Abstract of Master's Dissertation

No.1

Course	MPH	Name	Yasushi Miyauchi
Thesis Title	Excitatory amino acids, possible causative agents of nodding syndrome in eastern Africa		

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Background :

Nodding syndrome (NS) is a progressive disease characterized by nodding symptoms clinically with children in eastern Africa. The burden with NS children is heavy not only mentally but financially for themselves and their family. However, the cause and curative of NS have been unknown yet. NS is one type of epilepsy and kainic acid-treated model in experimental animals is well known for epilepsy model of human. In this study, I examined similarities of clinical symptoms and histological cerebral changes in kainic acid-treated rat compared with NS pathogenesis. In addition, I considered the possibility kainic acid agonist may be causative substance for NS.

Objectives :

Objectives of this study is to investigate a possibility of excitatory amino acids as causative agents of NS. Rats were treated with excitatory amino acids and the similarities between these animal models and human NS were examined in terms of clinical symptoms and histopathological changes. In particular, the association of kainic acid with NS was examined.

Methods :

After kainic acid and quisqualic acid were administered in rats, clinical signs in rats were observed. Histological lesions were investigated in kainic acid- or quisqualic acid-treated rat brains and expression of tau protein, GFAP and Iba-1 in kainic acid-treated rat brains were examined at 24 hours, 8 days and/or 29 days post-administration.

＊ The abstract, containing background, objectives, methods, results and conclusion should not exceed 300-500words and printed double sided on A4 paper)

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No.2

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Further study was conducted by literatures reviewing to find candidate substances that exhibit kainic acid receptor agonist and additionally, estimation of human toxicity was conducted for the substance.

Results :

Kainic acid induced epileptic symptoms including nodding accompanied by drooling in rats and bilateral neuronal cell death in the hippocampus, piriform cortex, amygdaloid nucleus and thalamic nucleus of rat brain. In the regions observed neuronal cell death, the overexpression of phosphorylated tau protein in neurons and the increasing of gliosis with time were seen immunohistochemically. These results showed the similarities in clinical symptoms and histological cerebral lesions with the NS and kainic acid-treated rat epilepsy model. On the other hand, in this study, quisqualic acid-treated rats shown hypolocomotion, but induced no epileptic symptoms and histological cerebral lesions.

Tricholomic acid, contained in mouldy maize (*Ustilago maydis)* was suggested to be a potential candidate for kainic acid receptor agonist by searching the previous reports. In addition, from estimation study of human toxicity, the human exposure oral dose showing epileptic symptoms of kainic acid was at 0.2 -2 mg/kg and the intake of tricholomic acid was estimated at 0.6 mg/kg when the child ingests *U. maydis*.

Conclusion :

In kainic acid-treated rat epilepsy model, similarities in clinical symptoms and histological changes to NS were shown. The possibility that tricholomic acid, one of kainic acid receptor agonist, shows epileptic symptoms in children is indicated.