Social Neuroscience

Progress and Implications for Mental Health

John T. Cacioppo,[1] David G. Amaral,[2] Jack J. Blanchard,[3] Judy L. Cameron,[4] C. Sue Carter,[5] David Crews,[6] Susan Fiske,[7] Todd Heatherton,[8] Marcia K. Johnson,[9] Michael J. Kozak,[10] Robert W. Levenson,[11] Catherine Lord,[12] Earl K. Miller,[13] Kevin Ochsner,[14] Marcus E. Raichle,[15] M. Tracie Shea,[16] Shelley E. Taylor,[17] Larry J. Young,[18] and Kevin J. Quinn[10]

[1]University of Chicago, [2]University of California, Davis, [3]University of Maryland, [4]University of Pittsburgh, [5]University of Illinois at Chicago, [6]University of Texas, Austin, [7]Princeton University, [8]Dartmouth University, [9]Yale University, [10]National Institute of Mental Health, [11]University of California, Berkeley, [12]University of Michigan, [13]Massachusetts Institute of Technology, [14]Columbia University, [15]Washington University in St. Louis, [16]Brown University, [17]University of California, Los Angeles, [18]Emory University School of Medicine

ABSTRACT—*Social neuroscience is a new, interdisciplinary field devoted to understanding how biological systems implement social processes and behavior. Social neuroscience capitalizes on biological concepts and methods to inform and refine theories of social behavior, and it uses social and behavioral constructs and data to inform and refine theories of neural organization and function. We focus here on the progress and potential of social neuroscience in the area of mental health. Research in social neuroscience has grown dramatically in recent years. Among the most active areas of research we found are brain-imaging studies in normal children and adults; animal models of social behavior; studies of stroke patients; imaging studies of psychiatric patients; and research on social determinants of peripheral neural, neuroendocrine, and immunological processes. We also found that these areas of research are proceeding along largely independent trajectories. Our goals in this article are to review the development of this field, examine some currently promising approaches, identify obstacles and opportunities for future advances and integration, and consider how this research can inform work on the diagnosis and treatment of mental disorders.*

It is estimated that hominids have walked the earth for the past 7 million years. *Homo sapiens* have evolved within approximately the last 1% of that period (Calvin, 2004), and only the last 5% to 10% of this brief span has brought an array of human achievements that we now take for granted. Humans were not the first bipedal creatures or the first to use tools, but humans, apparently uniquely, contemplate the history of the earth, the reach of the universe, the origin of the species, and the genetic blueprint of life.

The properties of *Homo sapiens* that were responsible for our success as a species are debatable, but it is clear that the number of genes and the size of the human brain are themselves insufficient explanations. Estimates among biologists a decade ago were that 100,000 genes were needed for the cellular processes responsible for human social behavior. However, it is now clear that humans have only a quarter that number of genes (Pennisi, 2005). The prefrontal cortex is thought to be particularly important for critical behaviors such as executive function and working memory, yet the ratio of prefrontal to total cortical gray matter is no greater in humans than it is in nonhuman primates (e.g., Schoenemann, Sheehan, & Glotzer, 2005), and although humans may have more cortical neurons than other mammals, they have barely more than whales and elephants (Roth & Dicke, 2005). The specialized capacities of humans may result from increased number of synapses in the brain, greater cell-packing density, and higher neural-conduction velocities, raising the overall information-processing capacity of the human brain (Roth & Dicke, 2005). Other specialized capacities of humans range from hands with fingers and thumbs to social perception and cognition (e.g., imitation, theory of mind) and social bonding and language. Together, these properties promote complex and coordinated collective actions (e.g., Cacioppo, Berntson, Adolphs, et al., 2002; Calvin, 2004; Hrdy, 2005; Roth & Dicke, 2005). Accordingly, the human brain has evolved to

Address correspondence to John T. Cacioppo, Center for Cognitive and Social Neuroscience, University of Chicago, 5848 S. University Avenue, Chicago, IL 60637, e-mail: cacioppo@uchicago.edu; or to Kevin J. Quinn, National Institute of Mental Health, 6001 Executive Blvd., MSC 9637, Bethesda, MD 20892, e-mail: kquinn@mail.nih.gov.

deal with complex social coordination that supports higher social cognitive functions such as imitation, communication, empathy, theory of mind, interactions, relationships, and collective enterprises.

Social interactions and relationships have a fundamental role in both the development and treatment of human physical and mental diseases (e.g., Giles, Glonek, Luszcz, & Andrews, 2005; House, Landis, & Umberson, 1988). Social processes and behavior are definitive of most mental disorders: A defining feature of autism spectrum disorder is impairment of social cognition and affiliation (Lim, Bielsky, & Young, 2005; Wetherby et al., 2004); schizophrenia is characterized by a profound social anhedonia (Horan & Blanchard, 2003); depression and perceived social isolation are distinct but related mental states (Cacioppo, Hughes, Waite, Hawley, & Thisted, 2006; Hooley, Gruber, Scott, Hiller, & Yurgelun-Todd, 2005); Williams-Beuren syndrome is characterized by hypersociability combined with increased nonsocial anxiety (Meyer-Lindenberg et al., 2005); and psychopathy is characterized by a lack of empathy and the formation of transient and exploitive interpersonal relationships (Harpur, Hare, & Hakstian, 1989). What is considered abnormal behavior in mental disorders depends in part on the cultural context in which it is observed (see Szasz, 1960; cf. Murphy, 1976). Indeed, Ahn, Novick, & Kim (2003) found that the social context could affect whether behavior was seen as acceptable or clinically relevant.

There have been important advances in our understanding of the links between the mind, brain, and behavior over the past century, but it has been conventional to conceptualize individuals as somewhat isolated units of analysis and each life stage as an independent period. Social neuroscience has emerged since the early 1990s as an interdisciplinary field devoted to understanding how biological systems implement social processes and behavior, capitalizing on biological concepts and methods to inform and refine theories of social processes and behavior, and using social and behavioral concepts and data to inform and refine theories of neural organization and function. Our goals in this article are to review the development of this field, examine some currently promising approaches, identify obstacles and opportunities for future advances, and consider how this research can inform work on the diagnosis and treatment of mental disorders.

A strictly biological approach might understand development and behavior to stem from evolved anatomical structures and genetic programs that operate within living cells, isolated from social influences, and the brain to be a biological machine. From the perspective of many biological scientists during most of the 20th century, the contributions of the social world to behavior could be considered later, if at all. Accordingly, social factors were viewed as being of minimal interest with respect to the basic development, structure, or processes of the brain. To the extent that social factors were suspected of being relevant, their consideration would so complicate the study of brain and behavior that they were not a priority.

The approach of social scientists throughout most of the 20th century was no less focused than that of biologists. World wars, a great depression, and civil injustices made it amply clear that social and cultural forces were too important to address to await the full explication of cellular and molecular mechanisms. Thus, biological events and processes were routinely ignored.

Despite this historical independence of biological and social sciences, evidence for a "social brain" in nonhuman primates and humans has accrued (Brothers, 1990). Individuals with damage to the amygdala and associated inferior portions of the temporal cortex exhibit decreased affect to threatening stimuli and increased ratings of the trustworthiness of social stimuli (Adolphs, Tranel, & Damasio, 1998). Prosopagnosics, who typically have bilateral lesions in the occipital lobes near the temporal lobes, do not undergo a change in personality but have another disturbing problem that alters their social behavior: They no longer recognize the faces of those they once knew (e.g., spouses), even though at some level the brain still recognizes these individuals as they show larger skin conductance responses to familiar faces (Tranel & Damasio, 1985). The Capgras syndrome, typically associated with bilateral lesions in the temporal and right fronto-parietal cortices (Signer, 1994), is characterized by an individual insisting that others who are emotionally close to them have been replaced by physically identical imposters. In the Fregoli syndrome, typically associated with right hemisphere dysfunction, the individual perceives strangers as familiar individuals—that is, people are perceived as physically different but psychologically identical to familiar individuals (e.g., Mojtabai, 1994; Oyebode & Sargeant, 1996).

In addition to the impact of the brain on social behavior, social behavior was found to have substantial impact on the brain. Early social interactions, for instance, are important in normal brain and behavioral development. Tactile contact is a stronger determinant of mother–infant attachment than feeding is (Harlow & Harlow, 1973). In rodents, early tactile deprivation reduces the number of glucocorticoid receptor (stress monitoring and dampening) binding sites in the hippocampus and frontal cortex. These changes are persistent and, as a consequence, the negative feedback to stress hormones is diminished, and stress reactivity as a pup and as an adult is elevated (Meaney, Sapolsky, & McEwen, 1985). In human children, attachment and communication are so important that infants respond to faces and try to elicit a response soon after birth. Even in rare instances in which language is neither modeled nor taught, a form of language develops nevertheless (Goldin-Meadow & Mylander, 1984). Intentional action and the observation of intentional action by a conspecific have a shared neural notation (Rizzollati, Fadiga, Gallese, & Fogassi, 1996), which promotes positive social interactions, synchrony, and communication. Positive social interactions promote the release of oxytocin in the brain, which promotes social bonding and down-regulates reactivity to stressors (Uvnäs-Moberg, 1998). The release of testosterone in nonhuman male primates not only

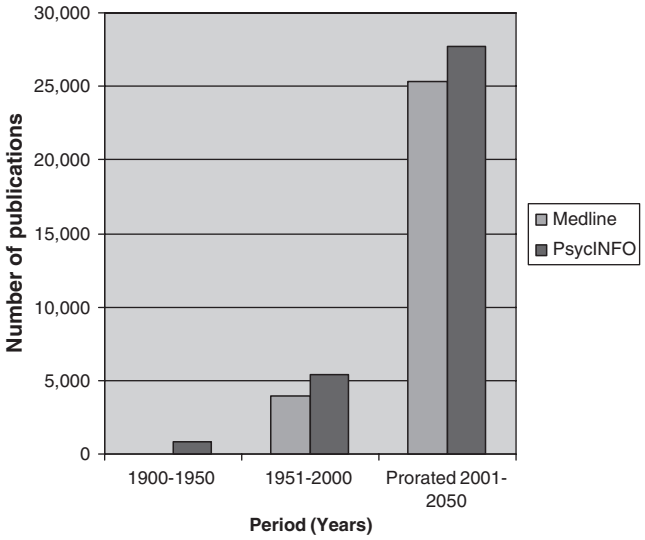

Fig. 1. Research (i.e., number of publications) crossing social and biological levels of analysis, by time period.

promotes sexual behavior, but the availability of receptive females influences their testosterone levels (Bernstein, Gordon, & Rose, 1983; Vandenbergh & Drickamer, 1974).

Mounting evidence for the importance of the relationship between social events and biological events has prompted biological scientists, cognitive scientists, and social scientists to collaborate more systematically, with a common view that the understanding of mind and behavior could be enhanced by an integrative analysis that encompassed brain, cells, and genes. The mean number of articles per year published in which the keywords "social" and "biology" or "biological" are found in Medline (designated in blue) and PsycINFO (designated in red) for the periods 1900 to 1950, 1951 to 2000, and prorated for 2001 to 2050 are illustrated in Figure 1. These data suggest a striking rise in interest and research crossing social and biological levels of analysis. The growth in this research suggests that linking the neurosciences and social sciences is indeed practical and indicates potential for a common scientific language that can establish bridge principles needed to connect the theoretical terms of these sciences.

Recent studies indicate, for instance, that single genes can affect aspects of social behavior (Ferguson et al., 2000); specific regions of the cortex are activated by faces (Grill-Spector, Knouf, & Kanwisher, 2004); the region of the rostral anterior cingulate involved in physical pain is also involved in the pain of social rejection (Eisenberger, Lieberman, & Williams, 2003); the pain of loneliness is largely heritable (Boomsma, Cacioppo, Slagboom, & Posthuma, 2005; Boomsma, Willemse, Dolan, Hawkley, & Cacioppo, 2006); individuals with frontal variant frontotemporal dementia, compared to individuals with Alzheimer's dementia, have normal general cognition but severely impaired social cognition (Gregory et al., 2002); and a mother's behavior affects DNA methylation and, thus, the brain, as well as the subsequent behavior of her offspring toward *their* offspring (Weaver et al., 2004).

An assumption underlying social neuroscience is that all human social behavior is implemented biologically. However, it does not follow that the concepts of biology can by themselves directly describe or explain social behavior, or that "molecular" forms of representation provide the only or best level of analysis for understanding human behavior or mental disorders. Constitutive reductionism, a systematic approach to investigating the parts to better understand the whole, should not be conflated with substitutionism or eliminative reductionism. Constitutive reductionism is one of various approaches to better science based on the value of data derived from distinct levels of analysis to constrain and inspire the interpretation of data derived from others levels of analysis. In constitutive reductionism, the whole is as important to study as are the parts, for only in examining the interplay across levels of analysis can the design be ascertained. Furthermore, molar constructs developed by behavioral and social scientists provide a means of understanding highly complex activity without needing to specify each individual action by its simplest components, thereby providing an efficient approach to describing complex systems. By analogy, chemists who work with the periodic table on a daily basis use recipes rather than the periodic table to cook, but not because a particular food preparation cannot be coded by complex chemical expressions (cf. McGee, 2004). However, efficiency of expression is not the only issue: The concepts defining fine cuisine are not part of the discipline of chemistry. The theoretical terms of the behavioral and social sciences are similarly valuable in relation to those of biology, but can be informed and refined through integration with theories and methods from the neurosciences (Cacioppo, Berntson, Sheridan, & McClintock, 2000).

Although research that falls under the rubric of social neuroscience has a longer tradition, the term social neuroscience first appeared in a 1992 article calling for an integration of human and animal research traditions to create an interdisciplinary approach to understanding the biological mechanisms that implement social behavior and to using biological concepts and methods to develop and refine theories in the social and behavioral sciences (Cacioppo & Berntson, 1992; Cacioppo et al., 2002). Research in social neuroscience has grown dramatically since that time. Among the most active areas of research are brain imaging studies in normal children (e.g., Dapretto et al., 2006) and adults (e.g., Ochsner & Lieberman, 2001); animal models of social behavior (e.g., Insel & Fernald, 2004); studies of stroke patients (e.g., Adolphs, 2001); imaging studies of psychiatric patients (e.g., Frith & Frith, 1999); and research on social determinants of peripheral neural, neuroendocrine, and immunological processes (e.g., Padgett et al., 1998). These areas of research appear to be proceeding along largely independent trajectories, however.

In 2002, the National Institute of Mental Health (NIMH) issued a Request for Applications (RFA) on "Exploratory/

Developmental Grants in Social Neuroscience." The intent of this RFA was to provide a catalyst for the area and to elucidate mechanisms of social behavior. A number of grants involving humans and animals were funded, and by the summer of 2004 these projects were completed. The following year, NIMH convened a workshop to identify some of the most promising avenues of research, with an emphasis on ultimately understanding mental disorders. A conclusion of the workshop was that, although it was inevitable that a field as broad as social neuroscience would proceed along many different trajectories, more communication and integration across animal and human research using normal and patient samples would be beneficial. Several research approaches were identified that held special promise to advance multilevel interdisciplinary analyses of the biological mechanisms of social behavior. In the following sections, several of these approaches and the challenges they face are described, and the relevance of each to the diagnosis and treatment of psychiatric disorders are considered. Following this, a brief summary of the NIMH workshop (held in July 2005) is presented.

ANIMAL MODELS

An important goal of social neuroscience research is to understand the basic genetic and neurobiological mechanisms underlying human sociality. This information can then be used for the development of novel treatment strategies for clinical disorders associated with disrupted social behaviors. Unfortunately, basic and clinical human research has been severely limited in its ability to dissect the complex interactions of genes, the environment, and the neural circuits that make up the social brain. In contrast, animal models provide a powerful opportunity to manipulate molecular and neural systems in order to elucidate the neural mechanisms underlying normal social processes. Social neuroscientists utilizing animal models have focused primarily on the proximate mechanisms regulating reproductive behavior (Meisel & Sachs, 1994; Pfaff & Schwartz-Giblin, 1994), maternal behavior (Numan & Insel, 2003) and aggression (Olivier & Young, 2002), with more recent studies examining social recognition (Bielsky, Hu, Ren, Terwilliger, & Young, 2005; Ferguson, Aldag, Insel, & Young, 2001; Ferguson et al., 2000) and social bonding (Young & Wang, 2004). Research delineating the neuroendocrine regulation of sexual behavior emerged in the late 1960s and continues to provide an ever more detailed mechanistic knowledge of how gonadal steroids influence gene transcription and properties of specific neural circuits to regulate sexuality. Beginning in the mid-1960s, studies in the regulation of maternal behavior in rats and sheep elucidated the role of the hormones of pregnancy and lactation (e.g., estrogen, oxytocin, prolactin) in the initiation of maternal nurturing and bonding behaviors (Bridges, 1984; Bridges, DiBiase, Loundes, & Doherty, 1985; Kendrick, Keverne, & Baldwin, 1987; Moltz, Lubin, Leon, & Numan, 1970; Pedersen & Prange, 1979; Rosenblatt, 1969; Terkel & Rosenblatt, 1968). These and subsequent studies also emphasized the importance of experience in the development of maternal behavior and other complex behavioral traits. More recently, there has been heightened awareness of the value of animal models for understanding processes directly relevant to psychiatric disorders of the social brain.

In this era of genomics, there has been increasing interest in the role of specific genes in the regulation of behavioral processes. As a result, genetically engineered mice have emerged as an important experimental tool for dissecting the contributions of individual genes in the regulation of social processes. Knockout mice studies have provided important contributions to our understanding of the regulation of reproductive (Ogawa et al., 2000; Ogawa, Lubahn, Korach, & Pfaff, 1997; Rissman, Early, Taylor, Korach, & Lubahn, 1997), parental (Brown, Ya, Bronson, Dikkes, & Greenberg, 1996; Lucas, Ormandy, Binart, Bridges, & Kelly, 1998; Takayanagi et al., 2005), and aggressive behavior (Nelson et al., 1995), as well as social cognition in general (Bielsky et al., 2005; Bielsky, Hu, Szegda, Westphal, & Young, 2004; Ferguson et al., 2001). In addition to their value in understanding basic mechanisms of normal social behavior, several knockout mouse models have been proposed to be useful models of psychiatric disorders characterized by deficits in social behavior, including autism (Lim et al., 2005; Nicot, Otto, Brabet, & Dicicco-Bloom, 2004; Takayanagi et al., 2005; cf. Happé, Ronald, & Plomin, 2006). A recent study by Kwon et. al. (2006) shows that conditional, selective central nervous system deletion (cerebral cortex and hippocampus) of *PTEN*, a tumor suppressor gene, results in selective neuronal hypertrophy and alterations in social behavior that resemble features of autism spectrum disorder. Studies of oxytocin knockout mice nicely illustrate the power of knockout mouse studies in modeling neural processes of central importance in social neuroscience. Oxytocin knockout mice display a severe disruption in the ability to recognize mice they have previously encountered (Ferguson et al., 2000). Because these mice appear to function normally in other nonsocial cognitive and olfactory tasks, these studies suggest that oxytocin plays a specific role in regulating the neural processing of social signals. This deficit in social recognition is associated with a deficit in amygdala activation in the knockouts during a social encounter (Ferguson et al., 2001). A single infusion of oxytocin into the medial amygdala completely restores social recognition abilities in these mice. Thus, oxytocin acts in the medial amygdala to promote the processing of social cues necessary for individual discrimination. These findings may have relevance to autism, which is characterized by aberrant processing of visual social information as well as amygdala function (Schultz, 2005; Schultz et al., 2000). In fact, one study has reported decreased oxytocin levels in the plasma of children with autism relative to controls (Modahl et al., 1998). A recent study (Campbell et al., 2006) points to increased susceptibility for autism with a particular

variant of the *MET* gene. However, as with many psychiatric disorders, no single hormone, neurotransmitter, or gene will likely provide a complete account of the disorder. Although such factors may play a significant role, as serotonin does in depression, understanding such disorders ultimately will require a deeper understanding of the psychological mechanisms and social context within which such factors act.

Indeed, other studies in oxytocin knockout mice illustrate the importance of considering social context in behavioral studies. Initial reports suggested that oxytocin knockout female mice displayed normal maternal behavior (Nishimori et al., 1996; Young et al., 1997). However, these tests were conducted in standard mouse cages with isolated females. A more recent study examined the behavioral phenotype of oxytocin knockout mice in seminaturalistic housing conditions with complex social environments and found that 100% of the knockout females in this context displayed infanticidal behavior, compared to only 50% of the wild-type controls (Ragnauth et al., 2005). The influence of context on behavioral outcomes is further exemplified by a multisite behavioral analysis of several strains of mice. Even though the behavioral assays were performed using standardized procedures at each of three different locations, contradictory behavioral results were obtained in several instances, suggesting that subtle differences in housing or experimenter characteristics greatly influenced behavioral results (Crabbe, Wahlsten, & Dudek, 1999). As behavioral expression in clinical disorders is also context dependent, consideration of social context is critical when developing animal models of human social constructs.

No single animal model will encompass the complexity of human sociality or mental health. Therefore, comparative studies using a wide range of species are critical for modeling various aspects of human behavior. Microtine rodents, or voles, are one such model that have been particularly useful in providing insight into the nature and diversity of social behavior (Carter, DeVries, & Getz, 1995; Young & Wang, 2004). Prairie voles are highly social and form long-lasting social bonds between mates—a behavior not characteristic of laboratory strains of rats and mice. In contrast, the closely related meadow and montane voles are relatively asocial species and do not form social bonds. Pharmacological studies have demonstrated that the neuropeptides oxytocin and vasopressin play critical roles in establishing the social bonds between mates (Williams, Insel, Harbaugh, & Carter, 1994; Winslow, Hastings, Carter, Harbaugh, & Insel, 1993). Comparative and molecular studies suggest that species differences in brain expression patterns of the receptors for these peptides may be responsible for the species differences in behavior (Insel & Shapiro, 1992; Insel, Wang, & Ferris, 1994; Lim et al., 2004). Specifically, oxytocin and vasopressin receptors are concentrated in the nucleus accumbens and ventral pallidum—components of the mesolimbic dopamine reward circuitry—of the pair-bonding prairie vole, but not of the nonmonogamous montane and meadow voles. Examination of the vasopressin receptor gene in these species suggests that the evolution of a highly repetitive DNA element in the promoter region of the gene has resulted in the species differences in expression pattern (Young, Nilsen, Waymire, MacGregor, & Insel, 1999).

Unlike inbred strains of rats and mice, humans are genetically diverse. Thus, outbred species recently derived from natural populations provide the additional potential for understanding the neural mechanisms underlying behavioral diversity within a species. With more than 9,200 species and a vast array of social structures, birds offer opportunities to study genetic and neuronal differences between groups that differ only in one aspect of social behavior. Recent work has shown, for instance, that vasotocin neurons in the medial extended amygdala respond differently to social cues in birds that live in colonies compared to birds that do not (Goodson & Wang, in press). Studies in prairie voles have also begun to examine individual variation in social behavior. For example, instability in the highly repetitive DNA element of the vasopressin receptor has resulted in polymorphisms in this sequence among individual prairie voles. Selective breeding studies demonstrate that variations in this locus lead to individual differences in expression of the vasopressin receptor in the brain, as well as to individual differences in social behavior (Hammock & Young, 2005). Similar repetitive elements have been identified in the human vasopressin receptor gene, *avpr1a*, and polymorphisms in one of these sites have been shown to be in linkage disequilibrium with autism in two independent studies (Kim et al., 2001; Wassink et al., 2004).

Despite the advantages of avian and rodent models for elucidating basic neurobiological mechanisms underlying social processes, there are limitations. The evolution of the primate brain has undoubtedly shifted the relative contribution of subcortical and cortical structures in the regulation of social behavior. Thus nonhuman primate models are also critical for fully understanding the social brain. For example, amygdala lesion studies in neonatal rhesus macaques have provided important information on the role of the amygdala and the development of social behavior (Bauman, Lavenex, Mason, Capitanio, & Amaral, 2004). Other studies are examining the effects of early social experience on brain neurochemistry and adult social interactions in primates. These studies have revealed that male monkeys that experienced early social deprivation have decreased oxytocin concentrations in the cerebrospinal fluid compared to controls (Winslow, 2005; Winslow, Noble, Lyons, Sterk, & Insel, 2003), a finding that is interesting in light of the rodent studies on oxytocin.

The primate model has also contributed to the still-primitive definitions of the neural circuits of the social brain. Studies in primates, for example, first identified regions that are preferentially responsive to faces and facial expressions (Perrett, Hietanen, Oram, & Benson, 1992). More recently, brain regions purported to be involved in social function have received experimental validation in nonhuman primate studies (Rudebeck,

Buckley, Walton, & Rushworth, 2006). These studies emphasize the value of using an animal model that has brain regions implicated in normal human social behavior as well as social behaviors that are at least analogous to human social behaviors. And innovative new techniques (see, for example, Deaner, Khera, & Platt, 2005) allow sophisticated probing of subtle and complex social motivations and intentions.

Although animal models clearly have great potential for furthering our understanding of the normal functioning of the human brain and of psychopathologies of social behavior, several challenging issues must be addressed if the ultimate goal of this research is to be fully realized.

First, selection does not act on single genes nor on the entire genome, but on functionally related genes that form networks that respond as units. Individual genes, neurotransmitters, and brain regions do not function in isolation. Instead these functions are expressed through interacting systems in the context of neural circuits to produce behavioral phenotypes. Thus experimental designs that interrogate multiple molecular systems at multiple levels of analysis are needed to maximize our understanding of the neural mechanisms underlying social processes.

Second, no single animal model reflects the full behavioral phenotype of a given psychiatric condition. Furthermore, behavioral measures used by human and animal researchers are often not comparable. *Diagnostic and Statistical Manual of Mental Disorders–IV* (DSM-IV; American Psychiatric Association, 2000) classification of human disorders is not optimal for investigation of the neurobiological correlates of behavior in animal models. Therefore, it is critical that individual behavioral components of disorders be quantified and emphasized whenever possible. This approach would facilitate the development of animal models relevant to those disorders. Rather than modeling the disease based on DSM-IV criteria, animal models can more effectively provide insights into particular behavioral components of disorders. Increased communication between clinical and animal researchers is needed to develop optimum animal models to facilitate translational research.

Third, the effects of neuropeptides and of other neurochemical elements, including neurotransmitters, subcellular signaling systems, and other systems yet to be discovered, require a functional central and autonomic nervous system. Physical states and reactions of the body, including the status of the central and autonomic nervous system, can influence the readiness of an individual to engage in social behaviors, form attachments, and regulate reactivity to social and physical challenges (Porges, 2003). Dynamic and noninvasive methods for assessing physiology and behavior under conditions of normal social stimuli and interactions are essential to the future of this field.

Fourth, genes are not expressed in isolation any more than social behavior has meaning outside of society. Both are in dynamic flux with the immediate environment that the gene/individual finds itself, which in turn establishes the timing, pattern, and conditions of expression. This important point has been recognized by molecular biologists and behavioral biologists alike: "Taken together, the relations of genes, organisms, and environments are reciprocal relations in which all three elements are both causes and effects" (Lewontin, 2000, p. 100). Hence, it is imperative, when considering complex behaviors and their underpinnings, to view the behaviors as a cumulative process or as the result of experiences up to that point in time and, simultaneously, as the precursor for what will follow.

The concept of translational research implies that research in preclinical animal models will lead to analogous studies in humans. However, applying discoveries originating from animal research to human studies is often impeded by the lack of experimental tools needed to engage the relevant neural systems in humans, as well as a lack of communication between animal and human social neuroscientists. For example, there is an extensive body of animal research implicating oxytocin and vasopressin in modulating various aspects of social behavior, but there is a paucity of studies examining these systems in humans. This is changing, however, with recent studies showing that intranasal oxytocin enhances the buffering effect of social support on stress responsiveness (Heinrichs, Baumgartner, Kirschbaum, & Ehlert, 2003). The development of positron emission tomography ligands to examine oxytocin and vasopressin receptor densities in the human brain would be very helpful in determining whether these systems are dysregulated in psychiatric disorders.

A complementary approach to the investigation of the social and neural contributions to social behavior is to focus on the developmental trajectories of and dependencies between biological and social processes in human and nonhuman animals. We turn to this approach next.

DEVELOPMENTAL APPROACHES

Ontogenetic and epigenetic processes, learning, and different forms of cognitive and affective experience that occur across the lifespan all contribute to variations among individuals. An individual's behavior is influenced by the experiences that accumulate throughout its life. Early experiences shape how individuals will respond to later experiences, and later experiences modify the effects of these earlier experiences (Crews & Groothuis, 2005). Difficulties with emotional regulation or the management of reactions to stressors also may be associated with atypical rearing experiences (Gunnar, 2005; O'Conner, Rutter, & the English and Romanian Adoptees Study Team, 2000). There is little doubt that deprivation and abuse can have negative consequences, but not all individuals who are subjected to deprivation and abuse show these negative outcomes. Early experiences may either increase or ameliorate vulnerabilities to psychopathology or other mental disorders including anxiety, depression, schizophrenia, and autism (Grossman et al., 2003; Teicher et al., 2003). Clues to the neural underpinning of social behavior are gradually emerging from studies of children

and nonhuman animals with atypical rearing experiences or differential amounts of early experience (Bowlby, 1969; Fleming, 2005; Harlow, 1959; Hrdy, 1999, 2005; Levine, 2001; Teicher et al., 2003).

Attempts to study the neurobiological causes and consequences of adverse early experiences, primarily in animal models, suggest that brain-derived neurochemicals, including oxytocin, arginine vasopressin (AVP), and corticotropin-releasing factor (CRF), or their receptors may have broad developmental consequences for physiology and behavior (Carter, 2003). In one recent study, children reared in orphanages and presumably neglected for roughly the first year of life were compared to children reared by their biological parents. Even after approximately 3 years of living with adoptive families, a significant proportion of the neglected children excreted lower levels of oxytocin and AVP than did family-reared children (Fries, Ziegler, Kurian, Jacoris, & Pollak, 2005). A related study of maternally deprived monkeys, when compared to mother-reared animals, also revealed a lower-than-normal level of oxytocin in samples of cerebrospinal fluid (Winslow, 2005).

These same peptides also play a role in the regulation of the hypothalamic-pituitary-adrenal (HPA) axis and could directly or indirectly influence emotionality or social behaviors. Oxytocin, in particular, is capable of down-regulating the HPA axis, and this effect applies to both rodents and humans (Carter, 1998, 2005; Heinrichs et al., 2003; Neumann, 2003). Oxytocin also regulates the autonomic nervous system, with potentially beneficial consequences for human behaviors and emotions (Porges, 2003). For instance, there is evidence that oxytocin can increase the capacity of individuals to show trust (Kosfeld, Heinrichs, Zak, Fischbacher, & Fehr, 2005). Thus, systems reliant on oxytocin may be part of a broad neural system capable of mediating the protective effects of positive social interactions and social support.

Of particular importance for social neuroscience are mechanisms responsible for individual and species differences in behavior. Genetic differences and epigenetic processes can alter subsequent thresholds for sociality, emotionality, and aggression. Epigenetic factors play a fundamental role in how the individual develops (Crews & McLachlan, 2006). Animal research has revealed that social experiences play a role in the development of individuality, probably in part by programming the nervous system (Weaver et al., 2004; Meaney & Szyf, 2005). At least some of the effects of early experience can be reversed by epigenetic manipulations in later life (Weaver et al., 2006). In this manner, epigenetic effects can cross generations, but it is important to keep in mind that only when the effect is incorporated into the germline will it persist without re-exposure of each new generation.

In the context of future translational research, it is interesting to note that exogenous peptide treatments in early life can reverse behavioral and physiological deficits in several models. Developmentally induced deficits such as those associated with prenatal stressors, including undernutrition (Olausson, Uvnäs-Moberg, 2003), certain drug treatments (Lee, Brady, Shapiro, Dorsa, & Koenig, 2005), or blocking the oxytocin receptor with oxytocin antagonists (Bales et al., 2007), can be reduced or reversed by later treatment with oxytocin. Knowledge of this aspect of oxytocin's action may have therapeutic significance given the association between developmental maltreatment and many forms of later psychopathology (Teicher et al., 2003; Winslow et al., 2003; Winslow, 2005).

Many of the consequences of early experiences, and especially social experiences, differ in males and females. It was originally assumed that sex differences were based primarily on genetics or genetically-regulated gonadal hormones. However, studies in animal models have illustrated the importance of social experiences in the later expression of differences between the sexes. For example, in prairie voles, early manipulations of oxytocin are capable of having long-lasting and sexually dimorphic effects on both social behaviors and the expression of oxytocin or AVP or receptors for these peptides (Bales et al., 2004; Carter, 2003). In female rats, the oxytocin receptor can be up-regulated by maternal licking and grooming, while in male rats the effects of maternal stimulation are more apparent as changes in the AVP receptor (Champagne, Diorio, Sharma, & Meaney, 2001; Champagne, Weaver, Diorio, Sharma, & Meaney, 2003; Francis, Young, Meaney, & Insel, 2002). These data support the general hypothesis that, in females, oxytocin may be a central component involved in the mediation of the long-lasting effects of early experience while, in males, AVP may be of particular importance. Sex differences in the effects of AVP seem to be especially apparent in the extended amygdala, bed nucleus of the stria terminalis (BNST), and lateral septum (DeVries & Simerly, 2002). Projections from sexually dimorphic areas may influence many functions, and knowledge of these systems may lead to a deeper understanding of sex differences in the reactions to stress or other emotional challenges (Taylor et al., 2000).

The hormones of the HPA axis also may regulate social behaviors, both in adulthood and during development (Carter & Roberts, 1997). Adrenal hormones, and specifically adrenal corticoids (cortisol in humans and corticosterone in rodents), are sensitive to social experiences, and hormones of the HPA axis can directly modulate pair-bond formation (DeVries, DeVries, Taymans, & Carter, 1995, 1996; DeVries & Simerly, 2002). In addition, there is evidence in rats that CRF receptors show life-long modifications as a function of early experiences, including those associated with maternal licking and grooming (Meaney & Szyf, 2005). Thus, hormones of the HPA axis have developmental consequences for various social and reproductive behaviors (Levine, 2001; Pedersen & Boccia, 2002), possibly interacting with both gonadal steroids and neuropeptides to modulate the expression of the characteristics of social behaviors, as well as reproductive behaviors. The involvement of early experience and the hormones of the HPA axis in the development of the central nervous system may be critically important to

the molding of both species and individual differences in sociality. Research examining the neural mechanism through which early social experiences influence the brain and behavior is a fertile area in social neuroscience.

In sum, understanding the mechanisms through which development impacts human behavior is a major challenge for social neuroscience in the 21st century. Knowledge of the neural consequences of early experience will be important to the understanding, treatment and eventual prevention of multiple types of psychopathology. Further research relating individual differences in neuropeptides to differences in experience and to the behavioral reactivity of normal and at-risk children, including those at risk as a result of child neglect or abuse, is needed. While the importance of addressing issues in developmental social neuroscience is clear, at the same time there is a clear need to understand and hopefully treat those individuals for whom the developmental trajectory has led to disorders and/or deficits in social behavior. In the next section, we turn to neuroimaging research in normal adults.

NEUROIMAGING AND SOCIAL PROCESSES

As noted above, human social behavior is complexly determined, with exquisite contextual and cultural controls evident in normal behavior. One important implication is that the expression of a specific social behavior may say little about the specific antecedent condition or cause. A focus on the level of simple, reflexive behavior, therefore, may not be sufficient for understanding how the brain generates complex behavior or the clinical manifestations of psychopathology. This has been apparent at least as far back as the case of Phineas Gage, whose orbitofrontal and ventromedial cortices were damaged in a construction accident in 1848. Although he "recovered" and attempted to return to work, he was described as no longer Gage, but there was no precise description of the alteration in his behavior (Damasio, 1994). This underscores the importance of delineating components of social behavior—a complex endeavor but one that might lead to an understanding of ordered and disordered social behaviors, their relationship to psychopathologies, the neural bases of such component behavioral processes, and specific diatheses for mental disorders.

Our current understanding of the neural bases of human social behavior is still quite limited. This is attributable less to a lack of interest in understanding the social brain than to the limited methods that have been available for investigating it. This has changed dramatically over the last two decades, as researchers have adopted the methods of cognitive neuroscience, and functional brain imaging in particular, to study social cognition and social behavior (see Adolphs, 2003; Cacioppo et al., 2003; Ochsner & Lieberman, 2001).

Developing an understanding of the neural bases of social behavior may benefit from a two-step process like that followed for research addressing purely cognitive deficits in clinical disorders. In this domain, basic cognitive neuroscience research first established models of working memory and related abilities, which were then applied to cognitive dysfunction in clinical disorders such as schizophrenia (see, e.g., Braver, Barch, & Cohen, 1999). Social neuroscience can follow this same two-step sequence. First, basic research can be used to establish normative models of the mechanisms that support social functioning in healthy individuals. Second, such models can provide conceptual and methodological bases for explaining how social behavior breaks down in various clinical disorders.

Brain imaging can play an important role in model development in that it can support the study of human social abilities involving higher cognitive processes that are difficult to study in animals. On the one hand, animal research has yielded detailed models of the molecular and subcortical bases of simple forms of emotional learning, affiliation, and bonding (e.g., Insel & Fernald, 2004; Quirk & Gehlert, 2003). On the other hand, human social behavior involves many processes that may not be fully captured by rodent (or even nonhuman primate) models of fear conditioning, pair bonding, and the like. The time is ripe for human imaging studies to build upon findings from animal models. Current human studies are exploring, for example, the brain mechanisms that allow people to use higher cognitive processes to access knowledge about themselves, draw inferences about the beliefs and feelings of others, regulate moods and emotions, and pursue long-term goals.

A fuller understanding of human social behavior requires multiple levels of analysis—from the individual, familial, and societal contexts that encourage people to inhibit or exhibit certain behaviors, thoughts, or emotions to genetic, molecular, and systems levels. As argued by Sarter, Berntson, and Cacioppo (1996), integrating animal research, lesion, and direct-stimulation studies and neuroimaging could provide converging evidence regarding the links between psychological function and the brain activity that implements it.

Social behavior can be classified into broadly defined subcategories including (a) self-perception, (b) self-regulation, (c) interpersonal perception, and (d) group processes. What is known about these categories, at multiple levels of analysis, and their implications for psychopathology?

Self-Perception

Self-concepts are fundamental to health and well-being. People like to have consistent self-concepts in consequential domains such as health and mental health. Psychotherapy requires effort, and choosing to participate, along with having to justify the effort, facilitates therapeutic change through cognitive-dissonance reduction (Axsom & Cooper, 1985). People often have positive illusions about themselves that maintain their mental health (Taylor & Brown, 1988), and people's psychological immune systems allow and maintain their recovery from negative life events (Gilbert, Pinel, Wilson, Blumberg, & Wheatley, 1998).

Self-concept drives self-expression in therapeutic writing that can have measurable effects on mental health (e.g., Pennebaker, 2004; see Frisina, Borod, & Lepore, 2004). Cutting-edge work in the domain of the social self includes improved theory-driven measurement (Kwan, John, Kenny, Bond, & Robins, 2004) and sensitivity to cultural and identity issues (Ellemers, Spears, & Doosje, 2002) that could be important for the acceptability of therapeutic interventions in an increasingly multicultural society.

Self-perception has important implications for specific psychopathologies. Some mental disorders, such as schizophrenia, involve disturbances in the perception of self or personal agency (Kircher & Leube, 2003; Sass & Parnas, 2003). Similarly, disturbances in the processing of self-relevant information exist in depression (Bargh & Tota, 1988; Murray, Whitehouse, & Alloy, 1999). Indeed, central to many theories of depression is the idea that people process information with regard to self through a negative filter (i.e., Beck's cognitive triad). Accordingly, a better understanding of the specific roles of brain regions involved in the mental representation of self might aid in the development of more effective cognitive rehabilitation strategies for the treatment of many psychological disorders, including depression, schizophrenia, and personality disorders.

A major focus, going back to the case of Phineas Gage, has been on the role of the prefrontal cortex. Numerous studies have found activity in prefrontal regions during tasks that require people to reflect on themselves or on others (Macrae, Moran, Heatherton, Banfield, & Kelley, 2004; Ochsner, Knierim, et al., 2004). This is the only area of the brain that receives input from all sensory modalities and is an area in which inputs from internal sources conjoin with information received from the outside world. For these reasons, the prefrontal cortex has been labeled the "chief executive" (Goldberg, 2001), responsible for subjective reactions to the outside world and for allowing efficient navigation in the social environment (e.g., Bechara, Damasio, Damasio, & Anderson, 1994; Damasio, 1994; Stuss, Gow, & Hetherington, 1992; Stuss & Levine, 2002; Stuss, Picton, & Alexander, 2001). Because of their interconnections with the rest of the brain, damage to the frontal lobes has widespread consequences, and it is likely that frontal lobe deficits are involved in a broad spectrum of psychopathological conditions, especially in terms of social impairments that accompany mental disorders (Beer, Heerey, Keltner, Scabini, & Knight, 2003).

Imaging studies have documented a unique role of the medial prefrontal cortex in self-relevant processing (e.g., Kelley et al., 2002; Macrae et al., 2004). The translational value of this research is supported by Moran, Macrae, Heatherton, Wyland, and Kelley (2006), who found that distinct neural circuits in adjacent regions of the prefrontal cortex subserve cognitive and emotional aspects of self-reflection. Whereas the medial prefrontal cortex responded only to material that was self-descriptive, the emotional impact of the material was resolved in an adjacent region of ventral anterior cingulate cortex (ACC). Importantly, prior research indicates that this region (i.e., Brodmann areas 24 and 25) is hypometabolic in unipolar depression (Buchsbaum et al., 1997; Drevets et al., 1997; M.S. George et al., 1997). Moreover, decreased metabolism in this region can be accompanied by a corresponding loss in cortical volume (Drevets et al., 1997), suggesting that some of the deficits associated with major depression may be attributable to a loss of functioning and volume in ventral regions of ACC. The functional significance of this finding is reflected in the differential activation of this region in response to the perception of emotional facial expressions between depressed and control subjects (e.g., Gotlib et al., 2005). In a particularly striking study, Mayberg and colleagues (2005) demonstrated that deep brain stimulation in this region was effective in alleviating depression in treatment-resistant patients. Understanding the role of the ventral ACC and adjacent parts of the medial prefrontal cortex in affective and self-relevant processing is likely to contribute to the development of effective treatments for depression and potentially other mental disorders as well.

Self-Regulation

An important human capacity in civilized societies is the ability to regulate and control thoughts and behavior. Self-regulation is viewed here as the higher-order (i.e., executive) control of lower-order processes, responsible for the planning and execution of behavior. Self-regulation not only refers to executive processes such as working memory, attention, memory, choice, and decision making, but also the control of emotion (covering issues of affect, drive, and motivation). Although humans have the capacity to delay gratification, control appetites and impulses, and persevere in order to attain goals, failures of self-regulation (e.g., drug abuse, domestic violence, binge eating) are among the most important and perplexing problems facing society. Self-regulation is important for all varieties of mental health treatment acceptance and compliance. Accordingly, understanding the nature of self-regulation, both its successful implementation and its failures, could provide valuable insights into mental disorders and their treatment.

Recent developments in cognitive neuroscience have increased understanding of the neural mechanisms of self-regulation, including three primary prefrontal circuits that are involved in executive function: the ventromedial/orbitofrontal cortex, the dorsolateral prefrontal cortex, and the ACC (Chow & Cummings, 1999; Kaufer & Lewis, 1999). For instance, research has implicated the ACC in decision monitoring and decision making (e.g. Bush et al., 2002; Elliot & Dolan, 1998; Liddle, Kiehl, & Smith, 2001), initiating the selection of an appropriate novel response from several alternatives (e.g., Raichle et al., 1994), performance monitoring (e.g., MacDonald, Cohen, Stenger, & Carter, 2000), action monitoring (Gehring & Knight, 2000; Paus, 2001), detection or processing of response conflict

(Gehring & Fencsik, 2001), error detection and processing (Carter et al., 1998; Kiehl, Liddle, & Hopfinger, 2000; Menon, Adleman, White, Glover, & Reiss, 2001), prediction of errors (Paulus, Hozack, Frank, Brown, & Schuckit, 2003), reward/punishment assessment (Knutson, Westdorp, Kaiser, & Hommer, 2000), and perception of physical and social pain (Eisenberger et al., 2003). All of these are relevant to the self-regulation of behavior. Nonhuman primate studies have provided converging evidence about the role of the frontal cortex in cognitive control (Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004).

Impairments in self-regulation and inhibition are relevant to a wide range of mental disorders, such as obsessive-compulsive disorder (OCD), Tourette's syndrome, autism, schizophrenia, and attention deficit disorder (e.g., Bush et al., 1999; Dehaene et al., 2003; Frith, 1992; Sheppard, Bradshaw, Purcell, & Pantelis, 1999; Stuss et al., 1992). It is not surprising, therefore, that ACC dysfunction has been associated with many mental health disorders—especially OCD and schizophrenia (e.g. Barch, Sheline, Csernansky, & Snyder, 2003; Dehaene et al., 2003; Johannes et al., 2001; Tamminga et al., 1992), disorders that exemplify problems with inhibitory control. In relation to OCD, it is argued that the process of comparing current status with the expectation of achieving a goal is disrupted. Other problems associated with damage to the ACC include mutism, diminished self-awareness, motor neglect, depression, emotional instability, apathy, loss of regulation of autonomic function, and severe disruption of social behavior (e.g., Devinsky, Morrell, & Bogt, 1995), all of which point to the ACC's vital function in self-regulation (Banfield, Wyland, Macrae, Munte, & Heatherton, 2004).

Imaging work has started to identify the neural mechanisms underlying internal inhibition or cognitive control of thoughts and behavior (e.g., Anderson et al., 2004). The inability to control unwanted thoughts is a central problem for mood disorders, OCD, and schizophrenia. In one recent study, subjects were required to suppress a particular thought, regulate all thoughts, or think freely about any thought. The results showed that the suppression of a *particular* thought led to greater activation in the ACC, when contrasted with the free-thought condition. Suppression of *all* thoughts was associated with greater bilateral activation in the insula and the right inferior parietal cortex, when compared with the free-thought condition (Wyland, Kelley, Macrae, Gordon, & Heatherton, 2003). Anderson and colleagues (2004) found that blocking the retrieval of unwanted memories was associated with activity in the dorsolateral prefrontal cortex. Understanding how people attempt to control unwanted thoughts, and how such efforts fail, could point to the etiology of some disorders and to treatment approaches.

In contemporary society, social stimuli are the most common elicitors of emotional responses. The self-regulation of emotions in social contexts, therefore, is important to successful social functioning. It is noteworthy in this context that the ability to self-regulate negative emotion is impaired in over half of DSM-IV Axis I disorders (e.g., depression) and most Axis II personality disorders (e.g., borderline personality disorder). Emotion regulation difficulties also influence physical health outcomes, such as cardiovascular disease (Mauss & Gross, 2004). Recent work has examined a cognitive form of emotion regulation, known as reappraisal, which involves reinterpreting the meaning of emotional events in unemotional terms. Reappraisal of aversive stimuli activates lateral prefrontal and anterior cingulate regions implicated in cognitive control and deactivates structures like the amygdala, which have been implicated in generating emotional responses (Beauregard, Levesque, & Bourgouin, 2001; Kalisch et al., 2005; Ochsner, Bunge, Gross, & Gabrieli, 2002; Ochsner, Ray, et al., 2004; Phan et al., 2005). These findings may be particularly relevant for disorders like depression, posttraumatic stress disorder (PTSD), and social phobia, which have shown heightened amygdala activity both at rest and in response to emotional cues (Furmark et al., 2004; Rauch et al., 2000; Sheline et al., 2001). Different medial prefrontal regions may play special roles in reappraisal. Dorsal regions implicated in thinking about others (Mitchell, Macrae, & Banaji, 2004; Ochsner, Knierim, et al., 2004) are involved when individuals make themselves more anxious by focusing on negative aspects of aversive images. By contrast, ventral regions implicated in evaluating the affective relevance of events (including the subgenual cingulate; Moran et al., 2006; Ochsner, Ludlow et al., 2006) are involved when individuals focus on the self-relevance of these images (Ochsner, Ray et al., 2004; Ray et al., 2005). These findings may have implications for distinct neural substrates for anxiety and depression, which have been related to increased activity in dorsal medial prefrontal cortices and reduced activity in ventral medial prefrontal and cingulate cortices, respectively (Drevets, 2001; Paulus, Feinstein, Simmons, & Stein, 2004; Sawamoto et al., 2000; Simpson, Drevets, Snyder, Gusnard, & Raichle, 2001). Potentially useful probes for characterizing the neural substrates of these disorders, including similarities and differences underlying the self-regulation of emotions elicited by humans (e.g., an attacker), animated but nonhuman stimuli (e.g., a tsunami), and nonsocial stimuli (e.g., a visual cliff), warrant investigation.

Interpersonal Perception and Group Processes

Social relationships are fundamentally important to people's health and well being. Epidemiological studies have found that deficits in social relationships are a risk factor for broad-based morbidity and mortality, with an age-adjusted effect equivalent to cigarette smoking (e.g., House et al., 1988). Whether we're empathically connecting with a friend who has lost a loved one or are trying to assess the honesty of a potential employee, the ability to understand the intentions, beliefs, and feelings of other people is necessary for both mundane and complex social interactions.

Recent brain imaging studies have revealed that distinct brain systems are important for person perception and suggest common processes underlying person perception and depression, social anxiety, PTSD, and autism.

Specific brain areas have been implicated in deciphering nonverbal cues that signal emotional states and behavioral intentions. It has been found that the physical features of a nonverbal cue and its affective and social value are processed by different structures. For example, face recognition has been shown to depend upon the integrity of a region of the inferior temporal cortex known as the fusiform face area (Grill-Spector et al., 2004; Kanwisher, McDermott, & Chun, 1997). Recognition of the emotions conveyed by a face, however, has been found to depend upon other structures that may decode specific emotions: The amygdala is particularly sensitive to fear faces (Adolphs et al., 1999; Breiter et al., 1996) even when they are presented so rapidly as to not be consciously perceived (Morris, Ohman, & Dolan, 1999; Whalen et al., 1998), and the anterior insula is particularly sensitive to expressions of disgust (Phillips et al., 1997).

The discovery that different neural structures process facial identity and facial affect has begun to inform clinical research (for review, see Phillips, Drevets, Rauch, & Lane, 2003). For example, imaging studies of face perception in clinical populations have now shown that children with autism fail to show normal activation of the fusiform face area (Pierce, Muller, Ambrose, Allen, & Courchesne, 2001; Schultz et al., 2000), that social phobics show heightened amygdala responses to neutral faces (Birbaumer et al., 1998), that individuals with PTSD show heightened amygdala responses to subliminal presentations of fear faces (Rauch et al., 2000), and that depressed individuals show a similar effect that resolves with successful drug treatment (Sheline et al., 2001).

Yet another set of structures is involved in attributing mental states and intentions to other people. A network of regions centered on the medial prefrontal and adjacent ACC has been shown to be critical for this ability (Gallagher & Frith, 2003). For example, medial prefrontal activation is found when individuals form impressions of others or figure out what they believe or feel (Gallagher & Frith, 2003; Mitchell et al., 2004; Ochsner, Knierim, et al., 2004). These findings could have important implications for understanding abnormal person perception in many disorders, including the tendency to misperceive the intentions of others in borderline personality disorder and social anxiety and the inability to understand others' intentions in autism (Frith, 2001). Intriguingly, studies now suggest that some medial prefrontal regions involved in perceiving others are also involved in accessing knowledge about one's own traits and emotional states (Mitchell, Banaji, & Macrae, 2005; Ochsner, Beer, et al., 2005; Ochsner, Knierim, et al., 2004), suggesting some overlap in regions involved in judging self and other. This finding has direct relevance to schizophrenia, which commonly involves confusion of one's own beliefs and feelings with those of other people. Strikingly, schizophrenics show reduced numbers of inhibitory interneurons in cingulate cortical regions implicated in person perception (Benes, 2000).

At a rudimentary level, the ability to differentiate between hostile and hospitable stimuli and to respond accordingly is fundamental to survival; all animals have simple reflexes for categorizing and approaching or withdrawing from certain classes of stimuli and for communicating with others. A remarkable feature of humans is the extent to which the evaluative discrimination of stimuli is shaped by learning, cognition, and appraisal processes (Berntson, Boysen, & Cacioppo, 1993). A hierarchy of evaluative discriminations, ranging from reflexive responses and automatic evaluations to self-reflective evaluations, constantly aids us in negotiating our social environments. This hierarchy forms the basis for human attitudes and preferences and can be modified in part by social interaction (Berntson & Cacioppo, in press; Cunningham & Zelazo, 2007). Recent neuroimaging data provide insights into the complex neural mechanisms underlying these iterative evaluative processes and point to specific deficits in decision making (Cunningham & Zelazo, 2007).

The stigma of physical and mental illness operates at the group or collective level of analysis. Because of stigma, people may resist acknowledging or recognizing their symptoms, delay diagnosis, avoid treatment, or terminate therapy, and these behaviors can precipitate relapse. Research has amply documented the stigma of certain group characteristics, including physical and mental illness (Crocker, Major, & Steele, 1998; Fiske, 1998).

The interplay of social psychological and neuroscience research is illustrated in a study showing that images of homeless people and drug addicts do not activate medial prefrontal neural regions typically implicated in processing social information. These data suggest that certain characteristics, such as mental illness, may cause observers sometimes to underperceive social aspects of its victims (Harris & Fiske, 2006). Dehumanization has critical import for the providers who treat, the public who view, and the families who surround those with mental illness.

The ability to understand, interact, and connect with others is essential for mental and physical well-being. So essential is this ability that social impairments have serious consequences both for individuals and for society. Given the critical importance of adaptive social functioning, it is essential that social neuroscience research address relevant psychological and neural mechanisms. Imaging research promises to help elucidate the neural operations that support healthy social function and the social dysfunction that characterizes many disorders of cognition, mood, and personality.

In sum, within the last decade, the development of neuroimaging methods has offered a new and more powerful extension of an old approach to understanding the mechanisms that underlie behavior. As we learn about the functional properties of different parts of the brain, this knowledge can guide understanding of other psychological processes. Of course, it is important to note

that neuroimaging data are only correlational with behavior and not necessarily the causal basis for behavior (Uttal, 2001). There is no simple one-to-one mapping between activity in a neural region and psychological function (one region is associated with many functions and one function is distributed across several regions), but there is consistency in the patterns of activity across studies, suggesting that distributed networks can be associated with psychological processes (e.g., Small & Nusbaum, 2004).

In addition, it is possible to intervene in the neural processing of specific brain regions, thereby testing causal hypotheses about the function of those locations. Each such intervention has its own set of caveats, and the localizationist assumptions about the specificity of any intervention are prone to overinterpretation. However, for decades the lesion model has been used to study the effects of localized brain regions on psychological and behavioral processes. Today it is possible to interrupt or alter neural processing in focal areas in animals' brains using exquisitely precise genetic-, electrophysiological-, and neurochemical-based techniques and to then evaluate the resulting effects. In humans, temporary interruption of neural activity using transcranial magnetic stimulation offers a similar tool with the potential to provide additional tests of causal hypotheses. Thus, neuroimaging research raises new questions and provides additional means for testing old ones.

INDIVIDUAL DIFFERENCES AND PSYCHOPATHOLOGY

In a seminal paper, Benton Underwood (1975) argued that individual differences provide a unique opportunity to test a wide range of psychological theories. Underwood argued that naturally occurring individual differences reveal the structure of psychological function and in fact may provide more robust insights than many conventional group-based methods. Kosslyn et al. (2002) extended and modified Underwood's argument to show that bridges between psychology and biology are easier to forge if individual differences are conceived within the framework of a general characterization of the population as a whole:

> [A]lthough all members of the same species share the same fundamental mechanisms, biological systems are notoriously redundant and complex, affording many different ways to accomplish the same goal. Thus, people (or other animals) may differ not only in the efficacy of specific mechanisms but also in the frequency with which particular mechanisms are recruited (which in turn would make some more salient than others). If some people tend to rely on one "strategy" (i.e., combination of processes), whereas others habitually rely on alternative strategies, pooling data from both groups may be uninformative at best and outright misleading at worst. Appropriately collected, group data can provide a good starting point, but individual differences need to be respected if researchers are to understand the nature of the alternative mechanisms. (Kosslyn et al., 2002, p. 341)

Mechanisms of social cognition and behavior can be investigated at many levels of analysis, ranging from the molecular to the social. Investigations across levels of analysis may benefit from attention to both group- and individual-level data.

Studies have repeatedly demonstrated that the immediate environment exerts a powerful influence over all kinds of social behavior and that this influence is greatly underestimated by actors and observers. When a person's social behaviors are underinfluenced by situational forces, as is often the case for individuals with serious psychopathology, these individual differences can stand out in the crowd and attract disapproval. However, individual differences in social behavior have sometimes been treated experimentally as noise to be minimized. The study of individual differences, or the variability observed around central tendencies, can be an important complement to the perspective on normative social processes in research on neural mechanisms (Kosslyn et al., 2002).

Phobias, depression, schizophrenia, autism, psychopathy, and PTSD are among the many psychopathologies characterized by abnormal emotional responses to an environmental situation. Studies of nonpatient populations have also found that a single stimulus can elicit a wide range of responses across individuals (Ekman & Davidson, 1994). Davidson and his colleagues showed that when participants receive stimuli that provoke withdrawal-related negative affect such as fear and disgust, the right prefrontal regions of the brain become more activated than the left (as measured by electroencephalogram, EEG). In contrast, when participants receive stimuli that evoke approach-related positive affect, the left prefrontal regions become more activated (e.g., Davidson, Ekman, Saron, Senulis, & Friesen, 1990). Davidson and colleagues reasoned that individual differences in the baseline amounts of activation in the left versus right prefrontal regions reflected predilections for activation and therefore could mediate the effects of environmental stimuli. Tomarken, Davidson, Wheeler, & Doss (1992) found adequate internal consistency, reliability, and test–retest stability for brain electrical activity measures of prefrontal activation asymmetry in a large number of participants, confirming its utility for assessing individual differences.

Davidson and colleagues hypothesized that if the left prefrontal regions mediate approach emotions and the right prefrontal regions mediate withdrawal emotions, then participants with greater baseline right-sided prefrontal activation should report greater dispositional negative affect on a standard paper-and-pencil measure. The data supported the prediction (Tomarken, Davidson, Wheeler, & Kinney, 1992; see also Sutton & Davidson, 1997). The extant research on frontal EEG asymmetry has revealed associations with child temperament (see Fox, Henderson, Rubin, Calkins, & Schmidt, 2001), self-report measures of affect and personality (e.g., Tomarken & Davidson, 1994), infant responses to maternal separation (Davidson & Fox, 1989), shyness and social anxiety (Schmidt, 1999), socioeconomic status (Tomarken, Dichter, Garber, & Simien, 2004), and

basal cortisol levels in monkeys (Kalin, Larson, Shelton, & Davidson, 1998).

Individual differences in frontal activation have been found to have important implications for social behavior. Children displaying social competence show greater relative left frontal activation while those displaying social withdrawal exhibit greater relative right frontal activation (Fox et al., 1995). Greater relative right frontal activation may interact with social behavioral style to predict maladaptive behavior (Fox, Schmidt, Calkins, Rubin, & Coplan, 1996). Further, right frontal asymmetry may interact with other indicators of temperament, as well as gender, to predict maladaptive social behavior in children (Henderson, Fox, & Rubin, 2001).

Given the role of individual differences in greater relative right frontal activity in negative affect and maladaptive social behavior, this region has been a focus for studies of clinical depression (Davidson, Pizzagalli, Nitschke, & Putnam, 2002). Importantly, the frontal asymmetry does not appear to be a simple correlate of current depression. Decreased activity of left relative to right frontal regions appears to be related to an enduring *vulnerability* for depression, because this asymmetry is evident in those who have recovered from the disorder (Henriques & Davidson, 1990) and in the at-risk offspring of mothers with a history of depression as measured in infants (Dawson, Grofer Klinger, Panagiotides, Hill, & Spieker, 1992; Field, Fox, Pickens, Nawrocki, 1995) and adolescents (Tomarken et al., 2004).

Amygdala activation to fear faces depends upon whether or not an individual *construes* a face as expressing fear or some other emotion, such as surprise. When a fear face is seen as expressing surprise, amygdala activation decreases and activity in the subgenual cingulate increases (Kim, Somerville, Johnstone, Alexander, & Whalen, 2003; Kim et al., 2004). This finding may have important implications for understanding abnormal emotion and social perception in disorders like depression, which show structural abnormalities and hypometabolism in subgenual ACC (mentioned earlier) in combination with amygdala hypermetabolism (Drevets, 2001). Future work holds the promise of relating clinical disorders to dysfunction in other brain regions, such as the superior temporal sulcus, that encode other socially meaningful nonverbal cues such as biological motion, the direction of eye gaze, and images of the body (Allison, Puce, & McCarthy, 2000; Downing, Jiang, Shuman, & Kanwisher, 2001; N. George, Driver, & Dolan, 2001; Puce & Perrett, 2003).

Recent imaging research has examined how neural circuits for facial emotion processing are related to genetic susceptibility for depression through a link with serotonin. Serotonin has been implicated in depression by the efficacy of serotonin reuptake inhibitor drugs (e.g., Tamminga, 1998). Serotonin gene variation has been found to moderate the influence of stress on depression (Caspi et al., 2003; Kendler, Kuhn, & Prescott, 2004). Individuals who carry at least one short allele of the promoter region of the serotonin transporter gene have increased risk for depression when exposed to life stressors (Caspi et al., 2003; Kendler et al., 2004).

To summarize thus far, investigations of the neural mechanisms underlying complex social behavior and psychopathology may benefit from greater attention to individual differences. Indeed, as detailed below, various psychopathologies can be characterized in terms of consistent differences from the norm in the degree to which a specific neural mechanism is activated.

All would probably also agree that an understanding of mental illness in its various forms will most certainly require an integration of information from multiple levels of scientific inquiry from the social and behavioral levels to the molecular and genetic levels (e.g., Anderson, 1998; Ilardi & Feldman, 2001). Achieving such an integration has been elusive both because the necessary techniques at all levels have not been available until recently and because communication among scientists and clinicians working at these different levels has been less than adequate. However, optimism that such integration might actually occur, with results that not only inform us in fundamental ways about human brain function but also result in benefit to patients, is fueled by several recent developments. Endophenotypes, measurable components unseen by the unaided eye along the pathway between genes and disease, have emerged as an important concept in the study of complex psychiatric diseases (Gottesman & Gould, 2003; Prathikanti & Weinberger, 2005). In addition, careful analyses of social behaviors have identified very specific individual component processes and behaviors that can serve the same role in the study of disorders as endophenotypes. Such component behaviors have been termed "behavioral endophenotypes," and they too make it possible to bring neuroscience (e.g., genetics, neuroimaging) methods to bear on given disease states.

Specifying behavioral endophenotypes may be important because social impairment and affective disturbances are aspects of all psychiatric disorders. Diagnostically, social dysfunction is either a core feature of a disorder (e.g., autism, social phobia, schizophrenia, any of the personality disorders) or serves as a marker of the functional impairment required to meet diagnostic threshold. Models addressing the etiology and course of disorders frequently involve social processes. For example, interpersonal processes have major theoretical roles in models relating not only to the development of depression (Daley & Hammen, 2002; Joiner, 1999; Hammen & Brennan, 2002), but also to substance use in adolescents (Walden, McGue, Iacono, Burt, & Elkins, 2004; Wills & Yaeger, 2003) and borderline personality disorder (Linehan, 1993). Interpersonal difficulties also play a significant prognostic role, as indicators of hostile or critical attitudes within families have been found to significantly predict relapse for a variety of disorders including schizophrenia, depression, bipolar disorder, and eating disorders (Butzlaff & Hooley, 1998; cf. Rosenfarb, Bellack, & Aziz, 2006). There are a number of areas where neurological studies of patients have

contributed to the understanding of psychopathology. In the remainder of this section, we return to our discussion of depression and briefly describe antisocial personality disorder as examples of how the integration of neuroscience and the study of social behavior has informed our understanding of these disorders.

Depression

Theories of depression have implicated interpersonal processes in this disorder (Coyne, 1999) as well as neural systems involved with emotion (Davidson et al., 2002), as discussed briefly in the previous section. Individuals with depression, as well as those at risk for depression, evidence a range of social deficits and appear to generate their own stressful social interactions (e.g., Daley & Hammen, 2002; Hammen & Brennan, 2002; Joiner, 1999). The development of theories of emotion and their systematic study in animals and humans have provided sophisticated perspectives on conceptualizing and studying how neural systems may be involved in the affective and social deficits observed in mood disorders (e.g., Davidson, 2000; Davidson et al., 2002; Heller, 1993; Heller, Nitschke, & Miller, 1998).

Drevets and colleagues (Drevets et al., 1997) studied patients with familial pure depressive disorder using positron emission tomography. They demonstrated abnormalities in brain circulation and metabolism in Brodmann areas 24 and 25 in the subgenual part of the medial prefrontal cortex, an area involved in self-referent and social information processing. In addition to these findings, they reported that this area of the brain appeared smaller in patients than in controls when measured with magnetic resonance imaging (MRI; see also Botteron, Raichle, Drevets, Heath, & Todd, 2002). This is an interesting finding in light of the role of interpersonal processes on the development of depression (Cacioppo et al., 2006; Daley & Hammen, 2002; Hammen & Brennan, 2002; Joiner, 1999).

Because of the high heritability of depressive symptoms in children and adolescents (Todd & Botteron, 2002), interest has turned to the role of genetic factors in determining the changes in the subgenual prefrontal cortex. In one of the most striking studies to date involving imaging and genetics (Pezawas et al., 2005), it was demonstrated that subjects with the short allele of a functional 5HT promotor polymorphism of the serotonin transporter gene have decreased volume of both the amygdala and the subgenual prefrontal cortex and show a functional uncoupling of the subgenual–amygdala circuitry. Subjects with this allele are known to have increased anxiety-related temperament traits, increased amygdala reactivity, and an elevated risk of depression. Whether or not the elevated risk of depression is secondary to the effects of these genetic factors on social processes and behaviors is not known.

Antisocial Behavior and Psychopathy

Antisocial personality disorder involves a range of social aberrations involving indifference to and violation of the rights of others. The related but more narrowly defined concept of psychopathy (Cleckley, 1976) focuses on social features (untruthfulness, superficial charm, unresponsiveness in interpersonal relations) and affective features (lack of remorse or shame, incapacity for love, and shallow affect) as key aspects of the syndrome (Cleckley, 1976; Hare, 1991). Deficits in aversive reactivity or fear are hypothesized to subserve these deficits in psychopathy (e.g., Fowles, 1980; Lykken, 1957). Diminished response to cues of threat or punishment is thought to mediate the failure to learn from punished responses, the callous exploitation, the lack of remorse, and the focus on immediate rewards that characterize psychopathy.

Consistent with this model, a functional MRI investigation revealed that the limbic–prefrontal circuit (involving amygdala, orbitofrontal cortex, anterior insula, and ACC) that was activated during fear conditioning (using slides of neutral faces) in normal individuals was not activated in psychopaths (Birbaumer et al., 2005). Accordingly, psychophysiological data indicate that psychopathy is related to deficient autonomic responding in anticipation of threatening events (for review, see Lykken, 1995) and inhibited startle to negative emotional stimuli (e.g., victim scenes; Levenston, Patrick, Bradley, & Lang, 2000). Prefrontal functional impairments have been proposed to relate to the behavioral and affective deficits seen in psychopathy (Morgan & Lilienfeld, 2000), as structural studies have indicated that antisocial personality disorder is associated with reduced prefrontal gray matter volume and that these prefrontal gray deficits are linked to electrodermal deficits (Raine, Lencz, Bihrle, LaCasse, & Colletti, 2000). These findings begin to provide an understanding of the neural contributions to the social-behavioral and affective deficits observed in psychopathy.

NIMH WORKSHOP FINDINGS

In July 2005, NIMH convened a workshop to examine the field of social neuroscience and to assess how the Institute's strategic mission in basic and clinical science could benefit from advances in this field. Workshop breakout sessions focused intensively on issues in four thematic areas:

- *Current Opportunities*: What are the greatest opportunities for major scientific advances in this field? What should be done to capitalize on these opportunities? What is the time frame for seeing significant benefits/findings (at the basic science level) from these new discoveries?
- *Impediments to Progress*: What are the most significant impediments to scientific progress in this field. What can be done to mitigate these impediments? How long will it take to overcome them?
- *Levels of Analysis*: How can we most effectively make connections across different levels of analysis in this field? What constitutes interdisciplinary research for social neuroscience? What benefits accrue from such an approach?

- *Clinical Implications*: Which clinical problems are poised to benefit most directly from new basic research in social neuroscience and behavior? What needs to happen scientifically for this to occur? What is a reasonable time frame for seeing clinical benefits accrue from basic research in this area?

A number of observations and suggestions emerged from the workshop as a whole, based not only on the breakout group reports but also on the comments and interactions that took place in the plenary session:

1. It is critically important to understand baseline states in the nervous system, as they are of fundamental importance to the generation of complex behaviors.
2. Emergent properties need to be carefully considered when studying complex systems, of which dynamic social interactions are a prime example.
3. Social context is a key modulator, even a determinant, of complex behavior. This makes it very important to take into consideration the effects of the experimental environment, especially the effects of the MRI scanning environment, when attempting to draw inferences about the neural bases of complex social behavior.
4. Basic research is by definition not translational, yet basic research is highly relevant to the NIMH mission. Basic research should be undertaken in the service of the NIMH mission.
5. Many psychiatric disorders have distinct developmental time courses. This points to the importance of developmental issues in social neuroscience.
6. The identification and study of endophenotypes will continue to be important for the understanding of psychiatric disorders. Psychiatric disorders are classified and diagnosed via observed and reported behavior, including social behavior. Social neuroscience approaches can be important for understanding psychiatric disorders through the linkage of social and psychological mechanisms to neural mechanisms.

A full workshop report is available at http://www.nimh.nih.gov/scientificmeetings/socialneuroscience.cfm.

Also, a subsequent NIMH funding-opportunity announcement in social neuroscience was published in 2006, details of which are available at http://grants.nih.gov/grants/guide/pa-files/PAR-06-389.html.

CONCLUSION

The human mind can be construed as a dynamic emergent property of an array of diverse elements: biological, psychological, and social. Early in life, growth trajectories and critical developmental stages take on particular importance for what emerges. Later, the deterioration of individual elements, such as anatomical structures, cognitive operations, and interpersonal relationships, can provide a glimpse into how these components contribute to the whole. For an unfortunate few, accidents and disease compromise physical, psychological, or social structures and processes, thus providing converging information on the contributions of the specific elements.

The capacity to form social bonds is not limited to humans. The mechanisms underlying social bonds are ancient and based on neural circuitry and endocrine processes rooted in mammalian evolution (Hammock & Young, 2005; Hrdy, 1999). The mechanisms of sociality are best understood in the context of their adaptive functions and their evolutionary, developmental, and social origins.

Understanding the human brain and mind, when healthy and in plight, requires the merging of multiple, distinct disciplines with translation across scientific perspectives and levels of analysis. The emerging field of social neuroscience constitutes such an approach. As understanding of the social brain advances, this knowledge can support understanding of mechanisms by which social factors and social deficits operate as causes and consequences of psychopathology. This perspective assumes mutual influences among biological and social factors in determining behavior. Accordingly, accounts of human function will be limited to the extent that any level of analysis is neglected.

Multilevel analyses of psychopathology require a range of expertise that is not likely to be found in solitary investigators. One can distinguish multidisciplinary from interdisciplinary approaches in this regard. While multidisciplinary research is characterized by the aggregation of expertise, interdisciplinary research is defined by synergies among experts that can transform both science and scientists. Interdisciplinary scientific research is riskier than multidisciplinary research since it is a group product rather than the simple sum of its individual products. Accordingly, interdisciplinary teams are more subject to failure than solitary and multidisciplinary scientific efforts are. But with this higher risk also comes a potential for higher payoffs. When interdisciplinary teams succeed, they have the potential to produce significant scientific innovations, make progress in solving what were thought to be intractable problems, and influence multiple disciplines.

Social neuroscience represents such an interdisciplinary approach to the study of mental health and disorders. The progress to date is promising, but this potential has yet to be realized. Work toward this goal could benefit from more interactions across investigators whose focus is on animal models, lesion patients, neuroimaging in normal and in patient populations, and peripheral neural mechanisms. There are at least two areas in psychopathology that research in social neuroscience might offer advances in the near term: the reliance to date on self-reports and the structure and diagnosis of psychopathology.

The reliance on self-report measures of psychological symptoms is problematic in that (a) the same symptoms may arise from different psychological disorders, (b) reports of symptoms might be biased according to social context (e.g., underreporting for self-presentational purposes, overreporting to

achieve secondary reinforcements), and (c) people may not have mental access to important aspects of the disorders. Dysphoria and perceived stress, for instance, are neither sensitive nor specific measures of psychological disorders.

The nature of the disorder may also influence an individual's ability to report on emotions or social functioning. For example, it is clear that, within the personality disorders, self-reports of dispositional tendencies diverge from collateral reports of peers or family members (e.g., Clifton, Turkheimer, & Oltmanns, 2005; Klonsky, Oltmanns, & Turkheimer, 2002). These findings and others underscore the importance of considering assessments across different response domains, and from various informants, in obtaining an accurate perspective on some aspects of emotional and social functioning in psychopathology.

Research on specific psychopathologies is also limited by the uncertain validity of diagnoses. Questions about validity emerge from a variety of sources, including the phenotypic heterogeneity observed within individuals sharing the same diagnosis (Clark, Livesley, & Morey, 1997; Widiger & Clark, 2000) and the frequent co-occurrence of different disorders within the same individual—the problem of comorbidity (Kessler, 1997; Lilienfeld, Waldman, & Israel, 1994; Newman, Moffit, Caspi, & Silva, 1998). The attempt to identify common factors within such heterogeneity (or to identify factors that are unique to a particular disorder when disorders frequently co-occur with other diagnoses) has proven difficult.

Several strategies to deal with this diagnostic dilemma are available. First, psychopathologists have recommended the adoption of symptom-based approaches that rely on the presence of a specific symptom to better understand underlying mechanisms within a disorder (Neale, Oltmanns, & Harvey, 1985; Persons, 1986). Thus, rather than examining the broad diagnosis of schizophrenia, one might focus on correlates of anhedonia (Blanchard, Mueser, & Bellack, 1998) or social dysfunction (Cohen, Mann, Forbes, & Blanchard, 2006) within this disorder. This ensures the presence of the feature that is being studied and allows for comparison groups comprised of patients with the same diagnoses but lacking the symptom (allowing for the control of such confounding variables as medication exposure).

A second and related strategy is to examine broader differentiable facets of a disorder. This approach has been used with success in the study of psychophysiology and emotional processing correlates of the "emotional-interpersonal" versus "social deviance" facets of psychopathy (Benning, Patrick, Hicks, Blonigen, & Krueger, 2003; Verona, Patrick, Curtin, Bradley, & Lang, 2004). Symptoms or factors may be used as dimensional correlates within a diagnosis or can be used to create categorical subdivisions or subtypes within disorders. Subtypologies have been employed in a variety of disorders including schizophrenia (Blanchard, Horan, & Collins, 2005; Kirkpatrick, Buchanan, Ross, & Carpenter, 2001) and psychopathy (Hicks, Markon, Patrick, Krueger, & Newman, 2004).

Finally, at the broadest level of analysis, cutting across diagnoses, models of the latent structure of psychopathology (Krueger, 1999; Krueger, Chentsova-Dutton, Markon, Goldberg, & Ormel, 2003) suggest that the study of core psychopathological processes underlying diverse diagnoses may be a more informative approach than focusing on the individual diagnostic manifestations of these core processes. To the extent that psychopathology is reflected in brain pathology, neurological research may make it possible to characterize specific psychopathologies in terms of the structural and functional operations of the brain in specific social contexts.

Delineation of the genetic code of multiple species (including humans), improved techniques ranging from molecular biology to systems-level electrophysiology, and continued improvements in the power of noninvasive functional imaging have dramatically increased the power we bring to bear on this area of research. We are poised to break fundamental new ground in the science of social behavior and to leverage the knowledge thus gained into breakthroughs in the understanding, diagnosis, and treatment of mental disorders. We believe that social neuroscience can be a fulcrum for enabling these breakthroughs. The promise of this field is clear, we now need to capitalize on that promise.

Acknowledgments—A workshop, "Social Neuroscience and Behavior: From Basic to Clinical Science," brought together the authors and enabled discussion of the issues described in this article. This workshop was supported by funds provided by the National Institute of Mental Health (NIMH) and was held July 15–16, 2005, in Washington, DC. The views contained in this article are those of the authors and are not to be construed as official or reflecting the views of the NIMH, The National Institutes of Health, or the Department of Health and Human Services.

REFERENCES

Adolphs, R. (2001). The neurobiology of social cognition. *Current Opinions in Neurobiology*, *11*, 231–239.

Adolphs, R. (2003). Cognitive neuroscience of human social behavior. *Neuroscience Reviews*, *4*, 165–178.

Adolphs, R., Tranel, D., & Damasio, A.R. (1998). The human amygdala in social judgment. *Nature*, *393*, 470–474.

Adolphs, R., Tranel, D., Hamann, S., Young, A.W., Calder, A.J., Phelps, E.A., et al. (1999). Recognition of facial emotion in nine individuals with bilateral amygdala damage. *Neuropsychologia*, *37*, 1111–1117.

Ahn, W., Novick, L., & Kim, N.S. (2003). Understanding behavior makes it more normal. *Psychonomic Bulletin and Review*, *10*, 746–752.

Allison, T., Puce, A., & McCarthy, G. (2000). Social perception from visual cues: Role of the STS region. *Trends in Cognitive Sciences*, *4*, 267–278.

American Psychiatric Association. (2000). Diagnostic and statistical manual of mental disoders (4th ed., text revision). Washington, DC: Author.

Anderson, M., Ochsner, K., Kuhl, B., Cooper, J., Robertson, E., Gabrieli, S., et al. (2004). Neural systems underlying the suppression of unwanted memories. *Science*, *303*, 232–235.

Anderson, N.B. (1998). Levels of analysis in health science: A framework for integrating sociobehavioral and biomedical research. *Annals of the New York Academy of Science*, *840*, 563–576.

Axsom, D., & Cooper, J. (1985). Cognitive dissonance and psychotherapy: The role of effort justification in inducing weight loss. *Journal of Experimental Social Psychology*, *21*, 149–160.

Bales, K.L., Plotsky, P.M., Young, L.J., Lim, M.M., Grotte, N.D., & Carter, C.S. (2004). Neonatal oxytocin manipulations have sexually dimorphic effects on vasopressin receptor binding in monogamous prairie voles. *Society for Neuroscience Abstracts*, *758*, 13.

Bales, K.L., Plotsky, P.M., Young, L.J., Lim, M.M., Grotte, N., Ferrer, E., & Carter, C.S. (2007). Neonatal oxytocin manipulations have long-lasting, sexually dimorphic effects on vasopressin receptors. *Neuroscience*, *144*, 38–45.

Banfield, J., Wyland, C.L., Macrae, C.N., Munte, T.F., & Heatherton, T.F. (2004). The cognitive neuroscience of self-regulation. In R.F. Baumeister & K.D. Vohs (Eds), *The handbook of self-regulation* (pp. 62–83). New York: Guilford.

Barch, D.M., Sheline, Y.I., Csernansky, J.G., & Snyder, A.Z. (2003). Working memory and prefrontal cortex dysfunction: Specificity to schizophrenia compared with major depression. *Biological Psychiatry*, *53*, 376–384.

Bargh, J.A., & Tota, M.E. (1988). Context-dependent automatic processing in depression: Accessibility of negative constructs with regard to self but not others. *Journal of Personality and Social Psychology*, *54*, 925–939.

Bauman, M.D., Lavenex, P., Mason, W.A., Capitanio, J.P., & Amaral, D.G. (2004). The development of social behavior following neonatal amygdala lesions in rhesus monkeys. *Journal of Cognitive Neuroscience*, *16*, 1388–1411.

Beauregard, M., Levesque, J., & Bourgouin, P. (2001). Neural correlates of conscious self-regulation of emotion. *Journal of Neuroscience*, *21*, RC165.

Bechara, A., Damasio, A.R., Damasio, H., & Anderson, S.W. (1994). Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition*, *50*, 7–15.

Beer, J.S., Heerey, E.A., Keltner, D., Scabini, D., & Knight, R.T. (2003). The regulatory function of self-conscious emotion: Insights from patients with orbitofrontal damage. *Journal of Personality and Social Psychology*, *85*, 594–604.

Benes, F.M. (2000). Emerging principles of altered neural circuitry in schizophrenia. *Brain Research Review*, *31*, 251–269.

Benning, S.D, Patrick, C.J., Hicks, B.M., Blonigen, D.M., & Krueger, R.F. (2003). Factor structure of the psychopathic personality inventory: Validity and implications for clinical assessment. *Psychological Assessment*, *15*, 340–350.

Bernstein, I.S., Gordon, T.P., & Rose, R.M. (1983). The interaction of hormones, behavior, and social context in nonhuman primates. In B.B. Svare (Ed.), *Hormones and aggressive behavior* (pp. 535–561). New York: Plenum Press.

Berntson, G.G., Boysen, S.T., & Cacioppo, J.T. (1993). Neurobehavioral organization and the cardinal principle of evaluative bivalence. *Annals of the New York Academy of Sciences*, *702*, 75–102.

Berntson, G.G., & Cacioppo, J.T. (in press). The neuroevolution of motivation. In J. Shah & W. Gardner (Eds.), *Handbook of motivation science*. New York: Guilford.

Bielsky, I.F., Hu, S.B., Ren, X., Terwilliger, E.F., & Young, L.J., (2005). The V1a vasopressin receptor is necessary and sufficient for normal social recognition: A gene replacement study. *Neuron*, *47*, 503–513.

Bielsky, I.F., Hu, S.-B., Szegda, K.L., Westphal, H., & Young, L.J. (2004). Profound impairment in social recognition and reduction in anxiety in vasopressin V1a receptor knockout mice. *Neuropsychopharmocology*, *29*, 483–493.

Birbaumer, N., Grodd, W., Diedrich, O., Klose, U., Erb, M., Lotze, M., et al. (1998). fMRI reveals amygdala activation to human faces in social phobics. *NeuroReport*, *9*, 1223–1226.

Birbaumer, N., Veit, R., Lotze, M., Erb, M., Hermann, C., Grodd, W., & Flor, H. (2005). Deficient fear conditioning in psychopathy: A functional magnetic resonance imaging study. *Archives of General Psychiatry*, *62*, 799–805.

Blanchard, J.J., Horan, W.P., & Collins, L.M. (2005). Examining the latent structure of negative symptoms: Is there a distinct subtype of negative symptom schizophrenia? *Schizophrenia Research*, *77*, 151–165.

Blanchard, J.J., Mueser, K.T., & Bellack, A.S. (1998). Anhedonia, positive and negative affect, and social functioning in schizophrenia. *Schizophrenia Bulletin*, *24*, 413–424.

Boomsma, D.I., Cacioppo, J.T., Slagboom, P.E., & Posthuma, D. (2006). Genetic linkage and association analysis for loneliness in Dutch twin and sibling pairs points to a region on chromosome 12q23-24. *Behavior Genetics*, *36*, 137–146.

Boomsma, D.I., Willemse, G., Dolan, C.V., Hawkley, L.C., & Cacioppo, J.T. (2005). Genetic and environmental contributions to loneliness in adults: The Netherlands Twin Register Study. *Behavior Genetics*, *35*, 745–752.

Botteron, K., Raichle, M.E., Drevets, W.C., Heath, A.C., & Todd, R.D. (2002). Volumetric reduction in left subgenual prefrontal cortex in early onset depression. *Biological Psychiatry*, *51*, 342–344.

Bowlby, J. (1969). *Attachment and Loss: Volume I. Attachment*. New York: Basic Books, Inc.

Braver, T.S., Barch, D.M., & Cohen, J.D. (1999). Cognition and control in schizophrenia: A computational model of dopamine and prefrontal function. *Biological Psychiatry*, *46*, 312–328.

Breiter, H.C., Etcoff, N.L., Whalen, P.J., Kennedy, W.A., Rauch, S.L., Buckner, R.L., et al. (1996). Response and habituation of the human amygdala during visual processing of facial expression. *Neuron*, *17*, 875–887.

Brenner, S.L., Beauchaine, T.P., & Sylvers, P.D. (2005). A comparison of psychophysiological and self-report measures of BAS and BIS activation. *Psychophysiology*, *42*, 108–115.

Bridges, R.S. (1984). A quantitative analysis of the roles of dosage, sequence, and duration of estradiol and progesterone exposure in the regulation of maternal behavior in the rat. *Endocrinology*, *114*, 930–940.

Bridges, R.S., DiBiase, R., Loundes, D.D., & Doherty, P.C. (1985). Prolactin stimulation of maternal behavior in female rats. *Science*, *227*, 782–784.

Brothers, L. (1990). The social brain: A project for integrating primate behavior and neurophysiology in a new domain. *Concepts in Neuroscience*, 1, 27–51.

Brown, J.B., Ya, H., Bronson, R.T., Dikkes, P., & Greenberg, M.E. (1996). A defect in nurturing in mice lacking the immediate early gene fosB. *Cell*, *86*, 1–20.

Buchsbaum, M.S., Wu, J., Siegel, B.V., Hackett, E., Trenary, M., Abel, L., et al. (1997). Effect of sertraline on regional metabolic rate in patients with affective disorder. *Biological Psychiatry*, *41*, 15–22.

Bush, G., Frazier, J.A., Rauch, S.L., Seidman, L.J., Whalen, P.J., Jenike, M.A., et al. (1999). Anterior cingulate cortex dysfunction in attention-deficit/hyperactivity disorder revealed by fMRI and the Counting Stroop. *Biological Psychiatry*, *45*, 1542–1552.

Bush, G., Vogt, B.A., Holmes, J., Dale, A.M., Greve, D., Jenike, M.A., & Rosen, B.R. (2002). Dorsal anterior cingulate cortex: A role in reward-based decision making. *Proceedings of the National Academy of Sciences, USA*, *99*, 523–528.

Butzlaff, R.L., & Hooley, J.M. (1998). Expressed emotion and psychiatric relapse. *Archives of General Psychiatry*, *55*, 547–552.

Cacioppo, J.T., & Berntson, G.G. (1992). Social psychological contributions to the decade of the brain: Doctrine of multilevel analysis. *American Psychologist*, *47*, 1019–1028.

Cacioppo, J.T., Berntson, G.G., Adolphs, R., Carter, C.S., Davidson, R.J., McClintock, M.K., et al. (2002). *Foundations in social neuroscience*. Cambridge, MA: MIT Press.

Cacioppo, J.T., Berntson, G.G., Lorig, T.S., Norris, C.J., Rickett, E., & Nusbaum, H. (2003). Just because you're imaging the brain doesn't mean you can stop using your head: A primer and set of first principles. *Journal of Personality and Social Psychology*, *85*, 650–661.

Cacioppo, J.T., Berntson, G.G., Sheridan, J.F., & McClintock, M.K. (2000). Multilevel integrative analyses of human behavior: Social neuroscience and the complementing nature of social and biological approaches. *Psychological Bulletin*, *126*, 829–843.

Cacioppo, J.T., Hughes, M.E., Waite, L.J., Hawkley, L.C., & Thisted, R.A. (2006). Loneliness as a specific risk factor for depressive symptoms: Cross sectional and longitudinal analyses. *Psychology and Aging*, *21*, 140–151.

Calvin, W.H. (2004). *A brief history of the mind: From apes to intellect and beyond*. Oxford, United Kingdom: Oxford University Press.

Campbell, D.B., Sutcliffe, J.S., Ebert, P.J., Militerni, R., Bravaccio, C., Trillo, S., et al. (2006). A genetic variant that disrupts MET transcription is associated with autism. *Proceedings of the National Academy of Sciences, USA*, *103*, 16834–16839.

Carter, C.S. (1998). Neuroendocrine perspectives on social attachment and love. *Psychoneuroendocrinology*, *23*, 779–818.

Carter, C.S. (2003). Developmental consequences of oxytocin. *Physiology & Behavior*, *79*, 383–397.

Carter, C.S. (2005). The chemistry of child neglect: Do oxytocin and vasopressin mediate the effects of early experience? *Proceedings of the National Academy of Sciences, USA*, *102*, 17237–17240.

Carter, C.S., Braver, T.S., Barch, D.M., Botvinick, M.M., Noll, D., & Cohen, J.D. (1998). Anterior cingulate cortex, error detection, and the online monitoring of performance. *Science*, *280*, 747–749.

Carter, C.S., DeVries, A.C., & Getz, L.L. (1995). Physiological substrates of monogamy: The prairie vole model. *Neuroscience and Biobehavioral Reviews*, *19*, 303–314.

Carter, C.S., & Roberts, R.L. (1997). The psychobiological basis of cooperative breeding. In N.G. Solomon & J.A. French (Eds.), *Cooperative breeding in mammals* (pp. 231–266). New York: Cambridge University Press.

Caspi, A., Sugden, K., Moffitt, T.E., Taylor, A., Craig, I.W., Harrington, H., et al. (2003). Influence of life stress on depression: Moderation by a polymorphism in the 5-HTT gene. *Science*, *301*, 386–389.

Champagne, F.A., Diorio, J., Sharma, S., & Meaney, M.J. (2001). Naturally occurring variations in maternal behavior in the rat are associated with differences in estrogen-inducible central oxytocin receptors. *Proceedings of the National Academy of Sciences, USA*, *98*, 12736–12741.

Champagne, F.A., Weaver, I.C., Diorio, J., Sharma, S., & Meaney, M.J. (2003). Natural variations in maternal care are associated with estrogen receptor alpha expression and estrogen sensitivity in the media preoptic area. *Endocrinology*, *11*, 4720–4747.

Chow, T.W., & Cummings, J.L. (1999). Frontal-subcortical circuits. In B.L. Miller & J.L. Cummings (Eds.), *The human frontal lobes* (pp. 3–26). New York: Guilford.

Clark, L.A., Livesley, W.J., & Morey, L. (1997). Personality disorder assessment: The challenge of construct validity. *Journal of Personality Disorders*, *11*, 205–231.

Cleckley, H. (1976). *The mask of sanity* (5th ed.). St. Louis, MO: Mosby, Inc.

Clifton, A., Turkheimer, E., & Oltmanns, T.F. (2005). Self- and peer perspectives on pathological personality traits and interpersonal problems. *Psychological Assessment*, *17*, 123–141.

Cohen, A.S., Mann, M., Forbes, C., & Blanchard, J.J. (2006). Specific cognitive deficits and differential domains of social functioning impairment in schizophrenia. *Schizophrenia Research*, *81*, 227–238.

Coyne, J.C. (1999). Thinking interactionally about depression: A radical restatement. In T.J. Joiner and J.C. Coyne (Eds.), *The interactional nature of depression: Advances in interpersonal approaches*, (pp. 365–392). Washington, DC: American Psychological Association.

Crabbe, J.C., Wahlsten, D., & Dudek, B.C. (1999). Genetics of mouse behavior: Interactions with laboratory environment. *Science*, *284*, 1670–1672.

Crews, D., & Groothuis, T. (2005). Tinbergen's fourth question, ontogeny: Sexual and individual differentiation. *Animal Biology*, *55*, 343–370.

Crews, D., & McLachlan, J.A. (2006). Epigenetics, evolution, endocrine disruptors, health and disease. *Endocrinology*, *147*(Suppl.), S4–S10.

Crocker, J., Major, B., & Steele, C. (1998). Social stigma. In D.T. Gilbert, S.T. Fiske, & G. Lindzey (Eds.), *Handbook of social psychology* (4th ed., Vol. 2, pp. 504–553). New York: McGraw Hill.

Cunningham, W.A., & Zelazo, P.D. (2007). Cognitive neuroscience of evaluation: An iterative reprocessing model. *Trends in Cognitive Science*, *11*, 97–104.

Daley, S.E., & Hammen, C. (2002). Depressive symptoms and close relationships during the transition to adulthood: Perspectives from dysphoric women, their best friends, and their romantic partners. *Journal of Consulting and Clinical Psychology*, *70*, 129–141.

Damasio, A. (1994). *Descartes' error: Emotion, reason, and the human brain*. New York: Grosset/Putnam.

Dapretto, M., Davies, M.S., Pfiefer, J.H., Scott, A.A., Sigman, M., Bookheimer, S.Y., & Iacoboni, M. (2006). Understanding emotions in others: Mirror neuron dysfunction in children with autism spectrum disorder. *Nature Neuroscience*, *9*, 28–30.

Davidson, R.J. (2000). Affective style, psychopathology, and resilience: Brain mechanisms and plasticity. *American Psychologist*, *55*, 1196–1214.

Davidson, R.J., Ekman, P., Saron, C., Senulis, J., & Friesen, W.V. (1990). Approach/withdrawal and cerebral asymmetry: Emotional expression and brain physiology: I. *Journal of Personality and Social Psychology*, *58*, 330–341.

Davidson, R.J., & Fox, N.A. (1989). The relation between tonic EEG asymmetry and ten month old emotional response to separation. *Journal of Abnormal Psychology*, *98*, 127–131.

Davidson, R.J., Pizzagalli, D., Nitschke, J.B., & Putnam, K. (2002). Depression: Perspectives from affective neuroscience. *Annual Review of Psychology*, *53*, 545–574.

Dawson, G., Grofer Klinger, L., Panagiotides, H., Hill, D., & Spieker, S. (1992). Frontal lobe activity and affective behavior in infants of mothers with depressive symptoms. *Child Development*, *63*, 725–737.

Deaner, R.O., Khera, A.V., & Platt, M.L. (2005). Monkeys pay per view: Adaptive valuation of social images by rhesus macaques. *Current Biology*, *15*, 543–548.

Dehaene, S., Artiges, E., Naccache, L., Martelli, C., Viard, A., Schurhoff, F., et al. (2003). Conscious and subliminal conflicts in normal subjects and patients with schizophrenia: The role of the anterior cingulate. *Proceedings of the National Academy of Science, USA*, *100*, 13722–13727.

Devinsky, O., Morrell, M.J., & Bogt, B.A. (1995). Contributions of anterior cingulate cortex to behaviour. *Brain*, *118*, 279–306.

DeVries, A.C., DeVries, M.B., Taymans, S.E., & Carter, C.S. (1995). Modulation of pair bonding in female prairie voles (*Microtus ochrogaster*) by corticosterone. *Proceedings of the National Academy of Sciences, USA*, *92*, 7744–7748.

DeVries, A.C., DeVries, M.B., Taymans, S.E., & Carter, C.S. (1996). Stress has sexually dimorphic effects on pair bonding in prairie voles. *Proceedings of the National Academy of Sciences, USA*, *93*, 11980–11984.

DeVries, G.J., & Simerly, R.B. (2002). Anatomy, development and functions of sexually dimorphic neural circuits in the mammalian brain. In D. Pfaff, et al. (Eds.), *Hormones, brain and behavior* (Vol. 4, pp. 137–192). San Diego: Academic Press.

Downing, P.E., Jiang, Y., Shuman, M., & Kanwisher, N. (2001). A cortical area selective for visual processing of the human body. *Science*, *293*, 2470–2473.

Drevets, W.C. (2001). Neuroimaging and neuropathological studies of depression: Implications for the cognitive-emotional features of mood disorders. *Current Opinion in Neurobiology*, *11*, 240–249.

Drevets, W.C., Price, J.L., Simpson, J.R., Jr., Todd, R.D., Reich, T., Vannier, M., et al. (1997). Subgenual prefrontal cortex abnormalities in mood disorders. *Nature*, *386*, 824–827.

Eisenberger, N.I., Lieberman, M., & Williams, K.D. (2003). Does rejection hurt? An fMRI study of social exclusion. *Science*, *302*, 290–292.

Ekman, P., & Davidson, R.J. (1994). *The nature of emotion: Fundamental questions*. New York: Oxford University Press.

Ellemers, N., Spears, R., & Doosje, B. (2002). Self and social identity. In S.T. Fiske, S.L. Schacter, & C. Zahn-Waxler (Eds.), *Annual review of psychology* (Vol. 53, pp. 161–186). Palo Alto, CA: Annual Reviews.

Elliot, R., & Dolan, R. (1998). Neural response during preference and memory judgments for subliminally presented stimuli: A functional neuroimaging study. *Journal of Neuroscience*, *18*, 4697–4704.

Ferguson, J.N., Aldag, J.M., Insel, T.R. & Young, L.J. (2001). Oxytocin in the medial amygdala is essential for social recognition in the mouse. *Journal of Neuroscience*, *21*, 8278–8285.

Ferguson, J.N., Young, L.J., Hearn, E.F., Matzuk, M.M., Insel, T.R., & Winslow, J.T. (2000). Social amnesia in mice lacking the oxytocin gene. *Nature Genetics*, *25*, 284–288.

Field, T., Fox, N.A., Pickens, J., & Nawrocki, T. (1995). Relative right frontal EEG activation in 3- to 6-month-old infants of "depressed" mothers. *Developmental Psychology*, *31*, 358–363.

Fiske, S.T. (1998). Stereotyping, prejudice, and discrimination. In D.T. Gilbert, S.T. Fiske, & G. Lindzey (Eds.), *Handbook of social psychology* (4th ed., Vol. 2, pp. 357–411). New York: McGraw-Hill.

Fleming, A.S. (2005). Plasticity of innate behaviors: Experiences throughout life affect maternal behavior and its neurobiology. In C.S. Carter, L. Ahnert, K.E. Grossmann, S.B. Hrdy, M.E. Lamb, S.W. Porges, & N. Sachser. *Attachment and bonding: A new synthesis* (pp. 137–168). Cambridge, MA: MIT Press.

Fowles, D.C. (1980). The three arousal model: Implications of Gray's two-factor learning theory for heart rate, electrodermal activity, and psychopathy. *Psychophysiology*, *17*, 87–104.

Fox, N.A., Henderson, H.A., Rubin, K.H., Calkins, S.D., & Schmidt, L.A. (2001). Continuity and discontinuity of behavioral inhibition and exuberance: Psychophysiological and behavioral influences across the first four years of life. *Child Development*, *72*, 1–21.

Fox, N.A., Rubin, K.H., Calkins, S.D., Marshall, T.R., Coplan, R.J., Porges, S.W., et al. (1995). Frontal activation asymmetry and social competence at four years of age. *Child Development*, *66*, 1770–1784.

Fox, N.A., Schmidt, L.A., Calkins, S.D., Rubin, K.H., & Coplan, R.J. (1996). The role of frontal activation in the regulation and dysregulation of social behavior during the preschool years. *Development and Psychopathology*, *8*, 89–102.

Francis, D.D., Young, L.J., Meaney, M.J., & Insel, T.R. (2002). Naturally occurring differences in maternal care are associated with the expression of oxytocin and vasopressin (V1a) receptors: Gender differences. *Journal of Neuroendocrinology*, *14*, 349–353.

Fries, A.B., Ziegler, T.E., Kurian, J.R., Jacoris, S., & Pollak, S.D. (2005). Early experience in humans is associated with changes in neuropeptides critical for regulating social behavior. *Proceedings of the National Academy of Sciences, USA*, *102*, 17237–17240.

Frisina, P.G., Borod, J.C., & Lepore, S.J. (2004). A meta-analysis of the effects of written emotional disclosure on the health outcomes of clinical populations. *Journal of Nervous and Mental Disease*, *192*, 629–634.

Frith, C.D. (1992). *The cognitive neuropsychology of schizophrenia*. Hillsdale, NJ: Erlbaum.

Frith, C.D., & Frith, U. (1999). Interacting minds—A biological basis. *Science*, *286*, 1692–1695.

Frith, U. (2001). Mind blindness and the brain in autism. *Neuron*, *32*, 969–979.

Furmark, T., Tillfors, M., Garpenstrand, H., Marteinsdottir, I., Langstrom, B., Oreland, L., & Fredrikson, M. (2004). Serotonin transporter polymorphism related to amygdala excitability and symptom severity in patients with social phobia. *Neuroscience Letters*, *362*, 189–192.

Gallagher, H.L., & Frith, C.D. (2003). Functional imaging of "theory of mind." *Trends in Cognitive Science*, *7*, 77–83.

Gehring, W.J., & Fencsik, D.E. (2001). Functions of the medial frontal cortex in the processing of conflict and errors. *Journal of Neuroscience*, *21*, 9430–9437.

Gehring, W.J., & Knight, R.T. (2000). Prefrontal-cingulate interactions in action monitoring. *Nature Neuroscience*, *3*, 516.

George, M.S., Ketter, T.A., Parekh, P.I., Rosinsky, N., Ring, H.A., Pazzaglia, P.J., et al. (1997). Blunted left cingulate activation in mood disorder subjects during a response interference task (the Stroop). *Journal of Neuropsychiatry and Clinical Neuroscience*, *9*, 55–63.

George, N., Driver, J., & Dolan, R.J. (2001). Seen gaze-direction modulates fusiform activity and its coupling with other brain areas during face processing. *NeuroImage*, *13*, 1102–1112.

Gilbert, D.T., Pinel, E.C., Wilson, T.D., Blumberg, S.J., & Wheatley, T.P. (1998). Immune neglect: A source of durability bias in affective forecasting. *Journal of Personality and Social Psychology*, *75*, 617–638.

Giles, L.C., Glonek, G.F.V., Luszcz, M.A., & Andrews, G.R. (2005). Effect of social networks on 10 year survival in very old Australians: The Australian longitudinal study of aging. *Journal of Epidemiology and Community Health*, *59*, 574–579.

Goldberg, E. (2001). *The executive brain: Frontal lobes and the civilized mind*. New York: Oxford University Press.

Goldin-Meadow, S., & Mylander, C. (1984). Gestural communication in deaf children: The effects and noneffects of parental input on early language development. *Monographs of the Society for Research in Child Development*, *49*, 1–121.

Goodson, J.L., & Wang, Y.A. (in press). Neural sensitivity to social valence evolves in relation to species-typical group size. *Proceedings of the National Academy of Sciences, USA*.

Gotlib, I.H., Sivers, H., Gabrieli, J., Whitfield-Gabrieli, S., Goldin, P., Minor, K., & Canli, T. (2005). Subgenual anterior cingulate activation to valenced emotional stimuli in major depression. *NeuroReport*, *16*, 1731–1734.

Gottesman, I.I., & Gould, T.D. (2003). The endophenotype concept in psychiatry: Etymology and strategic intentions. *American Journal of Psychiatry*, *160*, 636–645.

Gregory, C., Lough, S., Stone, V., Erzinclioglu, S., Martin, L., Baron-Cohen, S., & Hodges, J.R. (2002). Theory of mind in patients with frontal variant frontotemporal dementia and Alzheimer's disease: Theoretical and practical implications. *Brain*, *125*, 752–764.

Grill-Spector, K., Knouf, N., & Kanwisher, N. (2004). The fusiform face area subserves face perception, not generic within-category identification. *Nature Neuroscience*, *7*, 555–562.

Grossman, A.W., Churchill, J.D., McKinney, B.C., Kodish, I.M., Otte, S.L., & Greenough, W.T. (2003). Experience effects on brain development: Possible contributions to psychopathology. *Journal of Child Psychology & Psychiatry*, *44*, 33–63.

Gunnar, M.R. (2005). Attachment and stress in early development: Does attachment add to the potency of social regulators of infant stress? In C.S. Carter, L. Ahnert, K.E. Grossman, S.B. Hrdy, M.E. Lamb, S.W. Porges, & N. Sachser (Eds.), *Attachment and bonding: A new synthesis* (pp. 245–255). Cambridge, MA: MIT Press.

Hammen, C., & Brennan, P.A. (2002). Interpersonal dysfunction in depressed women: Impairments independent of depressive symptoms. *Journal of Affective Disorders*, *72*, 145–156.

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

Happé, F., Ronald, A., & Plomin, R. (2006). Time to give up on a single explanation for autism. *Nature Neuroscience*, *9*, 1218–1220.

Hare, R.D. (1991). *The Hare psychopathy checklist–Revised*. Toronto, Canada: Multi-Health Systems.

Harlow, H.F. (1959, July). Love in infant monkeys. *Scientific American*, *200*, 68–74.

Harlow, H.F., & Harlow, M.K. (1973). Social deprivation in monkeys. In W.T. Greenough (Ed.), *The nature and nurture of behavior: Readings from the Scientific American* (pp. 108–116). San Francisco: Freeman.

Harpur, T.J., Hare, R.D., & Hakstian, A.R. (1989). Two-factor conceptualization of psychopathology: Construct validity and assessment implications. *Psychological Assessment*, *1*, 6–17.

Harris, L.T., & Fiske, S.T. (2006). Dehumanizing the lowest of the low: Neuro-imaging responses to extreme outgroups. *Psychological Science*, *17*, 847–853.

Heinrichs, M., Baumgartner, T., Kirschbaum, C., & Ehlert, U. (2003). Social support and oxytocin interact to suppress cortisol and subjective responses to psychosocial stress. *Biological Psychiatry*, *54*, 1389–1398.

Heller, W. (1993). Neuropsychological mechanisms of individual differences in emotion, personality, and arousal. *Neuropsychology*, *7*, 476–489.

Heller, W., Nitschke, J.B., & Miller, G.A. (1998). Lateralization in emotion and emotional disorders. *Current Directions in Psychological Science*, *7*, 26–32.

Henderson, H.A., Fox, N.A., & Rubin, K.H. (2001). Tempermental contributions to social behavior: The moderating roles for frontal EEG asymmetry and gender. *Journal of the American Academy of Child and Adolescent Psychiatry*, *40*, 68–74.

Henriques, J.B., & Davidson, R.J. (1990). Regional brain electrical asymmetries discriminate between previously depressed and healthy control subjects. *Journal of Abnormal Psychology*, *99*, 22–31.

Hicks, B.M., Markon, K.E., Patrick, C.J., Krueger, R.F., & Newman, J.P. (2004). Identifying psychopathy subtypes on the basis of personality structure. *Psychological Assessment*, *16*, 276–288.

Hooley, J.M., Gruber, S.A., Scott, L.A., Hiller, J.B., & Yurgelun-Todd, D.A. (2005). Activation in the dorsolateral prefrontal cortex in response to maternal criticism and praise in recovered depressed and healthy control participants. *Biological Psychiatry*, *57*, 809–812.

Horan, W.P., & Blanchard, J.J. (2003). Emotional responses to psychosocial stress in schizophrenia: The role of individual differences in affective traits and coping. *Schizophrenia Research*, *60*, 271–283.

House, J.S., Landis, K.R., & Umberson, D. (1988). Social relationships and health. *Science*, *241*, 540–545.

Hrdy, S.B. (1999). *Mother nature: A history of mothers, infants, and natural selection*. New York: Pantheon Books.

Hrdy, S.B. (2005). Evolutionary context of human development. In C.S. Carter, L. Ahnert, K.E. Grossman, S.B. Hrdy, M.E. Lamb, S.W. Porges, & N. Sachser (Eds.), *Attachment and bonding: A new synthesis* (pp. 9–32). Cambridge, MA: MIT Press.

Ilardi, S.S., & Feldman, D. (2001). The cognitive neuroscience paradigm: A unifying metatheoretical framework for the science and practice of clinical psychology. *Journal of Clinical Psychology*, *57*, 1067–1088.

Insel, T.R., & Fernald, R.D. (2004). How the brain processes social information: Searching for the social brain. *Annual Review of Neuroscience*, *27*, 697–722.

Insel, T.R., & Shapiro, L.E. (1992). Oxytocin receptor distribution reflects social organization in monogamous and polygamous voles. *Proceedings of the National Academy of Sciences, USA*, *89*, 5981–5985.

Insel, T.R., Wang, Z., & Ferris, C.F. (1994). Patterns of brain vasopressin receptor distribution associated with social organization in microtine rodents. *Journal of Neuroscience*, *14*, 5381–5392.

Johannes, S., Wieringa, B.M., Nager, D.R., Rada, D., Dengler, R., Emrich, H.M., et al. (2001). Discrepant target detection and action monitoring in obsessive-compulsive disorder. *Psychiatry Research*, *108*, 101–110.

Joiner, T.E. (1999). Depression's vicious scree: Self-propagating and erosive processes in depression chronicity. *Clinical Psychology: Science & Practice*, *7*, 203–218.

Kalin, N.H., Larson, C.L., Shelton, S.E., & Davidson, R.J. (1998). Asymmetric frontal brain activity, cortisol, and behavior associated with fearful temperament in Rhesus monkeys. *Behavioral Neuroscience*, *112*, 286–292.

Kalisch, R., Wiech, K., Critchley, H.D., Seymour, B., O'Doherty, J.P., Oakley, D.A., et al. (2005). Anxiety reduction through detachment: Subjective, physiological, and neural effects. *Journal of Cognitive Neuroscience*, *17*, 874–883.

Kanwisher, N., McDermott, J., & Chun, M.M. (1997). The fusiform face area: A module in human extrastriate cortex specialized for face perception. *Journal of Neuroscience*, *17*, 4302–4311.

Kaufer, D.I., & Lewis, D.A. (1999). Frontal lobe anatomy and cortical connectivity. In B.L. Miller & J.L. Cummings (Eds.), *The human frontal lobes* (pp. 27–44). New York: Guilford.

Kelley, W.T., Macrae, C.N., Wyland, C., Caglar, S., Inati, S., & Heatherton, T.F. (2002). Finding the self? An event-related fMRI Study. *Journal of Cognitive Neuroscience*, *14*, 785–794.

Kendler, K.S., Kuhn, J.W., & Prescott, C.A. (2004). Childhood sexual abuse, stressful life events and risk for major depression in women. *Psychological Medicine*, *34*, 1475–1482.

Kendrick, K.M., Keverne, E.B., & Baldwin, B.A. (1987). Intracerebroventricular oxytocin stimulates maternal behaviour in the sheep. *Neuroendocrinology*, *46*, 56–61.

Kessler, R.C. (1997). The prevalence of psychiatric comorbidity. In S. Wetzler & W.C. Sandersen (Eds.), *Treatment strategies for patients with psychiatric comorbidity* (pp. 23–48). NY: Wiley.

Kiehl, K.A., Liddle, P.F., & Hopfinger, J.B. (2000). Error processing and the anterior cingulate: An event-related fMRI study. *Psychophysiology*, *37*, 216–223.

Kim, H., Somerville, L.H., Johnstone, T., Alexander, A.L., & Whalen, P.J. (2003). Inverse amygdala and medial prefrontal cortex responses to surprised faces. *NeuroReport*, *14*, 2317–2322.

Kim, H., Somerville, L.H., Johnstone, T., Polis, S., Alexander, A.L., Shin, L.M., et al. (2004). Contextual modulation of amygdala responsivity to surprised faces. *Journal of Cognitive Neuroscience*, *16*, 1730–1745.

Kim, S., Young, L.J., Gonen, D., Veenstra-VanderWeele, J., Courchesne, R., Courchesne, E., et al. (2001). Transmission disequilibrium testing of arginine vasopressin receptor 1A (AVPR1A) polymorphisms in autism. *Molecular Psychiatry*, *7*, 503–507.

Kircher, T.T., & Leube, D.T. (2003). Self-consciousness, self-agency, and schizophrenia. *Consciousness and Cognition*, *12*, 656–669.

Kirkpatrick, B., Buchanan, R.W., Ross, D.E., & Carpenter, W.T. (2001). A separate disease within the syndrome of schizophrenia. *Archives of General Psychiatry*, *58*, 165–171.

Klonsky, E.D., Oltmanns, T.F., & Turkheimer, E. (2002). Informant-reports of personality disorder: Relation to self-reports and future research directions. *Clinical Psychology: Science and Practice*, *9*, 300–311.

Knutson, B., Westdorp, A., Kaiser, E., & Hommer, D. (2000). FMRI visualisation of brain activity during a monetary incentive delay task. *NeuroImage*, *12*, 20–27.

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

Kosslyn, S.M., Cacioppo, J.T., Davidson, R.J., Hugdahl, K., Lovallo, W.R., Spiegel, D., & Rose, R. (2002). Bridging psychology and biology: The analysis of individuals in groups. *American Psychologist*, *57*, 341–351.

Krueger, R.F. (1999). The structure of common mental disorders. *Archives of General Psychiatry*, *56*, 921–926.

Krueger, R.F., Chentsova-Dutton, Y.E., Markon, K.E., Goldberg, D., & Ormel, J. (2003). A cross-cultural study of the structure of comorbidity among common psychopathological syndromes in the general health care setting. *Journal of Abnormal Psychology*, *112*, 437–447.

Kwan, V.S.Y., John, O.P., Kenny, D.A., Bond, M.H., & Robins, R.W. (2004). Reconceptualizing individual differences in self-enhancement bias: An interpersonal approach. *Psychological Review*, *111*, 94–110.

Kwon, C., Luikart, B.W., Powell, C.M., Zhou, J., Matheny, S.A., Zhang, W., et al. (2006). PTEN regulates neuronal arborization and social interaction in mice. *Neuron*, *50*, 377–388.

Lee, P.R., Brady, D.L., Shapiro, R.A., Dorsa, D.M., & Koenig, J.I. (2005). Social interaction deficits caused by chronic phencyclidine administration are reversed by oxytocin. *Neuropsychopharmacology*, *30*, 1883–1894.

Levenston, G.K., Patrick, C.J., Bradley, M.M., & Lang, P.J. (2000). The psychopath as observer: Emotion and attention in picture processing. *Journal of Abnormal Psychology*, *109*, 373–385.

Levine, S. (2001). Primary social relationships influence the development of the hypothalamic-pituitary-adrenal axis in the rat. *Physiology & Behavior*, *73*, 255–260.

Lewontin, R. (2000). *The triple helix*. Cambridge, MA: Harvard University Press.

Liddle, P.F., Kiehl, K.A., & Smith, A.M. (2001). Event-related fMRI study of response inhibition. *Human Brain Mapping*, *12*, 100–109.

Lilienfeld, S.O., Waldman, I.D., & Israel, A.C. (1994). A critical examination of the use of the term and concept of "comorbidity" in psychopathology research. *Clinical Psychology: Science and Practice*, *1*, 71–83.

Lim, M.M., Bielsky, I.F., & Young, L.J. (2005). Neuropeptides and the social brain: Potential rodent models for autism. *International Journal of Developmental Neuroscience*, *23*, 235–243.

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

Linehan, M.M. (1993). *Cognitive-behavioral treatment of borderline personality disorder*. New York: Guilford.

Lucas, B.K., Ormandy, C.J., Binart, N., Bridges, R.S., & Kelly, P.A. (1998). Null mutation of the prolactin receptor gene produces a defect in maternal behavior. *Endocrinology*, *139*, 4102–4107.

Lykken, D.T. (1957). A study of anxiety in the sociopathic personality. *Journal of Abnormal and Social Psychology*, *55*, 6–10.

Lykken, D.T. (1995). *The antisocial personalities*. Mahwah, NJ: Erlbaum.

MacDonald, A.W., Cohen, J.D., Stenger, V.A., & Carter, C.S. (2000). Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. *Science*, *288*, 1835–1838.

Macrae, C.N., Moran, J., Heatherton, T., Banfield, J., & Kelley, W. (2004). Medial prefrontal activity predicts memory for self. *Cerebral Cortex*, *14*, 647–654.

Mauss, I.B., & Gross, J.J. (2004). Emotion suppression and cardiovascular disease: Is hiding feelings bad for your heart? In L.A. Temoshok, I. Nyklicek, & A. Vingerhoets (Eds.), *The expression of emotion and health* (pp. 62–81). London: Brunner-Routledge.

Mayberg, H.S., Lozano, A.M., Voon, V., McNeely, H.E., Seminowicz, D., Hamani, C., et al. (2005). Deep brain stimulation for treatment-resistant depression. *Neuron*, *45*, 651–660.

McGee, H. (2004). *On food and cooking: The science and lore of the kitchen*. New York: Collier Books.

Meaney, M.J., Sapolsky, R.M., & McEwen, B.S. (1985). The development of the glucocorticoid receptor system in the rat limbic brain: II. An autoradiographic study. *Developmental Brain Research*, *18*, 159–164.

Meaney, M.J., & Szyf, M. (2005). Maternal care as a model for experience-dependent chromatin plasticity? *Trends in Neuroscience*, *28*, 456–463.

Meisel, R.L. & Sachs, B.D. (1994). The physiology of male sexual behavior. In E. Nobil & J.D. Neill (Eds.), *The physiology of reproduction* (Vol. 2, pp. 3–105). New York: Raven Press.

Menon, V., Adleman, N.E., White, C.D., Glover, G.H., & Reiss, A.L. (2001). Error-related brain activation during a Go/NoGo response inhibition task. *Human Brain Mapping*, *12*, 131–143.

Meyer-Lindenberg, A., Hariri, A.R., Munoz, K.E., Mervis, C.B., Mattay, V., Norris, C.A., & Berman, K.F. (2005). Neural correlates of genetically abnormal social cognition in Williams syndrome. *Nature Neuroscience*.

Mitchell, J.P., Macrae, C.N., & Banaji, M.R. (2004). Encoding-specific effects of social cognition on the neural correlates of subsequent memory. *Journal of Neuroscience*, *24*, 4912–4917.

Mitchell, J.P., Banaji, M.R., & Macrae, C.N. (2005). The link between social cognition and the self referential thought in the medial prefrontal cortex. *Journal of Cognitive Neuroscience*, *17*, 1306–1315.

Modahl, C., Green, L.A., Fein, D., Morris, M., Waterhouse, L., Feinstein, C. & Levin, H. (1998). Plasma oxytocin levels in autistic children. *Biological Psychiatry*, *43*, 270–277.

Mojtabai, R. (1994). Fregoli syndrome. *Australian & New Zealand Journal of Psychiatry*, *28*, 458–462.

Moltz, H., Lubin, M., Leon, M., & Numan, M. (1970). Hormonal induction of maternal behavior in the ovariectomized nulliparous rat. *Physiology & Behavior*, *5*, 1373–1377.

Moran, J.M., Macrae, C.N., Heatherton, T.F., Wyland, C.L., & Kelley, W.M. (2006). Neuroanatomical evidence for distinct cognitive and affective components of self. *Journal of Cognitive Neuroscience*, *18*, 1586–1594.

Morgan, B.A., & Lilienfeld, S.O. (2000). A meta-analytic review of the relation between antisocial behavior and neuropsychological measures of executive function. *Clinical Psychology Review*, *20*, 113–136.

Morris, J.S., Ohman, A., & Dolan, R.J. (1999). A subcortical pathway to the right amygdala mediating "unseen" fear. *Proceedings of the National Academy of Sciences, USA*, *96*, 1680–1685.

Murphy, J.M. (1976). Psychiatric labeling in cross-cultural perspective. *Science*, *191*, 1019–1028.

Murray, L.A., Whitehouse, W.G., & Alloy, L.B. (1999). Mood congruence and depressive deficits in memory: A forced recall analysis. *Memory*, *7*, 175–196.

Neale, J.M., Oltmanns, T.F., & Harvey, P.D. (1985). The need to relate cognitive deficits to specific behavioral referents of schizophrenia. *Schizophrenia Bulletin*, *11*, 286–291.

Nelson, R.J., Demas, G.E., Huang, P.L., Fishman, M.C., Dawson, V.L., Dawson, T.M., & Snyder, S.H. (1995). Behavioural abnormalities in male mice lacking neuronal nitric oxide synthase. *Nature*, *378*, 383–386.

Neumann, I.D. (2003). Brain mechanisms underlying emotional alterations in the peripartum period in rats. *Depression and Anxiety*, *17*, 111–121.

Newman, D.L., Moffit, T.E., Caspi, A., & Silva, P.A. (1998). Comorbid mental disorders: Implications for treatment and sample selection. *Journal of Abnormal Psychology*, *107*, 305–311.

Nicot, A., Otto, T., Brabet, P., & Dicicco-Bloom, E.M. (2004). Altered social behavior in pituitary adenylate cyclase-activating polypeptide type I receptor-deficient mice. *Journal of Neuroscience*, *24*, *8786–8795*.

Nishimori, K., Young, L.J., Guo, Q., Wang, Z., Insel, T.R., & Matzuk, M.M. (1996). Oxytocin is required for nursing but is not essential for parturition or reproductive behavior. *Proceedings of the National Academy of Science, USA*, *93*, 11699–11704.

Numan, M., & Insel, T.R. (2003). *The neurobiology of parental behavior*. New York: Springer-Verlag.

Ochsner, K.N., Beer, J.S., Robertson, E., Cooper, J., Gabrieli, J.D.E., Kihlstrom, J.F., et al. (2005). The neural correlates of direct and reflected self-knowledge. *NeuroImage*, *28*, 797–814.

Ochsner, K.N., Bunge, S.A., Gross, J.J., & Gabrieli, J.D. (2002). Rethinking feelings: An fMRI study of the cognitive regulation of emotion. *Journal of Cognitive Neuroscience*, *14*, 1215–1229.

Ochsner, K.N., Knierim, K., Ludlow, D., Hanelin, J., Ramachandran, T., & Mackey, S. (2004). Reflecting upon feelings: An fMRI study of neural systems supporting the attribution of emotion to self and other. *Journal of Cognitive Neuroscience*, *16*, 1746–1772.

Ochsner, K.N., & Lieberman, M.D. (2001). The emergence of social cognitive neuroscience. *American Psychologist*, *56*, 717–734.

Ochsner, K.N., Ludlow, D., Knierim, K., Hanelin, J., Ramachandran, T., Glover, G., et al. (2006). Neural correlates of individual differences in pain-related fear and anxiety. *Pain*, *120*, 69–77.

Ochsner, K.N., Ray, R.D., Cooper, J.C., Robertson, E.R., Chopra, S., Gabrieli, J.D.E., et al. (2004). For better or for worse: Neural systems supporting the cognitive down- and up-regulation of negative emotion. *NeuroImage*, *23*, 483–499.

O'Conner, T.G., Rutter, M., & the English and Romanian Adoptees Study Team. (2000). Attachment disorder behavior following early severe deprivation: Extension and longitudinal follow-up. *Journal of the American Academy of Child and Adolescent Psychiatry*, *39*, 703–712.

Ogawa, S., Chester, A.E., Hewitt, S.C., Walker, V.R., Gustafsson, J.A., Smithies, O., et al. (2000). Abolition of male sexual behaviors in mice lacking estrogen receptors alpha and beta (alpha beta ERKO). *Proceedings of the National Academy of Sciences, USA*, *97*, 14737–14741.

Ogawa, S., Lubahn, D.B., Korach, K.S., & Pfaff, D.W. (1997). Behavioral effects of estrogen receptor gene disruption in male mice. *Proceedings of the National Academy of Sciences, USA*, *94*, 1476–1481.

Olausson, H., Uvnäs-Moberg, K., & Sohlstrom, A. (2003). Postnatal oxytocin alleviates adverse effects in adult rat offspring caused by maternal malnutrition. *American Journal of Physiological Endocrinology and Metabolism*, *284*, E475–E480.

Olivier, B., & Young, L.J. (2002). Animal models of aggression. In K.L. Davis, D. Charney, J.T. Coyle, & C. Nemeroff (Eds.), *Neuropsychopharmacology: The fifth generation of progress* (pp. 1699–1708). Philidelphia: Lippincott, Williams, & Wilkens.

Oyebode, F., & Sargeant, R. (1996). Delusional misidentification syndromes: A descriptive study. *Psychopathology*, *29*, 209–214.

Padgett, D.A., Sheridan, J.F., Dorne, J., Berntson, G.G., Candelora, J., & Glaser, R. (1998). Social stress and the reactivation of latent herpes simplex virus type 1. *Proceedings of the National Academy of Sciences, USA*, *95*, 7231–7235.

Paulus, M.P., Feinstein, J.S., Simmons, A., & Stein, M.B. (2004). Anterior cingulate activation in high trait anxious subjects is related to altered error processing during decision making. *Biological Psychiatry*, *55*, 1179–1187.

Paulus, M.P., Hozack, N., Frank, L., Brown, G.G., & Schuckit, M.A. (2003). Decision making by methamphetamine-dependent subjects is associated with error-rate-independent decrease in prefrontal and parietal activation. *Biological Psychiatry*, *53*, 65–74.

Paus, T. (2001). Primate anterior cingulate cortex: Where motor control, drive and cognition interface. *Nature Reviews Neuroscience*, *2*, 417–424.

Pedersen, C.A., & Boccia, M.L. (2002). Oxytocin links mothering received, mothering bestowed and adult stress responses. *Stress*, *5*, 259–267.

Pedersen, C.A., & Prange, A.J., Jr. (1979). Induction of maternal behavior in virgin rats after intracerebroventricular administration of oxytocin. *Proceedings of the National Academy of Sciences, USA*, *76*, 6661–6665.

Pennebaker, J.W. (2004). Theories, therapies, and taxpayers: On the complexities of the expressive writing paradigm. *Clinical Psychology: Science and Practice*, *11*, 138–142.

Pennisi, E. (2005). Why do humans have so few genes? *Science*, *309*, 80.

Perrett, D.I., Hietanen, J.K., Oram, M.W., & Benson, P.J. (1992). Organization and functions of cells responsive to faces in the temporal cortex. *Philosophical Transactions of the Royal Society of London: Series B. Biological Sciences*, *335*, 23–30.

Persons, J.B. (1986). The advantages of studying psychological phenomena rather than psychiatric diagnoses. *American Psychologist*, *41*, 1252–1260.

Pezawas, L., Meyer-Lindenberg, A., Brabant, E.M., Verchinski, B.A., Munoz, K.E., Kolachana, B.S., et al. (2005). 5-HTTLPR polymorphism impacts human cingulate-amygdala interactions: A genetic susceptibility mechanism for depression. *Nature Neuroscience*, *8*, 828–834.

Pfaff, D.W., & Schwartz-Giblin, S. (1994) Cellular and molecular mechanisms of female reproductive behaviors. In E. Knobil & J.D. Neill (Eds.), *The physiology of reproduction* (2nd ed., Vol. 2, pp. 107–220). New York: Raven Press.

Phan, K.L., Fitzgerald, D.A., Nathan, P.J., Moore, G.J., Uhde, T.W., & Tancer, M.E. (2005). Neural substrates for voluntary suppression of negative affect: A functional magnetic resonance imaging study. *Biological Psychiatry*, *57*, 210–219.

Phillips, M.L., Drevets, W.C., Rauch, S.L., & Lane, R. (2003). Neurobiology of emotion perception. II: Implications for major psychiatric disorders. *Biological Psychiatry*, *54*, 515–528.

Phillips, M.L., Young, A.W., Senior, C., Brammer, M., Andrew, C., Calder, A.J., et al. (1997). A specific neural substrate for perceiving facial expressions of disgust. *Nature*, *389*, 495–498.

Pierce, K., Muller, R.A., Ambrose, J., Allen, G., & Courchesne, E. (2001). Face processing occurs outside the fusiform 'face area' in autism: Evidence from functional MRI. *Brain*, *124*, 2059–2073.

Porges, S.W. (2003). The polyvagal theory: Phylogenetic contributions to social behavior. *Physiology & Behavior*, *79*, 503–513.

Prathikanti, S., & Weinberger, D.R. (2005). Psychiatric genetics – the new era: Genetic research and some clinical implications. *British Medical Bulletin*, *73*, 107–122.

Puce, A., & Perrett, D. (2003). Electrophysiology and brain imaging of biological motion. *Philosophical Transactions of the Royal Society of London: Series B. Biological Science*, *358*, 435–445.

Quirk, G.J., & Gehlert, D.R. (2003). Inhibition of the amygdala: Key to pathological states? In P. Shinnick-Gallagher & A. Pitkänen (Eds.), *The amygdala in brain function: Basic and clinical approaches* (Vol. 985, pp. 263–325). New York: New York Academy of Sciences.

Ragnauth, A.K., Devidze, N., Moy, V., Finley, K., Goodwillie, A., Kow, L.M., et al. (2005). Female oxytocin gene-knockout mice, in a semi-natural environment, display exaggerated aggressive behavior. *Genes, Brain, & Behavior*, *4*, 229–239.

Raichle, M.E., Fiez, J.A., Videen, T.O., MacLeod, A.M., Pardo, J.V., Fox, P.T., & Petersen, S.E. (1994). Practice-related changes in human brain functional anatomy during non-motor learning. *Cerebral Cortex*, *4*, 8–26.

Raine, A., Lencz, T., Bihrle, S., LaCasse, L., & Colletti, P. (2000). Reduced prefrontal gray matter volume and reduced autonomic activity in antisocial personality disorder. *Archives of General Psychiatry*, *57*, 119–127.

Rauch, S.L., Whalen, P.J., Shin, L.M., McInerney, S.C., Macklin, M.L., Lasko, N.B., et al. (2000). Exaggerated amygdala response to masked facial stimuli in posttraumatic stress disorder: A functional MRI study. *Biological Psychiatry*, *47*, 769–776.

Ray, R.D., Ochsner, K.N., Cooper, J.C., Robertson, E.R., Gabrieli, J.D.E., & Gross, J.J. (2005). Individual differences in trait rumination and the neural systems supporting cognitive reappraisal. *Cognitive, Affective & Behavioral Neuroscience*, *5*, 156–158.

Ridderinkhof, K.R., Ullsperger, M., Crone, E.A., & Nieuwenhuis, S. (2004). The role of the medial frontal cortex in cognitive control. *Science*, *306*, 443–447.

Rissman, E.F., Early, A.H., Taylor, J.A., Korach, K.S., & Lubahn, D.B. (1997). Estrogen receptors are essential for female sexual receptivity. *Endocrinology*, *138*, 507–510.

Rizzolatti, G., Fadiga, L., Gallese, V., & Fogassi, L. (1996). Premotor cortex and the recognition of motor actions. *Cognitive Brain Research*, *3*, 131–141.

Rosenblatt, J.S. (1969). The development of maternal responsiveness in the rat. *American Journal of Orthopsychiatry*, *39*, 36–56.

Rosenfarb, I.S., Bellack, A.S., & Aziz, N. (2006). Family interactions and the course of schizophrenia in African American and White patients. *Journal of Abnormal Psychology*, *115*, 112–120.

Roth, G., & Dicke, U. (2005). Evolution of the brain and intelligence. *Trends in Cognitive Sciences*, *9*, 250–257.

Rudebeck, P.H., Buckley, M.J., Walton, M.E., & Rushworth, M.F. (2006). A role for the macaque anterior cingulate gyrus in social valuation. *Science*, *313*, 1310–1312.

Sarter, M., Berntson, G.G., & Cacioppo, J.T. (1996). Brain imaging and cognitive neuroscience: Toward strong inference in attributing function to structure. *American Psychologist*, *51*, 13–21.

Sass, L.A., & Parnas, J. (2003). Schizophrenia, consciousness, and the self. *Schizophrenia Bulletin*, *29*, 427–444.

Sawamoto, N., Honda, M., Okada, T., Hanakawa, T., Kanda, M., Fukuyama, H., et al. (2000). Expectation of pain enhances responses to nonpainful somatosensory stimulation in the anterior cingulate cortex and parietal operculum/posterior insula: An event-related functional magnetic resonance imaging study. *Journal of Neuroscience*, *20*, 7438–7445.

Schmidt, L.A. (1999). Frontal brain electrical activity in shyness and sociability. *Psychological Science*, *10*, 316–320.

Schoenemann, P.T., Sheehan, M.J., & Glotzer, D. (2005). Prefrontal white matter volume is disproportionately larger in humans than in other primates. *Nature Neuroscience*, *8*, 242–252.

Schultz, R. (2005). Developmental deficits in social perception in autism: The role of the amygdala and fusiform face area. *International Journal of Developmental Neuroscience*, *23*, 125–141.

Schultz, R., Gauthier, I., Klin, A., Fulbright, R., Anderson, A., Volkmar, F., et al. (2000). Abnormal ventral temporal cortical activity among individuals with autism and Asperger syndrome during

face discrimination. *Archives of General Psychiatry Journal*, *57*, 331–340.

Sheline, Y.I., Barch, D.M., Donnelly, J.M., Ollinger, J.M., Snyder, A.Z., & Mintun, M.A. (2001). Increased amygdala response to masked emotional faces in depressed subjects resolves with antidepressant treatment: An fMRI study. *Biological Psychiatry*, *50*, 651–658.

Sheppard, D.M., Bradshaw, J.L., Purcell, R. & Pantelis, C. (1999). Tourette's and comorbid syndromes: Obsessive compulsive and attention deficit hyperactivity disorder. A common etiology? *Clinical Psychological Review*, *19*, 531–552.

Signer, S.F. (1994). Localization and lateralization in the delusion of substitution: Capgras symptom and its variants. *Psychopathology*, *27*, 168–176.

Simpson, J.R., Jr., Drevets, W.C., Snyder, A.Z., Gusnard, D.A., & Raichle, M.E. (2001). Emotion-induced changes in human medial prefrontal cortex: II. During anticipatory anxiety. *Proceedings of the National Academy of Sciences, USA*, *98*, 688–693.

Small, S.L., & Nusbaum, H.C. (2004). On the neurobiological investigation of language understanding in context. *Brain and Language*, *89*, 300–311.

Stuss, D., Gow, C., & Hetherington, C. (1992). "No longer Gage": Frontal lobe dysfunction and emotional changes. *Journal of Consulting and Clinical Psychology*, *60*, 349–359.

Stuss, D.T., & Levine, B. (2002). Adult clinical neuropsychology: Lesions from studies of the frontal lobes. *Annual Review of Psychology*, *53*, 401–433.

Stuss, D.T., Picton, T.W., & Alexander, M.P. (2001). In S.P. Salloway, P.F. Malloy (Eds.), *The frontal lobes and neuropsychiatric illness* (pp. 101–109). Washington, DC: American Psychiatric Publishing.

Sutton, S.K., & Davidson, R.J. (1997). Prefrontal brain asymmetry: A biological substrate of the behavioral approach and inhibition systems. *Psychological Science*, *8*, 204–210.

Szasz, T.S. (1960). The myth of mental illness. *American Psychologist*, *15*, 113–118.

Takayanagi, Y., Yoshida, M., Bielsky, I.F., Ross, H.R., Kawamata, M., Onaka, T., et al. (2005). Pervasive social deficits but normal parturition in oxytocin receptor-deficient mice. *Proceedings of the National Academy of Sciences, USA*, *102*, 16096–16101.

Tamminga, C.A. (1998). Serotonin and schizophrenia. *Biological Psychiatry*, *44*, 1079–1080.

Tamminga, C.A., Thaker, G.K., Buchannan, R., Kirkpatrick, B.L., Alphs, L.D., Chase, T.N., & Carpenter, W.T. (1992). Limbic system abnormalities identified in schizophrenia using positron emission tomography with fluorodeoxyglucose and neocortical alterations with deficit syndrome. *Archives of General Psychiatry*, *49*, 522–530.

Taylor, S.E., & Brown, J.D. (1988). Illusion and well-being: A social psychological perspective on mental health. *Psychological Bulletin*, *103*, 193–210.

Taylor, S.E., Klein, L.C, Lewis, B.P., Gruenewald, T.L, Gurung, R.A., & Updegraff, J.A. (2000). Biobehavioral responses to stress in females: Tend-and-befriend, not fight-or-flight. *Psychological Review*, *107*, 411–429.

Teicher, M.H., Andersen, S.L., Polcari, A., Anderson, C.M., Navlta, C.P., & Kim, D.M. (2003). The neurobiological consequences of early stress and childhood maltreatment. *Neuroscience and Biobehavioral Reviews*, *27*, 33–44.

Terkel, J., & Rosenblatt, J.S. (1968). Maternal behavior induced by maternal blood plasma injected into virgin rats. *Journal of Comparative & Physiological Psychology*, *65*, 479–482.

Todd, R.D., & Botteron, K. (2002). Etiology and genetics of early onset mood disorders. *Child and Adolescent Psychiatric Clinics of North America*, *11*, 499–518.

Tomarken, A.J., & Davidson, R.J. (1994). Frontal brain activation in repressors and non-repressors. *Journal of Abnormal Psychology*, *103*, 339–349.

Tomarken, A.J., Davidson, R.J., Wheeler, R.E., & Doss, R.C. (1992). Individual differences in anterior brain asymmetry and fundamental dimensions of emotion. *Journal of Personality and Social Psychology*, *62*, 676–687.

Tomarken, A.J., Davidson, R.J., Wheeler, R.E., & Kinney, L. (1992). Psychometric properties of resting anterior EEG asymmetry: Temporal stability and internal consistency. *Psychophysiology*, *29*, 576–592.

Tomarken, A.J., Dichter, G.S., Garber, J., & Simien, C. (2004). Resting frontal brain activity: Linkages to maternal depression and socioeconomic status among adolescents. *Biological Psychology*, *67*, 77–102.

Tranel, D., & Damasio, A.R. (1985). Knowledge without awareness: An autonomic index of facial recognition by prosopagnosics. *Science*, *228*, 1453–1454.

Underwood, B.J. (1975). Individual differences as a crucible in theory construction. *American Psychologist*, *12*, 128–134.

Uttal, W.R. (2001). *The new phrenology: The limits of localizing cognitive processes in the brain*. Cambridge: MIT Press.

Uvnäs-Moberg, K. (1998). Oxytocin may mediate the benefits of positive social interactions and emotions. *Psychoneuroendocrinology*, *23*, 819–835.

Vandenbergh, J.G., & Drickamer, L.C. (1974). Reproductive coordination among free-ranging rhesus monkeys. *Physiology & Behavior*, *13*, 373–376.

Verona, E., Patrick, C.J., Curtin, J.J., Bradley, M.M., & Lang, P.J. (2004). Psychopathy and physiological response to emotionally evocative sounds. *Journal of Abnormal Psychology*, *113*, 99–108.

Walden, B., McGue, M., Iacono, W.G., Burt, A., & Elkins, I. (2004). Identifying shared environmental contributions to early substance use: The respective roles of peers and parents. *Journal of Abnormal Psychology*, *113*, 440–450.

Wassink, T.H., Piven, J., Vieland, V.J., Pietila, J., Goedken, R.J., Folstein, S.E., & Sheffield, V. (2004). Examination of AVPR1a as an autism susceptibility gene. *Molecular Psychiatry*, *9*, 968–972.

Weaver, I.C.G., Cervoni, N., Champagne, F.A., D'Alesio, A.C., Sharma, S., Seckl, J.R., et al. (2004). Epigenetic programming by maternal behavior. *Nature Neuroscience*, *7*, 847–854.

Weaver, I.C.G., Champagne, F.A., Brown, S.E., Dymov, S., Sharma, S., Meaney, M.J., & Szyf, M. (2005). Reversal of maternal programming of stress responses in adult offspring through methyl supplementation: Altering epigenetic marking later in life. *Journal of Neuroscience*, *25*, 11045–11054.

Wetherby, A.M., Woods, J., Allen, L., Cleary, J., Dickinson, H., & Lord, C. (2004). Early indicators of autism spectrum disorders in the second year of life. *Journal of Autism and Developmental Disorders*, *34*, 473–493.

Whalen, P.J., Rauch, S.L., Etcoff, N.L., McInerney, S.C., Lee, M.B., & Jenike, M.A. (1998). Masked presentations of emotional facial expressions modulate amygdala activity without explicit knowledge. *Journal of Neuroscience*, *18*, 411–418.

Widiger, T.A., & Clark, L.A. (2000). Toward DSM-V and the classification of psychopathology. *Psychological Bulletin*, *126*, 946–963.

Williams, J.R., Insel, T.R., Harbaugh, C.R., & Carter, C.S. (1994). Oxytocin administered centrally facilitates formation of a partner preference in prairie voles (*Microtus ochrogaster*). *Journal of Neuroendocrinology*, *6*, 247–250.

Wills, T.A., & Yaeger, A.M. (2003). Family factors and adolescent substance use: Models and mechanisms. *Current Directions in Psychological Science*, *12*, 222–226.

Winslow, J.T. (2005). Neuropeptides and non-human primate social deficits associated with pathogenic rearing experience. *International Journal of Developmental Neuroscience*, *23*, 245–251.

Winslow, J., Hastings, N., Carter, C.S., Harbaugh, C., & Insel, T. (1993). A role for central vasopressin in pair bonding in monogamous prairie voles. *Nature*, *365*, 545–548.

Winslow, J.T., Noble, P.L., Lyons, C.K., Sterk, S.M., & Insel, T.R. (2003). Rearing effects on cerebrospinal fluid oxytocin concentration and social buffering in rhesus monkeys. *Neuropsychopharmacology*, *28*, 910–918.

Wyland, C.L., Kelley, W.M., Macrae, C.N., Gordon, H.L., & Heatherton, T.F. (2003). Neural correlates of thought suppression. *Neuropsychologia*, *41*, 1863–1867.

Young, L.J., Nilsen, R., Waymire, K.G., MacGregor, G.R., & Insel, T.R. (1999). Increased affiliative response to vasopressin in mice expressing the vasopressin receptor from a monogamous vole. *Nature*, *400*, 766–768.

Young, L.J., & Wang, Z. (2004). The neurobiology of pair bonding. *Nature Neuroscience*, *7*, 1048–1054.

Young, L.J., Winslow, J.T., Wang, Z., Gingrich, B., Guo, Q., Matzuk, M.M., & Insel, T.R. (1997). Gene targeting approaches to neuroendocrinology: Oxytocin, maternal behavior, and affiliation. *Hormonal Behavior*, *31*, 221–231.