VULNERABILITY TRAITS EXHIBITED BY MAO-A HYPOMORPHIC MICE

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Introduction: Monoamine oxidase A (MAO-A) enzyme is the degrading enzyme of monoamines (e.g. serotonin, dopamine), which play age-specific roles in the etiopathogenesis of aggressive behavior (AB). Although AB is an innate physiological response to species survival, it has a multi-factorial origin based on the interaction between genetic and environmental factors. Accordingly, AB depends upon the interaction between early life adversities (e.g. child neglect, emotional/physical abuse) and low levels of MAO-A activity. Both early life adversities and AB are highly comorbid with substance abuse, thus raising the possibility that MAO-A may act as a risk/predictive factor also for drug abuse. We have recently shown that dysfunctional mesocortical dopamine signaling at pre-adolescence ties to AB in a hypomorphic mouse exhibiting a low activity variant of MAO-A (MAO^{Neo} mouse) when subjected to early life adversity (i.e., neonatal maternal separation, social isolation; ES). Notably, neonatal maternal separation is an animal model of depression that is also associated to dysregulation of the gut–microbiota–brain axis, thus contributing to susceptibility to stress-related psychiatric disorders. Conversely, accumulating evidence suggests that probiotic treatments can normalize stress-induced brain changes, and modulate endophenotypes associated with neuropsychiatric disorders.

Materials and methods: We, therefore, sought to determine whether i) a probiotic treatment might prevent the occurrence of an AB in $MAOA^{Neo}$–ES mice at pre-adolescence; ii) MAO-A genotype and ES might impact on psychostimulant effects elicited by cocaine at pre-adolescence.

Results: We found that i) a chronic regimen with probiotics (a mixture of diverse bacterial species such as L. Acidophilus, L. Rhamnosus, B. Lactis and B. Longus) did not prove useful as therapeutic adjuncts in preventing the manifestation of AB in $MAOA^{Neo}$–ES mice at pre-adolescence; ii) genetic background impacted on the responsiveness to both single and repeated administration of cocaine.

Conclusions: Our results reveal that genetic background heightens vulnerability traits (i.e., AB and cocaine abuse) displayed by $MAOA^{Neo}$ mice at pre-adolescence. Future investigations aimed at revealing synaptic, cellular and molecular underpinnings of this genetic by environmental interaction might be instrumental to the development of future preventative strategies for the occurrence of signs and symptoms of these neuropsychiatric disorders.