Environment International 161 (2022) 107094

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Early life exposure to residential green space impacts cognitive functioning in children aged 4 to 6 years

Yinthe Dockx [a], Esmée M. Bijnens [a,b], Leen Luyten [a], Martien Peusens [a], Eline Provost [a,c], Leen Rasking [a], Hanne Sleurs [a], Janneke Hogervorst [a], Michelle Plusquin [a], Lidia Casas [d,e,f], Tim S. Nawrot [a,f,*]

[a] Centre for Environmental Sciences, Hasselt University, Agoralaan Building D, 3590 Diepenbeek, Belgium
[b] Department of Human Structure and Repair, Ghent University Hospital, Ghent, Belgium
[c] Health Unit, Flemish Institute for Technological Research (VITO), Mol, Belgium
[d] Social Epidemiology and Health Policy, Department of Family Medicine and Population Health, University of Antwerp, Belgium
[e] Insitute for Environment and Sustainable Development (IMDO), University of Antwerp, Belgium
[f] Center for Environment and Health, Department of Public Health, Leuven University (KU Leuven)

ARTICLE INFO

Handling Editor: Zorana Jovanovic Andersen

Keywords:
Green Space
SDQ
CANTAB
Childhood

ABSTRACT

Introduction: During early childhood, neuronal networks are highly susceptible to environmental factors. Previous research suggests that green space exposure is beneficial for cognitive functioning. Here, we investigate the associations between residential green space exposure and behavioral problems and cognitive development in children aged four to six years.

Method: We included children participating in the ENVIR*ON*AGE birth cohort. Residential green spaces were calculated based on high-resolution land cover data within several buffers (50–1,000 m) around the residence. The children's behavior was assessed with the Strengths and Difficulties Questionnaire (SDQ) among 411 children. In addition, to evaluate cognitive function, 456 children completed four tasks of the Cambridge Neuropsychological Test Automated Battery (CANTAB). We used multivariate logistic and linear regression models while accounting for potential confounders and covariables.

Results: An interquartile (IQR) increase of residential green space within 50 m was associated with a 38% (95% CI: 56;14) lower odds of a child having hyperactivity problems. Additionally, we found a beneficial influence of residential green space in close proximity (50–100 m) on the attention and psychomotor speed, represented by the Motor Screening Task. For example, we found a decrease of 0.45 (95% CI: −0.82;-0.09) pixel units from target center with an IQR increase of residential green space in a 50 m buffer. In addition, we observed an improved visual recognition/working memory, represented by the Delayed Matching to Sample Task within all included buffers (50–1000 m). For example, we observed a decrease of 4.91% (95 %CI: −7.46;-2.36) probability of an error occurring if the previous trial was correct and a 2.02% (95 %CI: 0.08; 3.97) increase of correct trials with an IQR increase of green space within a 100 m buffer.

Conclusion: This study provides additional indications for a beneficial influence of green space exposure on the development of behavioral problems and cognitive function as young as four years of age.

1. Introduction

The period from conception until early childhood is highly sensitive to environmental exposures and contains various critical windows of susceptibility where extrinsic factors can influence the complex dynamics of development. One such intricate process involves the development of the brain and its neurocognitive maturation (Rice and Barone, 2000; World Health Organization, 2006). Although the brain remains relatively plastic over time, the increased flexibility of neural networks in early life and their changes in response to the environment are uniquely efficient in shaping the developing brain, which can have permanent effects in later life, such as effects on intelligence and academic performance (National Research et al., 2000).

Much of what we know about the environmental impact on early life

---

* Corresponding author at: Centre for Environmental Sciences, Hasselt University, Agoralaan Building D, 3590 Diepenbeek, Belgium.
E-mail address: tim.nawrot@uhasselt.be (T.S. Nawrot).

https://doi.org/10.1016/j.envint.2022.107094
Received 24 September 2021; Received in revised form 13 December 2021; Accepted 11 January 2022

cognitive development is derived from adverse or deprived conditions, such as the presence of toxins (Lanphear, 2015) or exposure to particulate matter (Calderón-Garcidueñas et al., 2016; Edwards et al., 2010). However, in recent years there is an increased interest in the potential beneficial health impacts of environmental factors on our mental development (James et al., 2015). Of particular interest is green space, especially in light of the ongoing degradation of green spaces through urbanization (Cotella, et al., 2020) despite the many possible underlying mechanisms through which green spaces can exert their beneficial effect. Biophysical-related pathways identify their capability to mitigate urban-related environmental hazards, such as outdoor air pollutants, noise and heat (Dadvand et al., 2015; Kuo, 2015). Additionally, the presence of green spaces observably promotes physical activity (Ward et al., 2016) as well as social interactions (Maas et al., 2009), both closely related to our mental well-being (Kahn and Kellert, 2002). Moreover, green space also regulates biodiversity, most notably environmental microbial communities (Dockx, 2021). Besides being explicitly involved in regulating our immune system, environmental microbial diversity might play a role in shaping the human microbiome, such as the gut microbiota, which can utilize our innate immune system to influence brain regulation (Galland, 2014; Rook, 2013).

Earlier experimental studies primarily focused on the short-term effects of green space on mental well-being. They established that the acute exposure to greener environments was related to a decrease in stress levels (Gidlow et al., 2016) and an increase in self-esteem (Barton et al., 2012). Similarly, in children, they found that short-term exposure to nature improved their attention (Schutte et al., 2017).

However, evidence is growing that supports also a relationship between long-term green space exposure and behavior and cognition in children. For instance, long-term exposure to green space was associated with a decreased risk of childhood-associated behavioral problems concerning emotion, conduct and hyperactivity (Amoly et al., 2014; Bijnens et al., 2020; Markevych et al., 2014) and associated with a lower risk of psychiatric disorders as found in a large-scale study covering more than 900,000 Danish individuals (Engemann et al., 2019). Additionally, studies found that children residing in an environment surrounded with more green could better memorize, were more attentive and had a higher intelligence quotient (Bijnens et al., 2020; Dadvand et al., 2017; Lee et al., 2021). However, most studies investigating cognitive function and green space examined school-aged children aged six to 12, whereas observable differences in cognitive capabilities are already present at the preschool age, which is an important developmental stage in children (National Research et al., 2000). In this study, we investigated the association between early life exposure to residential green space and behavior and cognitive functioning in children aged four to six years participating in the prospective Environmental influence on Aging in Early Life (ENVIR*ON*AGE) birth cohort.

2. Methods

2.1. Study design and population

ENVIR*ON*AGE is an ongoing prospective Belgian birth cohort initiated in 2010, that recruits mother-newborn pairs at the time of delivery in the East-Limburg Hospital (Genk, Belgium). Detailed information on the eligibility and recruitment process at birth is provided elsewhere (Janssen, 2017). When the child is between four and six years old, the mother and child are invited to participate in the follow-up phase. At the follow-up visit, written consent from the mothers is obtained and children give their oral permission. The participating mothers fill out several questionnaires to get information about the socio-demographic and lifestyle characteristics of the household. Additionally, mothers fill out the Strengths and Difficulties Questionnaire (SDQ) to evaluate the child's behavior using SDQ sub-scales and a Total Difficulties Score. Cognitive function is assessed using four tasks of the Cambridge Neuropsychological Test Automated Battery (CANTAB): the Motor Screening Task and Big/Little Circle, that evaluate attention and psychomotor speed, and the Spatial Span Test and Delayed Matching to Sample that evaluate the visual recognition/working memory. Details on the SDQ and the CANTAB are provided in the behavioral assessment and cognitive measurement sub-sections of the methods. The study protocol was approved by the ethical committees of the Hasselt University, and complied with the Helsinki Declaration (Janssen, 2017). The cohort participants, both at birth as well as at follow-up, are considered to be representative for the population in Flanders and are spatially distributed within the province of Limburg (Flanders, Belgium), including urban, suburban and rural areas (Janssen, 2017).

We attempted to contact 905 mother–child pairs of which the child was between four and six within the selected timeframe of December 10, 2014 to March 5, 2020. A participation flowchart is provided in the supplemental material (Supplemental Fig. 1). In total, 108 mother–child pairs were not included for participation because the child had died (n = 2), had a severe cognitive impairment (n = 1), moved abroad or too far from the examination center (n = 16), could not communicate adequately in Dutch (n = 9), or there was loss of contact (n = 80). In addition, the child reached six years of age before an appointment could be made (n = 27), 289 mothers refused to participate and 22 failed to come to the appointment. In total 459 mother–child pairs renewed their consent and participated in the follow-up study, resulting in a final participation rate of 57.5%. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Of the 459 participating children, there were 411 children with available data from the SDQ. Analysis with regard to cognitive functioning was done on 456 children with available CANTAB test results. We excluded 26 children from whom we had no information on average daily screen time (n = 19), that were influenced by a parent or sibling (n = 3), were distracted by the environment during the test (n = 2), or had trouble to understand any of the CANTAB tasks (n = 2). Furthermore, we looked separately into the four specific sections of the CANTAB cognitive tests, being the Motor Screening Task, Big/Little Circle Spatial Span Test and Delayed Match to Sample with results for 422, 423, 429, and 425 children, respectively. We excluded the results of each specific test in case of coughing, an incorrect registering screen, distraction by the parent or environment or a problem with the device (Supplemental Fig. 1).

2.2. Behavioral assessment

At the moment of the follow-up visit, the parents, mostly accompanying mothers (87.8%), were asked to fill out the Dutch version of the parent-administered SDQ once as developed by Goodman (Goodman, 2001). The questionnaire contains 25 statements regarding the child's behavior over the past six months to obtain four sub-scales assessing internalizing (peer relationship and emotional subscales) and externalizing (conduct and hyperactivity subscales) behavior. Each subscale consists of five items that can be scored 0, 1, or 2, and the total score on each domain can therefore range from 0 to 10. These sub-scales were combined to calculate a Total Difficulties Score (range, 0–40). For comparability with other European cohorts, we followed the commonly used British cut-off guidelines and categorized these four sub-scales and the Total Difficulties Score into discrete variables by grouping borderline and abnormal scores together to define a "not normal" category. Being not normal was thus defined when scores were found to be equal or above 3 for peer relationships, 4 for emotional behavior, 3 for conduct, 6 for hyperactivity and 14 for the Total Difficulties Score (Meltzer et al., 2003). This version of the SDQ has been proven to be highly reliable and has been validated as an appropriate screening method in children aged four to 16 (Goodman, 2001).

2.3. Cognitive measurements

We assessed the children's neurocognitive functioning using four tasks of the CANTAB (CANTAB, Cognitive assessment software, 2019) software on a touch-screen tablet. It was explained to the children at the beginning of the clinical examinations that we could stop each test at any moment if the child was uncomfortable or scared. A trained examiner gave instructions for each task according to a standardized script provided by the software developers, repeated once if the child was unsure or did not understand the task. Each test had trials that were not included in the calculated outcome variables. The CANTAB allows for reliable and well-founded measurements for executive functions as young as four years of age (Luciana, 2003). In total, the child was given four tasks to complete, of which the first two were designed to assess the attention and psychomotor speed and the last two were used to measure the child's visual recognition/working memory (Fig. 1).

The first two attention-related tasks included the Motor Screening Task and Big/Little Circle task. During the first cognitive test, the Motor Screening Task, the child had to press a series of ten crosses at different locations on the screen, one at a time, as quickly and accurately as possible. The cross was considered successfully selected if the point of touch was within a close radius around the target's center (based on a screen resolution of 640 × 350 pixels). This test assessed the average time in milliseconds it took for the child to successfully select the cross, further referred to as response latency, and the average pixel units between the touch and the center of the target on successful trials, referred to as error. The second cognitive test was the Big/Little Circle task. The child was presented with two differently sized circles and had to select the smallest circle as quickly as possible for the first 20 choices, and for the next 20 choices, the child was instructed to select the largest circle. This test measured the average time it took to touch the correct stimulus after it was displayed on the screen, further referred to as response latency.

After evaluating the child's attention and psychomotor speed, we further assessed the visual recognition/working memory. In the Spatial Span task, white boxes are shown on the screen, of which two briefly change color in a randomized sequence. The child had to reproduce the sequence after an auditory cue. If it did so correctly, the sequence was increased by one until the child could not correctly recall it in three consecutive attempts within the same sequence length. The outcome variable for this test was the maximum number of boxes the child could remember in the correct sequence, further referred to as span length. The fourth and final test was the Delayed Matching to Sample task. This task started with displaying a complex visual pattern (sample), which the child had to recognize from four similar patterns that were randomly presented. The patterns consisted of one being identical to the sample pattern, one having the same colors but different shapes, one having the same shape but different colors and finally one having different shapes and colors, referred to as the distractor. The selection of patterns to choose from was either presented simultaneous to the sample pattern or after a delay of either 0, 4 or 12 s after which the sample pattern was not displayed anymore for reference. This test assessed the percentage of total number of trials upon which the child answered correctly on their first try and the average time it took to select the correct answer on first try (response latency in milliseconds). Only latencies on the Delayed Matching to Sample task where the child achieved more than 25% correct trials were considered. Additionally, the test evaluated the probability of an error occurring if the previous trial was correctly answered.

2.4. Green space exposure

We geocoded the current residential addresses of the households at the follow-up visit to calculate a measure of green space exposure in five buffers around the residential address (50 m, 100 m, 300 m, 500 m and 1,000 m). All analyses were carried out using Geographic Information System (ArcGIS 10 software) functions. Green space was calculated using Groenkaart Vlaanderen (Green Map of Flanders) 2013. The land cover data is established on raster-segmentation classification using flight *ortho*-photos from 2012 commissioned by the Agency for Nature and Forest (ANB) and provides high-resolution (1x1m) information on natural elements, identified as all non-agricultural vegetation and further referred to as green space, validated with an overall accuracy of 95% (Vegetatiekaart, 2015). More information is provided in supplemental material and an overview of the classification processing is provided in supplemental Fig. 2.

2.5. Covariables

Information on lifestyle and certain clinical characteristics, such as age of the child and sex, was obtained using a questionnaire. Maternal education at the moment of examination was used to define

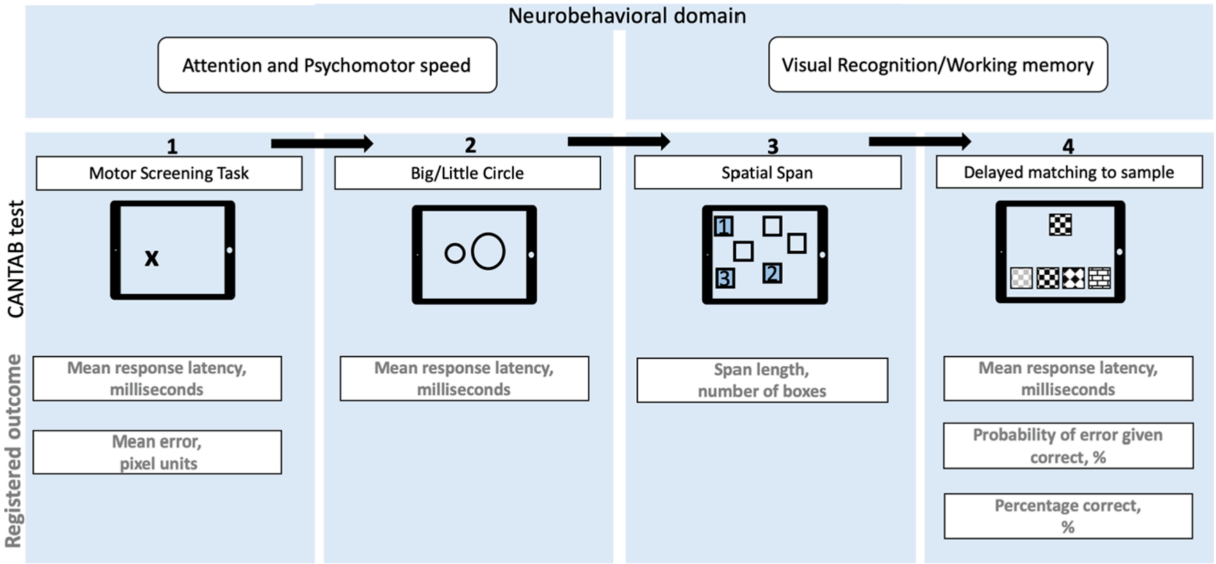

Fig. 1. Schematic representation of the cognitive CANTAB measurements and registered outcomes. Arrows indicate the sequence of the tests. While the child was administered the cognitive CANTAB tasks, the SDQ was filled out by the accompanying parent.

socioeconomic status and was coded as "low" (no diploma or primary school), "middle" (high school), or "high" (college or university degree). Average daily screen time, defined as watching television, playing computer games and tablet use, was used to estimate possible prior familiarization with tablet use or playing computer games and was coded as "none to less than 1 h per day", "1 to 2 h per day" and "more than 2 h per day". In addition, we also obtained information on the average amount the child sleeps, in hours, on a typical day and night.

The daily exposure levels to $PM_{2.5}$ (particulate matter with an aerodynamic diameter $\leq 2.5\ \mu m$, $\mu g/m^3$) and NO_2 ($\mu g/m^3$) at the residential address were obtained using a spatiotemporal interpolation method (Janssen et al., 2008), taking into account both land-cover data and pollution data from fixed monitoring stations in combination with a dispersion model (Lefebvre et al., 2011, 2013). We assessed overall model performance via a leave-one-out cross-validation, including 34 monitoring stations for $PM_{2.5}$ and 44 for NO_2. The validation statistics of the interpolation tool explained >80% of the spatial–temporal variability in the Flemish Region of Belgium for $PM_{2.5}$ and 78% for NO_2 (Maiheu, 2013). The model was additionally validated by linking the modelled residential $PM_{2.5}$ and BC levels with the biomarkers of internal exposure to nanosized black carbon particles in urine (Saenen, 2017) and placental tissue (Bové et al., 2019). These daily values were then averaged over the entire pregnancy and entire childhood, the latter to have an estimation of postnatal ambient air pollution exposure.

The time of day of the cognitive testing was used as a continuous variable in the main analyses, and categorized as follows for stratification in sensitivity analysis: morning (before 12 pm), early afternoon (from 12 pm up to 4 pm), and late afternoon (from 4 pm up to 6 pm).

2.6. Statistical analysis

For the statistical processing we used the R environment (R Development Core Team, 2019). To examine the associations between green space exposure and the child's behavior, we used multivariate logistic regression models for the SDQ sub-scales and the Total Difficulties Score, adjusted for several *a priori* chosen covariables. We included clinical characteristics such as the child's age at the time of the examination and their sex, as well as maternal education. Results are expressed as odd's ratios [95% confidence interval, CI] for an IQR increment in residential green space.

To investigate the association between green space exposure and cognitive functioning, using CANTAB outcomes, we log-transformed (natural base e) all latency data, i.e. response latency of the Motor Screening Task, Big/Little Circle test and Delayed Matching to Sample test, to better comply with assumptions of model linearity. First, we performed two principal component analyses (PCAs) where we made linear combinations of the CANTAB variables assessing the same neurocognitive domain. We then used the values of the first two principal components from each PCA, with a cumulative explained variance of more than 70%, as dependent variables in a multivariable linear regression model (Luyten et al., 2020). Additionally, we performed multivariable linear regression models to investigate the relationship between green space exposure and all individual outcome variables of the CANTAB cognitive tests. All models were adjusted for the same aforementioned covariables (child's age, sex and maternal education) and additionally adjusted for the child's average daily screen time and the time of the examination. Results are expressed as estimates [95% CI] for an IQR increment in residential green space. For data that were log-transformed, we back-transformed the estimates and expressed them as a percentage change.

To assess the robustness of our findings, we performed several sensitivity analyses on both the behavioral outcomes and the computerized measures of cognitive function. Regarding the exposure assessment (i.e. green spaces), we assessed the effect of surrounding green space in larger buffers (2000 m and 3000 m). In addition, we excluded children that ever moved to another home since birth. Further, we investigated several measures of postnatal air pollution exposure by separately adding to the main model the chronic exposure to $PM_{2.5}$ or NO_2 concentration averaged over the entire childhood. In addition, we investigated prenatal $PM_{2.5}$ exposure by adding to the main model the average daily residential concentrations of ambient $PM_{2.5}$ averaged over the entire pregnancy. For the models including CANTAB variables, we excluded children who showed any signs of possible disinterest while taking the cognitive tests to account for possible problems with the response validity. This exclusion was based on behavioral remarks and children seemingly pressing irregularly as collected from the touch patterns from the tablet. These were six results for the Motor Screening task, 12 results for the Big/Little Circle task, 24 results for the Spatial Span task and 38 results for the Delayed Matching to Sample task. Last, because a child's performance may depend on tiredness, we excluded children that performed the cognitive tests in the late afternoon (i.e. between 4 pm and 6 pm). In addition, we also adjusted the main model for the average amount the child sleeps on a typical day and night.

3. Results

3.1. Study population

Characteristics of the mother–child pairs with complete information (n = 430) were similar to eligible mother–child pairs that were invited but did not participate in the follow-up, further referred to as non-participants (n = 338), regarding maternal characteristics, including age of the mother at birth and the pre-pregnancy body mass index (BMI), and clinical characteristics such as the child's sex, gestational age, birth weight and birth length (Supplemental Table 1). However, compared with non-participants, participating mothers were more likely to have a higher educational degree and to be of European descent.

The characteristics of the follow-up visits and mother–child pairs of the ENVIRONAGE birth cohort included in this study are presented for each subset in Table 1. Most of the examinations were done in the early afternoon (58.1%). On average (min–max), the children were 4.5 (3.7–6.4) years old at the follow-up visit and approximately half were girls (51.6%). A minority of children had an average screen time of more than 2 h per day (9.8%), most children spent on average 1 to 2 h a day on this activity (54.2%). Accompanying mothers were on average (min–max) 35.1 (22.5–49.8) years old and the majority had a college education or higher (68.1%).

The characteristics of the four sub-scales and Total Difficulties score of the SDQ are summarized in Table 2. The largest group categorized as not normal was within the conduct sub-scale, where 104 (25.3%) children had conduct difficulties, followed by 101 (24.6%) children with hyperactivity difficulties, 89 (21.7%) with emotional difficulties, and lastly 67 (16.3%) children with peer relationship problems.

The outcomes for the four CANTAB tasks are summarized in Table 2. The median (p25-p75) response latency of the Motor Screening task, calculated as the mean time to successfully touch the target was 964.0 (812.8–1157.5) milliseconds. Additionally, the error of the Motor Screening task, was 14.3 (12.3–16.3) pixel-units removed from the center of the target. The response latency of the Big/Little Circle task, calculated as the average time to select the correct circle in the Big/Little Circle task was 1091.5 (965.0–1232.2) milliseconds. The number of boxes that could be reproduced in the correct sequence during the Spatial Span test was 3 (2–3). Finally, the time to select the correct pattern on the first try during the Delayed Matching to Sample task for all presented sample patterns was 4111.2 (3280.8 – 5070.5)milliseconds. The percentage of trials that were answered correctly on the first try was 45.0 (35.0–55.0) %.

The distribution of residential green space for all buffers (50 m to 1,000 m) for the SDQ and CANTAB subsets is presented in Table 3. The median residential green space ranged from approximately 46% within a 50 m radius up to approximately 55% within a 1,000 m radius. Moreover, the different buffers of residential green space were, as

Table 1
Characteristics of the mother–child pairs that performed the SDQ and CANTAB tests.

	SDQ subset (n = 411)	CANTAB subset (n = 430)
Characteristics of the visit		
Time of examination		
Morning	155 (37.7)	157 (36.5)
Early afternoon	236 (57.4)	250 (58.1)
Late afternoon	20 (4.9)	23 (5.3)
Characteristics of the child		
Age at follow-up visit, years	4.5 ± 0.4	4.5 ± 0.4
Sex		
Girl	213 (51.8)	222 (51.6)
Screen time		
None to less than 1 h/day	149 (37.8)	155 (36.0)
1-2 hours/day	206 (52.3)	233 (54.2)
>2 h/day	39 (9.9)	42 (9.8)
Missing information	17	0
Average amount of sleep on a typical day and night, hours	10.9 ± 1.1	10.9 ± 1.1
Characteristics of the mother		
Age of the mother at follow-up visit, years	35.1 ± 4.3	35.1 ± 4.2
Educational level at follow-up visit		
Low (no high school diploma)	19 (4.6)	20 (4.7)
Middle (high school diploma)	114 (27.7)	117 (27.2)
High (college degree or higher)	278 (67.6)	293 (68.1)
Characteristics of the household		
Moved		
Never moved	281 (68.4)	294 (68.4)
Childhood average daily PM$_{2.5}$ exposure, μg/m^3	12.1 ± 1.1	12.2 ± 1.2
Childhood average daily NO$_2$ exposure, μg/m^3	16.7 ± 3.1	16.2 ± 3.2
Pregnancy average daily PM$_{2.5}$ exposure, μg/m^3	13.9 ± 2.4	14 ± 2.5

Continuous data are presented as mean ± SD, categorical variables as n (%).

expected, highly positively correlated with each other, with the spearman rho ranging from 0.38 (between 50 m and 1,000 m) to 0.92 (between 300 and 500 m) (Supplemental Fig. 3).

3.2. Association between green space and behavior

After adjustment for age, sex and maternal education we found an overall trend of an inverse association between the proportion of residential green space in close buffers (50 and 100 m) and behavioral problems, although only statistically significant for hyperactive behavior. Here, we found that an IQR increase in green space within in a 50 m buffer surrounding the residential address was associated with a 38% (95% CI: 56 ; 14) lower odds of scoring not normal for hyperactivity problems (Table 4). No other behavioral outcomes were found to be associated with green space.

3.3. Association between green space and cognitive functioning

3.3.1. Attention and psychomotor speed

Principal components for the neurological domain of attention and psychomotor speed were obtained as linear combinations of the two outcomes of the Motor Screening Task and the outcome of the Big/Little Circle test. The first principal component explained 52% of the variance; the second, an additional 33%. Characteristics of the principal components used in the multivariable linear regression models are shown in the supplemental material (Supplemental Table 2). While accounting for the child's age, sex, maternal education, average daily screen time and time of examination, we observed an inverse association between green space in a 50 m and 100 m buffer and the second principal component ($P = 0.006$, $P = 0.002$, respectively).

Table 2
Description of the parent-administered SDQ including the 4 sub-scales and Total Difficulties Score (n and n %) in 411 children and the description of the 4 tasks (Motor Screening Task, Big/Little Circle, Spatial Span Test, Delayed Matching to Sample) of the CANTAB in 430 children of the ENVIR*ON*AGE birth cohort.

Strength and Difficulties categories	n (%)
Peer relationship behavior	
Normal	344 (83.7)
not normal	67 (16.3)
Emotional behavior	
normal	322 (78.3)
not normal	89 (21.7)
Conduct problems	
normal	307 (74.7)
not normal	104 (25.3)
Hyperactive behavior	
normal	310 (75.4)
not normal	101 (24.6)
Total Difficulties Score	
Normal	340 (82.7)
not normal	71 (17.3)

Outcomes of the CANTAB	n	min	p25	p50	p75	max
Motor Screening	422					
Response latency, milliseconds		535.1	812.8	964.0	1157.5	2961.8
Error, pixel units		6.7	12.3	14.3	16.3	23.0
Big/Little Circle	423					
Response latency, milliseconds		683.0	965.0	1091.5	1232.2	2719.9
Spatial Span	429					
Span Length		0	2	3	3	5
Delayed Match to Sample	423					
Response latency, milliseconds		945.7	3280.8	4111.2	5070.5	13994.7
Probability of error given correct answer		11.8	41.7	55.6	66.7	100.0
Percentage correct, %		0.0	35.0	45.0	55.0	90.0

Table 3
Distribution of the residential green space for five buffers (50 m to 1000 m) surrounding the residential address, presented for SDQ subset and CANTAB subset.

Green space (%)	min	p25	p50	p75	max
SDQ subset (n = 411)					
50 m buffer	3.64	35.61	46.14	58.91	92.02
100 m buffer	8.53	39.02	48.41	59.83	87.76
300 m buffer	11.84	41.54	51.81	61.41	89.66
500 m buffer	12.25	41.44	53.57	62.00	87.26
1000 m buffer	10.63	39.94	55.90	65.09	88.62
CANTAB subset (n = 430)					
50 m buffer	3.64	35.31	46.46	58.86	92.02
100 m buffer	8.53	38.86	48.52	59.73	87.76
300 m buffer	11.84	41.43	51.83	61.14	89.66
500 m buffer	12.25	41.39	53.25	62.11	86.39
1000 m buffer	10.63	39.82	55.06	65.13	88.62

Using multivariable linear regression model for each of the three separate test outcomes, adjusted for the aforementioned variables, we observed a significant inverse association between residential green space and the pixel distance from the target of the Motor Screening Task only in close-by buffers (50 m and 100 m) surrounding the residential address (Fig. 2 and Supplemental Table 3). An IQR increase in

Table 4
Overview of the 4 SDQ sub-scales (peer relationship, emotional, conduct, and hyperactivity) and Total Difficulties Score (divided into normal (reference) and not normal categories) in association with residential green space for 5 buffers (50 m to 1,000 m) surrounding the residential address. Multivariate logistic regression models were adjusted for age, gender and maternal education. Results are expressed as odd's ratio's [95% confidence interval] for an IQR increment in residential green space (estimates presented in bold are statistically significant p less than 0.05).

	50 m	**100** m	**300** m	**500** m	**1,000** ***m***
peer relationship	0.91 [0.63; 1.32]	0.95 [0.65; 1.37]	1.18 [0.82; 1.71]	1.21 [0.83; 1.76]	1.12 [0.74; 1.73]
emotional	1.05 [0.75; 1.46]	0.95 [0.68; 1.32]	0.88 [0.63; 1.21]	0.84 [0.61; 1.17]	0.81 [0.56; 1.17]
conduct	0.87 [0.63; 1.20]	0.89 [0.65; 1.23]	0.92 [0.67; 1.25]	0.92 [0.67; 1.26]	0.95 [0.66; 1.36]
hyperactivity	**0.62 [0.44; 0.86]**	0.75 [0.54; 1.03]	1.16 [0.85; 1.60]	1.02 [0.75; 1.41]	0.89 [0.62; 1.28]
Total Difficulties Score	0.74 [0.51; 1.06]	0.84 [0.58; 1.22]	1.18 [0.82; 1.71]	1.13 [0.78; 1.64]	1.07 [0.70; 1.64]

residential green space was associated with a decrease of 0.45 (95% CI: −0.82;-0.09) and 0.50 (95% CI: −0.87;−0.14) pixel unit distance from target within the 50 m and 100 m buffers respectively. No other cognitive outcomes for attention and psychomotor speed were found to be associated with green space.

3.3.2. *Visual recognition/working memory*

Principal components for the neurological domain of visual recognition/working memory were obtained as linear combinations of the outcome of the Spatial Span test and the three outcomes of the Delayed Matching to Sample task (Fig. 1). The first principal component explained 46% of the variance; the second an additional 25%. Characteristics of the principal components used in the multivariable linear regression models are shown in supplement (Supplemental Table 2). After adjusting for age, sex, maternal education, average daily screen time, and time of examination, we observed a significant negative association between green space and the first principal component in all buffers, with p-values ranging from 0.003 (100 m) to 0.03 (500 m).

With the multivariable linear regression models for each of the four separate test outcomes, adjusted for the aforementioned variables, we observed a significant negative association between green space and the probability of error if the previous trial was correct in the Delayed Matching to Sample task in all buffers (50 m-1,000 m). For instance, an IQR increase in residential green space within a 50 m buffer, was associated with a decrease of 3.12% (95% CI: −5.70 ; −0.54) probability of an error occurring. Associations with larger buffers are all in the same direction without substantial differences in the size of the effect (Fig. 2 and Supplemental Table 3). Moreover, we also found a significant positive association between residential green space and percentage of correct trials in the Delayed Matching to Sample task in all buffers (100 m-1000 m), with the exception of the 50 m buffer surrounding the residential address. For instance, an IQR increase in residential green space in the 100 m buffer was associated with an increase of 2.02% (95% CI: 0.08; 3.97) percent of correct trials in the Delayed Matching to Sample task.

3.4. *Sensitivity analyses*

In a first sensitivity analysis, we investigated the associations in two larger buffers (2000 m and 3000 m) of green space exposure surrounding the residential address and found additional significant associations for the Delayed Matching to Sample outcomes, i.e. the probability of error if the previous trial was correct, and the percentage of correct trials, in the same direction and without substantial differences in the size of the effect as observed for the main analyses (Supplemental Table 4).

In a second sensitivity analysis, we investigated the relationship between residential green space exposure and behavioral and cognitive outcomes for children who never moved during their lifetime (n = 281 and n = 294, respectively) (Supplemental Table 5). Here, we found the same significant inverse association between residential green space exposure and hyperactivity problems (n = 66 (23.5%)) in a 50 m buffer, and additionally this association was found to be significant in a 100 m buffer. Furthermore, an IQR increase in residential green space in the 50 m, 500 m and 1,000 m buffers surrounding the residence was associated with a significantly lower odds of the child scoring not normal for conduct problems (n = 66 (23.5%)). Overall, this resulted in a significant inverse association between residential green space and the SDQ Total Difficulties score (n = 44 (15.7%)). An IQR increase in residential green space was associated with a 50% (95% CI: 70 ; 19) and 40% (95% CI: 65 ; 2) lower odds of the child scoring not normal for total difficulties problems, within the 50 m and 100 m buffers, respectively. Regarding CANTAB outcomes, we observed minor changes to the previously reported associations.

In a third sensitivity analysis, we additionally adjusted the models regarding behavioral and CANTAB outcomes for the daily $PM_{2.5}$ exposure averaged over the entire childhood (n = 410 and n = 430, respectively). Here, we found no changes to the statistical significance of the observed associations (Supplemental Table 6). Replacing $PM_{2.5}$ by NO_2 in the model or replacing $PM_{2.5}$ childhood exposure by prenatal exposure did not alter the aforementioned results (results not shown).

In a fourth sensitivity analysis, we excluded children with any possible signs of disinterest whilst performing the cognitive tests (Supplemental Table 7). All observed associations remained significant. However, additionally we found a significant positive association between residential green space and the response latency of the Delayed Matching to Sample task. The latency increased with 4.96% (95% CI 0.04; 10.12) for every IQR increase in residential green space in the 50 m buffer.

In a final sensitivity analysis, we investigated the possibility of tiredness. We excluded children that performed the cognitive tests in the late afternoon (n = 407). This did not alter the previously reported associations much (Supplemental Table 8). Additionally, adjusting for the average amount the child sleeps in a typical day and night did not alter the results (results not shown).

4. Discussion

In this prospective birth cohort study, we used high-resolution green space information within multiple buffers surrounding the child's residence and evaluated child behavioral difficulties in addition to cognitive function testing by the CANTAB test battery in four to six year old children. The key finding of our analysis was that independent from pre- and postnatal air pollution and other covariables residential surrounding green space is associated with a reduction in hyperactive behavioral traits, had a beneficial effect on motor accuracy and improved visual memory-related tasks in children of four to six years.

We investigated the relationship between early life green space exposure and behavioral traits displayed in childhood, as represented by SDQ sub-scales and the SDQ Total Difficulties Score. Overall, we found a decrease in the likelihood of a child having problems in externalizing domains, such as conduct and hyperactivity behavior. The persistent association between residential surrounding green space exposure and hyperactivity is consistent with previous studies describing the potential of surrounding greenness to reduce the risk of ADHD or hyperactivity problems (Amoly et al., 2014; Thygesen et al., 2020). Similarly, we found the strongest association between hyperactivity and residential green space within close proximity to the residence. Our study suggests

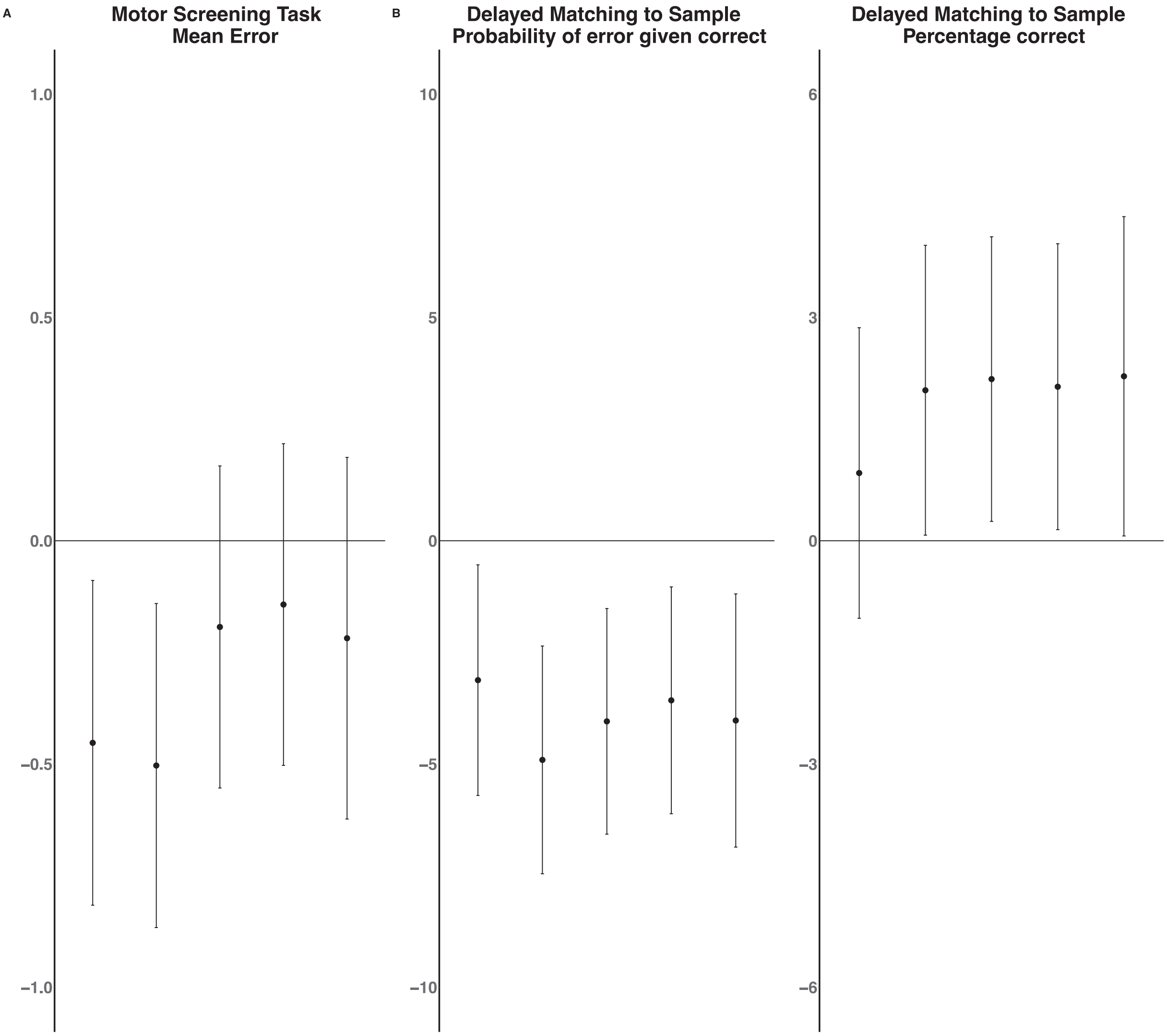

Fig. 2. Overview of the relevant CANTAB outcomes of the cognitive domain of **A** Attention and psychomotor Speed, represented by the Motor Screening Task and **B** Visual recognition/working memory, represented by the two outcomes of the Delayed Matching to Sample Task. Multivariate generalized linear models were adjusted for child's age, gender, maternal education, average daily screen time and time of examination. Results are expressed as regression coefficients and 95% CI error bars for an IQR increase in residential green space for 5 buffers (50 m to 1,000 m). Buffer-specific IQRs are given in the x-axis.

that even green space as close as 100 m surrounding the residential address might be relevant in preventing behavioral outcomes from early life onwards.

Besides behavioral characteristics, we also investigated the association between early life green space exposure and cognitive functioning, as represented by four CANTAB tasks. Analyses pertaining to performance on attention and psychomotor speed involved results from the Motor Screening Task and Big/Little Circle task. Here, we found children pressing more accurately in the Motor Screening Task, as shown by a significant decrease in pixel unit distance from the target center in association with the child's household residential green in close-by (50–100 m) buffers. Touch-performance is indicative of a child's attention and fine motor skills. The tapping touch-screen gestures used to complete the Motor Screening Task require certain dexterity skills (Nacher et al., 2015), acquired and refined during early childhood. This motor development is still relevant for children aged four to six years old, considering they are in the preoperational stage, as defined by Piaget's cognitive developmental theory, in which acquiring motor skills is still ongoing (Byrnes and Byrnes, 2008; Piaget, 2003). Touch accuracy is driven by complex sensorimotor skills and visuospatial processing pathways and inherently improves with age (Vatavu et al., 2015). Our results are in accordance with studies associating natural green environments with improved balance, motor coordination and attention in children (Chawla, 2015). Moreover, several studies have investigated the contribution of environmental stressors on childhood motor skills, connecting, amongst others, maternal depression and (airborne) pollutants to worse motor skill outcomes (Golding et al., 2014) which are both factors associated with surrounding green space (Dadvand et al., 2015; Kuo, 2015; Kahn and Kellert, 2002).

Analyses regarding the visual recognition/working memory, involved the Spatial Span test and Delayed Matching to sample task. Here, we observed that an increase in residential green space was associated with better childhood visual recognition/working memory, identified as children having more correct responses on their first try as well as having an approximately 4% lower probability of error if the previous trial was correct when contrasting the higher versus the lower green space. The processes involved in visual short-term recognition memory-related tasks are regulated by a diverse array of complex pathways in the brain and correspond strongly with the visual working memory (Oakes et al., 2013). This neurological domain undergoes significant development during infancy and early childhood, accompanying improvement in both visual attention and perceptual processing

(Buss et al., 2018; Toornstra, 2019). Furthermore, the visual working memory is involved with aspects of overall cognitive functioning, evidenced by its connection with intelligence and academic performance in later life (Raghubar et al., 2010; Bull et al., 2008). The observed beneficial influence of green space on the visual working memory is consistent with studies observing better memorization and a higher intelligence quotient in children (aged seven to 15) residing in homes surrounded with more green (Dadvand et al., 2015; Bijnens et al., 2020; Dadvand et al., 2018). Considering that visual working memory is innately attention-driven, our results are comparable to studies connecting environments with more green to better attention in childhood (Dadvand et al., 2017).

The complex interactions between green space and behavioral and cognitive outcomes are probably due to the several mechanisms through which green space can influence our health (Peters et al., 2021). First, green space is involved with biophysical-related processes such as the reduction of urban-related environmental hazards, including outdoor air pollutants, heat and noise (Dadvand et al., 2015; Kuo, 2015), which have been associated with higher scores for the hyperactivity subscale of the SDQ (Hjortebjerg et al., 2016) and worse motor skills outcomes (Golding et al., 2014; Lin et al., 2014). Furthermore, green space is hypothesized to provide bio-cognitive related benefits, including the potential to restore cognitive resources, which is important to improve directed-attention abilities (Groenewegen et al., 2006; Ohly et al., 2016). Moreover, green space has the potential to shape residential microbial communities (Dockx, 2021), which could influence behavioral traits displayed by children (Casas et al., 2019). However, the specific underlying processes responsible for the associations observed in the present study remain unclear. Therefore, more studies are still needed to differentiate the specific ways these neurological domains are driven by green space exposure.

We acknowledge a few limitations to our study. For our analysis, we used the green space exposure at the child's residence and did not take green space exposure at school into account. However, Flanders has excellent access to services, allowing most parents to opt for schooling near, on average 2.8 km, from the residential address (Pisman et al., 2018). Considering this range coincides with our largest calculated buffer in the sensitivity analysis, we expect this to cover, in part, the green space exposure at school, enabling us to get an indication on their total green space exposure. Furthermore, because we lack information on the actual time they spent outdoors and the access to green space, we cannot identify whether the positive contribution of green space is more related to biosocial characteristics, such as physical activity and social interactions. However, we observe significant associations of green space on cognition while adjusting for screen time, which is both indicative of sedentary behavior (Mineshita et al., 2021; Vriens et al., 2018) and, to a certain extent of social skills (Hinkley et al., 2018). In addition, there were more children from highly educated parents in our follow-up study compared with the baseline ENVIR*ON*AGE population, which may limit the generalizability of our findings of the full cohort and to the general population. Nevertheless, the number of women that followed higher education in Flanders is quite high (52.7%) (Bevolking naar onderwijsniveau (scholingsgraad)., 2020). A strength of this study is that our green space calculations were of high quality and high resolution, allowing us to identify the impact of non-agricultural green instead of a combination of vegetation used in NDVI (normalized difference vegetation index) calculations. Moreover, we used principal components and performed various sensitivity analyses and found minimal changes to the observed associations, indicating the results are robust and consistent. Furthermore, although we included several measures of residential green space and cognitive outcomes, we did not adjust for multiple comparisons, because the strongly correlated green space variables and cognitive outcomes do not provide a completely independent opportunity for a type I error. Instead of adjusting for multiple comparisons, we grounded the interpretation of our results on their consistencies among our different green spaces buffers and our hypothesized mechanisms. Furthermore, our study is among the first studies, that have investigated the relationship between green space exposure and the cognitive functioning of children as young as four years of age. Although cognitive testing is slightly more difficult to interpret because of age-related factors (Luciana and Nelson, 1998), we did account for a potential lack of motivation and thus inaccurate response validity. We, hereby found the same significant associations which further indicates the reliability of cognitive testing through CANTAB in children as young as four years of age. Moreover, all cognitive tests were performed in a standardized manner with trained researchers, limiting inter-observer bias and improving reliable data collection.

5. Conclusion

This study provides indications for a beneficial influence of residential green space exposure on neuropsychological development, including hyperactivity and cognitive function in children as young as four years of age. Moreover, we observed this association in multiple buffers surrounding the residential address, including close-by (50 m and 100 m) buffers, which might help provide an incentive to urban planners to consider green space as a powerful and inexpensive public health intervention.

CRediT authorship contribution statement

Yinthe Dockx: Writing – original draft, Investigation, Methodology, Formal analysis, Conceptualization. **Esmée M. Bijnens:** Writing – review & editing, Formal analysis, Methodology, Conceptualization. **Leen Luyten:** Writing – review & editing, Investigation. **Martien Peusens:** Writing – review & editing, Investigation. **Eline Provost:** Writing – review & editing, Investigation. **Leen Rasking:** Writing – review & editing, Investigation. **Hanne Sleurs:** Writing – review & editing, Investigation. **Janneke Hogervorst:** Writing – review & editing. **Michelle Plusquin:** Writing – review & editing. **Lidia Casas:** Writing – review & editing. **Tim S. Nawrot:** Writing – review & editing, Supervision, Methodology, Conceptualization.

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.

Acknowledgements

The authors thank all children and parents for taking part in the study. Graphical abstract was created with BioRender.com.

Funding

This investigation is supported by the EU research council "project ENVIRONAGE" (ERC-2012-StG 310890) and Flemish Scientific Fund (G073315N/G048420N).

Lidia Casas is recipient of a post-doctoral fellowship a of the Research Foundation Flanders (FWO), grant number 12I1517N. Esmée M Bijnens holds a fellowship from the Marguerite-Marie Delacroix foundation.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2022.107094.

References

Rice, D., Barone, S., 2000. Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models. Environ. Health Perspect. 108 (suppl 3), 511–533.

World Health Organization, 2006. Principles for evaluating health risks in children associated with exposure to chemicals, World Health Organization.

National Research, C. and D. Institute of Medicine Committee on Integrating the Science of Early Childhood, 2000 in *From Neurons to Neighborhoods:* The Science of Early Childhood Development, Shonkoff, J.P., Phillips, D.A. (Eds.), National Academies Press (US) Copyright 2000 by the National Academy of Sciences. All rights reserved: Washington (DC).

Lanphear, B.P., 2015. The Impact of Toxins on the Developing Brain. Annu. Rev. Public Health 36 (1), 211–230.

Calderón-Garcidueñas, L., Leray, E., Heydarpour, P., Torres-Jardón, R., Reis, J., 2016. Air pollution, a rising environmental risk factor for cognition, neuroinflammation and neurodegeneration: The clinical impact on children and beyond. Rev Neurol (Paris) 172 (1), 69–80.

Edwards, S.C., Jedrychowski, W., Butscher, M., Camann, D., Kieltyka, A., Mroz, E., Flak, E., Li, Z., Wang, S., Rauh, V., Perera, F., 2010. Prenatal exposure to airborne polycyclic aromatic hydrocarbons and children's intelligence at 5 years of age in a prospective cohort study in Poland. Environ Health Perspect 118 (9), 1326–1331.

James, P., Banay, R.F., Hart, J.E., Laden, F., 2015. A Review of the Health Benefits of Greenness. Curr. Epidemiol. Rep. 2 (2), 131–142.

Cotella, G., et al., 2020. ESPON SUPER – Sustainable Urbanisation and land-use Practices in European Regions. A GUIDE TO SUSTAINABLE URBANISATION AND LAND-USE.

Dadvand, P., Nieuwenhuijsen, M.J., Esnaola, M., Forns, J., Basagaña, X., Alvarez-Pedrerol, M., Rivas, I., López-Vicente, M., De Castro Pascual, M., Su, J., Jerrett, M., Querol, X., Sunyer, J., 2015. Green spaces and cognitive development in primary schoolchildren. PNAS 112 (26), 7937–7942.

Kuo, M., 2015. How might contact with nature promote human health? Promising mechanisms and a possible central pathway. Front. Psychol. 6, 1093.

Ward, J.S., Duncan, J.S., Jarden, A., Stewart, T., 2016. The impact of children's exposure to greenspace on physical activity, cognitive development, emotional wellbeing, and ability to appraise risk. Health Place 40, 44–50.

Maas, J., van Dillen, S.M.E., Verheij, R.A., Groenewegen, P.P., 2009. Social contacts as a possible mechanism behind the relation between green space and health. Health Place 15 (2), 586–595.

Kahn, P.H., S.R. Kellert, 2002. Children and Nature: Psychological, Sociocultural, and Evolutionary Investigations. In: Kahn, P.H., Kellert, S.R. (Eds.), The MIT Press.

Dockx, Y., et al., 2021. Residential green space can shape the indoor microbial environment. Environ. Res. 201, 111543.

Galland, L., 2014. The gut microbiome and the brain. J. Med. Food 17 (12), 1261–1272.

Rook, G.A., 2013. Regulation of the immune system by biodiversity from the natural environment: an ecosystem service essential to health. Proc. Natl. Acad. Sci. U S A 110 (46), 18360–18367.

Gidlow, C.J., Randall, J., Gillman, J., Smith, G.R., Jones, M.V., 2016. Natural environments and chronic stress measured by hair cortisol. Landscape Urban Plann. 148, 61–67.

Barton, J.o., Griffin, M., Pretty, J., 2012. Exercise-, nature- and socially interactive-based initiatives improve mood and self-esteem in the clinical population. Perspect. Public Health 132 (2), 89–96.

Schutte, A.R., Torquati, J.C., Beattie, H.L., 2017. Impact of Urban Nature on Executive Functioning in Early and Middle Childhood. Environ. Behav. 49 (1), 3–30.

Amoly, E., Dadvand, P., Forns, J., López-Vicente, M., Basagaña, X., Julvez, J., Alvarez-Pedrerol, M., Nieuwenhuijsen, M.J., Sunyer, J., 2014. Green and blue spaces and behavioral development in Barcelona schoolchildren: the BREATHE project. Environ. Health Perspect. 122 (12), 1351–1358.

Bijnens, E.M., Derom, C., Thiery, E., Weyers, S., Nawrot, T.S., Markevych, I., 2020. Residential green space and child intelligence and behavior across urban, suburban, and rural areas in Belgium: A longitudinal birth cohort study of twins. PLoS Med. 17 (8), e1003213.

Markevych, I., Tiesler, C.M.T., Fuertes, E., Romanos, M., Dadvand, P., Nieuwenhuijsen, M.J., Berdel, D., Koletzko, S., Heinrich, J., 2014. Access to urban green spaces and behavioural problems in children: Results from the GINIplus and LISAplus studies. Environ. Int. 71, 29–35.

Engemann, K., Pedersen, C.B., Arge, L., Tsirogiannis, C., Mortensen, P.B., Svenning, J.-C., 2019. Residential green space in childhood is associated with lower risk of psychiatric disorders from adolescence into adulthood. Proc. Natl. Acad. Sci. 116 (11), 5188–5193.

Dadvand, P., Tischer, C., Estarlich, M., Llop, S., Dalmau-Bueno, A., López-Vicente, M., Valentín, A., de Keijzer, C., Fernández-Somoano, A., Lertxundi, N., Rodriguez-Dehli, C., Gascon, M., Guxens, M., Zugna, D., Basagaña, X., Nieuwenhuijsen, M.J., Ibarluzea, J., Ballester, F., Sunyer, J., 2017. Lifelong Residential Exposure to Green Space and Attention: A Population-based Prospective Study. Environ. Health Perspect. 125 (9), 097016. https://doi.org/10.1289/EHP694.

Lee, K.-S., Choi, Y.-J., Cho, J.-W., Moon, S.-J., Lim, Y.-H., Kim, J.-I., Lee, Y.-A., Shin, C.-H., Kim, B.-N., Hong, Y.-C., 2021. Children's Greenness Exposure and IQ-Associated DNA Methylation: A Prospective Cohort Study. Int. J. Environ. Res. Public Health 18 (14), 7429. https://doi.org/10.3390/ijerph18147429.

Janssen, B.G., et al., 2017. Cohort Profile: The ENVIRonmental influence ON early AGEing (ENVIRONAGE): a birth cohort study. Int. J. Epidemiol. 46 (5), 1386–1387m.

Goodman, R., 2001. Psychometric properties of the strengths and difficulties questionnaire. J. Am. Acad. Child Adolesc. Psychiatry 40 (11), 1337–1345.

Meltzer, H., Gatward, R., Goodman, R., Ford, T., 2003. Mental health of children and adolescents in Great Britain (Reprinted from 2000). Int. Rev. Psychiatry (Abingdon, England) 15 (1-2), 185–187.

CANTAB, Cognitive assessment software, 2019. Cambridge Cognition. p. all rights reserved. www.cantab.com.

Luciana, M., 2003. Practitioner review: computerized assessment of neuropsychological function in children: clinical and research applications of the Cambridge Neuropsychological Testing Automated Battery (CANTAB). J. Child Psychol. Psychiatry 44 (5), 649–663.

Vegetatiekaart 2015: Digitale bos-, natuur- en groenkartering voor Vlaanderen op basis van digitale luchtopnames. 2017, Informatie Vlaanderen.

Janssen, S., Dumont, G., Fierens, F., Mensink, C., 2008. Spatial interpolation of air pollution measurements using CORINE land cover data. Atmos. Environ. 42 (20), 4884–4903.

Lefebvre, W., Vercauteren, J., Schrooten, L., Janssen, S., Degraeuwe, B., Maenhaut, W., de Vlieger, I., Vankerkom, J., Cosemans, G., Mensink, C., Veldeman, N., Deutsch, F., Van Looy, S., Peelaerts, W., Lefebre, F., 2011. Validation of the MIMOSA-AURORA-IFDM model chain for policy support: modeling concentrations of elemental carbon in Flanders. Atmos. Environ. 45 (37), 6705–6713.

Lefebvre, W., Degrawe, B., Beckx, C., Vanhulsel, M., Kochan, B., Bellemans, T., Janssens, D., Wets, G., Janssen, S., de Vlieger, I., Int Panis, L., Dhondt, S., 2013. Presentation and evaluation of an integrated model chain to respond to traffic-and health-related policy questions. Environ. Modell. Software 40, 160–170.

Maiheu, B., et al., 2013. Identifying the best available large-scale concentration maps for air quality in Belgium. Flemish Institute for Technological Research (VITO), Mechelen, Belgium.

Saenen, N.D., et al., 2017. Children's Urinary Environmental Carbon Load. A Novel Marker Reflecting Residential Ambient Air Pollution Exposure? Am. J. Respir. Crit. Care Med. 196 (7), 873–881.

Bové, H., Bongaerts, E., Slenders, E., Bijnens, E.M., Saenen, N.D., Gyselaers, W., Van Eyken, P., Plusquin, M., Roeffaers, M.B.J., Ameloot, M., Nawrot, T.S., 2019. Ambient black carbon particles reach the fetal side of human placenta. Nat. Commun. 10 (1), 3866.

R Development Core Team, R: A language and environment for statistical computing, 2019. R Foundation for Statistical Computing: Vienna, Austria.

Luyten, L.J., Dockx, Y., Madhloum, N., Sleurs, H., Gerrits, N., Janssen, B.G., Neven, K.Y., Plusquin, M., Provost, E.B., De Boever, P., Nawrot, T.S., 2020. Association of Retinal Microvascular Characteristics With Short-term Memory Performance in Children Aged 4 to 5 Years. JAMA Netw. Open 3 (7), e2011537.

Thygesen, M., Engemann, K., Holst, G.J., Hansen, B., Geels, C., Brandt, J., Pedersen, C.B., Dalsgaard, S., 2020. The Association between Residential Green Space in Childhood and Development of Attention Deficit Hyperactivity Disorder: A Population-Based Cohort Study. Environ. Health Perspect. 128 (12), 127011. https://doi.org/10.1289/EHP6729.

Nacher, V., Jaen, J., Navarro, E., Catala, A., González, P., 2015. Multi-touch gestures for pre-kindergarten children. Int. J. Hum Comput Stud. 73, 37–51.

Byrnes, J., Byrnes, James P., 2008. Piaget's theory. In: Haith, M.M., Benson, J.B. (Eds.), Encyclopedia of Infant and Early Childhood Development (vol. 2., pp. 543-552). New York, NY, USA: Elsevier. 2008. p. 543-552.

Piaget, J., 2003. The psychology of intelligence, Routledge.

Vatavu, R.-D., Cramariuc, G., Schipor, D.M., 2015. Touch interaction for children aged 3 to 6 years: Experimental findings and relationship to motor skills. Int. J. Hum Comput Stud. 74, 54–76.

Chawla, L., 2015. Benefits of Nature Contact for Children. J. Planning Literature 30 (4), 433–452.

Golding, J., Emmett, P., Iles-Caven, Y., Steer, C., Lingam, R., 2014. A review of environmental contributions to childhood motor skills. J. Child Neurol. 29 (11), 1531–1547.

Oakes, L.M., Baumgartner, H.A., Barrett, F.S., Messenger, I.M., Luck, S.J., 2013. Developmental changes in visual short-term memory in infancy: evidence from eye-tracking. Front. Psychol. 4 https://doi.org/10.3389/fpsyg.2013.00697.

Buss, A.T., Ross-Sheehy, S., Reynolds, G.D., 2018. Visual working memory in early development: a developmental cognitive neuroscience perspective. J. Neurophysiol. 120 (4), 1472–1483.

Toornstra, A., et al., 2019. Measuring visual matching and short-term recognition memory with the CANTAB® Delayed Matching to Sample task in schoolchildren: Effects of demographic influences, multiple outcome measures and regression-based normative data. Child Neuropsychol. 26, 1–30.

Raghubar, K.P., Barnes, M.A., Hecht, S.A., 2010. Working memory and mathematics: A review of developmental, individual difference, and cognitive approaches. Learn. Individual Differences 20 (2), 110–122.

Bull, R., Espy, K.A., Wiebe, S.A., 2008. Short-term memory, working memory, and executive functioning in preschoolers: longitudinal predictors of mathematical achievement at age 7 years. Dev. Neuropsychol. 33 (3), 205–228.

Dadvand, P., Pujol, J., Macià, D., Martínez-Vilavella, G., Blanco-Hinojo, L., Mortamais, M., Alvarez-Pedrerol, M., Fenoll, R., Esnaola, M., Dalmau-Bueno, A., López-Vicente, M., Basagaña, X., Jerrett, M., Nieuwenhuijsen, M.J., Sunyer, J., 2018. The Association between Lifelong Greenspace Exposure and 3-Dimensional Brain Magnetic Resonance Imaging in Barcelona Schoolchildren. Environ. Health Perspect. 126 (2), 027012. https://doi.org/10.1289/EHP1876.

Peters, A., Nawrot, T.S., Baccarelli, A.A., 2021. Hallmarks of environmental insults. Cell 184 (6), 1455–1468.

Hjortebjerg, D., Andersen, A.M.N., Christensen, J.S., Ketzel, M., Raaschou-Nielsen, O., Sunyer, J., Julvez, J., Forns, J., Sørensen, M., 2016. Exposure to Road Traffic Noise and Behavioral Problems in 7-Year-Old Children: A Cohort Study. Environ. Health Perspect. 124 (2), 228–234.

Lin, C.-C., Yang, S.-K., Lin, K.-C., Ho, W.-C., Hsieh, W.-S., Shu, B.-C., Chen, P.-C., 2014. Multilevel analysis of air pollution and early childhood neurobehavioral development. Int. J. Environ. Res. Public Health 11 (7), 6827–6841.

Groenewegen, P.P., van den Berg, A.E., de Vries, S., Verheij, R.A., 2006. Vitamin G: effects of green space on health, well-being, and social safety. BMC Public Health 6 (1). https://doi.org/10.1186/1471-2458-6-149.

Ohly, H., White, M.P., Wheeler, B.W., Bethel, A., Ukoumunne, O.C., Nikolaou, V., Garside, R., 2016. Attention Restoration Theory: A systematic review of the attention restoration potential of exposure to natural environments. J. Toxicol. Environ. Health B Crit. Rev. 19 (7), 305–343.

Casas, L., Karvonen, A.M., Kirjavainen, P.V., Täubel, M., Hyytiäinen, H., Jayaprakash, B., Lehmann, I., Standl, M., Pekkanen, J., Heinrich, J., 2019. Early life home microbiome and hyperactivity/inattention in school-age children. Sci. Rep. 9 (1) https://doi.org/10.1038/s41598-019-53527-1.

Pisman, A.V.S, Willems, P., Engelen, G., Poelmans, L., 2018. Ruimterapport (RURA) 2018 - Infographics, Omgeving, Editor, Brussel.

Mineshita, Y., Kim, H.-K., Chijiki, H., Nanba, T., Shinto, T., Furuhashi, S., Oneda, S., Kuwahara, M., Suwama, A., Shibata, S., 2021. Screen time duration and timing: effects on obesity, physical activity, dry eyes, and learning ability in elementary school children. BMC Public Health 21 (1). https://doi.org/10.1186/s12889-021-10484-7.

Vriens, A., Provost, E.B., Saenen, N.D., De Boever, P., Vrijens, K., De Wever, O., Plusquin, M., Nawrot, T.S., 2018. Children's screen time alters the expression of saliva extracellular miR-222 and miR-146a. Sci. Rep. 8 (1) https://doi.org/10.1038/s41598-018-26351-2.

Hinkley, T., Brown, H., Carson, V., Teychenne, M., Martinuzzi, A., 2018. Cross sectional associations of screen time and outdoor play with social skills in preschool children. PLoS ONE 13 (4), e0193700.

Bevolking naar onderwijsniveau (scholingsgraad). 2020.

Luciana, M., Nelson, C.A., 1998. The functional emergence of prefrontally-guided working memory systems in four- to eight-year-old children. Neuropsychologia 36 (3), 273–293.