Modeling Post-Traumatic Stress Disorder (PTSD) *in vitro*:
A mechanistic exploration of stress-induced neurobiological alterations

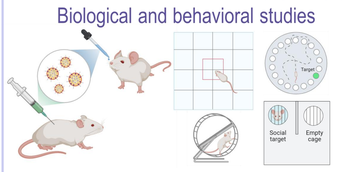
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Introduction

▲ **PTSD-*in vivo* Mus-Rat**
Biological and behavioral studies



Post-Traumatic Stress Disorder (PTSD) is a debilitating neuropsychiatric condition characterized by dysregulated neuronal signaling and neuroinflammatory responses. Existing models are primarily *in vivo*, which are costly and limited in studying human-specific mechanisms. To address this, we established an *in vitro* PTSD model using differentiated SH-SY5Y neurons, although it cannot fully replicate the complexity of the brain or behavioral aspects of PTSD (**Fig.1**)[1].

▼ **PTSD-*in vitro* Hsa**
Human-specific PTSD biological mechanisms



Aim of study

Dexamethasone (DEX) and related corticosteroids could be used as pharmacological **stressors *in vitro*** to **reproduce PTSD's stress-related molecular alterations.**

Materials and methods

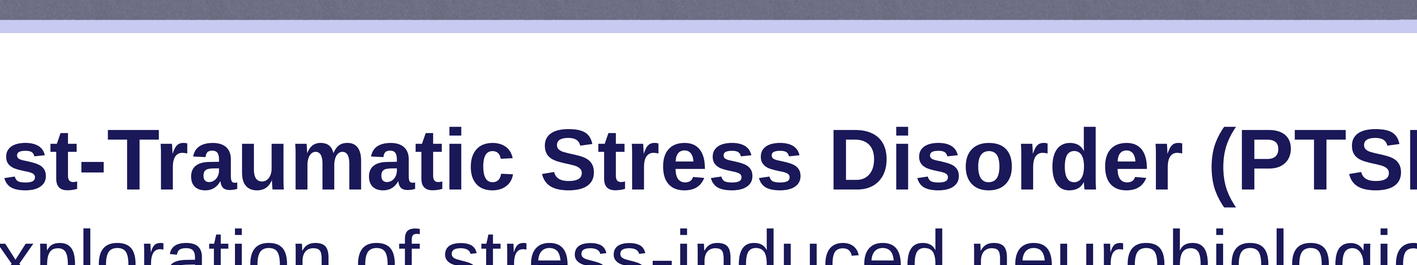
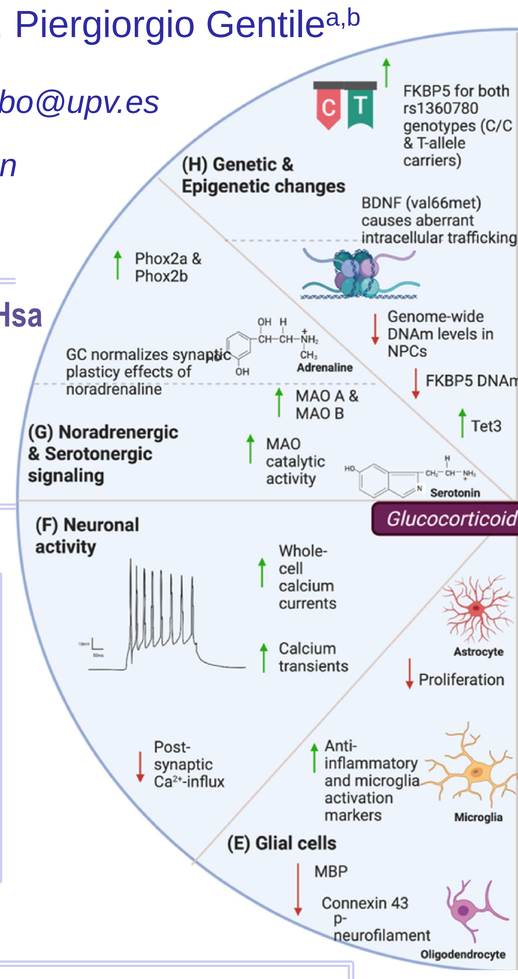


Fig. 1. Key findings of studies investigating glucocorticoid's neurobiological effects in vitro.[1]



Results and discussion

Differentiation of SH-SY5Y neuroblastoma cells into neuron-like phenotypes was successfully achieved through sequential treatment with retinoic acid and BDNF, as confirmed by morphological changes and increased neuronal maturity over time (**Fig. 2AB**).

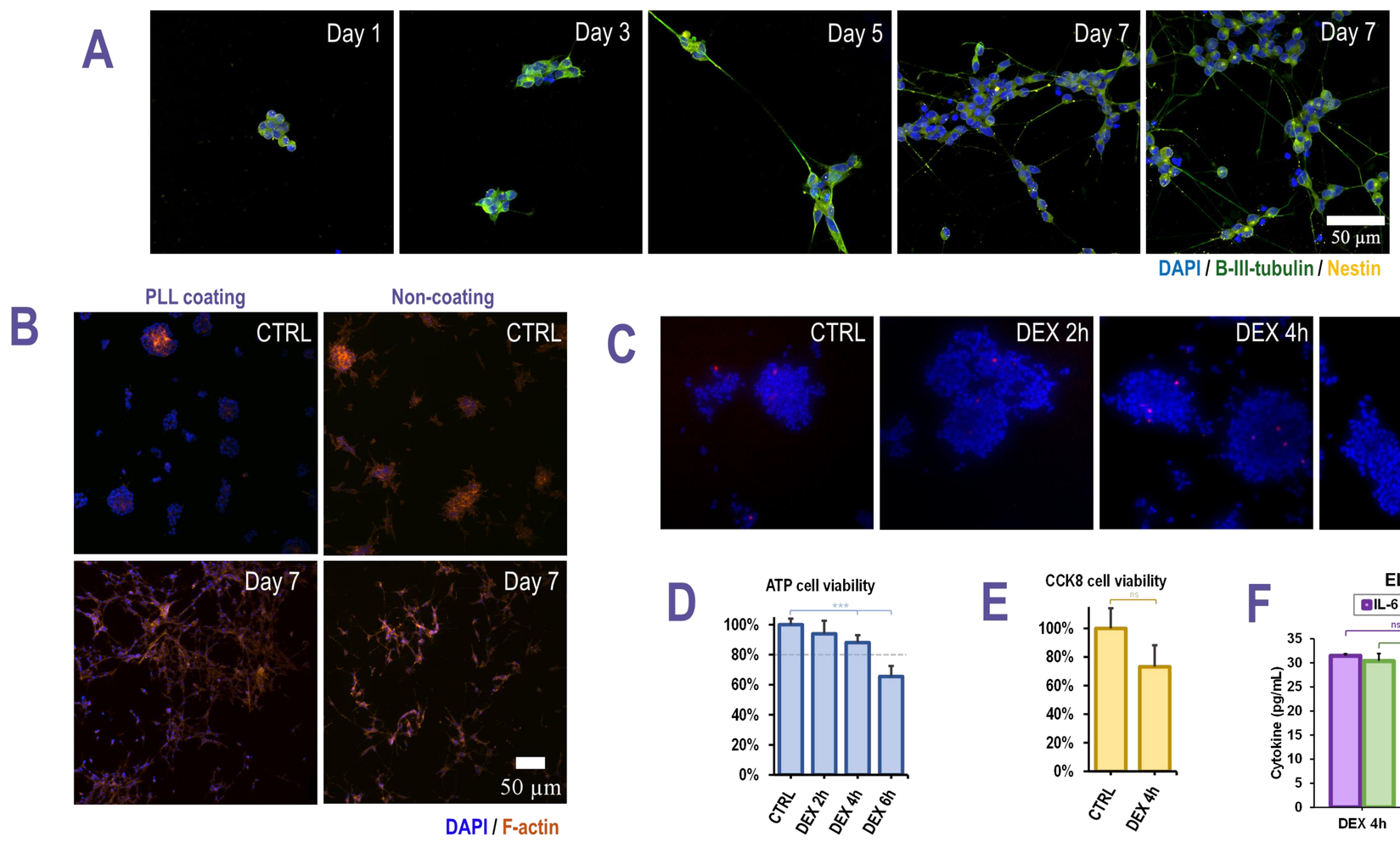


*Fig. 2. Cell differentiation to neuron: under confocal (**A**), and fluorescence (**B**) microscope; Stress-like PTSD 2D-in vitro modelling with dexamethasone (DEX) at 100 nM for 2-4-6h: Live/Dead (**C**), CellTitlerGlo viability (**D**), Cell-Counting Kit-8 (CCK8) (**E**), and ELISA IL-6 and TNF-α (**F**). One-way ANOVA statistics via GraphPad8.0: p-value < 0.001 (***), not-significant (ns).*

Exposure to dexamethasone (100 nM) induced time-dependent alterations in cellular metabolic activity, suggesting a stress-responsive phenotype[2,3]. Notably, short-term exposure appeared to modulate adaptive transcriptional responses, while prolonged treatment led to reduced cell viability and signs of mitochondrial dysfunction (**Fig. 2C-E**)[2-4]. These findings are consistent with stress-induced neurobiological alterations described in Post-Traumatic Stress Disorder, including impaired neuronal resilience and dysregulated inflammatory signaling, like the increasement of IL-6 and TNF-α proinflammatory cytokines (**Fig. 2F**)[4].

References

[1] Bassil, K. et al., 2023, 10.1016/j.ynstr.2023.100530
[2] Lugenbühl, J. F. et al., 2025, 10.1111/jne.70021
[3] Elmorsy, E. et al., 2024, 10.1016/j.steroids.2024
[4] Gupta, S. et al., 2022, 10.3390/cells11132034

Conclusions

This study establishes a reproducible 2D *in vitro* model of stress-induced neuronal dysfunction using differentiated SH-SY5Y cells and corticosteroid stimulation. The model recapitulates key molecular and cellular features associated with PTSD-related stress exposure, providing a controlled platform to investigate underlying mechanisms. Importantly, it enables the evaluation of targeted therapeutic strategies, including RNAi-based nanomedicine approaches, bridging fundamental neurobiology with translational applications.

Next Steps

Future work will focus on extending the model to higher-dose and chronic exposure conditions to better mimic sustained stress environments. Gene expression analysis via qPCR will be conducted to assess the regulation of neuroplasticity-associated markers, including BDNF, FKBP5, and PPP6C. Additionally, integration with nanocarrier delivery systems will be explored to evaluate the efficacy of targeted gene modulation strategies in reversing stress-induced neuronal alterations.

Acknowledgement

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