



HAL
open science

Diabetic neuropathic pain improvement by inhibition of constitutive 5-HT₆ receptor activity in rats

Nazarine Mokhtar, Marcin Drop, Frédéric Lamaty, Pawel Zajdel, Philippe Marin, Stéphane Doly, Christine Courteix

► To cite this version:

Nazarine Mokhtar, Marcin Drop, Frédéric Lamaty, Pawel Zajdel, Philippe Marin, et al.. Diabetic neuropathic pain improvement by inhibition of constitutive 5-HT₆ receptor activity in rats. Neuropathic Pain Special Interest Group (NeuPSIG) 2023 International Congress on Neuropathic Pain, Sep 2023, Lisbon, Portugal. hal-04324131

HAL Id: hal-04324131

<https://hal.science/hal-04324131v1>

Submitted on 5 Dec 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NoDerivatives 4.0 International License

Diabetic neuropathic pain improvement by inhibition of constitutive 5HT₆ receptor activity in rats - TH17

Nazarine Mokhtar¹, Marcin Drop^{2,3}, Frédéric Lamaty², Paweł Zajdel³, Philippe Marin⁴, Stéphane Doly¹, Christine Courteix¹

¹Neuro-Dol, Université Clermont- Auvergne, INSERM / ²IBMM, Université de Montpellier, CNRS, INSERM / ³Faculty of pharmacy, Jagiellonian University Medical College, Poland / ⁴Institut de Génomique Fonctionnelle, Université de Montpellier, CNRS, INSERM

Corresponding authors : nazarine.mokhtar@uca.fr & christine.courteix@uca.fr

Background

Chronic neuropathic pain affects 20% of patients with type 1 and 2 diabetes mellitus. In these patients, neuropathic pain is often associated with **cognitive deficits** and decreased quality of life. The **serotonin type 6 (5-HT₆)** receptor has recently emerged as a modulator of chronic pain and cognitive functions. The 5-HT₆ receptor interacts with intracellular proteins including **mTOR** (mechanistic Target Of Rapamycin), also involved in neuropathic pain and in the regulation of cognitive functions. The present study addresses the involvement of 5-HT₆ receptor constitutive activity and mTOR signaling in neuropathic pain in the experimental model of streptozocin (STZ)-induced diabetic (D) rats.

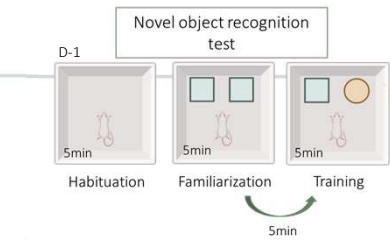
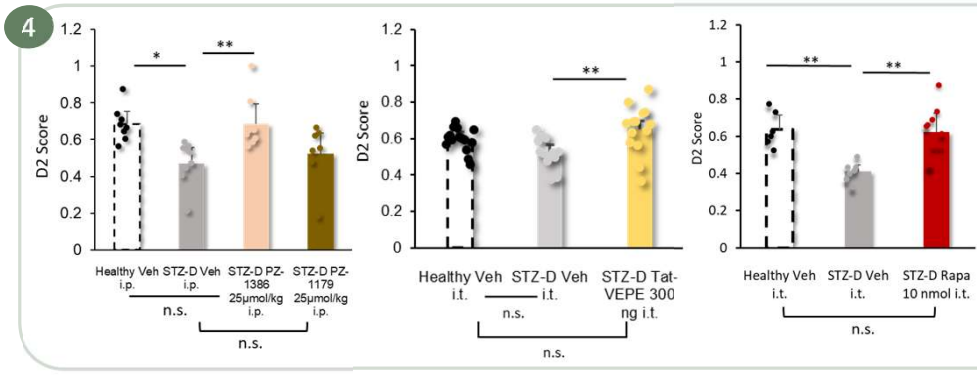
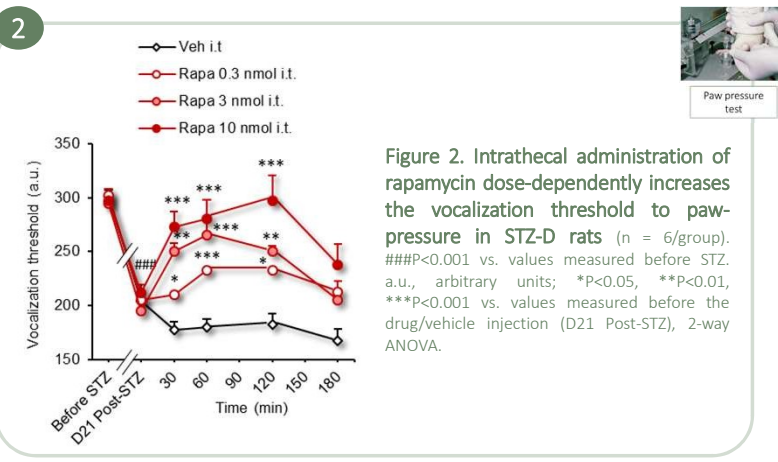
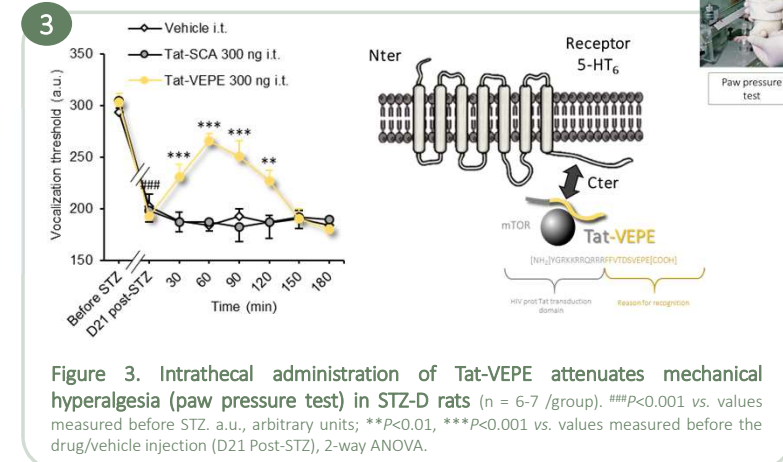
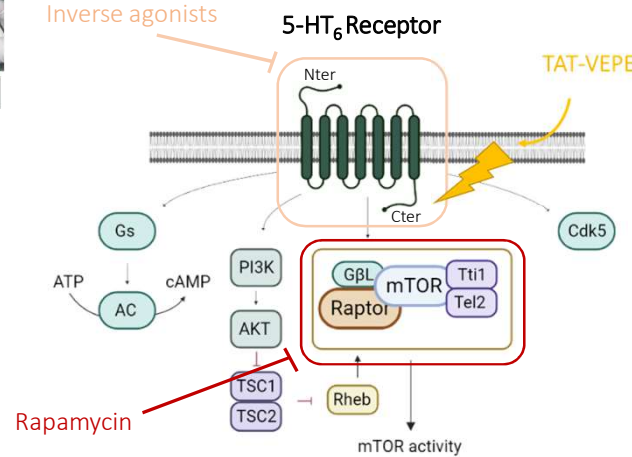
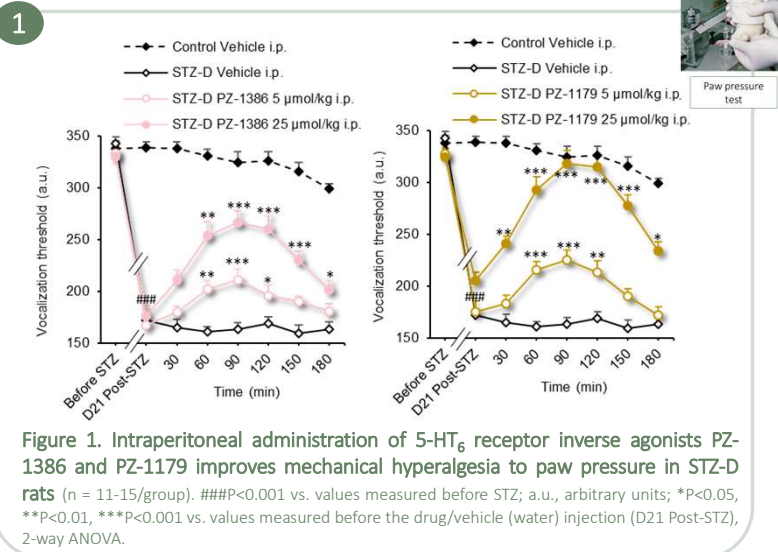
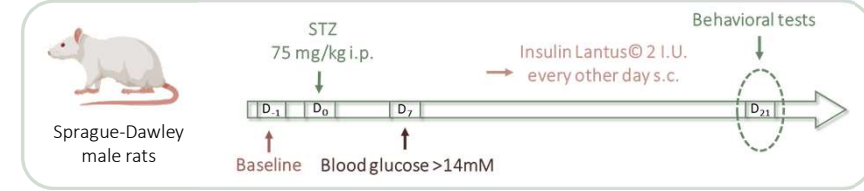


Figure 4. Injection of PZ-1386, Tat-VEPE or rapamycin but not PZ-1179 improves cognitive deficits (novel object recognition test) in STZ-diabetic (STZ-D) rats (n = 7-16/group). D2 score = exploration time of novel object/exploration time of both objects; *P<0.05, **P<0.01, vs. STZ-D Vehicle group, 1-way ANOVA.

Conclusion

These results suggest that the constitutive activity of the 5-HT₆ receptor has a harmful influence in **diabetic neuropathic pain**. Thus, **targeting 5-HT₆ receptor/mTOR complex activity** or 5-HT₆ receptors with inverse agonists represents new strategies to treat **painful diabetic neuropathy** and associated **cognitive co-morbidities**.