



# Angiotensin II type 1 receptor antibodies in multiple sclerosis: a new biomarker for disease activity?

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## Background & Objectives

Angiotensin II (AngII) is the major effector molecule of the renin-angiotensin system (RAS). It exerts its various actions on the cardiovascular and renal system mainly via the AngII type 1 receptor (AT1R). Ang II was shown to be a potent proinflammatory mediator and recent data highlight the role of the RAS in animal models of multiple sclerosis (MS)<sup>1,2</sup>. Activating antibodies to the AT1R may play a role for the outcome of T cell mediated diseases like renal allograft rejection<sup>3</sup>. Here we evaluate the role of anti-AT1R antibodies in multiple sclerosis (MS).

## Methods

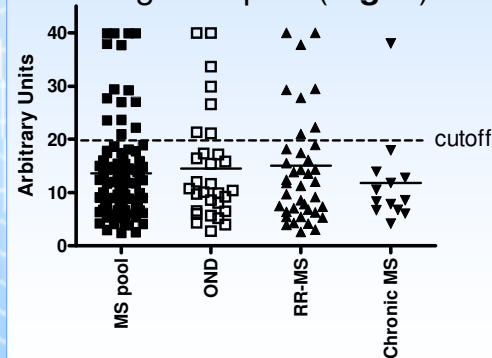
After obtaining informed consent, sera from patients with MS and respective controls were analyzed for the presence of activating anti-AT1R-antibodies by a newly

developed cellular ELISA based on cell lines transfected with the AT1R. MS patients were characterized for their disease course, treatment, and disease activity based on relapses, EDSS progression and MRI activity as defined by gadolinium enhancement of lesions.

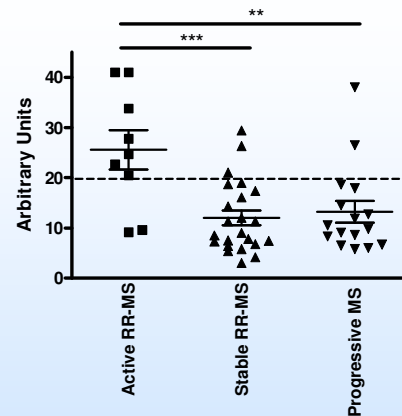
## Results

From 48 MS patients (29 female, 19 male, mean age 40), 67 % presented with a relapsing disease course. In the sera from these patients, significant reactivities towards the AT1R are present in 25 % of subjects. Anti-AT1R antibody titres were significantly higher in the subgroup of MS patients with recent disease activity in the past three months (mean SEM: 25.6 +/- 3.9 in patients with relapses or contrast enhancing lesions vs. 12 +/- 1.5 in patients with relapsing remitting MS without disease activity;  $p < 0.001$ , **Fig. 2**).

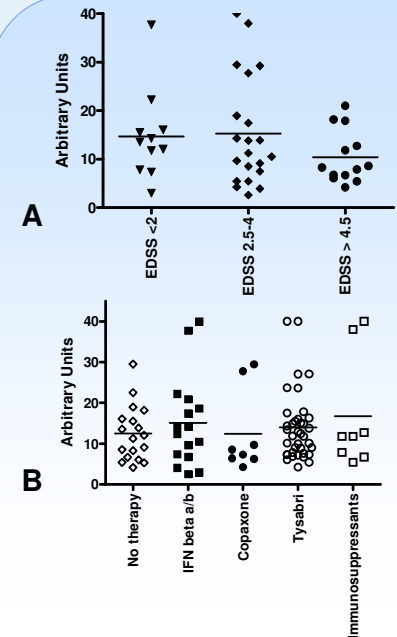
The presence of anti-AT1R antibodies was not associated with EDSS, duration of disease, or pre-existing therapies (**Fig. 3**).



**Fig. 1:** AT1R antibodies are present in a subgroup of MS patients and other neurologic diseases (OND: Huntington's disease)



**Fig. 2:** AT1R antibodies are significantly increased in the subgroup of relapsing-remitting MS patients (RR-MS) with recent disease activity.



**Fig. 3:** AT1R antibodies are not associated with EDSS (A) or disease modifying therapies (B).

## Conclusion

Anti-AT1R antibodies may be a biomarker for disease activity in MS with relapses. The detection of these antibodies may identify MS patients at risk who possibly benefit from a therapeutic modulation of the RAS.

## Literature

1. Stegbauer et al. PNAS 2009; 106(35):14942-7.
2. Platten et al. PNAS 2009; 106(35):14948-53.
3. Dragun et al. N Engl J Med. 2005; 352(6):558-69.