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Residential Surrounding Greenness and Cognitive Decline: A 10-Year Follow-up of the Whitehall II Cohort

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Background: Evidence on beneficial associations of green space with cognitive function in older adults is very scarce and mainly limited to cross-sectional studies.

Objectives: We aimed to investigate the association between long-term residential surrounding greenness and cognitive decline.

Methods: This longitudinal study was based on three waves of data from the Whitehall II cohort, providing a 10-y follow-up (1997–1999 to 2007–2009) of 6,506 participants (45–68 y old) from the United Kingdom. Residential surrounding greenness was obtained across buffers of 500 and 1,000 m around the participants' residential addresses at each follow-up using satellite images on greenness (Normalized Difference Vegetation Index; NDVI) from a summer month in every follow-up period.
Cognitive tests assessed reasoning, short-term memory, and verbal fluency. The cognitive scores were standardized and summarized in a global cognition *z*-score. To quantify the impact of greenness on repeated measurements of cognition, linear mixed effect models were developed that included an interaction between age and the indicator of greenness, and controlled for covariates including individual and neighborhood indicators of socioeconomic status (SES).

Results: In a fully adjusted model, an interquartile range (IQR) increase in NDVI was associated with a difference in the global cognition *z*-score of 0.020 [95% confidence interval (CI): 0.003, 0.037; $p=0.02$] in the 500-m buffer and of 0.021 (95% CI: 0.003, 0.039; $p=0.02$) in the 1,000-m buffer over 10 y. The associations with cognitive decline over the study period were stronger among women than among men.

Conclusions: Higher residential surrounding greenness was associated with slower cognitive decline over a 10-y follow-up period in the Whitehall II cohort of civil servants. https://doi.org/10.1289/EHP2875

Introduction

The proportion of people over 60 y old in the world is expected to nearly double from 12% to 22% between 2015 and 2050 (WHO 2015). In addition, the number of dementia cases has been predicted to double worldwide, rising to 115.4 million cases by 2050 (WHO 2012). Dementia involves the impairment of cognitive function, which has a major detrimental effect on well-being, functioning, and independent living at older age (WHO 2012). The risk for dementia and cognitive decline can be affected by exposure to urban-related stressors such as air pollution and noise (Cassarino and Setti 2015; Power et al. 2016; Tzivian et al. 2015, 2016). This is alarming because the increase in the elderly population coincides with ongoing urbanization worldwide. Currently, over half of the world population lives in cities, and it is projected that by 2050, almost two-thirds of the world population will live in urban areas (United Nations 2015).

Urban residents often have limited exposure to greenness, while such an exposure has been associated with better health (Fong et al. 2018; Nieuwenhuijsen et al. 2017). Studies have shown associations with improved mental health (Gascon et al. 2015) and self-perceived general health (Dadvand et al. 2016; Triguero-Mas et al. 2015) and reduced morbidity (James et al. 2015) and mortality (Gascon et al. 2016). Through the proposed pathways for these associations, green spaces could also have beneficial impacts on cognitive decline. First, greener neighborhoods are reported to foster social cohesion and social support (de Vries et al. 2013; Maas et al. 2009a), which in turn could decelerate cognitive decline (Holtzman et al. 2004). Second, exposure to greenness could reduce stress (Gong et al. 2016), which could reduce risk of cognitive decline (Marin et al. 2011). Furthermore, higher levels of physical activity have been demonstrated in older adults with higher greenness in their residential surroundings (Gong et al. 2014), which could have a protective effect against cognitive decline and dementia (Blondell et al. 2014). Last, greenness can reduce levels of noise and air pollution (Dadvand et al. 2012, 2015b), while these are risk factors for cognitive decline (Tzivian et al. 2015, 2016).

However, in our recent systematic review of available evidence on the association of long-term green space exposure with cognition over the life course (de Keijzer et al. 2016), we found that the existing studies on the association with cognitive decline are still very scarce and mainly include cross-sectional studies that have shown inconsistent results. Therefore, the aim of the present study was to investigate the association between long-term green space exposure and cognitive decline in the Whitehall II study.

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Methods

Study Population and Setting

The Whitehall II study is an ongoing cohort that started in 1985 with over 10,000 British civil servants. All civil servants between age 35 and 55 from 20 government departments in London were invited to participate in the study. Participants have been invited for follow-ups of medical examinations and questionnaires every 5 y. The present study included 10 y of follow-up with three follow-up points: baseline at 1997–1999 (the first follow-up in which cognitive function was assessed in the full cohort, when participants were 45–68 y old), and follow-ups in 2002–2004 and 2007–2009 (Figure 1). We included participants who had data available on medical examination and questionnaire at baseline and lived in England, Scotland, or Wales. The majority of participants in our study still lived in the southeast of England by the end of our study period; however, during the 10-y course of the study, the cohort spread over the United Kingdom (Figure S1). Participant's consent and research ethics approvals [University College London (UCL) ethics committee] are renewed at each follow-up; the latest approval was by the Joint UCL/UCL Hospitals (UCLH) Committee on the Ethics of Human Research (Committee Alpha), reference number 85/0938.

Exposure Assessment

Our exposure assessment was based on the characterization of outdoor greenness surrounding the residential address of each participant at each follow-up. We geocoded the addresses of each participant at each follow-up based on the centroid of their postcode. The data on postcodes' centroids were obtained from the postcode directory of the corresponding year, provided by the Office for National Statistics (Office for National Statistics 2017). In 2011, the postcodes in England and Wales held a median number of households of 14 [interquartile range (IQR): 20] and a median number of residents of 33 (IQR: 47) (Office for National Statistics 2013).

To assess greenness, we applied the Normalized Difference Vegetation Index (NDVI) derived from images obtained by the Moderate-Resolution Imaging Spectroradiometer (MODIS) onboard the Terra satellite (Didan 2015; Huete et al. 2002). NDVI is an indicator of greenness based on land surface reflectance of visible (red) and near-infrared (NIR) parts of spectrum (Weier and Herring 2000). It ranges between −1 and 1, with higher values indicating more greenness (i.e., photosynthetically active vegetation). Our applied NDVI maps had a spatial resolution of 250 m by 250 m and were obtained over a period of 16 d. To maximize the contrast in exposure, we looked for MODIS images with least cloud cover obtained between May and June (i.e., the maximum vegetation period of the year in our study region) of the relevant years to each follow-up from the Data Pool website of the National Aeronautics and Space Administration (NASA) Land Processes Distributed Active Archive Center [LP DAAC (Land Processes Distributed Active Archive Center) 2014]. Based on this search, we downloaded and merged our NDVI maps using the images described in Table S1 and Figure 2.

For each participant, separate sets of residential surrounding greenness estimates were abstracted for the address at each follow-up separately across buffers of 500 m and 1,000 m around the corresponding postcode centroid (3 follow-ups × 2 buffers = 6 exposure estimates per person). The 500-m buffer (hereafter direct neighborhood) was chosen to represent the direct environment around the home potentially more significant for older adults (Gong et al. 2014). Given the size of the postcode areas and the resolution of our NDVI maps, it was not feasible to choose buffers smaller than 500 m. The 1,000-m buffer (hereafter walkable neighborhood) was selected to represent the general distance that adults walk to reach places nearby the home, as discussed in a previous Whitehall II study (Stockton et al. 2016). Over 96% of the 500-m buffers and over 94% of the 1,000-m buffers included complete NDVI data (i.e., no missing values in the raster) (Table S1). We used the software ArcGIS (version 10; Esri) and GDAL (version 2.2.0; OSGeo Project) for the exposure assessment.

Cognitive Function

The participants of the Whitehall II cohort took four cognitive tests covering different aspects of cognitive function with a test–retest reliability ranging from 0.60 to 0.89 (Singh-Manoux et al. 2012, 2017). The tests assessed three domains: (*a*) Reasoning was evaluated using the Alice Heim 4 test of intelligence, which included 65 items of verbal and mathematical reasoning of increasing difficulty for which the participants had 10 min to answer. The participants could obtain a score between 0 and 65; (*b*) Phonemic and semantic verbal fluency were characterized using S words and Animal names, respectively. In the S words test, the participants were instructed to write down as many words beginning with the letter S as they could in 1 min, and in the Animals names test, they were asked to write down as many animal names as they could in one minute. The participants' scores were the number of words they wrote down; and (*c*) Short-

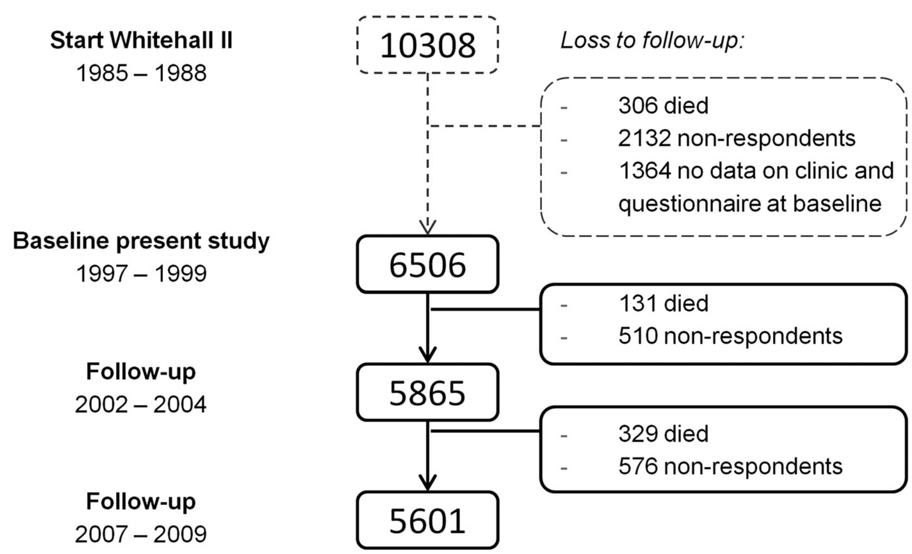

Figure 1. Flowchart of the study population.

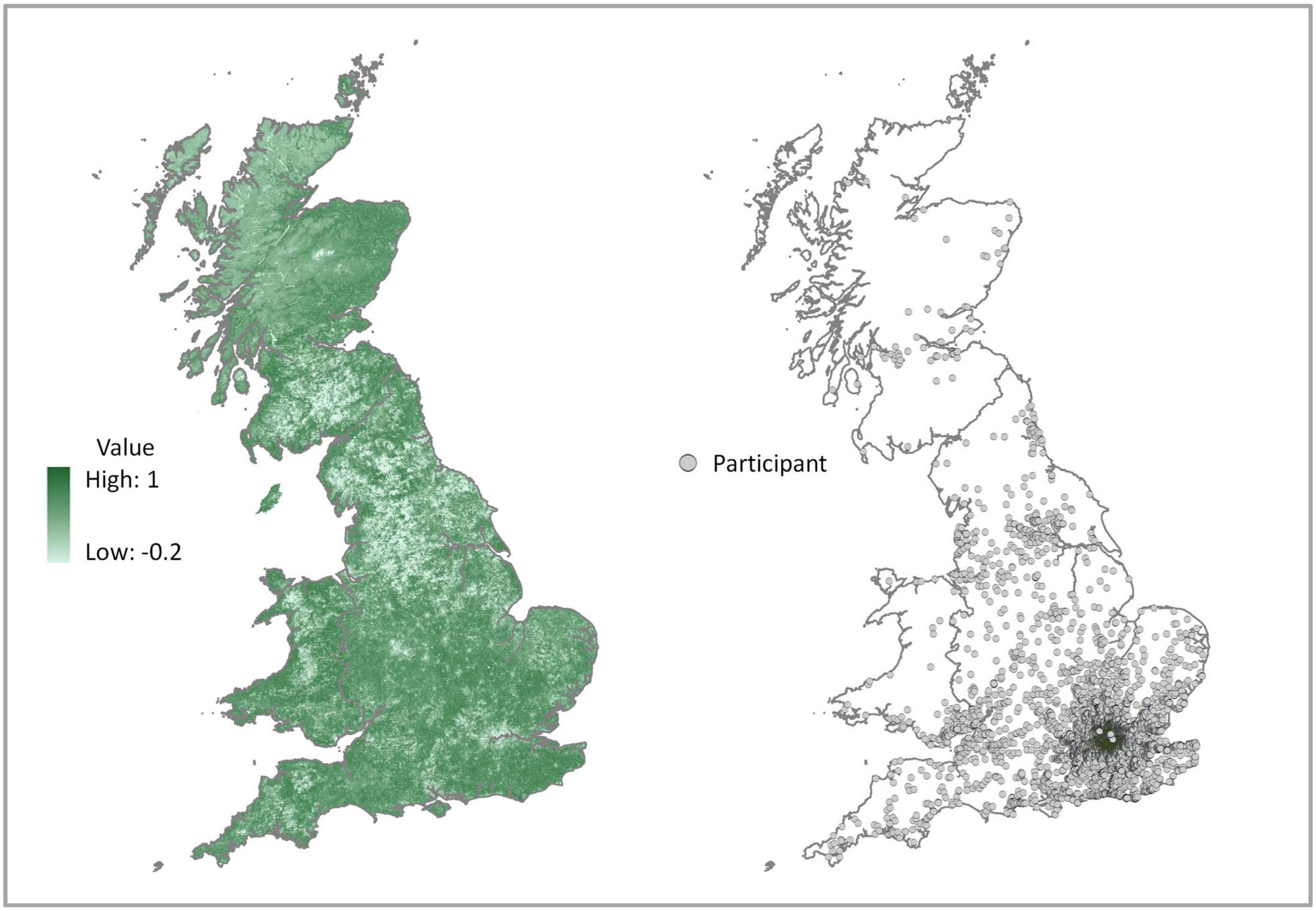

Figure 2. Normalized Difference Vegetation Index (NDVI) levels in the United Kingdom (May/June 2001) and the geographical distribution of the participants' postcodes at baseline. The maps were created using ArcGIS and ArcMap (both version 10; Esri) software.

term memory was assessed applying a free recall test in which 20 words of one or two syllables were read out loud with a 2-s interval, and the participants had 2 min to write down as many words as they remembered in any order. The participants' scores were the number of words they had remembered (with the potential range between 0 and 20).

Covariate Data

Data on demographic characteristics, socioeconomic status (SES), and lifestyle factors were collected in each follow-up. The demographic characteristics included age (continuous in years), gender, ethnicity (white or nonwhite), and marital status (married/cohabiting: yes or no). Lifestyle factors included diet (intake of fruit and vegetables: daily or less than daily), alcohol intake (frequency of consumption in the year prior to filling in the questionnaire: sometimes, daily, or never), and smoking status (current, past, or never). For SES, we used two individual-level and two area (neighborhood)-level indicators. The individual-level indicators included educational attainment and the employment grade based on the British civil service grades of employment [high (administrative), middle (professional and executive), and low (clerical)]. Following previous Whitehall II studies (Rusmaully et al. 2017; Singh-Manoux et al. 2012, 2017), education was categorized in three categories (lower secondary school or less, higher secondary school, and university or higher degree). The lower secondary school could be completed at age 16, while the higher secondary school was an additional 2 y of higher and more in-depth education, usually required for university admission (Trudel et al. 2016). For the neighborhood SES, we obtained data on the Index of Multiple Deprivation (IMD) (Noble et al. 2006) at lower-layer super output area (LSOA) level according to the 2001 Census. We collected the IMD data for each participant in each follow-up. LSOAs are the finest spatial units for which 2001 Census data on IMD is available. At baseline, our study participants lived in LSOAs with a median area of $0.4\,km^2$ (IQR: 0.2 to 0.9) (Office for National Statistics 2017). Since the total IMD includes different indicators in England than Wales or Scotland, we used the two domains (employment and income) that are comparable between the countries (Abel et al. 2016).

Furthermore, we used additional neighborhood variables at the LSOA level in each follow-up. First, we collected an indicator of rurality, using a definition of rurality by the Organization for Economic Cooperation and Development as administrative units with a population density lower than 150 inhabitants per km^2 (European Commission 2017). The population density for every participant at each follow-up was obtained at the LSOA level from the 2001 Census data (National Records of Scotland 2001; Office for National Statistics 2001). Second, we used two other domains of the IMD on crime and barriers to housing and services, collected at each follow-up. The crime score was based on the number of burglaries, thefts, criminal damage, and violence, but was only available for England. The barriers to housing and services scores were based on several indicators such as household overcrowding, road distance to a general practitioner (GP) surgery, road distance to a general store or supermarket, and road distance to a primary school. Last, we used data on land use in England on the LSOA level from the Generalised Land Use Database, obtained from the Office for National Statistics. We used the database of 2001 for the follow-ups in 1997–1999 and 2002–2004 and the database of 2005 for 2007–2009. The proportion of road area, path area, domestic buildings, and nondomestic buildings was calculated as a percentage of the total area in the LSOA at each follow-up.

Moreover, data on the potential mediators including physical activity, social support, and air pollution were used. Physical activity was assessed by questionnaire at every follow-up. The participants reported on their frequency and duration of participation in several physical activities (Sabia et al. 2012). Each type of physical activity was assigned a metabolic equivalent (MET) value and classified as mild, moderate, or vigorous physical activity. The total number of MET hours/week was used in the analysis separately for moderate and vigorous physical activity. Social support was assessed at baseline (1997–1999) and at the first follow-up (2002–2004) using a questionnaire on the number of family and friends in a person's network and the frequency of contact, and participation in social or religious activities (Singh-Manoux et al. 2005; Stringhini et al. 2012). The scaled responses were summed into a network index score, which was used in the analysis. In addition, for air pollution, the annual levels of particulate matter with an aerodynamic diameter ≤ 10 μm (PM_{10}) for each follow-up were obtained from the Department for Environment Food & Rural Affairs (Defra), modeled under Defra's Modelling of Ambient Air Quality contract (Defra 2016). The PM_{10} concentrations were modeled at a spatial resolution of 1,000 m by 1,000 m [approach described elsewhere (Grice et al. 2010; Stedman et al. 2005)]. Maps of a relevant year to each follow-up (2001, 2003, and 2008) were downloaded. We abstracted the average concentration in a 1,000-m buffer around each participant's postcode centroid for each follow-up (Tonne and Wilkinson 2013).

Statistical Analyses

Main analyses. The cognitive scores were converted to *z*-scores (using the distribution of the baseline measurements in 1997–1999) such that a positive score represents better cognitive functioning. The two fluency test scores (the S test and Animals test) were grouped together into one fluency *z*-score, and observations on all three domains were summarized and restandardized in a global cognitive score (global cognition) (Ozawa et al. 2016; Singh-Manoux et al. 2017). We tested the association between residential surrounding greenness and global cognition and the separate cognitive subscores including reasoning, fluency, and short-term memory (one at a time). For each analysis, we included all participants with available data on the corresponding cognitive score for at least one follow-up (Dadvand et al. 2015a; Ozawa et al. 2016; Singh-Manoux et al. 2017). To account for missing covariate data, multiple imputation was conducted by chained equations carrying out 25 imputations with 10 cycles for each imputation that generated 25 complete datasets (see Table S2 for details). These datasets were analyzed following the standard combination rules for multiple imputations (Spratt et al. 2010). Results were considered statistically significant at $p < 0.05$. Stata (version 14; StataCorp) was used for all analyses.

To take into account the repeated measurements for each participant, we used mixed effects models with the repeated cognitive test scores as outcomes (global cognition and each of the subscores separately), a measure of exposure to greenness as fixed predictor, and the person as random effect. An interaction between age (centered at 65 y and divided by 10 to give change over 10 y) and the indicator of greenness at each follow-up was used to quantify the impact of greenness on trajectories of cognitive decline separately for each cognitive score (Dadvand et al. 2015a; Sunyer et al. 2015). The main effect of greenness captured the baseline differences in cognitive function that were associated with greenness. The association with greenness was reported per IQR in average NDVI based on all study participants separately for each buffer size. The analyses were adjusted for a range of variables that were added to the model step-by-step. The fully adjusted models were controlled for gender, ethnicity, personal educational level, and the time-varying covariates including age, age squared (Liao et al. 2014; Singh-Manoux et al. 2017), marital status, the Whitehall employment grade, neighborhood SES (income and employment domains of IMD), diet, alcohol consumption, and smoking status. These confounders have been commonly used in cognition studies of the Whitehall II cohort (Hagger-Johnson et al. 2013; Ozawa et al. 2016; Singh-Manoux et al. 2012, 2017; Tonne et al. 2014) and in studies of the association between green space and cognition (de Keijzer et al. 2016).

Sensitivity analyses. First, we repeated the main analyses without using multiple imputation for missing covariate data (i.e., complete case analyses). Second, as rural areas generally have larger postcode areas (which could result in greater exposure misclassification) and by considering the potential modifying effect of urbanity/rurality on our investigated associations, we repeated the main analyses excluding observations from rural areas at each follow-up. Given the small proportion of study participants living in rural areas (<11%; Table 1), it was not possible to stratify the analyses based on urbanity/rurality. Third, we tested for the influence of country (England, Scotland, Wales) by repeating the analysis including only observations from England. There were not enough observations from Wales and Scotland (<4%; Table 1) to conduct analyses stratified by country. Fourth, the influence of ethnicity was tested by performing the analysis excluding nonwhite participants, as there were not enough nonwhite participants to stratify the analysis by ethnicity. Fifth, we evaluated potential confounding by other spatially distributed covariates by further adjusting (one at a time) for IMD crime score, IMD score for barriers to housing and services, road area density, path area density, domestic building density, and nondomestic building density as time-varying continuous variables.

Last, we tested for the influence of differential loss to follow-up on our findings using an inverse probability weighting approach (Weuve et al. 2012). This analysis was restricted to participants with a baseline observation for global cognition ($n = 5{,}850$). We estimated the participants' probability of completing the three follow-ups of the study by developing logistic regression models with completing three follow-ups (yes/no) as outcome together with age, age squared, global cognition score, gender, ethnicity, marital status, educational attainment, the British employment grade, the IMD income and employment domains, alcohol consumption, fruit and vegetable consumption, smoking status, subjective general health status, and residential surrounding greenness as predictors. To characterize subjective general health status, the participants were asked: "In general, would you say your health is . . ." with possible responses being one of the following five categories: excellent, very good, good, fair, or poor. We defined the weight for each participant as the inverse of the participant's predicted probability of completing the three follow-ups of the study, and applied it in the main model. Moreover, as not all participants who completed the study also had data available on the cognitive scores at all follow-ups, we created a second set of weights based on the inverse of a participant's probability of having complete observations for the cognitive scores in all three of the follow-ups using the same set of predictors. The inverse of these probabilities were the second set of weights that we applied in the main model.

Table 1. Description characteristics of participants and the cognitive scores over the study period.

Variables	No. at baseline[a]	1997–1999	2002–2004	2007–2009
Age; mean ± SD	6,506	55.73 ± 6.03	61.13 ± 6.03	65.98 ± 6.01
Male; *n* (%)	6,506	4,613 (70.9)	4,032 (71.6)	3,847 (72.3)
White; *n* (%)	6,506	5,945 (91.4)	5,177 (91.9)	4,910 (92.2)
Married/cohabiting; *n* (%)	6,191	4,864 (78.6)	4,422 (75.8)	4,172 (75.7)
Education	6,058			
University degree or higher; *n* (%)		2,229 (36.8)	1,968 (37.4)	1,909 (38.2)
Higher secondary education; *n* (%)		1,668 (27.5)	1,483 (28.2)	1,427 (28.5)
Lower secondary school or less; *n* (%)		2,161 (35.7)	1,806 (34.4)	1,666 (33.3)
Employment grade	6,474			
Administrative; *n* (%)		2,807 (43.4)	2,634 (46.9)	2,566 (49.1)
Professional and executive; *n* (%)		2,802 (43.3)	2,403 (42.8)	2,180 (41.6)
Clerical; *n* (%)		865 (13.4)	577 (10.3)	487 (9.3)
IMD income domain; mean ± SD	6,475	0.09 ± 0.08	0.09 ± 0.08	0.08 ± 0.07
Daily alcohol consumption last year; *n* (%)	6,307	2,824 (44.8)	2,570 (46.1)	2,398 (46.0)
Non-daily fruit and vegetable intake; *n* (%)	6,331	1,658 (26.2)	1,329 (23.8)	1,125 (21.4)
Current smokers; *n* (%)	6,438	634 (9.85)	419 (7.46)	264 (5.05)
Living in England; *n* (%)	6,477	6,338 (97.9)	5,481 (97.4)	5,137 (96.9)
Rural; *n* (%)	6,475	475 (7.34)	537 (9.55)	578 (10.91)
Cognitive scores; mean ± SD				
Global score	5,850	~0 ± 1	−0.210 ± 0.964	−0.331 ± 0.936
Reasoning	5,992	~0 ± 1	−0.209 ± 0.980	−0.236 ± 0.986
Fluency	5,990	~0 ± 1	−0.218 ± 0.924	−0.330 ± 0.899
Short-term memory	5,960	~0 ± 1	−0.018 ± 0.985	−0.270 ± 0.913
Residential surrounding greenness; median (first Q to third Q)				
NDVI: 500 m	6,475	0.58 (0.49–0.67)	0.60 (0.51–0.70)	0.63 (0.54–0.71)
NDVI: 1,000 m	6,476	0.59 (0.51–0.68)	0.61 (0.52–0.71)	0.64 (0.55–0.73)
EVI: 500 m	6,475	0.36 (0.29–0.44)	0.39 (0.31–0.47)	0.38 (0.31–0.48)
EVI: 1,000 m	6,476	0.38 (0.31–0.46)	0.40 (0.33–0.50)	0.39 (0.32–0.50)

Note: Data are presented as mean ± SD, n (%), and median (first Q to third Q). EVI, Enhanced Vegetation Index; IMD, Index of Multiple Deprivation; NDVI, Normalized Difference Vegetation Index; SD, standard deviation; Q, quartile.

[a]Number of available observations at baseline may differ from the total number of participants due to missing values.

Stratified analyses. We stratified the main analyses by gender, education (university or higher, higher secondary school, and lower secondary school or lower), and the tertiles of the IMD income domain to explore the variation in the association between greenness exposure and cognitive decline across the strata of gender and SES. The association with greenness was reported per IQR in average NDVI, calculated separately for each stratum.

Mediation analysis. Potential mediators were chosen a priory based on the literature. We tested for mediation of the association between NDVI and the global cognition score by physical activity (MET week of moderate or vigorous physical activity), air pollution (average annual concentration of PM_{10} in a 1,000-m buffer), and social support (social network score) following the four steps of Baron and Kenny (1986) as used in our previous studies of health benefits of green spaces (Dadvand et al. 2016; Zijlema et al. 2017). First, we tested for an association between residential surrounding greenness and the global cognition score as described in the main analyses. Then, we tested the association between greenness exposure and the mediators (one at a time) by using linear mixed effects models, including an interaction between age and the indicator of greenness at each follow-up with an identical set of covariates to the main analyses to quantify the association of greenness with the mediator at baseline and over the study period. Last, we added the mediator (one at a time) and the greenness exposure and their interaction terms with age to the main model (as described in the main analyses) to evaluate the association between the mediator and global cognition score adjusted for the greenness exposure as well as the association between greenness exposure and global cognition score adjusted for the mediator. We considered mediation if the exposure variable (greenness) was significantly associated with the mediator, the mediator was significantly associated with the outcome (cognitive function/decline), and the association between the exposure and the outcome (cognitive function/decline) was eliminated or weakened when the mediator was included in the model.

Alternative measure of greenness. The Enhanced Vegetation Index (EVI) is a vegetation index, which, compared to NDVI, is more robust to canopy structural variations (i.e., it is more accurate in characterizing greenness in densely vegetated areas) and less prone to influences by background soil (Huete et al. 2002). As NDVI, EVI is based on land surface reflectance of visible (red) and near-infrared parts of spectrum, but, in addition, includes canopy background adjustment that addresses nonlinear, differential NIR and red radiant transfer through a canopy, and coefficients of the aerosol resistance term, which uses the blue band to correct for aerosol influences in the red band (Huete et al. 2002). We obtained data for EVI from the same source (MODIS onboard the TERRA satellite) at the same resolution (250 m × 250 m) and for the same periods as NDVI (Table S1). Accordingly, we developed three separate sets of residential surrounding greenness estimates for each participant for the address at each follow-up separately across buffers of 500 m and 1,000 m around the corresponding postcode centroid (3 follow-ups × 2 buffers = 6 exposure estimates per person). The aforementioned main analysis was repeated using the EVI indicators as an alternative set of exposure.

Results

The study population consisted of 6,506 participants between 45 and 68 y at baseline (Figure 1) and had a median follow-up time of 10.4 y. Most of the participants were white (91%), male (71%), and married (79%), and over a third (36%) had a university degree or higher (Table 1). On average, global cognition declined by 0.331 standard deviations over the 10-y study period

(Table 1). Participants with missing data for covariates generally had lower global cognition z-scores and lower residential surrounding greenness (Table S3). At baseline, the average NDVI value was 0.58 in the direct neighborhood (500-m buffer) and 0.59 in the walkable neighborhood (1,000-m buffer), and slightly increased over the study period (Table 1). The correlations between the NDVI estimates at one follow-up and NDVI estimates at another follow-up were between 0.69 and 0.81 (Table S4).

Main Analyses

Higher residential surrounding greenness was associated with slower cognitive decline. In the fully adjusted model, 1-IQR increase in NDVI in a 500-m buffer surrounding the residence was associated with a difference in the global cognition score of 0.020 [95% confidence interval (CI): 0.003, 0.037] over 10 y (Model 4; Table 2). The unadjusted models, the models adjusted for demographic characteristics, and the models adjusted for demographic and lifestyle characteristics showed associations of residential surrounding greenness with baseline cognition and with cognitive decline over the study period (Models 1, 2, and 3; Table 2). The baseline association between an IQR increase in NDVI (500-m buffer) and global cognition was closer to the null in the fully adjusted model (Model 4, β: 0.012; 95% CI: −0.007, 0.031) than in models without adjustment for SES (e.g., for Model 3, β: 0.037; 95% CI: 0.018, 0.056), but the longitudinal association with cognitive decline was similar to estimates from the less adjusted models (Table 2).

When considering cognitive subscores separately, residential surrounding greenness was associated with slower decline in reasoning and fluency, but not in short-term memory (Model 4; Table 2). An IQR increase in NDVI in the 500-m buffer was associated with a difference of 0.022 (95% CI: 0.007, 0.038) in the reasoning z-score and a difference of 0.021 (95% CI: 0.002, 0.040) in the fluency z-score over the study period. Additionally, we observed a positive baseline association between residential surrounding greenness and reasoning (β: 0.021; 95% CI: 0.003, 0.038), while the positive baseline association with fluency was not statistically significant (β: 0.016; 95% CI: −0.005, 0.037), and the baseline association with short-term memory was almost null (β: −0.009; 95% CI: −0.035, 0.018) (Model 4, NDVI in the 500-m buffer, Table 2).

Estimated associations between residential surrounding greenness and the global cognition and individual cognitive subscores were similar for greenness in the direct neighborhood (500-m buffer) and greenness in the walkable neighborhood (1,000-m buffer) (Table 2).

Sensitivity Analyses

The associations were generally consistent with the main analyses when estimated using a complete case analysis (without imputing missing data), when restricted to participants who were white, from urban areas, or from England only (Table S5), and when adjusted for additional neighborhood characteristics (IMD scores for crime and barriers to housing and services, or four land use variables, in separate models) (Table S6). Associations with global cognition were slightly attenuated but generally consistent with the primary model when inverse probability weighting was used to account for potential bias due to differential loss to follow-up, including weights based on the probability of completing the study and of having complete data on the cognitive scores (Table S7).

Table 2. Difference (95% confidence interval) in global cognition and cognitive sub–z-scores at baseline and after 10 years of follow-up in association with a one interquartile range (IQR) increase in residential surrounding greenness (Normalized Difference Vegetation Index; NDVI).

	Model 1: Unadjusted		Model 2: Demographic factors		Model 3: + lifestyle		Model 4: + SES (main model)	
Exposure and outcome	Baseline	Difference	Baseline	Difference	Baseline	Difference	Baseline	Difference
NDVI: 500-m buffer								
Global cognition	0.076 (0.057, 0.095)	0.029 (0.012, 0.046)	0.040 (0.022, 0.059)	0.022 (0.005, 0.039)	0.037 (0.018, 0.056)	0.021 (0.004, 0.038)	0.012 (−0.007, 0.031)	0.020 (0.003, 0.037)
Reasoning	0.084 (0.066, 0.101)	0.029 (0.013, 0.044)	0.044 (0.027, 0.062)	0.022 (0.007, 0.037)	0.042 (0.024, 0.059)	0.021 (0.005, 0.036)	0.021 (0.003, 0.038)	0.022 (0.007, 0.038)
Fluency	0.083 (0.063, 0.104)	0.030 (0.011, 0.049)	0.047 (0.027, 0.068)	0.023 (0.004, 0.042)	0.043 (0.022, 0.064)	0.021 (0.002, 0.041)	0.016 (−0.005, 0.037)	0.021 (0.002, 0.040)
Short-term memory	0.052 (0.027, 0.077)	0.008 (−0.018, 0.034)	0.023 (−0.002, 0.049)	0.002 (−0.024, 0.028)	0.016 (−0.009, 0.042)	0.000 (−0.026, 0.026)	−0.009 (−0.035, 0.018)	−0.003 (−0.029, 0.022)
NDVI: 1,000-m buffer								
Global cognition	0.086 (0.066, 0.107)	0.031 (0.013, 0.049)	0.043 (0.023, 0.063)	0.023 (0.006, 0.041)	0.039 (0.019, 0.059)	0.022 (0.005, 0.040)	0.011 (−0.010, 0.031)	0.021 (0.003, 0.039)
Reasoning	0.110 (0.091, 0.129)	0.033 (0.016, 0.049)	0.061 (0.042, 0.080)	0.025 (0.009, 0.041)	0.057 (0.038, 0.076)	0.024 (0.008, 0.040)	0.033 (0.014, 0.052)	0.025 (0.009, 0.041)
Fluency	0.091 (0.069, 0.113)	0.034 (0.014, 0.054)	0.049 (0.026, 0.071)	0.026 (0.006, 0.047)	0.043 (0.021, 0.066)	0.025 (0.005, 0.045)	0.013 (−0.010, 0.036)	0.024 (0.004, 0.044)
Short-term memory	0.050 (0.024, 0.077)	0.002 (−0.025, 0.030)	0.017 (−0.010, 0.044)	−0.004 (−0.032, 0.023)	0.010 (−0.017, 0.037)	−0.006 (−0.033, 0.021)	−0.017 (−0.045, 0.011)	−0.010 (−0.037, 0.017)

Note: All estimates are from linear mixed effect models. Model 1: Unadjusted model including NDVI, age, age2, and age *x* NDVI. Model 2: Model 1 plus gender, ethnicity (white, nonwhite), and marital status (married/cohabiting: yes or no). Model 3: Model 2 plus alcohol use (frequency of consumption in the year prior to filling in the questionnaire: sometimes, daily, or never), diet (intake of fruit and vegetables: daily or less than daily), and smoking status (current, past, or never). Model 4: Model 3 plus education (lower secondary school or less, higher secondary school, and university or higher degree), employment grade (high, middle, or low), Index of Multiple Deprivation (IMD) income score, and IMD employment score. SES, socioeconomic status.

Table 3. Difference (95% confidence interval) in global cognition at baseline and over follow-up associated with a 1-interquartile range (IQR) increase in residential surrounding greenness (Normalized Difference Vegetation Index; NDVI) stratified by gender, education, and Index of Multiple Deprivation (IMD) income domain.

		NDVI (500-m buffer)				NDVI (1,000-m buffer)			
Modifier	*n*	IQR	Baseline	Difference	*p*-Int	IQR	Baseline	Difference	*p*-Int
Gender									
Men	4,537	0.168	0.016 (−0.006, 0.037)	0.007 (−0.013, 0.026)	—	0.167	0.014 (−0.008, 0.037)	0.006 (−0.014, 0.026)	—
Women	1,850	0.182	−0.001 (−0.038, 0.036)	0.048 (0.016, 0.081)	0.178	0.188	−0.002 (−0.043, 0.039)	0.055 (0.020, 0.090)	0.107
Education									
≥University	1,985	0.187	−0.015 (−0.049, 0.019)	0.019 (−0.010, 0.048)	—	0.183	−0.027 (−0.062, 0.009)	0.019 (−0.010, 0.049)	—
Higher secondary school	1,523	0.173	0.038 (0.002, 0.074)	0.035 (0.002, 0.068)	—	0.173	0.040 (0.001, 0.079)	0.037 (0.002, 0.072)	—
≤Lower secondary school	1,933	0.167	0.034 (0.005, 0.064)	−0.003 (−0.031, 0.024)	0.012	0.175	0.045 (0.012, 0.078)	−0.006 (−0.035, 0.024)	0.001
IMD income domain									
Tertile 1 (least deprived)	2,132	0.137	0.015 (−0.012, 0.042)	0.004 (−0.022, 0.030)	—	0.136	0.005 (−0.023, 0.045)	0.006 (−0.022, 0.034)	—
Tertile 2	1,878	0.156	−0.005 (−0.035, 0.025)	0.027 (−0.001, 0.055)	—	0.154	−0.006 (−0.038, 0.026)	0.024 (−0.005, 0.054)	—
Tertile 3 (most deprived)	1,810	0.159	0.027 (−0.008, 0.063)	0.029 (−0.002, 0.060)	0.098	0.153	0.031 (−0.005, 0.066)	0.025 (−0.005, 0.056)	0.215

Note: All estimates are from linear mixed effect models adjusted for age, age squared, gender, ethnicity, marital status, education, employment grade, area IMD employment and income domain, alcohol use, diet, and smoking. *p*-Int: The *p*-value for interaction was assessed by the Wald test comparing the main model to a model including an interaction between the modifier and NDVI (modifier x NDVI) and an interaction between the modifier, NDVI, and age (modifier x NDVI x age).

Stratified Analyses

When stratified by gender, residential surrounding greenness was positively associated with global cognition at baseline in men (β: 0.016; 95% CI: −0.006, 0.037 for NDVI in a 500-m buffer), but the association was null for women (β: −0.001; 95% CI; −0.038, 0.036). In contrast, the association between NDVI and the change in global cognition over time was positive for women (β: 0.048; 95% CI: 0.016, 0.081) and close to null for men (β: 0.007; 95% CI: −0.013, 0.026) (p-interaction = 0.178) (Table 3). When stratified by educational level, NDVI was negatively associated with the cognitive scores at baseline and positively associated with the difference in scores over time among those with a university education, positively associated with baseline cognitive scores and differences over time among those with a higher secondary school education, and positively associated with baseline scores but showed no association with differences over time among those in the low-education group (p-interaction = 0.01 and 0.001 for the 500-m and 1,000-m buffers, respectively) (Table 3). When the analyses were stratified by tertiles of the IMD income domain, residential surrounding greenness was positively associated with differences in global cognition over time among those living in areas within the highest (β: 0.029; 95% CI: −0.002, 0.060 for NDVI in a 500-m buffer) and middle tertiles of area deprivation (β: 0.027; 95% CI: −0.001, 0.055), while the association was close to null among those in the lowest tertile of area deprivation (β: 0.004; 95% CI: −0.022, 0.030) (Table 3). The baseline association of residential surrounding greenness and global cognition was positive among participants in the lowest and highest tertiles of area deprivation, but close to null among participants in the middle tertile (Table 3).

Mediation Analysis

Table 4 shows the results of mediation analysis for physical activity, air pollution, and social support (Baron and Kenny 1986). We considered mediation if the exposure variable (greenness) was significantly associated with the mediator, the mediator was significantly associated with the outcome (cognitive function/decline) after controlling for exposure, and the association between the exposure and the outcome was eliminated or weakened when the mediator was included in the model. The results did not suggest mediation of the association between residential surrounding greenness and the global cognition score by any of the investigated potential mediators.

Physical activity was not found to mediate the association between residential surrounding greenness and cognitive decline because greenness was not longitudinally associated with physical activity, and adjustment for physical activity in the main model did not notably change the association between residential surrounding greenness and global cognitive function (Table 4). With regard to air pollution and social network, higher residential surrounding greenness was significantly associated with lower levels of PM_{10} and a higher social network score (Table 4). However, PM_{10} and social network were not longitudinally associated with cognitive decline (Table 4), so they could not be considered as a mediator for the association between residential surrounding greenness and cognitive decline.

Alternative Measure of Greenness

The correlation between NDVI and EVI was strong (between 0.87 and 0.91) (Table S4). Consistent with the findings of our main analyses based on NDVI, higher residential surrounding greenness measured using EVI was associated with a slower decline in global cognition in both the direct neighborhood (β: 0.020, 95% CI: 0.004, 0.036) and walkable neighborhood (β: 0.020, 95% CI:

Table 4. Mediation analysis of the association between the global cognitive *z*-score (COG) and residential surrounding greenness (Normalized Difference Vegetation Index; NDVI).

Predictor	Outcome	NDVI (500-m buffer)		NDVI (1,000-m buffer)	
		Baseline	Difference	Baseline	Difference
Main model					
NDVI (not adjusted for mediators)	COG	0.012 (−0.007, 0.031)	0.020 (0.003, 0.037)	0.011 (−0.100, 0.031)	0.021 (0.003, 0.039)
Mediation by vigorous physical activity (VPA)					
NDVI	VPA	0.632 (0.444, 0.821)	0.075 (−0.111, 0.260)	0.637 (0.438, 0.836)	0.038 (−0.155, 0.232)
VPA (adjusted for NDVI)	COG	0.002 (0.001, 0.004)	−0.001 (−0.002, 0.000)	0.002 (0.001, 0.004)	−0.001 (−0.002, 0.000)
NDVI (adjusted for VPA)	COG	0.012 (−0.007, 0.031)	0.022 (0.005, 0.039)	0.012 (−0.009, 0.032)	0.023 (0.005, 0.041)
Mediation by moderate physical activity (MPA)					
NDVI	MPA	1.551 (1.206, 1.896)	0.295 (−0.0366, 0.627)	1.679 (1.313, 2.046)	0.330 (−0.017, 0.676)
MPA (adjusted for NDVI)	COG	0.001 (0.000, 0.002)	−0.001 (−0.002, 0.000)	0.001 (0.000, 0.002)	−0.001 (−0.002, 0.000)
NDVI (adjusted for MPA)	COG	0.012 (−0.007, 0.031)	0.021 (0.004, 0.038)	0.012 (−0.008, 0.033)	0.022 (0.004, 0.040)
Mediation by air pollution (PM_{10})					
NDVI	PM_{10}	−1.275 (−1.325, −1.225)	−0.256 (−0.304, −0.208)	−1.510 (−1.561, −1.459)	−0.256 (−0.305, −0.206)
PM_{10} (adjusted for NDVI)	COG	−0.007 (−0.013, −0.001)	0.003 (−0.003, 0.010)	−0.007 (−0.013, −0.001)	0.004 (−0.003, 0.011)
NDVI (adjusted for PM_{10})	COG	0.005 (−0.015, 0.025)	0.023 (0.003, 0.042)	0.002 (−0.020, 0.024)	0.025 (0.004, 0.046)
Mediation by social network (SN)					
NDVI	SN	0.043 (−0.062, 0.148)	0.102 (−0.001, 0.206)	0.043 (−0.065, 0.151)	0.117 (0.012, 0.222)
SN (adjusted for NDVI)	COG	0.004 (0.000, 0.008)	0.002 (−0.003, 0.006)	0.004 (0.000, 0.008)	0.002 (−0.003, 0.006)
NDVI (adjusted for SN)	COG	0.012 (−0.007, 0.031)	0.020 (0.003, 0.036)	0.011 (−0.010, 0.031)	0.021 (0.003, 0.038)

Note: All estimates are from linear mixed effect models adjusted for age, age squared, gender, ethnicity, marital status, education, employment grade, area IMD employment and income domain, alcohol use, diet, and smoking. Associations between outcomes and predictors represent the difference in the outcome for a 1-IQR increase in NDVI, a 1- metabolic equivalent (MET)/week increase in vigorous physical activity, a 1-MET/week increase in moderate physical activity, a 1-$\mu g/m^3$ increase in PM_{10}, or a 1-unit increase in social network score (range: 1–16).

0.003, 0.037) using the main model (Table S8). For the separate cognitive tests, EVI was associated with a slower decline in reasoning and fluency. Although higher greenness was associated with better cognitive function at baseline, the associations were not statistically significant. No significant associations were found with short-term memory.

Discussion

The present study investigated the association of long-term residential surrounding greenness with cognitive decline. Our study relied on the characterization of cognitive decline based on a battery of four cognitive tests repeated three times over a course of 10 y together with assessment of exposure to green spaces using two satellite-based indices of greenness. We observed that a 1-IQR increase in NDVI in a 500-m buffer surrounding participants' homes was associated with a slower decline in global cognition, with a difference in global cognition of 0.020 (95% CI: 0.003, 0.037) over the 10-y course of the study. Considering the separate cognitive test scores, we found similar associations with reasoning and fluency, where the same increase in residential surrounding greenness was associated with a slower decline of 0.022 (95% CI: 0.007, 0.038) in the reasoning score and 0.021 (95% CI: 0.002, 0.040) in the fluency score over the study period. The observed association may be modified by gender, as we observed that in men, residential surrounding greenness was positively associated with global cognition at baseline but not with cognitive decline over the study period, while in women, higher greenness was associated with a slower cognitive decline over the study period, but not with baseline cognitive function. The findings were robust to a wide range of sensitivity analyses. The results when using EVI as an alternative exposure for greenness were similar to the results when using NDVI, which is consistent with the high correlation found between these vegetation indices.

While we found an association between residential surrounding greenness and cognitive decline over the 10-y course of our study, we did not find a baseline association. Baseline estimates reflected the cross-sectional association between the cognitive test scores at baseline and the green space exposure occurring before the baseline follow-up, while our exposure assessment was based on the home address of participants during the study period. Our exposure assessment therefore did not include different address(es) where participants might have lived before the baseline follow-up, which could have resulted in a larger exposure misclassification for the baseline estimates compared with the longitudinal estimates based on the addresses during the 10-y course of the study (Dadvand et al. 2015a). Part of our observed larger estimates for 10-y decline might therefore reflect better characterization of exposure for the longitudinal analysis, but it could also be due to the window of vulnerability with cognitive decline being greater at older ages (Singh-Manoux et al. 2012). This might also explain why we observed the strongest associations for 10-y decline in reasoning that declines considerably during this period.

The analyses were adjusted for a wide range of potential confounders including two individual-level and two neighborhood-level socioeconomic indicators. Residential surrounding greenness was associated with better cognitive function at baseline and slower cognitive decline over the study period in all adjusted models, but the association with baseline cognitive function was not statistically significant after adjustment for the socioeconomic indicators, while the longitudinal association with cognitive decline remained statistically significant in the fully adjusted model (Model 4, Table 2). In stratified analyses, no clear trends in the associations with cognitive function were shown across strata of educational attainment or across strata of neighborhood SES (Table 3). Although we believe that residual confounding by SES was unlikely, it cannot be ruled out. In addition, further adjusting for other variables that may be spatially correlated with green space such as path and road density, crime, and barriers to housing and services did not result in a notable change in our findings (Table S6). We believe that this suggests that it is unlikely that our result was observed due to residual confounding by other neighborhood factors, although residual confounding cannot be ruled out.

Available Evidence

Residential greenness exposure was associated with reduced cognitive decline during a 10-y follow-up period, with small differences in global cognition scores and in subscale scores for reasoning and fluency. Evidence on the association between greenness exposure and cognitive functioning in older adults is very scarce and inconclusive (de Keijzer et al. 2016). A recent longitudinal study ($n = 281$) found that the proportion of parks within a 1,500-m buffer around the residence in childhood and adulthood was associated with a slower decline in cognitive function in later life (Cherrie et al. 2018). Previous studies reported associations between gardening and reduced incidence of dementia in older adults (>60 y old) (McCallum et al. 2007), and between walking in parks and improved cognitive function in older adults (>65 y old) (Prohaska et al. 2009). Furthermore, a cross-sectional study from England relying on questionnaire-based assessment of general cognitive function found a negative association between the percentage of surrounding green space and private gardens in the residential neighborhood and cognitive function in older adults (>65 y old) (Wu et al. 2015). Another cross-sectional study from Chicago, United States, found no association between the proportion of park area in the residential neighborhood and general cognitive functioning, assessed by a questionnaire, in adults aged 50 and over (Clarke et al. 2012).

We did not find any association between greenness and short-term memory. Although short-term memory showed a decline over the course of the study, this decline mainly occurred during later stages of our study. As shown in Table 1, the decline between the first two follow-ups was minimal and became larger between the last two follow-ups. Furthermore, the present study showed stronger associations of residential surrounding greenness with cognitive decline over time in women than in men, similar to the results found by Cherrie et al. (2018). Men and women have been shown to have different risk factors for cognitive decline and dementia (Lipnicki et al. 2013). Stratifying the analysis by education (high: university or higher, middle: higher secondary school, and low: lower secondary school or lower), we observed stronger baseline associations with global cognition in people within the two lower education groups in comparison with the people within the highest education group, while the longitudinal association was stronger in people the middle educational group in comparison to those within the lowest or highest education group. In addition, stratifying by area deprivation did not show a clear trend, though the association between residential surrounding greenness and cognitive decline over the study period was strongest among participants living in areas within the second and third tertiles of area deprivation. Previous studies found a stronger association between green space and health among lower socioeconomic groups (Cherrie et al. 2018; Gascon et al. 2015; Maas et al. 2009b), although not all studies replicate this observation, for example, for mortality (Crouse et al. 2017; James et al. 2016; Vienneau et al. 2017).

Potential Underlying Mechanisms

We tested a number of mechanisms that have been proposed for the association between greenness exposure and health, which could also be relevant in terms of such an association with cognitive decline. First, greener neighborhoods are reported to foster social cohesion and social support (Dadvand et al. 2016; de Vries et al. 2013; Maas et al. 2009a), which in turn could decelerate cognitive decline (Holtzman et al. 2004). However, in our study, a score of the social network was not found to be associated with cognitive decline over the study period. Second, higher levels of physical activity have been demonstrated in older adults with higher greenness in their residential surroundings (Gong et al. 2014), while higher physical activity has been associated with a lower risk for cognitive decline and dementia in previous research (Blondell et al. 2014). However, we did not find such a beneficial association between physical activity and cognitive decline, which was in agreement with the results of another recent study in the Whitehall II study (Sabia et al. 2017). In addition, mediation by physical activity was also not shown in a recent cross-sectional study of the association between natural outdoor environments and cognitive function in adults (Zijlema et al. 2017). Last, greenness can reduce levels of noise and air pollution (Dadvand et al. 2012, 2015b), while previous studies have identified noise and air pollution as risk factors for cognitive decline (Tzivian et al. 2015, 2016). However, air pollution was not found to be associated with cognitive decline in our study. Limitations in our exposure assessment of air pollution may be contributing to finding this null association. We only had PM_{10} (but not other particle metrics) levels available, and the spatial resolution of the modeled PM_{10} was coarse. This resulted in an indicator of background air pollution, while traffic-related pollution may be more important in explaining the association (Dadvand et al. 2015a). In addition to air pollution, other urban stressors such as noise may also be important mechanisms in associations with greenness, but were not measured in our study.

Strengths and Limitations

Our study had a number of strengths and weaknesses. Strengths include the use of a large, well-established cohort with a high response rate (e.g., at the study's baseline in 1997–1999, 86.3% of all eligible participants responded) (University College London 2016), which allowed a longitudinal study with repeated measurements of both greenness and cognitive functioning. Moreover, cognitive functioning was assessed using four objective tests covering different aspects of cognitive function. Additionally, the analyses were adjusted for a wide range of potential confounders including demographic, lifestyle, socioeconomic, and neighborhood characteristics.

Our study faced some limitations. First, the Whitehall II cohort is based on civil servants with underrepresentation of women and ethnic minorities, which might have affected the generalizability of our findings.

Second, we assessed exposure to greenness using satellite-based vegetation indices enabling us to take into account small green spaces (e.g., private gardens and street trees) in a standardized way. However, vegetation indices do not differentiate between different types of vegetation or land cover, and thus are not informative about the usability or quality of green spaces, nor do they provide any information on the actual use of green spaces. This could have influenced our observed associations. Due to the resolution of our NDVI maps and the fact that we used the centroid of postal code as the residential location of the participants, we could not use buffers smaller than 500 m. Smaller buffers could indicate greenness closer to home and perhaps visual access to green spaces, which could represent other relevant pathways underlying benefits of green spaces. As a result of using vegetation indices to characterize residential surrounding greenness, this study does not provide information on the specific characteristics in green spaces that are responsible for the findings. To inform policy making, information on the type, size, quality, and access to green spaces is needed. Moreover, we could not characterize exposure to greenness at workplace or other locations where participants might have spent significant amount of time. However, over the study period, many of the Whitehall II participants retired (27% at baseline, 44% in the next follow-up, and 66% in the last follow-up), and older adults generally tend to be more bound to their direct neighborhood environment (Yen et al. 2009). Furthermore, the use of postcode centroids instead of the location of the residential addresses might have led to exposure misclassification, particularly in large postcode areas that are more common in rural areas.

However, excluding participants from rural areas ($7-11\%$ of the study population) did not change our findings notably.

Additionally, the covariate data seemed to not be missing at random (i.e., participants with missing covariate data generally had lower global cognition *z*-scores and lower residential surrounding greenness) (Table S3). However, complete case analysis gave similar results to the analysis with multiple imputation. In addition, differential attrition (i.e., selection bias from selective mortality or loss to follow-up) is an important potential source of bias in longitudinal studies of cognitive decline (Weuve et al. 2012). However, we used an inverse probability weighting approach to take into account attrition over the study period and showed similar results as in our main analyses. Lastly, there remains a risk for potential residual confounding by unmeasured factors, although we adjusted for a wide range of individual and neighborhood variables.

Conclusion

We observed that higher residential surrounding greenness was associated with slower cognitive decline over a period of 10 y in adults aged 45–68 y at the beginning of the study. The rapid urbanization and aging population worldwide is resulting in an increase in the number of older adults living in urban areas where higher levels of air pollution (Power et al. 2016) and noise (Tzivian et al. 2015, 2016) could accelerate cognitive decline. Cognitive functioning is one of the most important determinants of well-being, functioning, and independent living at older age (WHO 2012). Our findings, if confirmed by future studies, may provide an evidence base for implementing targeted interventions aimed at decelerating cognitive decline in elderly residing in urban areas and hence improving their quality of life. Further research is needed to replicate our findings in other settings and climates and study the specific characteristics in green spaces that have most potential for enhancing healthy cognitive aging.

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