COULD TRIFLUOPERAZINE PROTECT PLASMA MEMBRANE Ca^{2+}-ATPase FROM OXIDATIVE STRESS INACTIVATION IN CORTICAL NEURONS?

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We previously showed that plasma membrane Ca^{2+}-ATPase (PMCA) is more sensitive to oxidative stress than endoplasmic reticulum Ca^{2+}-ATPase (SERCA), in membrane fractions from whole brain, by using Fe^{2+}/ascorbate or Fe^{2+}/ascorbate/H_2O_2 as prooxidants. In addition, we demonstrated that 20-100 µM of the known antipsychotic agent trifluoperazine (TFP) could efficiently prevent such inactivation (DOI 10.1007/s00221-006-0678-1). Now we are checking whether TFP protects PMCA from oxidative stress that may occur in physiopathological conditions. Fifty percent inhibition of PMCA was observed after incubation at 2µM Fe^{2+}/ 500µM ascorbate, in the absence or in the presence of 500 µM H_2O_2, for 10 or 5 min, respectively. PMCA inactivation was completely prevented by 100µM TFP. Possible TFP protection in rat brain primary neuronal cultures (PNC), subjected to oxidative stress, is now been verified. PMCA activity of PNC homogenates was characterized (~ 112?mol Pi. mg of protein^{-1}.h^{-1}). Cell toxicity in PNC was verified, after 24 hours of incubation, with either 50µM H_2O_2 or TFP 15 µM, using the MTT method (mitochondrial dysfunction). In both cases, 30-40% of PNC cells showed some dysfunction. No significant toxicity was observed with 5µM TFP, indicating that this concentration may be used as a possible PMCA protector against oxidative damage.

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