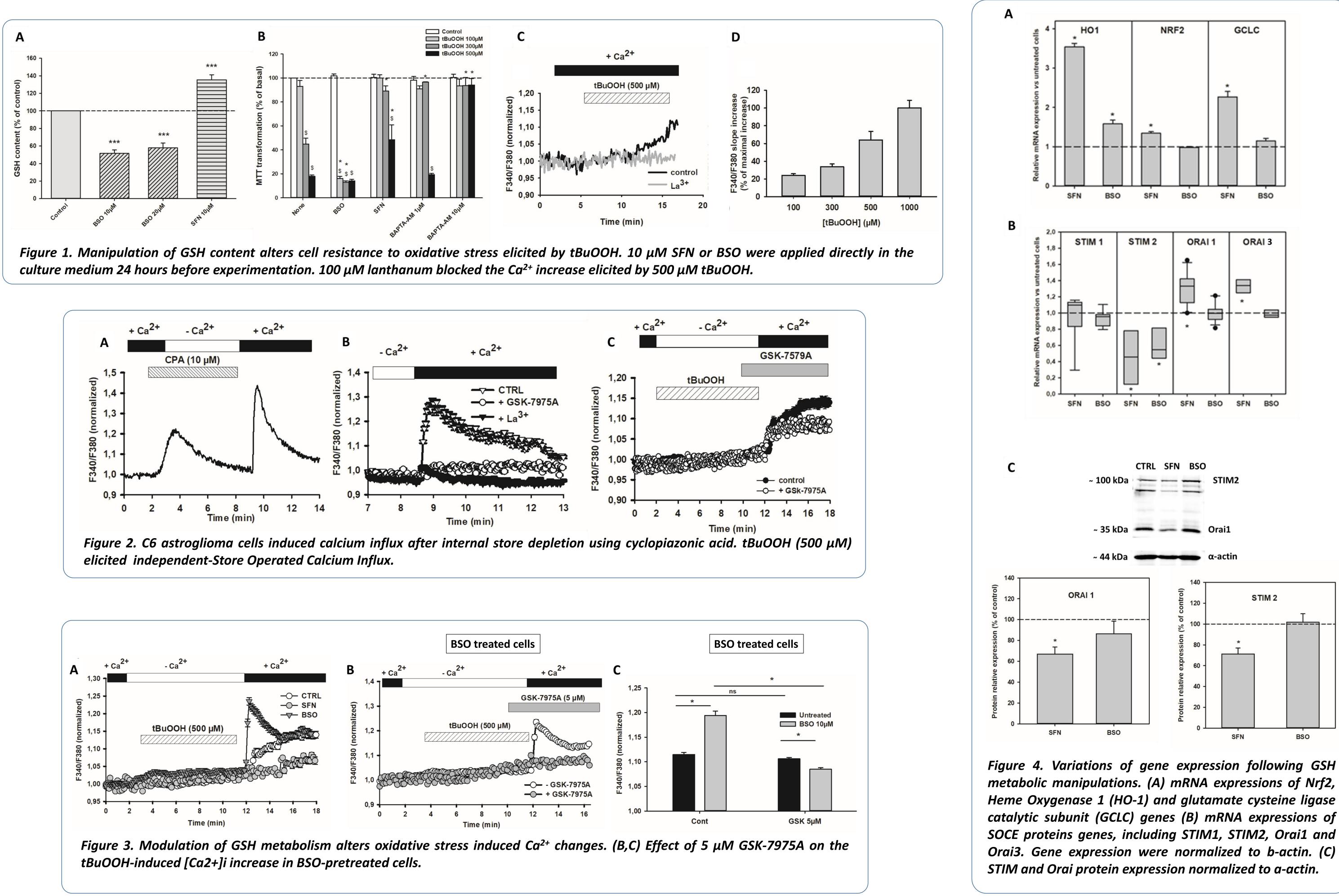
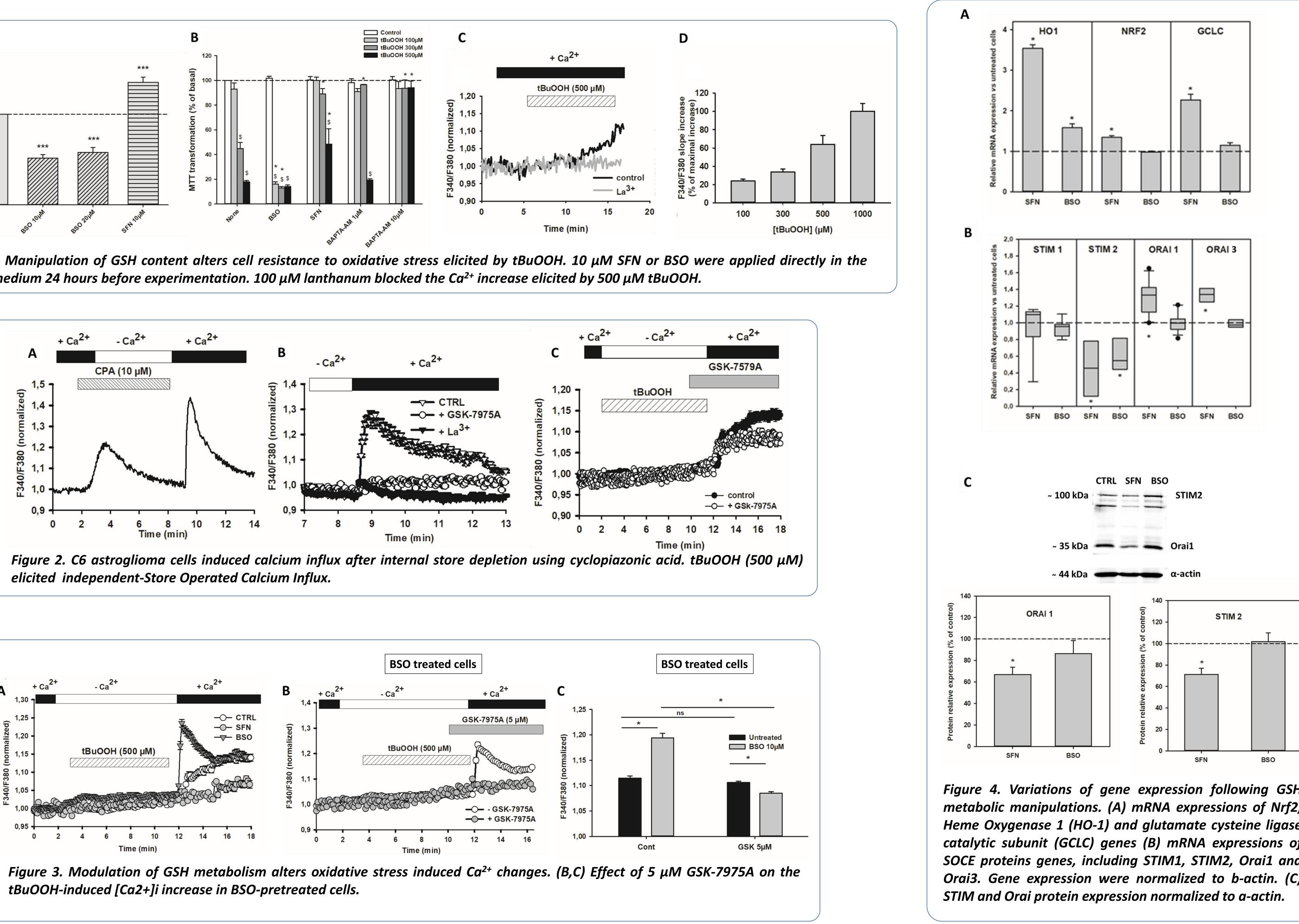
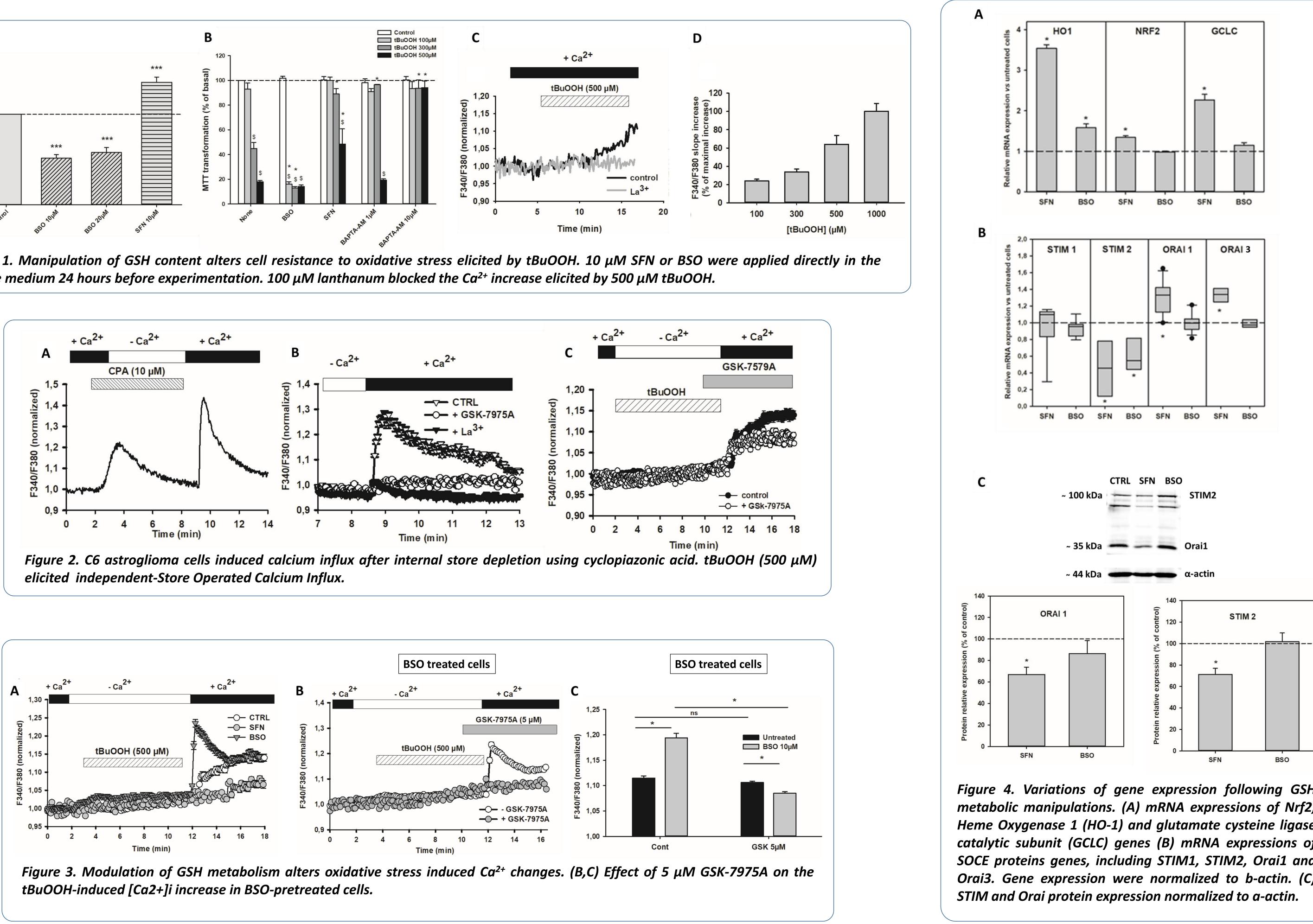
## Manipulations of GSH content modulate [Ca2+]i homeostasis in rat astroglioma cells



Oxidative stress is an aggravating factor of all neurological disorders, including neurodegenerative diseases. It is due to an exaggerated accumulation of reactive oxygen species (ROS) concomitant to decreased reduced glutathione (GSH) levels; the main antioxidant of brain cells produced by astrocytes in large amounts. Cell death triggered by oxidative damage results from intracellular calcium overload which is deleterious to cell activity. The mechanisms involved in these calcium increases are not fully understood. Here, we have thus investigated whether GSH could protect neurons against oxidative stress through the modulation of calcium homeostasis. For this, GSH cell content was manipulated by modulating its metabolism. To investigate the link between GSH content and calcium homeostasis, we pre-treated rat astroglioma cells (C6) with sulforaphane (SFN) to increase intracellular GSH levels, or buthionine sulfoximine (BSO) to decrease them, during 24 hours for both treatments.

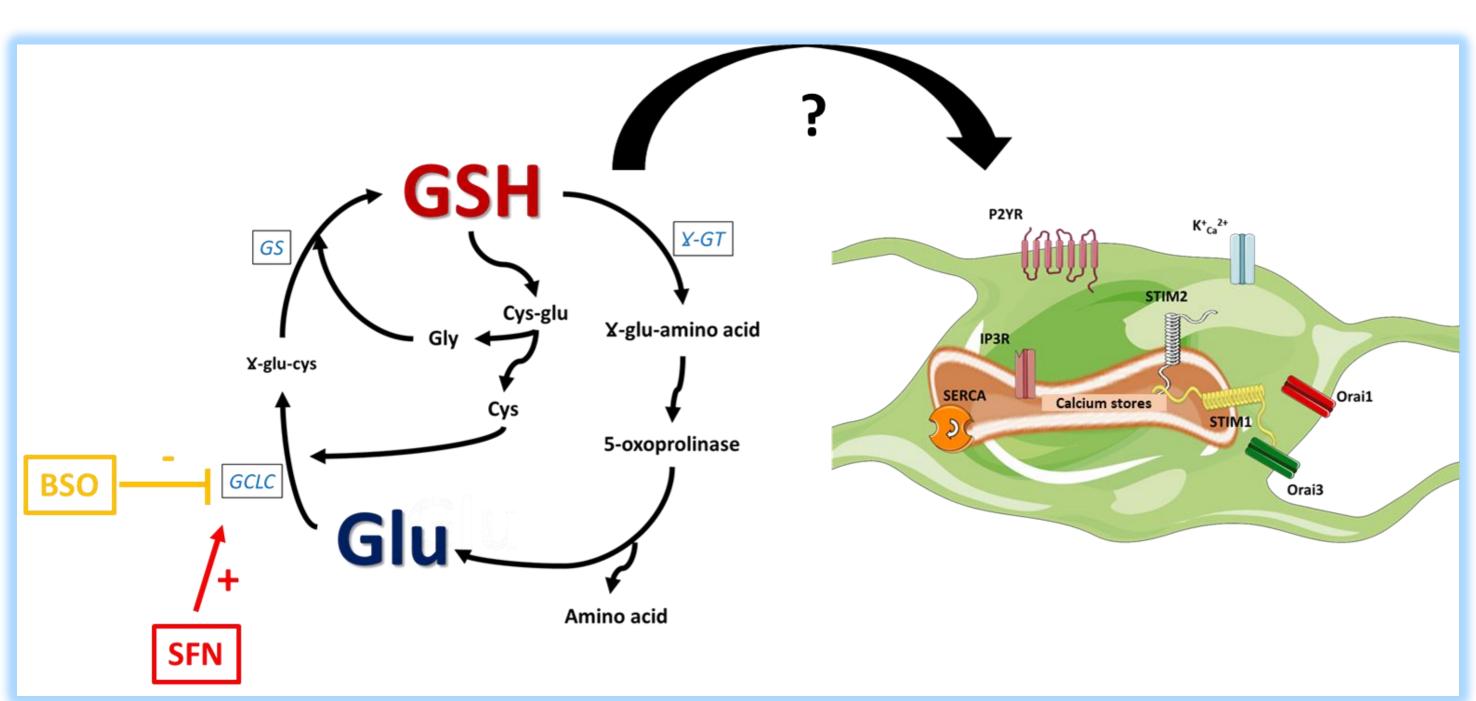




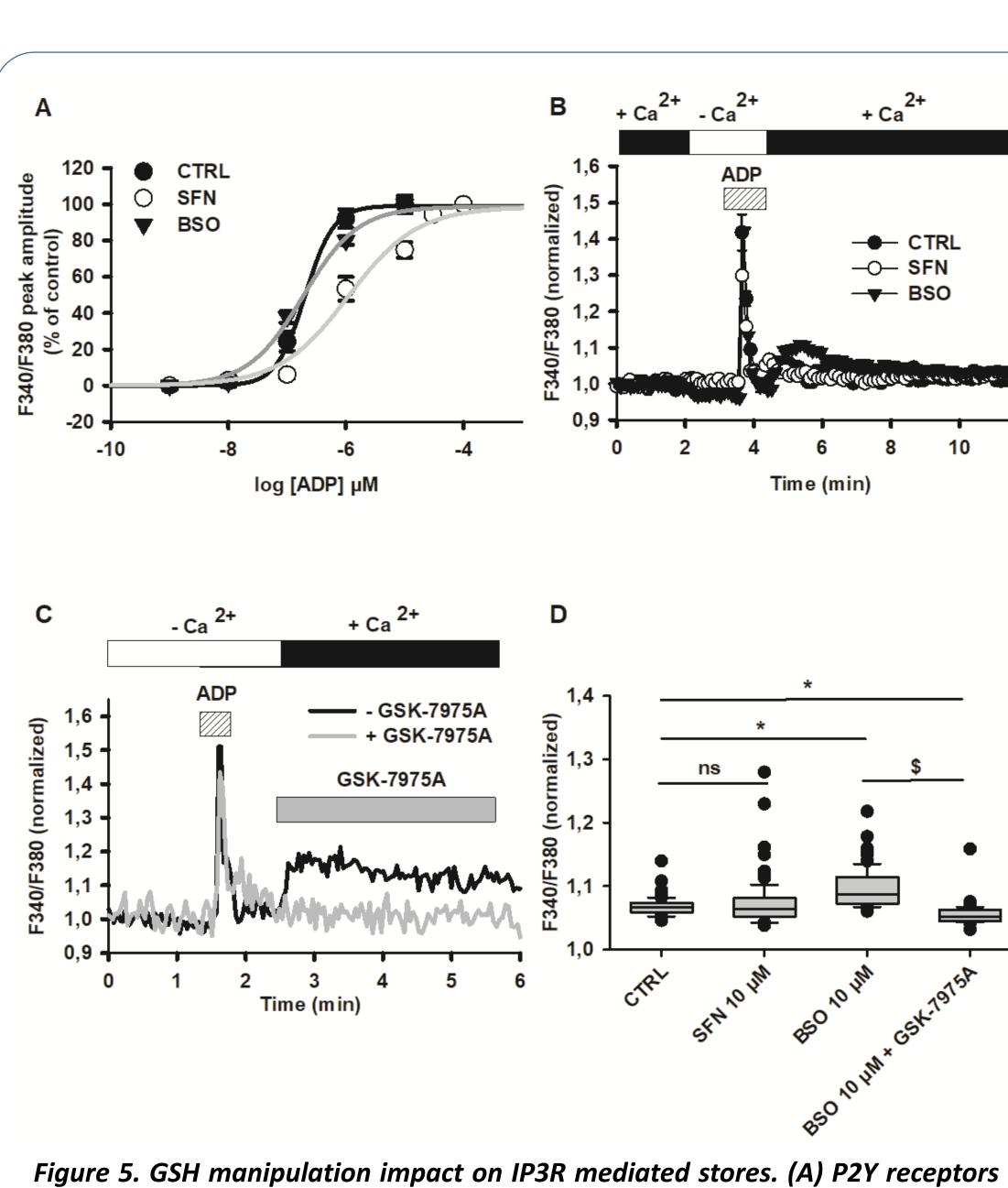


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+ Ca



were stimulated by increasing concentrations of ADP (1, 10, 100 nM and 1, 10 μM) in the absence of extracellular calcium and (D) the peak amplitude was determined (C) 5 µM of GSK-7975A were used 3 minutes prior extracellular calcium reinstatment.

We conclude that GSH cell content changes impact intracellular Ca2+ homeostasis in C6 glioma cells likely via sensitization/desensitization mechanisms of Calcium Release Activated Channels (CRAC). GSH depletion due to oxidative stress regulation could thus contribute to the alterations of Ca<sup>2+</sup> homeostasis in astrocytes under pathological conditions.





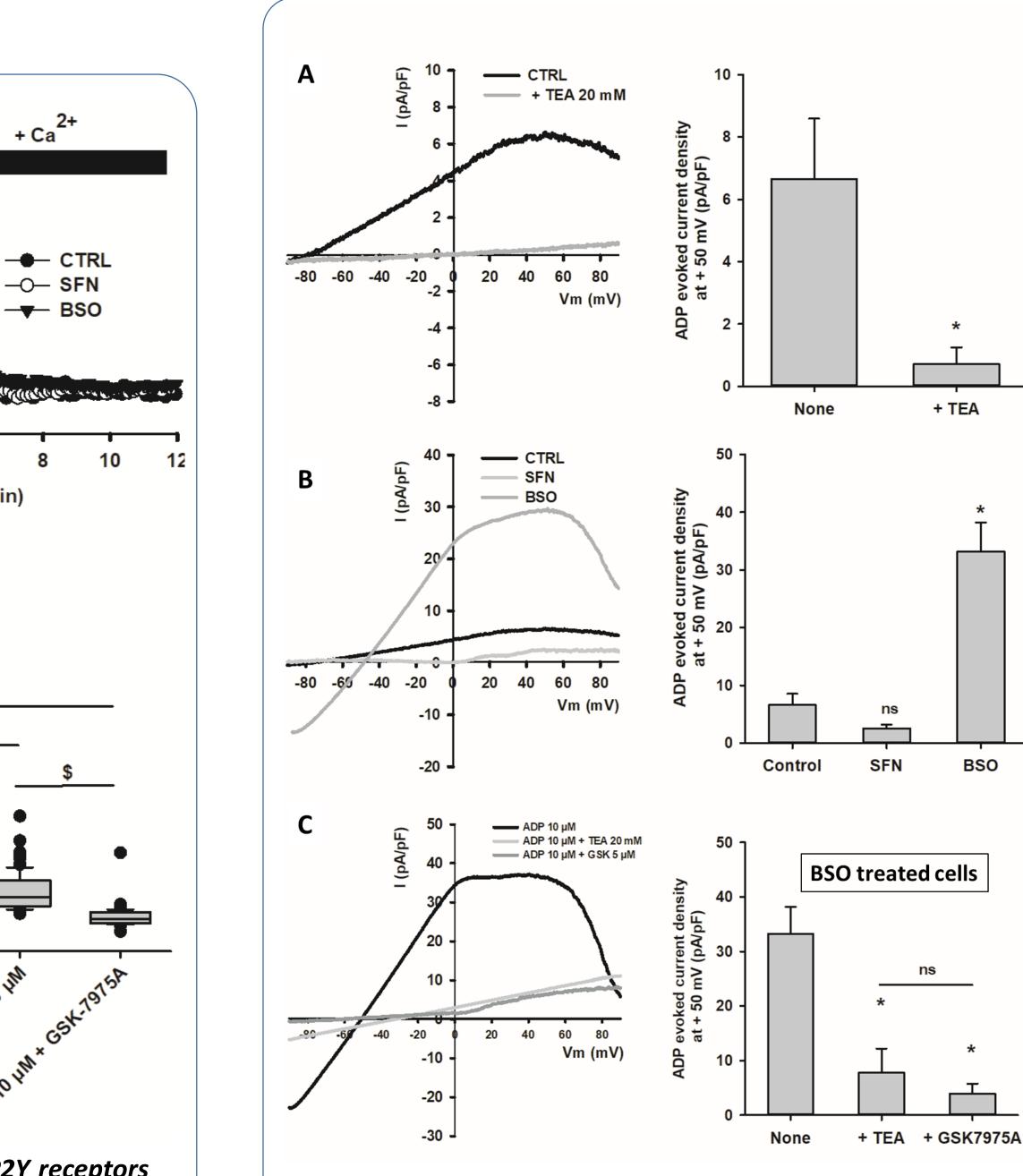


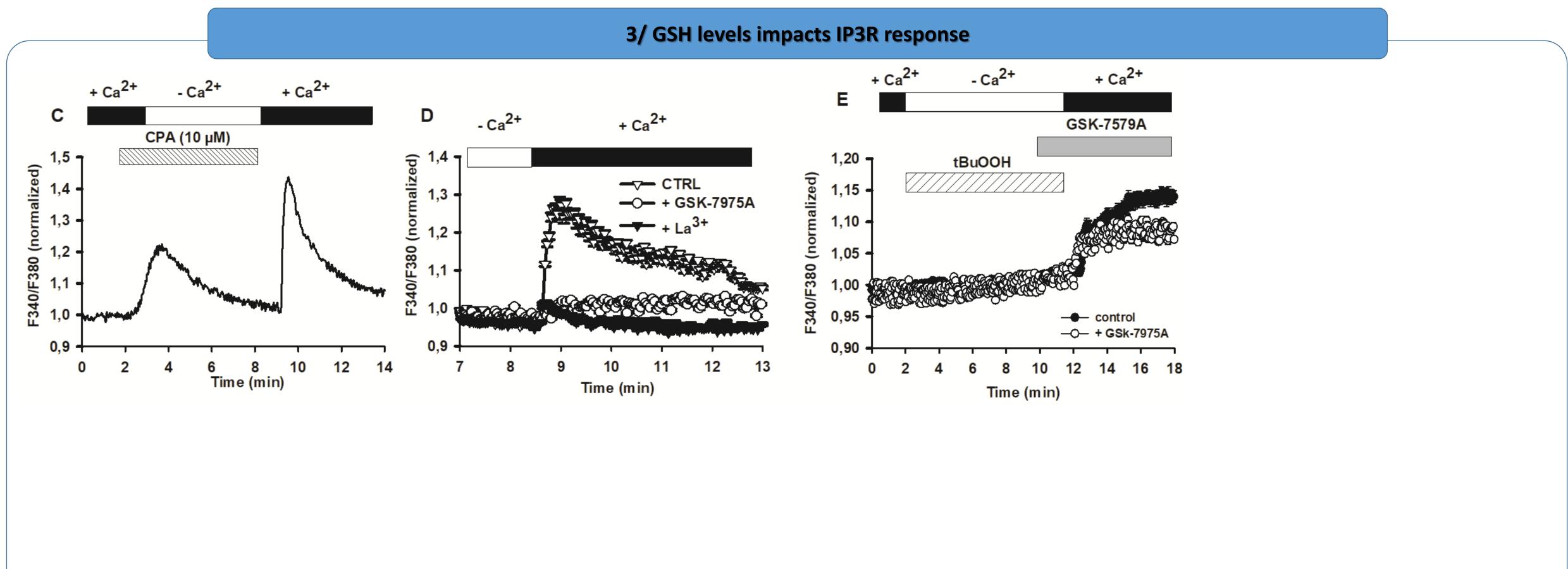
Figure 6. Impact on ADP mediated currents. Single traces of currents recorded after (A) 10  $\mu$ M ADP application on control cells either in the absence or in the presence of 20 mM TEA or not (B) 10 μM ADP application on control, BSO- and SFN pretreated cells (C) BSO-treated cells with 20 mM TEA or 5µM GSK 7579A are shown. Currents were recorded by applying voltage ramps from -100 to 100 mV every 10 seconds.

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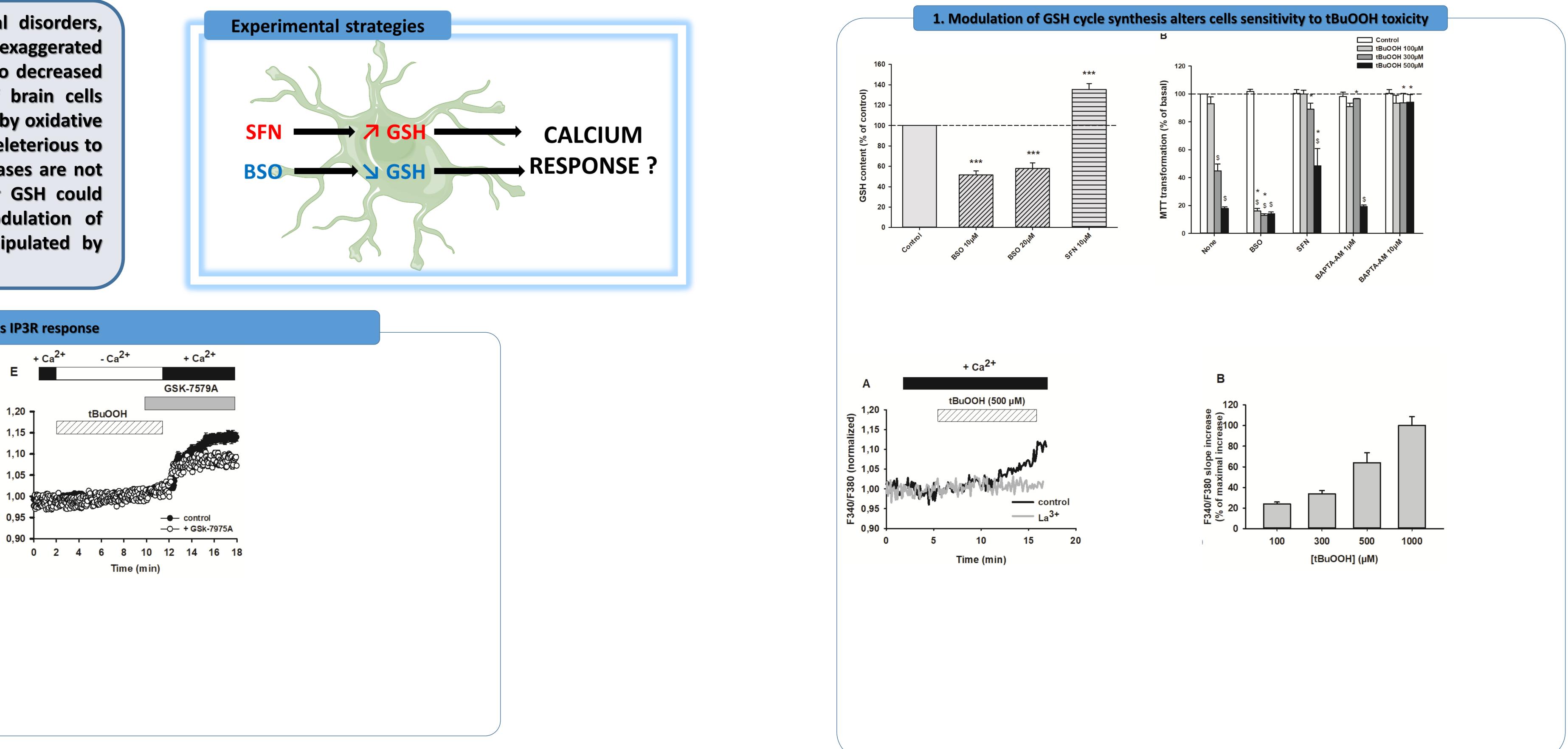
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## Manipulations of GSH content modulate [Ca2+]i homeostasis in rat astroglioma cells

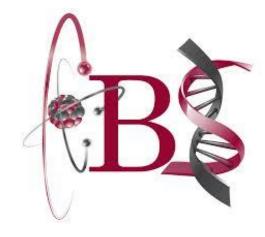
Oxidative stress is an aggravating factor of all neurological disorders, including neurodegenerative diseases. It is due to an exaggerated accumulation of reactive oxygen species (ROS) concomitant to decreased reduced glutathione (GSH) levels; the main antioxidant of brain cells produced by astrocytes in large amounts. Cell death triggered by oxidative damage results from intracellular calcium overload which is deleterious to cell activity. The mechanisms involved in these calcium increases are not fully understood. Here, we have thus investigated whether GSH could protect neurons against oxidative stress through the modulation of calcium homeostasis. For this, GSH cell content was manipulated by modulating its metabolism.

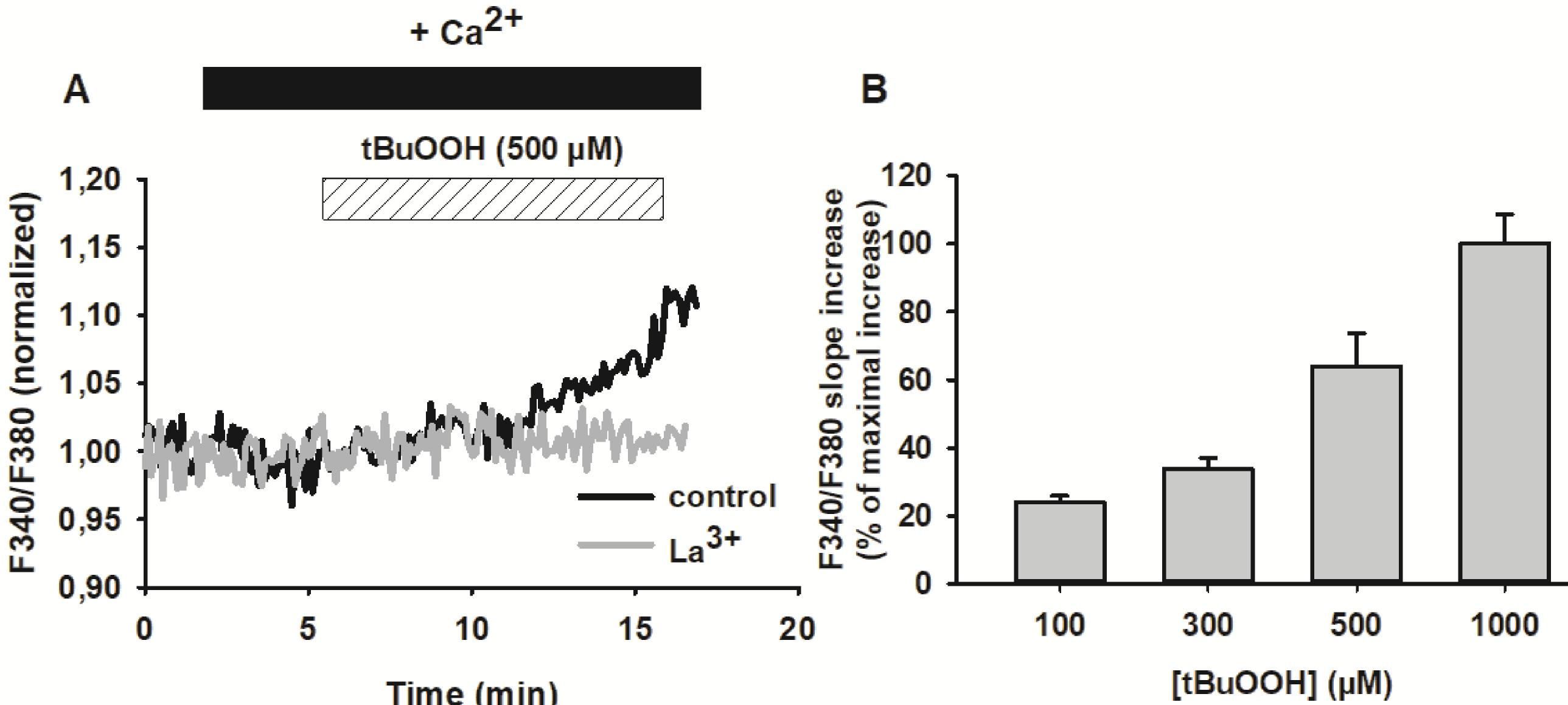


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Time (min)

