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


Introduction: Previous in vitro and in vivo studies have demonstrated the protective properties of lipid endocannabinoids against amyloid-β (Aβ) induced neurotoxicity. Lipid-derived endocannabinoid agonists such as 2-arachidonoylglycerol (2-AG) can exert their effects via both the extra- and intracellular cannabinoid receptor-1 (CB1). Pepcans are a group of haemoglobin derived peptide cannabinoids and are found throughout the CNS. They are cell-impermeant and act on the extracellular CB1 receptor as agonists/antagonists. The pepcan RVD-hemopressin (RVD) is a CB1 receptor agonist. 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 CB1 agonist RVD and lipid CB1 agonist 2-AG plus the CB1 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 CB1 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 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:**


