Modelling pre-trauma resilience and vulnerability factors for PTSD

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Background: Research identifying vulnerability and resilience factors that may affect an individual's likelihood of developing post-traumatic stress disorder (PTSD) is hampered by the dearth of information on those who are resilient and, although exposed to the trauma, remain unaffected by it.
Methods: Such a study eventuated in Canberra where the Centre for Mental Health Research is conducting a longitudinal study of over 7000 participants from three age groups. Reinterviewed participants were asked about their level of exposure and reaction to this trauma and their fire-related PTSD symptoms. Information on a range of sociodemographic, health and personality measures was collected both before and after the trauma.
Results: Almost 80% of Wave 2 respondents were exposed to the fire, while around 2000 reported having experienced fire-related PTSD symptoms in the week prior to their interview. Structural equation modeling of pre-trauma risk and resilience factors associated with PTSD symptoms was undertaken. When level of exposure and immediate reaction to the fire were taken into account, pre-trauma resilience measures had the greatest impact on PTSD symptoms. Those with higher levels of resilience were significantly less likely to report PTSD symptoms.
Conclusion: These findings indicate that reducing risk of PTSD by increasing individuals' levels of resilience in the face of specific traumas has the potential to be an effective strategy to limit the negative psychological impact of trauma exposure.

Clozapine invokes the EGF system to activate ERK: a novel target in treatment resistant schizophrenia?

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Background: The atypical antipsychotic drug clozapine is superior to all other drugs in treatment of refractory schizophrenia. This is likely to involve clozapine-inducing long-term neuronal adaptations contingent on drug-receptor activation of intracellular signaling to affect gene transcription. One candidate intracellular signaling pathway is the mitogen-activated protein kinase-extracellular signal-regulated kinase (ERK) cascade. This pathway regulates synaptic proliferation and plasticity, processes impaired in schizophrenia. We have previously reported that although clozapine and haloperidol acutely inhibited ERK activation in cortical neurons, only clozapine stimulated ERK with continued treatment. However, this stimulation was not through the canonical dopamine D2-Gi/o-PKA or the serotonin 5HT2A-Gq-phospholipase C-linked signaling pathways. Thus, we examined alternative signaling pathways that clozapine could mobilize to activate ERK including growth factor receptor systems.
Methods: Clozapine-induced phosphorylation of ERK1/2 in the absence or presence of growth factor receptor-specific inhibitors was measured in primary murine cortical cultures by Western immunoblotting. Results were normalized against vehicle and total ERK1 and 2 levels.
Results: The epidermal growth factor (EGF) receptor inhibitor, AG1478, caused significant dose-dependent inhibition of pERK1 (IC50 0.083 μM) and pERK2 (IC50 0.106 μM) in the presence of clozapine, whereas the platelet-derived growth factor receptor inhibitor, tyrphostin, A9 did not.
Conclusions: This is the first evidence that the effects of clozapine may involve a neuronal signaling system previously not linked to antipsychotic drug action. This presents a novel series of targets for exploration in the development of new therapeutics and insights into the pathology of schizophrenia.

The prevalence of depression in the North West Adelaide Health Study

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Background: The North West Adelaide Health Study is a population-based biomedical cohort study investigating the prevalence of chronic conditions and health-related risk factors. This study is based on a randomly selected group of individuals over the age of 18, who agreed to be involved in a longitudinal health study.
Methods: Over the past 18 months, 3488 participants were assessed. General demographic and socioeconomic data were collected. Participants were assessed for the presence of a number of chronic conditions including major depression. The presence of depression was assessed using the Center for Epidemiological Studies Depression Scale-D. A score of 16 or higher indicated mild depression. A score of 27 or higher was rated as moderate to severe depression.

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