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Hippocampal asymmetry: differences in the left and right hippocampus proteome in the rat model of temporal lobe epilepsy

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ABSTRACT

The hippocampus is a complex brain structure and undergoes severe sclerosis and gliosis in temporal lobe epilepsy (TLE) as the most common type of epilepsy. The key features of the TLE may be reported in chronic animal models of epilepsy, such as pilocarpine model. Therefore, the current study was conducted in a rat pilocarpine model of acquired epilepsy. Two-dimensional gel electrophoresis based proteomic technique was used to compare the proteome map of the left and right hippocampus in both control and epileptic rats. Generally, 95 differentially expressed spots out of 1300 spots were identified in the hippocampus proteome using MALDI-TOF-TOF/MS. Within identified proteins, some showed asymmetric expression related to the mechanisms underlying TLE imposed by pilocarpine. Assessment of lateralization at the molecular level demonstrated that expression of proteins involved in dopamine synthesis was significantly more in the right hippocampus than the left one. In the epileptic model, reduction in dopamine pathway proteins was accompanied by an increase in the expression of proteins involved in polyamine synthesis, referring to a new regulating mechanism. Our results revealed changes in the laterality of protein expression due to pilocarpine-induced status epilepticus that could present some new proteins as potential candidates for antiepileptic drug design.

Biological significance: In the current study, two-dimensional gel electrophoresis (2-DE) based proteomic technique was used to profile changes in the left and right hippocampus proteome after pilocarpine induced status epilepticus. Spots of proteome maps for two hemispheres were excised and identified with MALDI-TOF-TOF/MS. Analysis of proteome map of the left and right hippocampus revealed a lateralization at the molecular level, in which the expression of proteins involved in dopamine synthesis and release were significantly more in right hippocampi than the left ones in the normal rats. Also, the expression of proteins involved in polyamine synthesis significantly increased in epileptic hippocampus (considerably higher in right hippocampi), whilst the proteins which included in dopamine pathways were decreased. Our results revealed changes in the laterality of protein expression due to pilocarpine-induced status epilepticus that could present some new proteins as potential candidates for antiepileptic drug design.

1. Introduction

Epilepsy is a potentially life-shortening neurological disorder that occurs in ~1–2% of the population worldwide [1]. It is characterized by the periodic and unpredictable incidence of repetitive seizures accompanied by acute systemic and neural insults [2,3]. To understand the functional consequences of changes at the genetic level, assessing molecular changes mediated by the coded proteins and their spatial distribution are important for epilepsy researches. These factors can be best explored using animal models of epilepsy that mimic temporal lobe epilepsy (TLE) as prevalent type of epilepsy in human. Most of them are models of epileptic seizures rather than models of epilepsy [4,5]. Since epilepsy is characterized by spontaneous recurrent seizures (SRS), therefore an acute seizure that is electrically induced in normal non-epileptic animal cannot represent a model of epilepsy [6]. Among epileptic models, pilocarpine model reproduces key features of human TLE and is considered to be the best characterized model [7,8].

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