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Childhood exposure to green space – A novel risk-decreasing mechanism for schizophrenia?

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ABSTRACT

Schizophrenia risk has been linked to urbanization, but the underlying mechanism remains unknown. Green space is hypothesized to positively influence mental health and might mediate risk of schizophrenia by mitigating noise and particle pollution exposure, stress relief, or other unknown mechanisms. The objectives for this study were to determine if green space are associated with schizophrenia risk, and if different measures of green space associate differently with risk. We used satellite data from the Landsat program to quantify green space in a new data set for Denmark at 30 × 30 m resolution for the years 1985–2013. The effect of green space at different ages and within different distances from each person's place of residence on schizophrenia risk was estimated using Cox regression on a very large longitudinal population-based sample of the Danish population (943,027 persons). Living at the lowest amount of green space was associated with a 1.52-fold increased risk of developing schizophrenia compared to persons living at the highest level of green space. This association remained after adjusting for known risk factors for schizophrenia: urbanization, age, sex, and socioeconomic status. The strongest protective association was observed during the earliest childhood years and closest to place of residence. This is the first nationwide population-based study to demonstrate a protective association between green space during childhood and schizophrenia risk; suggesting limited green space as a novel environmental risk factor for schizophrenia. This study supports findings from other studies highlighting positive effects of exposure to natural environments for human health.

1. Introduction

Globally, 450 million people are estimated to suffer from some form of mental illness and the number is expected to increase.(World Health Organization, 2003) Loss of productivity costs national economies billions of dollars, and the economic burden is estimated to 3–4% of GNP for developed countries (World Health Organization, 2003). Increasing rates of mental illnesses have been linked to increasing urbanization and environmental degradation whereas access to green space has been linked to mental health benefits (James et al., 2015; Lee and Maheswaran, 2011; Sandifer et al., 2015; Sugiyama et al., 2008) but the mechanistic link remains unknown.

Since the beginning of the 19th century a number of studies have documented urban rural differences in the occurrence of schizophrenia, generally showing increasing occurrence of schizophrenia in urbanized areas (Faris and Dunham, 1939; Haukka et al., 2001; March et al., 2008; Mortensen et al., 1999; Pedersen and Mortensen, 2001). The underlying mechanism is likely linked to multiple factors, but hypotheses roughly fall within one of two main explanatory categories (DeVerteuil et al., 2007): 1) individuals with schizophrenia migrate into inner-city areas, or 2) disease development is disproportional in inner-cities because of environmental risk factors. Recent studies have shown only partial effects of selective migration, indicating that the urban environment itself is a risk factor (DeVerteuil et al., 2007; Pedersen, 2015; Vassos et al., 2016). A clear difference between urban and rural environments is the amount and types of green space. Green space is known to decrease air and noise pollution (Gidlöf-Gunnarsson and Öhrström, 2007; Nowak et al., 2006) and increase stress restoration (Annerstedt et al., 2013; Beyer et al., 2014; Grahn and Stigsdotter, 2010) – factors that have been linked to mental health and risk of developing schizophrenia

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(Freeman, 1994; Mortensen, 2000). However, with few exceptions, studies investigating which characteristics of green space are important for mental health are lacking (Annerstedt et al., 2012).

Schizophrenia risk could be associated with different measures of green space as well as the spatial distribution of green space – e.g., the quantity or heterogeneity of green space within a given distance from a person's place of residence. We would expect that the quantity is related to availability and density of the surrounding green space, which could be important for e.g. air and noise pollution levels, whereas the heterogeneity is related to variation of the surrounding green space, which could be important for the viewscape and the restorative qualities of the surrounding green space. Expansion of remote sensing programs and increased investments in satellites now provide users with high-resolution earth observation data that can be used to calculate objective measures of green space with broad temporal and spatial coverage (Henke and Petropoulos, 2013; Li and Weng, 2007; Ryznar and Wagner, 2001; Wu et al., 2014). However, satellite data has not been used before in studies of schizophrenia risk.

Assessing the influence of environmental risk factors, such as green space, on schizophrenia requires estimation of incidence rates in representative samples of the general population (Mortensen et al., 1999). Denmark offers a unique opportunity to study the potential association between schizophrenia and green space since place of residence and health of all citizens are recorded longitudinally in national registers. By using data from the Danish national registers we can account for effects of socioeconomic factors and family history allowing more robust estimation of the potential influence of green space on schizophrenia risk.

This is the first nationwide population-based study assessing the potential impact of green space on schizophrenia risk. Most studies of health and green space have focussed on quantity (van den Berg et al., 2015), but it is still unclear how green space is linked to mental health. Studies on landscape preference, restorative environments, and usability of green space suggest that the type and characteristics of green space is also important (Bratman et al., 2015; Carrus et al., 2015; Lee and Maheswaran, 2011). We addressed this question by linking the rich Danish population-based register on health and socioeconomic status with two different individual-level exposure during childhood to quantity and heterogeneity of green space from a new high-resolution data set. We used a measure of vegetation greenness, the normalized difference vegetation index (NDVI), calculated from remotely-sensed satellite images at each place of residence for all Danish residents covering the years 1985–2012. It is unclear at what distance green space potentially affects mental health (e.g. Ekkel and de Vries, 2017; Maas et al., 2009; Nutsford et al., 2013), and whether green space surrounding a persons' residence or green space within the neighbourhood is potentially more important. To test this, we examine the effect of green space at different residential proximities. We hypothesize that more green space (higher mean value of NDVI around the residence) reduces the risk of schizophrenia, and that this effect is strongest closest to the residence. Furthermore, as vulnerability to environmental risk factors may vary with age (Pedersen and Mortensen, 2001), we also examine at what age green space exposure is more important for the risk of schizophrenia.

2. Materials and methods

2.1. Study population

Denmark is a small, relatively homogeneous country with a population of 5.8 mill people and a total area of about 43,000 km^2. Distances within the country are small, with most people living within 25 km of a city with >30,000 inhabitants and a psychiatric hospital. The Danish Civil Registration System was established in 1968. For all Danish citizens, it contains a personal identification number and information on gender, date, place of birth, vital status, and parents' personal identification numbers. The personal identification number is used in all national registers, linking each individual to other national registers, e.g., containing information on health, contextual, and socioeconomic information. The study population included all persons born in Denmark 1985–2003 and who were alive and residing in Denmark at their 10th birthday (943,027 persons).

2.2. Assessment of schizophrenia and schizophrenia spectrum disorder

All individuals from the study population and their parents and siblings, were linked up to the Danish Psychiatric Central Research Register (Mors et al., 2011) to obtain information about schizophrenia. The Register contains information on all admissions to Danish psychiatric in-patient facilities since April 1st, 1969 and since 1995 also all contacts to psychiatric outpatient visit or emergency care. There are no private psychiatric in-patient facilities in Denmark. From 1969 to 1993 the diagnostics system used was the Danish modification of ICD-8 (World Health Organization, 1967) and from 1994 the ICD-10 (World Health Organization, 1992). Individuals were classified with schizophrenia and schizophrenia spectrum disorder if they had been admitted to a psychiatric facility, received outpatient care, or visited a psychiatric emergency care unit with a diagnosis of schizophrenia (ICD10: F20 and equivalent ICD-8 codes) and schizophrenia spectrum disorder (ICD10: F20–F29 and equivalent ICD-8 codes) (Pedersen et al., 2014). The date of onset was defined as the first contact diagnosed with the above-defined diagnosis.

2.3. Quantification of green space

We used two measures of green space covering the period of 1985–2013: 1) mean green space, and 2) spatial heterogeneity of green space. Both measures were calculated from the normalized difference vegetation index (NDVI) obtained from 30 m resolution remote sensing images from the Landsat archive (http://earthexplorer.usgs.gov/, accessed 2 February 2016). NDVI is calculated as the difference between absorbed (red) and reflected (near-infrared) light by vegetation following:

$$\mathrm{NDVI} = \frac{\mathrm{NIR} - \mathrm{RED}}{\mathrm{NIR} + \mathrm{RED}}$$

where NIR is the near-infrared and RED is the red band. NDVI is a commonly used and effective measure of green space (Lo, 1997; Rhew et al., 2011). Low values indicate sparse vegetation and high values indicate dense vegetation.

The Landsat archive contains satellite data of earth acquired by six satellites over >40 years. Over the years, the purpose and spatial focus of the Landsat program has changed, and as a result the availability of the data varies. The Landsat satellites provide images of 4–11 bands at 30–120 m resolution on a 16–18 day revisit cycle. We aimed to obtain images from the growing season in June, July, or August with none to low cloud cover for the entire country each year. The best data coverage comes from the later years, whereas data availability of the earliest years fluctuates. E.g. the satellite images from year 1978–1983 only cover parts of Zealand and the island of Bornholm. Also, due to technical difficulties some years in the time period are only partly covered or not covered at all (see Table S1 for details of each year).

All Landsat images were atmospherically corrected and converted to Top of Atmosphere (TOA) reflectance using ENVI version 5.1 to remove atmospheric effects such as water vapour and the position of the sun. Despite our best efforts to find cloud free images, some images were partly covered by clouds. For images with severe cloud cover (~5–30%), several images were downloaded covering the same area at different dates and merged to obtain a single complete image. Clouds were identified and masked loosely following the approach from Martinuzzi et al., 2007. Clouds on images from Landsat 8 (only for year 2013)

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