A subgroup of affective and schizophrenic spectrum psychoses may be related to mild encephalitis (ME) triggered by various infectious agents and/or due to autoimmune responses (Bechter 2001), a hypothesis gaining more and more plausibility from new results in various fields, though different pathogenetic explanations exist (Müller & Schwarz 2007; Yolken & Torrey 2008). Therapy resistant cases of suggested ME related spectrum psychoses were successfully treated by cerebrospinal fluid filtration (CSFF) (Bechter et al 2000), a method previously shown effective in Guillain-Barré syndrome (Wollinsky et al 2001), a neurological autoimmune disorder. Patients with psychoses treated by CSFF were followed up over years, majority showing sustained improvement (Bechter 2007). Unexpected was that comorbid chronic pain syndromes in patients with depression improved with CSFF within days. This observation, and certain topological aspects, were attributed to a possible direct interaction between CSF and nerves. Indeed, investigations in mammals, showed that CSF efflux along brain nerves and peripheral nerves physiologically occurs and such may exist analogous in humans. Therefore the hypothesis of a direct local interaction of CSF with brain nerves and peripheral nerves during efflux appears plausible and can explain unexplained symptoms in various human diseases, in which toxic or inflammatory CSF states are prevalent (examples to be presented). This hypothesis leads to new insights into the pathogenesis of symptoms in various neurological and psychiatric disorders and change of treatment approach. Yet, a bias toward central or cortical explanation of chronic pain syndromes neglecting or underestimating peripheral triggers appears prevalent.