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Title : Similar anomalies in the thalamic reticular nucleus of a mice model of redox dysregulation and of schizophrenia patients

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Abstract. Growing evidence points to a disruption of thalamo-cortical circuits in schizophrenia (SZ) and bipolar disorder (BD). It has been hypothesized that the thalamic reticular nucleus (TRN), a thin layer of inhibitory neurons that target thalamo-cortical neurons, could be affected in SZ because of its role in gating and shaping thalamo-cortical information flow and of its involvement in sleep spindle generation (known to be impaired in SZ). Recently, a postmortem study has shown that the numbers of TRN neurons expressing parvalbumin (PV), which form the main TRN neuronal population, are reduced in SZ and BD patients. The perineuronal net, a specialized extracellular matrix that densely enwraps many TRN neurons is also abnormal in both diseases. These TRN anomalies are not associated with the duration and age onset of the illness, and with the medication. Using rodent models, we find that the TRN neurons are prone to oxidative stress, a condition reported in both SZ and BD. Such a susceptibility to oxidative stress is already present in very young animals and leads to reduced number of TRN PV-immunoreactive neurons and abnormal perineuronal net as observed in patients. Furthermore, it alters the firing properties of TRN neurons in a way that is consistent with the sleep spindle deficits found in SZ. Thus, oxidative stress induced structural and functional alteration of the TRN is a potent pathological mechanism leading to aberrant thalamo-cortical communication and contributing to a large array of symptoms and sensory / cognitive deficits typical of these psychiatric disorders.