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### Title

Intrinsic (genotype) and extrinsic (environment) factors in the temporal patterns of nest-building process:

Effect of forced isolation in old female mice with normal and AD-pathological aging

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### Abstract

The impact of isolation has become a critical worldwide issue since the outbreak of the COVID-19 pandemic. In nursing homes, the physical distance measures forced the separation of old patients in restricted areas and rooms to avoid the spread of the virus. Similarly, older people living at home face severe restrictions as the best preventive strategy to protect their lives before vaccination is possible/effective. At the translational level, we recently demonstrated the impact of isolation in male 3xTg-AD mice for Alzheimer's disease and the increase of gross and fine motor activity. The latter was monitored through nesting, a species-typical ethological behavior used as a naturalistic approach to measuring animals' well-being and abilities in instrumental tasks. In the present work, we scored the nests and the nest-building process in old females under the effects of intrinsic (genotype, 3xTg-AD vs. C57BL/6]) and extrinsic (environment, forced isolation vs. social environment) factors. Nests were scored according to the ordinal Deacon Scale, whereas the temporal progress of nests construction was determined with a new parametric (numeric) measurement analog. The results confirmed previously described genotype differences, with worse nests in 3xTg-AD mice living under standard housing conditions than non-transgenic counterparts, at 48 and 72 hours. However, the genotype effect was lost under isolation, mainly due to isolated 3xTg-AD females enhancing nest-building behavior, while isolated non-transgenic counterparts were less efficient at 24h. The results also indicate that temporal patterns of the nest-building process are important to be considered when measuring the effects of intrinsic and extrinsic factors.

# **Keywords**

Environment; Social; Nesting; Daily life activities; COVID-19; Social isolation