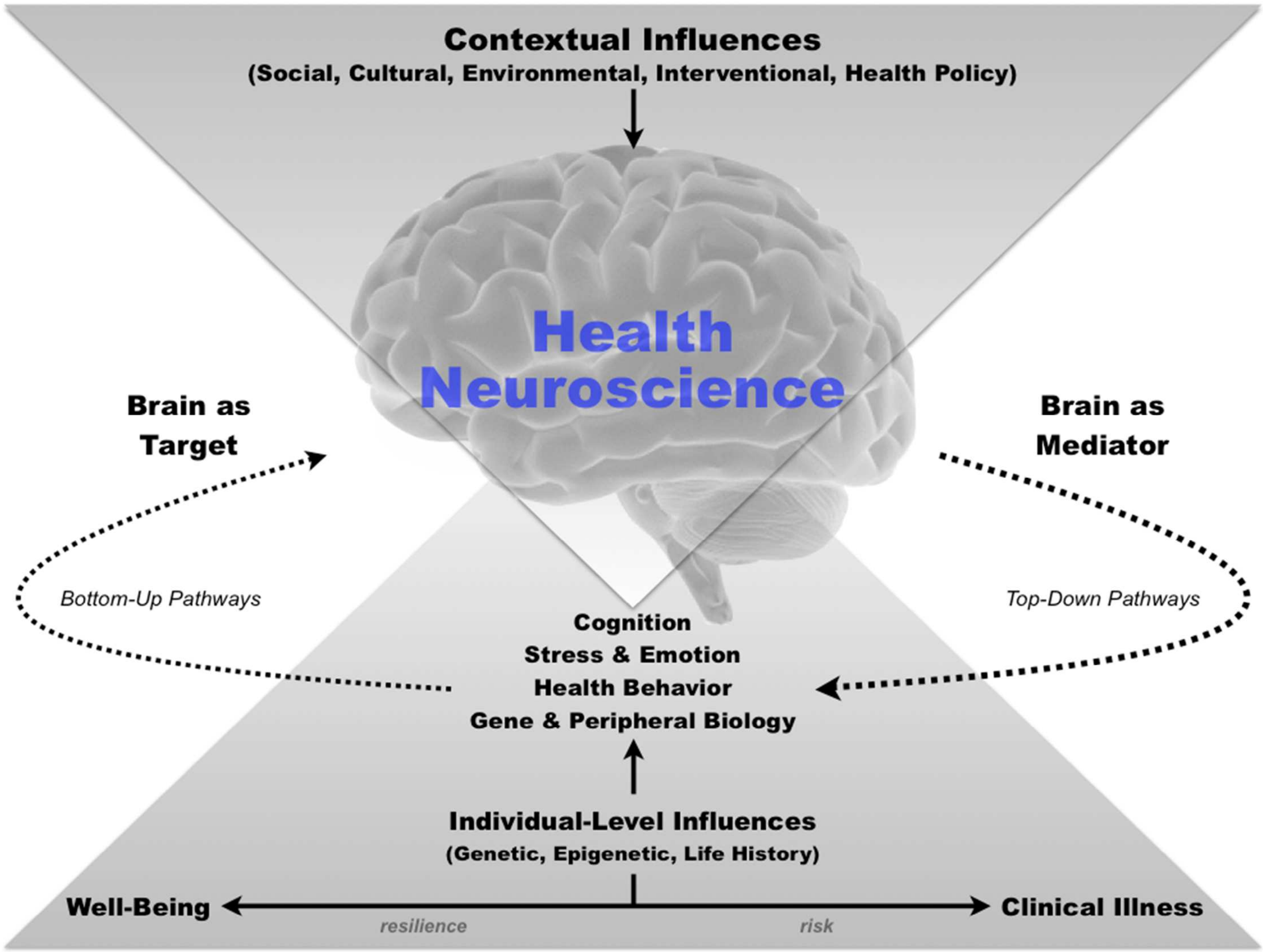
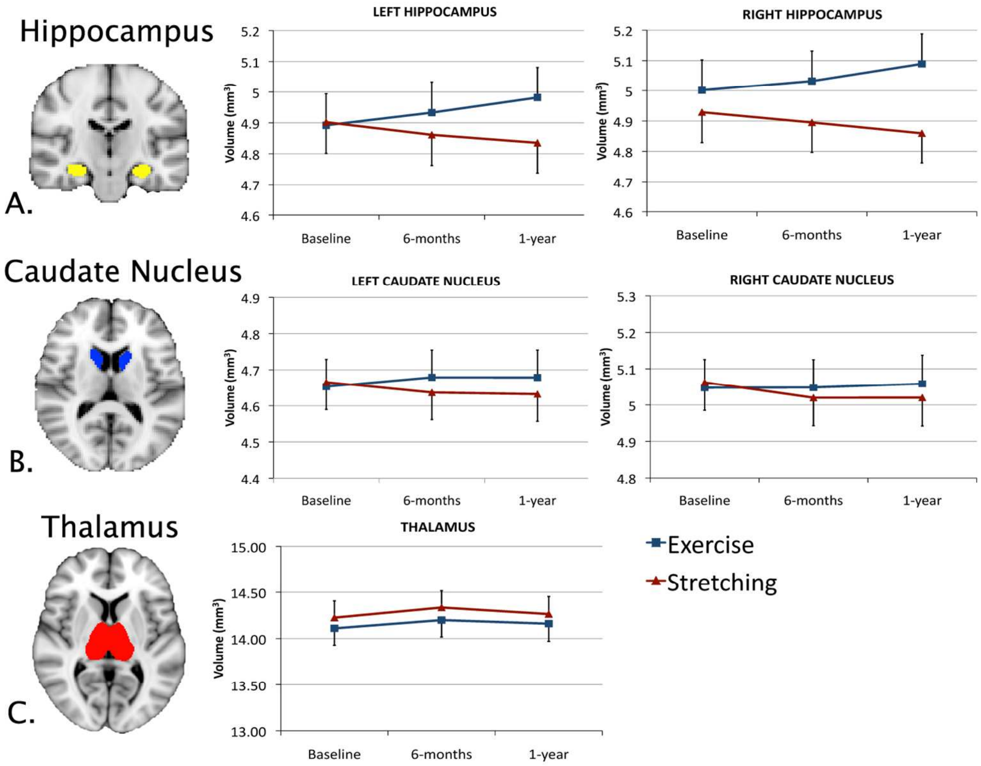
Figure 1. Health neuroscience is an interdisciplinary field at the interface of health psychology and neuroscience. Thematically, health neuroscience is concerned with understanding how the brain influences and is influenced by physical health across the lifespan—extending along a continuum shown at the bottom of the figure of optimal states of health and well being to states of disease risk, symptom expression, and clinical illness. Distal contextual influences at the top of the figure are viewed to impact physical health via downstream effects that are mediated by the brain, including social (e.g., familial and peer networks), cultural (e.g., valued group identities and shared practices), environmental (e.g., counties, neighborhoods, workplaces, etc.), interventional (e.g., efforts to change physical activity, diets, lifestyles, psychological states, etc.), and health policy (e.g., laws affecting the distribution of health resources, public health messaging and campaigns, etc.) influences. Proximal influences at the bottom of the figure are viewed to impact physical health via direct and interactive effects on the brain, as well as via mediating processes that affect and are affected by the brain, including genetic, epigenetic, developmental, and aging influences. Processes that bi-directionally and dynamically link the brain to states of health throughout life include factors that are widely studied in health psychology, but also studied historically in separate fields of study; namely, cognitive, stress, emotion, health behavioral, peripheral physiological, and gene expression processes. Health neuroscience studies are diverse and integrative, insofar as these processes

are viewed as being regulated by the brain via top-down (efferent) pathways and as influencing the brain via bottom-up (afferent) pathways. In this way, health neuroscience studies conceptualize measurements of brain function and structure as outcome variables that are dependent on bottom-up pathways and as independent variables that determine health processes via top-down pathways.

Figure 2. In this figure, Erickson and colleagues (2011) demonstrated that a 1 year randomized exercise intervention resulted in an increase in the size of the hippocampus relative to the control group, but no significant changes in the size of the caudate nucleus or thalamus. This example illustrates how a health behavior intervention (i.e., exercise) affects brain structure in ways that predict cognitive functioning.


Contextual Influences
(Social, Cultural, Environmental, Interventional, Health Policy)
Health
Neuroscience
Brain as
Target
Brain as
Mediator
Bottom-Up Pathways
Top-Down Pathways
Cognition
Stress & Emotion
Health Behavior
Gene & Peripheral Biology
Individual-Level Influences
(Genetic, Epigenetic, Life History)
Well-Being
Clinical Illness
resilience
risk


Hippocampus
A.
LEFT HIPPOCAMPUS
RIGHT HIPPOCAMPUS
Volume (mm³)
5.2
5.1
5
4.9
4.8
4.7
4.6
Baseline
6-months
1-year
Caudate Nucleus
B.
LEFT CAUDATE NUCLEUS
RIGHT CAUDATE NUCLEUS
4.9
4.8
4.7
4.6
4.5
4.4
5.3
5.2
5.1
5
4.9
4.8
Thalamus
C.
THALAMUS
15.00
14.50
14.00
13.50
13.00
Exercise
Stretching