Angiotensinogen, ACE-1 and ACE-2 expression in Alzheimer’s Disease and Vascular Dementia

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Introduction

Alteration of the renin angiotensin system (RAS) within the brain potentially contributes to the pathogenesis of Alzheimer’s disease (AD). ACE1 encodes angiotensin II converting enzyme-1 (ACE-1), a rate-limiting enzyme in the classical renin-angiotensin system (cRAS) responsible for the conversion of Ang-I (generated from angiotensinogen) to Ang-II. ACE-2 is the central enzyme in the generation of Ang (1-7) from Ang II and is a central mediator of the counter-regulatory RAS (rRAS) arm. In this study, we investigated the mRNA expression of ACE1, ACE2 and AGT; and protein levels of ACE1 in frontal cortex in dementia and examined their associations with the ACE1 variant (rs4343) (a proxy marker for the more commonly studied indel polymorphism) which is an established genetic risk factor for AD.

Materials and Methods

1. ACE1, ACE2 and AGT mRNA expression levels in frontal cortex

![Graph A](image1)

** conclusion: ACE1 mRNA expression, adjusted for the neuronal marker (NeuN), in frontal cortex for control and diseases groups with ACE1 genotype (One-way ANOVA test with Dunn’s post-hoc test, **p=0.0018)**

2. Neuronal ACE1 mRNA level in frontal cortex

![Graph B](image2)

** conclusion: ACE1 protein levels in frontal cortex in relation to disease groups (A) and ACE1 genotypes (B) (One way ANOVA test with Dunnett’s post hoc test, **p=0.0018)**

Conclusion

- ACE1 mRNA expression level, after adjusting to the neuronal marker, NeuN, was significantly lower in VaD brains (p=0.0026).
- ACE2 mRNA expression, after adjusting for GFAP, an astrocytic calibrator gene, was significantly lower in AD and Mixed brains compared to controls (p=0.042 and 0.046, respectively)
- AGT mRNA was expressed at significantly lower levels in AD, Mixed and VaD brains when adjusted for GFAP expression (p<0.002, <0.0001 and 0.0065, respectively)
- Individuals who were homozygous I/I i.e. at risk of AD, had lower neuronal ACE1 mRNA level compared to homozygous (D/D) (p=0.0013).
- ACE-1 protein level were unchanged in AD, VaD and Mixed cases compared to controls in frontal cortex but individuals with homozygous I/I had lower ACE-1 protein level compared to homozygous (D/D) in frontal cortex (p=0.0018).