Preface

The amygdala, or more properly the amygdaloid complex, is about 2.0 cm^3 on each side of the human brain. If a normal adult brain is approximately 1,300 cm^3, then the amygdala makes up about 0.3% of its volume. The human amygdala has about 12 million neurons on each side. This compares to estimates of 100 billion neurons in the entire brain and 20 billion in the cerebral cortex. By any quantitative measure, the amygdala makes up a very small portion of the human brain. Yet there is virtually no psychiatric or neurological disorder in which it has not been suggested to play an important role.

Why is the amygdala so popular in neuropsychiatry? And why edit a book on it? The answer to these questions is that despite its small size, the amygdala is one of the most densely connected structures in the brain. This feature of connectivity, in turn, fits very well with hypotheses about not only psychiatric illnesses (that they are disconnection or misconnection syndromes in many cases), but also the functions that the amygdala is thought to implement. First and foremost among these latter hypotheses is that the amygdala helps orchestrate global organismic states that we call "emotions"—states that are pervasively dysfunctional in psychiatric illness, but that also show considerable variation across individual differences in the healthy population. In short, the reason for interest in the amygdala derives from its pervasive role: In implementing emotional states, it modulates nearly every cognitive function one can think of.

Much of what we know about the function of the amygdala has come from studies in which it is damaged in one way or another, and the resulting alterations of behavior are evaluated. There are dangers in this

approach, since it is clear that all behaviors are subserved by many brain regions linked together in multiple functional systems. On the one hand, the brain does not resign itself to the damage of one of the component structures but attempts to reorganize in order to optimize its ability to deal with a complex environment. On the other hand, very convergent story lines for the function of the amygdala emanate from lesion studies in both humans and experimental animals. While the era of permanent lesions is rapidly giving way to strategies for genetically mediated transient inactivation, the hypotheses that are being tested with these new techniques have arisen from lesion studies.

Our goal in this book was to take stock of what has been learned from humans and nonhuman experimental animals that are living their lives without a functioning amygdala. We decided early on to focus primarily on research carried out in human patients and in nonhuman primates. However, it is clear that much of what is known about the amygdala has come from research in rodents. To represent this body of research, Sarro and Sullivan (Chapter 4) summarize their research on the role of the amygdala in the early development of behavior. Kim, Choi, and Lee (Chapter 5) provide an overview of their use of novel approaches toward quantifying fear in rodents in a controlled but naturalistic foraging task.

Since the book is heavily focused on primate studies, Schumann, Vargas, and Lee (Chapter 2) remind us of the complex neuroanatomical organization of the amygdaloid complex. Amaral (Chapter 3) provides a historical summary of the studies carried out in nonhuman primates that played a major part in our current appreciation of the role of the amygdala in emotional regulation. He also discusses the period of psychosurgery in which human patients received bilateral amygdalectomy for control of seizures and unmanageable behavior.

There are a number of chapters related to nonhuman primate research. Bliss-Moreau, Moadab, and Amaral (Chapter 6) and Bachevalier, Sanchez, Raper, Stephens, and Wallen (Chapter 7) describe studies in which rhesus monkeys receive lesions very early in life and are then raised in seminaturalistic environments with their mothers and social groups. These chapters raise the issue of plasticity and change in the effects of these early lesions as the animals mature. The effects of losing amygdala function as an adult in relation to anxiety are discussed by Oler, Fox, Shackman, and Kalin (Chapter 8). Murray and Rhodes (Chapter 9) explore the consequences relative to cognitive and emotional behavior of losing amygdala function in the mature rhesus monkey.

Several chapters in the book focus on patients who have the mysterious Urbach–Wiethe syndrome, which can often result in relatively selective, bilateral damage of the amygdala. Feinstein, Adolphs, and Tranel (Chapter 1) present the human perspective of living without an amygdala through interviews with patient S. M., who has been studied by

this group for several decades. Adolphs (Chapter 10) reviews data from several patients with Urbach–Wiethe syndrome and indicates that there are several challenges for the future of this research, including better delineation of the lesions, concurrent neuroimaging to quantify systems-level changes following amygdala lesions, and comparisons across different ages. Van Honk, Terburg, Thornton, Stein, and Morgan (Chapter 12) describe their studies of South African patients with Urbach–Wiethe syndrome and begin to raise the issue of whether alteration of function can be localized to one or more regions of the amygdala based on patients with subnuclear damage. And Patin and Hurlemann (Chapter 11) again raise the issue of compensatory adaptations after damage by studying monozygotic twins who are affected by Urbach–Wiethe syndrome.

There are relatively few individuals who have bilateral lesions of the amygdala due to disease, but unilateral amygdalectomy is still a common practice for the alleviation of epilepsy. Todd, Anderson, and Phelps (Chapter 13) describe one patient who apparently had unilateral damage to the amygdala on one side, then the removal of the opposite amygdala when she was 47 years old for treatment of her seizure disorder. They recount some of the sequelae of this loss of amygdala function in an adult.

The book ends with a synthesis chapter by Monk and Pine (Chapter 14), which delves into the role of the amygdala in psychiatric disorders. The Epilogue by Amaral and Adolphs looks back at what we have learned from lesions of the amygdala, what have been lost opportunities, and where the future of amygdala research may be heading.

We asked the authors to present their material in a way that would be accessible to researchers, clinicians, and the lay audience. Taken together, these chapters provide a glimpse into the worlds of individuals who have lost the ability to detect dangers in their environment and how that impacts their lives. They also tell a story of how the brain compensates for brain damage, particularly when it occurs early in life. However, the adaptation is never complete, and loss of the amygdala, with its unique structure and connections with other brain regions, has a lifelong impact on the individual.

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