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Research report

Social behaviors and acoustic vocalizations in different strains of mice

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HIGHLIGHTS

- In a social interaction task, social and acoustic parameters varied between strains.
- Social and acoustic parameters were independent of anxiety or locomotor features.
- C57BL/6J mice uniquely developed strong affiliative behaviors, with high call rates.

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ABSTRACT

Proposing a framework for the study of core functions is valuable for understanding how they are altered in multiple mental disorders involving prefrontal dysfunction, for understanding genetic influences and for testing therapeutic compounds. Social and communication disabilities are reported in several major psychiatric disorders, and social communication disorders also can occur independently. Being able to study social communication involving interactions and associated acoustic vocalizations in animal models is thus important. All rodents display extensive social behaviors, including interactions and acoustic vocalizations. It is therefore important to pinpoint potential genetic-related strain differences –and similarities- in social behavior and vocalization. One approach is to compare different mouse strains, and this may be useful in choosing which strains may be best suitable in modeling psychiatric disorders where social and communication deficits are core symptoms.

We compared social behavior and ultrasonic acoustic vocalization profiles in males of four mouse strains (129S2/Sv, C57BL/6J, DBA/2, and CD-1) using a social interaction task that we previously showed to rely on prefrontal network activity.

Our social interaction task promotes a high level of ultrasonic vocalization with both social and acoustic parameters, and further allows other measures of social behaviors. The duration of social contact, dominance and aggressiveness varied with the mouse strains. Only C57BL/6J mice showed no attacks, with social contact being highly affiliative, whereas others strains emitted aggressive attacks. C57BL/6J mice also exhibited a significantly higher rate of ultrasonic vocalizations (USV), especially during social interaction.

1. Introduction

Numerous mouse models have been suggested for studying neurodevelopmental disorders such as autism spectrum disorder and schizophrenia [27], which may also be associated with social and communication deficits (Silverman et al., 2010 for review). The C57BL/6J mouse is the most widely used inbred mouse strain in neuroscience research, especially for investigating models of cognition Banbury Conference, 2007. However, an increasing number of studies of social behaviors use mutant mice, which are generated on various genetic backgrounds. These studies report sometimes inconsistent data. Inconsistency could arise either because of the use of different social paradigms, or because of the use of different animal models, including different genetic strains. Although all rodents show developed social behaviors and social organization that make them useful models for studying social and communi-

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cation abilities and defects, they also show differences between strains. It is therefore important to determine which strain could be the most appropriate for studying social behaviors and vocalization. To date, there have been very few strain comparison studies combining social behavior and acoustic vocalization in adult male mice [1].

We compared social behavior and acoustic vocalization profiles, elicited in a social interaction task –SIT- which promotes acoustic vocalization, in four mouse strains: 129S2/Sv, C57BL/6J, DBA/2, and CD-1. We chose the C57BL/6J and DBA/2 strains because they are the most studied inbred strains of mice in behavioral pharmacology and neuropharmacology. In particular, their behavioral responses to dopaminergic agents, and functional and anatomical characteristics of their dopaminergic neurotransmitter system have been extensively described (e.g. [34,16]). However, the social and vocalization characteristics of C57BL/6J and DBA/2 mice have never been compared in adults. The 129S2/Sv strain was additionally chosen because it is the strain most commonly used to generate knockout and transgenic mouse lines [40]. Finally, CD-1 mice were chosen because, by contrast with the three other strains, they are outbred mice, and so likely to exhibit the widest range of variation of individual differences in their cognitive abilities [8]. CD-1 mice also are frequently used to study stereotypic behaviors, which is a common feature of psychiatric disorders [20]. In addition, C57BL/6J and 129S2/Sv are reputed to show very different levels of motor activity and anxiety-like behavior (for review see [10]). The 129S2/Sv strain has been reported to not perform well in cognitive tasks in contrast to the DBA/2 mice, which consistently are reported to show higher levels of learning and high levels of exploratory behavior [6].

While the assessment of motor differences can be relatively simple, as because movements are readily manifested and easily observable, the assessment of cognitive differences requires a greater attention to experimental design, sensitive tasks and appropriate controls. Likewise, social behaviors are complex integrative behaviors that involve multiple sensory and cognitive functions. We have previously developed and validated a social interaction task –SIT- that allows the investigation and characterization of an exhaustive social repertoire that occurs when dyads of mice are placed together for the first time in a novel environment [21,2,17,29]. The SIT also promotes ultrasonic vocalization in adult male mice, which can interact together without barriers, even in absence of any reproductive context [11], by contrast with other social tasks which elicit reproduction-related vocalizations but do not allow full body contact [12]. The experimental setting described here is therefore suitable for developing a better understanding of the social repertoire and social acoustic vocalization behaviors in mice. Although it would be of interest to investigate these traits in both sexes, we focused here on males as a beginning, in order to capitalize on our previous data which were also obtained in male mice.

The aim of our paper is thus to compare mouse strains for vocalizations and social behavior in order to determine which strains may be best suitable for use as background strains for transgenic or pharmacological models of psychiatric disorders involving social and communication deficits.

2. Materials and methods

2.1. Animals

79 male mice obtained from Charles Rivers Laboratories France (L'Arbresle Cedex, France) were used. We used C57BL/6J (n = 6), CD-1 (n = 15), DBA-2 (n = 13) and 129S2/Sv (n = 15) strains.

Mice arrived to the animal facility at five weeks of age, and were maintained in collective cages for five weeks and were thereafter housed individually. They were fed with standard chow and food and water were provided ad libitum. A circadian light cycle of 12 h light/12 h dark (on at 8 am) was maintained in the animal section. All experiments were performed during the light cycle, between 09:00 a.m. and 5:00 p.m. Experiments were conducted in accordance with the local regulations for animal experiments as well as the recommendations for animal experiments issued by the European Council (directives 219/1990 and 220/1990).

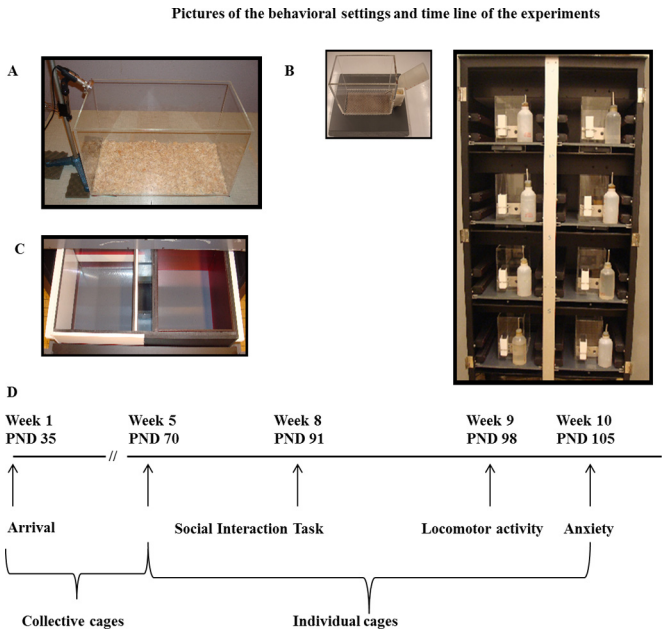

Fig. 1. Picture of the behavioral settings. A. Social interaction environment and recording of the ultrasonic vocalizations. B. Automatic actometer measuring locomotor activity over 24 h. C. Automatic light-dark box measuring anxiety-like behavior for a brightly illuminated environment as compared to a dark one. D. Time line of the behavioral experiments. Week 1 represent the first week of animals' arrival. PND 35 represent their age, i.e. 5 weeks hence 35 days of age.

2.2. Behavioral apparatus and analyses

The Social Interaction Task (SIT) was previously described in detail [17]. Briefly, it took place in a transparent plexiglas cage (50 cm long × 25 cm wide × 30 cm deep) located in a small novel experimental room with a diffuse 100 l× light. It contained a handful of clean sawdust (Fig. 1A). The experimental cage was located below a camera connected to a computer that recorded video of social behavior for subsequent off-line analyses.

Ultrasonic vocalizations were recorded during the SIT in dyads of mice of same age, sex and strain. A condenser ultrasound microphone Polaroid/CMPA was placed above the experimental chamber (Fig. 1A), high enough so that the receiving angle of the microphone covered the whole area of the test cage. It was connected to an ultrasound recording interface UltraSoundGate 416H, which was plugged into a computer equipped with the recording software Avisoft Recorder USG (sampling frequency: 250 kHz; FFT-length: 1024 points; 16-bit format). All recording hardwares and softwares were from Avisoft Bioacoustics (Berlin, Germany). Spectrograms were generated for each detected call to measure the number calls and their duration as previously [11,12] with the following characteristics: Blackman window, overlap: 87.5%, time resolution: 0.512 ms, frequency resolution 244 Hz. Frequencies of each call were processed using a custom MATLAB program [1,13], originally modified from code written by Timothy E. Holy [24] that is called 'Mouse Song Analyzer v1.3'. Briefly, the software computed the sonograms from each waveform (512 samples/block, half overlap), thresholded to