

# Treatment of major depression reduces arterial stiffness

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## Introduction

Major Depression is twice more common in women and evidence suggests that sex differences may exist in antidepressant pharmacokinetics and pharmacodynamics<sup>1</sup>.

Additionally, depression is recognized as a risk factor for cardiovascular disease. We previously showed, in a pilot study of 20 female severely depressed inpatients, that arterial stiffness (measured by Pulse Wave Velocity, PWV) was increased in comparison to non-depressed controls<sup>2</sup>.

In that study, increased arterial stiffness (PWV) was decreased following combination of short-term antidepressant, antipsychotic and/or electroconvulsive treatment.

These findings suggest that arterial stiffness may partly mediate the observed association between depression and cardiovascular adverse events in the short-term.

## Aim

We aim to expand on our previous findings and investigate whether long-term treatment for 21-24 weeks with a combination of a selective serotonin reuptake inhibitor and an atypical antipsychotic would lead to a sustained improvement in arterial stiffness in depressed outpatients. We further aimed to assess whether sex differences exist in this setting.

## Methods

In this open label flexible dose study, patients presenting to primary health care centers for treatment were included if suffering from major depression according to DSM-IV-TR diagnostic criteria, and scoring at least 19 in the 17-item Hamilton Depression Rating Scale (HDRS).

Only patients deemed suitable for treatment with a combination of citalopram 20–60 mg and risperidone 0.5–1 mg were included and those patients with a history of clinically overt cardiovascular disease were excluded.

All patients were scheduled to be examined at baseline and 21-24 weeks after treatment initiation. All patients were drug-free, except 11 out of 72 who were using benzodiazepines.

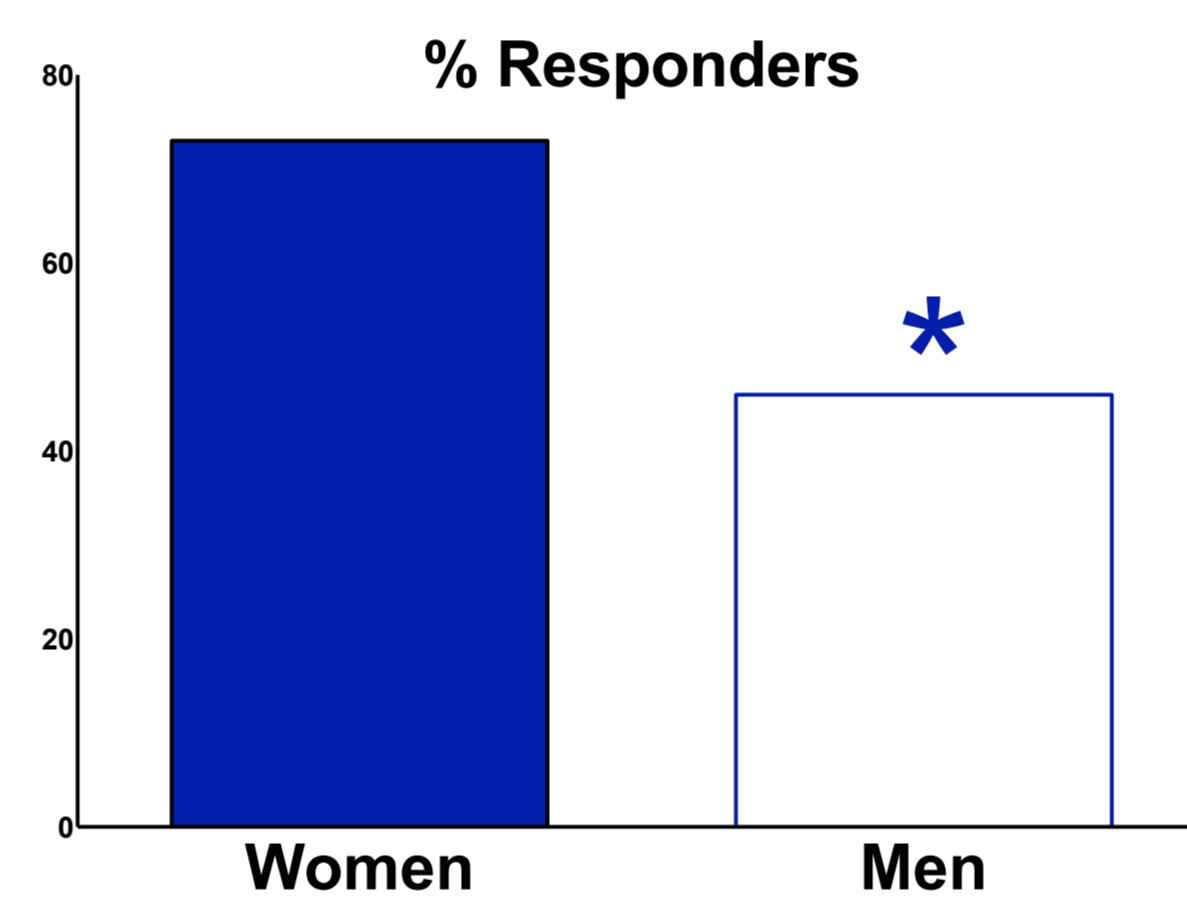
Arterial stiffness was assessed using a validated non-invasive device which allowed the recording and automatic calculation of pulse wave velocity (PWV)<sup>3</sup>.

## Results

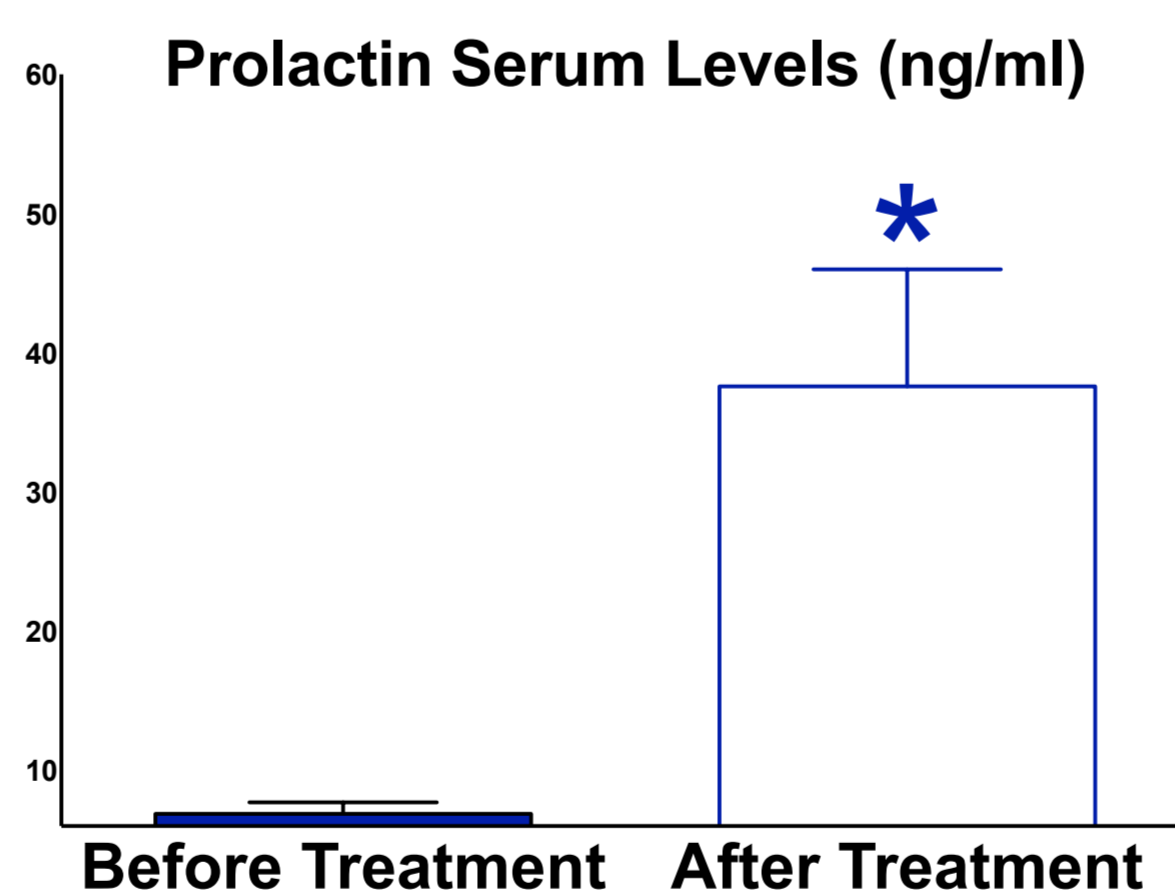
A total of 72 patients have been included and so far 36 patients (13 men, 23 women) have completed their follow-up vascular assessments after a 21-24 weeks long treatment period.

Those patients received a mean citalopram dose of 37 mg and a mean risperidone dose of 0.72 mg.

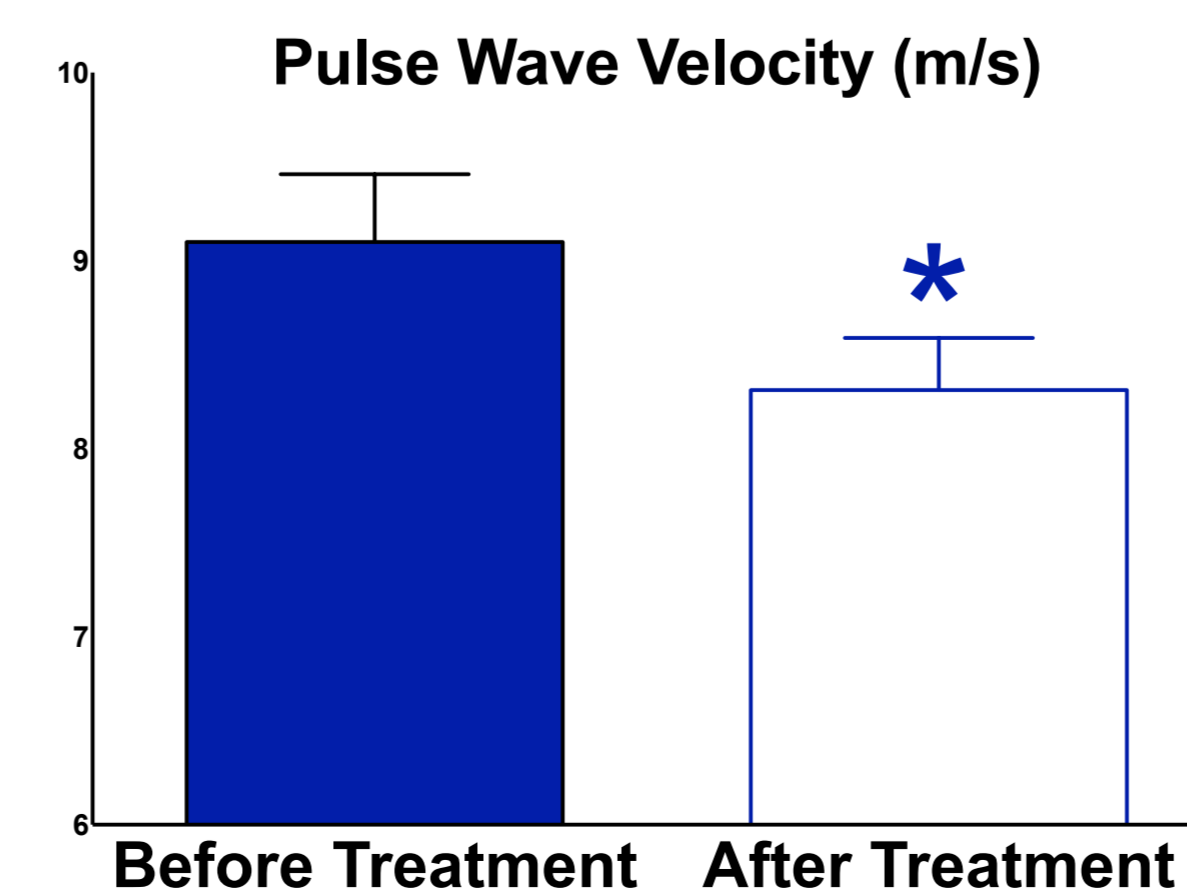
When response to treatment was defined as a 50% reduction in the HDRS, a remarkable 73% of female patients were classified as responders, whereas only 46% of male depressed patients responded to treatment.



In those patients having completed their follow-up assessment, no significant differences were found in blood biochemistry, except prolactin, which was increased on average by 80%.

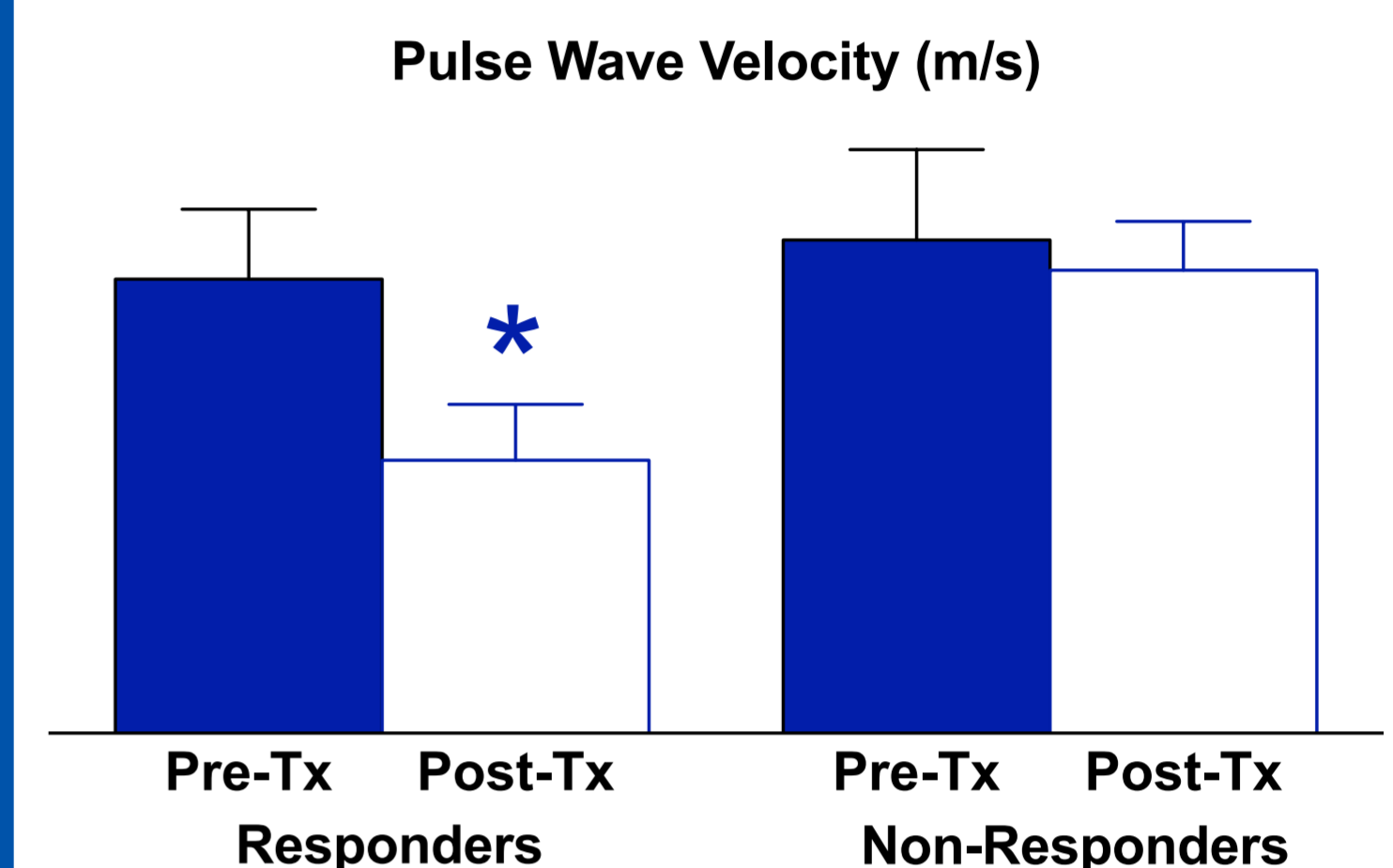


PWV decreased significantly after treatment ( $9.1 \pm 0.35$  vs.  $8.3 \pm 0.27$  Mean  $\pm$  SEM,  $p < 0.001$ , repeated measures analysis of variance).



## Results

The same analysis showed that patients who responded to treatment had a more pronounced reduction in arterial stiffness (PWV).



## Conclusion

Our preliminary results suggest that antidepressant treatment exerts not only an acute effect, as previously reported by our group, but also leads to a long-term sustained improvement of arterial stiffness.

Interestingly, in this on-going study a significant sex-differentiated response to the combined antidepressant/antipsychotic treatment of major depression was also remarked.

According to our preliminary results, the hypothesis of an interaction between gender, treatment response and arterial stiffness warrants further investigation.

## References

1. Kokras, N., Dalla, C., Papadopoulou-Daifoti Z., 2011. Sex differences in pharmacokinetics of antidepressants. *Expert Opin Drug Metab Toxicol* 7(2), 213–226.
2. Oulis, P., Kouzoupis, A., Kyrkou, K., Masdrakis, V.G., Georgiopoulos, G., Karapoulos, E., Georgiou, S., Karakatsanis, N.A., Lykka, M., Papadimitriou, G.N., Papamichael, C., Stamatelopoulos, K., 2010. Reversal of increased arterial stiffness in severely depressed women after 6-week antidepressant treatment. *J Affect Disord* 122(1), 164–166.
3. Ikonomidis, I., Stamatelopoulos, K., Lekakis, J., Vamvakou, G. D., & Kremastinos, D. T., 2008. Inflammatory and non-invasive vascular markers: the multimarker approach for risk stratification in coronary artery disease. *Atherosclerosis* 199(1), 3–11.

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