



# Modulation of ATP-Activated Calcium Intracellular Signaling by Methylglyoxal in Brain Microvascular Endothelial Cells



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## Background

The formation of advanced glycation end products (AGE) is one of the major factors involved in diabetic neuropathy, aging, neurodegenerative diseases, as well as inflammation [1]. *In vitro* models of neuroinflammation are commonly using the exposure of brain endothelial cells to methylglyoxal (MG), ubiquitous product of cell metabolism, that activates TRPA<sub>1</sub>, specific receptors present on the endothelial cells' plasma membrane [2].

## Aim

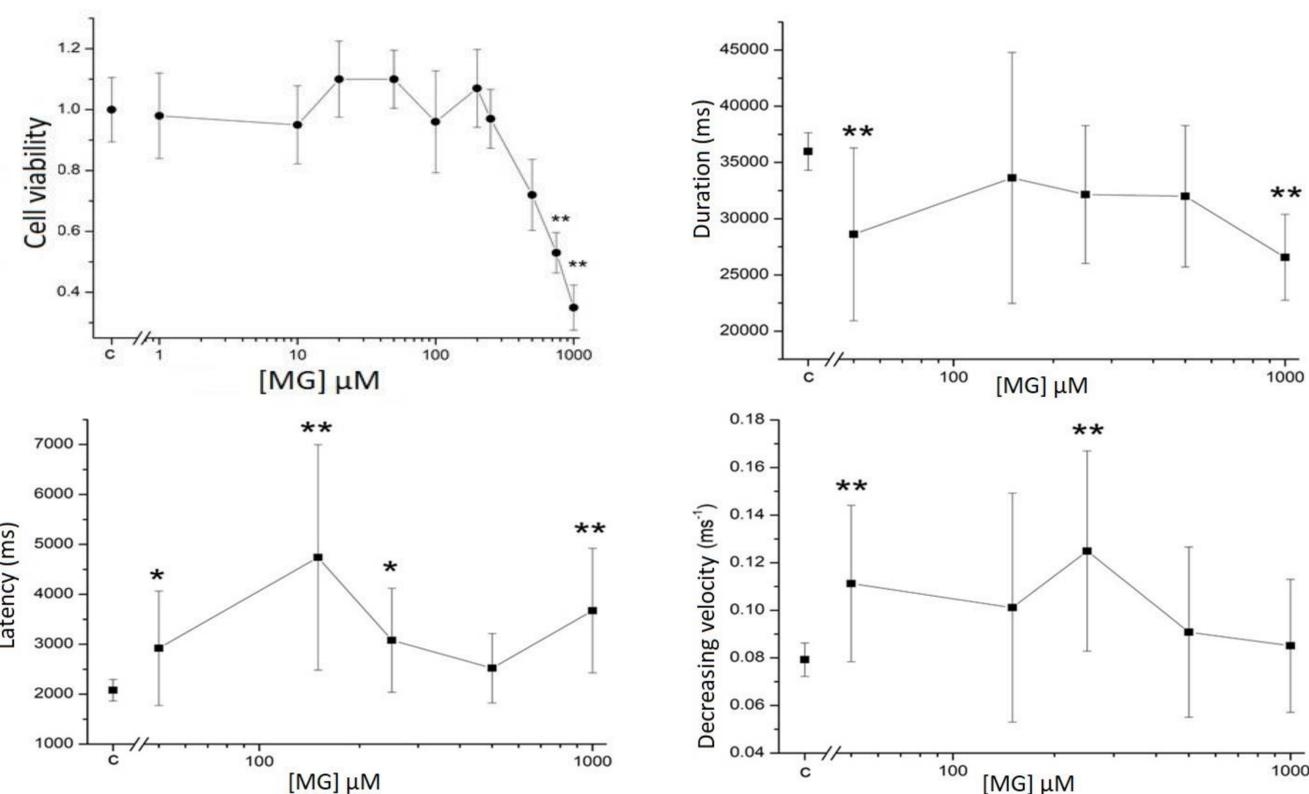
Our study is focused on understanding how exposure to MG affects the brain microvascular endothelial cells in bacterial infection conditions.

## Materials and methods

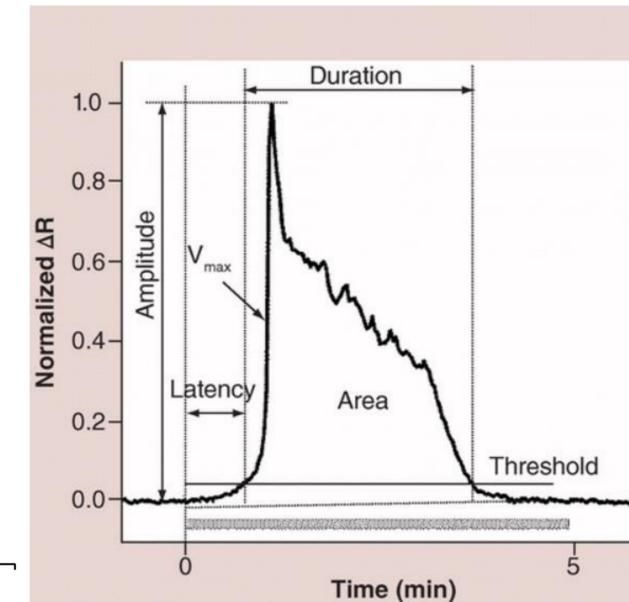
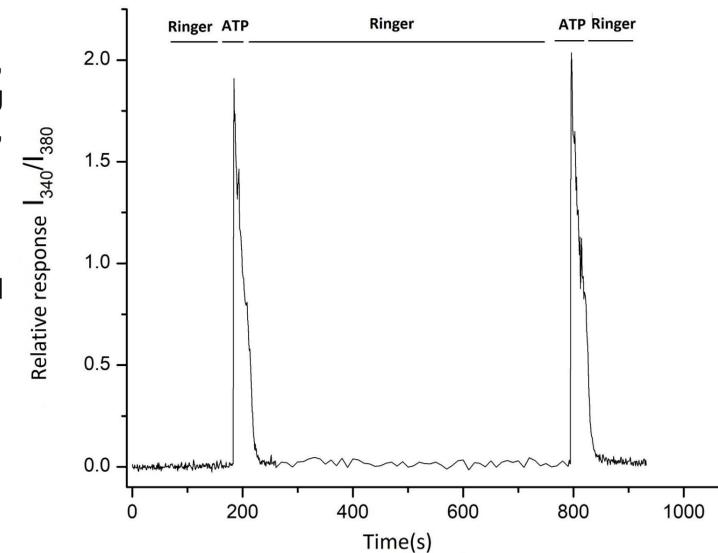
bEnd.3 cells (ATCC) were treated with methylglyoxal (1-1000  $\mu$ M) for 24h. Its effects were tested on MTT cell viability test and on cellular response to ATP quantified through calcium imaging experiments, cells being load with FURA-2AM. The used protocol is illustrated in the figure 1 and for each calcium transient recorded, it was used a MATLAB script previously developed [3] for characterizing a variety of specific parameters, illustrated in figure 2.

## Results

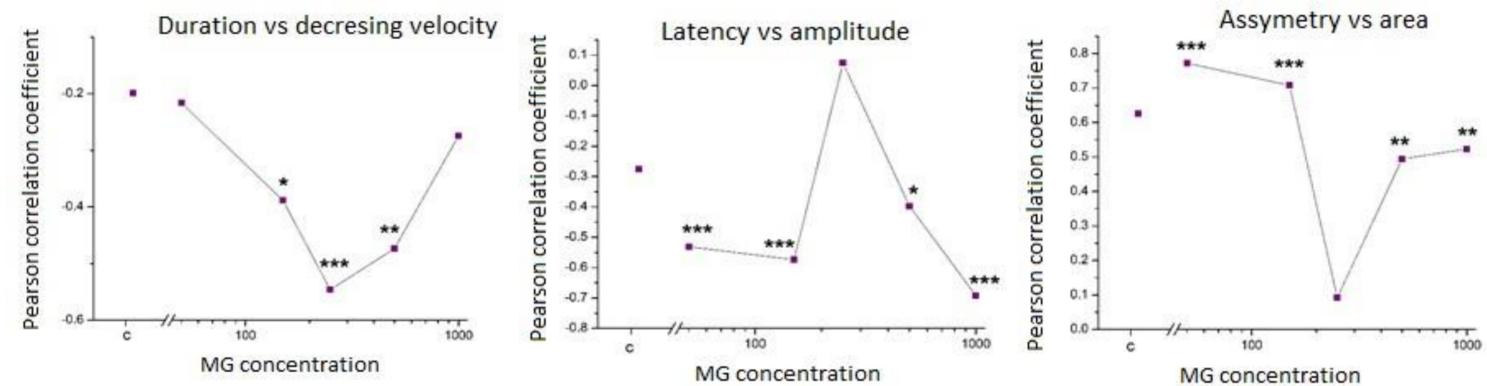
MG decreases the cell viability and transient duration, latency and decreasing velocity



The error bars show the standard deviation (SD). One-way ANOVA's p-values are given for each test with respect to control, with significance labels from Bonferroni post-hoc tests (\* 0.01<p<0.05; \*\* 0.001<p<0.01; \*\*\* p<0.001)



MG modifies the correlation degree between certain pairs of parameters



## Conclusions

- ✓ For higher concentrations (>150  $\mu$ M), MG affects the cell viability
- ✓ MG treatment induces a slower response after extracellular ATP binding to purinergic receptors
- ✓ Endogenous stimuli from bloodstream (MG) modulate ATP-induced calcium transients in endothelial cells from cerebral microvasculature

## References

- [1] Maryam Hussain et al., Novel insights in the dysfunction of human blood-brain barrier after glycation, Mechanisms of Ageing and Development 155 (2016) 48-54
- [2] Kuan-I Lee et al., Role of transient receptor potential ankyrin 1 channels in Alzheimer's disease, Journal of Neuroinflammation (2016) 13:92
- [3] Beatrice Mihaela Radu, Mihai Radu, Cristina Tognoli, Donatella Benati..., Paolo Francesco Fabene, Nanomedicine 2015, volume 10, number 22.