Plasma acetylated α-tubulin expression as an indicator of antidepressant effectiveness

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INTRODUCTION

- Microtubules are the primary component of the cytoskeleton.
- Alteration in the expression of microtubular proteins associated with microtubule dynamics and neuronal plasticity has been linked with the pathogenesis and treatment of major depressive disorder (MDD) [1].
- Acetylated α-Tubulin (Acet-Tub) is associated with less dynamic microtubules and was found to be increased in the hippocampus in a rat model of depression and rescued by antidepressant treatment [2].
- Burning Mouth Syndrome (BMS) is a neuropathic pain disorder having high comorbidity with MDD.

- **Aim: To explore the feasibility of plasma Acet-Tub as an indicator of antidepressant effectiveness.**

METHODS

Forced Swimming Test: Wistar rats (3-4 months;300-350g) were administered fluoxetine (10mg/kg, *i.p.*) 1h, 5h, and 24h, before forced swimming test (FST). FST was performed as previously described [3].

Rat Plasma: Wistar rats were sacrificed by decapitation and trunk blood was collected immediately following FST. Plasma was isolated from blood samples by centrifugation. Plasma samples were preserved using a protease inhibitor cocktail and stored at -80 °C. Samples were prepared with a protein concentration of 1 µg/µl.

Human Plasma: Venous blood was collected from 20 volunteers and plasma was aspirated following centrifugation. Samples were prepared with a protein concentration of 6 µg/ µl.

Infrared Western Blotting (IFWB): The expression of plasma Acet-Tub was measured using a protocol of IFWB adapted from previous studies [3]. Acet-Tub detection in human plasma was optimised.

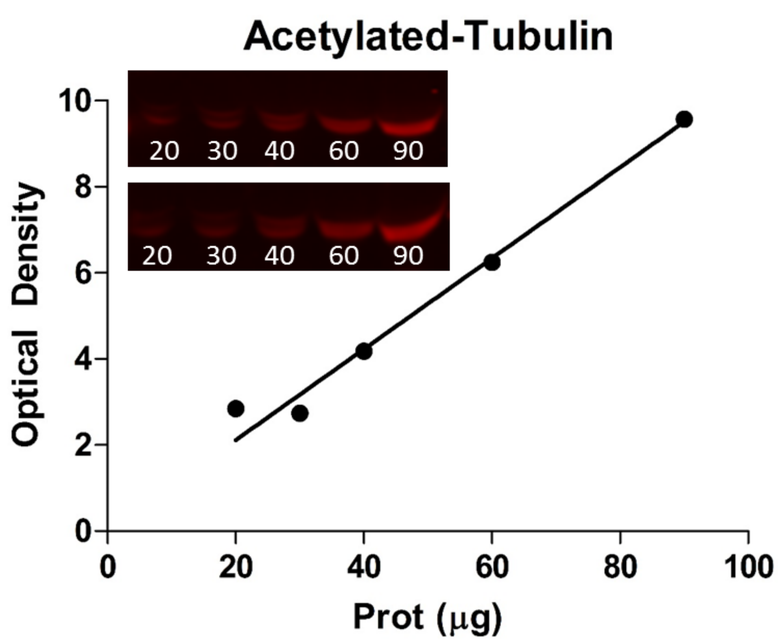

Figure 1. Human Plasma Acet-Tub Optimisation

Human plasma optimised to a signal linearity of R^2=0.9685. Optimal protein concentration determined to be 60µg/µl.

CONCLUSION

- Fluoxetine administration has behavioural antidepressant efficacy in the forced swimming test in Wistar rats.
- In conjunction with rat behavioural data, Acet-Tub expression normalised to transferrin in rat plasma is reduced after receiving fluoxetine treatment.
- BMS patients receiving antidepressant treatment showed reduced Acet-Tub expression compared to those not receiving antidepressant treatment.

- **Acet-Tub can be measured in human plasma and the first clinical data on a limited number of samples suggests the translational validity of Acet-Tub as an indicator of antidepressant efficacy.**

REFERENCES

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[2] Bianchi M and Baulieu EE (2012). 3β-Methoxy-pregnenolone (MAP4343) as an innovative therapeutic approach for depressive disorders. *Proceedings of National Academy of Sciences,* 109 (5): 1713-8.

[3] Ladurelle N, Gabriel C, Viggiano A, Mocaër E, Baulieu EE, Bianchi M (2012): Agomelatine (S20098) modulates the expression of cytoskeletal microtubular proteins, synaptic markers and BDNF in the rat hippocampus, amygdala and PFC. Psychopharmacology, 221, 493-509.

RESULTS

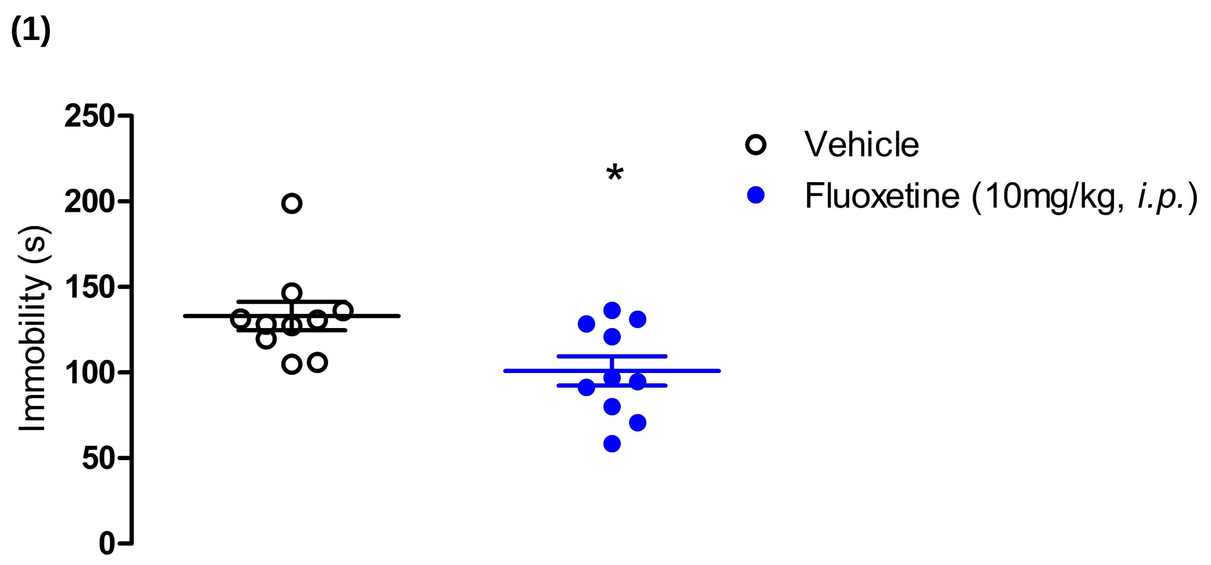

Figure 2. Fluoxetine Reduces Immobility in Forced Swimming Test

*Wistar rats (n=10) show reduced immobility in forced swimming test after receiving fluoxetine treatment 1h, 5h, and 24h pre-test vs vehicle(n=10)(*p<0.05). Student's t-test. Data: Mean ± SEM.*

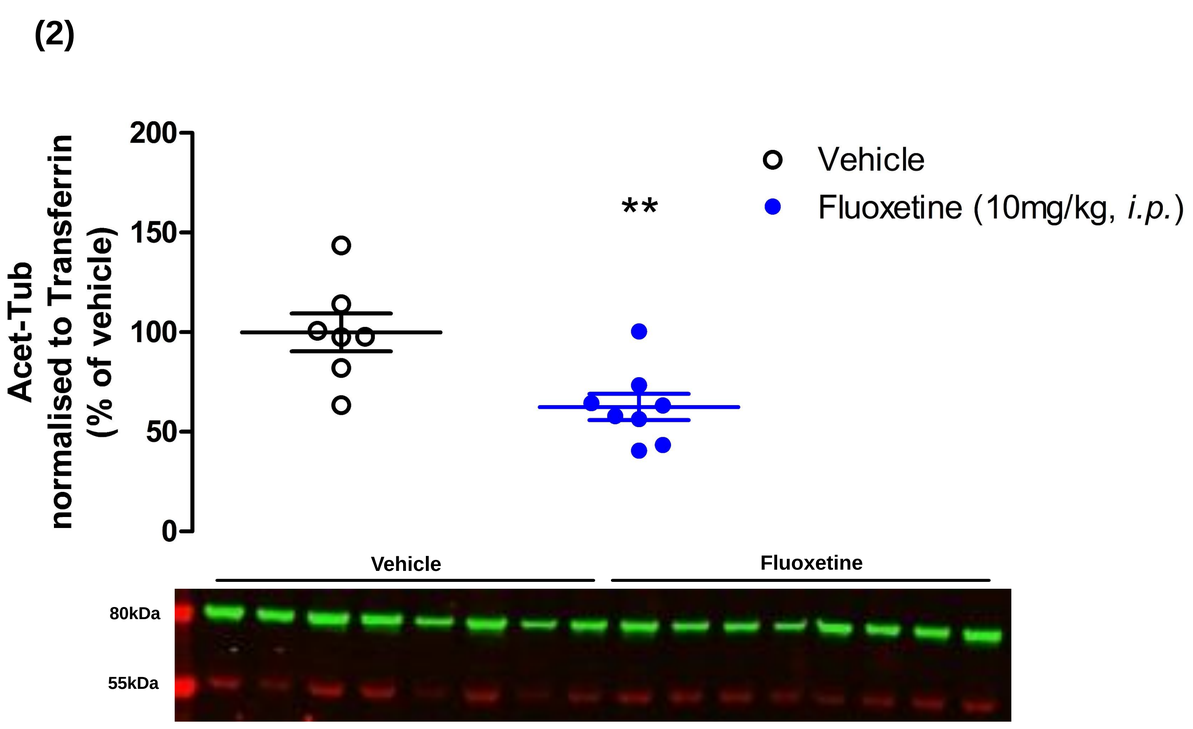

Figure 3. Fluoxetine Reduces Acet-Tub Expression in Rat Plasma

*Wistar rats (n=8) show a reduction in Acet-Tub expression normalised to transferrin following fluoxetine treatment 1h, 5h, and 24h pre-test vs vehicle (n=7)(**p<0.01). Student's t-test. Data: Mean ± SEM.*

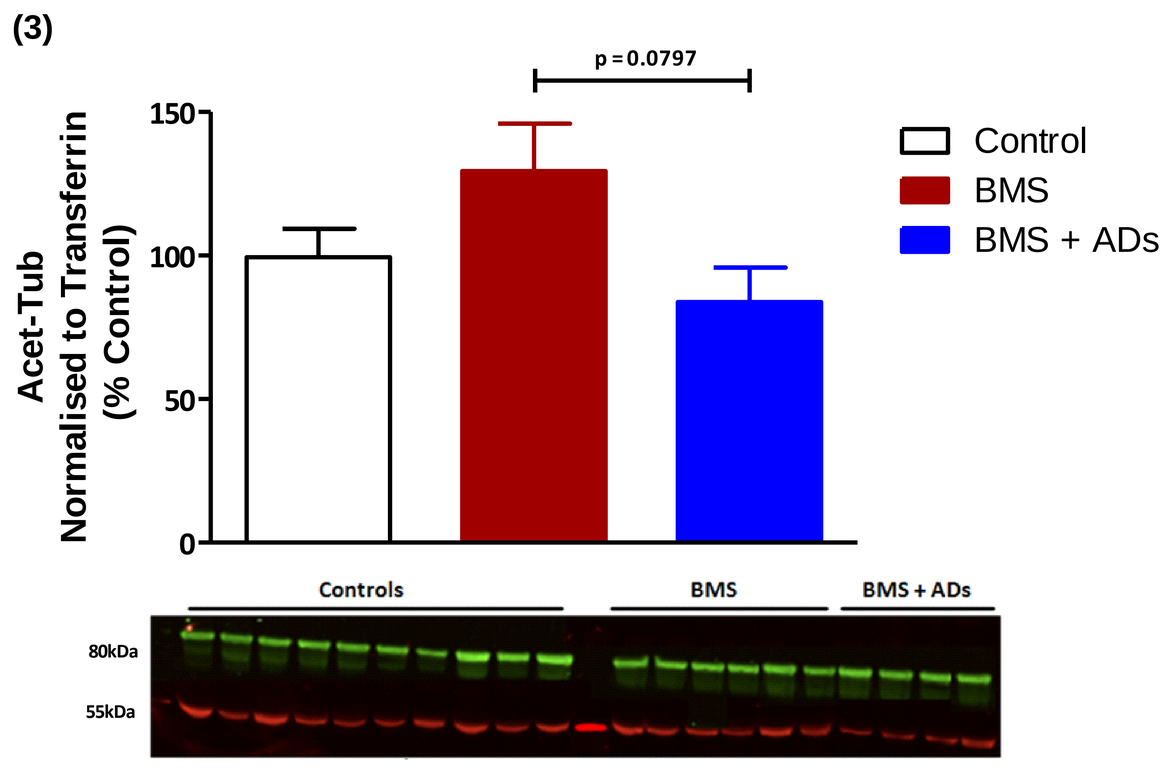

Figure 4. Antidepressant lower plasma Acet-Tub expression in patients with burning mouth syndrome

Plasma from BMS patients receiving antidepressant treatment (n=4) showed reduced Acet-Tub expression normalised to transferrin, compared to health controls (n=10) and BMS patients not receiving antidepressants (n=6). One-way ANOVA. Data: Mean ± SEM.

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