

# Behavioral and molecular consequences of a 'double-hit' challenge on the pathogenesis of mouse models of depression and amyotrophic lateral sclerosis (ALS)

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## Propositions

1. Experiencing a ‘double-hit’ of chronic stress and LPS-induced systemic inflammation increases depressive-like behaviors and inhibits aggression in a mouse model of depression (*this thesis*).
2. When present simultaneously, these factors do not act in an additive way, but result in a distinct behavioral and molecular response (*this thesis*).
3. The behavioral changes arising from the ‘double-hit’ are associated with suppression of pro-inflammatory cytokines and serotonin (5-HT)-mediated mechanisms both in the brain and in the periphery (*this thesis*).
4. In the FUS[1-359]-tg model of amyotrophic lateral sclerosis (ALS), LPS-induced systemic inflammation in pre-symptomatic mice exacerbates the emotional and molecular abnormalities caused by the FUS gene mutation (*this thesis*).
5. Individual susceptibility to stress-induced depressive-like syndrome in mice is associated with elevated COX2 and Iba-1 expression, and decreased Ki67 expression in the hippocampus (*this thesis*).

6. The use of COX-2 inhibitors in the management of depressive syndromes, such as major depressive disorder (MDD), may be an example of how the manipulation of the inflammatory response may be beneficial in the treatment of neuropsychiatric disorders (*valorization*).
7. The use of the ‘double-hit’ model to study the underlying mechanisms of neuropsychiatric disorders is highly valid, as it allows for the modeling of clinical conditions (*impact*).
8. “In life, unlike chess, the game continues after checkmate.”  
– Isaac Asimov, biochemist and science fiction writer.