Redox dysregulation in schizophrenia pathophysiology: Add-on trial with N-acetylcysteine (NAC) in early psychosis patients.

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INTRODUCTION
Oxidative stress, coupled with dysregulations of inflammation, NMDA receptors and dopamine, is involved in schizophrenia pathophysiology, affecting the integrity of parvalbumin interneurons (PVI)2. The antioxidant N-acetylcysteine (NAC):
• prevented physiological and behavioural alterations in schizophrenia rodent models presenting an elevated oxidative stress and PVI impairment in prefrontal cortex1,4,
• improved negative symptoms5, mismatch negativity6 and local synchronization7 in chronic SZ patients.

We studied NAC’s impact on symptoms and neurocognition in early psychosis (EP) patients, to explore whether glutathione (GSH)/redox markers could represent valid biomarkers to guide treatment.

CONCLUSION
In this 6-month clinical trial, NAC
• Increased peripheral and brain GSH level
• Improved speed processing

Moreover, NAC improved positive symptoms in patients with high blood oxidative marker, thus paving the way toward biomarker-guided treatment in early psychosis.

Limitations:
• Small sample size (n=61 for clinical evaluations; n=25 in MRS study)
• Modest severity of negative symptoms at baseline
• Power was lower than estimated: 36% of the patients might respond to NAC based on high blood GSH activity.

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METHODS

Study design
6 months, double-blind, placebo-controlled, randomized trial
Add-on therapy to standard medication: 2700 mg of NAC/day
Multi-centered trial: Lausanne and Boston

Inclusion criteria
• Male or female, 18-40 years old
• Diagnosis of psychotic disorder, reaching the psychosis threshold of the CAARMS
• ≤2 months of antipsychotic treatment

Exclusion criteria
• Organic mental disease / organic psychosis
• Severe cerebral trauma
• Mental retardation (IQ<70)
• Diagnosis of substance induced psychosis

DISCLOSURES
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