Synergic effect of exercises and nutrition on seizure activity and oxidative stress
간질모델에서 운동과 영양의 시너지 효과

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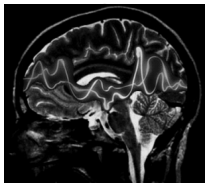
Introduction

What is seizure ?

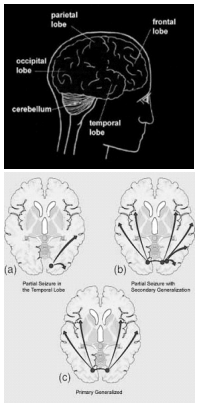
"**Seizure**" is a general term that refers to a sudden malfunction in the brain that causes someone to collapse, convulse, or have another temporary disturbance of normal brain function, often with a loss or change in consciousness.



Introduction

Classification of seizure

1. **Partial seizure** (focal seizure)
   - simple partial seizure
   - complex partial seizure
2. **Generalized seizure**
   - Petit mal seizure
   - Grand mal seizure

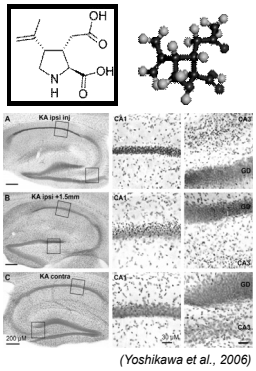


Introduction

Kainic acid (Kainate)

-**Specific agonist** for the kainate receptor which mimics the effect of glutamate

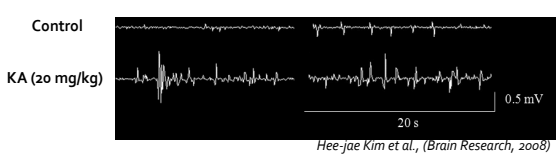
- Used in experiments to distinguish a receptor from the other ionotropic receptors such as **NMDA** and **AMPA**



(Yoshikawa et al., 2006)

Introduction

Kainic acid-induced seizure



Hee-jae Kim et al., (Brain Research, 2008)

Prolonged generalized seizure results in **neuronal injury** and **death** in the brain, and this damage presumably involve the **hippocampus** and **memory** impairments as the major neuronal sequel.

Introduction

Effect of exercise on seizure

In **animal** models, **regular exercise**

- Was found to **retard the development of amygdala kindling** in experimental animal models *(Arida et al., 1998).*

- **Reduced the number of seizure** *(Arida et al., 1999).*

- **Revert electrophysiological changes** in the hippocampus *(Arida et al., 2009).*

- **Induces positive plastic changes** in hippocampal formation of animals with epilepsy *(Arida et al., 1991).*

Introduction

Effect of exercise on seizure

In **human** studies, **regular exercise**

- A positive effect of physical exercise on seizure frequency and severity in people with epilepsy (Nakken, 1999).

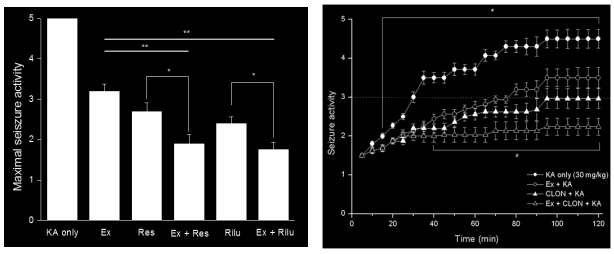
- Electroencephalography (EEG) findings have shown that interictal epileptiform activity remains unchanged or decreases during or immediately after exercise in the majority of patients studied (Esquivel et al., 1991)

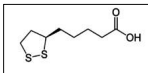
Previous reports (synergic effect)

Potential mechanisms for regulation of seizure activity

Antioxidant

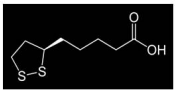
Adrenergic response

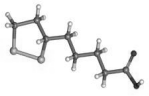




Introduction

Lipoic acid (LA)





Lipoic acid (**LA**), also known as **alpha lipoic acid** (**ALA**) and **thioctic acid.**

LA, as **growth factor**, first isolated in the late 1940s, with **ability to react with ROS**, it was determined to possess antioxidant properties in mitochondrial metabolism.

With current **anticonvulsant evidence** of LA on epilepsy induced by pilocarpine, clinical experiments test LA as a drug for potential treatment for neurological disorders such as depression, Parkinson's disease, and epilepsy.

Purpose

Taken together, previous researchers clearly demonstrated the effect of physical exercise and LA on brain damage or seizure activity by **attenuating oxidative stresses**. However potential synergic effect of physical exercise and LA on preventing seizure development has not been explored yet.

Therefore, in the present study, we investigated

the synergic effect of physical exercise and LA on kainic acid-induced seizure activity caused by oxidative stress?

Materials and Methods

Experimental groups

Experimental group	n
Control	9
KA only	9
Exercise + KA	9
LA + KA	9
LA + Exercise + KA	9

Adult male ICR mice weighing approximately 35 g each (8 week-old)

Materials and Methods

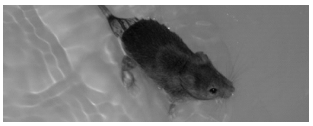
Physical exercise training

8 weeks swimming training (60 min sessions, 5 times per week)

1st week: adaptation to swimming without weights

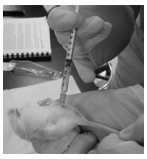
After the water-adaptation period, the mice were made to swim with weights (**5% of body weight**) in order **to improve endurance exercise capacity.**

(Arida et al., 1991).



Materials and Methods

Experimental procedure



Lipoic acid (40 mg/kg)
2 day pre-treatment

8 weeks swimming

Measuring seizure activity for 2 hours

KA (30 mg/kg)
(seizure induction)

Materials and Methods

Measuring of seizure activity

- Monitored for 2 h after the KA injection

Score	Behavior
0	Normal, rare wet dog shakes (WDS), or no convulsion
1	Intermediate number of WDS, rare focal convulsions affecting the head
2	Frequent WDS, frequent focal convulsions, or appearance of generalized convulsions
3	Frequent WDS, focal convulsions, or frequent appearance of generalized convulsions with rearing (but not falling)
4	Frequent WDS, focal convulsions, or frequent generalized convulsions with falling, jumping, and salivation
5	Continuous generalized seizures and death within 2 h

(Kim HJ et al., 2008)

Results

Body weight and endurance capacity

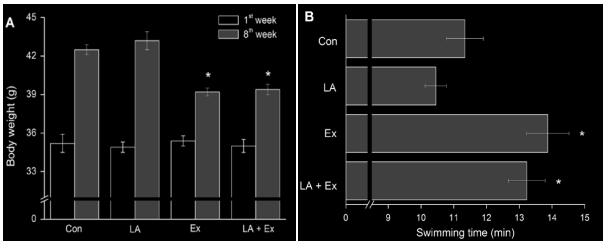
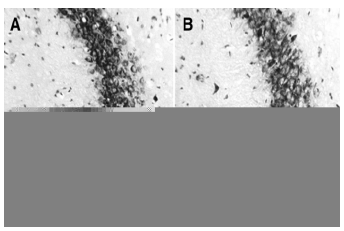


Fig. 1 Effect of 8 weeks of exercise training on body weight (a) and endurance capacity (b).
Values are mean ± ME for n = 9 in each group. *p<0.05 compared to control group (independent t test)

Results

Neuronal injury in hippocampus



KA (30 mg/kg, i.p.), Cresyl Violet
Hippocampus CA3 region

Hee-jae Kim et al., (Brain Research, 2008)

Results

Seizure activity and mortality

Fig. 2 Effect of exercise training and LA treatment on kainic acid induced seizure activity (a) and mortality (b). Values mean ± ME for n = 9 in each group. *p<0.05 compared to 뙿A only뛯group, and #p<0.05 compared to 뙿x + KA뛯or 뙿A + KA뛯group. a Kruskal–Wallis test with Dunn뮙test and kai square test