Methods: A literature review was conducted in order to address two questions: What is oxidative stress and how does oxidative stress come about?
Results: Oxidative stress is caused by an imbalance between the production of reactive oxygen and a biological system's ability to readily detoxify the reactive intermediates or easily repair the resulting damage. Disturbances in a cells normal redox state can cause toxic effects through the production of peroxides and free radicals that damage all components of the cell, including proteins, lipids, and DNA.
Conclusions: Interpretation of molecular investigations in schizophrenia might benefit from considering whether the results obtained could be the cause or consequence of oxidative stress. Causal findings could suggest more specific treatments for schizophrenia and allied disorders.

References

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SP38 - IS THERE EVIDENCE FOR OXIDATIVE STRESS IN THE PREFRONTAL CORTEX OF PATIENTS WITH SCHIZOPHRENIA?

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Background: Evidence suggests that oxidative damage exists in the brains of patients with schizophrenia, however, it is not yet clear how this is occurring. In the present study, we determined whether oxidative stress response markers are altered in the DLPFC of the human prefrontal cortex and whether changes in glial cells, such as astrocytes and microglia, may be contributing towards the schizophrenia neuropathology.
Methods: Utilizing a cohort of n=37/37 controls/schizophrenics from the Sydney NSW Tissue Resource Centre, we assessed gene expression changes by Taqman quantitative real-time PCR and protein expression alterations by western blotting.
Results and Conclusions: No significant changes were observed in mRNA expression of several biochemical markers of the oxidative stress response including SOD1, GPX3, and apoD between control and schizophrenics. Interestingly, age-dependent upregulation of apoD was not found in schizophrenia. We found no significant changes in GFAP expression compared to controls, moreover, age-dependent regulation of GFAP was not found. Interestingly, we found increased expression of a marker of total (Glut5) but not activated microglia (HLADR) protein. This suggests that cellular response to oxidative stress in the DLPFC may be altered in schizophrenia. Astrocytes responsible for neuronal support may not be responding to redox perturbations as age-dependent regulation of GFAP and apoD expressions are lost in schizophrenia, moreover, increased expression of total microglia with no change in activated microglia, GPX3 and SOD1 in schizophrenia may indicate a lack of free radical detoxification. Thus, glial cell dysfunction in schizophrenia may be an underlying factor in the neuropathology.

SP39 - THE SPECIFICITY OF PATHOGENIC OXIDATIVE STRESS IN SCHIZOPHRENIA

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Background: The role of oxidative stress has become an important factor in uncovering the pathophysiology of schizophrenia. There is substantial evidence to suggest not only downstream changes in oxidative defenses, but also more global changes including alterations to mitochondrial function, neurotrophins, and polymorphisms in genes associated with primary antioxidants. More and more these factors are being implicated in a variety of psychiatric disorders, indicating that oxidative stress is not specific to schizophrenia but may be a common feature of many disorders.
Method: The current presentation will provide an overview of the commonality of oxidative stress across several psychiatric illnesses, demonstrating a wider view of a continuum of psychiatric illness.
Results: As the field of oxidative biology and psychiatric illness expands it is becoming apparent that there are many more similarities in the underlying pathology of these disorders that first suspected.
Conclusions: Based on current literature, the notion of specificity of oxidative stress in schizophrenia is not supported. Changes in oxidative defenses are occurring in many psychiatric disorders. Further investigation of whether these changes are a consequence or a primary part of these disorders is required. This will not only provide a better understanding of these disorders, but also lead the way to new treatment targets.

SP40 - NEW THERAPIES TARGETING ANTIOXIDANT DEFENSE AND MEMBRANE INTEGRITY IN SCHIZOPHRENIA: A PREVENTION PERSPECTIVE

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Background: There is increasing evidence of impaired antioxidant defense systems, increased lipid peroxidation and abnormal levels of polyunsaturated fatty acids (PUFAs) in patients suffering from schizophrenia. The synthesis of the main intracellular redox regulator and cellular antioxidant, glutathione (GSH), was shown to be impaired in schizophrenia. A GSH deficit is associated with lipid membrane peroxidation during excessive oxidative stress.
Methods: Clinical trials were conducted with the objective of improving the GSH and/or the PUFAs status and of seeing the effects of such an improvement on the psychopathology and neurobiology of participants. N-Acetyl-Cysteine (NAC), a precursor of GSH and antioxidant itself, was administered to schizophrenia patients in Lausanne and Melbourne. An intervention with omega-3 PUFAs was conducted in Vienna.
Results: Treatment with NAC was accompanied by an amelioration of negative symptoms and global symptomatology and reduction of antipsychotic-induced akathisia. The mismatch negativity, an EEG component reflecting the functioning of NMDA receptors, was also improved. Treatment with omega-3 PUFAs reduced the risk of progression to psychotic disorders.
Conclusions: Based on the literature, mechanisms involving NMDA receptors function and cell membrane integrity will be proposed in an attempt to explain the actions of NAC and omega-3 PUFAs. The interesting findings will also be presented in a perspective of early intervention in psychosis.