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2	The relationship between natural outdoor environments and cognitive functioning and its mediators
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5	This is an Author's Original Manuscript of an article published by Elsevier in Environmental Research in
6	2017 available online at doi: 10.1016/j.envres.2017.02.017.
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11 12 13 14 15	Zijlema, W. L., Triguero-Mas, M., Smith, G., Cirach, M., Martinez, D., Dadvand, P., Gascon, M., Jones, M., Gidlow, C., Hurst, G., Masterson, D., Ellis, N., van den Berg, M., Maas, J., van Kamp I., van den Hazel, P., Kruize, H., Nieuwenhuijsen, M. J., Julvez. J. (in press). The relationship between natural outdoor environments and cognitive functioning and its mediators. Environmental Research, 27, 55, 268-275.

- 17 Title
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- 46 Running title
- 47 Natural outdoor environments and cognition
- 48
- 49

50 ACKNOWLEDGEMENTS

51 The research leading to these results has received funding from the European Community's Seventh 52 Framework Programme (FP7/2007-2013) under grant agreement no 282996. Margarita Triguero-Mas is 53 funded by a pre-doctoral grant from the Catalan Government (AGAUR FI-DGR-2013). Payam Dadvand is 54 funded by a Ramón y Cajal fellowship (RYC-2012-10995) awarded by the Spanish Ministry of Economy 55 and Competitiveness. ISGlobal is a member of the CERCA Programme, Generalitat de Catalunya. The 56 funders had no role in study design, data collection and analysis, decision to publish, or preparation of the 57 manuscript. This study has been funded by Instituto de Salud Carlos III through the projects "CP14/00108 58 & PI16/00261" (Co-funded by European Regional Development Fund "A way to make Europe"). Jordi 59 Julvez was funded by a Miguel Servet fellowship (MS14/00108) awarded by the Spanish Institute of Health 60 Carlos III (Ministry of Economy and Competitiveness).

61 COMPETING FINANCIAL INTERESTS DECLARATION

62 The authors declare they have no actual or potential competing financial interests.

63 ABSTRACT

64 Background

65 Urban residents may experience cognitive fatigue and little opportunity for mental restoration due to a

66 lack of access to nature. Natural outdoor environments (NOE) are thought to be beneficial for cognitive

67 functioning, but underlying mechanisms are not clear.

68 Objectives

- 69 To investigate the long-term association between NOE and cognitive function, and its potential mediators.
- 70 Methods
- 71 This cross-sectional study was based on adult participants of the Positive Health Effects of the Natural
- 72 Outdoor Environment in Typical Populations in Different Regions in Europe (PHENOTYPE) project.
- 73 Data were collected in Barcelona, Spain; Doetinchem, the Netherlands; and Stoke-on-Trent, United
- 74 Kingdom. We assessed residential distance to NOE, residential surrounding greenness, perceived amount
- of neighborhood NOE, and engagement with NOE. Cognitive function was assessed with the Color Trails
- 76 Test (CTT). Mediation analysis was undertaken following Baron and Kenny.
- 77 Results
- 78 Each 100m increase in residential distance to NOE was associated with a longer CTT completion time of
- 79 1.50% (95% CI 0.13, 2.89). No associations were found for other NOE indicators and cognitive function.
- 80 Neighborhood social cohesion was (marginally) significantly associated with both residential distance to
- 81 NOE and CTT completion time, but no evidence for mediation was found. Nor were there indications for
- 82 mediation by physical activity, social interaction with neighbors, loneliness, mental health, air pollution
- 83 worries, or noise annoyance.

84 Conclusions

- 85 Our findings provide some indication that proximity to nature may benefit cognitive function. We could86 not establish which mechanisms may explain this relationship.
- 87
- 88 Keywords: Natural outdoor environments; green space; cognition; mediation; environmental
- 89 epidemiology; built environment

90 INTRODUCTION

91 Natural outdoor environments (NOE) are places with natural ('green and blue') elements such as parks, 92 forests, and recreation areas. Contact with natural outdoor environments has been suggested to be beneficial 93 to human health and wellbeing [1]. However, a large proportion of the world's population currently lives 94 in urban areas, where they are often deprived of contact with nature. One particular concern of city living 95 is that residents may experience more stress than rural residents [2,3], making them more vulnerable to 96 developing mental illnesses [4]. Urban environments contain many stimuli that require directed attention 97 due to, for example, traffic and crowding. Directed attention refers to the effortful, conscious attention for 98 focusing on specific stimuli, while avoiding distractions. As a result, urban residents may experience more 99 cognitive fatigue and little opportunity for mental restoration [5].

100 The attention restoration theory (ART) proposes that directed attention, i.e. attention directed by cognitive 101 control processes, is restored by interaction with nature. Natural environments are thought to have minimum 102 requirements for directed attention, allowing for directed attention functions to restore [6]. According to 103 another theory, the stress reduction theory (SRT), nature helps to decrease stress by lowering states of 104 arousal and negative thoughts. Natural places with certain characteristics (e.g. visible horizons for spotting 105 of predators, availability of food) are from an evolutionary perspective better for survival, and may 106 automatically evoke positive responses [7].

107 Evidence for a relation between NOE and improved cognitive function mainly originates from experimental 108 studies typically focusing on short-term exposures (for a review, see [5]). Studies have observed 109 improvements in memory capacity and attention after walking in natural environments, compared to 110 walking in urban environments [8-12]. Other studies have evaluated visibility of NOE and relations with 111 cognition; it has been found that people with a window facing a green space reported less concentration 112 problems than those without a green view [13], and that people were less likely to be forgetful and 113 disorganized [14]. Similarly, students with the most natural window view had better directed attention than 114 those with built or concrete window views [15]. Even viewing pictures of natural environments resulted in 115 improved scores on attention tests [8,16]. Other observational studies evaluating the beneficial effects of 116 access to NOE on cognition have for example focused on working memory and behavioral development in 117 children [17,18] and on cognitive function and dementia in older adults [19,20]. A recent review 118 summarizing these studies reported that the number of available studies are limited and concluded that 119 current evidence for such an association is inadequate [21].

While most of the previous research focused on cognition benefits associated with NOE visibility, more indirect pathways may also be relevant to explore. Access to NOE may affect cognition indirectly by encouraging physical activity [22], facilitating social interaction [23], and by improving mood [24], which may all be beneficial for cognitive function [25,26]. Conversely, in environments with little nature, residents may be increasingly exposed to air pollution [27] and traffic noise [28]. The exposure to air pollutants and noise and related worries and annoyance may influence cognitive functions [29–32].

There is, however, little evidence of the mechanisms underlying the relation between cognitive function and NOE. Evidence about the duration of these effects and its causality is also lacking. Another unresolved question is what type of interaction with NOE is needed for beneficial cognition effects. While most previous observational studies focused on residential distance to nature or surrounding greenness, the actual engagement with and perceived amount of nature in ones surroundings may also be important [33].

To gain further insight into the relation between long-term exposure to nature and cognitive function, we investigated the association between multiple NOE indicators and performance on the Color Trails Test (CTT), which assesses attention and executive function. We also evaluated the potential mediating roles of physical activity, social interaction, mental health, air pollution worries, and noise annoyance.

135

136 METHODS

137 Study design and participants

138 The study was undertaken within the Positive Health Effects of the Natural Outdoor environment in Typical 139 Populations in different regions in Europe (PHENOTYPE) project. This project was established to 140 investigate the relationship between exposure to NOE and health and its underlying mechanisms in a sample 141 of residents from four European cities: Barcelona (Spain); Doetinchem (the Netherlands); Kaunas 142 (Lithuania); and Stoke-on-Trent (United Kingdom) [34]. Participants were recruited from 30 143 neighborhoods per city that were selected in order to have variability in access to natural outdoor 144 environments and socioeconomic status. From these neighborhoods, a random sample of 30-35 adults aged 145 18-75 were invited to participate, resulting in a sample of around 1000 participants per city (response rates 146 were 46.9% in Barcelona; 8.4% in Doetinchem; 21.3% in Kaunas; and 36.9% in Stoke-on-Trent, see further 147 details in [35]). Data were collected alongside a face-to-face questionnaire administered at participants' 148 residences during May-November 2013. In Kaunas (Lithuania), data were collected using a postal questionnaire and for this reason the CTT (our measure of cognitive function) could not be assessed in
participants from Kaunas. Therefore, in the current study, only data from Barcelona, Doetinchem, and
Stoke-on-Trent were used. All participants provided written informed consent and study protocols were
approved by the local ethical committees.

A total of 1628 participants completed the CTT. From this sample, participants with incomplete data regarding indicators of the natural environment (n=83), mediators (n=222), and covariates (n=26) were excluded from the corresponding analyses, leaving between n=1493 and n=1602 participants for the current analyses depending on the exposure and mediator (see Tables 2-5).

157

158 Characterization of the natural outdoor environment

NOE were characterized with data using geographical information systems (GIS) and face-to-face
questionnaires [34]. Participants' residential addresses were collected and subsequently geocoded.

Residential distance to NOE was based on Urban Atlas 2006 [36] (Barcelona and Stoke-On-Trent) and
Top10NL [37] (Doetinchem) databases. Both databases use a 1:10,000 scale and a minimum
represented unit of 0.25ha (Top10NL was adapted to be consistent with Urban Atlas). The Euclidean
distance from residences to natural spaces >1 hectare [38] was calculated for the following land use
categories: green urban areas (e.g. public gardens, parks) (14100), agricultural land, semi-natural areas,
wetlands (20000), forests (30000), water bodies (50000) [39].

167 Residential surrounding greenness was assessed with the normalized difference vegetation index 168 (NDVI). The NDVI is a measure of level of vegetation in a certain area and was derived from satellite 169 images available from Landsat 8 at a resolution of 30 m \times 30 m. We aimed to find cloud-free images 170 within the greenest season (May to September) in the relevant period for this study (2011-2013), and 171 obtained images from 16th April 2013 (Barcelona area), 21st July 2013 (The Netherlands East), and 172 21st April 2011 (Stoke-on-Trent). The NDVI is based on the fact that healthy vegetation absorbs most visible light and reflects large parts of near-infrared light, while sparse vegetation reflects more visible 173 174 light and less near-infrared light. Based on this distinction and excluding large water bodies, a value 175 between -1 and +1 was calculated, with higher values indicating higher density of green vegetation [40]. 176 The average NDVI values were calculated within (Euclidean) buffers of 100m, 300m, and 500m around 177 the residence, as was done in previous research [33,41].

Perceived amount of neighborhood NOE was assessed with questions 'How would you describe your
a) neighborhood, b) street c) window view in terms of green or blue space' with answers on a five-point
scale ranging from 'not at all' (1) to 'very' (5). With these questions a sum score of a, b and c questions
was calculated with higher scores indicating a higher degree of nature in the neighborhood.

Visits to NOE was assessed with questions 'How often did you visit a green or blue space in the last 4
weeks on purpose a) near your home, b) in your city, c) close to your city' with answers on a five-point
scale ranging from 'never' (1) to '(almost) daily' (5).

Total time spent visiting NOE was calculated by combining data on the number of visits to NOE (see above) with questions: 'How much time did you spend in a green or blue space a) near your home, b)
in your city, c) close to your city in the last four weeks', with answers on a 4-point scale ranging from
<1 hours (1) to 6-10 hours (4). Middle values of each answer category for frequency (e.g. <1
times/month was coded as 0.5 times/month) were multiplied with middle values of each answer category
for duration (e.g. <1 hours/month was coded as 0.5 hours/month) and summed.

191

192 Cognitive function

Cognitive function was assessed with the Color Trails Test (CTT). The CTT is a language- and culture-free neuropsychological test that measures visual attention, and effortful executive processing abilities [42]. The test consists of numbered coloured circles from 1 to 25 in pink and yellow. Participants are required to rapidly connect the circles in sequence, but to alternate between the pink and yellow colors. Such a task is thought to be demanding for sustained and divided attention, and poorer CTT results have been reported in ageing populations [43] and in clinical populations with impaired cognitive function [44].

199 The CTT was completed at the participant's home, after the completion of the structured face-to-face 200 questionnaire. Completion time and errors were recorded by the interviewer. Both were used as outcomes 201 in the current study, with shorter completion time and fewer errors reflecting better cognitive function. 202 Participants had 5 minutes to complete the test; if after 5 minutes the test was not completed, a CTT time 203 of 300 seconds was recorded. CTT test quality was recorded by the interviewer after completion of the test. 204 For example, if the participant had raised the pencil from the paper during the test, this was rated as 'poor 205 quality.'

206

207 Mediators

Physical activity was assessed with questions from the Short Questionnaire to Assess Health-enhancing
 physical activity (SQUASH) [45]. Total minutes per week of active commuting (walking and biking)
 and being physically active during leisure time were calculated and summed.

Social interaction with neighbors was assessed with the question 'How often do you have contact with
your neighbors?' and was scored on a 5-point scale ranging from 'at least once a week' (1) to 'seldom
or never' (5), and was dichotomized into ≥1 per month and <1 per month.

Loneliness was assessed with six statements based on the UCLA loneliness scale (e.g. feelings of isolation, feeling as part of a group of friends) [46]. Participants were asked to indicate to what extent they agreed with the statements on a 5-point scale ranging from 'totally agree' (1) to 'totally disagree'
 (5). A sum score was calculated with higher scores indicating greater feelings of loneliness.

Neighborhood social cohesion was assessed with the Social Cohesion and Trust Scale, consisting of 5
items (e.g. 'people are willing to help their neighbors') [47]. Questions were scored on a 5-point scale
and a sum score was calculated with higher scores indicating a higher degree of social cohesion.

Perceived mental health was assessed with 5 questions from the Medical Outcome Study Short Form
 (SF-36) mental health subscale, assessing nervousness and feelings of depression in the past month.
 Questions were scored on a 6-point scale ranging from 'all of the time' (1) to 'none of the time' (6). A
 sum score was calculated and transformed into a scale ranging from 0 to 100 according to guidelines
 [48] with higher scores indicating better mental health.

Traffic noise annoyance was assessed with one question about the degree of annoyance caused by traffic
noise, which was scored on a scale ranging from 'not annoyed at all' (0) to 'extremely annoyed' (10)
[49]. The response scale was transformed into a scale from 0 to 100, and a score of >72 was considered
being highly annoyed by traffic noise [50].

Worry about air pollution was assessed by asking to what extent participants were worried that the air
 pollution in their neighborhood could lead to health problems. Worries could be indicated on a scale
 ranging from 'not worried at all' (0) to 'extremely worried' (10). Participants were considered to be
 worried about air pollution when they scored >7.

234

235 Covariates

Covariates were chosen a priori based on previous literature [33,42,51]. Data on sex, age, educational level
(primary school or no education; secondary school/ further education (up to 18 years); university degree or

higher), time spent away from home, and start date of residence at the current address were obtained from

239 face-to-face questionnaires. Neighborhood socioeconomic status (low; intermediate; high) was based on

240 country-specific data, and CTT test quality (good; poor) was recorded by the interviewer.

241

242 Statistical analysis

243 Descriptive statistics were calculated for the total study population and separately for each of the three 244 cities. Parametric and non-parametric tests were used to test for significant differences between cities. To 245 account for clustering within cities and neighborhoods, associations were analyzed with multilevel analysis 246 with a random intercept defined at the city and neighborhood level. City-specific associations between the 247 NOE indicators and CTT were also investigated to evaluate differences between cities.

Mediation analysis was undertaken in four steps following Baron and Kenny (1986) and previous research [33]. Conditions for mediation are that the predictor variable (NOE) must affect the mediator; and that the mediator must affect the outcome variable (CTT); and that the association between the predictor and outcome is eliminated or weakened when the mediator is included in the model.

- The association between NOE and cognitive function. Linear and logistic multilevel models with
 random intercept for city and neighborhood were developed separately for CTT completion time (log
 transformed for normal distribution) and CTT errors (no errors/ 1 or more error(s)) as outcomes.
 Models were adjusted for age, sex, educational level, neighborhood socioeconomic status, time spent
 away from home, and CTT test quality.
- 257 2. <u>The association between NOE and mediators.</u> Multilevel models with random intercept for city and
 258 neighborhood were developed in which we specified the mediators physical activity, social
 259 interaction, loneliness, neighborhood social cohesion, mental health, air pollution worries, and noise
 260 annoyance as the outcome (one at a time), and indicators of NOE as the predictor. Models were
 261 adjusted for the same covariates as specified in step 1.
- 3. <u>The association between mediators and cognitive function.</u> Multilevel models with random intercept
 for city and neighborhood were developed in which we specified the mediators (see step 2) as
 predictors and the CTT as outcome. Models were adjusted for the same covariates as specified in step
 1.

266 4. <u>The association between NOE, mediators and cognitive function.</u> Mediators were added to the
267 multilevel models as specified in step 1, allowing for estimation of associations between indicators of
268 NOE and the CTT, while adjusting for the mediators.

Finally, if the conditions for mediation were met, the proportion of the total effect mediated (i.e. the combined effect of the exposure and mediator divided by the effect of the exposure) was calculated to quantify the relative contribution of each mediator. The proportion and the 95% confidence interval were obtained through bootstrapping [33].

The analyses in step 1 were repeated while excluding participants with a poor CTT test quality (n= 38; instead of using CTT quality as a covariate) to assess robustness of our findings. We also repeated analyses in step 1 while excluding those living at their residence <1 year (n=86) to assess whether residence time affected the results.

277 In order to report results in a consistent manner, we calculated the percentage difference per one unit 278 increase of the predictor for each of the estimates and 95% confidence intervals (except for CTT errors). 279 For log-transformed outcome variables, we calculated the exponential of the coefficients and subsequently 280 the percentage difference in the outcome per one unit increase of the independent variable: $(\exp(\beta)-1)*100$ 281 [53]. For odds ratios and coefficients for untransformed outcome variables the percentage difference was 282 calculated as (odds ratio-1)*100 or (β /range of outcome variable)*100. All analyses were performed in 283 STATA 14.1 [54]. Associations were considered statistically significant if the 95% confidence intervals 284 did not include zero (β) or one (odds ratios).

285

286 RESULTS

287 *Population characteristics*

Population characteristics are presented in Table 1. Participants were on average 48 (SD=15.2) years old and 54.1% were female. Median CTT completion time varied significantly between cities and was longest in Barcelona and shortest in Doetinchem. Over a quarter (28.5%) of the participants made one or more errors on the CTT and this was similar across the three cities. The median residential distance to NOE was largest in Barcelona, and much smaller in Doetinchem and Stoke-on-Trent (p<.001). Similarly, surrounding greenness was highest in Doetinchem, followed by Stoke-on-Trent, and lowest in Barcelona (p<.001). Also

 $\label{eq:294} the perceived amount of NOE in the neighborhood was lower in Barcelona than in the other cities (p<.001).$

- Furthermore, participants from Doetinchem visited NOE most often (p<.01) and spent most time there (p<.05), compared to participants from Barcelona and Stoke-on-Trent (Table 1). Correlations between objective NOE measures and the perceived amount of NOE ranged from -0.58 (residential distance to NOE) to 0.61 (residential surrounding greenness in 100m buffer). The use of NOE and objective NOE measures were less strongly correlated, we observed for example a correlation of -0.25 between residential distance to NOE and NOE visits, and 0.22 between residential surrounding greenness (100m buffer) and NOE visits (all correlations p<.001; Supplemental Material Table S1).
- 302

	Total (n=1628)	Barcelona, Spain (n=732)	Doetinchem, the Netherlands (n=567)	Stoke-on- Trent, UK (n=329)	p value
Females, %	54.1	52.3	57.6	51.8	>.05
Age, mean \pm SD	48.1 (15.2)	44.3 (15.2)	55.6 (12.1)	43.6 (15.4)	<.001ª
Educational level, %					<.001 ^b
Primary school	6.6	13.4	0.9	0.9	
Secondary school	45.3	37.6	44.0	65.1	
University degree	48.1	49.0	55.1	34.0	
Neighborhood SES, %					<.05°
Low	29.6	31.1	28.4	28.1	
Medium	35.0	31.7	39.9	33.8	
High	35.5	37.2	31.7	38.1	
CTT time (s), median	93 ± 54	107 ± 54	83 ± 38	90 ± 61	<.001 ^b
(IQR)					
CTT ≥1 errors, %	28.5	28.3	27.0	31.8	>.05
Residential distance to	119.6	310.2 (331.1)	45.5 (80.0)	83.2 (106.8)	<.001 ^t
NOE (m), median (IQR)	(243.2)				
Residential surrounding					
greenness, mean \pm SD					
100 m buffer	$0.38 \pm$	0.22 ± 0.09	0.54 ± 0.12	0.46 ± 0.08	<.001 ^t
	0.18				
300 m buffer	$0.39 \pm$	0.23 ± 0.11	0.55 ± 0.09	0.49 ± 0.09	<.001 ^b
	0.18				
500 m buffer	$0.40 \pm$	0.24 ± 0.11	0.57 ± 0.08	0.50 ± 0.09	<.001 ^b
	0.18				
Perceived amount of	7 (6)	5 (6)	10 (3)	7 (4)	<.001 ^t
NOE, median (IQR)					
NOE total visits last 4	11 (21)	8 (19.5)	18.5 (22)	8 (18.5)	<.01 ^a
wks, median (IQR)					
NOE total time spent	14.0	12.0 (30.5)	18.0 (27.8)	12.0 (44)	<.05 ^b
visiting (hours spent last 4	(31.5)		· /		
wks), median (IQR)	. ,				
Physical activity	420 (580)	240 (420)	670 (570)	360 (540)	<.05 ^b
min/week, median (IQR)	× -/		× /		

303 Table 1 Characteristics of study population

Social interaction	9.6	15.4	3.0	7.6	<.01 ^b
neighbors <1/month, %					
Social cohesion, mean \pm	13.0 ± 4	12.0 ± 3.0	14.0 ± 3.1	13.2 ± 3.7	<.001 ^b
SD					
Loneliness, median (IQR)	11 (5)	10 (5)	10 (4)	13 (3.5)	<.05 ^d
Mental health, median	80 (20)	76 (20)	84 (12)	76 (24)	<.05 ^b
(IQR)					
Air pollution worries, %	23.3	40.9	7.9	10.6	<.001 ^e
Noise annoyance, %	14.4	23.1	6.7	8.2	<.001 ^e
Hours away from home	10 (10)	10 (11)	11 (8)	8 (10)	<.05 ^b
(per week), median (IQR)					

304 CTT: color trails test; NOE: natural outdoor environments; NDVI: normalized difference vegetation index;
 305 SD: standard deviation; IQR: interquartile range. ^a NL different from SP and UK; ^b all groups differ; ^c NL
 306 different from SP; ^d UK different from SP and NL; ^e SP different from NL and UK.

307

308 Associations between natural outdoor environments and CTT

309 Each 100m increase in residential distance to NOE was associated with a longer CTT completion time of 310 1.50% (95% CI 0.13, 2.89) (Table 2). No associations were found between any of the other indicators of 311 NOE exposure and CTT completion time. No associations were found between any of the NOE indicators 312 and CTT errors (Table 2). City-specific associations between residential distance to NOE and CTT 313 completion time were only statistically significant for participants from Barcelona (Supplemental Material 314 Table S2). Similar to the pooled analyses, city-specific associations between the other indicators of natural 315 outdoor environments and CTT completion time and CTT errors were not statistically significant, with one 316 exception: we observed a significant association between surrounding greenness (in 500 m buffer) and 317 longer CTT completion time for participants from Doetinchem (Supplemental Material Table S2). 318 Sensitivity analysis showed that exclusion of participants with a poor CTT test quality (n=38) and those 319 with time of residence <1 year (n=86) did not change the results (data not shown).

320

321 Table 2 Associations between NOE and CTT completion time and errors

	% Difference in CTT	OR ≥ 1 CTT errors
	time	
	(95% confidence interval)	(95% confidence interval)
	liitei vai)	linter var)
Residential distance to NOE (per 100 m) (n=1602)	1.50 (0.13, 2.89)	1.02 (0.97, 1.07)
Residential surrounding greenness 100 m buffer per	-0.60 (-7.27, 6.55)	0.93 (0.74, 1.16)
IQR 0.313 (n=1602)		
Residential surrounding greenness 300 m buffer per	-0.27 (-8.59, 8.81)	0.91 (0.72, 1.16)
IQR 0.336 (n=1602)		

Residential surrounding greenness 500 m buffer per	-1.63 (-10.53, 8.15)	0.89 (0.70, 1.13)
IQR 0.349 (n=1602)		
Perceived amount of NOE in neighborhood (n=1599)	-0.13 (-0.78, 0.51)	1.01 (0.97, 1.05)
NOE visits (n=1602)	-0.04 (-0.15, 0.08)	1.00 (1.00, 1.01)
NOE total time spent visiting (n=1567)	-0.01 (-0.04, 0.03)	1.00 (1.00, 1.00)

322 CTT: color trails test; NOE: natural outdoor environments; OR: odds ratio; IQR: interquartile range. Models
 323 were adjusted for age, sex, educational level, neighborhood socioeconomic status, time spent away from
 324 home, and CTT test quality and random intercepts were specified for cities (n=3) and neighborhoods
 325 (n=93).

326

327 Associations between natural outdoor environments and potential mediators

328 No statistically significant associations were observed between residential distance to NOE and any of the

329 potential mediators (Table 3). The association between residential distance to NOE and neighborhood social

cohesion was marginally statistically significant (p=0.078) (Table 3).

331

332 Table 3 Associations between residential distance to NOE and potential mediators

	% Differe	nce (95% cor	fidence interval))			
	Physical activity	Social interactio	Social cohesion	Lonelines s	Mental health	Air pollution	Noise annoyanc
	(n=1526	n	neighborhoo	(n=1570)	(n=1590	worries	e
)	neighbors (n=1602)	d (n=1493))	(n=1601)	(n=1602)
Residentia	1.64	-1.20	-0.60	0.91	-0.25	4.76	5.08
1 distance	(-1.30,	(-13.15,	(-1.26, 0.07)	(-0.27,	(-0.71,	(-3.25,	(-4.39,
to NOE (per 100	4.67)	12.39)		2.11)	0.22)	13.43)	15.48)
(r • • • • • • • • • • • • • • • • • • •							

NOE: natural outdoor environments. Models were adjusted for age, sex, educational level, neighborhood
 socioeconomic status, time spent away from home, and CTT test quality, and random intercepts were
 specified for cities (n=3) and neighborhoods (n=93).

336

337 Associations between potential mediators and cognitive function

338 Higher loneliness and more air pollution worries were associated with longer CTT completion time, while

higher social cohesion and better mental health were related to shorter CTT completion time (Table 4).

340 Physical activity, social interaction with neighbors, and noise annoyance were not statistically significantly

associated with CTT time (Table 4).

342

343 Table 4 Associations between potential mediators and CTT time

Mediator

% Difference in CTT time

	(95% confidence interval)		
Physical activity (n=1602)	0.001 (-0.003, 0.005)		
Social interaction neighbors	-4.10 (-9.78, 1.94)		
(n=1602)			
Social cohesion neighborhood	-0.94 (-1.50, -0.37)		
(n=1493)			
Loneliness (n=1570)	1.48 (0.93, 2.04)		
Mental health (n=1590)	-0.22 (-0.34, -0.10)		
Air pollution worries (n=1601)	5.43 (0.79, 10.30)		
Noise annoyance (n=1602)	1.02 (-4.09, 6.41)		

344 CTT: color trails test. Models were adjusted for age, sex, educational level, neighborhood socioeconomic
345 status, time spent away from home, and CTT test quality and random intercepts were specified for cities
346 (n=3) and neighborhoods (n=93).

347

348 Associations between natural outdoor environments, mediators and cognitive function

349 Finally, none of the potential mediators were significantly associated with both residential distance to NOE

and CTT completion time. Since neighborhood social cohesion was (marginally) significantly associated

351 with both residential distance to NOE and CTT completion time, we investigated the association between

352 residential distance to NOE and CTT completion time, while adjusting for neighborhood social cohesion.

353 However, in this model, the association between residential distance to NOE and CTT completion time

354 increased slightly (Table 5). These results give no clear indication for mediation of the association between

residential distance to NOE and cognitive function by neighborhood social cohesion.

- 356
- 357 Table 5 Associations between distance to NOE, neighborhood social cohesion and CTT time

	% Difference in CTT time
	(95% confidence interval)
Residential distance to NOE	1.58 (0.19, 3.00)
(per 100 m)	
Social cohesion neighborhood	-0.91 (-1.48, -0.35)
(n=1493)	

NOE: natural outdoor environments; CTT: color trails test. Model was adjusted for age, sex, educational
 level, neighborhood socioeconomic status, time spent away from home, and CTT test quality and random
 intercepts were specified for cities (n=3) and neighborhoods (n=93).

361

362

363 DISCUSSION

364 An increase in residential distance to NOE was related to longer completion time of the CTT. This may

indicate that people living further away from nature have lower scores in cognitive function, specifically

366 for visual attention, and effortful executive processing abilities. There were no associations between

367 cognitive function and (i) residential surrounding greenness, (ii) perceived amount of NOE in
368 neighborhoods, and (iii) engagement with NOE. We found no clear indications for mediation by physical
369 activity, social interaction with neighbors, neighborhood social cohesion, loneliness, mental health, air
370 pollution worries, or noise annoyance.

371

372 Some of our results are in line with previous studies that also observed relations between access to NOE 373 and cognitive function. One previous observational study that was performed in primary schoolchildren 374 reported improvements in the development of working memory and attention after 12 months that was 375 related to surrounding greenness in residential, school and commuting areas [17]. Another study could not 376 find an association between proportion of parks in the neighborhood and cognitive function [19], while a 377 UK study found surrounding greenness and private gardens to be a risk factor for cognitive impairment and 378 dementia [20]. We are not aware of previous studies investigating the relation between access to NOE and 379 cognitive function measured with the CTT. Most of the other previous studies had an experimental design 380 and assessed short-term effects of exposure to nature [8,11,55]. We carried out an observational study, with 381 subjects in their residential environments, assessing a more general, and perhaps a more sustained relation 382 between NOE and cognitive function.

383

While residential distance to NOE was related to cognitive function, other indicators of NOE showed no consistent association with cognition. We found no evidence for an association between surrounding greenness, as measured with the NDVI, and cognitive function. The NDVI is relatively easy to obtain and provides a useful measure of residential greenness relevant for studies of potential cognitive benefits of natural outdoor environments. However, it's a rather coarse measure of greenness that does not differentiate between size, type and function of greenness [56].

390

Furthermore, we did not find an association between engagement with NOE and cognitive function. Engagement with nature may not reach its full potential for cognitive benefits when people are distracted with other things while they are in the natural space (e.g. mobile phones, crowding). Another explanation may be that especially the larger natural spaces are of importance for cognitive function, since spaces of >1 hectare were captured in the distance to natural outdoor environments indicator, while there was no such requirement in the other indicators. However, viewing nature from windows, which could include spaces as small as a street trees, has been related to benefits for cognitive function [15,55], but we did not find
such relations with our perceptions of NOE indicator which included window views. Lastly, another reason
may be that the unintentional use of NOE, which was not captured in our measure of engagement with
NOE, may be important for cognitive benefits, and may help explain our null findings.

401

402 We hypothesized that people living closer to nature feel less lonely, perceive higher social cohesion in their 403 neighborhood, and have more contact with their neighbors, but could not find clear evidence for this. A 404 Dutch study found that loneliness and shortage of social support mediated the relation between green space 405 and health, but found no support for a mediating role of contact with neighbors [23]. They hypothesized 406 that green spaces may be especially important for a sense of community through place attachment (i.e. the 407 bond between individuals and places) and not because of actual contact with neighbors [23]. In a study 408 about perceived greenness and mental health, social interaction with neighbors was not associated with 409 mental health, while social cohesion was. It was postulated that more close social interaction than was 410 assessed with their measure (e.g. waved, said hello, chatted) may be needed to confer health benefits [57]. 411 Another study found that urban gardening activities were beneficial for health through social involvement 412 and neighborhood attachment [58]. If proximity to NOE does reduce loneliness and enhance social 413 cohesion, it might support the hypothesis that this could partially mediate cognitive performance, as 414 perceived social isolation has been identified as a risk factor for poorer overall cognitive performance, faster 415 cognitive decline and poorer executive functioning [59]. The increase in cognitive load from worry and 416 chronic surveillance for threat in the environment associated with social isolation may leave fewer cognitive 417 resources to devote to completing the CTT, but the current results do not support this and further research 418 is needed.

419

We could not establish mediation by physical activity, mental health, air pollution worries, or noise annoyance. Two previous studies reported mediation of the relation between green space and general health by social cohesion, but physical activity was less important [33,51]. One explanation could be that both here and in previous studies, the mediation of physical activity in general was investigated, rather than activity in natural outdoor environments, which may have distorted the relation. Furthermore, stress may be an important mediator, since it was found to play a large role in explaining the relation between green space and health [51], and may also be relevant for the relation with cognitive function. Unfortunately, no data on stress were available in our sample. Another analysis of the Doetinchem PHENOTYPE data
revealed that the perceived sound quality (i.e. soundscape) of people's favorite NOE could contribute to
perceived restoration after visiting such a place [60].

430

431

432 No associations were found between any of the natural outdoor environment indicators and CTT errors. 433 While completing the CTT as fast as possible is thought to be associated with visual attention, completing 434 the CTT without errors is thought to be associated with impulse inhibition, another function related to 435 executive functioning [61]. Our findings might indicate that contact with nature is more related to 436 improvements in the visual attention functions, than with impulse inhibition. However, low variability of 437 CTT errors in our data may also be the reason for our null findings. Future research could further investigate 438 these and other aspects of cognitive function to establish what aspects of cognition may be relevant for 439 effects of NOE.

440

441 Our study has several strengths and limitations. Strengths are the use of a variety of objective and validated 442 instruments for exposure, mediators, and outcome assessments; and the investigation of different study 443 populations from three European countries using the same methodology. Cognitive function was assessed 444 with the CTT, which is regarded to be a language- and culture-free instrument. The use of such an 445 instrument is important considering the international nature of our study. One of the limitations includes 446 the relatively low response rates in our study, especially for Doetinchem. Non-response analysis for the 447 Doetinchem sample showed that respondents had less often poor general health and rated NOE to be of 448 higher importance for physical activity and relaxation compared to non-responders [35]. This might have 449 affected the generalizability of our study. Another limitation is the missing data for the CTT, with more 450 tests missing in Doetinchem and Stoke-on-Trent than in Barcelona, which resulted in unequal population 451 sizes. The cognition test was taken after the questionnaire was completed, but if this exceeded one hour, 452 the CTT was not taken. This may have resulted in potential bias by not having cognition test scores from 453 those participants that took longer to complete the questionnaire. However, it is unlikely that this is 454 associated with exposure to NOE and should not have introduced bias. We did observe that associations 455 between residential distance to NOE and CTT completion time were only statistically significant for 456 Barcelona, the city with the largest sample size, which may have driven the significant association in the

457 total sample. Another reason for this result might be that the smaller amount of NOE in Barcelona makes 458 it easier to detect associations, and when there already is a certain amount of NOE, increasing levels of 459 NOE have little additional value. Nonetheless, we must be cautious when interpreting these results 460 considering the possibility that our observed associations were due to chance. Although efforts were made 461 to take into account several covariates, estimates may have residual confounding by unknown factors that 462 could vary between study areas. Finally, with our mediation analysis we assume a certain sequence of 463 effects, while the cross-sectional nature of our study limits us to establish the directions of these effects. 464 This is a general limitation of cross-sectional studies and underlines the need for longitudinal studies to 465 gain knowledge on the potential causal link between NOE and cognition and its mechanisms [21].

466

467 CONCLUSIONS

468 In this cross-cultural study, we found an association between distance to NOE and CTT completion time, 469 providing some indication that proximity to nature may benefit cognitive function, particularly visual 470 attention. We observed no associations between other exposure indicators of NOE and cognitive function, 471 nor could we establish mediation by physical activity, social interaction with neighbors, neighborhood 472 social cohesion, loneliness, mental health, air pollution worries, or noise annoyance. When future research 473 provides more evidence for an association between nature and cognition, and when more knowledge 474 becomes available on what particular form of nature is beneficial to cognitive health and to whom, these 475 findings could have implications for urban spatial planning policies targeted at improving access to nature 476 in cities.

477

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