Ultrasonic communication deficits in p50 KO mice and effect of maternal enrichment

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INTRODUCTION

Mice emit ultrasonic vocalizations (USVs) under different social conditions: pups maternal separation, juveniles play and adults mating and social investigation. The USVs measurement has become an important instrument for behavioral phenotyping in neurodevelopmental disorders (NDDs). Many studies have shown the fundamental role of maternal enrichment with long-term positive effects on brain and behavior in mouse models of NDDs. In this study, we wanted to investigate if mice lacking the NF-κB p50 subunit (p50 knock-out, KO) that are a mouse model of NDDs, had alterations in ultrasonic communication and if these calling patterns were influenced by maternal behavior.

MATERIALS AND METHODS: USVs of wild type (WT), p50 KO and KO pups exposed to maternal enrichment (KO enriched) were recorded using an ultrasound sensitive microphone and quantitatively analyzed by Avisoft software. Each syllable was categorized manually.

RESULTS: We previously demonstrated that p50 KO mice had cortical structure alterations and social behavior impairment. In this study, USVs analysis showed that p50 KO and KO enriched pups emitted more and longer vocalizations compared to WT pups. During adulthood, p50 KO and KO enriched emitted less USVs than WT mice. In addition, an altered qualitative ultrasonic communication in p50 KO mice has been found. Interestingly, maternal enrichment had no effects on USVs number, duration and type in p50 KO mice.

CONCLUSIONS: This study investigated the relationship between maternal enrichment and USVs in a mouse model of NDDs. USVs anaylisis revealed social communication alterations in p50 KO mice; these deficits were not recovered by maternal enrichment, stregthening the fact that genetic backgound prevails on evironmental enrichment.

RESULTS

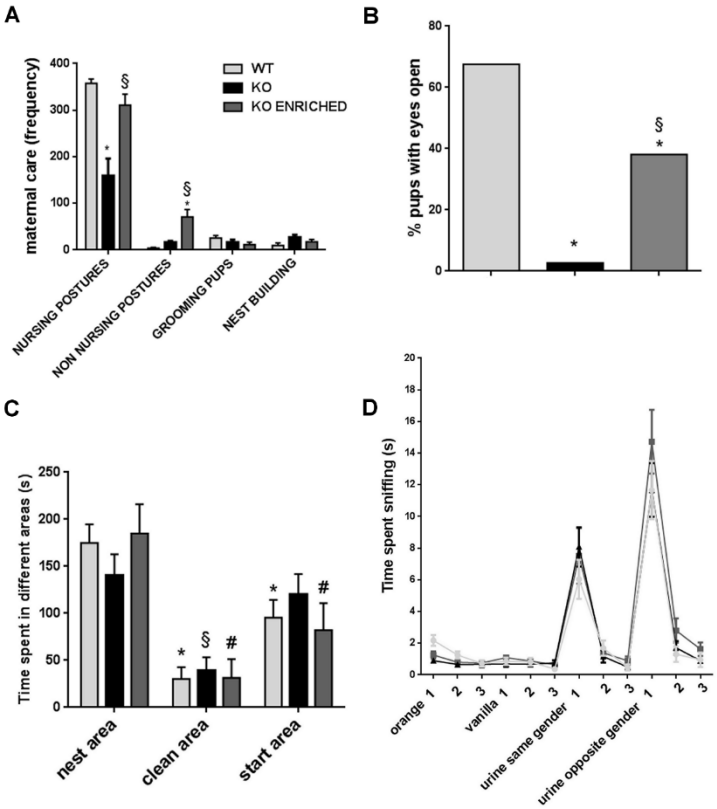

Figure 1. Maternal care assessment and developmental traits in WT, KO and KO enriched mice.
(A) Detailed representation of different maternal activities frequency in WT, KO and KO enriched pups from postnatal day (PND) 1 to 7. *p < 0.05 for KO and KO enriched vs WT pups and §p < 0.05 for KO enriched vs KO pups (Two-way ANOVA, followed by Tukey's post-test analysis). *p < 0.05 for KO and KO enriched vs WT pups and §p < 0.05 for KO enriched vs KO pups (One-way ANOVA, followed by Tukey's post-test analysis). (C) Social recognition was evaluated in the homing test on PND 14 by measuring the time in seconds (s) spent in the nest area, in the clean and in start area. *p < 0.05 for time spent in the clean area or start area vs time spent in nest area for WT; §p < 0.05 for time spent in the start area vs time spent in nest area for KO; #p < 0.05 for time spent in the clean area vs time spent in nest area for KO enriched and #p < 0.05 for time spent in the start area vs time spent in nest area for KO enriched (Two-way ANOVA, followed by Sidak's post-test analysis). (D) Graphic representattion of data collected during olfactory habituation/dishabituation test by measuring the time spent by adolescent mice in sniffing cotton-tipped swabs satured with different odours. (Two-way ANOVA, followed by Sidak's post-test analysis).

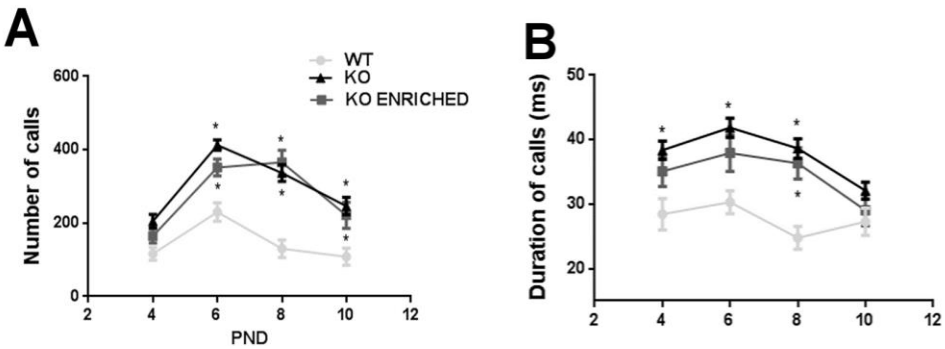

Figure 2. Quantitative analysis of ultrasonic communications in WT, KO and KO enriched pups.
(A) Number and (B) duration of vocalizations on PND 4, 6, 8 and 10 in response to social separation during a three minute session. *p < 0.05 for KO and KO enriched vs WT pups (Two-way ANOVA, followed by Sidal's post-test analysis).

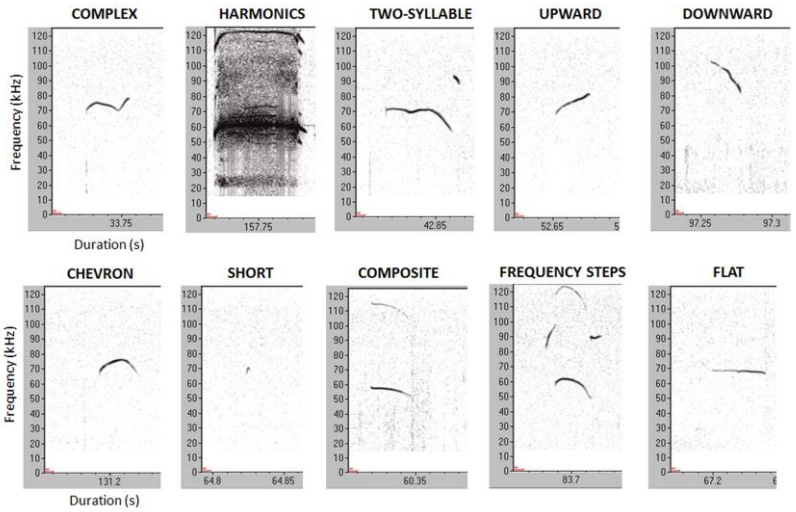

Figure 3. Examples of classification. Typical spectrograms of USVs classified into different calls categories emitted by WT pups.

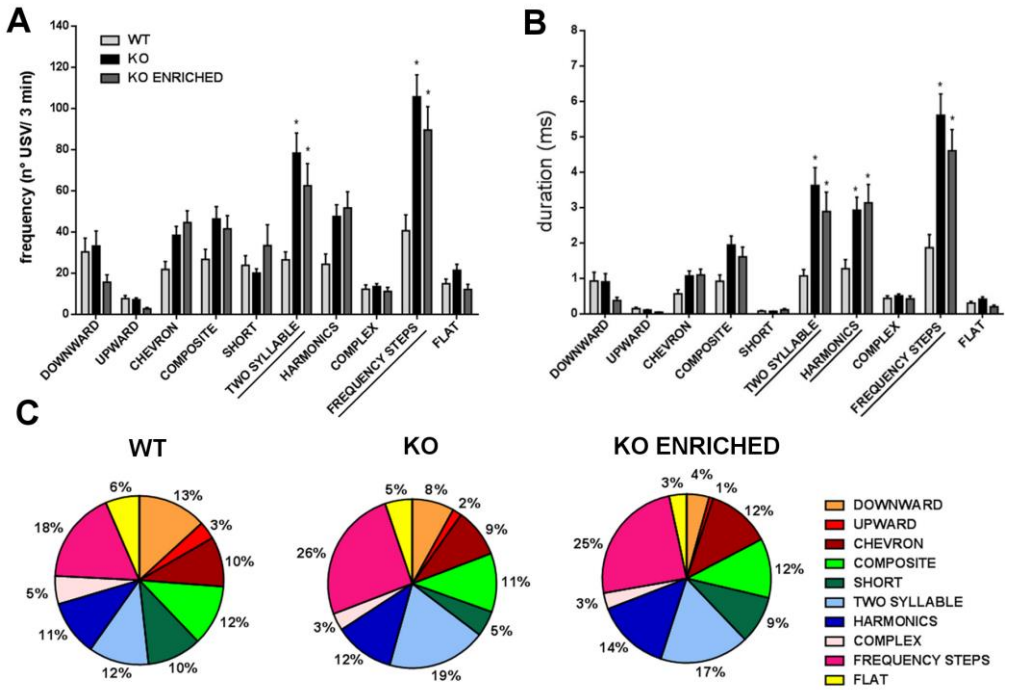

Figure 4. Qualitative analysis of ultrasonic communication in WT, KO and KO enriched pups.
(A) Number and (B) duration of USVs different categories on PND 6 during 3 minutes of USVs test. *p < 0.05 for KO and KO enriched vs WT pups (Two-analysis ANOVA, followed by Sidak's post-test analysis). (C) Proportion of different calls typologies expressed as the percentages in pie graphs.

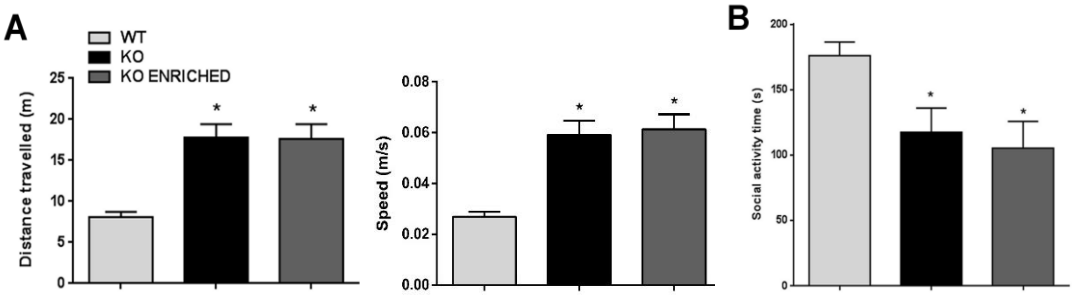

Figure 5. Exploratory and social behavior of WT, KO and KO enriched adult mice.
(A) Graphic representation of data collected in the open field test by automatically measuring the total distance travelled and the speed. *p < 0.05 for KO and KO enriched vs WT mice (One-way ANOVA, followed by Tukey's post-test analysis). (B) time spent by WT, KO and KO enriched adult mice in doing social activities during the male-female social interaction test. *p < 0.05 for KO and KO enriched vs WT mice (One-way ANOVA, followed by Dunnet's post-test analysis).

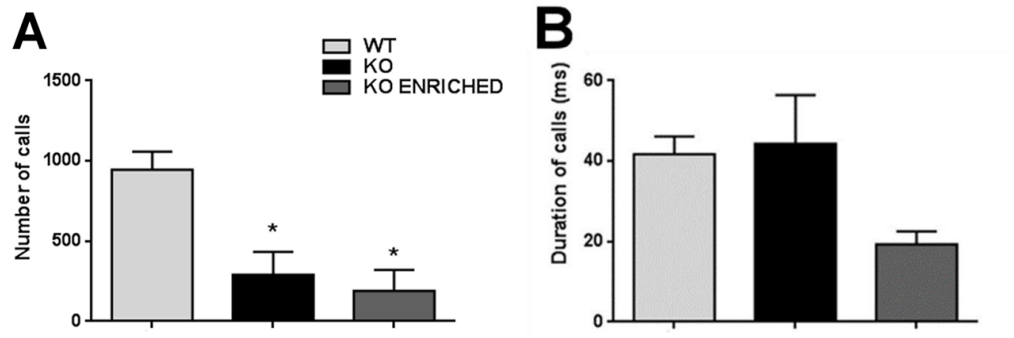

Figure 6. Quantitative analysis of ultrasonic communication in WT, KO and KO enriched adult mice.
(A) Number and (B) duration of USVs emitted by adults during male-female social interaction tetst. *p < 0.05 for KO and KO enriched vs WT mice (One-way ANOVA, followed by Sidak's post-test analysis).

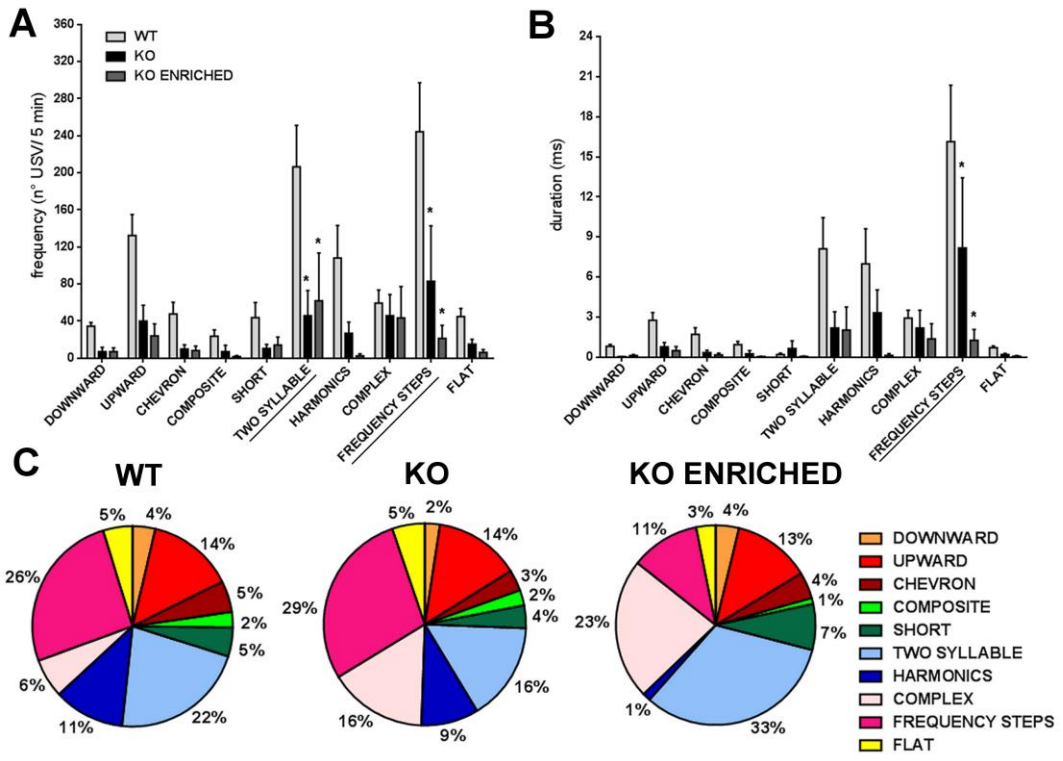

Figure 7. Qualitative analysis of ultrasonic communication in WT, KO and KO enriched adults.
(A) Number and (B) duration of different calls categories of WT, KO and KO enriched adult mice. *p < 0.05 for KO and KO enriched vs WT mice (Two-way ANOVA, followed by Sidak's post-test analysis). (C) Proportion of different calls typologies expressed as percentages in pie graphs.