

Intrinsic and extrinsic factors in the bizarre patterns elicited in the open-field test in male and female mice with normal and AD-pathological aging under social or isolated housing conditions [†]

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Abstract

Bizarre behaviors (BB) are elicited in animals during stressful conditions and behavioral markers of disease/sickness relevant to animal welfare. These behaviors are disregarded in most experimental screenings due to their low incidence and short duration, despite their translational value mimicking disruptive behaviors associated with neurological/psychiatric diseases. However, we previously reported experimental conditions with conspicuous BB incidence: 1) the 3xTg-AD mice for Alzheimer's disease *vs.* wild-types; 2) the open-field test (OF) *vs.* other tests; 3) + 6 months of age and female sex; 4) at older ages (+13 months) male 3xTg-AD mice also exhibit more circling behavior (BB-CB) than control mice; 5) early neonatal handling reduces BB; whereas 6) they are enhanced by d-galactose-induced accelerated aging. In the present work, we studied the BB patterns elicited in the OF using a longitudinal design with sixty-six 13-month-old male/female mice with normal/AD-pathological aging under social/isolated housing conditions, aimed to explore the effects of intrinsic (genotype, sex) and extrinsic (environment) factors (n=7-8/group). BB were recorded in 39% of animals. Sex, re-test at an older age, and genotype factors differentiated two BB patterns: higher circling behavior (BB-CB, n=12) in wild-type and males, whereas higher backward movements (BB-BM, n=14) in 3xTg-AD, females, and older age. Isolation increased the incidence of freezing, mostly in 3xTg-AD mice, and exerted a modulatory role in BB, but interaction effects with other factors led to residual significance. The results point to BB-BM as the most pervasive BB pattern in this animal model, which is also sensitive to the progress of aging/disease.

Keywords

bizarre behaviors; animal welfare; Alzheimer's disease; aging; social isolation; gender perspective