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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 (Aβ) 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 (CB_1)[3]. Pepcans are a group of haemoglobin derived peptide cannabinoids and are found throughout the CNS[3]. They are cell-impermeant and act on the extracellular CB_1 receptor[3,4] as agonists/antagonists. The pepcan RVD-hemopressin (RVD) is a CB_1 receptor agonist[3]. The aim of this study was to determine whether RVD is protective against Aβ toxicity.

Method: This study employed MTT cell viability assays to investigate the effects of the peptide CB_1 agonist RVD and lipid CB_1 agonist 2-AG plus the CB_1 antagonist AM281 on Aβ 25-35 induced neurotoxicity in human neuroblastoma SH-SY5Y cells. Data was analyzed by one-way analysis of variance (ANOVA).

Results: RVD (0.01-10μM) had no effect on 10μM Aβ 25-35 induced neurotoxicity in SH-SY5Y cells, whereas 2-AG (0.02-10μM; $P<0.05$ vs Aβ 25-35 alone) promoted a concentration dependent inhibition (Figure 1A). The CB_1 antagonist AM281 (10μM) had no effect on RVD (10μM) plus 10μM Aβ 25-35, however it abolished the protective effects of 2-AG (10μM; $P<0.05$ vs Aβ 25-35 alone) on 10μM Aβ 25-35 induced neurotoxicity (Figure 1B).

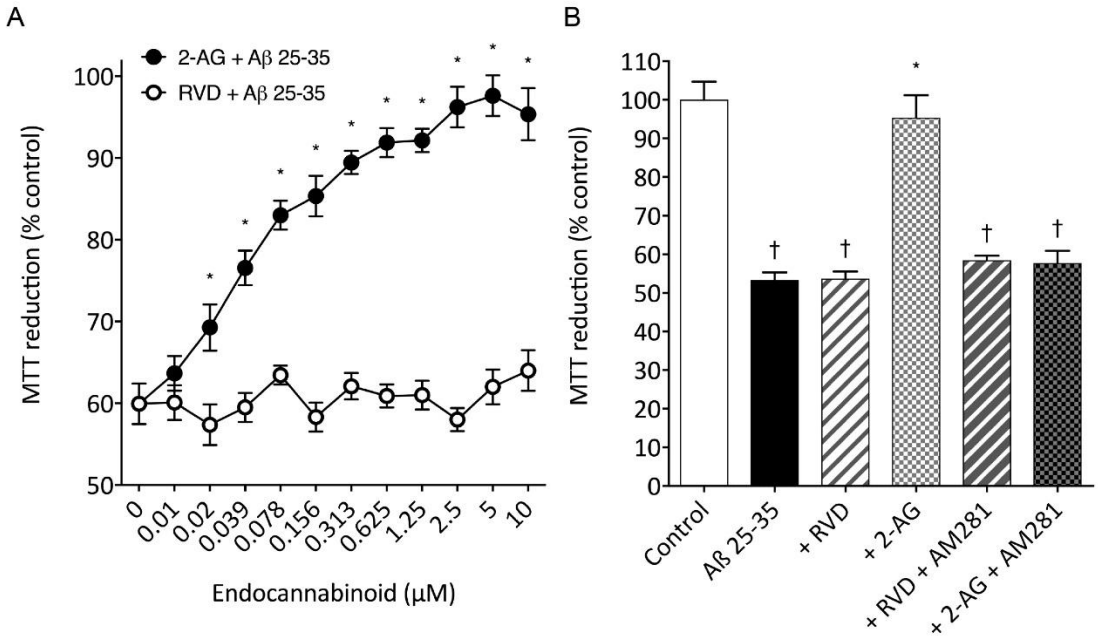

Figure 1. (A) Dose-response curves for RVD plus 10μM Aβ 25-35 and 2-AG plus 10μM Aβ 25-35 on MTT reduction in SH-SY5Y cells. **(B)** SH-SY5Y cells were exposed to 10μM Aβ 25-35 alone, or plus 10μM RVD alone or 10μM RVD and 10μM AM281 or 10μM 2-AG alone or 10μM 2-AG and 10μM AM281 and cell viability determined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

Conclusion: In conclusion, the peptide cannabinoid RVD is non-protective against Aβ 25-35 induced neurotoxicity in SH-SY5Y cells. Lipid based endocannabinoids, such as 2-AG, are protective against Aβ 25-35 induced neurotoxicity[1]. Our results support the suggestion that endocannabinoid neuroprotection against Aβ involves the intracellular CB_1 receptor rather than the extracellular CB_1 receptor[5].

References:

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