
Commentary on Residential Location Papers by Whitfield et al. (2005) and Willemsen et al. (2005)

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Of all the different psychiatric phenotypes, a dose–response relationship with urbanicity has been reported most consistently and with by far the greatest effect size for psychosis (van Os, 2004). In addition, this effect has its impact through continuous or repeated exposure on developing children and adolescents, that is, the time window of exposure is not around the time of birth nor around the time of onset of psychotic disorder (typically in young adulthood), but in between (Marcelis et al., 1999; Pedersen & Mortensen, 2001a). Recent studies in Germany, Greece, the United Kingdom and the Netherlands (e.g., Spauwen et al., 2004; van Os et al., 2001) have shown that the increased level of risk for psychotic disorder in urban populations is not phenotypically silent, because the prevalence of at-risk mental states characterized by subtle psychosis-like phenomena is also higher in urban areas, independent of the increased rate of psychotic disorder, and independent of service use, sociodemographic factors including ethnic group, drug use, size of social network and neuropsychological impairment (Pedersen & Mortensen, 2001a; Pedersen & Mortensen, 2001b; van Os et al., 2001).

The association between psychosis and urbanicity does not appear to be a noncausal genetic epiphenomenon involving a mechanism of gene–environment correlation, as change in the urbanicity exposure during childhood also results in a change in risk for adult schizophrenia (Pedersen & Mortensen, 2001a). The genes that contribute to the risk of schizophrenia therefore do not appear to induce spatial selective mobility, suggesting a possible true causal influence on psychosis in the urban environment.

Therefore, the findings reported by Whitfield and colleagues and Willemsen and colleagues are highly relevant for psychosis research (Whitfield et al., 2005; Willemsen et al., 2005). If environmental factors in the urban environment contribute to psychosis risk then individuals who move to urban areas are at greater risk than those who do not, and knowledge about the factors determining increased risk of exposure would be useful. The question is to what degree these factors are of genetic and/or environmental origin.

The comparability between the two studies is limited. Just as the heritability of alcoholism will likely differ as a function of societal availability (severe restriction resulting in alcohol use only by those who are genetically most predisposed), so may the genetic influence on urban mobility vary as a function of base rate of the outcome: 10% in Australia versus around 30% to 50% (*very heavy* and *heavy* urbanization) in the Netherlands. More evidence of genetic influence in Australia therefore may in part be the result of the lower base rate. In addition, the Australian study defined urbanicity in terms of distance to the centre of a big city, which is known to include predictable neighborhood socioeconomic status differentials that may represent a genetic source of variation. Another possible factor involved is co-twin closeness, which is greater in monozygotic (MZ) than in dizygotic (DZ) twins (Tambs et al., 1995; Tambs et al., 1985). Creating within-pair discordance in place of residence is therefore occurring against a greater emotional barrier in MZ than in DZ twins, and this may be more relevant in Australia (resulting in greater apparent genetic influence), as the maximum distance by which two persons in the Netherlands can be separated is bridged by a train journey of only 4.5 hours.

There are likely to be only very few human characteristics beyond any genetic influence. The studies from Australia and the Netherlands suggest that in young adulthood, the age range at which the psychotic disorder typically declares itself, environmental more than genetic factors may influence exposure to the risk environment that urbanicity represents.

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