The impact of lithium on prooxidant-antioxidant balance in human plasma \textit{in vitro} and in neuronal cell lines

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\section*{Introduction}

``Disturbance in prooxidant-antioxidant balance in favour of the former, leading to potential damage'' (Nies, 1992)

- patients with BD have increased lipid peroxidation (acute manic and depressive episodes, remission).
- a potential role of glutamate-induced oxidative stress in BD?
- excessive generation of ROS triggered by mitochondrial dysfunction in BD?

\section*{Methods}

\textbf{Human plasma in vitro:}
- plasma samples from healthy volunteers;
- plasma incubation (24h, 37°C);
- without the drug;
- with lithium alone (0.67 or 1.0 mmol/l);
- with lithium and haloperidol (10g/ml);
- incubated with various concentrations of lithium (0.67 mmol/l and 1.0 mmol/l) and haloperidol (10ng/ml) for 48h;
- Cells were pretreated with various concentrations of lithium (0.67 mmol/l and 1.0 mmol/l) and haloperidol (10ng/ml) for 24h and then treated with hydrogen peroxide (100µM) for another 24h;
- Lipid peroxidation and cell viability were measured.

\textbf{Lipids peroxidation (LP) measurement by the concentration of thiobarbituric acid reactive substances (TBARs) (Rice-Evans).}

\textbf{Determinaion of total antioxidant capacity (TAC) with ABTS radical-cation (ABTS\textsuperscript{+})-decolorization assay (Re).}

\section*{Results}

We observed:
- no influence of lithium on lipid peroxidation (fig. 1) nor TAC (fig. 2) in human plasma \textit{in vitro};
- increase in lipid peroxidation in samples with combination of lithium and haloperidol in human plasma \textit{in vitro} (fig. 3), no difference in TAC between the samples;
- no influence of lithium, haloperidol and combination of lithium and haloperidol on lipid peroxidation in SH-SYSY neuroblastsoma cells (fig. 3);
- no influence of pretreatment with lithium, haloperidol and combination of lithium and haloperidol on lipid peroxidation in SH-SYSY neuroblastsoma cells treated with hydrogen peroxide (fig. 4);
- higher viability in SH-SYSY neuroblastsoma cells incubated with lithium (fig. 5); no influence of haloperidol and combination of lithium and haloperidol on cells viability.

\section*{Conclusions}

- Lithium in concentrations used in psychiatry does not influence oxidative stress parameters in \textit{in vivo} conditions (human plasma, neuroblastsoma cells) in a short-period observation (24 or 48h) what is consistent with some of the previous studies;
- Lithium in combination with haloperidol increases lipid peroxidation compared to control, lithium or haloperidol alone, thus one should be careful prescribing these drugs together; the mechanism may be responsible for some side effects (e.g. neurotoxicity) of the combination;
- inconsistency of research in the field causes necessity for further studies to assess lithium impact on oxidative stress parameters in \textit{in vivo} conditions, in a long-period observation, in neutral and prooxidative environment (patients with bipolar disorder);
- further studies may provide additional data regarding the possible involvement of oxidative stress in the pathophysiology of BD and in the therapeutic effects of lithium.

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