

Bate palmas mutant mice as a model of Kabuki syndrome: Higher susceptibility to infections and vocalization impairments?

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Abstract

The recessive mutant mouse *bate palmas* (*bapa*) arose from N-ethyl-N-nitrosourea mutagenesis. Previous studies of our group revealed some behavioral impairments and a mutation in the lysine (K)-specific methyltransferase 2D (Kmt2d) gene. Because mutations in the KMT2D gene in humans are mainly responsible for Kabuki syndrome, this study was proposed to validate *bapa* mice as a model of Kabuki syndrome. Besides other symptoms, Kabuki syndrome is characterized by increased susceptibility to infections and speech impairments, usually diagnosed in the early childhood. Thus, juvenile male and female *bapa* mice were studied in different developmental stages (prepubertal period and puberty). To induce sickness behavior and to study infection susceptibility responses, lipopolysaccharide (LPS) was used. To study oral communication, ultrasonic vocalizations were evaluated. Behavioral (open-field test) and central (astrocytic glial fibrillary acidic protein [GFAP] and tyrosine hydroxylase [TH]) evaluations were also performed. Control and *bapa* female mice emitted 31-kHz ultrasounds on prepubertal period when exploring a novel environment, a frequency not yet described for mice, being defined as 31-kHz exploratory vocalizations. Males, LPS, and puberty inhibited these vocalizations. *Bapa* mice presented increased motor/exploratory behaviors on prepubertal period due to increased striatal TH expression, revealing striatal dopaminergic system hyperactivity. Combining open-field behavior and GFAP expression, *bapa* mice did not develop LPS tolerance, that is, they remained expressing signs of sickness behavior after LPS challenge, being more susceptible to infectious/inflammatory processes. It was concluded that *bapa* mice is a robust experimental model of Kabuki syndrome.

KEYWORDS

astrocytes, dopamine, LPS, open field, RRID:AB_10013382, RRID:AB_11214323, sickness behavior, ultrasonic vocalizations