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Urban green is more than the absence of city: Structural and functional neural basis of urbanicity and green space in the neighbourhood of older adults

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HIGHLIGHTS

- We investigated the association between brain and Urban Fabric and Green in old age.
- Urban Fabric is negatively, Urban Green positively associated with p/sACC grey matter.
- Neither Urban Fabric (UF), Green (UG) nor p/sACC is related to mental health measures.
- But a resting-state measure in p/sACC showed a negative association with UF.
- Although UF is often seen as the opposite of UG additional variance in p/sACC structure is explained.

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ABSTRACT

The relationship between urbanization, the brain, and human mental health is subject to intensive debate in the current scientific literature. Particularly, since mood and anxiety disorders as well as schizophrenia are known to be more frequent in urban compared to rural regions.

Here, we investigated the association between cerebral signatures, mental health and land use indicators (Urban Fabric and Urban Green) within a 1 km radius around the home address of 207 well-characterized older adults.

We observed a negative association between Urban Fabric coverage and a positive association between Urban Green coverage and grey matter volume in perigenual/subgenual anterior cingulate cortex (p/sACC). Although p/sACC has repeatedly been associated with depressive symptoms, neither brain structure nor land use categories were related to measures of mental health. However, resting-state measure in p/sACC showed a negative association with Urban Fabric in our healthy sample, reminiscent of previous reports on major depression where p/sACC is often found to be reduced in activation. Interestingly, hierarchical regression analyses showed that Urban Green accounted for *additional* variance in brain structure beyond Urban Fabric. We take this finding as an exploratory result that hints at potentially salutogenic elements of green spaces (e.g. terpenes, nature sounds)

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that go beyond the absence of the detrimental elements of urban contexts (e.g. traffic noise, air pollution), which may inform the future search of environmental factors affecting mental health and disease.

Urbanization is steadily increasing with more than half of the world's population living in urban areas today. Urban settings are a relatively new phenomenon in phylogenesis and their impact on human well-being and mental health has not yet been fully understood. However, it has been repeatedly shown that mood and anxiety disorders as well as schizophrenia are more frequent in urban compared to rural regions (Peen and Dekker, 2004; Peen et al., 2010; Purtle et al., 2019; Vassos et al., 2012). But the specific links between urban living and psychiatric diseases are still unknown. According to the so-called "drift hypothesis" urban and rural differences are caused by selective migration, meaning that individuals with diseases or more susceptible individuals move to cities. However, there is a considerable number of studies arguing against this hypothesis (Norman et al., 2005; van der Ven et al., 2015; Verheij et al., 1998) and favouring the "breeder hypothesis" instead, positing that urban and rural differences are caused by the exposure to environmental factors. Most of the psychiatric literature aimed at explaining the urban–rural differences, focuses on detrimental effects of urbanicity (e.g. traffic noise, air pollution). Interestingly, green spaces such as parks and forests have repeatedly been shown beneficial for mental health. A recent study has demonstrated a reduced risk for developing psychiatric disorders during adolescence and adulthood when children grew up in green areas (Engemann et al., 2019). Exposure to green seems to have protective effects not only in childhood but also during adulthood. A British study found that individuals who moved to a greener area had better mental health three years post movement (Alcock et al., 2014). In addition, acute exposure to green spaces such as a walk in a forest or park has been shown to improve mood and stress markers (Kondo et al., 2018) as well as cognitive functioning (Ohly et al., 2016; Stevenson et al., 2018), maybe with particularly strong effects in individuals with reduced psychological regulatory capacity (Tost et al., 2019). However, relevant causal links and mechanisms are unclear. In particular, not much is known on how exposure to urbanicity leads to increases in stress and a reduction in well-being, or how green space may alleviate these effects. Especially in the current mental health literature, urbanicity and green space are mainly considered mutually exclusive, leaving it an open question whether it is the detrimental effect of urbanicity or the protective effect of green space or a combination of both that explain the underlying mechanisms of the findings cited above.

Studies initially used neuroimaging methods to address the question how the brain may be involved in the observed effects of environment on mental health. In a functional neuroimaging study current city living (compared to town or rural living) was associated with increased amygdala activity during a stressful mental calculation task (Lederbogen et al., 2011), which is interesting because the amygdala has been related to stress processing. In the very same study having been brought up in an urban environment during the first 15 years of life was associated with brain activity in the perigenual anterior cingulate cortex (pACC), a brain regions that is involved in multiple cognitive functions but has also been related to psychiatric disease (Goodkind et al., 2015). This seminal study, focussing on brain function, was followed by several studies investigating associations between living environment and brain structure. The first study reported a negative association between grey matter volume in dorsolateral prefrontal cortex (DLFPC) and pACC (in men only) and urban upbringing (Haddad et al., 2015). Urban upbringing was quantified by means of an urbanicity score assuming a constant gradient between cities with>100.000 inhabitants (coded as "3″), towns with 10.000–100.000 inhabitants (coded as "2") and rural regions with<10.000 inhabitants (coded as "1"), as it multiplies the coding with the years participants report to have lived in the respective environment. This again illustrates the prevalent view in mental health research that there is a continuum between urban and rural living. In a study on children in Barcelona, lifelong green exposure has been shown to be positively associated with grey matter volume in prefrontal cortex, in left premotor cortex and with white matter volume in right prefrontal regions, in the left premotor region, and in both cerebellar hemispheres (Dadvand et al., 2018).

Taken together, previous evidence has suggested that urban upbringing is associated with decrements in lateral and medial prefrontal cortex, whereas green space exposure was in turn associated with increases in similar brain regions. The similarity of regions involved may invite to the interpretation that exposure to urbanicity and to green space takes place on a single continuum, and the effects are mutually exclusive. However, this question has to our knowledge never been directly addressed concerning the association with brain structure. It, hence, remains unclear whether green space and urbanicity function as two sides of a coin or exert truly different influences on the brain that need to be considered as different effects.

Within the present analysis we relate brain structure to a proxy for urbanicity (Suarez-Rubio and Krenn, 2018), instead of grouping participants based on coarse categories such as urban, town or rural living environment. Accordingly, we focus on the land use category Urban Fabric including areas related to industry, commercial areas and transportation of the European Urban Atlas around participants' home address (Agency, 2016), assuming that areas where buildings, urban structures and transport networks are dominating the surface area, they represent what is most likely implied by the concept of urbanicity employed in previous studies (Besteher et al., 2017; Haddad et al., 2015; Lammeyer et al., 2019). Also, we address the question whether it is worthwhile to consider Urban Green (e.g. parks, zoos, gardens) as an additional factor over and above the respective reduction of Urban Fabric and therewith a potential reduction of the negative factors of urbanicity.

1. Methods

1.1. Participants and study design

Participants from the Berlin Aging Study II (BASE-II, (Bertram et al., 2014)) were recruited to take part in a neuroimaging study. Eligible participants were invited to take part in a magnetic resonance imaging (MRI) session consisting of 341 older adults. Since the neuroimaging software does not support missingness, we had to restrict the analysis to participants of whom georeferencing and MRI data were available (n = 207 older adults). Mean age in years was 70.1 years (*SD* = 3.77, age range 61–82), with 129 individuals (62.3%) being male. On average the participants had 14.01 years of education (SD = 2.89) and their household income was on average 1752 Euros. None of the participants took any medication that may have affected memory function or had a history of head injuries, medical (e.g., heart attack), neurological (e.g., epilepsy), or psychiatric disorders (e.g., depression). The study was approved of by the ethics committees of German Psychological Society. Participants signed written informed consent including consent for publication and received monetary compensation for their participation in BASE-II and the MRI study. The data-set has been published previously elsewhere (Kühn et al., 2017).

1.2. MRI acquisition

All images were acquired on a Siemens Tim Trio 3 Tesla scanner (Erlangen, Germany) using a 32-channel head coil. The T1 weighted images were obtained using a three-dimensional T1-weighted magnetization prepared gradient-echo sequence (MPRAGE) based on the ADNI protocol (http://www.adni-info.org) (repetition time (TR) = 2500 ms; echo time (TE) = 4.77 ms; TI = 1100 ms, acquisition matrix = 256 × 256 × 176, flip angle = 7°; 1 × 1 × 1 mm voxel size). Whole brain functional images were collected using a T2*-weighted eco-planar imaging (EPI) sequence sensitive to blood-oxygen level dependent (BOLD) contrast (time of repetition (TR) = 2000 ms, echo time (TE) = 30 ms, acquisition matrix = 216 × 216 × 129, flip angle = 80°, slice thickness = 3.0 mm, distance factor = 20%, voxel size 3 × 3 × 3 mm^3, 36 axial slices, using parallel imaging (GRAPPA)). 300 image volumes aligned to anterior commission- posterior commission (AC-PC) were acquired. Participants were shown a cross on the screen and were instructed to fixate it.

1.3. Voxel-based morphometry (VBM) preprocessing

We performed our pre-processing and whole brain image analyses using the toolboxes SPM12 (version v7388) and CAT12 (version r1450) (Structural Brain Mapping Group, University of Jena). The toolboxes were run with Matlab R2016b (MathWorks Inc., Natick, MA).

Pre-processing steps were conducted following recommendations for the default CAT12 segmentation routine for cross-sectional data (http://dbm.neuro.uni-jena.de/cat12/CAT12-Manual.pdf). CAT12 uses a DARTEL (diffeomorphic anatomical registration through exponentiated lie algebra) template and Geodesic Shooting templates in MNI space that were derived from n = 555 healthy control subjects of the IXI-database (http://brain-development.org/). Then warped gray matter (GM) segments are created and modulation with Jacobian determinants was applied in order to preserve the volume of a particular tissue within a voxel leading to a measure of GM volume. Finally, images were smoothed with a kernel of 8 mm. Then whole brain correlation analyses were run on the GM maps for Urban Fabric and Urban Green using sex, age, total intracranial volume (TIV) and household income as nuisance variables. To extract the mean of the GM values within a ROI, the marsbar toolbox (version 0.44, (Brett et al., 2002)) was used. Significant clusters are displayed superimposed on the colin 27 average brain (ch2better (Holmes et al., 1998)) using MRIcron. To relate the resulting significant clusters to previous cytoarchitectonic and functional connectivity based parcellations we used the SPM Anatomy toolbox (Eickhoff et al., 2007).

1.4. Resting-state preprocessing

The first five volumes were discarded to allow the magnetisation to approach a dynamic equilibrium. Part of the data pre-processing, including slice timing, head motion correction (a least squares approach and a 6-parameter spatial transformation) and spatial normalization to the Montreal Neurological Institute (MNI) template (resampling voxel size of 3 mm × 3 mm × 3 mm), were conducted using the SPM12 and Data Processing Assistant for (Resting-State) Brain Imaging (DPABI, (Yan et al., 2016)). A spatial filter of 4 mm FWHM (full-width at half maximum) was used. Participants showing head motion above 3 mm of maximal translation (in any direction of x, y or z) and 1.0° of maximal rotation throughout the course of scanning were excluded.

After pre-processing, linear trends were removed. Then the functional MRI (fMRI) data were temporally band-pass filtered (0.01–0.08 Hz) to reduce low-frequency drift and high-frequency respiratory and cardiac noise (Biswal et al., 1995). To obtain a voxel-wise resting-state measurement of the BOLD signal we computed the fractional amplitude of low-frequency fluctuation (fALFF) using DPABI. fALFF represents the relative contribution of low frequency oscillations to the total detectable frequency range and is calculated taking the power within a frequency range and dividing it by the total power in the whole detectable frequency range (Zou et al., 2008). To create standardized maps, each subjects' map was transformed into Z-scores.

1.5. Urban land use data

The land use data was taken from the European Urban Atlas, provided by the European Environment Agency. The classification of land in the present study into the respective categories follows the classification of land in the European Urban Atlas 2006 (Agency, 2016). The dataset contains polygon features representing real-world features characterised by very small areas. All areas>0.25 ha or 10 m feature length's for the reference year 2006 are assigned exclusively to well-defined land use categories. The category Urban Green is defined as land for predominantly recreational use including gardens, parks and suburban natural areas used as parks (14100: Green urban areas). Forests and other green fields are considered Urban Green areas in case there are traces of recreational use and they are surrounded by urban structures. Therefore, forests within an urban setting, that is, patches of parks canopied by trees, fall into the category of Urban Green.

The category Urban Fabric contains mostly residential structures, but also downtown areas including central business districts and areas with partial residential use. The different subclasses of Urban Fabric represented in the in the European Urban Atlas are distinguished by their degree of soil sealing rather than by type of building. We decided to sum all subcategories of Urban Fabric (11100: Continuous urban fabric, 11210: Discontinuous dense urban fabric, 11220: Discontinuous medium density urban fabric, 11230: Discontinuous low density urban fabric, 11240: Discontinuous very low density urban fabric) to one score and also included the category of industrial, commercial, public, military and private units (12100), as well as the transportation related land use categories: fast transit roads (12210), other roads (12220), railways (12230), port areas (12300) and airports (12400), However for simplicity we refer to this sum of land use classes as "Urban Fabric" in the following. Urban Fabric and Urban Green are measured as the percentage of the area covered by the land use category in a pre-defined radius of 1 km around households, respectively.

1.6. Household income data

As an approximation of the socio-economic status we computed the household income as the monthly net amount of income which has been adjusted to the size of the household based on the OECD (Organisation for Economic Cooperation and Development)-modified equivalence scale (Hagenaars et al., 1994).

1.7. Mental health-related questionnaires

We assessed *depressive affect* by means of a 3-item subscale of the Positive and Negative Affect Schedule (PANAS-X (Watson and Clark, 1994)) as well as subscales summarizing *positive and negative affect*. To assess *neuroticism* we used a 3-item subscale of the short version of the Big Five Inventory (John et al., 1991; Lang et al., 2001). ***Stress*** has been assessed using the Perceived Stress Scale (Cohen et al., 1983). The 10 items were reduced to 8 items (we omitted item 6 and 9 based on scale properties in a pilot study).

1.8. Data analysis

In search of neural correlates of urban living we ran a whole-brain analysis using Urban Fabric within 1 km radius around the household and the same for Urban Green while controlling for sex, age, household income and total intracranial volume (TIV). The resulting brain maps were thresholded with $p < 0.001$ and the statistical extent threshold was used combined with a non-stationary smoothness correction based on permutation (Hayasaka et al., 2004) as implemented in the CAT12 toolbox to correct for multiple comparisons.

In an exploratory follow-up analysis, we associated the mean extracted grey matter volume values of the cluster obtained in the VBM analysis with mental health parameters.

To explore functional brain data in the clusters resulting from the whole-brain structural analysis we extracted the mean fractional amplitude of low frequency fluctuations (fALFF) score of each participant from the cluster in which the structural correlates of Urban Fabric and Urban Green overlapped (multiplication of masks). fALFF is an indicator of local brain functionality at rest. Then we ran correlation analyses between Urban Fabric and Urban Green with fALFF values correcting for age, sex and household income.

We then conducted multiple hierarchical linear regression analyses predicting mean grey matter volume extracted from the significant cluster resulting from VBM structural analysis. Variables were entered in three steps to assess their incremental predictive value. The covariates age, sex, household income and TIV were added first, independently of non-significant bivariate correlations with the dependent variable as controlling for their potential influence is commonly considered mandatory in brain-structural analyses. In a second and third step, the variables of interest were added.

2. Results

On average the coverage of Urban Fabric was 78.34% (SD = 20.22), and 6.79% (SD = 9.03) of Urban Green within 1 km around the households. Urban Fabric and Urban Green showed a moderately negative correlation ($r(207) = -0.339$; $p < 0.001$).

2.1. Brain structural correlates of Urban Fabric and Urban Green

In a brain structure whole-brain correlation analysis we found that Urban Fabric was negatively associated with grey matter volume in perigenual anterior cingulate cortex (ACC) extending into subgenual ACC, henceforth referred to as p/sACC, after controlling for age, sex, household income and TIV (peak MNI coordinate: 2,28,-2; 202 voxels; Fig. 1, blue). Hence, more Urban Fabric in a 1 km radius around the home address of participants was associated with less p/sACC grey matter volume. To exactly identify the location, we consulted cytoarchitectonic maximum probability maps (Palomero-Gallagher et al., 2015) indicating that 25% of the cluster were located in Area 33 and 18.2% in Area p24ab.

Then we ran a second structural whole-brain correlation analysis while exchanging the Urban Fabric predictor with the predictor of Urban Green and found a largely overlapping cluster of significant correlations in p/sACC (peak MNI coordinate: 3,28,-2; 307 voxels; Fig. 1, red), reflecting, however, a *positive* association between the p/sACC and Urban Green. In other words, more Urban Green in a 1 km radius around the home addresses of participants was associated with *more* p/sACC grey matter volume. To exactly identify the location, we consulted cytoarchitectonic maximum probability maps (Palomero-Gallagher et al., 2015) indicating that 22.2% of the cluster were located in Area 33 and 21.6% in Area p24ab.

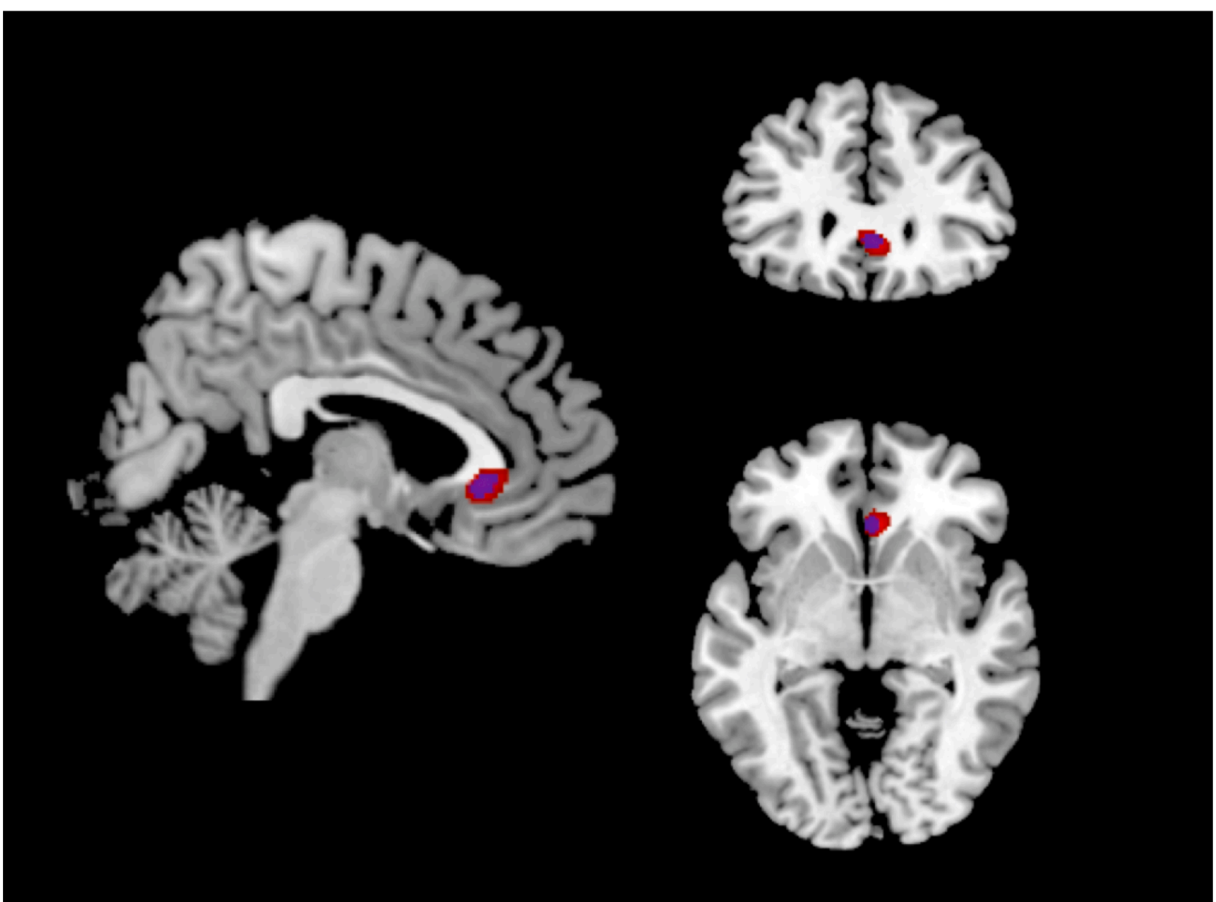

Fig. 1. Blue = significant cluster in perigenual ACC (p/sACC) resulting from a negative whole brain correlation with Urban Fabric (MNI coordinate: 2,28,-2; 252 voxels), red = significant cluster in p/sACC resulting from a positive whole brain correlation with Urban Green (MNI coordinate: 3,28,-2; 307 voxels), violet = overlap of the two clusters (nuisance variables: sex, age, total intracranial volume, household income). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

2.2. Association with mental-health variables

Given that psychiatric disorders including mood disorders are more frequent in cities as compared to more rural regions (Peen et al., 2007) and p/sACC has been frequently associated with depressivity (Janiri et al., 2019; Kühn & Gallinat, 2013; Wise et al., 2017), we set out to explore the association between exposure to Urban Fabric and Urban Green as well as its neural structural correlates in p/sACC with scores measuring positive affect, negative affect, depressivity, perceived stress and neuroticism in our healthy sample (while controlling for age, sex, household income and TIV for the analysis in which brain variables were included). No significant associations were observed, neither for Urban Fabric or Urban Green ($p > 0.18$) nor for the grey matter cluster in p/sACC where the results of Urban Fabric and Urban Green analysis overlapped ($p > 0.29$).

2.3. Resting-state (fALFF) in p/sACC

Within the structural cluster identified in p/sACC, in which we observed overlap for the Urban Fabric and the Urban Green whole-brain analysis, we extracted fALFF and computed correlations between mean fALFF and Urban Fabric and Urban Green. We found no significant association to Urban Green, $r(179) = 0.096$, $p = 0.20$, but a significant negative association between Urban Fabric and fALFF, $r(179) = -0.191$, $p = 0.010$, indicating that more Urban Fabric around the home address was associated with less resting-state activation in p/sACC.

2.4. Regression analyses

In order to further explore the relationship between Urban Fabric, Urban Green and the brain, and to test whether Urban Green explains any additional variance over and above Urban Fabric we ran the following regression analyses.

Model-I included the demographic variables age, sex, household income as well as TIV as predictors for grey matter volume in p/sACC (determined based on a whole-brain correlation with the regressor Urban Fabric). As can be seen from Table 1, none of the predictors exhibited a significant effect on volume of p/sACC ($F_{(4, 202)} = 1{,}21$, n.s.). However, predictors were kept in the model as these variables are standard variables that are commonly controlled for in analyses of brain volume.

In Model-II, we then added the percentage of Urban Fabric to the model. As can be seen from Table 1, percentage of Urban Fabric in the surrounding area was significantly negatively related to p/sACC-volume ($F_{(5, 201)} = 3.52$, $p < 0.05$). Individuals with a higher percentage of Urban Fabric in their direct surrounding had *smaller* p/sACC. Although, overall, the amount of explained variance was small ($R^2 = 0.081$), the incremental effect of percentage of Urban Fabric was significant ($\Delta R^2 = 0.057$). This is not surprising, since the region of interest from which the mean was extracted resulted from a whole-brain correlation of grey matter volume with Urban Fabric. Strictly speaking, such a model could be considered as double dipping, however our goal was to compare Model-II with Model-III.

In Model-III we additionally added the percentage of Urban Green in the direct surrounding of the individuals to the analyses ($F_{(6, 200)} = 4.85$, $p < 0.001$). As can be seen, Urban Green exhibited a significant effect over and above Urban Fabric and the control variables, implying that those with more Urban Green in their immediate environment had *larger* p/sACC structures (Table 1). The incremental effect on explained variance was significant ($\Delta R^2 = 0.046$) leading to a total of explained variance of $R^2 = 0.127$. Hence, overall, Model-III explained about 13% of the variance in the volume of p/sACC. Moreover, the variance inflation factor (VIF) of Urban Fabric in Model-III was VIF = 1.148 and of Urban Green VIF = 1.171, with both values not indicating strong multicollinearity (O'Brien, 2007) within the model. An additionally tested interaction effect between Urban Fabric and Urban Green was not significant (β=- 0.076, $t_{(199)}$=–0.759, ns.).

The results are almost identical when the outcome variable is mean grey matter volume in the p/sACC region in which the cluster from the Urban Fabric and Urban Green analyses overlap.

In order to relate the present finding to our previous report (Kühn et al., 2017) in which we found a positive association between amygdala integrity and forest within 1 km radius around the home address, we computed a correlation between mean grey matter volume in the region of overlap between the two whole brain analyses with Urban Fabric and Urban Green and the mean grey matter volume of bilateral amygdala (Tzourio-Mazoyer et al., 2002) and observed a significant positive correlation, $r(201) = 0.198$, $p = 0.005$, between the two regions (while controlling for age, sex, household income, TIV). No significant association was observed to the two land use classes (Urban Fabric and Urban Green) and grey matter volume in the amygdala ($p > 0.21$).

Table 1
Standardized results of regression analyses predicting the mean of the p/sACC cluster resulting from a whole brain correlation with Urban Fabric.

Predictor	Model		
	I	II	III
Sex	0.08	0.09	0.08
Age in years	−0.08	−0.06	−0.06
Household income	0.07	0.07	0.11
TIV	0.12	0.14	0.11
Urban Fabric		−0.24*	−0.16*
Urban Green			0.23*
R^2	0.023	0.081	0.127
ΔR^2		0.057*	0.046*

Note: We report standardized beta values. TIV = total intracranial volume; * = $p < 0.05$

3. Discussion

Within the scope of the present study we aimed at investigating associations between brain structure (and function) and Urban Fabric as a proxy for urbanicity (Suarez-Rubio and Krenn, 2018) and Urban Green around the homes of older participants living in Berlin. Moreover, we set out to explore whether Urban Green, which has been repeatedly demonstrated to enhance well-being and mental health (Alcock et al., 2014; White et al., 2013), is more than just the flip side of Urban Fabric as implicitly assumed by a multitude of neuroimaging/mental health studies and may constitute an additional relevant factor above and beyond Urban Fabric in the explanation of brain structure, with Urban Green having a larger predictive value than Urban Fabric.

3.1. Structural neural correlates of Urban Fabric and Urban Green in p/sACC

We observed a negative association between Urban Fabric and grey matter volume in a cluster located between pACC and sACC. In an independent analysis using Urban Green as a regressor we found an overlapping cluster in p/sACC with more grey matter volume the more Urban Green was present in a 1 km radius around the home address of participants. In our previous report (Kühn et al., 2017) on the same data set, in which we reported a positive association between forest in the neighbourhood of participants and amygdala integrity, we used a region of interest comprising the entire ACC as defined by the automated anatomical labeling (AAL) atlas (Tzourio-Mazoyer et al., 2002), which clearly spans a larger area then the cluster now observed in p/sACC. Interestingly, here we did not observe a significant relationship with Urban Green in the neighbourhood of participants and the p/sACC. However, we did observe a significant positive association between grey matter volume in the p/sACC cluster and bilateral amygdala, potentially suggesting that the two regions are functionally related.

3.2. No relationship to mental health-related variables

The psychiatric literature has frequently associated sACC with depression (Drevets et al., 2008; Jaworska et al., 2016). In healthy participants sACC activation has repeatedly been found when participants were in a sad mood, because they were exposed to pictures, or music or led to recall negative experiences, which elicited this affect (George et al., 1995; Phan et al., 2002; Smith et al., 2011). Interestingly, sACC activation was especially pronounced when healthy participants ruminated about a memory (Kross et al., 2009) or down-regulated negative affective responses in fear extinction paradigms (Diekhof et al., 2011).

Urbanicity in turn has likewise been associated with depression, with higher prevalence rates in urban areas (Peen and Dekker, 2004; Peen et al., 2010) and higher psychological distress associated with urban characteristics around the home address of healthy individuals (Gong et al., 2016). At the same time, the potential opposite, namely experimental exposure to nature, has been shown to result in positive short-term mental health effects (Barnes et al., 2018). However, in the present sample of healthy older adults we found no evidence for an association neither between mental health variables, namely positive affect, negative affect, depressivity, perceived stress, and neuroticism and grey matter volume extracted from the region in p/sACC where the results of the Urban Green and Urban Fabric whole-brain analyses overlapped, nor directly with the variables capturing Urban Green and Urban Fabric within the neighbourhood of the participants. In contrast, a recent study on older adults did report a positive association between urbanicity and depressive symptoms e.g. in the US (Pun et al., 2019). A possible explanation for the lack of a significant relation could lie in the participants of the BASE sample itself. We explicitly included healthy individuals with no history of psychiatric disorders. Also, the sample was rather educated with a comfortable household income, indicating that financial resources and living conditions were probably not exerting extra stress on participants. Also, individual mental health variables were assessed with brief subscales due to overall design-demands of the study. It is possible that small effects in a healthy sample could not be detected with our instruments.

3.3. Functional resting-state activity in p/sACC

In order to characterize the cluster in p/sACC, in which we observed the structural effect, also in terms of functional resting-state connectivity, we extracted the mean fALFF from the overlapping region of the Urban Fabric and Urban Green analyses and observed no significant association with Urban Green but a significant negative association with Urban Fabric. Several *meta*-analyses on resting-state abnormalities in depression have likewise reported reduced activation in the p/sACC in patients compared to healthy controls (Kaiser et al., 2015; Northoff et al., 2011). Although neither Urban Fabric, Urban Green, nor grey matter volume in p/sACC were related to mental health variables, the negative resting-state correlation with Urban Fabric constitutes a piece of evidence pointing at a potential connection between the p/sACC brain region related to Urban Fabric and Urban Green and disturbances in the mental health domain. However, the lower activation in depressed patients is not found in all studies, other *meta*-analyses report a hyperactivation instead (Kühn & Gallinat, 2013). Therefore, further research on the impact of Urban Fabric on resting state activity in p/sACC and mental health is needed.

3.4. Urban Green as an additional explanatory factor

Moreover, we aimed to explore whether it is worthwhile to consider Urban Green as an additional factor, when focussing on neuroimaging variables over and above the associated respective reduction of Urban Fabric. This question could be empirically tested because Urban Green and Urban Fabric, though mutually exclusive, only showed a moderate negative correlation. Given that Urban Green has previously been shown to enhance well-being and mental health (Alcock et al., 2014; White et al., 2013) it may constitute an important (potentially salutogenic) factor to consider, when investigating effects of living environment on the brain. A previous study that associated green space with perceived general health in urban and rural regions also concluded that there is an effect of the continuum between urban and rural regions, with less urban regions showing higher general health ratings, with the amount of green space having an independent positive effect on people's health at all degrees of urbanicity (Maas et al., 2006). The results of our regression analyses also suggest that Urban Green (although it has a very similar structural correlate in p/sACC), explains additional variance in the explanation of grey matter volume in p/sACC above and beyond the contribution of Urban Fabric. The results shed new light on the interpretation of previous studies reporting brain structural correlates in association with an urbanicity score (Besteher et al., 2017; Haddad et al., 2015; Lammeyer et al., 2019) and those focussing on the relationship between brain and green space (Dadvand et al., 2018; Kühn et al., 2017). Rather than interpreting those studies as addressing different ends of the same environmental continuum, as frequently done in the mental health and neuroimaging literature, it may well be that green spaces provide qualitatively different potentially salutogenic effects (e.g. terpenes (Li et al., 2009), physiological effects described in response to forest bathing (Park et al., 2010), nature sounds (Medvedev et al., 2015)) above and beyond the mere absence of potentially detrimental elements of urban contexts (e.g. traffic related noise, air pollution). This perspective may inform the search of detrimental aspects of city living on the development of mental health problems, since also the absence of green should be considered as a driving factor.

3.5. Limitations and future directions of research

An important limitation of our study is that we cannot draw strong causal inferences about the observed associations, given that individuals have not been randomly assigned to their home addresses. To unravel causal effects, longitudinal research is needed. Also, different methodological approaches should ideally be applied to show the causal direction of effects and to further understand the unique contribution of Urban Fabric and Urban Green. From the present analyses we cannot infer whether and how there is a protective effect of Urban Green or whether the underlying mechanism of the effect is better described differently. However, we believe that our study prepares the ground and warrants further analyses as the results clearly point towards a true effect of each entity. We also acknowledge that our analyses are exploratory in nature and would need replication in an independent sample in order to be interpreted as stable findings. Ideally, the present study would have been preregistered.

4. Conclusion

Taken together we observed a negative association between Urban Fabric in the neighbourhood of older adults and a positive association between Urban Green and grey matter volume in p/sACC. Although p/sACC has repeatedly been associated with depression, neither brain structure nor the land use categories Urban Fabric or Urban Green were related to mental health variables. A resting-state marker (fALFF) in p/sACC showed a negative association with Urban Fabric, which is in line with previous data in psychiatric disease where p/sACC has been found to be less activated in depression. Importantly, we found that it is worthwhile to consider Urban Green as an additional positive factor over and above the potentially negative effects of urbanicity, given that it accounted for additional variance in brain structure. We conclude that green spaces potentially harbour salutogenic elements that go beyond the mere absence of potentially detrimental elements of urban contexts. Therewith the absence of green rather than only the stressors within cities maybe worthwhile considering when attempting to unravel the higher prevalence of certain mental disorders in urban contexts.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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