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THE IMPACT OF SOCIAL STATUS ON PSYCHIATRIC DISEASE SUSCEPTIBILITY - AN INFLAMMATORY MODEL

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INTRODUCTION

Chronic inflammation of the brain during the prenatal period, infancy, childhood, adolescence and adulthood has a significant impact on brain structures involved in cognition and mental health (Lupien 2009). Specific effects on the brain, behaviour and cognition are related to the timing and duration of exposure to inflammation, and in some instances, interactions between gene affects and past exposure to environmental adversity (Lupien 2009). There is a growing focus on neuroinflammation playing a significant role in psychiatry; schizophrenia (Shen et al. 2008), bipolar disorder (Hope et al. 2009), autism (Vargas et al. 2005) and psychosis (Masopust et al. 2011).

Here we highlight the effects of social status which is described here as a pathogenic factor, on susceptibility to inflammatory disease and discuss how this relationship holds potential implications for the field of psychiatry.

ACKNOWLEDGING SOCIAL STATUS

The origin of 'racial', 'class' and 'ethnic' disparities in health has recently become the centre of some debate, with proposals for addressing disparity focused on individual-orientated prevention by alterations to lifestyle (Link & Phelan 2000). Poor diet, sedentary lifestyle, smoking and excessive alcohol intake are widely regarded as key predisposing factors and thus potential targets for change (Wallace & Wallace 2010).

A second theory currently gaining increasing support is that social status plays a fundamental role in the prediction of morbidity and mortality (Packard et al. 2011). Factors such as status rank, job uncertainty and de-facto deprivation are credited with having just as significant an effect on a person's morbidity as the other risk factors discussed (Link & Phelan 2000).

SOCIAL STATUS AND INFLAMMATORY DISEASE

Inflammatory diseases appear to be more prominent amongst individuals of a lower social status (Packard et al. 2011). Kiecolt-Glaser et al. (2002) discusses the implications of social status in a range of inflammatory conditions including; carotid artery disease, respiratory disease, arthritis, and diabetes.

A particular focus has observed correlations between social class and inflammatory markers such as C-reactive protein (CRP) (Schafer et al. 2011), interleukin 6 (IL-6) (Gruenewald et al. 2009) and fibrinogen (Friedman & Herd 2010) in carotid artery sclerosis. In coronary disease the spectrum is wider involving, white blood cell count, von Willebrand factor (vWF), factor VIII, activated protein C (APC) resistance, plasma viscosity, fibrin D-dimer and platelet count (Ramsay et al. 2008).

In children suffering with asthma, it was observed that airway inflammation, determined by exhaled nitric oxide (FeNO), demonstrated and inverse correlation with socioeconomic status (Chen et al. 2010). It is thought that this may be a result of decreased activity of cyclic AMP response element binding protein (CREB), nuclear factor Y (NF-Y) and increased nuclear factor kappaB (NF-κB) (Chen et al. 2009). These pathways are known to regulate catecholamine and inflammatory signalling in immune cells (Chen et al. 2009).

Assessed using the Carstairs index, social deprivation was associated with an increased risk of dislocation and mortality at 90 days after a total hip replacement (Clement et al. 2011). A Danish case–control study found that this risk was highly associated with rheumatoid factor positive RA and not rheumatoid factor-negative RA (Pedersen et al. 2006). This study confirmed previous Scandinavian reports that arthritis was 40% more likely in less educated classes (Bengtsson et al. 2005).

Finally, a recent study back by the Scottish government has indicated a role for social status in cognitive decline (Packard et al. 2011). Choice Reaction Time, the Stroop test, and Auditory Verbal Learning Tests all demonstrated a significant decline associated with lower social status.

THE ROLE OF INFLAMMATION IN PSYCHIATRY

Our hypothesis stems from the recent focus in psychiatry; specifically the consensus that inflammation plays a key role in conditions such as schizophrenia

(Shen et al. 2008), bipolar disorder (Hope et al. 2009), autism (Vargas et al. 2005) and psychosis (Masopust et al. 2011).

Early studies by Coplan et al. (1996) highlight the potential implications of neuroinflammation on the pathophysiology of psychiatric disorders. They evince that the induction of stressful living conditions will result in elevated concentrations inflammatory proteins (Reyes & Sawchenko 2000).

In schizophrenia, increase placental tumour necrosis factor (TNF-α) & IL-6 has been linked to onset of the condition (Shen et al. 2008). Where in adult patients there was significantly raised sIL-2Rα, IL-1RA and CRP (Suvisaari et al. 2011). This is in addition to observations of upregulation of the transcription factor NF-κB (Song et al. 2009). These results are evident throughout most peripheral cells with increased generation of reactive oxygen species (ROS) in platelets from schizophrenic patients being observed (Dietrich-Muszalska et al. 2005)

Similar molecular patterns have been observed in autism. Specifically, aberrant expression of NF-κB has been demonstrated both centrally (Young et al. 2011) and peripherally (Naik et al. 2011). This was accompanied with raised profiles in the cerebrospinal fluid (CSF)(Vargas et al. 2005). Specifically, tumour growth factor-beta 2 (TGF-β2), IL-6, macrophage chemoattractant protein-1 (MCP-1), vascular endothelial growth factor (VEGF), interferon-gamma (IFN-γ), fibroblast growth factor (FGF-9), PARC & insulin-like growth factor binding protein-3 (IGFBP-3) were shown to be markedly raised (Vargas et al. 2005).

Similarly, plasma levels of sTNF-R1 and vWf were statistically significantly increased in bipolar disorder patients compared to controls (Hope et al. 2009). Weigelt et al. (2011) support the concept that monocytes are in a pro-inflammatory state in severe psychiatric conditions. They noted that in particular TREM-1 gene expression is significantly increased in monocytes of bipolar patients.

There has been circulating concern that antipsychotic medication can increase inflammatory markers (Suvisaari et al. 2011). However, recent investigations have demonstrated that D-dimers, factor VIII and sP-selectin plasma levels were significantly increased in the group of patients with acute psychosis as compared with healthy volunteers (Masopust et al. 2011). Others found raised IL-1RA and CRP in persons with affective psychosis and almost significantly higher TNF-α compared to their matched controls (Suvisaari et al. 2011). Additionally, sIL-2Rα, a marker of T-cell activation, was associated with depressive symptoms, schizophrenia, and affective psychosis (Suvisaari et al. 2011).

THE POTENTIAL ROLE OF SOCIAL STATUS IN PSYCHIATRY

Interestingly, the consensus when analysing psychiatric data is to control for age, gender, ethnicity and multi-factoral disease. The importance of social status is often overlooked as a prerequisite to a diseased state. Instead, environmental factors associated more frequently with lower social status, are used as disease state predictors. Nevertheless, there is accumulating data to suggest that social status plays a significant independent role in systemic inflammatory disease (Packard et al. 2011).

As our knowledge of how inflammation contributes to psychiatric conditions develops, it is becoming increasingly necessary to consider social status as a risk factor for these conditions. Chronic inflammation of the brain has a significant impact on brain structures involved in cognition and mental health (Lupien 2009) and furthering our understanding of this could prove important in future data collection and both the recognition and treatment of disease.

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