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Urban social stress – Risk factor for mental disorders. The case of schizophrenia

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ABSTRACT

Living in an urban environment is associated with an increased prevalence of specific mental health disorders, particularly schizophrenia. While many factors have been discussed as possible mediators of this association, most researchers favour the hypothesis that urban living stands as a proxy for an increased exposure to social stress. This factor has been recognized as one of the most powerful causes for the development of mental disorders, and appears to correlate with the markedly increased incidence of schizophrenia in urban minority groups. However, the hypothesis that the general urban population is exposed to increased levels of social stress has to be validated. Pursuing the goal of understanding how social stress acts as a risk factor for mental disorder in urban populations must include factors like social conditions, environmental pollutants, infrastructure and economic issues.

1. Introduction

The continuous expansion of urban regions constitutes one of the most radical changes in our environment at the beginning of the 21st century. It is estimated that by the year 2050, 67% of the global population will live in urban areas (United Nations, 2012). In addition to profound effects on economy and ecology, this process has major implications for health. Both physical and mental health of city dwellers may be affected by varying degrees of population density, social interaction, physical activity and exposure to noise, toxins and light. In general, health is better in urban than in rural areas, mainly because of better education, higher rates of employment and easier access to health care (Dye, 2008). However, reliable information on these conditions is hard to extract, as the urban environment is inhomogeneous. Therefore, the statement of a health advantage of city dwellers may be correct on a general level, however, it may not apply for specific diseases or for inhabitants of a distinct neighbourhood.

2. Urban-rural differences in mental disorder risk

Despite the general health advantage of city dwellers, incidence (the rate at which new disease events occur in a population) and prevalence (the number of events, e.g., a given disease, in a given population at a designated time) of specific mental disorders seem to be increased in this population. Meta-analytic studies report that among individuals living in cities, the prevalence of all psychiatric disorders is increased by 38%, of mood disorders by 39%, and of anxiety disorders by 21%, as compared to inhabitants of rural areas (Peen et al., 2010). Adjustment for potential confounders like age, gender, marital status, social class or ethnicity had limited impact on these findings, indicating that these population characteristics do not substantially contribute to the observed disparities.

The most striking urban-rural difference in mental disorder risk is the increased incidence of schizophrenia in people born and raised in urban areas (van Os et al., 2010). Schizophrenia is a serious mental disorder affecting approximately 0.5–1% of the world population, leading to major suffering and disability in many patients (Insel, 2010). The first report on the increased incidence of schizophrenia in urban areas dates back to 1939 (Faris and Dunham, 1939), when increased incidence rates for this disorder were observed in densely populated inner city areas of Chicago, as compared to the city's periphery. The increased schizophrenia incidence in urban areas has been corroborated by subsequent studies (Häfner et al., 1965; Mortensen et al., 1999; Kirkbride et al., 2006), including demonstration of a dose–response relationship (Pedersen and Mortensen, 2001). A systematic review of the literature reported an increase in schizophrenia risk among city dwellers of 1.92 in males and 1.34 in females (Kelly et al., 2011). Interestingly, the effect of exposure to the urban environment seems to be strongest during the time period from birth to age 15 (Pedersen and Mortensen, 2001), as compared to exposure later in life (Marcelis et al., 1999).

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Many researchers believe that urbanicity stands as a proxy for environmental factors that await identification. Possibilities discussed in the literature (Krabbendam and van Os, 2005) include socioeconomic adversities, environmental pollution, exposure to toxins and infectious agents, drug abuse, and others. However, the difference in schizophrenia incidence persisted when analyses were adjusted for many of these variables, indicating that these factors probably exert no major effect on the association. The social drift hypothesis also addressed this issue and proposed that individuals with pre-existing mental disorders tend to move to a socioeconomic lower status and to cluster in urban areas, thus raising the false impression that city living predisposes to increased psychosis risk. However, several observations argue against this hypothesis. First, there is both a dose–response relationship between duration of exposure to urbanicity and morbidity risk and a nearly linear association between city size and psychosis incidence, indicating that the urban-rural difference constitutes the etiologic factor (Pedersen and Mortensen, 2001). Second, in subjects with high psychosis risk, moving to a rural area attenuates schizophrenia incidence (Pedersen and Mortensen, 2001). This reversibility also argues in favour of urbanicity itself, not social drift, as the causative agent. Third, in migrants, the effect of city living on schizophrenia incidence is greatest among second-generation individuals (Cantor-Graae and Selten, 2005). This observation is not easily explained by social drift as the primary event. In conclusion, the factors mentioned above seem an unlikely explanation for the observed urban-rural difference in mental disorders incidence. Currently, many researchers favour the hypothesis that the urban environment stands as a proxy for increased exposure to social stress.

3. Social stress – risk factor for mental disorders

During evolution, processing and performing complex social interaction emerged as a key factor driving the development of larger brains in primates and humans (Dunbar and Shultz, 2007). Social skills that are necessary for profiting from diversification of knowledge, for refining commercial relationships or for building tactical alliances in order to expand power, substantially contributed to the success of the human species. A supportive social environment turned out as one of the most important conditions necessary for mental and physical health. Therefore, acute loss of group support may be perceived as fundamental threat, eliciting a stress reaction comparable to acute physical endangerment (Eisenberger and Cole, 2012). But also more chronic forms of social stress are of interest, as exposure to a socially stressful environment often expands over a period of weeks, months or years. For example, long-lasting social isolation has a considerable impact on both physical and mental health, as it is associated with an increased risk of depression, anxiety, coronary heart disease, and death (House, 2001). The impact of social stress as a risk factor for both mental and physical disease is corroborated by findings that highlight the beneficial impact of social support. This factor emerged as a powerful resource to mitigate the effects of acute stress (Heinrichs et al., 2003). Finally, the presence of this factor is associated with a reduction of mortality exceeding the influence of physical activity, smoking cessation and lower body-mass index (Holt-Lunstad et al., 2010).

Stress research, neuroscience and epidemiology have substantially contributed to elucidate the role of social stress as a risk factor for mental disorders. Stress research has identified potent ingredients of acute social stress. Exposure to tasks that were uncontrollable and included social threat, i.e. failure in front of significant others, were associated with the most profound activation of the endocrine stress response (Dickerson and Kemeny, 2004). Pathways through which stress exposure increases the risk of disease manifestation have been investigated in most major mental disorders. They vary according to type of stressor, exposure time and subject characteristics. In 1997, Walker and Diforio (Walker and Diforio, 1997) proposed the “neural diathesis-stress model”, and suggested that the interaction of specific genetic and environmental factors resulted in increased stress system activation, thus facilitating onset, exacerbation and relapse of schizophrenia. According to this model, stressful events are associated with an abnormal activity of the hypothalamic-pituitary-adrenal(HPA)axis, triggering a cascade of events leading to dysfunction of dopaminergic neurotransmission and neural circuits relevant for psychosis symptom generation (van Winkel et al., 2008). Significant stress-associated dopamine release in the ventral striatum in healthy volunteers (Pruessner et al., 2004) and stress-responsive system dysfunction in schizophrenic patients upon exposure of to an experimental social stressor (Brenner et al. 2009) both support this hypothesis. Furthermore, prolonged exposure to stress seems to be capable of inducing architectural changes in specific brain areas such as the prefrontal cortex which mediates the highest-order cognitive abilities (Arnsten, 2009). Chronic stress was also found to be associated with a decrease in volume in of the hippocampus, a structure central to memory storage and retrieval (Sapolsky, 1996). Interestingly, the hippocampus is also involved in HPA system regulation, as this structure exerts a tonic inhibition on stress system activity, which subsides with stress exposure. Through this mechanism, hippocampal damage may result in enduring HPA system overactivity, further aggravating damage to brain structures via prolonged cortisol exposure.

Neuroscience has made substantial progress in exploring the neural circuits that support social function and process social stress. Segmentation of social cognition differentiates social perception, attribution and categorization. During these processes, social stimuli that arise from other group members are detected and analysed, and behaviour is interpreted as indicating a specific mental state (Meyer-Lindenberg and Tost, 2012). The emotional and motivational appraisal of social stimuli is processed in a neural mutually interacting circuit involving the brain regions amygdala, insulate, subgenual anterior cingulate cortex (ACC) as well as the orbitofrontal cortex. This circuit closely interacts with the brain structures that direct the stress-responsive systems including the HPA system. The smooth functioning of these neural circuits may be endangered by genetic and environmental factors. Several lines of evidence indicate that the maturing brain is vulnerable to environmental stressors especially in genetically predisposed subjects (Heim and Binder, 2012). For example, the action of the hypothalamic neuropeptides oxytocin and vasopressin differs in carriers of genetic variants encoding the receptor for these molecules (Chen et al., 2011; Hammock and Young, 2005). Exposure to social stress is associated with a profound effect on these receptors, affecting function and structure of hypothalamic-limbic circuits. In the case of schizophrenia, animal data indicate that early life exposure to social stress is associated with both increased mesolimbic dopamine reactivity and psychosis related phenotype in adulthood (Lieberman et al., 1997).

Recent work has combined functional magnetic resonance imaging techniques and stress research tools to identify the brain mechanisms that are involved in translating the effect of city living on social stress processing (Lederbogen et al., 2011). It was shown that in healthy adults, exposure to an urban environment during the first 15 years of life was associated with an increased activation of the ACC, a key structure of the limbic system involved in both processing social information and regulating stress-responsive system activation. The association between early-life urbanicity