

Neuronal Mechanisms of Epilepsy: An Experimental Study with Kindling

メタデータ	言語: jpn 出版者: 公開日: 2022-06-30 キーワード (Ja): キーワード (En): 作成者: Wada, Yuji メールアドレス: 所属:
URL	https://doi.org/10.24517/00066701

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1994 Fiscal Year Final Research Report Summary

Neuronal Mechanisms of Epilepsy : An Experimental Study with Kindling

Research Project

Project/Area Number

05670802

Research Category

Grant-in-Aid for General Scientific Research (C)

Allocation Type

Single-year Grants

Research Field

Psychiatric science

Research Institution

Kanazawa University

Principal Investigator

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Project Period (FY)

1993 - 1994

Keywords

EPILEPSY / KINDLING / SEROTONIN / RECEPTOR

Research Abstract

In order to clarify the neuronal mechanisms of epilepsy, we conducted neuropharmacological research on brain serotonin (5-HT) using hippocampal kindling, an experimental model of temporal lobe epilepsy.

In 1993, we examined the effects of intra-hippocampal microinjection of a 5-HT_{1A} receptor agonist (8-OH-DPAT) on hippocampal kindled seizures and suggested that the 5-HT_{1A} receptor subtype has an inhibitory action against the generation of hippocampal seizure activity. We also examined the effects of selective 5-HT reuptake inhibitors with antidepressant properties (fluoxetine and paroxetine), and found that the systemic administration of these compounds shortened the duration of generalized convulsion. In addition, the microinjection study of fluoxetine showed the antiepileptic action of fluoxetine against hippocampal seizure generation.

In 1994, we examined acute and chronic effects of fluoxetine upon hippocampal seizures. Its single administration did not affect hippocampal seizure


activity, whereas fluoxetine at a dose of 10 mg/kg significantly elevated the hippocampal afterdischarge threshold when administered 1 week after its daily treatment for 21 days. The inhibitory effect of acute fluoxetine was also observed in rats receiving a 21-day treatment of gepirone, a 5-HT_{1A} receptor agonist.


Based on these experiment, the 5-HT system is suggested to play an inhibitory role in hippocampal seizure activity. Our results indicate that the effect of long-term fluoxetine administration relate to the well-demonstrated evidence that fluoxetine, upon its long-term administration, can facilitate net 5-HT neurotransmission through desensitization of presynaptic 5-HT autoreceptors. It is also suggested that selective 5-HT reuptake inhibitors possess clinical efficacy on depressive symptoms in patients with seizure disorder.


Research Products (8 results)


All Other

All Publications (8 results)

[Publications] Wada Y, Nakamura M., Hasegawa H, Yamaguchi N: "Effect of serotonin uptake inhibiting antidepressants on hippocampal kindled seizures in cats" Neuroscience Research Communications. 12. 119-124 (1993) 


[Publications] Wada, Y, Nakamura M, Hasegawa H, Yamaguchi N: "Microinjection of the serotonin uptake inhibitor fluoxetine elevates hippocampal seizure threshold in rats" Neuroscience Research Communications. 13. 143-148 (1993) 


[Publications] Wada, Y, Nakamura M., Hasegawa, H., Yamaguchi N.: "Intra-hippocampal injection of 8-OH-DPAT inhibits partial and generalized seizures induced by kindling stimulation in cats" Neuroscience Letters. 159. 179-182 (1993) 

[Publications] Wada, Y, Shiraishi J., Nakamura M: "Prolonged but not acute fluoxetine administration produces its inhibitory effect on hippocampal seizures in rats" Psychopharmacology. (印刷中). (1995) 

[Publications] Wada Y, Nakamura M, Hasegawa H, Yamaguchi N: Neuroscience Research Communications. 12. 119-124 (1993) 

[Publications] Wada Y, Nakamura M, Hasegawa H, Yamaguchi N: Neuroscience Research Communications. 13. 143-148 (1993) 

[Publications] Wada Y, Nakamura M, Hasegawa H, Yamaguchi N: Neuroscience Letters. 159. 179-182 (1993) 

[Publications] Wada Y, Shiraishi J, Nakamura M: Psychopharmacology. in press. 

URL: https://kaken.nii.ac.jp/report/KAKENHI-PROJECT-05670802/056708021994kenkyu_seika_hokoku_

Published: 1996-04-14