Neurobiology of Grooming Behavior

Grooming is among the most evolutionary ancient and highly represented behavior in many animal species. It represents a significant proportion of an animal's total activity and between 30% and 50% of their total awake time. Recent research has demonstrated that grooming is regulated by specific brain circuits and is sensitive to stress, as well as to pharmacological compounds and genetic manipulation, making it ideal for modeling affective disorders that arise as a function of stressful environments, such as stress and post-traumatic stress disorder. Over a series of 12 chapters that introduce and explain the field of grooming research and its significance for the human and animal brain, this book covers the breadth of grooming animal models while simultaneously providing depth in introducing the concepts and translational approaches to grooming research. The book is written primarily for graduates and researchers within the neuroscientific community.

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Preface

Grooming and related behaviors

Behavioral and pharmacological research continues to play a crucial role in modern neuroscience, often spearheading new and innovative techniques and models that further our understanding of the intricate workings of the nervous system. This is particularly evident in the arena of mental health research where, with the help of animal models and novel genetic or pharmacological treatments, new insights and theories are evolving to conceptualize more accurately common brain disorders such as anxiety, depression, obsessive–compulsive disorder (OCD), and schizophrenia.

These advances are allowing for an unprecedented examination of the heritable and environmental factors that contribute to disease pathogenesis. However, although there has been marked progress, the biological substrates of many of these disorders remain unclear. To establish a more concrete understanding of these disorders, a careful dissection of experimental phenotypes must be pursued. In this way, every aspect of behavior is a potentially fruitful source of experimental data that can provide clues to the contributing mechanisms.

One important example of such a behavior is grooming. Grooming is a very highly represented behavior in many animals, comprising a large proportion of their waking time. It serves an incredibly diverse range of purposes in the life of the animal from chemocommunication to basic hygiene. It is a natural behavior, yet it can be induced as part of an experimental procedure and has been shown to be sensitive to stress and bidirectionally sensitive to anxiolytic and anxiogenic drugs in rodents, making it an ideal focal point for high-throughput behavioral studies.

In the clinic, this behavior plays a similarly important role. The complexity of human grooming behavior, of course, goes beyond simple measures of hygiene and mate attraction. However, it has proven to be an invaluable tool in clinical

diagnostic assessment. Abnormalities in human self-grooming are often a component of disorder symptomology, and there are a variety of grooming disorders, such as trichotillomania, that involve behaviors like biting the nails or picking at the skin, which are indicative of a larger mental health issue.

The span of grooming behavior will be explored here in the following chapters, providing an updated summary of current research on this important topic. The opening chapter of the book will give a concise introduction, providing a comprehensive summary of past research on grooming behavior. It includes an exposition of the theoretical justifications in grooming studies, and how these are evolving to give researchers an accurate view of this quickly developing field.

The causes of grooming behaviors and environmental factors that affect them are a very active area of research. Continuing on this theme, another chapter specifically explores grooming as a response to olfactory stimuli. Here, the authors detail their research on grooming phenotypes that differentially self-groom when they come into contact with different conspecifics, and discuss the implications of this research for viewing grooming as a vehicle for targeted social communication. The olfactory component of grooming also plays a key role in animal reproductive behaviors, and the chapter examines this as a way that mate eligibility is conveyed.

Along with olfactory communication, grooming serves many other practical roles in animal behavior, and is often accompanied by behavior-associated hair loss known as barbering. These are complex, ethologically rich behaviors with sensitivity to alterations in activity and microstructure. Another chapter elucidates the utility of grooming analysis for assessing stress in individual animals, testing of psychotropic drugs, phenotyping mutant or transgenic animals, as well as selecting proper strains for experimental modeling of affective disorders. The chapter will also discuss ethologically based approaches to the assessment of animal grooming and barbering activity, present examples of genetic variation leading to altered grooming and barbering phenotypes in rodents, and summarize the growing value of these two phenotypes for translational neurobehavioral research.

In addition to barbering, there are additional forms of social grooming behavior that entail physical contact between conspecifics. Social grooming, as well as rough-and-tumble play, caressing, and hand-shaking, are all touching behaviors that are an integral part of social communication. One chapter will review the neurochemical pathways that regulate these behaviors, as well as the touch-induced changes in mood across mammals. Touching (as an important form of communication) will be discussed, with a focus on the subcortically regulated emotional state of the interactants and the cortically mediated modulation of the touching behavior that allows animals to use physical contact in a more strategic manner.

As mentioned before, grooming is also highly sensitive to pharmacological treatments, and is increasingly recognized as a reliable marker of stress-related disturbances in animal models of neuropsychiatric disorders. One chapter details the past and current literature examining induced grooming in phencyclidine-treated rats. Relevant data about the effects of this drug on grooming patterning and hygiene efficiency, and how this related to both normal and abnormal stress responses will be presented, followed by a discussion on how the qualitative observations from this study may be beneficial in identifying hygienic and stress-related irregularities in animal models.

Grooming has been shown to be regulated by a variety of factors, one of them being hormonal levels. The effect of estrogen on this behavior, as both the estrogen-synthesizing enzyme and estrogen receptors are present in the brain and have roles in several neural circuits, will be examined in another chapter. The research presented will show how the distribution of estrogen-sensitive cells in the brain corresponds to regions that control sexual differentiation, masculine and feminine sexual behaviors, aggressive behaviors as well as grooming, and will review the observations from both animal models and clinical patients indicating that estrogen has a modulatory effect on grooming and related behaviors.

The absence of grooming behaviors in an animal can be as important and significant to the translational validity of models as robustly grooming phenotypes. There are symptoms of social withdrawal that occur in many neuropsychiatric disorders, including some of the most common such as depression. Another chapter will introduce this issue, highlighting social withdrawal phenotypes like barbering behaviors. The research will focus on these aspects in a potential mouse model of schizophrenia, a knockout for the PLCβ1 gene. The authors will explain how abnormal phospholipid metabolism has been implicated in the pathogenesis of schizophrenia, and how phospholipase C (PLC) β1 has been shown to be reduced in specific brain areas of patients with schizophrenia. This chapter will also discuss the interesting array of grooming-related phenotypes and the possible signaling mechanisms that may be affected in this model, as well as its applicability as a model of schizophrenia.

In line with the animal models, another chapter will discuss the effect of brain lesions on grooming behaviors and how new information on neurobehavioral pathways can be derived using these methods. The chapter will detail research on electrical stimulation of the midline cerebellum and striatum in rats, and lesioning methods using either surgery or genetic mutations that indicate that the cerebellum, basal ganglia, and neocortical brain regions contribute to grooming behaviors. It will also discuss *Grid2*^{Lc} mutant mice with selective cerebellar atrophy, and *Girk2*^{Wv} mutants with combined cerebellar and substantia nigra atrophy that display different effects on grooming. Their results implicating cerebello–neocortical

pathways in the completion of grooming chains, and a striato–pallido–neocortical pathway in the serial ordering of grooming chains, will also be presented in this chapter.

The role of the striatum in grooming behaviors will be specifically explored in another chapter. The research presented here will review the evidence for the role of the striatum in implementing the fixed action pattern of the grooming chain in the rat. In addition, the support for the involvement of the dorsolateral striatal subregion involved in the production of this movement sequence and the general functional significance of implementation by striatal circuitry is discussed. The authors also introduce the possibility that the general nature of striatal function of "implementing" chains of information crosses different functional boundaries between movement and reward information.

Taking a broader look at grooming-related behaviors, the next chapter will focus on the circuits surrounding barbering behavior. Many aspects still remain unclear to researchers and even the very existence of the behavior seems to be a paradox to some. Barbering behavior will be explained from an ethological perspective in an effort to resolve the barbering paradox by asking how and why barbering behavior occurs. The authors will also discuss the phylogenetic underpinnings of barbering, by comparing and contrasting the occurrence of hair-plucking behavior. The chapter reviews the developmental processes that underlie barbering behavior, with specific attention to known risk factors, learning, the laboratory environment, and transgenic mice. The authors will also review the behavioral mechanisms, eliciting stimuli, and physiological mechanisms that might mediate barbering, and outline the role of cortico–striatal circuitry in abnormal repetitive behavior in general, how it can be used to delineate disorders, and insights it provides into barbering.

Potentially maladaptive behaviors such as barbering are not uncommon in both laboratory rodents and clinical psychiatric patients alike. Human grooming disorders, such as trichotillomania, nail biting, and skin picking, are possibly linked to conditions like OCD. However, within current psychiatric classification systems trichotillomania is currently conceptualized as an impulse control disorder and nail biting and skin picking are not yet included in the official nomenclature. One clinical chapter outlines the debate over whether grooming disorders should form a separate category, or whether they should be classified as OCD spectrum disorders, impulse control disorders, or as body-focused repetitive behaviors. This chapter will also discuss these diagnostic and taxonomic issues particularly as they pertain to clinical practice.

Keeping with the theme on trichotillomania, another clinical chapter will review new advances in genetic, family, neurocognitive, neuroimaging, and neuropharmacological studies on this impulse control disorder. A particular focus will

be given to new research that shows interesting similarities between trichotillomania, other impulse control disorders, and OCD, while also revealing important differences in some endophenotypic measures. The chapter will also discuss neural abnormalities in the amygdalo–hippocampal formation and frontal–subcortical circuits are discussed and how animal models of these disorders may prove to be a fruitful avenue for future research.

In conclusion, the book conveys the message that grooming is an ethologically relevant, robustly observed behavior that can be dissected with high-throughput phenotyping techniques. By understanding the behavior, the researchers can now maximize the translational significance of the data and get closer to new diagnostic tools, as well as treatments and preventions. These chapters represent a wide and thorough perspective into a very important behavior that is proving indispensible to translational mental health research. The authors have been selected from an international conglomeration of top experts in their respective fields, and have contributed data that are driving today's research. The themes range from pharmacological to genetic to behavioral, covering a wide spectrum of basic and clinical neuroscientific disciplines. However, this book has been designed to serve as a useful source of literature for both the introductory student, as well as for the experienced researcher.

The editors would like to thank the National Alliance for Research on Schizophrenia and Depression (NARSAD), the world's leading charity dedicated to mental health research, for their generous support of this work. We hope that this book can help further the goal of discovering preventions and cures for neuropsychiatric illnesses through innovative translational scientific research.