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The Association between Residential Green Space in Childhood and Development of Attention Deficit Hyperactivity Disorder: A Population-Based Cohort Study

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Background: Access to green space has been hypothesized to have a beneficial impact on children's mental well-being and cognitive development. The underlying mechanisms of the mental health benefits of green space are not fully understood, but different pathways have been suggested, such as the psychologically restoring capacities of green space, the ability to facilitate physical activity and social cohesion, and the mitigation of exposure to air pollution.

Objectives: In this nationwide cohort study, we investigated associations between residential green space in early childhood and a clinical diagnosis of attention deficit hyperactivity disorder (ADHD).

Methods: The cohort included individuals, who were born in Denmark between 1992 and 2007 ($n = 814{,}689$) and followed for a diagnosis of ADHD from age 5, during the period 1997–2016. We used the normalized difference vegetation index (NDVI) as a measure of vegetation greenness surrounding each residential address in a quadratic area of 210 m × 210 m in which the residence was located in the center of the quadrate. Individual exposure to green space was calculated as the average of NDVI surrounding each individual's residential address (or addresses if more than one) between birth and the fifth birthday. Multilevel modeling was used to estimate the incidence rate ratios (IRRs) with 95% confidence intervals (CI) for ADHD, according to exposure level and adjusted for calendar time, age, sex, parental socioeconomic status, neighborhood level socioeconomic status, and urbanicity.

Results: Individuals living in areas defined by sparse green vegetation (lowest decile of NDVI) had an increased risk of developing ADHD, compared with individuals living in areas within the highest decile of NDVI (IRR = 1.55; 95% CI: 1.46, 1.65). Adjusting for the known confounders attenuated the result, but the association remained (IRR = 1.20; 95% CI: 1.13, 1.28).

Conclusion: Our findings suggest that lower levels of green space in residential surroundings, during early childhood, may be associated with a higher risk of developing ADHD. https://doi.org/10.1289/EHP6729

Introduction

Attention deficit hyperactivity disorder (ADHD) is a heritable and highly prevalent (Dalsgaard et al. 2020) neurodevelopmental disorder with childhood onset and core symptoms of inattention, hyperactivity, and impulsivity, which often persist into adolescence and adulthood. The etiology of ADHD is still not fully understood, but both genetic and environmental risk factors (e.g., prenatal and perinatal factors, environmental toxins, and psychosocial factors) (Thapar et al. 2012) may increase susceptibility to develop ADHD (Demontis et al. 2017; Faraone and Larsson 2018).

Access to green space has been suggested to have a beneficial impact on children's cognitive development and mental health, including ADHD (Gascon et al. 2015; McCormick 2017; Tillmann et al. 2018; Vanaken and Danckaerts 2018). Studies have reported that access to green space was associated with improved cognitive skills in children and better scores on tests of attention in schoolchildren (Dadvand et al. 2015a, 2017), and several observational studies have investigated the association between green space and ADHD or symptoms of ADHD. A cross-sectional study by Amoly et al. found that residential surrounding green space had a positive impact on ADHD symptoms in school-age children (Amoly et al. 2014), and a study by Markevych et al. found that access to urban green spaces was associated with fewer behavioral problems. The results were most consistent with hyperactivity/inattention problems (Markevych et al. 2014). A third study found that greater residential proximity to city parks was associated with fewer ADHD symptoms in children (Balseviciene et al. 2014), and a more recent study by Markevych et al. found that residential green space was associated with a reduced risk of a diagnosis of ADHD (Markevych et al. 2018). Finally, a longitudinal cohort study by Donovan et al. suggested that increased minimum greenness was associated with a lower risk of developing ADHD (Donovan et al. 2019), and a cross-sectional study by Yang et al. found that greater levels of greenness near schools or kindergartens were associated with lower odds of ADHD in Chinese children (Yang et al. 2019).

The underlying mechanisms for these potential associations are not fully known, but different pathways have been suggested. Green environments are widely believed to enhance psychological restoration including attention restoration and stress recovery. Inattention and concentration difficulties are symptoms of ADHD, and the attention-restoration theory suggests that these symptoms are reduced by access to green environments (Stevenson et al. 2018). In addition, a few experimental studies have reported that symptoms of inattention were reduced in children with ADHD

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when playing in green environments (Kuo and Taylor 2004; van den Berg and van den Berg 2011). Furthermore, studies have found that children with ADHD have lower gut microbial diversity and that increased microbial exposure from the environment can improve the microbial diversity (Aerts et al. 2018; Kuo 2015; Prehn-Kristensen et al. 2018). Finally, the ability of green spaces to alleviate negative effects of environmental stressors such as air pollution have also been suggested as potential mechanisms (Dadvand et al. 2012; 2015b; Nowak et al. 2006). Exposure to higher levels of air pollution has been adversely associated with ADHD or symptoms of ADHD (Forns et al. 2016; Min and Min 2017; Mortamais et al. 2017; Newman et al. 2013; Siddique et al. 2011; Thygesen et al. 2020), and consequently, a supposed beneficial association between green space and ADHD may partly be explained by lower air pollution levels in green areas.

In this nationwide population-based cohort study, we exploit the unique research possibilities of combining Danish registry data, with yearly information on green space, daily concentrations of air pollutants by geographical coordinates, complete residential history of all cohort members, validated clinical diagnoses of ADHD, individual-level data on parental education and income, and neighborhood-level data on education, income, and unemployment. The primary aim of this study was to investigate the potential impact of residential green space in early childhood on the risk of ADHD, and because it is not fully known whether the proximity of green space to a residence has an impact on the association between green space and ADHD, we investigated the association between green space and ADHD at different proximities. Finally, we wanted to investigate whether the association between green space and ADHD was influenced by the presence of air pollution.

Materials and Methods

Study Population

The study population included all singletons born in Denmark between 1 January 1992 and 31 December 2007, who were alive and resident in Denmark on their fifth birthday, whose parents were both born in Denmark, and whose mothers were residents in Denmark at the time of conception, defined as 9 months before giving birth. To identify the study population of 814,689 individuals, we used the Danish Civil Registration System (CRS) (Figure S1). The CRS was established in Denmark in 1968 (Pedersen et al. 2006) and includes all people who had a residence in Denmark on 1 April 1968 onward. Since then, all residents in Denmark have been assigned a unique 10-digit personal identification number, which is stored in the CRS together with information such as sex, date and place of birth, vital status (e.g., date of death or date of exit from Denmark), the personal identification numbers of the parents, information about current and former residential addresses in Denmark, and dates of all residential changes. The personal identification number is the key that enables exact individual-level linkage between all Danish National registers.

Exposure Window

From the CRS we identified the cohort members' residential addresses between birth and the fifth birthday and used geographical coordinates obtained from the Danish Register on Official Standard Addresses and Coordinates to link the addresses with information on green space (NDVI) and daily concentrations of air pollution [NO_2 and fine particulate matter with aerodynamic diameter ≤ 2.5 μm ($PM_{2.5}$)] in this period. For each individual, we calculated the average exposure levels of NDVI, NO_2 and $PM_{2.5}$ between birth and the fifth birthday, accounting for residential changes in Denmark. If an individual had a residence in another country during these 5 y, it was not possible to assign exposure status for this period residing outside of Denmark. Individuals who had less than 4 years of exposure information during the period were excluded from the study population, whereas we calculated an average of the 4 y for individuals who had only 4 years of exposure information.

An exposure window from birth to the fifth birthday was chosen because the incidence (Dalsgaard et al. 2020) and validity (Overgaard et al. 2019) of a diagnosis of ADHD before this age is very low. Defining clinical hyperactivity can be more challenging in a preschool child because such symptoms alone are also often seen among typically developing preschoolers (Tandon et al. 2011). Another reason for defining the exposure window as the first 5 years of life was to have equal time of exposure for all individuals in the study population, to ensure temporality (i.e., that the exposure precede the outcome), and to follow-up all cohort members at the same age.

Green Space Exposure Assessment

As an indicator of green space surrounding an individual's residential address, we used a standardized measure of vegetation greenness, the normalized difference vegetation index (NDVI), which is based on land surface reflectance of visible (RED) and near-infrared (NIR) parts of spectrum (Weier and Herring 2020). The NDVI is a commonly used measure of green space (Lo and Faber 1997; Rhew et al. 2011) and is calculated as the difference between absorbed and reflected (near-infrared) light by vegetation $\mathrm{NDVI} = (\mathrm{NIR} - \mathrm{RED})/(\mathrm{NIR} + \mathrm{RED})$, where NIR is the near-infrared, and RED is the red region of spectral reflectance. Values of NDVI range between -1 and 1, with the lowest values indicating absence or only sparse vegetation, most often found in city areas and along the coastline of Denmark, whereas the highest values of NDVI indicate more photosynthetically active greenness (denser vegetation), which is mostly found in rural areas or in city parks.

The NDVI values were calculated with comprehensive temporal and spatial coverage using high-resolution digital information on spectral reflectance, provided by sensors on satellites. Satellite data of the earth, acquired by six satellites for more than 40 y and available from the American Landsat archive, were used for this purpose. This approach has earlier been described in more detail and followed in two studies by Engemann et al. (Engemann et al. 2018, 2019).

For each year between 1985 and 2015, residential green space was measured as the average of NDVI in a quadratic area (exposure zones) of 210 m × 210 m around each residential address in Denmark. For each quadratic area, the place of residence was located in the center of the quadrate; for sensitivity analyses, this procedure was repeated for quadratic areas of 330 m × 330 m, 570 m × 570 m, 930 m × 930 m around all Danish residential addresses. Finally, these data were linked to all addresses of the cohort members by geographical coordinates.

Assessment of ADHD

In Denmark, public health care, including mental health care, is free of charge for the whole population, which enables a good national coverage of the registries. Information on clinical diagnoses of ADHD among cohort members was primarily obtained from the Danish Psychiatric Central Research Register (DPCR) and secondarily from the Danish National Patient Register (DNPR). The DPCR contains information on all inpatient admissions to Danish psychiatric facilities since 1969, and from 1995 also has information on all contacts to outpatient psychiatric departments and visits

to psychiatric emergency care units. The DNPR holds information on all inpatient admissions to public hospitals in Denmark since 1977 and outpatient visits from 1995 onward.

A diagnosis of ADHD is, in Denmark, based on the International Classification of Diseases, 10th Revision, Diagnostic Criteria for Research (ICD-10-DCR) codes F90x (Hyperkinetic disorders) or F98.8 (Attention deficit disorder without hyperactivity), and always assessed by child and adolescent psychiatrists. The ICD-10-DCR was adopted for use in Denmark in 1994, and a diagnosis of ADHD in the DPCR is considered to be of high validity (Mohr-Jensen et al. 2016). Date of diagnosis of ADHD was defined as the first day with the diagnosis (inpatient or outpatient contact), and individuals with an incident diagnosis of ADHD before their fifth birthday were excluded from the cohort. The reason for excluding individuals with ADHD before 5 years of age was to ensure that the exposure preceded the outcome.

Air Pollution

To investigate whether the association between green space and ADHD is influenced by the presence of air pollution, we adjusted for nitrogen dioxide (NO_2) and $PM_{2.5}$. We used information about daily concentrations of NO_2 and $PM_{2.5}$ from the Danish air pollution modeling system THOR (Brandt et al. 2003; Brandt 2001b, 2001a, 2001c) to estimate a level of air pollution exposure for each individual. The THOR system consists of a coupling of air pollution models, including the Danish Eulerian Hemispheric Model (DEHM) and the Urban Background Model (UBM), which cover different geographical areas and have different resolutions. The DEHM, which handles long-range atmospheric transport and chemical transformations of 80 chemical species on the intercontinental and regional scales, covers the northern hemisphere with a relatively high resolution over Denmark (5.6 km × 5.6 km). UBM is a high-resolution model that covers Denmark, taking atmospheric transport and chemistry on a 1 km × 1 km resolution into account. The emission inventory for Denmark is based on the SPREAD model (Plejdrup et al. 2016) on a similar high resolution and includes emissions from all sectors (e.g., traffic, industry, power production, residential heating, agriculture, etc.). The air pollution models are driven by meteorology using the WRF model (Skamarock et al. 2008). The modeled long-term averages for NO_2 and $PM_{2.5}$ in Denmark have been validated against measured concentrations of the pollutants (Brandt et al. 2001, 2003, 2012; Im et al. 2018).

Statistical Analysis

Due to the multilevel structure of the data (individuals within municipalities), we conducted multilevel Poisson regression using the procedure proc glimmix in SAS version 9.4 (SAS Institute Inc). The resulting estimates were incidence rate ratios (IRRs) with 95% confidence intervals (CIs). An IRR of 1.00 indicates no association between exposure (green space) and outcome (ADHD). All individuals in the cohort were followed from their fifth birthday until the date of first diagnosis of ADHD, death, disappearance, emigration from Denmark or end of study (31 December 2016) (whichever came first). The average measure of green space (NDVI) was fitted in categorical deciles, a numeric trend variable representing the highest vs. the lowest decile and a continuous variable representing a decrease of 0.1 NDVI. All estimates were adjusted for age, calendar time, and sex, and in three extended models, we made further adjustments. Overall, four models were fitted: *a*) adjustment for age, calendar year, and sex; *b*) adjustment for age, calendar year, sex, and parental socioeconomic status (SES); *c*) adjustment for age, calendar year, sex, parental SES, and neighborhood-level SES; *d*) adjustment for age, calendar year, sex, parental SES, neighborhood-level SES, and urbanicity. In the analyses, age and calendar time were treated as time-dependent variables, whereas all other variables were treated as variables independent of time. All covariates were accessed for the year the cohort member was born, and when information on covariate data was not available, we performed complete-case analysis.

Age, sex, and parental SES were included to control for individual and socioeconomic confounding factors. Parental SES has been associated with an increased risk of ADHD in children (Dalsgaard et al. 2015; Larsson et al. 2014), and we obtained information from Statistics Denmark about parental education (highest completed education in four categories, primary school, short education, medium long education, and higher education) and parental income (gross income in quintiles adjusted for inflation and gender differences). In the following sections, parental SES will be defined as parental education and income and phrased as parental SES. Indicators of neighborhood-level SES is included to describe the effects that lie beyond the individually determined risk of ADHD and is measured as the proportion of individuals with low income, the proportion of individuals with low education and the proportion of individuals outside the workforce in the municipality (the smallest administrative unit in Denmark). The incidence of ADHD diagnoses has been observed to differ geographically (Madsen et al. 2015), and degree of urbanization was included in the model to determine to what degree the association between green space and ADHD was independent from urbanization. Degree of urbanicity was included as a categorical variable on five levels: *a*) the capital; *b*) the suburbs of the capital; *c*) municipalities, where the largest city has more than 100,000 inhabitants; *d*) municipalities, where the largest city has between 10,000 and 100,000 inhabitants; and *e*) municipalities with largest towns having fewer than 10,000 inhabitants.

Incidence of a diagnosis of ADHD has increased over the years, and we addressed these temporal changes in incidence of ADHD by adjusting for calendar time in our main analyses. Moreover, we performed an analysis stratified on birth year and found comparable estimates of the association in all strata. In all, we performed six stratified analyses including an interaction term; *a*) stratification by year of birth (in three groups) due to increasing prevalence rates of diagnosed ADHD (Atladottir et al. 2015); *b*) stratification by sex, because the prevalence is considerably higher in males than females; *c*) stratification by urbanicity; *d*) stratification by geographical regions in Denmark, because the incidence of ADHD (Madsen et al. 2015) and the NDVI differ geographically across Denmark; *e*) stratification by parental SES; and *f*) stratification by neighborhood-level SES.

To investigate whether the association between green space and ADHD was influenced by the presence of air pollution, we calculated the percentage of the associations between green space and ADHD, which could be explained by air pollution as $([1-(\beta m/\beta)]\times 100)$, where βm was the regression coefficient in the model including the air pollutant and β was the regression coefficient in the model not including the air pollutant.

We performed several sensitivity analyses. In the main analyses, individual exposure to green space was defined as an averaged measure of NDVI based on values for each year from birth to the fifth birthday, and NDVI was measured within the quadratic exposure zone of 210 m × 210 m. In the "Results" and "Discussion" sections, the results presented are based on these analyses. However, it is not fully known whether the distance to green space is important for the association between green space and ADHD. To test this hypothesis, we investigated the association between green space and ADHD at

different proximities, in a sensitivity analysis, using the three exposure zones (330 m × 330 m, 570 m × 570 m, and 930 m × 930 m zones) instead of an exposure zone of 210 m × 210 m. In addition, we performed an analysis of the association between green space and ADHD when NDVI was measured at different ages between birth and 5 years of age, instead of an averaged measure of NDVI within the first 5 years of life. Finally, we investigated whether associations were influenced by shared factors within families by studying only firstborn children in the study population.

Ethics

This study was approved by The Danish Protection Agency and the Danish Health and Medicines Authority. All personal information from the registers was anonymized when used for research purposes; and by Danish law, ethical approval is not required for register-based studies.

Results

The study population included 814,689 individuals born in Denmark between 1 January 1992 and 31 December 2007 (Figure S1). During the study period, 29,697 individuals (3.65%) were diagnosed with ADHD, during 9,770,746 person-years of risk from 1997 until 2017 (Table 1). Mean age at first ADHD diagnosis was 11.5 y [standard deviation (SD) 4.32], and individuals in the study population were followed for up to 19 y (mean = 12 y; SD 4.75 y). For 6,825 individuals (0.84%), follow-up was ended before the end of the study (i.e., censored) because they emigrated from Denmark (0.70%), disappeared (0.01%), or died (0.13%).

Green Space and ADHD

Level of residential green space was measured as NDVI in an exposure zone of 210 m × 210 m and ranged from −0.58 to 0.8. The lowest values indicate a sparse vegetation, which is typically found in the city centers, and the highest values indicate a denser vegetation in, e.g., forest areas, rural areas, or in city parks (Figure 1). We found that NDVI was inversely associated with ADHD. Living in residences surrounded by the lowest level of NDVI was associated with a higher risk of ADHD, when compared with individuals living in residences surrounded by the highest level of NDVI (IRR: 1.55; 95% CI: 1.46, 1.65) (Table 2). This association was robust to adjustment for parental SES, although slightly attenuated (IRR: 1.21; 95% CI: 1.14, 1.28), whereas further adjustments for area-level SES and urbanicity did not change the result (IRR: 1.20; 95% CI: 1.13, 1.28) (Table 2). Likewise, in a trend analysis, where NDVI was fitted numerically, we found the same inverse relationship, because children living in areas surrounded by the lowest levels of NDVI had a 1.43-fold (95% CI: 1.37, 1.49) increased risk of ADHD, compared with individuals living in residences surrounded by the highest level of NDVI. Again, adjusting for parental SES attenuated the association (IRR: 1.16; 95% CI: 1.11, 1.22), whereas further adjustments for area-level SES and urbanicity did not change the results (IRR: 1.16; 95% CI: 1.11, 1.22) (Table 2). For every 0.1 *decrease* in NDVI, the risk of ADHD increased by 3% (IRR: 1.03; 95% CI: 1.02, 1.03) in the fully adjusted model.

Stratified analyses of green space and ADHD in a fully adjusted model showed that low levels of NDVI were associated with increased risk of ADHD across birth-year groups, sex, and region, but the strength of the association differed. Stronger associations were found in the oldest birth-year groups, in females, and in the North Denmark region (Table S1). Stratifying on urbanicity and parental SES showed an increased risk of ADHD across all urbanicity levels except for the capital suburb, and exposure to low levels of NDVI increased the risk of ADHD on all levels of parental income and parental education except for individuals having a mother with a long education (Table S1). Regarding neighborhood-level SES, the strongest association was found in municipalities with the highest proportion of low income or highest proportion of low education or highest proportion of unemployment (Table S1).

Investigating the Role of Air Pollution

When the analyses estimating the effects of green space on the risk of ADHD were adjusted for air pollution (i.e., NO_2 and $PM_{2.5}$), the association was attenuated (Table 3). Using the difference-of-coefficient method, we calculated how much of the associations between green space and ADHD could be explained by air pollution, and found that NO_2 could explain 21.28% of the association (Table 3), whereas the presence of $PM_{2.5}$ explained 5.42% of the association.

Sensitivity Analyses

We investigated the association between green space and ADHD at three additional proximities. We used exposure zones of 330 m × 330 m, 570 m × 570 m and 930 m × 930 m quadratic areas of exposure and found that children living in areas having the lowest level of NDVI had an increased risk of ADHD compared with children living in areas having the highest level of NDVI. The results were similar to our earlier results using an exposure zone of 210 m × 210 m, but with a slightly weaker association in relation to the largest exposure zone of 930 m × 930 m (see Table S1). In another sensitivity analysis in which NDVI was measured at different ages (age 1, 2, 3, 4, and 5) and analyzed in separate models, we found that the association between NDVI and ADHD was strongest at age 5 compared to ages 1 to 4, but overall the strongest association was found when using the average measure of NDVI for the period between birth and age 5 as in our main analyses (Table S2). Because the total study population included siblings, we investigated the robustness of the results in the main analyses by studying firstborn children in the study population, and found that the association between NDVI and ADHD was attenuated but remained robust (Table S3).

Discussion

In this prospective study of a nationwide cohort, we found that children who in early life lived in residences with low levels of green space (NDVI) surrounding the residential addresses had an increased risk of ADHD, when compared to children living in a residence surrounded by high levels of green space. Differences in proximity of green space to a residence showed similar associations concerning the four different exposure zones, however, with a slightly weaker association for the most distant exposure zone. These findings indicate that living in a residential area with higher density of green space in early life may lower the risk of developing ADHD. Our results are supported by previous studies, which also found associations between higher levels of residential green space and lower risk of ADHD (Amoly et al. 2014; Donovan et al. 2019; Markevych et al. 2018; Yang et al. 2019) and lower severity of ADHD symptoms (Amoly et al. 2014).

Potential Pathways

Many different pathways have been suggested to explain potential mental health benefits of green space. Research based on the two theories, the *stress reduction theory* (Ulrich 1983; Ulrich et al. 1991) and the *attention restoration theory* (Kaplan and Kaplan 1989;

Table 1. Distribution of 29,697 cases of ADHD and 9,770,746 person-years at risk in the overall cohort.

	Number of cases with ADHD	Number of person-years at risk in total in the cohort	Incidence rate per 10,000 person-years
Year of birth			
1992–1996	10,253	4,682,352.47	21.9
1997–2001	10,655	3,096,788.89	34.4
2002–2007	8,789	1,991,604.54	44.1
Sex			
Male	20,420	4,973,694.16	41.1
Female	9,277	4,797,051.74	19.3
Region in Denmark			
North Denmark	2,751	1,102,336.62	25.0
Central Denmark	8,112	2,363,555.83	34.3
South Denmark	5,667	2,215,020.19	25.6
Capital region	8,591	2,707,981.79	31.7
Zealand	4,576	1,381,851.48	33.1
Degree of urbanization at birth[a]			
Capital	3,171	1,136,790.33	27.9
Capital suburb	4,010	1,201,872.57	33.4
Municipalities with a town with >100,000 inhabitants	2,966	1,171,198.67	25.3
Municipalities with a town with 10,000–100,000 inhabitants	8,893	2,773,159.44	32.1
Other municipalities (largest town <10,000 inhabitants)	10,621	3,481,479.72	30.5
Missing	36	6,245.17	90
Mother's level of education[a]			
Primary school	11,409	2,169,404.59	52.6
Short education	13,463	4,947,213.78	27.2
Medium long education	3,908	2,036,361.2	19.2
Long education	720	580,955.64	12.4
Missing	197	36,810.71	53.5
Father's level of education[a]			
Primary school	10,919	2,124,245.83	51.4
Short education	15,169	5,540,432.09	27.4
Medium long education	1,954	1,171,251.65	16.7
Long education	1,049	832,717.29	12.6
Missing	606	102,099.03	59.3
Mother's level of income[b]			
Below the 20th percentile	824	194,441.59	42.4
20th to the 40th percentile	4,393	839,004.45	52.4
40th to the 60th percentile	14,085	3,752,154.26	37.5
60th to the 80th percentile	8,497	3,773,234.86	22.5
Above the 80th percentile	1,898	1,211,910.73	15.7
Father's level of income[b]			
Below the 20th percentile	585	113,376.48	51.6
20th to the 40th percentile	2,207	391,452.09	56.4
40th to the 60th percentile	4,892	982,753.53	49.8
60th to the 80th percentile	10,990	3,187,737.30	34.5
Above the 80th percentile	11,002	5,092,107.37	21.6
Missing	21	3,319.14	63.3
Accumulated mean NDVI (210 m × 210 m) in deciles			
1st decile (−0,588142–0,162019)	3,413	1,181,692.12	28.9
2nd decile (0,1625203–0,2542293)	3,227	1,116,921.65	28.9
3rd decile (0,2542301–0,3145785)	3,115	1,057,289.32	29.5
4th decile (0,3145791–0,3618568)	2,989	998,719.91	29.92
5th decile (0,3618578–0,4039548)	3,048	953,622.57	32.0
6th decile (0,4039552–0,4422902)	2,931	911,696.23	32.1
7th decile (0,4422906–0,4770624)	2,828	870,574.88	32.5
8th decile (0,4770632–0,5123291)	2,881	863,872.45	33.3
9th decile (0,5123299–0,5561148)	2,761	888,147.35	31.1
10th decile (0,5561150–0,7973234)	2,504	928,209.42	27.0

Note: Cohort consisted of 814,689 children born 1992–2007. ADHD, attention deficit hyperactivity disorder; NDVI, normalized difference vegetation index.
[a]Highest finished education measured at the end of the year of the child's birth.
[b]Level of income at the year of the child's birth.

Kaplan and Talbot 1983; Kaplan 1995), argue that individuals with access to environments of high restorative quality (e.g., green areas) during periods of restoration will attain greater health benefits, in comparison with individuals who only have access to environments with lower restorative quality (Hartig 2007). Environments that promote stress reduction could be beneficial in relation to a reduction in ADHD symptoms, because stress can exacerbate symptoms in individuals with ADHD (Randazzo et al. 2008). In addition, difficulties

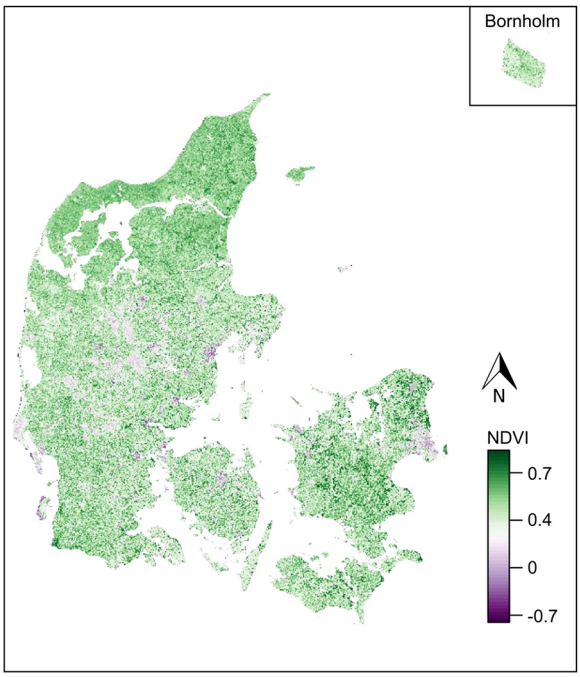

Figure 1. Map of Denmark showing the distribution of the normalized difference vegetation index (NDVI). NDVI was calculated as the yearly mean for the period 1985–2013. High values of NDVI is indicative of dense vegetation such as multilayered forests, whereas low values of NDVI indicate areas with no or very little vegetation such as parking lots.

with concentration, which is also associated with ADHD, may also be improved when individuals are exposed to restorative environments as proposed by the attention restoration theory. Other authors promote social cohesion and physical activity as underlying mechanisms of potential beneficial effects of access to green space, because green space may act as a facilitator by providing a setting for social contact and outdoor play in the neighborhood. Social cohesion in a neighborhood has been associated with human health and improved mental well-being in general (Fone et al. 2014; Rios et al. 2012), and researchers have suggested that playing in green areas reduced symptoms of inattention in children with ADHD (Kuo and Taylor 2004; van den Berg and van den Berg 2011). Improved functioning of the immune system and regulation of inflammatory responses, due to increased exposure to microorganisms from green areas, has also been suggested as a potential mechanism, because poor immune functioning could potentially impair brain development (Kuo 2015; Rook 2013; Rook et al. 2014). Proponents of the biophilia hypothesis also proposed that access to nature during the early postnatal period might be associated with beneficial structural changes in the developing brain (Kahn and Kellert 2002; Kellert 2005). This hypothesis was supported by another study by Dadvand et. al., who found that living in greener neighborhoods was associated with favorable effects on children's brain development and cognitive function (Dadvand et al. 2018).

In addition, exposure to noise has been suggested to increase symptoms of ADHD in children (Tiesler et al. 2013), and the ability of green space to alleviate noise exposure is considered a possible mechanism, because it may reduce the annoyance and stress caused by noise (Gidlöf-Gunnarsson and Öhrström 2007). Finally, research has suggested that green space reduces levels of air pollution, either simply because there is less traffic in green areas or through the filtering effect of plants (dry deposition of pollutants) (Bowler et al. 2010; Dadvand et al. 2012, 2015b). Exposure to air pollution has been associated with an increased risk of developing ADHD (Forns et al. 2016; Min and Min 2017; Mortamais et al. 2017; Newman et al. 2013; Siddique et al. 2011; Thygesen et al. 2020), and because green space and air pollution are highly correlated, the seemingly beneficial effect of green space could be partly explained by individuals' exposure to lower levels of air pollution. In a study on green space and cognitive development in schoolchildren, Dadvand et. al. found that higher levels of green space surrounding school boundaries were associated with lower levels of traffic-related air pollution and reported a positive association between green space and cognitive development in the children. This association was in part mediated by a reduced exposure to air pollution (Dadvand et al. 2015a). In this study, we investigated the potential influence of NO_2 and

Table 2. Incidence rate ratios (IRRs) for ADHD by NDVI within an exposure zone of 210 m × 210 m and in different adjustment models.

NDVI[a] deciles	Base adjustment[b] IRR (95% CI)	Base adjustment and individual SES[c] IRR (95% CI)	Base adjustment, individual- and neighborhood-level SES[d] IRR (95% CI)	Base adjustment, individual and neighborhood-level SES and urbanicity[e] IRR (95% CI)
1	1.55 (1.46, 1.65)	1.21 (1.14, 1.28)	1.20 (1.13, 1.28)	1.20 (1.13, 1.28)
2	1.46 (1.38, 1.55)	1.21 (1.14, 1.29)	1.21 (1.15, 1.29)	1.21 (1.15, 1.29)
3	1.40 (1.33, 1.48)	1.20 (1.13, 1.27)	1.20 (1.14, 1.27)	1.20 (1.14, 1.27)
4	1.34 (1.26, 1.41)	1.16 (1.10, 1.23)	1.17 (1.10, 1.24)	1.17 (1.10, 1.24)
5	1.35 (1.28, 1.42)	1.20 (1.14, 1.27)	1.21 (1.14, 1.28)	1.21 (1.14, 1.28)
6	1.29 (1.22, 1.36)	1.16 (1.10, 1.23)	1.16 (1.10, 1.23)	1.16 (1.10, 1.23)
7	1.24 (1.17, 1.31)	1.13 (1.07, 1.20)	1.13 (1.07, 1.20)	1.13 (1.07, 1.20)
8	1.23 (1.17, 1.30)	1.14 (1.08, 1.21)	1.15 (1.08, 1.21)	1.15 (1.08, 1.21)
9	1.15 (1.09, 1.21)	1.09 (1.03, 1.15)	1.09 (1.03, 1.15)	1.09 (1.03, 1.15)
10	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
NDVI[f] High vs. low	1.43 (1.37, 1.49)	1.16 (1.11, 1.22)	1.16 (1.11, 1.22)	1.16 (1.11, 1.22)
Per 0.1 NDVI decrease	1.07 (1,06, 1.07)	1.03 (1.02, 1.03)	1.03 (1.02, 1.03)	1.03 (1.02, 1.03)

Note: ADHD, attention deficit hyperactivity disorder; CI, confidence interval; IRR; incidence rate ratio; NDVI, normalized difference vegetation index; SES, socioeconomic status.
[a]Multilevel modeling was used to estimate the association between NDVI in deciles measured at 210 m × 210 m around an individual's residential address between age 0 and 5 y and the outcome of ADHD in a cohort of 814,689 individuals born in Denmark 1992–2007 and who were followed from 1997 until 2017.
[b]Adjusted for age, calendar year, and sex.
[c]Adjusted for age, calendar year, sex, and mother's and father's level of education and income.
[d]Adjusted for age, calendar year, sex and proportion of low income, low education, and unemployment at municipal level.
[e]Adjusted for age, calendar year, sex, mother's and father's level of education and income, urbanicity and proportion of low income, low education, and unemployment at municipal level.
[f]Multilevel modeling was used to estimate the association between NDVI as numeric deciles measured at 210 m × 210 m around an individual's residential address between age 0 and 5 y and the outcome of ADHD in a cohort of 814,689 individuals born in Denmark 1992–2007 and who were followed from 1997 until 2017.

Table 3. Incidence rate ratios ADHD by NDVI within an exposure zone of 210 m × 210 m and adjusted for NO_2 and $PM_{2.5}$.

NDVI[a] deciles	Adjusted for NO_2[b] IRR (95% CI)	Adjusted for $PM_{2.5}$[c] IRR (95% CI)
1	1.16 (1.09, 1.23)	1.19 (1.12, 1.27)
2	1.18 (1.11, 1.25)	1.20 (1.14, 1.28)
3	1.17 (1.10, 1.25)	1.19 (1.13, 1.26)
4	1.14 (1.07, 1.21)	1.16 (1.10, 1.23)
5	1.18 (1.12, 1.25)	1.20 (1.13, 1.27)
6	1.14 (1.08, 1.20)	1.15 (1.09, 1.22)
7	1.12 (1.05, 1.18)	1.13 (1.07, 1.19)
8	1.13 (1.07, 1.20)	1.14 (1.08, 1.21)
9	1.08 (1.02, 1.14)	1.09 (1.03, 1.15)
10	1.00 (ref)	1.00 (ref)
NDVI[d]	1.13 (1.07, 1.18)	1.15 (1.10, 1.21)
High vs. low		
% explained[e]	21.28%	5.42%

Note: ADHD, attention deficit hyperactivity disorder; CI, confidence interval; IRR, incidence rate ratio; NDVI, normalized difference vegetation index; NO_2, nitrogen dioxide; $PM_{2.5}$, fine particulate matter.

[a]Multilevel modeling was used to estimate the association between NDVI in deciles measured at 210 m × 210 m around an individual's residential address between age 0 to 5 y and the outcome of ADHD in a cohort of 814,689 individuals born in Denmark 1992–2007 and who were followed from 1997 until 2017.

[b]Adjusted for age, calendar year, sex, mother's and father's level of education and income, urbanicity and proportion of low income, low education, and unemployment at municipal level and NO_2.

[c]Adjusted for age, calendar year, sex, mother's and father's level of education and income, urbanicity and proportion of low income, low education, and unemployment at municipal level and $PM_{2.5}$.

[d]Multilevel modeling was used to estimate the association between NDVI in deciles measured at 210 m × 210 m around an individual's residential address between age 0 to 5 y and the outcome of ADHD in a cohort of 814 689 individuals born in Denmark 1992–2007 and who were followed from 1997 until 2017.

[e]Percentage of the association between NDVI and ADHD explained by air pollutant calculated as $[1-(\beta_{air}/\beta_{base})]\times 100$.

$PM_{2.5}$ on the association between green space and ADHD and found that the association may partly be explained by the presence of especially NO_2. Whether reduced air pollution levels in green areas are due to less traffic or dry deposition of pollutants is unclear. However, researchers have recently reported that for practical planting schemes and PM from all sources, the reduction is not expected to be more than a few percent, and in relation to NO_2 there is also only very little benefit for air quality (AQEG 2018). Regarding the effect of less traffic in green areas, future studies should examine the role of both traffic-related and nontraffic-related air pollutants in relation to green space.

Strengths and Limitations

The Danish national registers offer a unique possibility to perform longitudinal cohort studies (Schmidt et al. 2019) because they enable lifelong follow-up of each individual, hold substantial health information of each individual (e.g., clinical diagnoses of mental disorders) as provided by health professionals, and information on socioeconomic factors for all individuals in Denmark.

SES is known to correlate with both residential area and mental disorders and could confound the estimated effects of residential access to green space on the risk of ADHD. To minimize this possible confounding, we included individual-level data on parental level of education and income, measured the year the child was born (i.e., prior to exposure) for all cohort members. To be able to adjust for this potential confounder in a study of the total population is a major strength of our study. In Denmark, diagnostic assessment and treatment of ADHD is provided through the governmental health care system. The diagnosis of ADHD is always assessed by a child and adolescent psychiatrist and based on the International Classification of Diseases. Diagnoses of ADHD in the Danish registers are of high validity, whereas most previous studies have based their outcomes on dimensional measurements of ADHD symptoms from questionnaires or computer tests. A significant strength in our study is also the use of a state-of-the-art high-resolution air pollution model system, developed for Denmark and run over a period of 40 y, and as an indicator of green space, we used the NDVI, a commonly used measure of green space. The NDVI was calculated from remotely sensed satellite images covering each residential address in Denmark and linked, together with NO_2 and $PM_{2.5}$, with historical information on residential addresses of each individual in the cohort the first 5 years of life, thereby taking all cohort members' residential changes into account.

However, our study also has important limitations. The prenatal period is considered a critical period for brain development, and studies have shown that maternal stress during pregnancy can affect development of ADHD symptomatology in the offspring (Grizenko et al. 2012). Access to green space has also been associated with reduced stress and improved mental health among adults (Engemann et al. 2019; Gascon et al. 2015), and therefore including the prenatal period could influence the association between green space exposure in the postnatal period and development of ADHD. Future studies on green space exposure should include the prenatal period and at the same time investigate which trimester of the pregnancy is the most important. Furthermore, we did not have information about noise exposure or type of vegetation in the residential surroundings, which could influence how the individuals in our study population used the surrounding green space. Children do not spend time only at home because most children in Denmark attend day care programs. This is also a limitation of the study, and future studies should include levels of green space measured in day care surroundings. Also, in this study, large water bodies were excluded, but smaller water bodies, which generate negative NDVI values, were not excluded and could to some extent average out positive NDVI values of green areas.

In addition, we had no information about other natural environments, like blue space, that research has also found to be associated with improved mental well-being and behavioral development in schoolchildren (Amoly et al. 2014). An important limitation when investigating the influence of air pollution is that we used a difference-of-coefficient method, which does not allow evaluating the 95% CI, and therefore this method is not completely adequate to estimate a potential mediating effect of air pollution. In future studies, methods such as the nonparametric bootstrap method should be used to construct the 95% CI of the indirect effects. Finally, most previous studies used areal or network buffers around the addresses to evaluate mean NDVI, whereas our study used a quadratic area, in which the residential address was located in the center of the quadrate, and results can be influenced by the type of buffer that has been chosen for a study (Oliver et al. 2007).

Conclusion

This nationwide population-based cohort included 814,689 individuals who were followed for up to 19 y, and the study included detailed spatial data on exposure (green space) and outcome (a diagnosis of ADHD) for the same period. This is, to our knowledge, the largest study on this topic so far. In conclusion, our results suggest that higher levels of green space in the residential area during early childhood may be associated with a lower risk of developing ADHD.

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