Neuroscience and Well-Being

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Abstract:

Abundant evidence highlights the important role of personality traits, age, and social relationships in the experience of subjective well-being. Experiential factors influence well-being, and evidence shows that specific forms of training, such as physical exercise and mindfulness meditation, can produce strong and enduring beneficial effects on well-being. These factors also shape the structure and function of our brains throughout the lifespan, with fascinating implications for our well-being. However, understanding how well-being is created (and changed) by our brains has only recently become the focus of neuroscientific investigations. In this chapter, we review recent neuroscientific evidence revealing how the neurocircuitries underlying personality traits (i.e., optimism, negative bias, self-esteem, extraversion, and neuroticism), successful emotional aging, and social relationships (i.e., love and loneliness) contribute to well-being, and how these circuits and systems are altered in chronic stress, anxiety, and depression. Identifying the neural correlates of well-being can illuminate the processes that cause higher levels of well-being, which, in turn, can inform promising training interventions that can induce neuroplastic changes and help people live happier, healthier, and more successful lives.

Keywords: Affective biases, Neuroplasticity, Prefrontal cortex, Amygdala, Orbitofrontal cortex, Ventral striatum.

The study of well-being has deep philosophical roots dating back to Aristotle, who proposed that well-being has at least two components: hedonia and eudaimonia (Aristotle, 2009; Seligman, Steen, Park, & Peterson, 2005). The term "hedonic" originates in the ancient Greek word "Hedone", which means pleasure. Hedonic well-being is exemplified in Ed Diener's concept of subjective well-being, which encompasses a combination of positive affect and life satisfaction. Thus, hedonic well-being highlights positive affect as a defining feature of well-being. Eudaimonic well-being emphasizes aspects of a life experienced as meaningful (with purpose, growth, etc.), and may or may not be accompanied by positive affect. Studying the neural substrates of eudaimonic well-being is more challenging, as it is harder to define life meaning and to link it to specific brain regions or networks. Therefore, in this chapter we will focus mostly on the hedonic component of well-being.

Subjective well-being is influenced by a combination of individual characteristics, such as genetics, personality traits (Lucas & Diener, 2008), and age (Carstensen et al., 2011), by psychosocial factors, such as having a reasonable income (Diener & Oishi, 2000; Luhmann, Schimmack, & Eid, 2011), being married (Diener, Gohm, Suh, & Oishi, 2000), or having meaningful social relationships (Cacioppo & Patrick, 2008), as well as by lifestyle-related factors, such as exercise (Hassmén, Koivula, & Uutela, 2000) and engagement in mindfulness meditation (Carmody & Baer, 2008). Although a large amount of evidence accumulated during the last decade has advanced our understanding of the roles of these factors in the experience of subjective well-being, a number of essential issues remain unclear. Among these, a key issue refers to the brain mechanisms supporting well-being, which could help clarify *why some people experience greater well-being than others*, *what might go wrong in affective disturbances, and how different types of interventions can enhance brain function and well-being*. Recent brain imaging advances enabling the investigation of the neural correlates of positive emotions and overall well-being have provided essential contributions to answering these fundamental questions.

The goal of this chapter is to review recent neuroscientific evidence revealing how the different brain regions and systems contribute to well-being, how these are different in affective disturbances, and

how this knowledge about the brain can inform interventions aimed at helping people lead happier, healthier, and more successful lives. We start with a general overview of the brain and how it works, while also introducing some of the main brain regions typically involved in general emotion processing and in positive emotions associated with well-being (pleasure, reward). Then, we examine how the structure and function of these regions is different in people experiencing low levels of well-being, such as in stress and affective disorders (anxiety and depression). Next, we review evidence pointing to links between various brain regions and factors that contribute to well-being, including individual differences (i.e., personality- and age-related) and psychosocial factors (i.e., social connectedness). Finally, we conclude with evidence highlighting changes in the brain resulting from interventions focused on increasing well-being.

Neural Correlates of Well-Being

Brief Introduction to How the Brain Works

All of our mental life—our thoughts, emotions, memories, and decisions—is brought about by the physical substance of the brain. To understand how the brain enables well-being, it is necessary to first understand the basics of its organization (or structure), function, and modes of communication. All brain activity depends on the workings of neurons—cells that carry information from one place to another through a combination of electrical and chemical signals. Information is transferred between neurons at synapses, and is typically mediated by chemical signaling molecules, called neurotransmitters. The most relevant neurotransmitters that facilitate the enjoyment of a wide range of experiences and the desire to engage in these experiences are dopamine and opioids (the endogenous brain variety of opiates) (Kringelbach & Berridge, 2010). The outer layer of the brain forms the cerebral cortex, which is responsible for many of the attributes that we consider inherently human, like language, reasoning, and imagination. The cerebral cortex is divided into four lobes. The frontal lobe, the front section of the brain, is involved in the planning, guidance, and evaluation of behavior. The parietal lobe, located in the middle section of the brain, is involved in integrating information from multiple sensory modalities within the body, and information from memory. The temporal lobe, located in the bottom section of the brain, is associated with auditory processing, memory, visual item recognition, and emotion. Finally, the occipital lobe, located at the back of the brain, is mainly involved in processing visual information. Below the cortex, in the center of the brain, are the subcortical structures, which contain many of the core areas involved in emotion and reward processing, and contributing to the experience of well-being. An abundance of neuroscientific evidence indicates that the subjective experience of happiness, pleasure, rewards, and general well-being depends on shared or overlapping networks of interacting subcortical and cortical regions. These networks involved in processing emotions and rewards include subcortical structures such as the amygdala, ventral tegmental area, nucleus accumbens, and ventral pallidum, and portions of the prefrontal cortex regions, including the medial prefrontal cortex, orbitofrontal cortex, anterior cingulate cortex, and insula.

Neural Correlates of Emotion

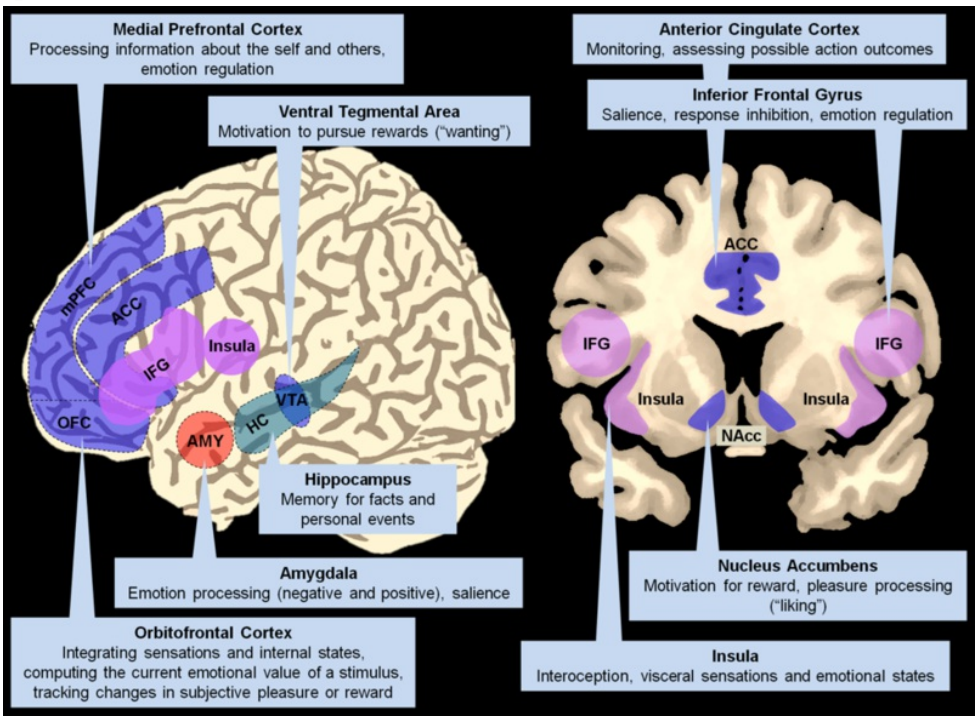
Emotion processing has been associated with a wide range of interacting brain regions (Lindquist, Wager, Kober, Bliss-Moreau, & Barrett, 2012). In this review we focus on regions that have been typically associated with well-being. A region that plays a critical role in the detection of emotional information and in learning the emotional significance of the information is the *amygdala (AMY)*, a small, almond shaped subcortical region located deep in the brain, in the temporal lobe. Traditionally, the AMY was linked exclusively to processing negative emotions, such as fear and anger. However, current views also highlight the AMY's role in processing positive emotions, and more generally in detecting salient stimuli (Adolphs, 2008, 2009; Dolcos, Iordan, & Dolcos, 2011; Whalen, 2007). Positive experiences increase the release of dopamine, the most important neurotransmitter for the experience of reward or pleasure, which makes the AMY react stronger to positive events and experiences, and send signals to the nearby hippocampus (HC) to remember such experiences.

The main cortical areas involved in emotion processing are located in the frontal lobe, which consists of a number of regions. The most relevant for well-being are the prefrontal cortex regions (especially its medial and orbital parts), the inferior frontal cortex, and the anterior cingulate cortex. The *prefrontal cortex (PFC)*, which comprises the anterior regions of the frontal lobe, takes part in the more complex aspects of planning, organizing, and executing behavior. The *medial PFC (mPFC)* plays important roles in processing information about the self and others, emotion regulation, and emotional decision making. The *orbitofrontal cortex (OFC)*, the most ventral part of the PFC, is especially involved in the experience of pleasure, happiness, and well-being. Located just above the orbits, this region receives input from the external senses (vision, hearing, touch, smell, and taste), as well as input related to the internal states of the body (via the insula, described below). By comparing the properties of an external

stimulus (e.g., sweet, friendly) with the body's current internal state, the OFC (especially its mid-anterior part) computes the current emotional value of a stimulus at a particular moment, and tracks changes in the subjective pleasure or reward. The *inferior frontal cortex (IFC)*[1] is involved in a diverse range of processes, such as basic processing of emotional and salient information, response inhibition, and emotion regulation. Another frontal lobe structure, the *anterior cingulate cortex (ACC)* is connected to many brain areas, including the PFC and AMY, which allows this region to have an important integrative role in emotion, self-monitoring, and reward anticipation. The ACC is involved in assessing the value of responses; that is, whether an action is likely to elicit a reward or punishment, which is different from the role of the OFC, which computes whether a stimulus is currently rewarding or punishing. Overall, there is also evidence that the left PFC plays a more specialized role in positive affect and approach-driven behaviors, whereas the right hemisphere is involved in negative affect and withdrawal/avoidance-driven behaviors, but this evidence is not discussed in details here (Davidson, 2004; Eddington, Dolcos, Cabeza, & Strauman, 2007; Eddington et al., 2009; Herrington et al., 2010).

Another brain region involved in emotion processing is the *insula*, which is an area of cortex tucked between the frontal and temporal lobes. Commonly known for its role in disgust, the insula actually has a wider role in emotional processing, being involved in monitoring the internal states of a body. The more complex whole-body sensations associated with emotional states, like feelings of happiness, sadness, or elation, are processed in the anterior insula, whereas basic visceral sensations like pain, temperature, or fatigue are processed in the posterior insula. Figure 1 highlights these brain regions and their main roles.

Figure 1. Neural circuitry of well-being emphasized in the present review. The areas circumscribed by dotted lines shown in the left panel illustrate brain regions located deep inside the brain. Note that the highlighted regions are meant to give a general idea of the locations in the brain, whereas delineations used for analysis might target specifically gray or white matter and use nomenclature specific to one or the other.



Neural Correlates of Reward

Neuroscientific evidence has shown that positive experiences engage a set of reward brain centers, which paint a "hedonic gloss" on some of our experiences. Before talking about these reward centers, we need to define the concept of reward. Reward consists of three components (Berridge & Kringelbach, 2015). The first component is the one most associated with reward, which is the actual pleasure or *liking*. The second component is the motivation for reward, or *wanting.* The third component is *learning* about future rewards based on past experiences. "Liking" is the core process of hedonic pleasure, whereas "wanting" refers to the motivation to obtain the reward, or the incentive salience. "Liking" is a present-moment, interoceptive feeling of well-being, whereas "wanting" is a future expectation of well-being. In

addition to these psychological dissociations, "liking" and "wanting" can be also dissociated at the neuroanatomical and neurochemical levels. "Wanting" is generated by more widely distributed subcortical brain circuits, especially by the mesolimbic dopamine system, which connects the dopamine-rich ventral tegmental area to the nucleus accumbens (see Figure 1). The *ventral tegmental area* contains many neurons that produce dopamine. The *nucleus accumbens* (NAcc), a subcortical structure located deep inside the brain, contains many dopamine receptors. Dopamine released from the mesolimbic system into the NAcc regulates the incentive salience of the stimuli. In addition to dopamine, other neurotransmitters, including opioids (natural brain neurochemicals similar to opiate drugs), also contribute to the incentive salience or "wanting" (reviewed in Berridge, 2009). "Liking" is generated by more restricted brain regions than "wanting", and is also more restricted neurochemically. "Liking" is enhanced by opioid stimulation in opioid hotspots such as the NAcc and the ventral pallidum. Although dopamine was considered by many as playing a role in sensory pleasure, recent evidence suggests that dopamine is only involved in "wanting" something, but not necessarily in "liking" it (Berridge & Kringelbach, 2015). Therefore, "liking" and "wanting" are different aspect of pleasure, and they involve different neurotransmitters. Opioids are the ones causing people to enjoy the experience, and dopamine keeps them coming back for more. While the "liking" component of reward is relatively understudied, the "wanting" part is very well studied, especially in the form of addiction.

In summary, no single brain area is responsible for the experience of emotion, pleasure, and reward. Rather, a number of brain regions interact to produce the different types of emotional experiences that accompany well-being.

When Things Go Wrong: Stress, Anxiety, and Depression

As described above, the experience of positive emotions, pleasure, and well-being is supported by the normal functioning of a number of brain regions and their interconnections[2]. Disturbances in the structure and function of these regions can reduce the ability to experience positive emotions and pleasure, which is commonly seen in chronic stress, anxiety, and depression.

Stress and the Brain

Everyone experiences stress in their life—from minor stressors such as a traffic jam or financial difficulties to major stressors such as divorce or the loss of a loved one. Stressors can cause a wide range of emotional responses, from mild alertness, to a sense of being overwhelmed and literally feeling stressed out. However, not all stress is bad. Acute or moderate stress (eustress), or what we commonly refer to as basic fight-or-flight response, not only helps people get out of danger in unexpected emergency situations, but can also have beneficial effects on people's health, strengthening the immune and cardiovascular systems. However, chronic stress, that is stress extending over longer periods of time, with no end in sight, can have deleterious effects on brain structure and function, and on people's health and well-being, leading to increased incidence of disease, such as generalized anxiety disorder, major depressive disorder, and post-traumatic stress disorder (PTSD) (Dohrenwend & Dohrenwend, 1974; Kendler, Gardner, & Prescott, 1999; Monat, Lazarus, & Reevy, 2007). Before describing the effects of stress on the brain, we need to understand how stress works.

Exposure to stressors activates the body's stress response (the fight-or-flight response), which involves the production of hormones and neurochemicals in the brain. Two key hormones are cortisol, which helps activate our brain and senses to increase alertness to better deal with emergency situations, and adrenaline, which gets the body immediately activated and aroused for action. Cortisol hard-wires the pathways between the AMY, which is important for emotions and for learning about aversive stimuli, and the adjacently located HC, which is critical for episodic memories. The hippocampal cells have the largest number of cortisol receptors in the brain, making the HC highly receptive to any change in cortisol levels. Short exposure to cortisol improves hippocampal activity and memory, but prolonged exposure to high levels of cortisol damages hippocampal cells. Patients with conditions associated with long-term stress exposure, such as depression and PTSD, have significantly shrunken HC (Arnone, McIntosh, Ebmeier, Munafo, & Anderson, 2012; Bonne et al., 2008; Koolschijn, van Haren, Lensvelt-Mulders, Hulshoff Pol, & Kahn, 2009; McEwen, Nasca, & Gray, 2016), suggesting that long-term cortisol exposure has destroyed their hippocampal cells. They also show changes in the size and connectivity of the AMY (Hamilton, Siemer, & Gotlib, 2008; McEwen et al., 2016; Morey et al., 2012). Increased stress in patients with these conditions puts the AMY into overdrive, and the increased AMY activity is accompanied by reduced activity in the PFC (Bremner, 2006).

Anxiety, Depression, and the Brain

Anxiety and depression are associated with symptoms of reduced well-being, such as negative

affective biases (Cisler, Bacon, & Williams, 2009; Eysenck, Derakshan, Santos, & Calvo, 2007; Gotlib, Krasnoperova, Yue, & Joormann, 2004), and enhanced encoding of negative stimuli (Hamilton & Gotlib, 2008; Russo et al., 2006). In addition, structural and functional neuroimaging evidence indicates that brain regions implicated in emotion and reward processing are altered in anxiety and depression. For example, individuals with anxiety and depression tend to show decreased volume in frontal lobe regions such as the OFC and ACC (Arnone et al., 2012; Koolschijn et al., 2009; Shang et al., 2014; Talati, Pantazatos, Schneier, Weissman, & Hirsch, 2013), as well as in medial temporal regions such as the HC and AMY (Alemany et al., 2013; Arnone et al., 2012; Fisler et al., 2013; Hayano et al., 2009; Irle et al., 2010; Koolschijn et al., 2009; Meng et al., 2013), suggesting that these conditions are linked to structural changes in key regions engaged during processing and integration of emotional and motivational signals.

Furthermore, anxiety and depression have been linked to reduced integrity of the structural connections between these brain regions, including between the frontal lobe and the AMY (Cullen et al., 2010; de Kwaasteniet et al., 2013; Kim & Whalen, 2009; Zhang et al., 2012), supporting the idea that the structure within and between key brain regions involved in emotion and reward processing are altered in anxiety and depression. Moreover, anxiety and depression are associated with aberrant brain activity, including communication between brain regions when the brain is "at rest" (i.e., resting state functional connectivity). For instance, anxiety is characterized by reduced resting state connectivity between PFC and the AMY (Hahn et al., 2011; Kim et al., 2011), and depression by increased resting state connectivity within a network of brain regions implicated in autobiographical memory, and decreased connectivity within a network implicated in cognitive control, relative to healthy individuals (Rayner, Jackson, & Wilson, 2016). These findings suggest that maladaptive cross-talk between brain regions occurs in anxiety and depression even when not engaged in a particular task. During tasks, individuals with anxiety or depression tend to show enhanced response in AMY to negative stimuli compared to control groups (Etkin & Wager, 2007; Groenewold, Opmeer, de Jonge, Aleman, & Costafreda, 2013), consistent with the idea that anxiety and depression influence the mechanisms subserving emotion processing.

Together, these findings identify brain mechanisms underlying chronic stress and reduced mental health, which are key factors in understanding the neuroscience of well-being, and highlight potential targets for preventive and therapeutic interventions aimed at decreasing susceptibility and increasing resilience against affective conditions to support improved well-being.

Factors Influencing Well-Being:

The Role of Individual Differences and Social Relationships

Important insight into understanding well-being has been offered by research clarifying the neural substrates of individual differences that play a role in promoting enhanced well-being and protecting against symptoms of reduced well-being. Among these, the most studied are individual differences in personality and age, which are discussed here. The role of social relationships is also discussed, with a focus on *love* and *loneliness*.

Personality, the Brain, and Well-Being

Personality influences many aspects of our lives, including our emotions, thoughts, and ultimately our well-being. Although a breadth of personality characteristics can be considered in the context of well-being, the present discussion focuses on several key factors that emerge from the literature, including *optimism, negative bias, self-esteem, and Big 5 traits.*

Optimism, a deep-rooted mindset defined as the dispositional tendency for people to hold generalized favorable expectancies about their future (Carver, Scheier, & Segerstrom, 2010), has been shown to be associated with coping behavior (Nes & Segerstrom, 2006), to be beneficial in times of adversity (Carver et al., 2010), and to promote psychological well-being (Andersson, 1996; Carver et al., 2010). Optimism is not just feeling good or thinking positively—it also helps us stay engaged in important tasks with important rewards (Scheier & Carver, 1985). Optimism leads to increased well-being because by expecting to do well, people will increase their engagement and persistence, being therefore more likely to achieve their goals.

Emerging evidence shows that optimism is associated with the structure and function of the brain. Structurally, trait optimism has been associated with greater volume in reward-related (Grabenhorst & Rolls, 2011; Kringelbach & Berridge, 2009; Phelps, Lempert, & Sokol-Hessner, 2014) and approach-oriented (Eddington et al., 2007) processing regions, such as the OFC (Dolcos, Hu, Iordan, Moore, & Dolcos, 2016). Moreover, optimism has been shown to mediate the relation between the OFC and symptoms of reduced well-being, thus demonstrating that increased volume in this brain region can play a

protective role against anxiety through increased optimism (Dolcos et al., 2016). In addition to the OFC, trait optimism has also been associated with a region of the ACC (rostral anterior cingulate cortex, rACC) when imagining future positive events vs. future negative events (Sharot, Riccardi, Raio, & Phelps, 2007). This region, known to be involved in self-reflection (Moran, Macrae, Heatherton, Wyland, & Kelley, 2006; Paulus & Frank, 2003) and assessing the salience of emotional and motivational information (Bush, Luu, & Posner, 2000), has also shown increased functional connectivity with the AMY when imagining future positive events compared to imagining negative events (Sharot et al., 2007).

Research examining the brain chemistry associated with optimism (Fox, 2013) posits that the optimistic mindset is rooted in the "sunny brain", the pleasure center of the brain, whereas the pessimistic mindset is rooted in the "rainy brain". The sunny brain consists of neurons in a core reward region, the NAcc, that forms links with neurons in particular areas of the PFC, and seems to be left lateralized (Davidson & Irwin, 1999). Converging evidence from healthy and clinical studies support these lateralization findings, suggesting that the two hemispheres are differentially engaged in these fundamental approaches to life (reviewed in Hecht, 2013).

Overall, the reviewed evidence highlights the role of the OFC, rACC, and NAcc in supporting optimism, and points to brain-personality mechanisms promoting enhanced well-being as well as protecting against reduced well-being.

Negative Bias. Another important aspect of understanding the neural correlates of well-being is clarifying the links between individual differences in *affective biases* that influence well-being. Positive affective biases tend to be observed in optimistic individuals and are associated with indicators of improved well-being (Segerstrom, 2001), whereas negative affective biases tend to be observed in individuals with emotional disorders and are associated with indicators of reduced well-being (Cisler et al., 2009; Eysenck et al., 2007; Gotlib et al., 2004). Negative affective biases are often expressed as enhanced sensitivity to negative or threatening information (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007), and likely reflect compromised executive control of attention (Cisler et al., 2009) and impairment of the ability to inhibit prepotent responses and to resist interference to task-irrelevant distracters.

Negative attentional biases can be captured by tasks like the Affective Go/No-Go, in which participants are asked to respond to target stimuli and withhold from responding to distracter stimuli, while targets and distracters differ in affective valence. A negative affective bias can be detected by an increased speed and/or accuracy in participant responses when attending to negatively (vs. positively) valenced information (Schulz et al., 2007). This pattern is typically shown by patients with affective disorders, whereas the opposite pattern is typically shown by healthy participants (Erickson et al., 2005). Together, these results support the idea that negative biases in attention can be targeted to clarify potential links between impaired control mechanisms and affective disorders. Structural and functional imaging evidence has linked the IFC with performance in Go/No-Go tasks (Brown et al., 2015; Brown et al., 2012; Liddle, Kiehl, & Smith, 2001; Swick, Ashley, & Turken, 2008, 2011). Structural damage to the IFC is associated with higher error rates (Swick et al., 2008), and greater IFC activity has been seen in no-go trials (Liddle et al., 2001), particularly for negative emotional contexts (Brown et al., 2012), consistent with the idea that IFC helps to inhibit prepotent responses and is differentially engaged by emotional stimuli. Furthermore, the IFC responses to affective stimuli seem to be modulated by trait anxiety (Fales, Becerril, Luking, & Barch, 2010). More specifically, Fales et al. (2010) showed that higher anxiety was associated with greater activation within the left IFC in response to fearful (vs. neutral) targets, while lower anxiety was associated with greater activation to happy (vs. neutral) targets. Extending these previous findings, a recent study (Hu & Dolcos, 2017) showed that trait anxiety was negatively correlated with left IFC volume, and positively correlated with a negative bias in reaction time. Furthermore, trait anxiety mediated the negative association between the IFC volume and the negative bias measure, thus demonstrating that decreased volume in this brain region is linked to negative affective bias through anxiety.

Overall, extant evidence highlights the influence of negative affective bias in attention, and points to the IFC as a region both structurally and functionally associated with executive control. Available evidence shows that negative affective bias tends to be associated with enhanced sensitivity to negative or threatening information, possibly linked to compromised executive control of attention, and subserved by alterations of underlying brain mechanisms. In turn, negative affective bias plays a key role in understanding the neurophysiological substrates of well-being.

Self-Esteem is another important factor that has been shown to greatly predict well-being (Diener, 2009). Self-esteem typically refers to one's global attitudes about oneself (Rosenberg, 1965). Interestingly, evidence suggests that when happiness decreases, self-esteem decreases as well (Laxer, 1964; Wessman & Ricks, 1966), suggesting that the relation between these factors might be bidirectional (Diener, 2009).

At a neural level, self-esteem has been shown to be associated with both the structure and function of the brain. Structurally, self-esteem has been linked to greater HC volume, in both younger and older adults, suggesting a potential protective role against challenges such as stress (Pruessner et al., 2005). Self-esteem is also associated with the structural connections between regions, such as the white matter integrity between the mPFC and the ventral striatum (Chavez & Heatherton, 2015), consistent with the role of these brain regions in processing information about the self and positive affective processes such as reward, respectively. Functionally, self-esteem has been linked to modulation of brain activity both at rest and during tasks. Greater self-esteem was associated with greater resting state functional connectivity between the ventral mPFC and the HC (and between the cuneus/lingual gyrus and right dorsolateral PFC and ACC) (Pan et al., 2016), consistent with the idea that brain networks supporting self-referential, memory, and cognitive control-related processes support self-esteem. Furthermore, tasks involving social exclusion or social feedback have shown that self-esteem modulates the engagement of ACC and mPFC responses (Onoda et al., 2010; Somerville, Kelley, & Heatherton, 2010). For instance, individuals with lower self-esteem relative to a high self-esteem group reported greater social pain in response to social exclusion, and had both greater response in ACC and greater connectivity between ACC and PFC (Onoda et al., 2010). These findings are consistent with the idea that self-esteem influences brain mechanisms engaged for interpretation of social signals and can lead to differential outcomes relevant to well-being.

Together, extant evidence suggests that self-esteem and the associated neural correlates influence factors of well-being. Self-esteem appears to be greatly linked to indices such as happiness, and is supported by both the structure and function of the brain. Hence, continuing research on these relations will refine and improve understanding and promotion of well-being.

Big 5 Traits. Yet another important aspect of understanding individual differences and the brain regions subserving well-being is the role of *general* personality factors. The link between the brain and well-being is complex, and might be better understood if individual differences in general personality traits are also taken into account. Personality is commonly studied using the Big 5 model, which includes the dimensions of extraversion, neuroticism, agreeableness, conscientiousness, and openness to experience (Costa & McCrae, 1992). Whereas the Big 5 have been shown to be linked to measures of well-being, most findings focus on extraversion and neuroticism, which are also the focus of this review (for details about agreeableness, conscientiousness, and openness to experience, see DeNeve & Cooper, 1998; Gutierrez, Moreno-Jimenez, Garrosa, & Puente, 2005; Hayes & Joseph, 2003). Extraversion is typically defined as a trait reflecting sensitivity to reward and positive affect, whereas neuroticism generally encompasses sensitivity to punishment and negative affect. Extraversion is linked to indicators of increased well-being, such as positive affect (DeNeve & Cooper, 1998; Gutierrez et al., 2005), enhanced recall of positive memories (Mayo, 1983; Rusting, 1999) and maintaining a positive mood after retrieval of positive personal memories (Denkova, Dolcos, & Dolcos, 2012). In contrast, neuroticism is associated with indicators of decreased well-being, such as negative affect, reduced life satisfaction, reduced happiness, and a tendency to recall negative information (Bradley & Mogg, 1994; DeNeve & Cooper, 1998; Gutierrez et al., 2005).

Available evidence links extraversion and neuroticism to the structure and function of the brain. For example, extraversion is positively associated with the medial OFC (DeYoung et al., 2010). Neuroticism is negatively linked to AMY volume (Hu et al., *in press*), and positively linked to the volume of regions engaged by sensitivity to punishment, negative emotion, and emotional dysregulation (mid-cingulate gyrus and caudate) (DeYoung et al., 2010). These traits have also been linked to other structural aspects such as cortical thickness (Riccelli, Toschi, Nigro, Terracciano, & Passamonti, 2017), and the structural connections between brain regions (i.e., white matter) (Xu & Potenza, 2012), as well as to the function of the brain. For instance, resting state functional connectivity measures have shown that extraversion and neuroticism are differentially associated with activity in networks of brain regions while at rest (Adelstein et al., 2011; Sampaio, Soares, Coutinho, Sousa, & Goncalves, 2014), consistent with the idea that these traits are linked to regions engaged in processes such as emotion regulation, self-evaluation, and reward (Adelstein et al., 2011; Andrews-Hanna, Reidler, Sepulcre, Poulin, & Buckner, 2010). Moreover, extraversion and neuroticism influence brain responses, especially in the AMY and HC, during tasks that involve emotional learning (Haas & Canli, 2008; Hooker, Verosky, Miyakawa, Knight, & D'Esposito, 2008). Overall, the reviewed evidence highlights the role of general personality factors as possible targets for better understanding susceptibility, and improving resilience, against emotional disturbances.

Successful Aging, the Brain, and Well-Being

Healthy aging is generally associated with improved emotional functioning and well-being (Carstensen et al., 2011; Mather, 2012; Scheibe & Carstensen, 2010). Brain imaging findings parallel this behavioral evidence, suggesting that healthy aging is associated with relatively preserved structural integrity in regions typically involved in the processing and valuation of emotional information (AMY,

mPFC), whereas it is associated with marked anatomical (Fjell et al., 2009; Raz, Ghisletta, Rodrigue, Kennedy, & Lindenberger, 2010; Raz et al., 2005) and physiological (Fabiani, 2012; Reuter-Lorenz & Park, 2014) losses in specific brain structures typically involved in executive control and emotion regulation (lateral PFC). Of note, given that the mPFC is also involved in some forms of emotion regulation (Roy, Shohamy, & Wager, 2012) and does not seem to show significant age-related cortical volume loss, it is possible that older adults may rely more on this structure in controlling their emotional responses (Mather, 2016).

In the context of overall preserved emotional functioning and well-being in aging, considerable evidence supports the idea of an age-related *positivity effect* in emotional perception, attention, and memory, by which older adults tend to pay greater attention to and remember more positive information (Charles, Mather, & Carstensen, 2003; Isaacowitz, Wadlinger, Goren, & Wilson, 2006; Knight et al., 2007; Mather & Carstensen, 2003) and show reduced processing of negative information (Grühn, Scheibe, & Baltes, 2007; Wood & Kisley, 2006), compared to younger adults (see also Mather, 2016; Reed & Carstensen, 2012; Reed, Chan, & Mikels, 2014). In order to explain this age-related positivity effect and its impact on well-being, a few models of emotional aging have been proposed. According to the *Socioemotional Selectivity Theory* (SST; Carstensen, Fung, & Charles, 2003), older adults' preference for positive over negative information is driven in part by their prioritization of more present-focused motivational goals related to emotional meaning and satisfaction, which in turn enhances their well-being. The SST model interprets the positivity effect as a consequence of enhanced top-down modulation by the PFC/ACC influencing AMY response (Dolcos, Katsumi, & Dixon, 2014; St. Jacques, Dolcos, & Cabeza, 2010), thus emphasizing the role of motivational goals in emotion regulation (Carstensen et al., 2003). Another influential model called the *Aging Brain Model* (ABM; Cacioppo, Berntson, Bechara, Tranel, & Hawkley, 2011) interprets it as a consequence of impaired bottom-up processing of negative arousing stimuli by the AMY in older adults, considering that its response to positive stimuli may be relatively unimpaired by advancing age (Cacioppo et al., 2011). It is important to note, however, that there is evidence identifying activation of overlapping areas of the AMY between younger and older adults in processing negative stimuli (Dolcos et al., 2014; St. Jacques et al., 2010). Therefore, it is unlikely that the age-related reduction in AMY activity can be explained by impaired functioning of this region, as posited by the ABM.

In addition to reduced processing of negative stimuli, available evidence points to the link between enhanced processing of positive/rewarding stimuli and increased psychological well-being in aging. For instance, among a sample of middle-aged and older adults, those who showed sustained activity in the striatum, which is typically involved in the processing of various types of reward, over time in response to viewing positive pictures also reported overall greater levels of well-being (Heller et al., 2013). Moreover, striatal activation related to the viewing of positive stimuli mediated the relationship between well-being and daily levels of the stress hormone cortisol. In particular, greater levels of well-being were associated with increased activation in the striatum during positive picture processing, which in turn was associated with decreased levels of cortisol (Heller et al., 2013). Overall, these findings suggest that sustained engagement of the striatum in positive emotion processing is a key factor associated with well-being and adaptive regulation of stress necessary for maintaining health (see also Ryff, Heller, Schaefer, Van Reekum, & Davidson, 2016).

Taken together, these findings suggest that healthy aging is associated with an age-related positivity effect in emotion processing, as reflected in reduced processing of negative stimuli and enhanced processing of positive stimuli. This age-related positivity effect appears to be subserved by brain regions involved in basic/bottom-up processing (e.g., AMY, striatum) and those involved in higher-order/top-down processing and control (e.g., PFC, ACC) of emotional information. Successful engagement of these regions may in turn lead to improved subjective well-being in older adults.

Social Relationships, the Brain, and Well-Being

Humans are fundamentally a social species, sharing a strong need to interact with others. Social relationships can provide enjoyment and can feel rewarding (Kahneman, Krueger, Schkade, Schwarz, & Stone, 2004). They give people access to the benefits of shared resources, security, and social support (Baumeister & Leary, 1995), and have a protective role, being associated with a variety of positive outcomes ranging from lower rates of mortality (House, Landis, & Umberson, 1988) and increased survival from heart attacks (Seeman, 1996) to physical (Holt-Lunstad, Smith, & Layton, 2010) and mental/subjective well-being across the lifespan. On the flip side, however, the perceived absence of social relationships, or loneliness, makes people feel more unsafe and threatened in social contexts (Cacioppo et al., 2011; Cacioppo & Patrick, 2008), and is associated with increased risk of depression (Cacioppo, Hawkley, & Thisted, 2010; Cacioppo, Hughes, Waite, Hawkley, & Thisted, 2006) and other negative outcomes.

Interactions with others are so critical for our survival that we developed larger brains and complex neural networks to be able to understand other people and to predict their intentions. Interestingly, when at rest, the brain's pattern of activity looks very similar to when people are thinking about others, oneself, and the relation of oneself to other people (Mars et al., 2012). This has led some scientists to believe that "our brains are built to practice thinking about the social world and our place in it" (Lieberman, 2013). As such, it should not be surprising that a lack of interactions with the social world, and especially perceived loneliness, has deleterious effects on health through its effects on the brain (Cacioppo & Hawkley, 2009). The neural substrates supporting social cognition/behavior consist of many cortical and subcortical regions, each involved in several distinct processes. Most of the structures that we have talked about as being important in processing emotions and rewards are also important for social behavior. These include the AMY, the OFC, and the ventral striatum (especially the NAcc, caudate nucleus, and the putamen). Additional brain regions are also involved in social relationships. The next paragraphs review structural and functional changes in the brain associated with the involvement in dyadic or more extended social relationships (i.e., love and social networks), and the perceived absence of social relationships (i.e., loneliness).

Love is a complex and rewarding mental state involving cognitive and goal-directed behavioral components (Bianchi-Demicheli, Grafton, & Ortigue, 2006). The different kinds of love (e.g., passionate, maternal) are important predictors of positive emotions, happiness, and satisfaction (Myers, 1992). Evidence indicates both common and dissociable circuits for different kinds of love (e.g., romantic vs. maternal). Functional brain imaging evidence (Bartels & Zeki, 2000; Bartels & Zeki, 2004) shows that all types of love engage subcortical dopaminergic reward-related brain systems (involving dopamine and oxytocin receptors), which play an important role in goal-directed motivation, reward, and pair-bonding (Ortigue, Bianchi-Demicheli, Patel, Frum, & Lewis, 2010). However, the different types of love also involve distinct neural networks inside and outside the dopaminergic network (Bartels & Zeki, 2004; Fisher, Aron, & Brown, 2005). For instance, passionate love engages the ventral tegmental area (part of the brain's reward circuit, associated with the motivation to pursue rewards) and the caudate nucleus (associated with reward detection and expectation). Maternal love recruits similar brain areas, with a specific involvement of the periaqueductal gray matter, an area that receives direct connections from the limbic emotional system, and contains a high density of receptors (vasopressin) that are important in maternal bonding and in pain suppression during intense emotional experiences like childbirth.

Interestingly, the presence of a loved one is not only rewarding, but it may act as a buffer against pain or stress. Showing female participants pictures of a loved male while receiving painful stimulation was associated with reduced reported pain intensity (Master et al., 2009), and such an analgesic effect correlated with activity in the reward-related NAcc (Younger, Aron, Parke, Chatterjee, & Mackey, 2010). Holding a partner's hand, relative to holding the hand of a stranger or squeezing a ball, produced similar effects (Master et al., 2009). Moreover, love also reduces critical social assessment of others. For instance, when people look at their loved partners, the neural circuits that are normally associated with critical social assessment (AMY, temporo-parietal junction, and mPFC) of other people are suppressed, whereas regions involved in reward and attachment (caudate nucleus, putamen, medial insula, ACC) are activated (Bartels & Zeki, 2000). In sum, love facilitates positive emotions, by connecting the NAcc with the PFC, and reduces negative emotions, such as social judgment, by connecting the NAcc to the AMY.

Loneliness has been linked to a number of psychological states that contribute to morbidity and mortality, including increased depression (Booth, 2000; Cacioppo et al., 2010; VanderWeele, Hawkley, Thisted, & Cacioppo, 2011) and lower subjective well-being (Kong, Zhao, & You, 2013; VanderWeele, Hawkley, & Cacioppo, 2012). Loneliness also influences individuals' perception and appraisal of the world. There is behavioral and neural evidence that loneliness increases attention to potential threats from the social world (Cacioppo & Hawkley, 2009), and is associated with increased worry about being evaluated negatively, as well as with higher levels of perceived threat in social situations (even when there is no increased likelihood of being rejected; Jones, Freemon, & Goswick, 1981). Lonely people also tend to feel more unsafe, compared to non-lonely people. They tend to appraise other individuals as more threatening, and to isolate themselves when confronted with stressors, rather than actively looking for the help and support of others (Berscheid & Reis, 1998; Cacioppo & Hawkley, 2005).

Loneliness involves multiple brain mechanisms, and produces significant changes in both brain structure and function. Recent structural brain imaging studies have identified relationships between loneliness and the density of gray and white matter in different regions of the brain. Loneliness was negatively correlated with the gray matter density in the left posterior superior temporal sulcus (pSTS), an area involved in processing biological motion and social perception (Kanai et al., 2012); the pSTS size was also related to poorer performance in a social perception task. Loneliness has also been associated with widespread reduction in white matter density in areas related to self- and social-cognition (bilateral inferior

parietal lobe, the right anterior insula, and left posterior temporo-parietal junction), as well as areas associated with empathy (the left pSTS and right lateral PFC) and self-efficacy (dorsomedial PFC) (Nakagawa et al., 2015). In addition to these structural changes, neuroimaging evidence also reveals functional changes associated with perceived loneliness in a number of brain regions involved in the detection of threat (AMY, ACC, the ventrolateral PFC, and the insula; Cacioppo et al., 2013; Eisenberger & Lieberman, 2005; Eisenberger, Lieberman, & Williams, 2003), and managing the demands of complex social contexts (OFC, mPFC, STS, temporo-parietal junction; Bickart, Hollenbeck, Barrett, & Dickerson, 2012; Cacioppo, Norris, Decety, Monteleone, & Nusbaum, 2009; Cacioppo et al., 2016; Eisenberger & Cole, 2012; Klumpp, Angstadt, & Phan, 2012).

Overall, the evidence reviewed in this section illustrates the essential role of social relationships for our happiness and well-being. Our brains are wired to be social, and this wiring of our brains motivates us to engage in relationships with others, which in turn, increases positive emotions, enjoyment, and feelings of reward. The fact that by simply enhancing social connections in our everyday lives we can enhance our well-being highlights the need to develop interventions focused on educating the social brain.

Enhancing Well-Being through Brain Building Interventions

The brain is a dynamic system, which responds to environmental demands and generates goals and actions, and hence its anatomical structure and physiology continuously change throughout our life. This ability to physically change and to maintain this change is known as *neuroplasticity*. Neuroplasticity has fascinating implications for our well-being! A growing body of evidence suggests that neuroplasticity is associated with variations in brain activity, which might come from experience (May, 2011), training/learning (Draganski & May, 2008), clinical status (Cahn et al., 2002), or injury (Sidaros et al., 2009). Plasticity allows our brains incredible flexibility, and evidence shows that our experiences can make real changes in the structure and function of our brains. This means that we have the power to change our brains for the better. Although the mechanisms underlying neuroplasticity are still an area of active research, it may describe a result of Hebbian learning, which posits that repeated patterns of neuronal firing lead to increased synaptic connectivity (Hebb, 1949), and suggests that these alterations might lead to changes in brain structure, such as gray matter volume (Boyke, Driemeyer, Gaser, Buchel, & May, 2008; Draganski et al., 2004; Draganski et al., 2006) and white matter connections between brain regions (Tang, Lu, Fan, Yang, & Posner, 2012), as well as brain function (Dayan & Cohen, 2011). Notably, extant evidence points to the possibility that interventions can be performed to improve well-being and the underlying structure and function of the brain (Davidson & McEwen, 2012). This idea has led to new and emerging research targeting different forms of training interventions to improve well-being and the brain. Areas in this domain include physical training and mindfulness training.

Physical Activity, the Brain, and Well-Being

Physical activity has been consistently associated with profound benefits for brain structure and function, and overall well-being. Engaging in physical activity might be enjoyable, and is associated with increased positive mood (Steptoe, Kimbell, & Basford, 1998; Yeung, 1996) and decreased negative mood (McIntyre, Watson, & Cunningham, 1990; Raglin & Wilson, 1996; Steptoe, Kearsley, & Walters, 1993). More important than these transient effects on mood are the more enduring effects of physical exercise, reflected in reduced stress and symptoms of anxiety and depression (Blumenthal et al., 2007; Silveira et al., 2013), prevention of the onset of depression (Schuch et al., 2016), and overall improved well-being (Penedo & Dahn, 2005). How is physical activity relieving the detrimental effects of stress and improving mood and well-being? Physical exercise changes the way the brain processes the information, and even more importantly, it changes the brain, having a positive effect on the structure and function of a number of brain regions (Foster, 2015), including the HC and the PFC. Although the exact mechanisms underlying the beneficial effects of physical activity on the human brain and well-being are not clear, extant research attributes these advantageous effects to a number of factors, including changes in neurotransmitters and neurogenesis – that is, the capability to recruit, in some specific areas of the adult brain, more neurons, showing cellular and synaptic plasticity abilities (Garcia-Segura, 2009). We will review these effects in turn below.

A possible neurobiological mechanism underlying these beneficial effects of exercise is the increased synthesis and release of neurotransmitters and neurotrophins, which could result in neurogenesis and neuroplasticity (Dishman et al., 2006). A critical mechanism involved in depression seems to be the depletion of a category of neurotransmitters called monoamines, including serotonin and norepinephrine (López-Muñoz & Alamo, 2009). Animal models provide evidence that, similar to the effects of antidepressants, regular aerobic exercise increases serotonergic and noradrenergic levels in the brain (Chaouloff, 1989; de Coverley Veale, 1987; Meeusen & De Meirleir, 1995; Van Praag, 1982). For instance,

treadmill training and wheel running have been linked to increased levels of norepinephrine in the HC and frontal cortex in rodents (Dishman, 1997; Dunn, Reigle, Youngstedt, Armstrong, & Dishman, 1996). Exercise has also been associated with increases in the synthesis of serotonin (Chaouloff, 1997; Dunn & Dishman, 1991; Meeusen & De Meirleir, 1995; Wilson & Marsden, 1996).

Accumulating evidence shows that physical exercise has a strong influence on inducing neuroplasticity (Voss et al., 2013), increasing the levels of the brain derived neurotrophic factor (BDNF). Research in rodents has shown that 20 days of voluntary wheel running increased BDNF levels in the HC and caudal neocortex (Meeusen & De Meirleir, 1995; Russo-Neustadt, Beard, & Cotman, 1999). The increase in BDNF increases functioning in the serotonergic system and may promote neuronal growth. Research in humans confirms the beneficial effects of physical exercise on neurogenesis. A 3-month fitness training (Pereira et al., 2007) study in a small group of middle-aged participants showed increases in measures of cerebral blood volume (CBV) in a region of the HC (i.e., the dentate gyrus). The location of the CBV changes in the dentate gyrus is interesting, given that previous animal evidence has shown neurogenesis in these very specific regions.

Physical activity interventions have also been shown to have positive effects in children, producing changes in brain structure and function. Research shows that more active children have greater HC volume (Chaddock, Erickson, Prakash, Kim, et al., 2010), along with greater basal ganglia volume (Chaddock, Erickson, Prakash, VanPatter, et al., 2010), and greater white matter integrity (Schaeffer et al., 2014). In addition, they show increased and more efficient patterns of brain activity (Voss, Nagamatsu, Liu-Ambrose, & Kramer, 2011), and superior executive and cognitive control performance (Chaddock et al., 2012; Davis et al., 2011; Hillman et al., 2014).

Most studies on the effects of exercise in humans have been done in the elderly. These studies have demonstrated that exercise improves older adults' cognitive abilities in various domains (and the associated neural mechanisms), or more directly, subjective well-being (reviewed in Bamidis et al., 2014; Gajewski & Falkenstein, 2016; Hillman, Erickson, & Kramer, 2008; Kramer & Erickson, 2007). Greater physical activity and cardiorespiratory fitness have been associated with reduced age-related cognitive declines and a lower risk for dementia in older adults (Buchman et al., 2012; Sofi et al., 2011). Furthermore, mounting evidence suggests that aerobic exercise interventions, such as those involving walking or dancing, lead to enhanced cognitive abilities and subjective well-being in older adults (Awick et al., 2017; Awick et al., 2015; Colcombe & Kramer, 2003; Kattenstroth, Kalisch, Holt, Tegenthoff, & Dinse, 2013; Netz, Wu, Becker, & Tenenbaum, 2005). Recent brain imaging studies in this population have shown that physical exercise induces both structural and functional changes in a variety of brain regions. For instance, weekly aerobic walking was associated with increased volume of the anterior HC in older adults, which was in turn positively associated with improvements in spatial memory performance due to exercise (Erickson et al., 2011). Similar beneficial effects of exercise have also been identified with respect to neural functioning. In particular, older adults who had undergone aerobic training for six months showed increased activity in the lateral PFC and parietal cortex and decreased activity in the ACC during a challenging task involving conflict resolution and selective attention; these participants also showed improvements in behavioral performance on the task (Colcombe et al., 2004). Overall, these findings suggest that exercise interventions can enhance the ability of the aging brain to effectively allocate neural resources, which in turn leads to improved performance on a cognitively challenging task (see also Voss et al., 2011).

In summary, exercise has beneficial effects by increasing the production of neurotransmitters such as serotonin and noradrenaline, by stimulating the growth factor and blood flow, and by stimulating adult neurogenesis.

Mindfulness Training, the Brain, and Well-Being

In recent years, there has been growing interest in the use of mindfulness-based training and intervention programs to improve well-being and to identify the underlying brain mechanisms associated with such improvements (Chiesa & Serretti, 2010; Fox et al., 2014; Gotink, Meijboom, Vernooij, Smits, & Hunink, 2016; Lomas, Ivtzan, & Fu, 2015). Mindfulness generally refers to "the awareness that emerges through paying attention on purpose, in the present moment, and non-judgmentally to the unfolding of experience moment by moment" (Kabat-Zinn, 2003). Training programs focusing on mindfulness typically target skills aimed at reducing distressing symptoms, including those associated with psychological disorders and somatic conditions.

Behaviorally, mindfulness training tends to mediate improved indices of well-being, such as decreased stress, rumination, and trait anxiety, as well as increased positive states of mind, psychological well-being, quality of life, and self-compassion (Branstrom, Kvillemo, Brandberg, & Moskowitz, 2010; Carmody & Baer, 2008; Nyklicek & Kuijpers, 2008; Shapiro, Brown, & Biegel, 2007; reviewed in Visted, Vollestad, Nielsen, & Nielsen, 2015). Notably, mindfulness training has been targeted in many different

populations. For example, mindfulness interventions have been tested in healthy and clinical populations (Chiesa & Serretti, 2010; Fox et al., 2014; Gotink et al., 2016; Lomas et al., 2015), including groups with psychological conditions such as anxiety (Vollestad, Nielsen, & Nielsen, 2012; Vollestad, Sivertsen, & Nielsen, 2011) and depression (Jain, Walsh, Eisendrath, Christensen, & Cahn, 2015; Kuyken et al., 2016; van der Velden et al., 2015). Mindfulness-based interventions have also been tested in different age groups, such as children and adolescents (Kallapiran, Koo, Kirubakaran, & Hancock, 2015), young and middle-aged adults (Fox et al., 2014), and older adults (Ehrenbrusthoff, Ryan, Schofield, & Martin, 2012). Although there is much heterogeneity of the practices and goals of mindfulness interventions when applied to these various groups, available evidence generally points to improvement in intervention outcomes (Quaglia, Braun, Freeman, McDaniel, & Brown, 2016; Visted et al., 2015).

At a neural level, mindfulness interventions have been shown to induce changes in both the structure and function of the brain. Structural studies have associated mindfulness training with increased gray matter volume or density in the cingulate cortex (Hölzel et al., 2011), insula (Murakami et al., 2012), and HC (Hölzel et al., 2011). Evidence for structural changes in the AMY seems a bit less clear (Hölzel et al., 2010; Murakami et al., 2012; Pickut et al., 2013), and is perhaps influenced by other factors such as sample demographics. However, overall, available evidence appears consistent with the idea that mindfulness engages brain regions that are key for body awareness, memory, and emotion (Fox et al., 2014). Mindfulness and meditation practice have also been associated with modulation of structural connectivity between brain regions. For example, meditation practice has been linked to changes suggesting enhanced connectivity within and between hemispheres of the brain (Luders et al., 2012; Tang et al., 2010), which is consistent with the idea that mindfulness and meditation training can improve the underlying connections in the brain that support attentional self-regulation processes (Luders et al., 2012). At the functional level, mindfulness training was associated with changes in the resting state functional connectivity between the so-called default mode and salience networks (Doll, Hölzel, Boucard, Wohlschläger, & Sorg, 2015), consistent with the idea that interactions between brain networks support the ability to attend to current experience without judgment. Moreover, mindfulness training appears to also influence brain responses when engaged in tasks, such as paradigms that involve responding to, or regulating response to, emotional stimuli. A study by Creswell and colleagues (2007), for example, showed that when labeling emotions, the AMY was negatively associated with lateral PFC activation in more mindful individuals. This evidence seems consistent with the idea that mindfulness training modulates the neural mechanisms involved in emotional processes.

Although how mindfulness interventions alter brain structure is still an open question that is being investigated, a number of possible mechanisms have been proposed (reviewed in Tang, Hölzel, & Posner, 2015). An account referred to as “use-dependent plasticity” (Bütefisch et al., 2000; Kleim et al., 2002; Kleim, Barbay, & Nudo, 1998; Nudo, Milliken, Jenkins, & Merzenich, 1996; for reviews of relevant studies in humans see Draganski & May, 2008; May, 2011) suggests that there is a relation between the structure of the brain and its level of use. This account may describe a result of Hebbian learning as mentioned above (Hebb, 1949), and suggests that these structural changes might lead to alteration in brain structure (Draganski et al., 2006). Consistent with the Hebbian learning model, it is possible that repeated engagement in mindfulness affects brain structure through expansions of existing synapses and dendrites, or creation of new synapses. It is also possible that engaging in mindfulness induces the formation of new neurons or myelin sheaths that help insulate the connections between neurons. Another possibility is that mindfulness influences autonomic and immune activity, which might help preserve or restore neurons. Alterations in these mechanisms at the level of brain cells might contribute to overall changes in the volume of brain regions and the integrity of the connections between them.

In sum, extant evidence on mindfulness training and the brain suggests that mindfulness interventions can enhance well-being, and modulate the structure and function of the brain. Available evidence highlights the benefits of mindfulness training, and further research in this area will continue to refine understanding of the effective practices and underlying neural mechanisms, in order to better promote well-being.

Conclusion

Taken together, the diverse body of neuroscientific evidence reviewed in this chapter reveals that factors known to play critical roles in well-being, such as personality traits, age, and social relationships, are influenced by subtle differences in the volume, function, and connectivity of a network of emotion- and reward-related regions. Our mind is highly plastic, and what we think, feel, and do changes the physical structure of the brain, and the function of different brain circuits. Given that the brain circuits supporting positive emotions and rewards are remarkably malleable, we have the amazing ability to reshape our brains, to change our affective mindsets, and to improve our well-being. One way to enhance well-being is

to address the rising tide of chronic stress, anxiety, and depression, conditions that have negative impacts on the life and well-being of an increasing number of people worldwide. Another way is to engage in activities that have positive impacts on our minds and bodies. Being physically active and engaging in mindfulness meditation are known to produce many physiological changes in our body, but they can also produce striking changes in the structure, function, and communication between the brain regions supporting well-being, helping us to lead happier and healthier lives. This suggests that well-being might be enhanced through training. Future research is needed to tap further into the enormous potential benefits of these training activities and to determine whether such training can produce changes with long-lasting consequences.

Endnotes

[1]It is important to consider the distinction between cortices and gyri when discussing neural correlates. Anatomically, cortex usually refers to gray matter in particular, while gyrus might refer to both gray and white matter. Depending on the goal of a study, the focus might be specifically on the gray matter of a particular region, in which case it is referred to as cortex (e.g., inferior frontal cortex, IFC), or the focus might be on a region of interest that does not distinguish between gray and white matter, and thus it is referred to as gyrus (e.g., inferior frontal gyrus, IFG). Hence, in the text and Figure 1 both cortical and gyral terms appear.

[2]Current brain imaging techniques allow noninvasive mapping of the anatomical and functional connections among distant brain regions. Structural connectivity refers to the "integrity" of the anatomical connections linking sets of neuronal elements. These connections refer to the white matter fibers linking different areas of the brain, and are often measured using a special magnetic resonance imaging approach called diffusion tensor imaging, or DTI. Functional connectivity evaluates the interconnections between spatially separated brain regions that occur at rest (resting state functional connectivity), or when a subject is performing an explicit task.

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