

**Amygdala Responses to
Novel Fearful vs Familiar Neutral**

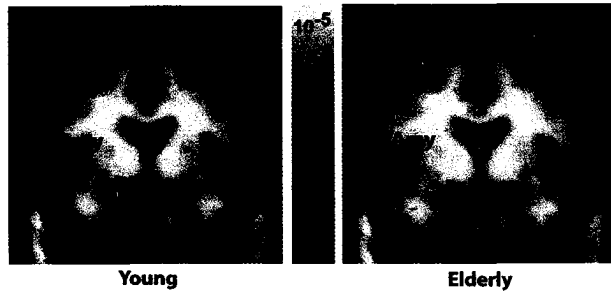


PLATE 17.2. Similar amygdala responses to human faces in young and elderly subjects. Coronal Talairach T1-weighted images with superimposed colorized statistical maps demonstrating similar amygdala activation in young ($n = 18$) and elderly ($n = 18$) subjects. The activations shown are for the comparison between novel fearful faces and familiar neutral faces. From Wright, Wedig, et al. (2006). Copyright 2006 by Elsevier. Adapted by permission.

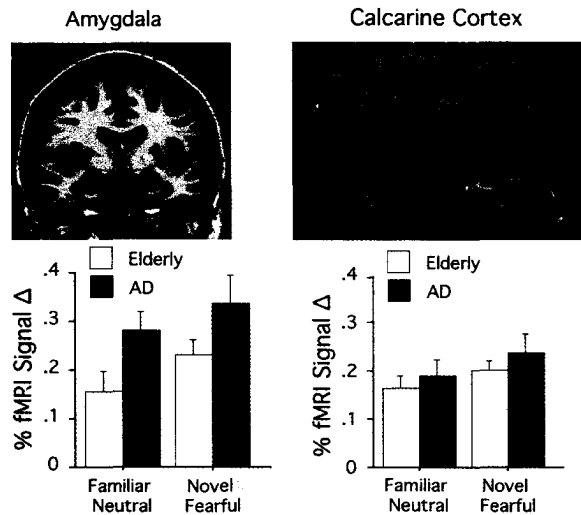


PLATE 17.3. Exaggerated amygdala responses to human faces in AD. Left upper panel shows high-resolution coronal MRI image demonstrating amygdala tracings used for anatomically based fMRI analyses. Bar graphs show percent (%) blood-oxygen-level-dependent (BOLD) signal change for elderly controls ($n = 12$) and patients with mild AD ($n = 12$). Bar graphs below show right amygdala responses to familiar neutral and novel fearful faces versus fixation. The amygdala in the patients with AD versus the healthy elderly subjects had significantly greater responses to both face conditions. Right upper panel shows the partially inflated reconstruction of the medial cortical surface demonstrating the right calcarine cortex parcellation (CCtx, purple). This was used for anatomically based fMRI analyses. The medial prefrontal cortex (PFC), medial temporal lobe (MTL), and parietal cortex (PC) are indicated. Bar graphs below show similar responses in the calcarine cortex of the two subjects groups. From Wright, Dickerson, et al. (2007). Copyright 2007 by the Society of Biological Psychiatry. Adapted by permission.

CHAPTER 13

**The Human Amygdala
in Social Function**

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What is the role of the amygdala in social function? Although this question has been the topic of considerable research, many past studies have addressed this question only indirectly, in the context of research on emotion or learning. In such studies, the sights, sounds, and smells of conspecifics have been used to induce emotional states or to influence learning. These social stimuli are often the most effective in producing emotional responses. But what gives these stimuli their potency in the production of affect and influence on learning? The social environment is first encountered immediately after birth in the form of mother–infant interactions and continues to be of tremendous importance throughout an animal’s lifespan. The bond formed with the mother is necessary for the survival of an organism (at least for most mammals), and this bond influences social behavior from infancy through adulthood. The primacy of the social environment in the survival of an organism makes it necessary for neural mechanisms to acclimate quickly to and learn from social situations. While many neural structures are involved in this process, the amygdala occupies a central position in both the recognition of and response to socially salient stimuli.

Perhaps an appropriate reformulation of the question at the beginning of the chapter is this: To *what* in the social environment does the amygdala respond? Some researchers have postulated that it is *ambiguity* or *relevance* to which the amygdala is sensitive (Sander, Grafman, & Zalla, 2003; Whalen, 1998). Stimuli that predict threat some of the time, as in a partial reinforce-

ment schedule, produce greater amygdala-dependent conditioned responses than those that consistently predict threat do (Lloyd & Kling, 1991). With regard to the human social environment, Whalen (1998) has argued that the amygdala response to facial expressions of fear (and, by extension, the facial fear recognition deficit in patients with amygdala damage) is due to the inherent ambiguity expressed in the fearful face. Whereas angry faces indicate both a threat and the source of that threat, fearful faces indicate only the presence of a threat, but not its source. In this view, the amygdala response is in the service of disambiguating the threat stimulus. Taken to its logical extreme, what could be more ambiguous than our social environment? Stimuli in the social environment include family members, coworkers, potential mates, potential enemies, and many others; they constitute a multifaceted system of interactions, which are sometimes predictable, but never certain. We humans by nature attempt to explain other humans' behavior, which is often erratic and can constitute threats to our survival, or at least to our well-being. In this sense, then, activation of the amygdala while we are navigating our social environment is an index of the amygdala's role in deciphering ambiguity.

We postulate that the unpredictable nature of social interactions is what influences amygdala function (and perhaps even its structure, although this is beyond the scope of our analysis). Within this chapter, we describe work showing the specific instances in which the amygdala is implicated in the processing of inherently unpredictable social stimuli. We begin by describing some of the early work done in nonhuman primates and discussing how this work influenced subsequent work in humans. Next, we review recent work on social cognition and the amygdala, which has used functional neuroimaging and neurophysiology approaches in humans. We then turn to descriptions of some rare amygdala-damaged patients we have had an opportunity to study, and discuss these patients in terms of both their performance on social tasks and their real-life social behavior. We conclude with a proposal for an integrative model of the functions of the human amygdala in social processing.

HISTORICAL CONTEXT, FOCUSING ON ANIMAL RESEARCH

Some of the earliest writings on the role of the amygdala in behavior emphasized its social function (Brown & Schafer, 1888). Klüver and Bucy (1937), in their classic paper on the behavior of rhesus monkeys that had undergone bilateral removal of the temporal lobes (including the amygdala, hippocampus, and surrounding cortex), included descriptions of altered sexual behavior and increased tameness toward humans and conspecifics. This work was followed by many studies documenting changes in social behavior, and increased compliance with experimenters, in monkeys with bilateral damage limited primarily to the amygdala (Dicks, Myers, & Kling, 1968; Thompson, Bergland, & Towfighi, 1977; Weiskrantz, 1956). The specific results of

amygdala damage in animals depended on the age of the animals at the time the damage occurred, the dominance status of the animals in their social hierarchy, and how the animals were housed (laboratory cage housing vs. a natural habitat).

In a classic study assessing the effects of amygdala damage on social behavior in the wild, Dicks and colleagues (1968) examined the effects of juvenile-onset and adult-onset lesions to the amygdala (and uncus) in rhesus monkeys. Animals that received the operation as juveniles (between 2 and 3 years of age) showed a transient social impairment, following which these animals rejoined their social group and within a month of the procedure were behaving within normal limits of social behavior. By contrast, the adult-onset cases were unable to display appropriate social signals, resulting in social ostracism. During the initial social reintroduction, both the adult- and juvenile-onset cases were described as "retarded in their ability to foresee and avoid dangerous confrontations." They did not show appropriate submissive gestures toward more dominant animals. Although the juvenile-onset animals were able to overcome these social impairments, the adult-onset cases were not so fortunate and, forced to live on their own, died within a month of the operation. On the basis of findings with animals having either early- or adult-onset amygdala damage, Thompson and colleagues (1977) suggested that damage to the amygdala did not result merely in tameness or placidity, but that these animals were "slow in conforming to the social etiquette normally associated with a subordinate status and behave in ways that prolong the hostility directed at them." This conclusion is more in tune with the idea that damage to the amygdala results in inappropriate responses to ambiguous social cues, rather than merely producing a pattern of tameness.

More recent research has assessed the effects of amygdala damage on the development of social behavior by examining the effects of neonatal amygdala damage on social interactions (Bauman, Lavenex, Mason, Capitanio, & Amaral, 2004a, 2004b). These authors have shown that the amygdala is not essential for the development of social behavior in rhesus monkeys. Damage to the amygdala does, however, alter certain aspects of social function. The primary social effect of neonatal amygdala damage—like that previously described for adult-onset lesions—is an inability to appreciate the threat value of a situation and to modify behavior accordingly. The amygdala, then, plays a modulatory role: While the development of fundamental social behavior with both the mother and peers proceeds (mostly) normally after early-onset amygdala damage, these animals are unable to regulate their social behavior later in life, especially in response to potentially fear-inducing situations. This pattern of results is analogous to that reported for the role of the amygdala in long-term declarative memory. Although the amygdala is not essential for the encoding, consolidation, and retrieval of memories, it does play a modulatory role. Specifically, the amygdala participates in the enhancement of memory for emotionally arousing material (Buchanan & Adolphs, 2004; McGaugh, Cahill, & Roozendaal, 1996). Just as normal memory performance develops

in monkeys or humans with amygdala damage, social development proceeds normally for the most part. It is only in certain social situations in which differences in social behavior or emotional memory are evidenced following amygdala damage.

These findings in animals with early- and adult-onset amygdala damage are instructive, in that they relate to the patterns of deficits seen in humans with amygdala damage due to either a developmental disease process or adult-onset changes in amygdala function, as we review in more detail later in this chapter.

NEUROPHYSIOLOGY AND FUNCTIONAL IMAGING IN PRIMATES

The altered social behavior described after damage to the amygdala suggests that it is involved in processing social signals—specifically, those related to potential threat—and modifying behavior accordingly. Neurophysiology and neuroimaging studies have allowed for the assessment of the specific stimuli in the social environment that activate the amygdala.

Neurophysiological studies have shown that neurons in the primate amygdala are responsive to faces (Leonard, Rolls, Wilson, & Baylis, 1985) and other social stimuli (Brothers & Ring, 1993; Brothers, Ring, & Kling, 1990). Leonard and colleagues (1985) described neurons in the basal accessory nucleus of the amygdala in the rhesus macaque that responded selectively to human and monkey faces. Similar findings have since been reported from single-neuron activity measured from the human amygdala (Fried, MacDonald, & Wilson, 1997). These results suggest a mechanism whereby amygdala damage could result in the altered social behavior previously documented in monkeys following amygdalotomy. If neurons in the amygdala are responsive to faces, and specifically to the faces of individuals within a dominance hierarchy, then damage to these neurons may result in an inability either to recognize members of a hierarchy or to produce the proper behavioral response to those individuals. This deficit, then, may alter the social and affective behavior of an individual in the presence of animals above or below that individual in the dominance hierarchy. Interestingly, Leonard and colleagues found that face-responsive neurons in the amygdala were slower to respond to facial stimuli than were neurons in the superior temporal sulcus area (110–200 msec compared to 90–140 msec, respectively). This delayed response suggests that the amygdala is receiving preprocessed information from cortical areas sensitive to social stimuli. The amygdala may utilize this processed social information, orchestrating the proper affective response when presented with an unpredictable social situation.

Other studies have shown that the amygdala response in social situations is potentiated when the situations can be interpreted as ambiguous (Kling, Steklis, & Deutsch, 1979; Lloyd & Kling, 1991; Whalen, 1998). Kling and

colleagues (1979) showed that amygdala activity in squirrel monkeys increased when animals were presented with ambiguous social behaviors by conspecifics, such as approach or genital inspection. A number of outcomes are possible in these situations, including aggression or sexual behavior. Amygdala activity was greatest in the conditions characterized by uncertainty than in any other conditions in the experiment, including situations involving overt physical aggression. Interestingly, these authors also found increased amygdala activity in a study in which squirrel monkeys were placed in a nonsocial situation in which they had previously received uncued—and therefore unpredictable—shock (Lloyd & Kling, 1991). Amygdala activity in the uncued shock chamber was greater than that recorded in a chamber in which shock had been presented reliably. These authors suggested that unpredictability, in the behavior of conspecifics as well as in the possibility of shock, was what elicited the amygdala activity.

Following from neurophysiological and neuropsychological studies, researchers have used functional neuroimaging techniques such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) to address the role of the human amygdala in social function. The results of many of these studies are discussed at length in other chapters in this volume, but we describe a selection of those studies that have specifically addressed social functioning.

The initial finding of amygdala response to facial expression stimuli in humans came from a PET study in which subjects viewed faces expressing fearful and happy expressions (Morris et al., 1996). Results of this study showed increased left amygdala activity in response to faces morphed to show higher intensity of fear, and decreased activity in response to faces showing higher intensity of happiness. These authors further showed that greater amygdala activity while subjects were viewing fearful faces was associated with greater activity in an area of visual cortex, whereas reduced amygdala activity during the viewing of happy faces was associated with reduced visual cortical activity (Morris et al., 1998). These data, and more recent research (Richardson, Strange, & Dolan, 2004; Vuilleumier, Richardson, Armony, Driver, & Dolan, 2004), indicate that the amygdala has a modulatory influence on other areas of the brain during the processing of social and emotional stimuli. These findings, along with those from neurophysiological studies of primates, indicate the central position that the amygdala occupies in the processing of social stimuli. It receives processed information via pathways from cortical regions, such as the superior temporal sulcus (Amaral, Price, Pitkanen, & Carmichael, 1992), but it also feeds back to higher-level visual cortex in response to socially salient information (Morris et al., 1998).

The face is a primary source of social information for primates, but other bodily expressions can also signal the social and emotional state of others (Atkinson, Dittrich, Gemmell, & Young, 2004). Several studies have shown amygdala activity to social signals arising from body expressions (Bonda, Petrides, Ostry, & Evans, 1996; de Gelder, Snyder, Greve, Gerard, & Had-

jikhani, 2004; Hadjikhani & de Gelder, 2003). In this work, subjects were presented with images of actors showing bodily expressions of fear, compared to expressions of happiness and nonemotional expressions (de Gelder et al., 2004). Importantly, the facial expressions of the actors depicted in the stimuli were blurred, to control for effects of facial expression on neural activity. Results of these studies showed activity in a network of regions, including the amygdala and fusiform cortex, in the processing of bodily emotional expressions. The amygdala was especially responsive to bodily expressions of fear. This work suggests that the amygdala is not merely sensitive to social signals from the face, but also to other channels of expression, such as those emanating from body posture (although see Adolphs & Tranel, 2003, for a discussion of the pattern of emotion recognition from bodily responses after amygdala damage).

Just as much of the work on the neural response to social stimuli has focused on facial signals, much of the work on the role of the amygdala in processing social stimuli in primates has focused on the visual domain. By contrast, work in other animals has sampled other sensory domains, such as olfaction (Knuepfer, Eismann, Schutze, Stumpf, & Stock, 1995) and audition (Gil-da-Costa et al., 2004; LeDoux, Farb, & Ruggiero, 1990). We note that the relative importance of the visual environment in guiding primate behavior has probably placed selection pressure on the neural structures involved in visual processing. The results of functional neuroimaging studies of the neural response to social stimuli indicate that the amygdala may show a preferential response to social stimuli presented in the visual domain. This could be due to a sampling bias, though, because research on social sounds and smells is less commonly reported than that focusing on visual social signals. In fact, several studies have shown pronounced amygdala responses to odorants (Gottfried, O'Doherty, & Dolan, 2002; Savic, Gulyas, Larsson, & Roland, 2000; Zald & Pardo, 1997); however, the social effects of odorants on human behavior remain unclear (Preti & Wysocki, 1999).

Research on the role of the human amygdala in the realm of auditory social processing has produced mixed results. Work in this area has used two different types of stimuli: nonverbal vocalizations, and affective prosody of spoken words and sentences. Several studies have shown that the amygdala responds to vocal nonverbal emotional expressions, such as screaming and crying (Morris, Scott, & Dolan, 1999; Phillips et al., 1998; Sander & Scheich, 2001). These findings complement results from a study showing impaired recognition of nonverbal emotional expressions in a patient with bilateral amygdala damage (Scott et al., 1997). Studies examining the neural response to another auditory expression of emotion, affective prosody, have not generally reported amygdala activity (Buchanan et al., 2000; Wildgruber et al., 2004; Wildgruber, Pihan, Ackermann, Erb, & Grodd, 2002). Similarly, two studies have shown normal recognition of affective prosody after bilateral amygdala damage (Adolphs & Tranel, 1999; Anderson & Phelps, 1998b). The results of these studies suggest that the amygdala may be a necessary compo-

nent in the processing of nonverbal social information, but that it does not play an integral role in the processing of the affective inflection of spoken language. It may be that the amygdala is responsive to nonverbal auditory stimuli that are more intense and phylogenetically older, such as screams and crying; by contrast, the affective intonation of spoken language may be processed more by cortical regions and less by the amygdala. The distinction between effects of verbal and nonverbal auditory social cues on amygdala activity has not been systematically addressed, however. In spite of the lack of amygdala involvement in the processing of affective prosody, two studies have shown amygdala activity in response to cross-modal presentations of face and voice, wherein amygdala activity is greatest when face and voice both express fear (Dolan, Morris, & de Gelder, 2001; Ethofer et al., 2006). This work supports findings from animal research describing a role for the amygdala in the binding of information across sensory modalities (Murray & Mishkin, 1985; although see Nahm, Tranel, Damasio, & Damasio, 1993, for an exception).

ANATOMY AND NEUROPSYCHOLOGY OF HUMAN AMYGDALA DAMAGE

Although several psychiatric illnesses are thought to involve pathology in the amygdala, overt neurological damage to this structure is not all that common. Posttraumatic stress disorder, the other anxiety disorders, schizophrenia, depression, and autism have all been linked to amygdala pathology (Aggleton, 1992, 2000). On the basis of functional imaging studies, the evidence for amygdala dysfunction in mood disorders is fairly strong (Davidson & Irwin, 1999; Drevets, 2000); however, it leaves open the question of whether such functional abnormality in fact arises from pathology within the amygdala, or is a consequence of pathology elsewhere that has a distal effect on amygdala function. One model of phobias, for instance, is that there is abnormal prefrontal regulation of amygdala function, resulting in an inability to down-regulate amygdala activity as a function of the context in which a stimulus occurs. Similar distal effects on evoked amygdala activation may account for many of the abnormal blood-oxygenation-level-dependent (BOLD) responses in cognitive activation studies that have been reported in a variety of other psychiatric illnesses. In autism, histological and volumetric MRI studies have found abnormal amygdala cell density or volume through development—providing perhaps a stronger link directly to the amygdala as a possible source of pathology in this disorder, and a basis for explaining abnormal amygdala activation in people with autism in fMRI studies. Nonetheless, insofar as autism is a developmental disorder, even these findings leave open the question of primary pathology in the brain.

The most common neurological cause of amygdala damage is medial temporal lobe epilepsy. Depending on the severity and years of duration of the epilepsy, medial temporal lobe sclerosis can damage structures in the medial

temporal lobe that include the amygdala (and prominently also the hippocampus). A fairly common elective surgery for the treatment of medically refractory epilepsy is neurosurgical temporal lobectomy. This also results in variable damage to the amygdala, depending on clinical criteria and the particular approach of the surgeon. In some cases resection of the amygdala is complete, whereas in others there is only damage to adjacent white matter. In all these cases, however, the damage is unilateral and is never selective to the amygdala. Nonetheless, unilateral amygdala damage resulting from temporal lobectomy accounts for by far the largest sample of neurological subjects with amygdala damage (Plate 13.1a in color insert).

Less common is bilateral damage to the medial temporal lobe resulting from encephalitis. Limbic encephalitis and herpes simplex encephalitis are two examples of inflammatory illnesses that can disproportionately damage the medial temporal lobe, and generally do so bilaterally (Plate 13.1b). When severe, such encephalitis can result in complete bilateral destruction of the amygdala; however, it is never selective, typically involving adjacent hippocampal, entorhinal, and parahippocampal regions, and consequently resulting in a dense amnesic syndrome that makes interpretation of the patients' performances on many experimental tasks a challenge.

There are a very few cases of neurological patients who have relatively selective damage to the amygdala. In such patients, the vagaries of a stroke, epilepsy, or surgery result in damage that is relatively restricted to the amygdala on one side or even bilaterally to some extent. One such important patient is S. P., who has been studied in detail by Phelps and colleagues (Anderson & Phelps, 1998a, 2000, 2001). Another is D. R. who has been studied by Young and colleagues (Calder, Young, Perrett, Etcoff, & Rowland, 1996; Young et al., 1995). The most neuroanatomically selective lesion cases can arise in extremely rare individuals who have Urbach–Wiethe disease. This disease, also called lipoid proteinosis, is due to a mutation in the gene coding for extracellular matrix protein 1 and shows an autosomal recessive inheritance pattern (Hamada et al., 2002). Roughly half of the affected individuals have calcifications of medial temporal lobe structures, usually bilateral and often encompassing the amygdala, entorhinal cortex, and surrounding white matter (Hofer, 1973). Little is known about the developmental time course of these calcifications, or about the cellular processes that result in calcification. There appears to be an early developmental calcification of vasculature in the affected structures, followed by atrophy. Several such patients have been studied by Markowitsch and colleagues, who have documented some progression in the disease, and consequences for emotion and memory processing (Babinsky et al., 1993; Markowitsch et al., 1994; Siebert, Markowitsch, & Bartel, 2003).

We have studied two patients with Urbach–Wiethe disease, S. M. (Adolphs, Damasio, Tranel, Cooper, & Damasio, 2000; Tranel & Hyman, 1990) and A. P. Both patients are female; at this writing, S. M. is 40 years old,

and A. P. is 19 years old. Although we do not know the exact onset of their amygdala lesions, both patients presented with bilateral, fairly symmetrical, and relatively restricted lesions to the amygdala when we first scanned them (in her early 20s for S. M. and at age 14 for A. P.), and their neuroanatomy has been stable since. Their lesions are portrayed in panels c and d of Plate 13.1 (in color insert); Plates 13.2 (in color insert) and 13.3 (in color insert) provide further views of A. P.'s lesions. We are conducting additional studies of these rare patients—using high-angular-resolution diffusion-weighted imaging to generate probabilistic maps of anatomical connectivity; using magnetic resonance spectroscopy to examine abnormal metabolites in the region of the lesion, as well as in distal targets of the amygdala; and using cognitive activation studies (echo planar imaging [EPI] with BOLD contrast). For the latter, it is important also to document the possible distortions of the magnetic field that could result from the different magnetic susceptibility of the calcifications in the amygdala compared to surrounding tissue. As shown in Plate 13.2, however, this appears to be a nearly negligible effect, thus perhaps making it possible to examine functional activity even in close proximity to the lesion.

Neuropsychological Profiles of S. M. and A. P.

S. M.'s neuropsychological profile has been described in detail elsewhere (Adolphs & Tranel, 2000; Tranel & Hyman, 1990), and is updated and summarized in Table 13.1. The neuropsychological profile of A. P. has not been published before. S. M. has 12 years of formal schooling and lives independently. A. P. is currently enrolled in college. Both patients are fully right-handed (+100 on the Geschwind–Oldfield questionnaire). We briefly summarize the neuropsychological profiles of the two patients below; Table 13.1 provides quantitative information.

Behavioral Observations

In all testing sessions in our laboratory, S. M. and A. P. have been alert, fully oriented, and entirely cooperative. Their attention and cognitive stamina are intact. S. M.'s interpersonal behavior has been remarkable for a somewhat coquettish, disinhibited style, and this has remained constant across the years. She tends to be very friendly with experimenters and other laboratory personnel, and she has a very comfortable, "hands-on" style of interaction that goes somewhat beyond the norm for conventional U.S. Midwestern culture. However, her behavior is not inappropriate, and she is capable of focusing on specific task and situational demands. It is important to emphasize that S. M. does not exhibit true features of the classic Klüver–Bucy syndrome (Klüver & Bucy, 1937). A. P.'s presentation is reminiscent of S. M.'s, but her interpersonal behavior is less disinhibited. She is friendly and cooperative, and very open and forthcoming in her social interactions. Her parents have noted that

TABLE 13.1. Neuropsychological Profiles for S. M. and A. P.

Test/function	Score/result	
	S. M.	A. P.
Part A: Intellect and academic achievement		
Wechsler Adult Intelligence Scale (WAIS-R for S. M., WAIS-III for A. P.) (age-corrected scaled scores)		
Verbal IQ	86	92
Information	8	10
Digit Span	9	10
Vocabulary	7	10
Arithmetic	6	9
Comprehension	7	9
Similarities	10	8
Performance IQ	95	106
Picture Completion	10	8
Picture Arrangement	14	8
Block Design	9	13
Object Assembly	7	10
Digit Symbol-Coding	7	13
Full Scale IQ	88	98
Wide Range Achievement Test (WRAT-R for S. M., WRAT-III for A. P.) (standard scores)		
Reading	79	113
Spelling	91	118
Arithmetic	72	102
Part B: Memory		
Wechsler Memory Scale—Revised (indexes)		
Verbal Memory Index	90	—
Visual Memory Index	93	—
General Memory Index	89	—
Attention/Concentration Index	87	—
Delayed Recall Index	88	—
Rey Auditory-Verbal Learning Test (AVLT) (# words recalled/15)		
Trial 1	5	6
Trial 2	9	10
Trial 3	11	11
Trial 4	14	13
Trial 5	13	15
30-minute delayed recall	10	12
30-minute delayed recognition (#/30)	29	30
Benton Visual Retention Test		
Number correct (maximum = 10)	5	10
Number errors	7	t0
Complex Figure Test (30-minute recall)	14/36	28/36 (continued)

TABLE 13.1. (continued)

Test/function	Score/result	
	S. M.	A. P.
Part C: Speech and linguistic functions		
Speech		
Fluency	Hoarse	Hoarse
Paraphasias	Normal	Normal
Articulation	None	None
Prosody	Normal	Normal
Linguistic functions		
Boston Naming Test	47/60	46/60
Sentence repetition	15th %ile	—
Reading comprehension 9/10	—	—
Writing	Normal	Normal
Controlled Oral Word Association Test	3rd %ile	3rd %ile
Token Test	44/44	—
Part D: Visuo perceptual and visuoconstructional functions		
Facial Recognition Test	90th %ile	85th %ile
Judgment of Line Orientation	22nd %ile	>74th %ile
Hooper Visual Organization Test	25.5/30	24/30
Complex Figure Test (copy)	32/36	36/36
Drawing to dictation		
Clock	Normal	Normal
House	Normal	Normal
Person	Normal	Normal
Three-dimensional block construction	29/29	—
Grooved Pegboard Test		
Right hand	5th %ile	37th %ile
Left hand	9th %ile	38th %ile
Part E. Executive control and related functions		
Wisconsin Card Sorting Test		
Number Correct	68	73
Errors	27th %ile	25th %ile
Perseverative responses	53rd %ile	32nd %ile
Nonperseverative errors	18th %ile	58th %ile
Perseverative errors	84th %ile	8th %ile
Number of categories	6 (>16th %ile)	6 (>16th %ile)
Trail-Making Test		
Part A	45	54
Part B	35	42

(continued)

TABLE 13.1. (continued)

Test/function	Score/result	
	S. M.	A. P.
Tower of Hanoi (# moves; means for age-matched controls in brackets)		
Trial 1 [80.6]	120	120
Trial 2 [61.4]	97	53
Trial 3 [63.6]	57	61
Trial 4 [59.8]	88	120
Tower of London		
Minimum moves	86	—
Excess moves	20	—
% above optimal strategy	23	—
Part F: Standardized personality assessment		
Minnesota Multiphasic Personality Inventory (MMPI-2 for S. M., MMPI-A for A. P.) (<i>T</i> -scores)		
Scale <i>L</i>	66	58
Scale <i>F</i>	48	42
Scale <i>K</i>	59	57
Scale 1	72	46
Scale 2	51	46
Scale 3	68	48
Scale 4	75	41
Scale 5	66	59
Scale 6	56	41
Scale 7	67	43
Scale 8	68	45
Scale 9	53	39
Scale 0	49	34
Part G: Further tests of social function		
Bar-On Emotional Quotient Inventory, short form (<i>z</i> -scores)		
TRA (Intrapersonal)	-0.7	0.07
TER (Interpersonal)	0.6	-0.02
SMS (Stress Management)	-0.3	1.0
AS (Adaptability)	-0.8	0.3
GMS (General Mood)	-0.5	-0.9
PIS (Positive Impression)	-1.2	0.2
EQ (Total Emotional Quotient)	-0.8	-0.1
Endler Multidimensional Anxiety Scales (nonsocial anxiety)	All in the normal range	All in the normal range
Endler Multidimensional Anxiety Scales (social anxiety)	All in the normal range	All in the normal range

(continued)

TABLE 13.1. (continued)

Test/function	Score/result	
	S. M.	A. P.
Social Problem Solving Inventory, Revised (<i>z</i> -scores)		
PPO	0.4	-0.5
NPO	-0.1	-0.3
PDF	-1.2	0.2
GAS	0.5	0.1
DM	-1.0	0.3
SIV	-0.8	-0.1
RPS	-0.7	0.1
ICS	0.8	-1.8
AS	0.1	-0.8
RAW (overall score)	-0.3	1.0
NEO Personality Inventory (<i>z</i> -scores)		
Neuroticism	-0.6	-0.1
Extraversion	2.0	-2.0
Openness	0.5	1.1
Agreeableness	-0.8	-1.0
Conscientiousness	-1.4	0.5

she tends to “trust” people too easily, and the parents have made an effort to teach her to be more wary of strangers. A. P.’s behavior in the laboratory setting is entirely appropriate. We discuss the “social cognition” of the patients in more detail in the next section.

Intellect and Academic Achievement

Part A of Table 13.1 presents data from the Wechsler Adult Intelligence Scale (WAIS) and the Wide Range Achievement Test (WRAT). S. M.’s IQ scores have remained stable across time. Her intellectual abilities range from the lower end of the average range to the upper end of the low average range—within typical expectations, given her educational and occupational background. Academic achievement skills range from average (spelling) to borderline (reading, arithmetic), commensurate with her educational background. A. P.’s intellectual abilities fall mainly in the average range, although a couple of her WAIS Performance subtest scores are high average (Block Design, Digit Symbol-Coding). All of the IQ scores for A. P. are in the average range. A. P. scored in the high average range on the Reading and Spelling subtests of the WRAT, and in the average range on the Arithmetic subtest. Like S. M., A. P. shows no indication of defects on any of the intellectual and achievement subtests.

Memory

Performances on various memory tests for the two patients are enumerated in Part B of Table 13.1. S. M.'s performances on all various components of the Wechsler Memory Scale—Revised are fully within normal expectations. As judged from the Rey Auditory–Verbal Learning Test (AVLT), S. M.'s ability to acquire and retain verbal information is intact. The same is true of A. P., who had a perfect 15/15 score on Trial 5 of the AVLT, and a perfect delayed recognition score of 30/30. S. M. has a mild weakness in the domain of nonverbal, visual memory (Benton Visual Retention Test, Complex Figure Test recall), which has characterized her profile over many years and has remained stable across time. A. P. scored perfectly on the Benton Visual Retention Test, and her performance on the Complex Figure Test recall is normal. Overall, both patients demonstrate essentially normal ability to acquire and retain declarative information, although S. M. may have a mild weakness for nonverbal, visuospatial material.

Speech and Linguistic Function

The findings for speech and linguistic function assessment are enumerated in Part C of Table 13.1. Both patients have markedly hoarse speech, characteristic of persons with Urbach–Wiethe disease (and both patients have had multiple vocal cord operations). With this exception, the speech of both patients is normal in every respect: Fluency, articulation, and prosody are intact, and there are no paraphasic errors. Linguistic functioning is also intact in both patients. However, both patients performed defectively (3rd percentile) on the Controlled Oral Word Association Test, which could suggest an “executive functioning” defect (see below).

Visuoperceptual and Visuoconstructional Functions

Part D of Table 13.1 enumerates data for tests of visuoperceptual, visuospatial, and visuoconstructional functioning in the two patients. For both patients, these abilities are essentially intact across the board (although S. M.'s psychomotor skills, as indexed by the Grooved Pegboard Test, are somewhat weak). These are important findings, especially in the realm of visual perception, and it is worth reiterating that there is no indication that the patients suffer from any type of basic visual information-processing disturbance that might contribute to their many defective performances on tests of facial emotion recognition and other related experiments reviewed elsewhere in this chapter.

Executive Control and Related Functions

Data for executive control and related functions are enumerated in Part E of Table 13.1. Both patients produced normal performances on the Wisconsin

Card Sorting Test and on the Trail-Making Test. By contrast, both of them demonstrated some difficulty with the Tower of Hanoi task, and as noted above, both produced relatively poor performances on the Controlled Oral Word Association Test. Thus the data hint at some mild “executive functioning” defects—something we have noted previously for S. M.

Personality Assessment

Part F of Table 13.1 summarizes the *T*-scores from the Minnesota Multiphasic Personality Inventory (MMPI), a standard measure of personality and psychopathology. The important conclusion to be drawn from these data is that neither S. M. nor A. P. evidences any form of significant psychopathology. The profiles are not suggestive, nor is there any evidence from their everyday lives, of a formal psychiatric diagnosis. Neither patient has ever manifested clinically significant depression or anxiety.

Further Tests of Social Functioning

Additional test scores are summarized under Part G of Table 13.1, all in *z*-scores from published norms. Again, what is most notable here is that neither patient's scores are abnormal, and in those cases where there might be a trend toward abnormality, they often go in opposite directions. In particular, there is no evidence of impairment on the Bar-On Emotional Quotient Inventory or on measures of anxiety, including social anxiety. Consistent with the results from the MMPI given in Part F, there is no evidence of psychopathology from the NEO Personality Inventory.

SOCIAL COGNITION FOLLOWING AMYGDALA DAMAGE

Our earlier work and considerable work by others suggested the view that the amygdala is “specialized” for processing information about fear. Amygdala lesions resulted in a disproportionate impairment in the recognition of fear from facial expressions, compared to other emotions (Adolphs, Tranel, Damasio, & Damasio, 1994; Calder, Young, Rowland, & Perrett, 1996), and viewing facial expressions of fear resulted in amygdala activation in healthy individuals (Morris et al., 1996; Whalen et al., 2001). Although it is now clear that the amygdala is not so specialized for fear, but processes a broader range of emotions, it remains the case that S. M. is much more impaired in recognizing fear from facial expressions than in recognizing other emotions. Patient S. M. has been especially informative here because of the specificity of both her lesion and her impairment (Adolphs et al., 2000; Tranel & Hyman, 1990; see Plate 13.1d in color insert). On a series of tasks, S. M. has shown disproportionate impairment in recognizing the intensity of fear from faces (Adolphs

et al., 1994). When asked to rate the intensity of fear and of other emotions in facial expressions, S. M. was relatively selectively impaired in regard to faces showing fear, with a much slighter impairment also in conceptually related emotions, such as surprise and anger. In addition, it was found that S. M. was impaired in her ability to judge the level of arousal of emotions with negative valence (unpleasant emotions), including fear, anger, disgust, and sadness. Since fear is normally judged to be one of the most arousing unpleasant emotions, S. M.'s impairment may be disproportionate to fear for this reason.

The amygdala's role is not limited to making judgments about basic emotions, but includes a role in making social judgments. This fact was already suggested by earlier studies in nonhuman primates (Kling & Brothers, 1992; Kliiver & Bucy, 1937; Rosvold, Mirsky, & Pribram, 1954), which demonstrated impaired social behavior after amygdala damage. It has been corroborated in recent times by studying monkeys with more selective amygdala lesions, and by using more sophisticated ways of assessing social behavior (Emery & Amaral, 1999; Emery et al., 2001); it has also been shown now in humans. Building on these findings, some recent studies suggest a general role for the amygdala in so-called "theory-of-mind" abilities—the collection of abilities whereby we humans attribute internal mental states, intentions, desires, and emotions to other people (Baron-Cohen et al., 2000; Fine, Lumsden, & Blair, 2001). Relatedly, the amygdala shows differential habituation of activation to faces of people of a different race from the viewer (Hart et al., 2000), and amygdala activation has been found to correlate with race stereotypes of which the viewer may be unaware (Phelps et al., 2000). However, the amygdala's role in processing information about race is still unclear: Other brain regions, in extrastriate visual cortex, are also activated differentially as a function of race (Golby, Gabrieli, Chiao, & Eberhardt, 2001), and lesions of the amygdala do not appear to impair race judgments (Phelps, Cannistraci, & Cunningham, 2003).

In studies using faces as stimuli, we found that subjects with bilateral amygdala damage were also impaired in judging the untrustworthiness of faces from their appearance. Although they were able to judge trustworthy-looking faces normally, both in terms of the absolute ratings these faces were given and in terms of their relative rank order, subjects with bilateral amygdala damage failed to rate normally those faces that are normally judged to look the least trustworthy (Adolphs, Tranel, & Damasio, 1998). The impairment consisted of two components: a general positive bias for rating faces normally judged to look untrustworthy, and an inability to rank or discriminate those faces in terms of their perceived trustworthiness. The finding was followed up by a functional imaging study, which corroborated the basic finding: Activation of the amygdala was correlated with the judged untrustworthiness of the face. That study also found activation to perceived untrustworthiness in the insula, and it was able to show that amygdala activation to untrustworthy faces held even when other factors were minimized: The stimuli were all direct

gaze, all faces were male, and emotion ratings were used as covariates in the analysis (Winston, Strange, O'Doherty, & Dolan, 2002).

Another study examined recognition of social emotion in individuals with amygdala damage, using a set of stimuli developed by Baron-Cohen for research into theory-of-mind abilities in people with autism. When shown faces that signal complex and social mental states, patients with bilateral amygdala damage performed disproportionately worse than comparison subjects (Adolphs, Tranel, & Baron-Cohen, 2002). Furthermore, the impairment held when just the eye region of the faces was shown, consistent with the idea that the eyes signal considerable social information that depends on the amygdala for its processing.

Although we will come back to the role of specific facial features, such as the eyes, it is worth noting a study in which the importance of the face, relative to other visual information, was examined. S. M.'s inability to recognize fear (as well as the impairments of other subjects with unilateral and bilateral amygdala damage) was relatively specific to faces, as opposed to other contextual visual information (Adolphs & Tranel, 2003). In that experiment, subjects were presented with scenes showing people that included facial expressions, as well as with the same scenes with the faces erased. Whereas nondisabled subjects' performance accuracy in judging the emotion decreased when the faces were erased (as one would predict, given that the face is a potent source of social information), the performance of subjects with amygdala damage did not suffer the same decrement. Indeed, for negative emotions, subjects with bilateral amygdala damage performed better when they were shown the stimuli with the faces erased than when the faces were present—presumably indicating that when the faces were present, they attempted to recognize them but got them wrong (Figure 13.1).

One interpretation of the data, and one that is still likely to be part of the story, proposed that the amygdala would link two kinds of representations: a visual representation of the other person's face one is viewing; and a somatic representation that would simultaneously represent one's own emotional response to seeing the person's face, as well as the presumed emotional state of that person (Adolphs, 2002). This link effected by the amygdala could be fairly direct (via direct projections from the amygdala to the insula, an interoceptive somatosensory cortex), or more indirect (via first eliciting an actual emotional response in the viewer's body that could then subsequently be represented in structures like the insula). There are now several studies indicating that the observation of another person's emotional state recruits structures like the insula (Jackson, Meltzoff, & Decety, 2005; Singer et al., 2004), which is also involved in representing one's own somatic states. Interestingly, the insula has been hypothesized (Craig, 2002; Damasio, 1999) and recently shown (Critchley, Wiens, Rotshtein, Oehman, & Dolan, 2004) to be associated with the conscious experience of one's own body state. This suggests that one person's knowledge of another person's emotional state through

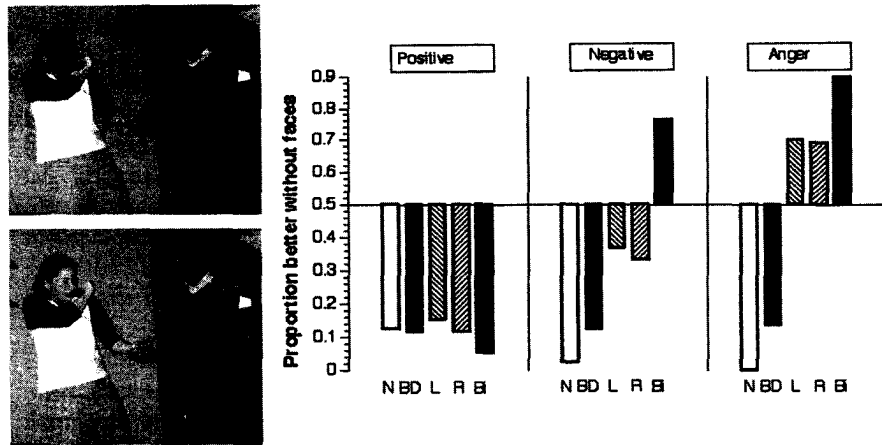


FIGURE 13.1. Recognition of emotion from emotional scenes with facial expressions or with erased faces. *Left:* Examples of the stimuli. *Right:* Performance accuracy in recognizing basic emotions. Bars going downward represent better accuracy on scenes with faces; bars going upward represent better accuracy on scenes with faces erased. Data are broken down for positive emotions, negative emotions, and anger. N, healthy comparison subjects; BD, brain-damaged subjects with no amygdala damage; L, R, subjects with unilateral left or right amygdala damage from surgical temporal lobectomy; Bi, subjects with complete bilateral amygdala damage. From Adolphs and Tranel (2003). Copyright 2003 by Elsevier. Reprinted by permission.

simulation of his or her presumed somatic state relies on a simulation that is explicit, in the sense of providing conscious access to the emotion being simulated. That is, the simulation mechanism through which one infers another person's emotion is empathic: It involves actually feeling (aspects of) the emotion of the other person.

In one study from our laboratory, we found evidence supporting a role for simulation in emotion recognition (Adolphs et al., 2000). In a lesion study of 108 patients with focal brain damage, it was found that lesions in right somatosensory cortices (including the insula) were associated with impairments in the ability to recognize emotion from other people's facial expressions. One interpretation of the findings was as follows: In order to trigger an image of the somatosensory state associated with an emotion, a viewer uses structures that link perception of the stimulus (the facial expression seen) to a somatic response (or directly to the representation thereof). One route for triggering such an emotional response to viewing another person's expression in the first place would be structures such as the amygdala.

This account of how one person might infer another's emotional state via an essentially simulation-based mechanism (Goldman & Sripada, 2005) has turned out to be an incomplete picture. A key recent insight has been that

the generative nature of cognition is driven not only by the inferences made once sensory information has been perceived; it is driven also by the possibility of discovering new information in the environment in the first place. We humans explore our environment, and we actively seek out social information. This idea was borne out in a more recent study (Adolphs et al., 2005) of Patient S. M., who, as discussed above, is impaired in the ability to use information from a diagnostic facial feature—the eye region of the face. To establish this, we used a new technique to assess the use of visual information from faces (Gosselin & Schyns, 2001, 2002). The method is called “bubbles” and addresses an important open question: What is it about certain faces that makes them look fearful? This method, akin to reverse correlation, randomly samples a stimulus space to extract those components of the space that drive behavioral discrimination. We used a three-dimensional search space for faces: the two dimensions (x, y) of the image plane, plus a dimension of spatial frequency into which the face has been decomposed (Figure 13.2). Thus a given trial shows only randomly revealed areas of the face at each spatial frequency band, determined by the number of bubbles (e.g., the sample stimulus shown at the far bottom right of Plate 13.4 in color insert). The more bubbles there are, the more area of the face is revealed to a viewer. The viewer then makes a judgment based on what is revealed. Regressing performance across all the trials (the dependent measure) onto the bubbles masks used in each trial (the predictor variables) yields a z -score for each sampled region of the image space. The entire image search space can then be statistically thresholded to reveal those portions of the image search space at which there was a significant association between the part of the face that was revealed and performance accuracy.

In order to visualize this statistically thresholded search space, it is superimposed on a face base image (one of the images that was sampled in the first place). The result is what is shown in Plate 13.4a: Those regions of the face that are visible are the portions of the face search space within which there was a statistically reliable association (at $p < .05$) between showing that region

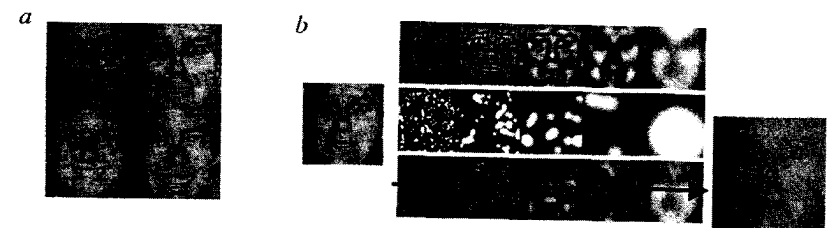


FIGURE 13.2. Construction of “bubbles” stimuli. (a) Four initial faces were normalized and (b) sampled at five bands of spatial frequencies to yield the final stimuli that subjects saw (far bottom right). Total bubbles provided were adjusted online to maintain performance throughout the task at 75% correct. From Adolphs et al. (2005). Copyright 2005 by the Nature Publishing Group. Reprinted by permission.

and the viewer's performance accuracy in classifying the stimulus as "happy" or "afraid." One interpretation of Plate 13.4a (in color insert) is that it depicts the visual information that viewers rely on to make judgments about the face. We found that S.M. failed to use the eye region of faces effectively in order to discriminate fear (Plate 13.4a).

These findings fit well with other results showing amygdala activation to fearful eyes (Morris, deBonis, & Dolan, 2002), or only to the briefly presented whites of eyes (Whalen et al., 2004). A further role for the amygdala in processing aspects of faces comes from studies of the interaction between facial emotion and eye gaze. The direction of eye gaze in other individuals' faces is an important source of information about their emotional state, intention, and likely future behavior. Eye gaze is a key social signal in many species (Emery, 2000), especially apes and humans, whose white sclera makes the pupil more easily visible and permits better discrimination of gaze. Human viewers make preferential fixations onto the eye region of others' faces (Janik, Wellens, Goldberg, & Dell'Osso, 1978)—a behavior that appears early in development and may contribute to the socioemotional impairments seen in such developmental disorders as autism (Baron-Cohen, 1995). Eyes signal important information about emotional states, and there is evidence from functional imaging studies that at least some of this processing recruits the amygdala (Baron-Cohen et al., 1999; Kawashima et al., 1999; Wicker, Perrett, Baron-Cohen, & Decety, 2003). The interaction between facial emotion and direction of eye gaze has been explored only very recently. It was found that direct gaze facilitated processing of approach-oriented emotions such as anger, whereas averted gaze facilitated the processing of avoidance-oriented emotions such as fear (Adams, Gordon, Baird, Ambady, & Kleck, 2003), and that this processing facilitation correlated with increased activation of the amygdala in a functional imaging study (Adams & Kleck, 2003).

In fact, we found that the deficit was even more basic: The reason why S. M. did not use information about the eye region effectively was that she did not fixate the eye region in the first place (Plate 13.4b). This finding is based on her eye-tracking performance during an emotion judgment task, to assess where she directed her gaze when viewing face stimuli. We instructed S. M. to direct her gaze onto the eyes of other people's faces, and found that this manipulation temporarily allowed her to generate a normal performance on a fear recognition task in which she was otherwise severely impaired. We could thus trace a causal chain from an impaired inclination spontaneously to fixate the eyes in other people's faces, to an impaired ability to make use of information from the eye region of faces, to our earlier reported impairments in judgments about the emotional and social nature of those faces (Adolphs et al., 1994, 1998).

It is worth noting two key further results from the study of patient S. M. described above (Adolphs et al., 2005). S. M. failed to fixate the eyes in any face, not just facial expressions of fear. In fact, she simply failed to explore faces in general, which included a failure to direct her gaze toward the eye

region. We have attributed the finding that this general impairment resulted in a relatively specific impairment in fear recognition to the further fact that the eye region of the face is in fact the most diagnostic for signaling fear, rather than other emotions, on our discrimination task (Smith, Cottrell, Gosselin, & Schyns, 2005). Interestingly, unpublished data indicate that S. M. does fixate the eye region when the faces are shown inverted (Adolphs, Buchanan, & Tranel, unpublished data). So, while the brain does not first need to know that a face is showing fear in order for the impaired eye fixations to occur, it apparently does need to know that the stimulus is a face.

A second point worth noting is that the explicit instruction to fixate the eyes in faces, while rescuing S. M.'s impaired recognition of fear, did so only transiently (as long as that block of the experiment lasted). When later asked to view faces, S. M. spontaneously reverted to her lack of exploration of the face, and once again showed impaired fear recognition. One reason why the improvement was not more permanent may well be that S. M. was unaware that she failed to fixate the eyes, as she was unaware that her performance in fear recognition was impaired. This raises further questions: Why did she not ask about her performance? Why did she not notice that she failed to fixate the eyes? These questions point toward a broader interpretation of the impairment: S. M., as a result of damage to her amygdala, lacks a normal mechanism to explore the environment. One aspect of this impairment is a failure to fixate the eyes in faces, to explore them normally with her gaze. Another aspect of the impairment in this particular experiment was a failure to question what was going on in any way, or to monitor her own performance during the experiment. In both instances, there remains a passive ability to process sensory information, but the instrumental component of seeking out such information in the first place has been severely compromised. This interpretation is related to other proposals of amygdala function in social exploration (Sander et al., 2003) and stimulus disambiguation (Whalen, 1998), and fits also with the known role of the amygdala in modulating attention in both animals (Holland & Gallagher, 1999) and humans (Anderson & Phelps, 2001; Vuilleumier, Armony, Driver, & Dolan, 2001). It raises important open questions: Can the amygdala's role in decision making be formalized as a role in exploring new choice options? Is its role disproportionate for exploring social options, or does it play an entirely domain-general role in exploring options regardless of their social nature (Adolphs, 2003)?

It has been well established that the amygdala is critical for processing various aspects of emotion, and in particular for perceiving negative emotions such as fear. One question that has remained unanswered, though, is whether S. M. has a normal phenomenological experience of emotion, especially negative emotion. To explore this, we designed a study in which two experienced clinical psychologists who were not provided any background information regarding S. M. conducted interviews with her (Tranel, Gullickson, Koch, & Adolphs, 2006). The psychologists were asked to interview S. M. to determine whether she exhibited any psychopathology, with a special eye toward her

emotional phenomenology. Both of them reached the conclusion that S. M. expressed a normal range of affect and emotion, and neither felt that she warranted a formal psychiatric diagnosis. However, they both noted that S. M. was remarkably dispassionate when relating highly emotional and traumatic life experiences, and they noted that she did not seem to have a normal sense of distrust and "danger." Indeed, to the psychologists, S. M. came across as a "survivor"—as being "resilient" and even "heroic" in the way she had dealt with adversity in her life. In full light, however, these observations reflect the fact that S. M. is missing from her phenomenology of life some of the deepest negative emotions, in a manner that parallels her defect in perceiving such emotions in external stimuli. These findings have interesting parallels with recent animal work (cf. Bauman et al., 2004b), and they provide valuable insights into the emotional life of an individual with complete bilateral amygdala damage.

AN INTEGRATIVE MODEL FOR THE SOCIAL FUNCTIONS OF THE HUMAN AMYGDALA

In this chapter, we have provided evidence for a model of amygdala function in social processing. On the basis of previous work suggesting a role for the amygdala in processing ambiguity and/or relevance (Sander et al., 2003; Whalen, 1998), we suggest that the social environment constitutes an especially ambiguous set of stimuli, and that the amygdala is critically involved in the disambiguation of such sets of stimuli. This model provides a parsimonious account of data from lesion studies of nonhuman primates and humans, as well as from neurophysiology and functional neuroimaging studies. The framework treats the amygdala as making a contribution to the motivation to seek out certain stimuli, or certain features of stimuli, at the expense of others. This role may well be analogous to a filter (enabling an individual to disregard information that is irrelevant), and it may also involve actively seeking out information. Together, these components can specify what is salient in the environment—what needs to be paid attention to, what should be assigned priority for further processing, and what stimuli have a premium on behavioral modulation.

The prediction and comprehension of others' behavior are clearly extremely important aspects of social functioning. There are any number of ways that conspecifics—whether they are rhesus monkey cage mates or coworkers in an office—may behave. The accurate recognition of conspecific behavior may proceed without explicit awareness in healthy individuals. An inability to understand the ambiguous behavior of others could produce profound deficits in social functioning, as evidenced by monkeys with early-onset bilateral amygdala damage. The altered affiliation and social withdrawal behaviors of these animals may reflect the inability to make sense of socially

relevant situations without a functioning amygdala. It is perhaps no surprise, then, that one of the hallmarks of proper social development is a predictable (unambiguous) relationship between a mother and infant (Bowlby, 1969). The descriptions of monkeys with neonatal amygdala lesions demonstrate abnormal relationships between infants and mothers initially, and this abnormality is later evidenced between these infants and their peers (Bauman et al., 2004a, 2004b). It is an intriguing possibility that such altered relationships between mothers and amygdala-damaged infants set the stage for later abnormalities in social behavior.

The instrumental role for the amygdala in seeking out potentially relevant social information we have sketched above needs, of course, to be situated with the amygdala as one component in a distributed neural system. Given the evidence for fast subcortical visual inputs to the amygdala (Johnson, 2005), as well as slower but more fine-grained visual information conveyed through cortical routes (Amaral et al., 1992), an important open question concerns the point in time at which the amygdala comes into play. There are rapid visually evoked responses even to fairly complex social scenes (Oya, Kawasaki, Howard, & Adolphs, 2002), demonstrating that at least some superordinate categorization of such stimuli in terms of their social meaning can occur within about 120 msec. One possibility is that the amygdala's modulation of eye movements and visual attention, perhaps in part via its projections back to visual cortices, comes into play very early and depends largely on subcortical visual inputs. This would make it possible, in principle, for the amygdala to modulate visual attentional processing in visual cortices (Anderson & Phelps, 2001; Vuilleumier et al., 2004) at the earliest processing times—before the cortical information has even reached the amygdala. This attentional modulation at early processing times by the amygdala may then be followed by a longer-latency role, based on cortical visual inputs as well as contextual modulation and self-regulation, in which it triggers emotional responses and participates in a simulation-based reconstruction of social information. It would seem likely that these two components depend, moreover, on separate nuclei within the amygdala.

WHAT WE THINK

This chapter raises two potentially conflicting views. Clearly, the amygdala is important for aspects of social cognition and social behavior; equally clearly, it is involved in aspects of attention, emotion, and memory that have nothing at all to do with social behavior (e.g., fear conditioning). So does the amygdala contribute something essential that is specific to social cognition? If so, what?

As we speculate on answers to this question, two points are worth making. Given the many functions in which the amygdala has been implicated, and given that it consists of over a dozen nuclei in primates, it will participate in both social and nonsocial aspects of cognition and behavior. Nonetheless, the question above

remains: Are there some aspects of amygdala function that are socially specialized? The second point is that it is not clear that there is any aspect of social cognition that does not have a nonsocial basis. Nonetheless, the question remains whether certain features of social cognition make processing demands unlike those posed by nonsocial stimuli.

Rather than trying to identify a single aspect of information processing that might distinguish social cognition and the amygdala's role in it, we may do better to acknowledge that social cognition is distinguished by the sheer variety of processes that come into play, and the way in which they need to be integrated. We are reminded here of the hodological analysis of Young, Scannell, Burns, and Blakemore (1994), which represents the amygdala as centrally connected in a multidimensional scaling representation. By modulating social cognition at the earliest times as well as at later times, at attention, perception, memory, decision making, and emotional reaction, the amygdala may be particularly well positioned to contribute what is the hallmark of social cognition: modulating all of cognition.

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PART III

Human Amygdala Dysfunction