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Comprehensive multi-parametric behavioral analysis of neuroinflammation

Recently developed various automated video assessment systems that measure mouse behavior produce enormous data sets. The analysis of such multidimensional behavioral data is a difficult task. The questions such as what parameters to use and how to combine similar behavioral parameters into various categories require an application of unbiased statistical approaches. We have developed simple and at the same time powerful protocol of behavioral analysis using R programming. Using this protocol in a mouse model of multiple sclerosis we have characterized a behavioral signature of neuroinflammation. Multiple sclerosis is an autoimmune disease of the central nervous system. Recently, we have discovered an endogenous pathway that limits inflammation in a multiple sclerosis-like diseases in mice. One of the key molecules of these pathways is Nlrx1 that belongs to Nlr family of proteins. Nlrs bind multiple proteins inside cells thus redirecting molecular signaling. Using state-of-the-art automated behavioral platform, we demonstrate that Nlrx1 inhibits progression of the diseases in a mouse model of MS. Furthermore we were able to construct mice with an increased predisposition to MS. These mice demonstrate the spontaneous appearance of the disease without any immunization. This model helped us to dissociate the sickness behavioral profile from the behavioral signature of neuroinflammation. We have grouped 33 behavioral activities into clusters and factors that enabled us to reveal signs of neuroinflammation within the first week after the disease induction. In addition, we noted significant differences in the circadian rhythm of mice with the neuroinflammatory component. In conclusion, the approach that we used in our study to analyze behavioral signature of neuroinflammation presents highly sensitive, automated, and easy-to-use tool that can be applied to evaluate progression of neurodegenerative diseases and various treatment paradigms.

Biography

Denis Gris has started his scientific career with the Master's and PhD in Neuroscience at Dr. Lynn Weaver's laboratory at the University of Western Ontario. He studied the role of inflammation in spinal cord injury. He discovered that the influx of neutrophils is detrimental for recovering after spinal cord injury. Using anti CD11d antibody as a treatment, he demonstrated that animals recovered faster and better after the treatment. Also, he showed that severe spinal cord injury results in massive inflammatory reactions throughout the body leading to the syndrome similar to multiple organ dysfunction syndromes. He continued his education in Dr. Jenny P-Y Ting's laboratory as a post-doctoral fellow at the University of North Carolina at Chapel Hill. There he studied in detail mechanism of activation of innate and adaptive immune responses. In collaboration with Dr. Wen, Dr. Eitas, Dr. Allen, and other members of the laboratory, he studied inflammation during obesity which leads to insulin resistance; innate and adaptive responses during multiple sclerosis. In summary, his role in this laboratory was to define the role of the novel family of immunoregulatory proteins (NLRs) in different human diseases. Currently,he is a member of the Immunology Program at the University of Sherbrooke and he is studying neuro-immune interactions during healthy state and disease.

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