EPILEPSY AS A MODEL FOR STUDYING NEURAL NETWORKS Hrvoje Hećimović Zagreb Epilepsy Center, University Hospital, Zagreb, Croatia hecimovic@inet.hr

Epilepsy is a chronic disorder that adversely affects social, vocational, and psychological functioning. Despite the variety and complexity of the negative clinical associations with epilepsy, depression is remarkably prevalent in patients with epilepsy.

An estimated 30-55% of persons with refractory epilepsy have major depression, and depression has a stronger correlation than seizure frequency with quality of life (1). Available data indicate that epilepsy and depression may share a common neural network, and the clinical expression of disease results from underlying brain dysfunction rather than social and vocational disability (2). The brain regions commonly involved in various types of epilepsies, such as the hippocampus and amygdala in temporal lobe epilepsy and subcortical nuclei in idiopathic generalized epilepsies, are important components of current models of depression (3). Increased understanding of mechanisms of depression in epilepsy is not only crucial for improving care of many persons with seizures, but may also yield useful information about principal mechanisms underlying both depression and epileptogenicity. Recent neuroimaging studies associated depression with specific cerebral structural and functional disturbances, suggesting that a dysfunction in neural networks underlie mood changes (4).

Current evidence suggests that smaller hippocampal volume in humans is not only a hallmark of mesial temporal lobe epilepsy, but is also associated with depression, and functional imaging studies point to dysfunction in the fronto-limbic network in patients with major depressive disorder (5). This is also in concord with reports from animal, lesional, and human postmortem studies. Understanding neuroanatomy and interconnectivity of the structures, neurotransmitter pathways and molecular mechanisms implicated in this dysfunction creates a basis to understand clinical expression of the disease (6). The fronto-limbic pathway presents a model to study a network dysfunction associated with epileptogenicity and mood changes.

1. Kanner AM, Balabanov A (2002) Depression and epilepsy: how closely related are they? Neurology 58:S27-S39.

2. Gilliam F, Santos J., Vahle V, Carter J, Brown K, Hecimovic H (2004) Depression in epilepsy: ignoring clinical expression of neuronal network dysfunction? Epilepsia 45 Suppl 2:28-33.:28-33.

3. Seminowicz DA, Mayberg HS, McIntosh AR, Goldapple K, Kennedy S, Segal Z, Rafi-Tari S (2004) Limbicfrontal circuitry in major depression: a path modeling metanalysis. Neuroimage 22:409-418.

4. Drevets WC (2001) Neuroimaging and neuropathological studies of depression: implications for the cognitive-emotional features of mood disorders. Curr Opin Neurobiol 11:240-249.

5. Sheline YI (2003) Neuroimaging studies of mood disorder effects on the brain. Biol Psychiatry 54:338-352.

6. Buckner RL, Head D, Parker J, Fotenos AF, Marcus D, Morris JC, Snyder AZ (2004) A unified approach for morphometric and functional data analysis in young, old, and demented adults using automated atlas-based head size normalization: reliability and validation against manual measurement of total intracranial volume. Neuroimage 23:724-738.