Neurobiological substrates of personality: A critical overview

Tal Yarkoni

University of Colorado Boulder

Draft of 01/31/2013

Abstract

Interest in the neurobiological substrates of personality has increased substantially in recent years as a result of the widespread availability of powerful new methods for investigating brain structure and function. This chapter provides a critical overview of the personality neuroscience literature. The first section discusses a number of methodological considerations that arise when attempting to study personality at a biological level. The second section selectively reviews recent work on the structural and functional neural correlates of personality, focusing on examples that illustrate principles of broad applicability in personality neuroscience. Finally, the third section discusses the conceptual implications of the reviewed work, focusing particularly on ways in which personality psychologists and neuroscientists can benefit maximally from a synergistic, interdisciplinary approach. The overarching aim is to provide personality psychologists with minimal familiarity with the biological literature with a sense of both the strengths and the limitations of a neurobiological perspective.

The assertion that the brain is the proximal source of human behavior is no longer controversial. Virtually all contemporary scientists accept that our thoughts, feelings and actions reflect electrochemical impulses occurring within our central or peripheral nervous systems rather than the mysterious influence of an immaterial soul. But if the brain is the proximal source of all people's behavior, it follows that it's also the proximal source of individual *differences* in behavior: Where we observe that two people behave differently (on average) in similar situations, we can conclude that some aspect of their brain structure and function must also be different. Affirming that all personality differences are ultimately biological differences doesn't deny the crucial role of environment and culture in guiding the developmental trajectory and expression of personality; it simply recognizes that the brain is the proximal mediator of those more distal influences. Identifying the neural mechanisms that support stable differences in personality—whatever their distal origin—is the focus of the emerging field of personality neuroscience.

In this chapter, I provide an overview of recent work at the interface of personality and neurobiology, with a particular emphasis on cognitive and systems neuroscience approaches. I make no attempt at an exhaustive review; indeed, a major theme of the chapter is to argue that 'grand model' approaches that seek one-to-one mappings between biological mechanisms and the various dimensions of major psychometric models (e.g., the Big Five) are fundamentally unlikely to succeed. Instead,

I focus on three goals. First, I discuss a number of methodological considerations that arise when attempting to study personality at a biological level. Second, I selectively review recent work on the structural and functional neural correlates of personality, focusing on examples that illustrate principles of broad applicability in personality neuroscience. Third, I discuss the conceptual implications of the reviewed work, focusing particularly on ways in which personality psychologists and neuroscientists can benefit maximally from a synergistic, interdisciplinary approach. The overarching aim is to provide personality psychologists with minimal familiarity with the biological literature with a sense of both the strengths and the limitations of a neurobiological perspective.

Methodological Considerations

Although the focus of the present review is substantive rather than methodological, a number of important methodological considerations are worth keeping in mind when evaluating the extant literature on the neurobiology of personality. I focus on three issues here: (i) the pernicious effects of the small samples typically used in neurobiological investigations of personality; (ii) the difficulty in drawing causal inferences from correlational biological data; and (iii) the complex relationship between psychometric descriptions of personality at a between-subject level and causal processes underlying behavior that unfold at a within-subject level. These issues are by no means new; by and large, they echo concerns that many other

researchers have raised over the past few decades, often in the context of older psychophysiological methods (e.g., Hans J. Eysenck, 1997; Gale & Edwards, 1983; Guilford, 1975). They are worth reiterating here, however, because while novel methods such as functional MRI have many important benefits over older techniques, they are not panaceas for long-standing methodological and conceptual concerns, and in some cases are actually more susceptible to certain problems (e.g., the high cost of fMRI tends to encourage small sample sizes).

Small sample sizes produce an illusion of highly selective, very strong effects

When the first functional magnetic resonance imaging (fMRI) studies of personality were conducted in the early 2000s, the strength of the results surprised many researchers. Consider an early study by Canli and colleagues (T Canli et al., 2001), who presented 14 participants with pictures from the International Affective Picture System (IAPS; (Lang, Bradley, & Cuthbert, 1999)) during scanning, and observed remarkably strong ($r > .74$) correlations between the traits of Extraversion and Neuroticism and brain activity changes in specific regions such as the amygdala, striatum, and middle frontal gyrus in response to affective pictures. These early studies offered what seemed like a remarkably clear explanation of the neural mechanisms underlying very broad personality traits: they reflected individual differences in the broad disposition of the brain's affective systems to respond to emotionally salient

stimuli, consistent with previous behavioral work interpreting Extraversion and Neuroticism in terms of increased positive and negative reactivity, respectively (Larsen & Ketelaar, 1989, 1991; Rusting & Larsen, 1997).

Many personality psychologists, upon first seeing the results of such studies, might have had the reaction that they were working in the wrong field. After all, if cognitive neuroscientists could routinely identify variables that explained more than half of the variance in complex traits, why bother conducting behavioral studies where correlations of .2 or .3 between personality and other variables are sometimes considered a best-case scenario (Meyer et al., 2001; Roberts, Kuncel, Shiner, Caspi, & Goldberg, 2007)? But the love affair didn't last very long. Over the past few years, researchers both within and outside the neuroscience community have come to appreciate that the results produced by small-sample neuroimaging studies (and to a large extent other kinds of neuroscientific investigations) are, too put it delicately, too optimistic.

The most obvious problem is that small studies have low power to detect all but extremely large effects (J. Cohen, 1988); consequently, in cases where activation changes are widely distributed over the brain, but are relatively weak in magnitude, researchers are liable to identify only a small fraction of true effects (Yarkoni & Braver, 2010; Yarkoni, 2009). More insidiously, however, low power will also tend to dramatically inflate statistically significant effects (i.e., those that happen to pass some critical

statistical threshold), because when power is low, the only way to detect a given effect is to capitalize on chance to some degree (Gelman & Weakliem, 2009; Ioannidis, 2008; Yarkoni, 2009)[1]. Personality psychologists who work primarily at a behavioral level and have the luxury of collecting (relatively) large samples should consequently keep in mind that statistically significant results reported in neurobiological studies of personality are likely to look more selective and much stronger than they actually are.

Misconceptions about the brain/mind relationship

Many people implicitly hold dualistic views about the mind, and this appears to be true of both lay people and a surprising number of scientists and mental health professionals (Ahn, Proctor, & Flanagan, 2009; Demertzi et al., 2009; Miresco & Kirmayer, 2006). Implicitly dualistic pronouncements are found in many studies—particularly those drawing on behavioral genetic evidence. For instance, Sutin and colleagues motivated a recent study of the neural correlates of Openness to Experience by suggesting that since "approximately 50% of the variance in Openness is heritable … This genetic influence suggests a strong biological basis" (p. 2797, Sutin, Beason-Held, Resnick, & Costa, 2009). Costa and McCrae (1992a) similarly suggested that "there are

[1] Lest personality psychologists experience a moment of schadenfreude, it's worth noting that this problem also afflicts behavioral research to a lesser extent, and remains widely underappreciated. It is very common to see personality researchers interpret the magnitude of their statistically significant effects in the context of other researchers' findings without giving any consideration to potential differences in sample sizes. In many cases, differing sample sizes will be sufficient to completely explain the differences in distribution of effect sizes (e.g., see 2/5/13 7:22 PM for an illustration in the context of personality effects on word use).

good reasons to suspect that all five factors have some biological foundation, because measures of all five have shown evidence of heritability" (p. 658). But if one is serious about the idea that there are no non-material influences on behavior, such pronouncements do not make sense. Whatever else may be true, 100% of the reliable variance in behavior must ultimately be mediated through biological mechanisms. Knowing that a personality trait is highly heritable does not make it any more or less biologically-based (Turkheimer, 1998). By the same token, knowing that a trait has a biological basis does not imply that it is fixed or immutable, as many people—including mental health professionals (Miresco & Kirmayer, 2006)—intuitively suppose. Since any influence of the environment on personality must also be mediated by the brain, the mere identification of neural correlates of personality says nothing about the relative malleability or stability of behavior.

A related and underappreciated point is that observing a correlation between a personality variable and a biological variable does not in and of itself validate the utility or importance of that personality variable. Personality psychologists sometimes appeal to neurobiological or genetic evidence in an effort to ground specific psychometric models of personality. This sentiment was perhaps best captured in an influential article by Costa and McCrae entitled "four ways the Five Factors are basic" (Costa & McCrae, 1992a). The authors argued that since all five factors of the FFM have identifiable neural correlates and show high heritability, the FFM must, in effect, capture nature at its true

joints. But if we accept that 100% of the reliable variance in *every* personality trait must ultimately reflect differences at the neural level, observing a correlation between personality and the brain provides no specific support for any particular model of personality. One could certainly argue that some measures of personality do a better job of carving nature at its joints than others—i.e., they show strong correlations with a few well-defined biological variables rather than weak correlations with many different variables—but such a conclusion must be supported by a careful comparative analysis involving multiple measures and well-delineated neurobiological constructs. The mere presence of correlations with biological variables does not in and of itself validate a psychometric model, as it could not conceivably be otherwise.

Reconciling individual differences with process models

Lastly, it is important to remember that there is a large gap between descriptive psychometric models of personality based on individual differences in overt behavior or self-report, and process models that aim to identify the mechanisms that produce behavior within a given individual. That there is a relationship between the two is undeniable; as Underwood (1975) influentially pointed out:

> If we include in our nomothetic theories a process or mechanism that can be measured reliably outside of the situation for which it is serving its theoretical

> purpose, we have an immediate test of the validity of the theoretical formulation … The assumed theoretical process will necessarily have a tie with performance which reflects (in theory) the magnitude of the process. Individuals will vary in the amount of this characteristic or skill they "possess." (p. 130).

However, the relationship between individual differences and process model approaches need not be a transparent one. For a variety of reasons, the joints at which people vary from one another the most need not be the same ones that play the largest role in explaining mean-level changes in behavior. For example, many neurobiological models of emotion assign the amygdala a central role in detecting and signaling the presence of salient stimuli in the environment—particularly threatening ones (LeDoux, 2000; Zald, 2003). Although it is likely that variation in amygdala function does indeed partly explain individual differences in conceptually related traits like Neuroticism (see below), this relationship is not strictly entailed; it may well be the case that other mechanisms are more important in generating differences between individuals. Put differently, there is no guarantee that any particular psychometric model of individual differences in personality will map onto underlying biological process models in any straightforward way. In fact, as I argue below, a clear-cut relationship between the two is likely to be the exception rather than the rule.

Neurobiological Bases of Personality: a Selective Review

In this section, I selectively review work on the neurobiological bases of personality. The review cannot hope to be comprehensive, as the extant literature is far too large to adequately capture in one chapter. Instead, I focus attention on select examples from the literature that illustrate important principles more broadly applicable to the biological study of personality. Moreover, in contrast to several previous reviews (e.g., T Canli, 2004; Deyoung & Gray, 2008) the present review is organized by biological level of description and methodological approach rather than by personality trait. This approach reflects the view (discussed in more detail in the final section) that the partitioning of traits found in standard psychometric model of personality is a pragmatic abstraction, and that the dimensions of common psychometric models have no special biological status. Thus, in place of 'grand model' approaches, the present review emphasizes the need for domain-specific personality models that focus on specific clusters of behaviors. For examples of such domain-specific reviews, the reader is referred to previous work—e.g., the many excellent chapters in a volume edited by Canli (2006).

Neurotransmission

A great deal of research on the biological substrates of personality has focused on individual differences in neurotransmission. Neurotransmitters are endogenous

chemicals that transmit signals across synapses, effectively constituting the primary form of information flow between neurons. Although dozens of distinct neurotransmitters have been identified, personality scientists have focused attention predominantly on modulatory neurotransmitters such as dopamine and serotonin, which exert diffuse effects on information processing throughout the brain. Perhaps the most influential such model was developed by Cloninger and colleagues (Cloninger, Svrakic, & Przybeck, 1993; Cloninger, 1987), who proposed a mapping between three major dimensions of the Temperament and Character Inventory (TCI)—Novelty Seeking, Reward Dependence, and Harm Aversion—and the neurotransmitters dopamine, norepinephrine, and serotonin, respectively.

Although Cloninger's model of personality is an elegant one, it is also clearly wrong in many respects (cf. Deyoung & Gray, 2008; Paris, 2005). While a number of studies have reported positive support for one or more of Cloninger's three proposed associations (e.g., (Hansenne & Ansseau, 1999; Hennig, Toll, Schonlau, Rohrmann, & Netter, 2000; Ruegg et al., 1997; Stuettgen, Hennig, Reuter, & Netter, 2005)), these associations are relatively non-specific; it’s now abundantly clear that each of the three TCI dimensions is reliably associated with individual differences in other neurotransmitter systems. For example, the dimension of novelty-seeking has been linked not only to dopaminergic differences, but also to biological markers of individual differences in serotonergic (Netter, Hennig, & Roed, 1996; Tyrka et al., 2006),

noradrenergic (Gerra et al., 1999), glucocorticoid (Piazza et al., 1993), and cannabinoid (Van Laere et al., 2009) function, among others. Conversely, each of the neurotransmitter systems in question is linked to multiple traits; for example, serotonin is variously implicated in differences in dispositional negative affect, behavioral inhibition, aggression, and impulsivity (for reviews, see Carver & Miller, 2006; J. A. Gray, 1987; K P Lesch & Merschdorf, 2000; Klaus Peter Lesch, Zeng, Reif, & Gutknecht, 2003; Olivier & Van Oorschot, 2005). Against such a backdrop, positive corroboration of putative trait-neurotransmitter associations is relatively uninformative; one also needs to establish that the posited effects are meaningfully larger than the many other associations that have been identified in the literature but are not predicted by Cloninger's model (or most others).

A case study in complexity: dopamine and personality. To illustrate the complexity inherent in trying to identify neurotransmission differences associated with personality, consider the case of dopamine. Dopamine is known to play a central role in reward, and extensive evidence suggests that a cluster of traits conceptually related to reward-seeking—including extraversion, novelty-seeking, behavioral activation, etc.—are associated to some degree with dopamine function. Perhaps the most influential dopamine-related model of personality is Depue and Collin's (1999) 'incentive facilitation' account linking variation in the mesolimbic dopamine pathway—which projects from the ventral tegmental area (VTA) to the nucleus accumbens, orbitofrontal

cortex, and other regions implicated in affect and motivation—to the agentic aspects of extraversion. The key postulate of Depue's model is that extraverts are likely to exert greater energy in pursuit of reward-related goals in virtue of having increased dopaminergic transmission. In this respect, Depue's work aligns with behavioral work suggesting that extraverts show increased reactivity to positive affective stimuli (Larsen & Ketelaar, 1991; Rusting & Larsen, 1997), as well as a number of fMRI and PET studies reviewed in the next sections.

Although the extraversion-mesolimbic DA hypothesis is arguably the best-supported neurotransmission-related account of personality, several important qualifiers are worth noting. First, while the mesolimbic DA pathway is commonly construed as the brain's central reward pathway, with virtually all drugs of abuse exerting at least a partial influence there (Nestler, 2005; Pierce & Kumaresan, 2006), the brain contains at least two other major dopaminergic pathways—the nigrostriatal and mesocortical pathways, implicated in motor control and a variety of motivational and cognitive functions, respectively. The relationship between personality and DA function within these latter pathways is not well characterized; however, there is indirect evidence suggesting that DA function within these pathways may be related to quite different traits. For instance, in large population-based samples, dispositional anxiety and pessimism appear to prospectively predict long-term onset of Parkinson's Disease (which is caused by degeneration of DA neurons in the nigrostriatal pathway), whereas

extraversion and novelty-seeking show no such association (Arabia et al., 2010; Bower et al., 2010; Weisskopf, Chen, Schwarzschild, Kawachi, & Ascherio, 2003).

Second, though often discussed in the context of Extraversion, an incentive facilitation account of DA cuts across traditional dimensional accounts of personality such as the Big Five. In Depue's (1999) model, increased DA transmission within the reward system is associated specifically with the agentic aspects of extraversion, and not with affiliative aspects. More generally, individual differences in the function of the reward system are liable to exert at least a small influence on a large number of traits—for instance, there is evidence for the involvement of the reward system in mediating not only appetitive behaviors, but also certain avoidance-related behaviors (Ikemoto & Panksepp, 1999; Salamone, 1994). The important point to note is that this lack of isomorphism with conventional personality measures is not a weakness of the biological theory; it simply reflects the reality, which is that there is little reason to expect biological mechanisms to cut personality at the same joints as psychometric approaches. If anything, one might argue the opposite—that biological considerations offer a principled way to distinguish between accounts that are otherwise equivocal at the psychometric level (cf. Block, 1995; Hans J Eysenck, 1992). I return to this point later.

Third, the nature of the association between DA levels and personality appears to depend on a number other factors. One complicating factor is that there are at least five types of dopamine receptors, each with different spatial distributions (Levey et al.,

1993; Meador-Woodruff et al., 1996) and somewhat different—and even opposing (Self, Barnhart, Lehman, & Nestler, 1996)—functions (for review, see Beaulieu & Gainetdinov, 2011). Another complication is that dopamine operates at both tonic and phasic timescales, with the two signals playing different roles in motivated behavior (J. D. Cohen, Braver, & Brown, 2002; Niv, 2007). Individuals may differ in either the baseline level of DA transmission or in the magnitude of the transient DA response to specific stimuli. From a theoretical standpoint, one would expect quite different relationships with personality for tonic and phasic DA. High tonic DA transmission should facilitate agentic behavior by stabilizing goal representations—in line with accounts that emphasize incentive facilitation and behavioral approach (Depue & Collins, 1999; J. A. Gray, 1987). Conversely, individuals with low basal DA levels and large phasic DA responses may be driven to novelty- or sensation-seeking behavior in an effort to elicit pleasurable DA release, as other theorists have suggested (e.g., Cloninger, 1987).

The bottom line is that while there is strong evidence linking variation in dopamine function to traits such as extraversion and novelty-seeking, the mapping is far from isomorphic. Non-dopaminergic mechanisms undoubtedly contribute to each of these traits to a considerable extent, and conversely, dopaminergic mechanisms demonstrably play a role in many other personality traits. Moreover, the dopamine molecule may exert opposing effects on personality depending on where in the brain it is released, what type of dopamine receptor it binds to, the temporal dynamics

governing its release, and many other factors. This type of complexity almost certainly holds not only for dopamine and extraversion, but for other personality traits as well. It likely also explains why, despite promising findings in early small-sample studies (e.g., Benjamin et al., 1996; K P Lesch et al., 1996), large-sample molecular genetic studies have now clearly precluded the presence of common genetic variants (including those known to modulate the function of neurotransmitter systems) that account for more than a tiny fraction of the variance in traits like extraversion or novelty-seeking (De Moor et al., 2010; Munafò & Flint, 2011; Munafò, Yalcin, Willis-Owen, & Flint, 2008; Verweij et al., 2010).

A case study in (relative) simplicity: neuropeptides and attachment. Although the above considerations suggest that the mapping between personality and underlying neurotransmitter systems is likely to be much more complicated than is widely appreciated, this complexity should not be taken to imply that the situation is hopeless. While it is clearly too simplistic to say that (agentic) extraversion reflects the operation of the dopamine system, it is equally clear that dopamine does play an important role in extraversion, even if the details remain to be worked out. More generally, there are a number of instances—at least in the animal literature—where the mapping between complex behaviors and underlying mechanisms appears to be, at least superficially,

much simpler[2]. A striking example is found in the literature on mating behavior and attachment in voles. Researchers have studied a number of vole species that are very similar genetically and behaviorally, yet differ strikingly in their mating patterns. Specifically, some species, such as the prairie vole, are monogamous and mate for life, whereas other species, such as the montane and meadow voles, are non-monogamous (for reviews, see T R Insel & Young, 2001; Thomas R Insel, 2010). A well-replicated finding is that it is possible to "turn" monogamous voles non-monogamous, or vice versa, by experimentally manipulating the neural expression of the neuropeptides oxytocin and vasopressin. For example, blockade of vasopressin receptors in the ventral pallidum in monogamous prairie voles prevents pair bonding (M M Lim & Young, 2004), whereas experimentally inducing expression of vasopressin receptors in the ventral pallidum of typically nonmonogamous meadow voles is sufficient to induce pair bonding (M M Lim et al., 2004).

Although sexual behavior has been relatively overlooked in the study of human personality (for discussion, see Schmitt & Buss, 2000), there is little question that individuals show stable differences in their proclivity towards long-term versus short-term mating, and that these differences have important implications (Buss & Schmitt, 1993; Jonason, Li, Webster, & Schmitt, 2009; Simpson & Gangestad, 1991). From a personality psychology standpoint, the vole literature is about as clean an animal model

[2] I hasten to emphasize that the 'simplicity' here is entirely relative to the preceding discussion; there is no doubt that at a systems or molecular level, even the 'simple' example given here is grossly lacking in detail.

of personality differences as one can hope for: isolated genetic variants are associated with well-delineated neurobiological differences that in turn produce very large behavioral differences. Moreover, differences in oxytocin and vasopressin receptor distribution not only explain between-species differences, but also individual differences in attachment and mating behavior within a given vole species (Hammock & Young, 2005; Ophir, Gessel, Zheng, & Phelps, 2012; Ophir, Wolff, & Phelps, 2008). The vole findings thus offer a striking example of the way in which large individual differences in behavior can potentially emerge from relatively small differences at the biological and genetic level.

Of course, what holds for voles is unlikely to hold to nearly the same degree in humans. For one thing, the spatial distribution of oxytocin and vasopressin receptors is known to differ considerably in humans (Loup, Tribollet, Dubois-Dauphin, & Dreifuss, 1991; Tribollet, Arsenijevic, & Barberis, 1998); for another, the determinants of most behaviors in humans—including attachment and mating behavior—are undoubtedly much more complex. Nonetheless, given that oxytocin and vasopressin have broadly conserved functions across mammalian species (Miranda M Lim & Young, 2006; Ross & Young, 2009), it is likely that some portion of the variance in attachment-related traits in human populations also reflects variation in neuropeptide systems. Interestingly, a number of human studies have observed naturally occurring correlations between peripheral oxytocin or its metabolites and differences in attachment or trust-related

traits and behaviors (Tops, Van Peer, Korf, Wijers, & Tucker, 2007; Uvnäs-Mobcrg, Widström, Nissen, & Björvell, 1990; Zak, Kurzban, & Matzner, 2005), and experimental administration of oxytocin appears to produce related changes in social behavior (Guastella, Mitchell, & Dadds, 2008; Kosfeld, Heinrichs, Zak, Fischbacher, & Fehr, 2005; Zak, Stanton, & Ahmadi, 2007).

Functional neuroimaging studies

Functional neuroimaging techniques measure the spatiotemporal dynamics of brain function by acquiring repeated images of the brain as it performs various tasks. Over the past two decades, researchers have used functional neuroimaging techniques to probe individual differences in personality and cognitive ability in literally thousands of studies. In this section I selectively review this literature, with an emphasis on two particular techniques: function magnetic resonance imaging (fMRI) and positron emission tomography (PET). Although many other techniques remain in widespread use—most notably, electroencephalography (EEG/ERP), which has been used to investigate personality for over 70 years (for reviews, see (Gale, 1983; Thibodeau, Jorgensen, & Kim, 2006; Wacker, Chavanon, & Stemmler, 2010))—these two techniques play an increasingly dominant role in the literature, and are the focus of the present review.

A cautionary note is warranted here: most of the studies reviewed in this section—particularly the fMRI studies—have employed sample sizes that are very small (typically, $n < 30$) by the conventions of personality psychology. Moreover, because neuroimaging studies are expensive to run, researchers often include extensive batteries of questionnaire measures as an afterthought, and only report personality findings in the event that they obtain striking results. The net effect is that publication bias—a perennial problem in science (Dwan et al., 2008; Young, Ioannidis, & Al-Ubaydli, 2008)—is likely to be particularly strong for functional neuroimaging studies of personality. One should consequently interpret many of the findings discussed in this section with caution (for additional discussion, see Yarkoni, 2009; Yarkoni & Braver, 2010).

Functional MRI studies. The most widely used functional neuroimaging technique at present is functional magnetic resonance imaging (fMRI). FMRI is an indirect measure of neural activity; it measures local changes in blood flow, which have been shown to track neuronal firing rates and local field potentials (LFPs) reasonably well (N K Logothetis & Wandell, 2004; Nikos K Logothetis, 2008). The major benefit of fMRI is that it provides whole-brain coverage with reasonably good spatial resolution (typically 1 – 3 mm), though it has relatively poor temporal resolution (1 – 2 seconds).

Since the fMRI literature on personality is immense, the present review is necessarily selective. I focus on three issues in particular: (i) the role of emotional reactivity in personality; (ii) the possibility of identifying personality-related neural differences in the absence of behavioral differences; and (iii) recent work investigating personality-related differences in functional connectivity between brain regions.

The role of emotional reactivity. Many fMRI studies of personality have focused on the role of emotional reactivity in personality—particularly in Neuroticism and Extraversion, two traits found in virtually every major personality taxonomy (Zelenski & Larsen, 1999). In an influential early study, Canli and colleagues found that Neuroticism and Extraversion were associated with increased neural reactivity to negative and positive emotional pictures, respectively, with effects observed in a number of cortical and subcortical regions, including the amygdala, basal ganglia, and frontal cortices (T Canli et al., 2001). A number of other studies have replicated and extended these findings. Theory-congruent personality-related activations in affect-linked regions have been reported during perception of emotional faces (T Canli, Sivers, Whitfield, Gotlib, & Gabrieli, 2002), affective pictures (Kehoe, Toomey, Balsters, & Bokde, 2011), risky decision-making (Paulus, Rogalsky, Simmons, Feinstein, & Stein, 2003), and painful thermal stimulation (Ochsner et al., 2006), among others. One caveat, however, is that the spatial location of personality-related activation shows relatively little consistency across these studies (possibly due to the low power of small-sample

studies; Yarkoni, 2009). Moreover, a number of seemingly contradictory effects have also been reported (Britton, Ho, Taylor, & Liberzon, 2007; De Gelder, Van De Riet, Grèzes, & Denollet, 2008; Hutcherson, Goldin, Ramel, McRae, & Gross, 2008; Kret, Denollet, Grèzes, & De Gelder, 2011), and a still much larger number of null results likely lurk in researchers' file drawers (e.g., the present author is aware of at least 4 unpublished analyses that found no relationship between affect-linked personality traits and neural reactivity to affective stimuli).

Personality differences without behavioral differences. An interesting class of fMRI studies has focused on situations where personality may produce changes in neural activity in the absence of overt behavioral differences. For example, several studies of working memory and executive control have observed neuroticism or extraversion-related changes in activity in regions such as the anterior cingulate and dorsolateral PFC—regions heavily implicated in effortful cognition (Duncan & Owen, 2000; Duncan, 2010; Yarkoni, Barch, Gray, Conturo, & Braver, 2009)—in the absence of differences in task performance (Basten, Stelzel, & Fiebach, 2011; Fales et al., 2008; Jeremy R Gray et al., 2005; Yücel et al., 2007). Such effects are often interpreted from the standpoint of neural *efficiency*: if extraverts are capable of obtaining an equivalent level of performance given reduced brain activity (J R Gray & Braver, 2002; Jeremy R Gray et al., 2005), one might conclude that extraverts perform working memory tasks more efficiently (cf. Lieberman & Rosenthal, 2001). Conversely, if anxious individuals

perform equivalently well on a task but show greater activation in cognitive control regions (Fales et al., 2008), the excess activation might reflect anxiety-induced arousal increases and/or simultaneous emotion regulation, in line with Eysenck's *processing efficiency theory* (M W Eysenck, Derakshan, Santos, & Calvo, 2007; Michael W Eysenck & Calvo, 1992), which holds that anxiety increases one's motivation to perform well while decreasing one's capacity. Such studies underscore the promise of fMRI to provide a window into cognitive processes even in the absence of overt behavioral changes. A major caveat, however, is that inferring cognitive function solely from observed brain activation—a strategy commonly referred to as *reverse inference*—can be a risky proposition (R A Poldrack, 2006; Russell A Poldrack, 2011; Yarkoni, Poldrack, Van Essen, & Wager, 2010) unless supported by quantitative evidence, and becomes even more risky when activation changes are interpreted in the absence of behavioral differences (Yarkoni & Braver, 2010).

Differences in functional connectivity. In addition to localization studies, which focus on identifying brain regions in which mean-level changes in activity are associated with other variables, neuroimaging researchers place increasing emphasis on understanding the functional relationships between different regions. *Functional connectivity* analyses seek to characterize the dynamics governing the coactivation and interaction of different regions. An extensive literature has identified a set of relatively conserved and highly distributed brain networks that play distinct roles in cognition

(M. D. Fox et al., 2005; Smith et al., 2009). A number of recent studies have sought to characterize the role of personality in modulating differences in functional connectivity. For example, Cremers and colleagues found that the connectivity between the amygdala and medial frontal regions varied as a function of neuroticism when making judgments about emotional faces (Cremers et al., 2009). Neurotic individuals showed greater coupling between the amygdala and dorsomedial PFC, and reduced coupling between the amygdala and dorsal anterior cingulate cortex (ACC)—findings the authors interpreted as evidence that neurotic individuals exhibit greater self-referential processing of potential threat and decreased top-down control over the amygdala. Intriguingly, recent studies suggest that personality-related differences in functional connectivity may be discernible during the resting state (e.g., Adelstein et al., 2011; Li, Qin, Jiang, Zhang, & Yu, 2012; Ryan, Sheu, & Gianaros, 2011)—a finding that should make large-sample fMRI investigation of personality more feasible, as resting state scans are commonly included in a large proportion of fMRI studies.

PET studies. One important limitation of fMRI is that it measures only *changes* in brain activity, and not absolute levels. This limitation is problematic in the context of personality and individual differences, because such differences may be apparent at baseline yet elicit incremental changes in activation only under very specific conditions. For example, one might expect Neuroticism to modulate activation when processing

threatening stimuli, but it's unclear what prediction (if any) one would make about its influence on activation during a task involving, say, mental arithmetic. Consequently, fMRI studies that select the wrong experimental task run the risk of failing to detect meaningful personality effects.

In contrast to fMRI, a technique called Positron Emission Tomography (PET)—which involves injection of radioactive tracers designed to bind to specific molecules—can measure baseline differences in overall blood flow. Although PET is used sparingly nowadays due to its invasive nature and relative high cost, it remains useful when trying to assess baseline differences in brain function. For example, Zald and colleagues used PET to show that high trait negative affect was associated with increased baseline blood flow in the ventromedial PFC (Zald, Mattson, & Pardo, 2002)—a region implicated in the regulation of autonomic responses and emotional experience (Ongür & Price, 2000; Quirk & Beer, 2006), and which is known to also run 'hot' in individuals with depression (Drevets, Savitz, & Trimble, 2008).

Interestingly, there is little or no PET evidence to support the link between trait negative affect and increased amygdala activity that has been observed in fMRI studies. With the exception of one small human study (Fischer, Tillfors, Furmark, & Fredrikson, 2001) and one very large study in rhesus monkeys (Oler et al., 2010), PET studies investigating the relationship between negative emotional traits and regional cerebral activation have overwhelmingly failed to report any association in the amygdala (e.g.,

Deckersbach et al., 2006; Fischer, Wik, & Fredrikson, 1997; Hakamata et al., 2009; Sugiura et al., 2000), despite the likely publication bias favoring such a positive finding. One can conclude either that the amygdala-trait negative affect relationship is specific to affective reactivity (rather than baseline hedonic tone), or that it is much smaller—and therefore more difficult to detect—than one might suppose.

In addition to quantifying baseline blood flow, PET should theoretically also be instrumental in probing the relationship between personality and neurotransmitter function *in vivo*, because radioactive tracers can be designed to bind selectively to specific receptors. Numerous studies have investigated the relationship between personality and the major monoamine neurotransmitters—particularly serotonin and dopamine. Unfortunately, a review of the extant literature suggests that mixed and contradictory findings predominate. For example, theoretical models of serotonin function frequently ascribe serotonin a role in the constraint and regulation of affective behavior—and particularly of negative affect (Carver & Miller, 2006; Depue & Spoont, 1986). However, PET studies of 5-HT (i.e., serotonin) binding in relation to personality traits such as neuroticism, anxiety, and hostility have produced contradictory findings, even when probing the same 5-HT receptor type and measuring the same personality traits. In some cases, increased 5-HT binding potential is inversely correlated with negative affect-related traits (Moresco et al., 2002; Tauscher et al., 2001); in other cases, the association is positive (Frokjaer et al., 2008; Takano et al., 2007; Veronica Witte et al.,

2010); and in still other cases, third variables (e.g., gender) appear to moderate the direction of association within a single study (Soloff, Price, Mason, Becker, & Meltzer, 2010).

Structural imaging studies

In contrast to functional neuroimaging studies of personality, which probe the relation between personality differences and the dynamic operation of the brain, structural neuroimaging studies search for associations with stable differences in structure—e.g., differences in the relative size of different brain regions, strength of connectivity between regions, etc. One advantage of structural techniques over functional techniques like fMRI is that the former rely on stationary images of the brain, and do not require careful selection of the experimental task. Since virtually every fMRI study requires the incidental acquisition of a structural MRI scan (to facilitate localization of brain activation), it is much easier for researchers to conduct very large-sample structural studies.

Voxel-based morphometry studies. The most widely used structural neuroimaging method is known as voxel-based morphometry (VBM). VBM is a fully automated method that identifies brain regions in which variation in the density or concentration of gray or white matter correlate with other variables (e.g., personality scores). It has been used to investigate a wide range of personality dimensions and

behavioral traits, ranging from impulsivity (Matsuo et al., 2009; Schilling et al., 2011) to placebo responding (Schweinhardt, Seminowicz, Jaeger, Duncan, & Bushnell, 2009). However, relatively few findings have been replicated, and even when replications are available, the data are often equivocal. For instance, one of the best-replicated findings is that anxiety-related traits such as Neuroticism and Harm Avoidance are associated with gray matter volume reductions in memory- and emotion-linked medial temporal lobe (MTL) regions such as the hippocampus (DeYoung et al., 2010; Kapogiannis, Sutin, Davatzikos, Costa, & Resnick, 2012; Yamasue et al., 2008) and amygdala (Omura, Todd Constable, & Canli, 2005; Spampinato, Wood, De Simone, & Grafman, 2009). These findings converge with experimental animal studies showing that stress induces cell death and volumetric reductions in the hippocampus (for review, see (Sapolsky, 1999)) and correlational clinical studies that have found smaller MTL structures in patients with PTSD and other anxiety-related disorders (Du et al., 2011; Karl et al., 2006). Yet even this seemingly robust finding is challenged by other VBM studies—some with very large sample sizes—that have observed positive correlations in the same structures (Barrós-Loscertales et al., 2006; Cherbuin et al., 2008; Iidaka et al., 2006). It is presently unclear what might explain such discrepant findings. Arguably the most powerful way to address this question would be through quantitative meta-analyses, which could examine the effects of different measures, methodological procedures, and covariates; however, to the best of my knowledge, no such meta-analyses have been conducted yet.

It is also important to note that VBM is not necessarily a measure of *stable* structural differences. At face value, one might suppose that individual differences in gross anatomy—like the volume of relatively large brain regions—would be highly reliable over time. Yet the brain shows considerable plasticity, and very large changes in VBM-based measures of regional volume have been observed following just a few weeks of practice (Draganski et al., 2004; Granert et al., 2011; Hölzel et al., 2010; Woollett & Maguire, 2011). To illustrate, consider a recent VBM study that found that people with more Facebook friends (a variable highly correlated with self-reported Extraversion; Gosling, Augustine, Vazire, Holtzman, & Gaddis, 2011) have increased gray matter concentration in superior and middle temporal sulcus regions previously implicated in the representation of agency and social information (Kanai, Bahrami, Roylance, & Rees, 2012). Although it is tempting to conclude that people with a greater inherent capacity to process social information might be better equipped to enjoy or exploit social situations, an alternative interpretation is that the enlargement of brain regions implicated in social cognition is an epiphenomenal by-product of Extraverts' increased tendency to engage in social interaction. While these possibilities cannot be disambiguated in correlational VBM studies, an elegant monkey study recently provided additional insight. Sallet and colleagues imaged 23 monkeys housed in social groups of varying sizes and observed that monkeys with greater social exposure showed an expansion of the STS (Sallet et al., 2011), consistent with a practice-based

explanation for the human volumetric findings (though not precluding a dispositional explanation). Taken together, these findings underscore the difficulty in drawing causal conclusions based on correlational evidence—even when that evidence stems from studies of gross anatomical structure—and highlight the utility of relating individual differences findings to process models that can be tested experimentally in both humans and animals.

Structural connectivity. In addition to volumetric approaches such as VBM, recent advances in structural imaging—most notably diffusion tensor imaging (DTI; Le Bihan et al., 2001) and related techniques, which use the diffusion of water molecules along axonal fibers to identify white matter tracts—provide a window into the relative integrity of white matter tracts that connect different neural circuits. Emerging studies provide promising evidence that differences in brain connectivity may explain part of the variation in personality. For example, distinct white matter pathways within the striatum appear to differentially predict the traits of novelty-seeking and reward dependence (M. X. Cohen, Schoene-Bake, Elger, & Weber, 2009), with tract strength between the ventral striatum and amygdala correlating positively with novelty-seeking, and tract strength between striatal and frontal regions correlating positively with reward dependence.

In another study, greater integrity of a white matter tract between the amygdala and ventromedial PFC was associated with reduced trait anxiety, consistent with the

notion that difficulty down-regulating emotion may be a precipitating factor for dispositional anxiety (Kim & Whalen, 2009) However, the apparent selectivity of this finding may simply reflect low power: at least two studies, one of them particularly large (n = 263), suggest that negative affect-related traits (Neuroticism and Harm Aversion) are associated with much more widely distributed reductions in white matter integrity (Westlye, Bjørnebekk, Grydeland, Fjell, & Walhovd, 2011; Xu & Potenza, 2011). It is presently unclear whether this difference is genetically mediated, or reflects developmental or environmental influences—for example, neurotic individuals chronically experience greater stress, and cortisol is implicated in cerebral atrophy (Starkman et al., 1999; Uno et al., 1994).

Implications for the Study of Personality

Having selectively reviewed recent findings on the neural substrates of personality, I now turn to discuss some more general implications for the study of personality.

Personality is multiply determined

Perhaps the most important conclusion to take away from the preceding review is that there appear to be few if any one-to-one mappings between psychometrically

defined personality traits and underlying biological mechanisms. This conclusion has important implications for the way personality psychologists and neuroscientists interact and collaborate. Anecdotally, personality psychologists used to thinking in terms of well-established psychometric models such as the Big Five sometimes experience frustration at neuroscientists' minimal regard for the constraints imposed by such models—e.g., the seemingly haphazard use of personality measures that may have face validity but don't necessarily bear a clear-cut relationship to established dimensional models such as the FFM. However, as the literature reviewed above illustrates, the biological substrates of personality are complex, and there is no particular reason (save perhaps for convention) to privilege any particular psychometric model when studying personality at a biological level. To the contrary, it is highly implausible to suppose that the vast range of biological mechanisms that contribute to observable differences in personality will happen to respect psychometric models in anything but the very loosest sense. A far more realistic assumption is that a very large number of biological factors contribute to any given trait, with individual pathways each contributing only a small portion of the variance.

For their part, neuroscientists interested in characterizing the biological mechanisms underlying specific dimensions of personality should appreciate that psychometric models of personality do offer important benefits, even if the dimensions posited by these models don't map cleanly onto biological mechanisms. Perhaps most

importantly, the psychometric and behavioral literature on personality provides a 'nomological network' (Cronbach & Meehl, 1955) of personality—a large-scale mapping of the associative relationships between different constructs. Knowing how strongly or weakly two or more psychometric constructs are related can provide valuable insights into the likely relationship between underlying biological mechanisms. For example, one does not need to reify the NEO-PI-R Extraversion facets of Warmth or Excitement-Seeking to appreciate that the relatively low correlation between the two (Costa & McCrae, 1992b) should have important implications for the overlap (or lack thereof) between the various neurobiological mechanisms that contribute to either trait.

An integrative, multi-level approach to personality

Taking these considerations into account, the most productive approach may be to view the relationship between psychometric and biological levels of descriptions in terms of mutual, but relatively weak, constraints. Ultimately, there must be *some* mapping between constructs at different levels, but this does not mean that psychometric models need to respect biological taxonomies or vice versa. It would be unreasonable to expect psychometricians to pursue the development of an Amygdala Personality Scale, and equally unreasonable to demand that neurobiologists identify the brain's Openness to Experience system. An appreciation of other levels of analysis should inform and constrain one's work without necessarily determining its course.

A particularly helpful approach may be to draw on the information-processing terminology of cognitive psychology as an intermediate bridge between the psychometric and biological levels of description. That is, personality dimensions that are psychometrically well defined can be mapped onto putative cognitive mechanisms, and these abstract cognitive mechanisms are then in turn mapped onto plausible neurobiological substrates. To some degree this strategy is already applied in personality psychology; for instance, the notion that extraversion and neuroticism reflect variation in reactivity to positive and negative stimuli is an appeal to an abstract level of information processing, and neuroimaging efforts to identify brain systems that mediate this effect can be viewed as attempts to identify the neurobiological implementation of those information-processing principles.

To illustrate the approach on a broader scale, consider the (daunting) task of identifying the neural substrates of, say, Neuroticism. For reasons reviewed above, it is unlikely that any single pathway or biological variable will contribute more than a small fraction of the variance in Neuroticism scores. But one can readily identify many different mechanisms that could individually play a small role. At an abstract information-processing level, mechanisms that could plausibly contribute to increased Neuroticism might include: increased perceptual sensitivity to potential threats (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & Van IJzendoorn, 2007); stronger emotional responses to stressors (Bolger & Schilling, 1991; Cook, Hawk, Davis, &

Stevenson, 1991; Gross, Sutton, & Ketelaar, 1998); difficulty disengaging attention from perceived threats (E. Fox, Russo, Bowles, & Dutton, 2001); an associative learning system that conditions more rapidly to aversive outcomes (Zinbarg & Mohlman, 1998); an inability to consciously down-regulate negative affect via top-down cognitive control mechanisms (Bishop, 2009); and so on.

In turn, each of these mechanisms (which undoubtedly also interact in complex ways) can then be mapped onto multiple potential biological substrates. To take just one example, individual differences in reactivity to negative emotional stimuli—a unitary construct at a psychological level—could, at the neural level, be reflected in differences in gray matter volume or density in limbic regions; in tonic ventromedial prefrontal inhibition of brainstem nuclei involved in affective responses (Amat et al., 2005; Amat, Paul, Watkins, & Maier, 2008); in the function of the corticotropin-releasing hormone system that modulates the stress response (Ellis, Jackson, & Boyce, 2006); in complex inhibitory and excitatory influences of different serotonin receptors in ventromedial PFC, amygdala, and other regions (Fisher et al., 2011; Hammack et al., 2009; Lowry, Johnson, Hay-Schmidt, Mikkelsen, & Shekhar, 2005); and in the structural or functional coupling between inferotemporal object recognition circuits and limbic affective circuits (Ahs et al., 2009; Vuilleumier & Driver, 2007), to name just a few possibilities. Individually, such mechanisms are likely to account for only a very small proportion of the variance in Neuroticism—and would undoubtedly each also

contribute to other traits—but taken together, would explain the phenotypic variability that, at a behavioral level, manifests as a seemingly coherent construct.

The benefits of a multi-level approach

The application of a multi-level approach would benefit the study of personality in several ways. First, a biological perspective can help avoid reification of psychometric constructs and remind researchers that there is rarely if ever a fact of the matter about how personality dimensions *should* be defined and delineated psychometrically. A sizeable portion of the personality literature has focused on deriving comprehensive structural models of personality, seeking to address questions like: Are there three, five, or eleven major dimensions of personality (Ashton & Lee, 2007; Costa & McCrae, 1992a; H J Eysenck, 1991; Jackson, Paunonen, Fraboni, & Goffin, 1996)? Is there anything beyond the Big Five (Lee, Ogunfowora, & Ashton, 2005; Paunonen & Jackson, 2000; Saucier & Goldberg, 1998; Schmitt & Buss, 2000)? How many levels should the hierarchy of personality contain (Costa & McCrae, 1995; DeYoung, Quilty, & Peterson, 2007; Digman, 1997)?

While there may be pragmatic answers to such questions (e.g., it is probably easier to develop and apply five-dimensional models than twelve-dimensional ones), one must be careful not to mistake a pragmatic desire for parsimony for an insight into causal necessity. From a mathematical standpoint, an infinite number of causal models

can produce any given pattern of correlational data (the so-called 'inverse problem'). Although simple linear solutions (e.g., those derived through factor analysis) may be preferable to complex non-linear ones from a psychometric standpoint, the reality is that real-world biological systems are rife with redundancy and non-linear interactions. A priori, there is no reason to expect anything remotely approaching a one-to-one mapping between psychometrically defined dimensions and underlying biological mechanisms, and there are any number of reasons to expect otherwise. This point has been raised frequently by leading personality psychologists and psychometricians over the decades (Block, 1995; Hans J. Eysenck, 1997; Guilford, 1975; McAdams, 1992)(Levenson, 1983), but nevertheless remains underappreciated. An explicit emphasis on the cognitive and neural mechanisms that produce behavior can help focus attention towards substantive questions about the causal mechanisms that produce behavior and away from purely descriptive questions to which there is not likely to be a definitive answer.

Second, a multi-disciplinary approach can inform theoretical issues at one level of analysis by identifying relevant sources of evidence at other levels. Consider the aforementioned question as to how the trait of Impulsivity should be conceptualized. Under the NEO-PI-R, Impulsivity is labeled as a facet of Neuroticism (Costa & McCrae, 1992b). However, the trait can also be conceptualized in other ways—e.g., in terms of low persistence/conscientiousness or high novelty- or sensation-seeking. One influential

proposal formalized in the four-factor UPPS model (J. Miller, Flory, Lynam, & Leukefeld, 2003; S P Whiteside & Lynam, 2001) is that different aspects of impulsivity—which include urgency, perseverance, lack of premeditation, and sensation-seeking—map onto different traits in other typologies (e.g., the Impulsivity, Excitement Seeking, Self-Discipline, and Deliberation facets of the NEO-PI-R, respectively). While pragmatically useful, this partitioning remains purely descriptive; for instance, it does not explain *why* the different aspects of Impulsivity should be scattered across other domains despite having moderate-to-strong positive intercorrelations (Stephen P Whiteside, Lynam, Miller, & Reynolds, 2005).

A cognitive/biological perspective can directly complement psychometric approaches by framing the issue in terms of shared and distinct biological pathways. For instance, an increased ability to actively maintain long-term goal representations in mind—a capacity thought to rely heavily on prefrontal cortical mechanisms (E. K. Miller & Cohen, 2001)—may represent a relatively general contributor to decreased impulsivity, and particularly to perseverance and premeditation. Greater reactivity to negative emotional stimuli may increase urgency but *de*crease sensation-seeking (since danger cues inhibit risk-taking behavior); weaker top-down regulation of emotion may increase both sensation-seeking and urgency; and so on. From this perspective, understanding the relationship between different aspects of personality is not simply a matter of finding a pragmatically useful way to partition the variance at a psychometric

level; it is also a matter of identifying many-to-many mappings between brain systems and behaviors. One must accept, however, that these mappings will be characterized by high redundancy—i.e., many different mechanisms will contribute to any given behavior, often in complex ways (e.g., even though urgency and sensation-seeking are positively correlated overall, greater negative emotional reactivity might influence the two traits in opposite ways).

Third, and perhaps most importantly, simultaneous consideration of personality at multiple levels of analysis can help generate novel theoretical models and empirical predictions. This approach is exemplified by much of the research reviewed in this chapter. It is evident in theorists like Eysenck, Cloninger, and Depue's insistence on grounding theoretical models of personality in biological constructs, in translational approaches that use animal models to generate and test predictions that might also help explain human personality, and in work that draws on process models of emotional reactivity to bridge between affective personality traits and underlying biological systems, among many other lines of research. While it is probably fair to say that we still understand only a small fraction of what there is to understand about the biology of personality, there is also little doubt that our current understanding has benefited immeasurably from integrative work that attempts to bridge between the behavioral, cognitive, and biological domains rather than focusing exclusively on any one level.

Conclusions

The selective review presented here conveys both bad news and good news. The bad news is that achieving a comprehensive understanding of the biological mechanisms underlying personality is almost certain to be an enterprise orders of magnitude more complex than psychometrically characterizing the structure of personality at a behavioral level. In view of this complexity, it is unreasonable to expect one-to-one mappings to emerge between familiar traits such as Neuroticism or Extraversion and underlying mechanisms. Instead, researchers interested in the biology of personality are likely to achieve greater success by adopting domain-specific approaches that seek to identify the many mechanisms that contribute to particular clusters of behaviors—and to accept that these clusters may cut across traditional dimensional boundaries.

Additionally, because the great majority of studies investigating the neural bases of personality have used relatively small samples, and often report statistically significant findings opportunistically, it is difficult to establish the ground truth regarding which neural systems are associated with which traits. There is a vital need for (a) quantitative meta-analyses that attempt to synthesize the results of the many hundreds of published studies and (b) much larger primary studies that use sample sizes comparable to those used in behavioral studies of personality.

The good news is that the tools needed to pursue such an undertaking are now widely available. From structural and functional neuroimaging techniques in humans to electrophysiological and lesion techniques in animals, researchers interested in investigating the biological mechanisms underlying personality are now able to probe brain function with remarkable precision at multiple levels of analysis. The results of such investigations will continue to advance our understanding of individual differences in brain structure and function, ultimately revealing how such differences explain stable differences in behavior. So long as we accept the inherent complexity of this monumental task and focus on developing integrative models that span multiple mechanisms at different levels of analysis, the field of personality neuroscience is certain to have a bright future.

References

Adelstein, J. S., Shehzad, Z., Mennes, M., DeYoung, C. G., Zuo, X.-N., Kelly, C., … Milham, M. P. (2011). Personality Is Reflected in the Brain's Intrinsic Functional Architecture. (M. Valdes-Sosa, Ed.)*PLoS ONE*, *6*(11), e27633. doi:10.1371/journal.pone.0027633

Ahn, W.-K., Proctor, C. C., & Flanagan, E. H. (2009). Mental Health Clinicians' Beliefs About the Biological, Psychological, and Environmental Bases of Mental Disorders. *Cognitive Science*, *33*(2), 147–182. doi:10.1111/j.1551-6709.2009.01008.x

Ahs, F., Pissiota, A., Michelgård, A., Frans, O., Furmark, T., Appel, L., & Fredrikson, M. (2009). Disentangling the web of fear: amygdala reactivity and functional connectivity in spider and snake phobia. *Psychiatry Research*, *172*(2), 103–108.

Amat, J., Baratta, M. V, Paul, E., Bland, S. T., Watkins, L. R., & Maier, S. F. (2005). Medial prefrontal cortex determines how stressor controllability affects behavior and dorsal raphe nucleus. *Nature Neuroscience*, *8*(3), 365–371.

Amat, J., Paul, E., Watkins, L. R., & Maier, S. F. (2008). Activation of the ventral medial prefrontal cortex during an uncontrollable stressor reproduces both the immediate and long-term protective effects of behavioral control. *Neuroscience*, *154*(4), 1178–1186.

Arabia, G., Grossardt, B. R., Colligan, R. C., Bower, J. H., Maraganore, D. M., Ahlskog, J. E., … Rocca, W. A. (2010). Novelty seeking and introversion do not predict the long-term risk of Parkinson disease. *Neurology*, *75*(4), 349–357.

Ashton, M. C., & Lee, K. (2007). Empirical, theoretical, and practical advantages of the HEXACO model of personality structure. *Personality and social psychology review an official journal of the Society for Personality and Social Psychology Inc*, *11*(2), 150–166.

Bar-Haim, Y., Lamy, D., Pergamin, L., Bakermans-Kranenburg, M. J., & Van IJzendoorn, M. H. (2007). Threat-related attentional bias in anxious and nonanxious individuals: a meta-analytic study. *Psychological Bulletin*, *133*(1), 1–24.

Barrós-Loscertales, A., Meseguer, V., Sanjuán, A., Belloch, V., Parcet, M. A., Torrubia, R., & Avila, C. (2006). Behavioral Inhibition System activity is associated with increased amygdala and hippocampal gray matter volume: A voxel-based morphometry study. *NeuroImage*, *33*(3), 1011–1015.

Basten, U., Stelzel, C., & Fiebach, C. J. (2011). Trait anxiety modulates the neural efficiency of inhibitory control. *Journal of Cognitive Neuroscience*, *23*(10), 3132–3145.

Beaulieu, J.-M., & Gainetdinov, R. R. (2011). The physiology, signaling, and pharmacology of dopamine receptors. *Pharmacological Reviews*, *63*(1), 182–217.

Benjamin, J., Li, L., Patterson, C., Greenberg, B. D., Murphy, D. L., & Hamer, D. H. (1996). Population and familial association between the D4 dopamine receptor gene and measures of Novelty Seeking. *Nature Genetics*, *12*(1), 81–84.

Bishop, S. J. (2009). Trait anxiety and impoverished prefrontal control of attention. *Nature Neuroscience*, *12*(1), 92–98.

Block, J. (1995). A contrarian view of the five-factor approach to personality description. *Psychological Bulletin*, *117*(2), 187–215.

Bolger, N., & Schilling, E. A. (1991). Personality and the problems of everyday life: the role of neuroticism in exposure and reactivity to daily stressors. *Journal of Personality*, *59*(3), 355–386.

Bower, J. H., Grossardt, B. R., Maraganore, D. M., Ahlskog, J. E., Colligan, R. C., Geda, Y. E., … Rocca, W. A. (2010). Anxious personality predicts an increased risk of Parkinson's disease. *Movement disorders official journal of the Movement Disorder Society*, *25*(13), 2105–2113.

Britton, J. C., Ho, S.-H., Taylor, S. F., & Liberzon, I. (2007). Neuroticism associated with neural activation patterns to positive stimuli. *Psychiatry Research*, *156*(3), 263–267.

Buss, D. M., & Schmitt, D. P. (1993). Sexual strategies theory: an evolutionary perspective on human mating. *Psychological Review*, *100*(2), 204–32. doi:10.1037//0033-295X.100.2.204

Canli, T. (2004). Functional brain mapping of extraversion and neuroticism: learning from individual differences in emotion processing. *Journal of Personality*, *72*(6), 1105–1132.

Canli, T, Sivers, H., Whitfield, S. L., Gotlib, I. H., & Gabrieli, J. D. (2002). Amygdala response to happy faces as a function of extraversion. *Science*, *296*(5576), 2191.

Canli, T, Zhao, Z., Desmond, J. E., Kang, E., Gross, J., & Gabrieli, J. D. (2001). An fMRI study of personality influences on brain reactivity to emotional stimuli. *Behavioral Neuroscience*, *115*(1), 33–42.

Canli, Turhan. (2006). *Biology of personality and individual differences*. New York, New York, USA: The Guilford Press.

Carver, C. S., & Miller, C. J. (2006). Relations of serotonin function to personality: current views and a key methodological issue. *Psychiatry Research*, *144*(1), 1–15.

Cherbuin, N., Windsor, T. D., Anstey, K. J., Maller, J. J., Meslin, C., & Sachdev, P. S. (2008). Hippocampal volume is positively associated with behavioural inhibition (BIS) in a large community-based sample of mid-life adults: the PATH through life study. *Social cognitive and affective neuroscience*, *3*(3), 262–269.

Cloninger, C. R. (1987). A systematic method for clinical description and classification of personality variants. A proposal. *Archives of General Psychiatry*, *44*(6), 573–588.

Cloninger, C. R., Svrakic, D. M., & Przybeck, T. R. (1993). A psychobiological model of temperament and character. *Archives of General Psychiatry*, *50*(12), 975–990.

Cohen, J. (1988). *Statistical Power Analysis for the Behavioral Sciences*. Lawrence Erlbaum Assoc Inc.

Cohen, J. D., Braver, T. S., & Brown, J. W. (2002). Computational perspectives on dopamine function in prefrontal cortex. *Current Opinion in Neurobiology*, *12*(2), 223–229.

Cohen, M. X., Schoene-Bake, J.-C., Elger, C. E., & Weber, B. (2009). Connectivity-based segregation of the human striatum predicts personality characteristics. *Nature Neuroscience*, *12*(1), 32–34.

Cook, E. W., Hawk, L. W., Davis, T. L., & Stevenson, V. E. (1991). Affective individual differences and startle reflex modulation. *Journal of Abnormal Psychology*, *100*(1), 5–13.

Costa, P. T., & McCrae, R. R. (1992a). Four ways five factors are basic, *13*(6), 653–665.

Costa, P. T., & McCrae, R. R. (1992b). *Revised NEO Personality Inventory (NEO PI-R) and NEO Five-Factor Inventory (NEO-FFI): Professional Manual*. Psychological Assessment Resources.

Costa, P. T., & McCrae, R. R. (1995). Domains and facets: Hierarchical personality assessment using the Revised NEO Personality Inventory. *Journal of Personality Assessment*, *64*(1), 21–50.

Cremers, H. R., Demenescu, L. R., Aleman, A., Renken, R., Van Tol, M.-J., Van Der Wee, N. J. A., … Roelofs, K. (2009). Neuroticism modulates amygdala--prefrontal connectivity in response to negative emotional facial expressions. *NeuroImage*, *49*(1), 963–970. doi:10.1016/j.neuroimage.2009.08.023

Cronbach, L. J., & Meehl, P. E. (1955). Construct validity in psychological tests. *Psychological Bulletin*, *52*(4), 281–302.

De Gelder, B., Van De Riet, W. A. C., Grèzes, J., & Denollet, J. (2008). Decreased differential activity in the amygdala in response to fearful expressions in Type D personality. *Neurophysiologie clinique Clinical neurophysiology*, *38*(3), 163–169.

De Moor, M. H. M., Costa, P. T., Terracciano, A., Krueger, R. F., De Geus, E. J. C., Toshiko, T., … Derringer, J. (2010). Meta-analysis of genome-wide association studies for personality. *Molecular Psychiatry*, *17*(April), 1–13. doi:10.1038/mp.2010.128

Deckersbach, T., Miller, K. K., Klibanski, A., Fischman, A., Dougherty, D. D., Blais, M. A., … Rauch, S. L. (2006). Regional cerebral brain metabolism correlates of neuroticism and extraversion. *Depression and Anxiety*, *23*(3), 133–138. doi:10.1002/da

Demertzi, A., Liew, C., Ledoux, D., Bruno, M.-A., Sharpe, M., Laureys, S., & Zeman, A. (2009). Dualism persists in the science of mind. *Annals Of The New York Academy Of Sciences*, *1157*, 1–9.

Depue, R. A., & Collins, P. F. (1999). Neurobiology of the structure of personality: dopamine, facilitation of incentive motivation, and extraversion. *Behavioral and Brain Sciences*, *22*(3), 469–491.

Depue, R. A., & Spoont, M. R. (1986). Conceptualizing a serotonin trait. A behavioral dimension of constraint. *Annals of the New York Academy of Sciences*, *487*, 47–62.

Deyoung, C. G., & Gray, J. R. (2008). Personality neuroscience : explaining individual differences in affect , behaviour and cognition. (P. J. Corr & G. Matthews, Eds.)*Biological Perspectives*, 323–346.

DeYoung, C. G., Hirsh, J. B., Shane, M. S., Papademetris, X., Rajeevan, N., & Gray, J. R. (2010). Testing predictions from personality neuroscience. Brain structure and the big five. *Psychological Science*, *21*(6), 820–828.

DeYoung, C. G., Quilty, L. C., & Peterson, J. B. (2007). Between facets and domains: 10 aspects of the Big Five. *Journal of Personality and Social Psychology*, *93*(5), 880–896.

Digman, J. M. (1997). Higher-order factors of the Big Five. *Journal of Personality and Social Psychology*, *73*(6), 1246–1256.

Draganski, B., Gaser, C., Busch, V., Schuierer, G., Bogdahn, U., & May, A. (2004). Neuroplasticity: Changes in grey matter induced by training. *Nature*, *427*(6972), 311–312. doi:10.1038/427311a

Drevets, W. C., Savitz, J., & Trimble, M. (2008). The subgenual anterior cingulate cortex in mood disorders. *CNS Spectrums*, *13*(8), 663–681.

Du, M.-Y., Wu, Q.-Z., Yue, Q., Li, J., Liao, Y., Kuang, W.-H., … Gong, Q.-Y. (2011). Voxelwise meta-analysis of gray matter reduction in major depressive disorder. *Progress in neuropsychopharmacology biological psychiatry*, *36*(1), 11–16. doi:10.1016/j.pnpbp.2011.09.014

Duncan, J. (2010). The multiple-demand (MD) system of the primate brain: mental programs for intelligent behaviour. *Trends in Cognitive Sciences*, *14*(4), 172–179.

Duncan, J., & Owen, A. M. (2000). Common regions of the human frontal lobe recruited by diverse cognitive demands. *Trends in Neurosciences*, *23*(10), 475–483.

Dwan, K., Altman, D. G., Arnaiz, J. A., Bloom, J., Chan, A.-W., Cronin, E., … Williamson, P. R. (2008). Systematic Review of the Empirical Evidence of Study Publication Bias and Outcome Reporting Bias. (N. Siegfried, Ed.)*PLoS ONE*, *3*(8), 31.

Ellis, B., Jackson, J., & Boyce, W. (2006). The stress response systems: Universality and adaptive individual differences. *Developmental Review*, *26*(2), 175–212. doi:10.1016/j.dr.2006.02.004

Eysenck, H J. (1991). Dimensions of personality: 16, 5 or 3? Criteria for a taxonomic paradigm, *12*(8), 773–790.

Eysenck, Hans J. (1992). Four ways five factors are not basic, *13*(6), 667–673.

Eysenck, Hans J. (1997). Personality and experimental psychology: The unification of psychology and the possibility of a paradigm. *Journal of Personality and Social Psychology*, *73*(6), 1224–1237.

Eysenck, M W, Derakshan, N., Santos, R., & Calvo, M. G. (2007). Anxiety and cognitive performance: attentional control theory. *Emotion Washington Dc*, *7*(2), 336–53.

Eysenck, Michael W, & Calvo, M. G. (1992). Anxiety and performance: The processing efficiency theory, *6*(6), 409–434.

Fales, C. L., Barch, D. M., Burgess, G. C., Schaefer, A., Mennin, D. S., Gray, J. R., & Braver, T. S. (2008). Anxiety and cognitive efficiency: Differential modulation of transient and sustained neural activity during a working memory task. *Cognitive Affective Behavioral Neuroscience*, *8*(3), 239–253. doi:10.3758/CABN.8.3.239

Fischer, H., Tillfors, M., Furmark, T., & Fredrikson, M. (2001). Dispositional pessimism and amygdala activity: a PET study in healthy volunteers. *NeuroReport*, *12*(8), 1635–1638.

Fischer, H., Wik, G., & Fredrikson, M. (1997). Extraversion, neuroticism and brain function: A PET study of personality. *Personality and Individual Differences*, *23*(2), 345–352.

Fisher, P. M., Price, J. C., Meltzer, C. C., Moses-Kolko, E. L., Becker, C., Berga, S. L., & Hariri, A. R. (2011). Medial prefrontal cortex serotonin 1A and 2A receptor binding interacts to predict threat-related amygdala reactivity. *Biology of Mood Anxiety Disorders*, *1*(1), 2. doi:10.1186/2045-5380-1-2

Fox, E., Russo, R., Bowles, R., & Dutton, K. (2001). Do threatening stimuli draw or hold visual attention in subclinical anxiety? *Journal of experimental psychology General*, *130*(4), 681–700.

Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., & Raichle, M. E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences*, *102*(27), 9673–9678.

Frokjaer, V. G., Mortensen, E. L., Nielsen, F. A., Haugbol, S., Pinborg, L. H., Adams, K. H., … Knudsen, G. M. (2008). Frontolimbic serotonin 2A receptor binding in healthy subjects is associated with personality risk factors for affective disorder. *Biological Psychiatry*, *63*(6), 569–576.

Gale, A. (1983). Electroencephalographic studies of extraversion-introversion: a case study in the psychophysiology of individual differences. *Personality and Individual Differences*, *4*(4), 371–380. doi:10.1016/0191-8869(83)90002-8

Gale, A., & Edwards, J. (1983). Psychophysiology And Individual Differences: Theory, Research Procedures, And The Interpretation Of Data. *Australian Journal of Psychology*, *35*(3), 361–379. doi:10.1080/00049538308258749

Gelman, A., & Weakliem, D. (2009). Of Beauty, Sex and Power. *American Scientist*, *97*(4), 310. doi:10.1511/2009.79.310

Gerra, G., Avanzini, P., Zaimovic, A., Sartori, C., Bocchi, M., Timpano, R., … Brambilla, U. (1999). Neurotransmitters , Neuroendocrine Correlates of Sensation-Seeking Temperament in Normal Humans. *Neuropsychobiology*, *39*, 207–213.

Gosling, S. D., Augustine, A. A., Vazire, S., Holtzman, N., & Gaddis, S. (2011). Manifestations of personality in online social networks: self-reported facebook-related behaviors and observable profile information. *Cyberpsychology behavior and social networking*, *14*(9), 483–488.

Granert, O., Peller, M., Gaser, C., Groppa, S., Hallett, M., Knutzen, A., … Siebner, H. R. (2011). Manual activity shapes structure and function in contralateral human motor hand area. *NeuroImage*, *54*(1), 32–41.

Gray, J R, & Braver, T. S. (2002). Personality predicts working-memory-related activation in the caudal anterior cingulate cortex, *2*(1), 64–75.

Gray, J. A. (1987). *The psychology of fear and stress*. Cambridge: Cambridge University Press.

Gray, Jeremy R, Burgess, G. C., Schaefer, A., Yarkoni, T., Larsen, R. J., & Braver, T. S. (2005). Affective personality differences in neural processing efficiency confirmed using fMRI. *Cognitive, Affective, & Behavioral Neuroscience*, *5*(2), 182–190.

Gross, J. J., Sutton, S. K., & Ketelaar, T. (1998). Relations Between Affect and Personality : Support for the Affect-Level and Affective-Reactivity Views. *Personality and Social Psychology Bulletin*, *24*(3), 279–288. doi:10.1177/0146167298243005

Guastella, A. J., Mitchell, P. B., & Dadds, M. R. (2008). Oxytocin Increases Gaze to the Eye Region of Human Faces. *Biological Psychiatry*, *63*(1), 3–5. doi:10.1016/j.biopsych.2007.06.026

Guilford, J. P. (1975). Factors and factors of personality. *Psychological Bulletin*, *82*(5), 802–814.

Hakamata, Y., Iwase, M., Iwata, H., Kobayashi, T., Tamaki, T., Nishio, M., … Inada, T. (2009). Gender difference in relationship between anxiety-related personality traits and cerebral brain glucose metabolism. *Psychiatry Research*, *173*(3), 206–211.

Hammack, S. E., Guo, J.-D., Hazra, R., Dabrowska, J., Myers, K. M., & Rainnie, D. G. (2009). The response of neurons in the bed nucleus of the stria terminalis to serotonin: implications for anxiety. *Progress in neuropsychopharmacology biological psychiatry*, *33*(8), 1309–1320.

Hammock, E. A. D., & Young, L. J. (2005). Microsatellite instability generates diversity in brain and sociobehavioral traits. *Science*, *308*(5728), 1630–1634.

Hansenne, M., & Ansseau, M. (1999). Harm avoidance and serotonin. *Biological Psychology*, *51*(1), 77–81.

Hennig, J., Toll, C., Schonlau, P., Rohrmann, S., & Netter, P. (2000). *Endocrine responses after d-fenfluramine and ipsapirone challenge: further support for Cloninger's tridimensional model of personality. Neuropsychobiology* (Vol. 41, pp. 38–47).

Hutcherson, C. A., Goldin, P. R., Ramel, W., McRae, K., & Gross, J. J. (2008). Attention and emotion influence the relationship between extraversion and neural response. *Social cognitive and affective neuroscience*, *3*(1), 71–79.

Hölzel, B. K., Carmody, J., Evans, K. C., Hoge, E. A., Dusek, J. A., Morgan, L., … Lazar, S. W. (2010). Stress reduction correlates with structural changes in the amygdala. *Social cognitive and affective neuroscience*, *5*(1), 11–17.

Iidaka, T., Matsumoto, A., Ozaki, N., Suzuki, T., Iwata, N., Yamamoto, Y., … Sadato, N. (2006). Volume of left amygdala subregion predicted temperamental trait of harm avoidance in female young subjects. A voxel-based morphometry study. *Brain Research*, *1125*(1), 85–93.

Ikemoto, S., & Panksepp, J. (1999). The role of nucleus accumbens dopamine in motivated behavior: a unifying interpretation with special reference to reward-seeking. *Brain Research. Brain Research Reviews*, *31*(1), 6–41.

Insel, T R, & Young, L. J. (2001). The neurobiology of attachment. *Nature Reviews Neuroscience*, *2*(2), 129–136. doi:10.1038/35053579

Insel, Thomas R. (2010). The challenge of translation in social neuroscience: a review of oxytocin, vasopressin, and affiliative behavior. *Neuron*, *65*(6), 768–779.

Ioannidis, J. (2008). Why most discovered true associations are inflated. *Epidemiology*, *19*(5), 640–648.

Jackson, D. N., Paunonen, S. V, Fraboni, M., & Goffin, R. D. (1996). A five-factor versus six-factor model of personality structure, *20*(1), 33–45.

Jonason, P. K., Li, N. P., Webster, G. D., & Schmitt, D. P. (2009). The Dark Triad : Facilitating a Short-Term Mating Strategy in Men. *European Journal of Personality*, *18*(November 2008), 5–18. doi:10.1002/per

Kanai, R., Bahrami, B., Roylance, R., & Rees, G. (2012). Online social network size is reflected in human brain structure. *Proceedings of the Royal Society B Biological Sciences*, *279*(October), 1327–1334.

Kapogiannis, D., Sutin, A., Davatzikos, C., Costa, P., & Resnick, S. (2012). The five factors of personality and regional cortical variability in the baltimore longitudinal study of aging. *Human brain mapping*. doi:10.1002/hbm.22108

Karl, A., Schaefer, M., Malta, L. S., Dörfel, D., Rohleder, N., & Werner, A. (2006). A meta-analysis of structural brain abnormalities in PTSD. *Neuroscience & Biobehavioral Reviews*, *30*(7), 1004–1031.

Kehoe, E. G., Toomey, J. M., Balsters, J. H., & Bokde, A. L. W. (2011). Personality modulates the effects of emotional arousal and valence on brain activation. *Social cognitive and affective neuroscience*, *in press* -. doi:10.1093/scan/nsr059

Kim, M. J., & Whalen, P. J. (2009). The structural integrity of an amygdala-prefrontal pathway predicts trait anxiety. *Journal of Neuroscience*, *29*(37), 11614–11618.

Kosfeld, M., Heinrichs, M., Zak, P. J., Fischbacher, U., & Fehr, E. (2005). Oxytocin increases trust in humans. *Nature*, *435*(7042), 673–676.

Kret, M. E., Denollet, J., Grèzes, J., & De Gelder, B. (2011). The role of negative affectivity and social inhibition in perceiving social threat: an fMRI study. *Neuropsychologia*, *49*(5), 1187–1193.

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1999). International affective picture system (IAPS): Instruction manual and affective ratings. *The Center for Research in Psychophysiology, University of Florida*.

Larsen, R. J., & Ketelaar, T. (1989). Extraversion, Neuroticism, and susceptibility to positive and negative mood induction procedures. *Personality and Individual Differences*, *10*(12), 1221–1228.

Larsen, R. J., & Ketelaar, T. (1991). Personality and susceptibility to positive and negative emotional states. *Journal of Personality and Social Psychology*, *61*(1), 132–140.

Le Bihan, D., Mangin, J. F., Poupon, C., Clark, C. A., Pappata, S., Molko, N., & Chabriat, H. (2001). Diffusion tensor imaging: concepts and applications. *Journal of Magnetic Resonance Imaging*, *13*(4), 534–546.

LeDoux, J. E. (2000). Emotion circuits in the brain. *Annual Review of Neuroscience*, *23*, 155–184.

Lee, K., Ogunfowora, B., & Ashton, M. C. (2005). Personality Traits Beyond the Big Five: Are They Within the HEXACO Space? *Journal of Personality*, *73*(5).

Lesch, K P, Bengel, D., Heils, A., Sabol, S. Z., Greenberg, B. D., Petri, S., … Murphy, D. L. (1996). Association of anxiety-related traits with a polymorphism in the serotonin transporter gene regulatory region. *Science*, *274*(5292), 1527–1531.

Lesch, K P, & Merschdorf, U. (2000). Impulsivity, aggression, and serotonin: a molecular psychobiological perspective. *Behavioral sciences the law*, *18*(5), 581–604.

Lesch, Klaus Peter, Zeng, Y., Reif, A., & Gutknecht, L. (2003). Anxiety-related traits in mice with modified genes of the serotonergic pathway. *European Journal of Pharmacology*, *480*(1-3), 185–204.

Levenson, R. W. (1983). Personality research and psychophysiology: General considerations. *Journal of Research in Personality*, *17*(1), 1–21.

Levey, A. I., Hersch, S. M., Rye, D. B., Sunahara, R. K., Niznik, H. B., Kitt, C. A., … Ciliax, B. J. (1993). Localization of D1 and D2 dopamine receptors in brain with

subtype-specific antibodies. *Proceedings of the National Academy of Sciences of the United States of America*, *90*(19), 8861–8865.

Li, Y., Qin, W., Jiang, T., Zhang, Y., & Yu, C. (2012). Sex-Dependent Correlations between the Personality Dimension of Harm Avoidance and the Resting-State Functional Connectivity of Amygdala Subregions. (Y.-F. Zang, Ed.)*PLoS ONE*, *7*(4), e35925. doi:10.1371/journal.pone.0035925

Lieberman, M. D., & Rosenthal, R. (2001). Why introverts can't always tell who likes them: multitasking and nonverbal decoding. *Journal of Personality and Social Psychology*, *80*(2), 294–310.

Lim, M M, Wang, Z., Olazabal, D. E., Ren, X., Terwilliger, E. F., & Young, L. J. (2004). Enhanced partner preference in a promiscuous species by manipulating the expression of a single gene. *Nature*, *429*(6993), 754–757.

Lim, M M, & Young, L. J. (2004). Vasopressin-dependent neural circuits underlying pair bond formation in the monogamous prairie vole. *Neuroscience*, *125*(1), 35–45.

Lim, Miranda M, & Young, L. J. (2006). Neuropeptidergic regulation of affiliative behavior and social bonding in animals. *Hormones and Behavior*, *50*(4), 506–517.

Logothetis, N K, & Wandell, B. A. (2004). Interpreting the BOLD signal. *Annual Review of Physiology*, *66*, 735–769.

Logothetis, Nikos K. (2008). What we can do and what we cannot do with fMRI. *Nature*, *453*(7197), 869–878.

Loup, F., Tribollet, E., Dubois-Dauphin, M., & Dreifuss, J. J. (1991). Localization of high-affinity binding sites for oxytocin and vasopressin in the human brain. An autoradiographic study. *Brain Research*, *555*(2), 220–32. doi:10.1016/0006-8993(91)90345-V

Lowry, C. A., Johnson, P. L., Hay-Schmidt, A., Mikkelsen, J., & Shekhar, A. (2005). Modulation of anxiety circuits by serotonergic systems. *Stress Amsterdam Netherlands*, *8*(4), 233–46. doi:10.1080/10253890500492787

Matsuo, K., Nicoletti, M., Nemoto, K., Hatch, J. P., Peluso, M. A. M., Nery, F. G., & Soares, J. C. (2009). A voxel-based morphometry study of frontal gray matter correlates of impulsivity. *Human Brain Mapping*, *30*(4), 1188–1195.

McAdams, D. P. (1992). The five-factor model in personality: A critical appraisal. *Journal of Personality*, *60*(2), 329–361.

Meador-Woodruff, J. H., Damask, S. P., Wang, J., Haroutunian, V., Davis, K. L., & Watson, S. J. (1996). Dopamine receptor mRNA expression in human striatum and neocortex. *Neuropsychopharmacology*, *15*(1), 17–29.

Meyer, G. J., Finn, S. E., Eyde, L. D., Kay, G. G., Moreland, K. L., Dies, R. R., … Reed, G. M. (2001). Psychological Testing and Psychological Assessment: A Review of Evidence and Issues. *American Psychologist*, *56*(2), 128–165.

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience*, *24*, 167–202.

Miller, J., Flory, K., Lynam, D., & Leukefeld, C. (2003). A test of the four-factor model of impulsivity-related traits. *Personality and Individual Differences*, *34*(8), 1403–1418. doi:10.1016/S0191-8869(02)00122-8

Miresco, M. J., & Kirmayer, L. J. (2006). The Persistence of Mind-Brain Dualism in Psychiatric Reasoning About Clinical Scenarios. *American Journal of Psychiatry*, *163*(11), 913–918.

Moresco, F. M., Dieci, M., Vita, A., Messa, C., Gobbo, C., Galli, L., … Fazio, F. (2002). In vivo serotonin 5HT(2A) receptor binding and personality traits in healthy subjects: a positron emission tomography study. *NeuroImage*, *17*(3), 1470–1478.

Munafò, M. R., & Flint, J. (2011). Dissecting the genetic architecture of human personality. *Trends in Cognitive Sciences*, *15*(9), 395–400.

Munafò, M. R., Yalcin, B., Willis-Owen, S. A., & Flint, J. (2008). Association of the dopamine D4 receptor (DRD4) gene and approach-related personality traits: meta-analysis and new data. *Biological Psychiatry*, *63*(2), 197–206.

Nestler, E. J. (2005). Is there a common molecular pathway for addiction? *Nature Neuroscience*, *8*(11), 1445–1449.

Netter, P., Hennig, J., & Roed, I. S. (1996). *Serotonin and dopamine as mediators of sensation seeking behavior. Neuropsychobiology* (Vol. 34, pp. 155–165).

Niv, Y. (2007). Cost, benefit, tonic, phasic: what do response rates tell us about dopamine and motivation? *Annals Of The New York Academy Of Sciences*, *1104*(1), 357–376.

Ochsner, K. N., Ludlow, D. H., Knierim, K., Hanelin, J., Ramachandran, T., Glover, G. C., & Mackey, S. C. (2006). Neural correlates of individual differences in pain-related fear and anxiety. *Pain*, *120*(1-2), 69–77.

Oler, J. A., Fox, A. S., Shelton, S. E., Rogers, J., Dyer, T. D., Davidson, R. J., … Kalin, N. H. (2010). Amygdalar and hippocampal substrates of anxious temperament differ in their heritability. *Nature*, *466*(7308), 864–868.

Olivier, B., & Van Oorschot, R. (2005). 5-HT1B receptors and aggression: a review. *European Journal of Pharmacology*, *526*(1-3), 207–217.

Omura, K., Todd Constable, R., & Canli, T. (2005). Amygdala gray matter concentration is associated with extraversion and neuroticism. *NeuroReport*, *16*(17), 1905–1908.

Ongür, D., & Price, J. L. (2000). The organization of networks within the orbital and medial prefrontal cortex of rats, monkeys and humans. *Cerebral Cortex*, *10*(3), 206–219.

Ophir, A. G., Gessel, A., Zheng, D.-J., & Phelps, S. M. (2012). Oxytocin receptor density is associated with male mating tactics and social monogamy. *Hormones and behavior*, *61*(3), 445–53. doi:10.1016/j.yhbeh.2012.01.007

Ophir, A. G., Wolff, J. O., & Phelps, S. M. (2008). Variation in neural V1aR predicts sexual fidelity and space use among male prairie voles in semi-natural settings. *Proceedings of the National Academy of Sciences of the United States of America*, *105*(4), 1249–1254.

Paris, J. (2005). Neurobiological dimensional models of personality: a review of the models of Cloninger, Depue, and Siever. *Journal of Personality Disorders*, *19*(2), 156–170.

Paulus, M. P., Rogalsky, C., Simmons, A., Feinstein, J. S., & Stein, M. B. (2003). Increased activation in the right insula during risk-taking decision making is related to harm avoidance and neuroticism. *NeuroImage*, *19*(4), 1439–1448.

Paunonen, S. V, & Jackson, D. N. (2000). What Is Beyond the Big Five? Plenty! *Journal of Personality*, *68*(5), 821–835.

Piazza, P. V, Deroche, V., Deminière, J. M., Maccari, S., Le Moal, M., & Simon, H. (1993). Corticosterone in the range of stress-induced levels possesses reinforcing properties: implications for sensation-seeking behaviors. *Proceedings of the National Academy of Sciences of the United States of America*, *90*(24), 11738–11742.

Pierce, R. C., & Kumaresan, V. (2006). The mesolimbic dopamine system: the final common pathway for the reinforcing effect of drugs of abuse? *Neuroscience & Biobehavioral Reviews*, *30*(2), 215–238.

Poldrack, R A. (2006). Can cognitive processes be inferred from neuroimaging data. *Trends in Cognitive Sciences*, *10*(2), 59–63.

Poldrack, Russell A. (2011). Inferring Mental States from Neuroimaging Data: From Reverse Inference to Large-Scale Decoding. *Neuron*, *72*(5), 692–697. doi:10.1016/j.neuron.2011.11.001

Quirk, G. J., & Beer, J. S. (2006). Prefrontal involvement in the regulation of emotion: convergence of rat and human studies. *Current Opinion in Neurobiology*, *16*(6), 723–727.

Roberts, B. W., Kuncel, N. R., Shiner, R., Caspi, A., & Goldberg, L. R. (2007). The Power of Personality: The Comparative Validity of Personality Traits, Socioeconomic Status, and Cognitive Ability for Predicting Important Life Outcomes. *Perspectives on Psychological Science*, *2*(4), 313–345. doi:10.1111/j.1745-6916.2007.00047.x

Ross, H. E., & Young, L. J. (2009). Oxytocin and the neural mechanisms regulating social cognition and affiliative behavior. *Frontiers in Neuroendocrinology*, *30*(4), 534–547.

Ruegg, R. G., Gilmore, J., Ekstrom, R. D., Corrigan, M., Knight, B., Tancer, M., … Golden, R. N. (1997). *Clomipramine challenge responses covary with Tridimensional Personality Questionnaire scores in healthy subjects. Biological Psychiatry* (Vol. 42, pp. 1123–1129).

Rusting, C. L., & Larsen, R. J. (1997). Extraversion, neuroticism, and susceptibility to positive and negative affect: A test of two theoretical models. *Personality and Individual Differences*, *22*(5), 607–612. doi:10.1016/S0191-8869(96)00246-2

Ryan, J. P., Sheu, L. K., & Gianaros, P. J. (2011). Resting state functional connectivity within the cingulate cortex jointly predicts agreeableness and stressor-evoked cardiovascular reactivity. *NeuroImage*, *55*(1), 363–370.

Salamone, J. D. (1994). The involvement of nucleus accumbens dopamine in appetitive and aversive motivation. *Behavioural Brain Research*, *61*(2), 117–133.

Sallet, J., Mars, R. B., Noonan, M. P., Andersson, J. L., O'Reilly, J. X., Jbabdi, S., … Rushworth, M. F. S. (2011). Social network size affects neural circuits in macaques. *Science (New York, N.Y.)*, *334*(6056), 697–700. doi:10.1126/science.1210027

Sapolsky, R. M. (1999). Glucocorticoids, stress, and their adverse neurological effects: relevance to aging. *Experimental Gerontology*, *34*(6), 721–732.

Saucier, G., & Goldberg, L. R. (1998). What is beyond the Big Five. *Journal of Personality*, *66*(4), 495–524.

Schilling, C., Kühn, S., Romanowski, A., Banaschewski, T., Barbot, A., Barker, G. J., … Gallinat, J. (2011). Common structural correlates of trait impulsiveness and perceptual reasoning in adolescence. *Human Brain Mapping*, *000*, n/a–n/a. doi:10.1002/hbm.21446

Schmitt, D. P., & Buss, D. M. (2000). Sexual dimensions of person description: Beyond or subsumed by the Big Five, *34*(2), 141–177.

Schweinhardt, P., Seminowicz, D. A., Jaeger, E., Duncan, G. H., & Bushnell, M. C. (2009). The anatomy of the mesolimbic reward system: a link between personality and the placebo analgesic response. *Journal of Neuroscience*, *29*(15), 4882–4887.

Self, D. W., Barnhart, W. J., Lehman, D. A., & Nestler, E. J. (1996). Opposite modulation of cocaine-seeking behavior by D1- and D2-like dopamine receptor agonists. *Science*, *271*(5255), 1586–1589.

Simpson, J. A., & Gangestad, S. W. (1991). Individual differences in sociosexuality: evidence for convergent and discriminant validity. *Journal of Personality and Social Psychology*, *60*(6), 870–883.

Smith, S. M., Fox, P. T., Miller, K. L., Glahn, D. C., Fox, P. M., Mackay, C. E., … Beckmann, C. F. (2009). Correspondence of the brain's functional architecture during activation and rest. *Proceedings of the National Academy of Sciences of the United States of America*, *106*(31), 13040–13045.

Soloff, P. H., Price, J. C., Mason, N. S., Becker, C., & Meltzer, C. C. (2010). Gender, personality, and serotonin-2A receptor binding in healthy subjects. *Psychiatry research*, *181*(1), 77–84. doi:10.1016/j.pscychresns.2009.08.007

Spampinato, M. V., Wood, J. N., De Simone, V., & Grafman, J. (2009). Neural correlates of anxiety in healthy volunteers: a voxel-based morphometry study. *The Journal of neuropsychiatry and clinical neurosciences*, *21*(2), 199–205.

Starkman, M. N., Giordani, B., Gebarski, S. S., Berent, S., Schork, M. A., & Schteingart, D. E. (1999). *Decrease in cortisol reverses human hippocampal atrophy following treatment of Cushing's disease. Biological Psychiatry* (Vol. 46, pp. 1595–1602).

Stuettgen, M., Hennig, J., Reuter, M., & Netter, P. (2005). Novelty Seeking but not BAS is associated with high dopamine as indicated by a neurotransmitter challenge test using mazindol as a challenge substance. *Personality and Individual Differences*, *38*(7), 1597–1608. doi:10.1016/j.paid.2004.09.025

Sugiura, M., Kawashima, R., Nakagawa, M., Okada, K., Sato, T., Goto, R., … Fukuda, H. (2000). Correlation between human personality and neural activity in cerebral cortex. *NeuroImage*, *11*(5 Pt 1), 541–546.

Sutin, A. R., Beason-Held, L. L., Resnick, S. M., & Costa, P. T. (2009). Sex differences in resting-state neural correlates of openness to experience among older adults. *Cerebral Cortex*, *19*(12), 2797–2802.

Takano, A., Arakawa, R., Hayashi, M., Takahashi, H., Ito, H., & Suhara, T. (2007). Relationship between neuroticism personality trait and serotonin transporter binding. *Biological Psychiatry*, *62*(6), 588–592.

Tauscher, J., Bagby, R. M., Javanmard, M., Christensen, B. K., Kasper, S., & Kapur, S. (2001). Inverse relationship between serotonin 5-HT(1A) receptor binding and anxiety: a [(11)C]WAY-100635 PET investigation in healthy volunteers. *The American Journal of Psychiatry*, *158*(8), 1326–1328.

Thibodeau, R., Jorgensen, R. S., & Kim, S. (2006). Depression, anxiety, and resting frontal EEG asymmetry: a meta-analytic review. *Journal of Abnormal Psychology*, *115*(4), 715–729.

Tops, M., Van Peer, J. M., Korf, J., Wijers, A. A., & Tucker, D. M. (2007). Anxiety, cortisol, and attachment predict plasma oxytocin. *Psychophysiology*, *44*(3), 444–449.

Tribollet, E., Arsenijevic, Y., & Barberis, C. (1998). Vasopressin binding sites in the central nervous system: distribution and regulation. *Progress in Brain Research*, *119*, 45–55.

Turkheimer, E. (1998). Heritability and biological explanation. *Psychological Review*, *105*(4), 782–791.

Tyrka, A. R., Mello, A. F., Mello, M. F., Gagne, G. G., Grover, K. E., Anderson, G. M., … Carpenter, L. L. (2006). Temperament and hypothalamic-pituitary-adrenal axis function in healthy adults. *Psychoneuroendocrinology*, *31*(9), 1036–1045.

Underwood, B. J. (1975). Individual differences as a crucible in theory construction. *American Psychologist*, *30*(2), 128–134. doi:10.1037/h0076759

Uno, H., Eisele, S., Sakai, A., Shelton, S., Baker, E., DeJesus, O., & Holden, J. (1994). Neurotoxicity of glucocorticoids in the primate brain. *Hormones and Behavior*. Elsevier. doi:10.1006/hbeh.1994.1030

Uvnäs-Mobcrg, K., Widström, A. M., Nissen, E., & Björvell, H. (1990). Personality traits in women 4 days postpartum and their correlation with plasma levels of oxytocin and prolactin. *Journal of Psychosomatic Obstetrics Gynecology*, *11*(4), 261–273. doi:10.3109/01674829009084422

Van Laere, K., Goffin, K., Bormans, G., Casteels, C., Mortelmans, L., De Hoon, J., … Pieters, G. (2009). Relationship of type 1 cannabinoid receptor availability in the human brain to novelty-seeking temperament. *Archives of General Psychiatry*, *66*(2), 196–204.

Veronica Witte, A., Flöel, A., Stein, P., Savli, M., Mien, L.-K., Wadsak, W., … Lanzenberger, R. (2010). Aggression is related to frontal serotonin-1A receptor distribution as revealed by PET in healthy subjects. *Human Brain Mapping*, *30*(2), 339.

Verweij, K. J. H., Zietsch, B. P., Medland, S. E., Gordon, S. D., Benyamin, B., Nyholt, D. R., … Wray, N. R. (2010). A genome-wide association study of Cloninger's temperament scales: implications for the evolutionary genetics of personality. *Biological Psychology*, *85*(2), 306–317.

Vuilleumier, P., & Driver, J. (2007). Modulation of visual processing by attention and emotion: windows on causal interactions between human brain regions. *Philosophical Transactions of the Royal Society of London - Series B: Biological Sciences*, *362*(1481), 837–855.

Wacker, J., Chavanon, M.-L., & Stemmler, G. (2010). Resting EEG signatures of agentic extraversion: New results and meta-analytic integration. *Journal of Research in Personality*, *44*(2), 167–179. doi:10.1016/j.jrp.2009.12.004

Weisskopf, M. G., Chen, H., Schwarzschild, M. A., Kawachi, I., & Ascherio, A. (2003). Prospective study of phobic anxiety and risk of Parkinson's disease. *Movement disorders official journal of the Movement Disorder Society*, *18*(6), 646–651.

Westlye, L. T., Bjørnebekk, A., Grydeland, H., Fjell, A. M., & Walhovd, K. B. (2011). Linking an anxiety-related personality trait to brain white matter microstructure: diffusion tensor imaging and harm avoidance. *Archives of General Psychiatry*, *68*(4), 369–377.

Whiteside, S P, & Lynam, D. R. (2001). The Five Factor model and impulsivity: using a structural model of personality to understand impulsivity, *30*, 669–689.

Whiteside, Stephen P, Lynam, D. R., Miller, J. D., & Reynolds, S. K. (2005). Validation of the UPPS impulsive behaviour scale: a four-factor model of impulsivity. *European Journal of Personality*, *19*(7), 559–574. doi:10.1002/per.556

Woollett, K., & Maguire, E. (2011). Acquiring "the Knowledge" of London's layout drives structural brain changes. *Current Biology*, *21*(24), 2109–2114.

Xu, J., & Potenza, M. N. (2011). White matter integrity and five-factor personality measures in healthy adults. *NeuroImage*, *59*(1), 800–807. doi:10.1016/j.neuroimage.2011.07.040

Yamasue, H., Abe, O., Suga, M., Yamada, H., Inoue, H., Tochigi, M., … Kasai, K. (2008). Gender-common and -specific neuroanatomical basis of human anxiety-related personality traits. *Cerebral cortex (New York, N.Y. : 1991)*, *18*(1), 46–52. doi:10.1093/cercor/bhm030

Yarkoni, T. (2009). Big Correlations in Little Studies: Inflated fMRI Correlations Reflect Low Statistical Power. Commentary on Vul et al. (2009). *Perspectives on Psychological Science*, *4*(3), 294–298. doi:10.1111/j.1745-6924.2009.01127.x

Yarkoni, T. (2010). Personality in 100,000 Words: A large-scale analysis of personality and word use among bloggers. *Journal of Research in Personality*, *44*(3), 363–373. doi:10.1016/j.jrp.2010.04.001

Yarkoni, T., Barch, D. M., Gray, J. R., Conturo, T. E., & Braver, T. S. (2009). BOLD correlates of trial-by-trial reaction time variability in gray and white matter: a multi-study fMRI analysis. *PLoS ONE*, *4*(1).

Yarkoni, T., & Braver, T. S. (2010). Cognitive neuroscience approaches to individual differences in working memory and executive control: Conceptual and methodological issues. In A. Gruszka, G. Matthews, & B. Szymura (Eds.), *Handbook of Individual Differences in Cognition*.

Yarkoni, T., Poldrack, R. A., Van Essen, D. C., & Wager, T. D. (2010). Cognitive neuroscience 2.0: building a cumulative science of human brain function. *Trends in Cognitive Sciences*, *14*(11), 496–489. doi:10.1016/j.tics.2010.08.004

Young, N. S., Ioannidis, J. P. A., & Al-Ubaydli, O. (2008). Why Current Publication Practices May Distort Science. *PLoS Medicine*, *5*(10), 5.

Yücel, M., Harrison, B. J., Wood, S. J., Fornito, A., Clarke, K., Wellard, R. M., … Pantelis, C. (2007). State, trait and biochemical influences on human anterior cingulate function. *NeuroImage*, *34*(4), 1766–1773.

Zak, P. J., Kurzban, R., & Matzner, W. T. (2005). *Oxytocin is associated with human trustworthiness. Hormones and Behavior* (Vol. 48, pp. 522–527). Elsevier.

Zak, P. J., Stanton, A. A., & Ahmadi, S. (2007). Oxytocin Increases Generosity in Humans. (S. Brosnan, Ed.)*PLoS ONE*, *2*(11), 5.

Zald, D. H. (2003). The human amygdala and the emotional evaluation of sensory stimuli. *Brain Research. Brain Research Reviews*, *41*(1), 88–123.

Zald, D. H., Mattson, D. L., & Pardo, J. V. (2002). Brain activity in ventromedial prefrontal cortex correlates with individual differences in negative affect. *Proceedings of the National Academy of Sciences of the United States of America*, *99*(4), 2450–2454.

Zelenski, J. M., & Larsen, R. J. (1999). Susceptibility to affect: a comparison of three personality taxonomies. *Journal of Personality*, *67*(5), 761–791.

Zinbarg, R. E., & Mohlman, J. (1998). *Individual differences in the acquisition of affectively valenced associations. Journal of Personality and Social Psychology* (Vol. 74, pp. 1024–1040).