

418 - Digging signatures modeling anxiety and OCD disorders in very old age and end-of-life Alzheimer's disease and the effect of social isolation: A translational neuroscience approach in times of coronavirus pandemic (COVID-19).

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The severity of the current scenarios in this pandemic will leave important psychological traces. In fact, the first clinical reports available already refer to increased incidence of depression and anxiety disorders such as obsessive-compulsive disorder (OCD) and post-traumatic stress disorder. At the translational level, modelling of such neuropsychiatric alterations in animal models relays in neuroethological perspectives since response to fearful situations and traumatic events, critical for survival and adaptation to the environment, are strongly preserved in phylogeny. In the wild, mice dig as a 'defensive behavior' which is considered to reflect the anxiety state of animals. In the laboratory, mice dig vigorously in deep bedding to bury food pellets or small objects they may find. Thus this behavior, initially used to screen anxiolytic activity was later proposed to better model meaningless repetitive and perseverative behaviors characteristic of OCD or autism spectrum disorders. In the present work, we have studied the digging ethograms in normal and advanced AD-related pathological aging using wildtype and the 3xTg-AD mice, a genetic model of Alzheimer's disease that presents AD-cognitive dysfunction but also a conspicuous BPSD-like phenotype. We also studied the effects of isolation in this respect, using very old (18 month-old) 3xTg-AD mice that survived to their cage mates, as mortality rates in this animal model are high after 13 months of age. Two digging paradigms, involving different anxiogenic and contextual situations were used to investigate the digging patterns in these very old males with normal and AD-pathological aging, as well as the effects of isolation. The temporal course and intensity of this behavior was found increased in those 3xTg-AD mice that had lost their 'room partner' and lived isolated. However, when they were tested under neophobia conditions, incidence of this behavior was smaller and the pattern of digging was disrupted. The results show that this combined paradigm unveils distinct features of digging signatures that can be useful to provide an animal model for these perseverative behaviors and their interplay with anxiety states, which represent an important part of BPSD or can now emerge as a result of the enhancement of obsessive-compulsive behaviors by social-isolation.