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Review

From models to mechanisms: Odorant communication as a key determinant of social behavior in rodents during illness-associated states

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ABSTRACT

Pheromones and other social odor cues convey rich information among rodents. Social investigation is described as a key element in olfactory communication, which involves motivated approaches to conspecifics and other socially relevant stimuli. This behavior is activated by the detection of social cues to gather information about conspecifics for subsequent strategies such as avoidance or further approach, thereby determining the extent and nature of physical contact that ensues. This feature indicates a useful way for describing the process of social communication in distance-based manner. In particular, airborne odorant signals in rodent species guide social investigation at a distance, and provide information regarding the health status of the odor donors. In this review, we will address the role of the inflammatory response in the release of odor cues that involve information about several illness-associated conditions (bacterial or parasitic infection, stressor exposure, etc.). We will provide an overview of how sex and developmental epoch in odor donors serve as predictors of subsequent social behavior. We conclude that inflammatory processes have a profound impact on social behavior through a direct effect on the sick individual (i.e., reduced motivation to engage in social interaction), while the release of illness-related, aversive odor cues from the sick individual serves to inhibit social investigation by healthy conspecifics. Together, this dual impact of acute illness is thought to minimize disease transmission across individuals and promote healthy group living.

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1. Introduction

Rodents such as mice and rats, the most commonly used animal models in neuroscience, are highly social species that form complex social systems in the wild (Grant and Mackintosh, 1963; Whishaw et al., 2001; Lacey and Sherman, 2007). They have developed several types of social communication for gathering information through visual, auditory, and olfactory senses and for engaging in physical contact through tactile and taste senses and other behavioral responses (Wyatt, 2003). These involve a complex system of sensory and behavioral components between conspecifics including the abilities to recognize and identify other individuals (Winslow and Camacho, 1995; Wyatt, 2003; Insel and Fernald, 2004). This investigation–recognition strategy heavily relies on the physical distance toward conspecific-relevant stimuli (e.g., Blanchard et al., 2001, 2003; Brennan and Keverne, 2004; Broad and Keverne, 2008). In this review, we will argue that the distance-based feature of social communication between conspecifics provides a useful way to analyze the processes of social behavior and its underlying mechanisms. This review will focus on describing illness-associated social cues that mediate social behavior at a distance, and possible neural mechanisms modulating the release of this social cue.

2. Distance-based social strategies

2.1. Sensory modalities and physical distance from social stimuli

While nocturnal species use olfactory cues in the assessment of conspecifics, most mammals combine this information with auditory and tactile senses as modalities for conspecific communication (Eisenberg and Kleiman, 1972; Brown, 1979; Eisenberg, 1981). While vocal components such as ultrasound vocalization (Blumberg, 1992; Burgdorf et al., 2005; Litvin et al., 2007) or alarm calling (Brudzynski, 2005; Hollen and Radford, 2009) play a key role in communication at close proximity, olfactory components obtained via odorants provide complementary, and further qualitative information about the current state of a social partner. Auditory signals exchanged with conspecifics or alarm cries of conspecifics are particularly important for group-living animals (Owings and Morton, 1998; Litvin et al., 2007; Hollen and Radford, 2009). Rapid-onset rapid-offset auditory signals are useful in acute emergencies and real-time communication, while olfactory signals typically have a delay between signal emission and reception (Eisenberg and Kleiman, 1972; Brown, 1979). Such odor cues are shown to remain functionally for at least 24 h without the presence of odor owners in the mouse (Hurst et al., 1998; Hurst and Beynon, 2004). Additionally, volatile chemicals and small molecules composed of odorant cues are able to disperse in air or water (Brown and Macdonald, 1985; Brennan and Keverne, 2004). As a result, scent odors may provide information to a wider range of recipients concerning the locations of animals that could no longer be present there (Brown and Macdonald, 1985; Blanchard et al., 2003; Hurst and Beynon, 2004).

The laboratory rodent species utilizes odorant signals such as scent marking (Brown and Macdonald, 1985; Arakawa et al., 2007b). They deposit scent marks from anogenital scent glands or urinary components, thereby producing an individual odor signature composed of rich information such as sex, social rank, sexual receptivity, hormonal status, and health/illness status of odor donors (Mykytowycz and Goodrich, 1974; Natynczuk and Macdonald, 1994; Popik and van Ree, 1998; Stopka et al., 2007). Odor signatures also play a key role in the establishment of territorial boundary and mating processes (Hurst and Beynon, 2004; Arakawa et al., 2008b). Recent studies have indicated that the information contained in an individual odor signature depends on the distance of the odor recipients to odor sources (Hurst et al., 2001).

2.2. Odor information process through volatile and non-volatile chemicals

Odorant chemicals can be grouped into airborne volatile and non-volatile components (Brennan and Kendrick, 2006; Hurst, 2009). Animals detect airborne scents by volatile chemical components and small airborne peptides via olfactory receptors primarily in the olfactory epithelium of the main olfactory system (Brennan and Keverne, 2004; Broad and Keverne, 2008). This pathway causes the detection of scents to be at some distance from their source. When animals detect scents in the air, the scent components are assessed based on their approximate adaptive value and stimulate animals to either approach the source in order to gain further information, or to avoid the social source that may involve potential dangers. In this way, the odor components inform conspecifics to about whether attraction or alarm would be an appropriate response to the conspecific. These airborne molecules are known to contain information about genetic and sex differences (Schaefer et al., 2002; Keller et al., 2006a, b), age (Osada et al., 2003, 2008), and current health status such as stress (Mykytowycz and Goodrich, 1974; Wheeler, 1976; Novotny et al., 1985; Schaal et al., 2003), parasitation (Kavaliers et al., 2000, 2005a), and illness (Yamazaki et al., 2002; Arakawa et al., 2010a). In contrast, non-volatile scents are comprised of fixed information such as an individual's genetic signature, provided by proteins such as the major urinary proteins (MUPs) (Bacchini et al., 1992; Hurst et al., 2001, 2005; Armstrong et al., 2005) and major histocompatibility complex (MHC) associated peptides (Brown et al., 1987; Brown, 1995; Boehm and Zufall, 2005; Lanyon et al., 2007).

In order to detect non-volatile components, animals must then approach and make nasal contact with the scent source indicating an expenditure of energy and time consumption to gain further information (Keverne, 1999; Leinders-Zufall et al., 2000; Pankevich et al., 2004). When animals make nasal contact with a scent source or a conspecific that releases odor, non-volatile molecules of the odor source are pumped to, and detected mainly by, the vomeronasal organ of the accessory olfactory system (Meredith, 1994; Halpern and Martinez-Marcos, 2003; Breer et al., 2006). Therefore, the detection of airborne scents may be necessary to activate the delivery of non-volatile scent via the nasal pumping system (Hurst and Beynon, 2004; Keller et al., 2006a). Although recent findings suggest that the main and accessory olfactory systems can detect and process both volatile and non-volatile chemosignals (Restrepo et al., 2004; Spehr et al., 2006a), differences in the type of chemosignals based on volatility appear to mediate specific behavioral responses and, therefore, information gathering strategies would be altered based on the distance to the source of the social cues.

2.3. Body parts associated social investigation

When animals approach and make contact with a conspecific, they engage in intense social investigation that consists of sniffing and licking facial and anogenital areas, as well as other body parts (Grant and Mackintosh, 1963; Brown and Macdonald, 1985) (Fig. 1). Some of the behavioral postures described as social behaviors are strongly associated with investigation strategies to exocrine body glands (Barnett, 1958; Blanchard et al., 1975, 1977, 1998). Given that non-volatile chemostimuli require active nasal pumping of air to be detected by olfactory receptors, it seems that animals detect non-volatile chemostimuli as well as volatile molecules through sniffing those body areas, each of which may produce differential odor information.

Through detailed observation of social behavior in a semi-natural colony, it has been shown that mice display particular features of social interaction; mice typically accept approaches to