**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.

**RESULTS**

**Figure 2. Fluoxetine Reduces Immobility in Forced Swimming Test**

Wistar rats (n=10) showed 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.

**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**