PRION PROTEIN IS A KEY DETERMINANT OF ALCOHOL SENSITIVITY THROUGH THE MODULATION OF N-METHYL-D-ASPARTATE RECEPTOR (NMDAR) ACTIVITY

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The cellular prion protein (PrPc) is absolutely required for the development of prion diseases, however its physiological functions in the central nervous system remain elusive.

Using a combination of behavioral, electrophysiological and biochemical approaches on transgenic mouse models, we provide strong evidence for a novel physiological role of PrPc at synaptic level. Indeed, PrP knock-out mice present a greater sensitivity to the sedative effects of ethanol compared to wild-type control mice. In addition, we show that PrPc is required to induce acute tolerance to ethanol by modulating the N-methyl-D-aspartate receptor function. This effect requires the activation of a Src-protein tyrosine kinase dependent intracellular signaling pathway. Together, our results reinforce the concept of a crucial role of PrPc in synaptic function.