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Analysis of Ultrasonic Vocalizations in a Rat Model of Fragile X Syndrome

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Abstract

Fragile x syndrome (FXS) is a leading known inherited form of autism and autism spectrum disorders (ASD), with deficiencies in communication and sensory processing. It is caused by a mutation in the fragile x mental retardation (Fmr1) gene. Analogous to human communication, rats engage in social communication in the form of ultrasonic vocalizations (USVs). The purpose of this research is to determine if mutations associated with ASD recapitulate the core social deficit features of this disease in animal models. The abnormal structure of USVs of the Fmr1 rat model of FXS will determine abnormal and disrupted social communication [2,5].

Wild Type (WT) and Fmr1-KO rats were exposed to 3 different call-inducing conditions. Fmr1-KO rats generated less USVs than the WT rats across all conditions. Analysis of different categories of calls revealed that loss of Fmr1 expression caused less varied (flat) calls to be generated. When compared to WT rats, Fmr1-KO rats produced less frequency-modulated calls in all conditions [3]. Examination of USVs in autism models can serve as a platform for determining the efficacy of potential pharmacological interventions for ASD.

Goals

- To investigate how the Fmr1-KO rat model of FXS exhibits abnormal social communication in the form of altered ultrasonic vocalizations (USVs).
- To understand how call type specific deficits shed light on the complex pathophysiology of autism that are possibly shared across species [1].

Materials and Methods

- Fmr1-KO and wild type (WT) rats were exposed to 3 different call-inducing conditions: isolation, female scent, and familiar pair (See fig. 1) [6].
- 2 minute long USVs were recorded for each condition, using the Avisoft-SASLAB Pro software and equipment.
- All USV analysis was completed using Adobe Audition
- A trained observer, blind to animal genotype and experimental condition, conducted analysis.
- USV lengths were determined by computing the difference of end and start times of each.
- Total number of USVs between Fmr1-KO and WT groups per condition were quantified manually
- The frequency modulation of all USVs were determined by computing the difference in beginning and end frequency of each USV. Calls with greater than 5kHz differences were categorized as frequency modulated then further classified in to up-sweep and down-sweep calls.

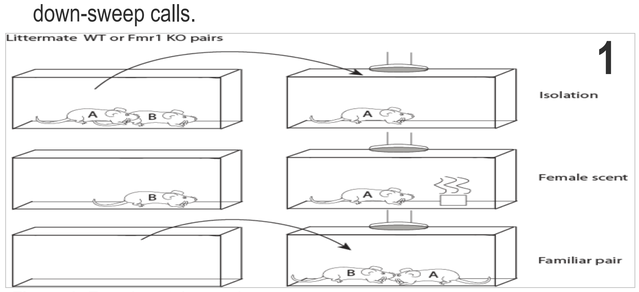
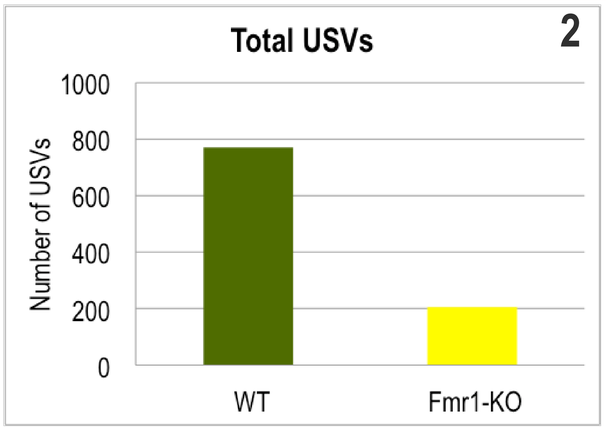


Figure 1: Experimental procedure

Results



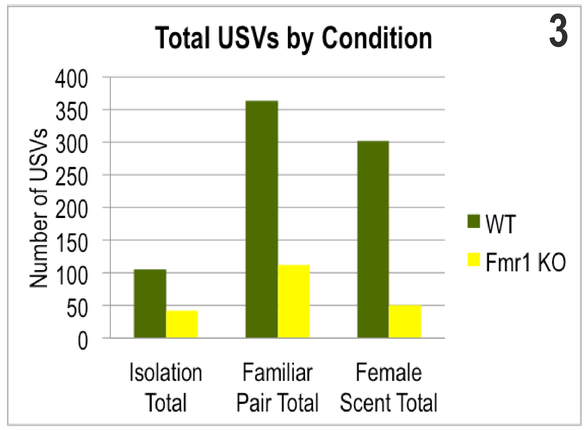


Figure 2: Fmr1-KO rats generated less USVs than WT rats (n=6 animals).
Figure 3: FMr1-KO rats emitted less USVs than WT across all conditions. Fmr1-KO and WT rats emitted most of their USVs during the familial pairing condition. The least number of calls for both groups were generated in the isolation induced condition.

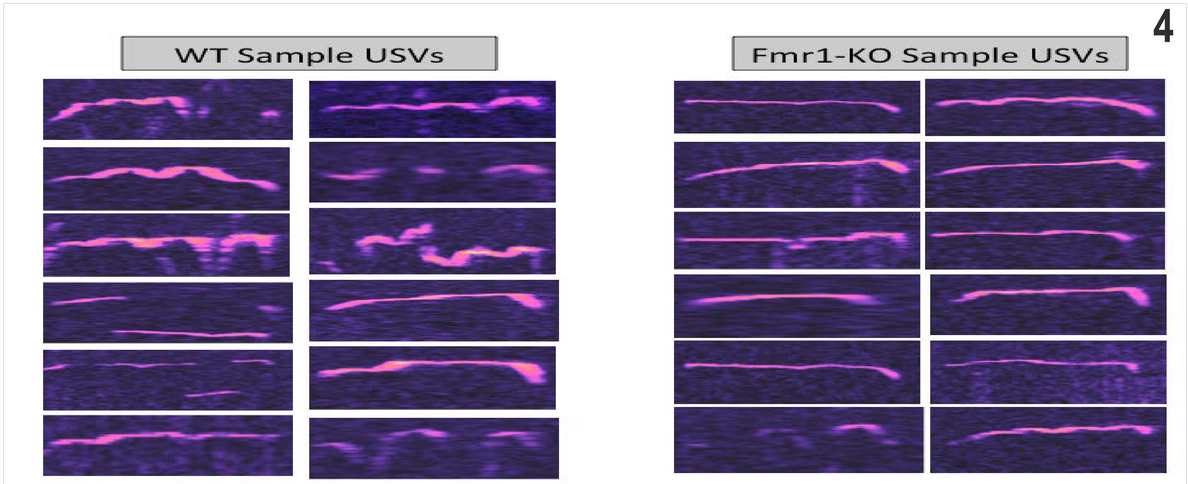
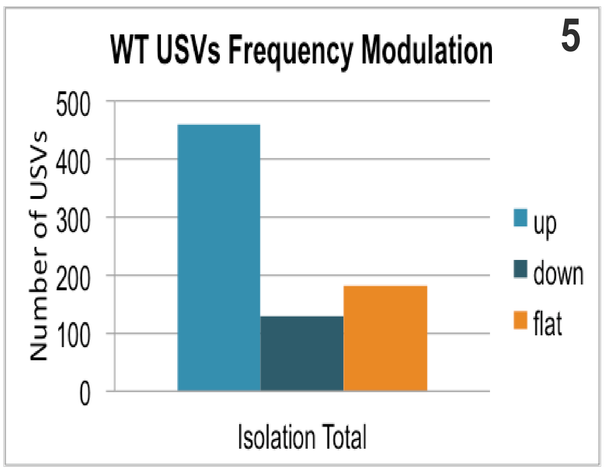


Figure 4: Sample WT and Fmr1-KO USVs.



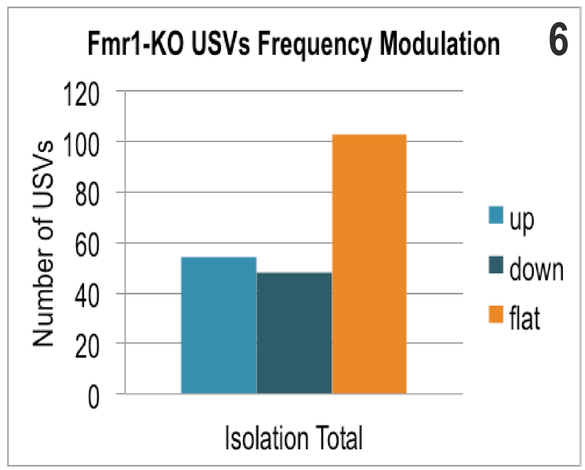


Figure 5&6: Analysis of different categories of USVs reveal that the structure of Fmr1-KO rat calls are less varied (mostly flat). Whereas, WT rats produce mostly varied and up-sweeping calls.

Conclusion and Future Works

SUMMARY

- WT generated more USVs than the Fmr1-KO rats, across all conditions.
- The Fmr1-KO rats generated less frequency modulated (flatter) USVs compared to those emitted by the WT group.
- These differences display call type specific deficits, which suggests that Fmr1-KO rats have abnormal social communication.
- Examination of USVs in autism models can serve as a platform for determining the efficacy of pharmacological interventions [4].

NEXT STEP

- Further collection and analysis of WT and Fmr1-KO USVs will provide important insights into the social brain and help to elucidate genetic, neurochemical and neuroanatomical factors underlying autism as well as other neuropsychiatric disorders characterized by social deficits such as schizophrenia and bipolar disorder [2].

POTENTIAL RESEARCH PROJECTS

- Analyze behavioral and neural responses to playback of these USVs. These will provide further insight into the social brain.

Acknowledgements

I would like to thank Dr. Richard Salvi for letting me contribute to the research in the Center for Hearing and Deafness. I would also like to acknowledge Dr. Benjamin D. Auerbach for teaching and guiding me through experiments.

References

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