Abnormal high frequency oscillations: a core feature in rat models of schizophrenia

NMDA receptor antagonists have been used for many years to model key aspects of schizophrenia. Abnormal activity of limbic structures, as demonstrated by neurochemical, electrophysiological, molecular and metabolic studies, has been suggested to underpin the psychotomimetic actions of NMDA receptor antagonists. The nucleus accumbens (NAc), is central to several hypotheses of the pathophysiology of schizophrenia. Here, we have recorded electrophysiological activity of the NAc in freely moving rats and show that high frequency oscillations (HFO, 130-180 Hz) fulfill 4 criteria as a biomarker in models of schizophrenia. 1) HFO are the dominant frequency band affected by systemic and local (into the NAc) administration of NMDAR antagonists. 2) HFO are associated with emergence from ketamine anesthesia. 3) HFO are potentiated in the MAM neurodevelopmental model of schizophrenia. 4) Atypical antipsychotics reduce the frequency of HFO. The occurrence of aberrant oscillations in the NAc may coordinate abnormal HFO recorded in other brain regions (where HFO has also been reported after NMDA administration). Together, these findings suggest that HFO may be pathologically important and be a useful biomarker for therapeutic development.