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Conference Paper Abstract

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Effect of RVD-hemopressin on amyloid- β induced toxicity in human SH-SY5Y neuroblastoma cells

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Introduction: Previous *in vitro* and *in vivo* studies have demonstrated the protective properties of lipid endocannabinoids against amyloid- β (A β) induced neurotoxicity^{1,2}. Lipid-derived endocannabinoid agonists such as 2-arachidonoylglycerol (2-AG) can exert their effects via both the extra- and intracellular cannabinoid receptor-1 (CB₁)³. Pepcans are a group of haemoglobin derived peptide cannabinoids and are found throughout the CNS³. They are cell-impermeant and act on the extracellular CB₁ receptor^{3,4} as agonists/antagonists. The pepcan RVD-hemopressin (RVD) is a CB₁ receptor agonist³. The aim of this study was to determine whether RVD is protective against A β toxicity.

Method: This study employed MTT cell viability assays to investigate the effects of the peptide CB₁ agonist RVD and lipid CB₁ agonist 2-AG plus the CB₁ antagonist AM281 on A β 25-35 induced neurotoxicity in human neuroblastoma SH-SY5Y cells. Data was analyzed by one-way analysis of variance (ANOVA).

Results: RVD (0.01-10 μ M) had no effect on 10 μ M A β 25-35 induced neurotoxicity in SH-SY5Y cells, whereas 2-AG (0.02-10 μ M; $P < 0.05$ vs A β 25-35 alone) promoted a concentration dependent inhibition (Figure 1A). The CB₁ antagonist AM281 (10 μ M) had no effect on RVD (10 μ M) plus 10 μ M A β 25-35, however it abolished the protective effects of 2-AG (10 μ M; $P < 0.05$ vs A β 25-35 alone) on 10 μ M A β 25-35 induced neurotoxicity (Figure 1B).

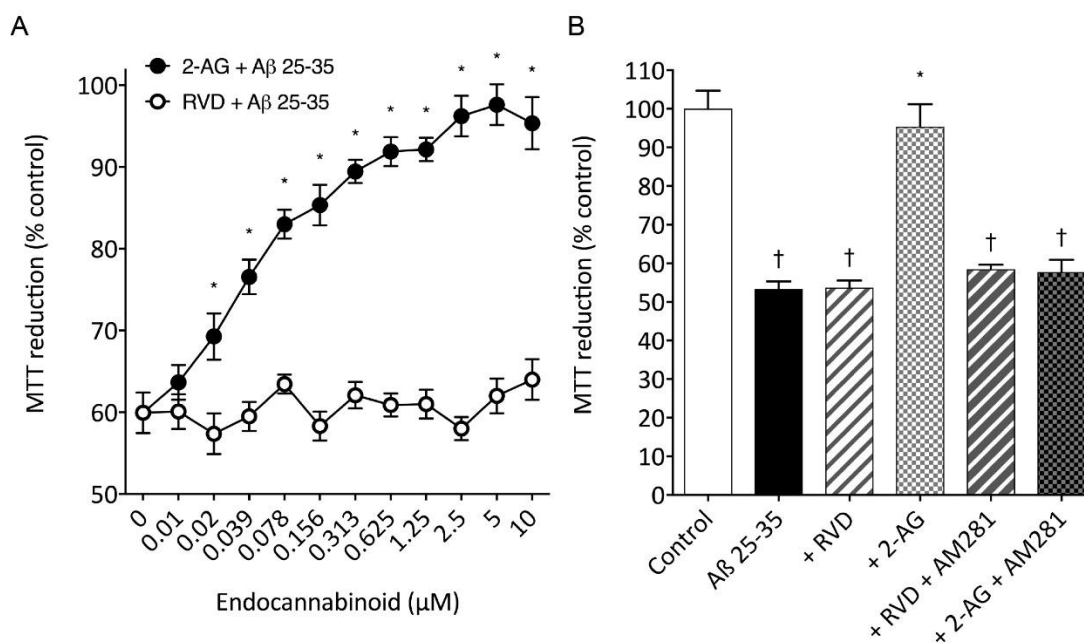


Figure 1. (A) Dose-response curves for RVD plus 10 μ M A β 25-35 and 2-AG plus 10 μ M A β 25-35 on MTT reduction in SH-SY5Y cells. (B) SH-SY5Y cells were exposed to 10 μ M A β 25-35 alone, or plus 10 μ M RVD alone or 10 μ M RVD and 10 μ M AM281 or 10 μ M 2-AG alone or 10 μ M 2-AG and 10 μ M AM281 and cell viability determined by MTT reduction. Results are mean \pm SEM ($n=8$ for each data point); * = $P < 0.05$ vs A β 25-35 alone; † = $P < 0.05$ vs control; (one-way ANOVA).

Conclusion: In conclusion, the peptide cannabinoid RVD is non-protective against A β 25-35 induced neurotoxicity in SH-SY5Y cells. Lipid based endocannabinoids, such as 2-AG, are protective against A β 25-35 induced neurotoxicity¹. Our results support the suggestion that endocannabinoid neuroprotection against A β involves the intracellular CB₁ receptor rather than the extracellular CB₁ receptor⁵.

References:

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