

warrants further investigation of these associations. Moreover, the cross-sectional design of most of these studies limits their ability to establish the causal nature of such associations.^{5-7,10} In addition, it would be interesting to study these associations across different developmental periods, because both the type of activities and cognitive development varies across ages.^{2,12} We aimed to investigate the association between physical activity and sedentary behavior at preschool age and working memory at primary school age, and the association between physical activity and sedentary behavior at primary school age and working memory at adolescence.

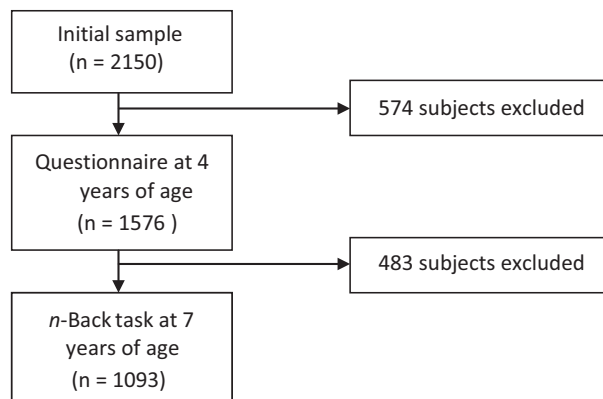
Methods

This study was conducted in the context of the population-based INMA (Infancia y Medio Ambiente [Environment and Childhood]) birth cohort across 4 Spanish regions: Menorca (n = 530), Valencia (n = 855), Sabadell in Catalonia (n = 657), and Gipuzkoa in Basque Country (n = 638).¹³ In Menorca (the older subcohort), women attending antenatal care were recruited over a 12-month period starting in mid 1997, whereas in Valencia, Sabadell, and Gipuzkoa (the younger subcohorts), recruitment took place between 2003 and 2008. In total, 1093 children in the younger subcohorts and 307 in the older subcohort who had data available on both lifestyle habits and cognitive function were included in the current study (Figure). All participants gave written informed consent before enrollment in the subcohorts. Each subcohort obtained study approval from the ethics committee in its corresponding region.

Data on extracurricular physical activity and sedentary behavior were collected through questionnaires administered to parents (mainly the mother) when children were 4 years of age in the younger subcohorts, and when children were 6 years of age in the older subcohort (Appendix; available at www.jpeds.com). We focused on extracurricular physical activity because it is more variable among children than school physical activity, which is highly standardized across Spain. Parents answered the following question regarding physical activity, "During a typical week, how long does your child perform extracurricular exercise in each day, eg, dance/swimming lessons, or just playing, running, cycling, skating, swimming, etc.?" In Menorca, the question did not include outdoor playing, walking, and cycling, because structured physical activity is more beneficial for cognitive development than unstructured physical activity at this age.² Parents were able to specify more than 1 activity in Gipuzkoa and Sabadell.

In all regions, parents answered the following question regarding TV viewing: "How many hours does your child watch TV per week?" Parents reported other sedentary behaviors through the question, "Outside school, how long does your child dedicate to games or sedentary activities (eg, puzzles, books, dolls, homework, computer/video games)?" Because the questions were not identical in all the regions, we harmonized the answers a posteriori. We transformed categorical variables to continuous variables as minutes and hours per day (Appendix).

Younger subcohorts (Valencia, Sabadell, and Gipuzkoa)



Older subcohort (Menorca)

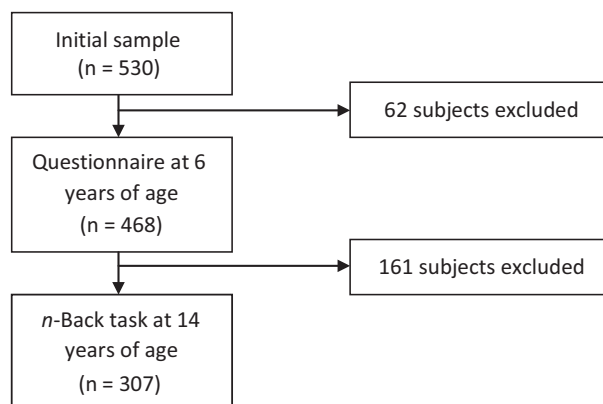


Figure. Flowchart of the study population.

These continuous variables were then converted to hours per week. In Menorca, we excluded TV watching from sedentary behavior by subtracting the value obtained in the specific TV watching question.

We tested working memory using computerized *n*-back task¹⁴ at 7 years of age in the younger subcohorts and at 14 years of age in the older subcohort. This instrument has been validated in the Spanish general population.¹⁵ The duration of the sessions was 25 minutes. Briefly, in the *n*-back task, participants have a sequence of stimuli on the computer screen, one at a time, and they have to respond (hit a button) when the current stimulus matches the one presented *n* steps before. The specific visual *n*-back task used consisted of a series of numbers, and 3 levels of difficulty or loads (1-, 2-, and 3-back). Stimuli were presented in a fixed central location on a white background for a 1500-ms duration with a 1000-ms interstimulus interval. Participants completed 3 blocks (1-, 2-, and 3-back) with each block being consisted of 25 trials. Targets never appeared in the first 3 trials of each block and 33% of stimuli of the following trials were targets. In the present study, we used 2-back as the main outcome, because it showed better properties than the 1- and 3-back tasks (eg, clear age-dependent slope and little learning effect) in a previous study.¹⁶ Addi-

tionally, we analyzed the difference between 1- and 2-back performances by subtracting the scores between both tasks to study whether the lifestyle habits affected scores changes owing to the increase in *n*-back load or task difficulty.¹⁷ This outcome controls for individual performance, and therefore increases its reliability. We measured overall accuracy (including both hits and correct rejections), and *d'*, a measure of detection subtracting the normalized false alarm rate from the hit rate: (*Z* hit rate - *Z* false alarm rate). This outcome indicates subject's sensitivity to detect the signal (target) against the noise (nontargets).

Accurate age at the time of test was calculated based on the date of birth and the date of neuropsychological testing session. We used maternal education (no or primary school, secondary school, or university) as a surrogate for socioeconomic status. This information was collected during the first trimester of pregnancy through a questionnaire.

Statistical Analyses

We dichotomized physical activity and sedentary behavior variables by their median values in each subcohort. We used dichotomous instead of continuous variables to homogenize the variables among subcohorts, because the values were not comparable among them owing to differences in the questions. For the 3 younger subcohorts, we merged the categorical variables in a new variable that gathered the low and high categories of each subcohort. The 2-back accuracy was truncated at 100% of correct responses and *d'* at 3.91 score (ie, the maximal possible *d'* score). We developed Tobit regression models,¹⁸ which are suitable for the truncated data, to test the associations between the lifestyle habits and 2-back performance. This model uses all observations, both those below and above the limit, to estimate the regression line. We applied linear regression models to test the associations between the lifestyle habits and 2- vs 1-back performance change. We developed separate models for each lifestyle habit and for each age

group (2 outcomes × 3 exposures × 2 age groups = 12 regressions in total). We used pooled analyses to combine the younger subcohorts. The confounders included in our models were sex, age, and maternal education, because previous literature has indicated that these variables could be associated with both lifestyle habits and cognitive performance.^{12,19} Final models were adjusted additionally for subcohort in the pooled analyses. We also performed stratified analyses for boys and girls to study possible effect modification by sex in the association between early lifestyle habits and later working memory.

We used R (3.0.2; R Foundation for Statistical Computing, Vienna, Austria) and Stata 12.1 (Stata Corporation, College Station, Texas) to perform the statistical analyses.

Results

The region-specific characteristics of the participants are described in **Table I**. Boys and girls were distributed similarly in all the regions. Among the younger subcohort participants, 64% and 12% obtained the maximum 1-back and 2-back accuracy scores, respectively. Among the older subcohort participants 85% and a 57% obtained the maximum 1-back and 2-back accuracy scores. The mean *n*-back scores were higher (ie, better performance) in the oldest (Menorca) subcohort compared with those obtained in the youngest subcohort (Sabadell; **Table I**). The change between 1-back and 2-back scores was smaller in the older subcohort than in the younger subcohorts. In **Table I**, we show the median hours per week spent in extracurricular physical activity, TV watching, and other sedentary behaviors by subcohort, which were used as cutoff points to create the dichotomous exposure variables.

Table II shows the percentage of children in each lifestyle category stratified by sex and maternal education. In the younger subcohorts (Valencia, Sabadell, and Gipuzkoa), boys spent more time performing extracurricular physical activity

Table I. Characteristics of the participants

	Younger subcohorts			Older subcohort
	Valencia (n = 437)	Sabadell (n = 492)	Gipuzkoa (n = 164)	Menorca (n = 307)
Baseline				
Sex, n (% females)	217 (49.7)	232 (47.2)	83 (50.6)	157 (51.1)
Age, mean (SD)	4.3 (0.1)	4.4 (0.2)	4.5 (0.3)	6.1 (0.1)
Maternal education, n (%)				
Primary or low	116 (26.5)	111 (22.6)	21 (12.8)	150 (48.9)
Secondary	188 (43.0)	208 (42.3)	60 (36.6)	90 (29.3)
University	133 (30.4)	158 (32.1)	83 (50.6)	46 (15.0)
Missing	0 (0)	15 (3.1)	0 (0)	21 (6.8)
Extracurricular physical activity (h/wk), median	2.0	14.2	15.0	1.8
TV watching (h/wk), median	9.0	9.4	8.0	7.0
Other sedentary behaviors (h/wk), median	7.0	9.0	6.8	14.0
Follow-up, mean (SD)				
Age	7.6 (0.2)	6.7 (0.5)	7.9 (0.1)	14.6 (0.2)
1-back (accuracy)	95.1 (10.4)	92.7 (12.9)	99.0 (3.0)	98.6 (3.7)
1-back (<i>d'</i>)	3.4 (0.9)	3.2 (1.0)	3.8 (0.4)	3.7 (0.6)
2-back (accuracy)	83.1 (15.3)	81.6 (14.5)	90.3 (7.4)	96.2 (5.5)
2-back (<i>d'</i>)	1.7 (1.2)	1.6 (1.1)	2.3 (1.1)	3.3 (0.9)
2-back vs 1-back (accuracy)	-12.0 (12.8)	-11.0 (12.6)	-8.7 (7.5)	-2.4 (6.3)
2-back vs 1-back (<i>d'</i>)	-1.7 (1.3)	-1.6 (1.3)	-1.5 (1.2)	-0.4 (1.0)

Table II. Percentage of participants in each category (low/high) of lifestyle activities by sex and maternal education categories

	Extracurricular physical activity (%)			TV watching (%)			Other sedentary behaviors (%)		
	Low	High	<i>P</i> value*	Low	High	<i>P</i> value*	Low	High	<i>P</i> value*
Younger subcohorts (Valencia, Sabadell, and Gipuzkoa)									
Sex (%)									
Female	50.8	46.6		52.4	44.2		43.9	54.4	
Male	49.2	53.4	.092	47.6	55.8	.004	56.1	45.6	<.0001
Maternal education (%)									
Primary	22.3	22.7		18.9	27.6		22.3	23.8	
Secondary	42.9	42.3		40.9	44.4		42.2	42.4	
University	34.9	35.0	.977	40.2	28.0	<.0001	35.5	33.7	.775
Older subcohort (Menorca)									
Sex (%)									
Female	52.3	48.9		54.6	45.4		48.7	56.0	
Male	47.7	51.1	.338	45.5	54.6	.079	51.3	44.0	.137
Maternal education (%)									
Primary	52.2	52.6		49.5	57.4		54.7	48.1	
Secondary	32.4	29.5		28.9	34.7		30.9	32.7	
University	15.5	18.0	.815	20.7	7.9	.017	14.4	19.2	.453

*Fisher exact test.

and watching TV, and girls spent more time engaged in other sedentary behaviors. In Menorca, the percentage of boys was slightly higher in the high physical activity and high TV watching groups, whereas the percentage of girls was higher in the group of high levels of other sedentary behaviors. Children whose mothers had lower education spent more time watch-

ing TV than those of higher educational background, both in the younger and older subcohorts.

Less active children at 4 years of age showed reductions in 2-back performance at 7 years of age compared with more active children, but these associations were not significant (Table III). Children who had low levels of extracurricular physical

Table III. Adjusted associations between preschool and primary school age lifestyle habits and *n*-back performance at primary school age (Valencia, Sabadell, and Gipuzkoa) and adolescence (Menorca)

		Younger subcohorts (Valencia, Sabadell and Gipuzkoa)		Older subcohort (Menorca)	
		2-back Coef.* (95% CI)	2-back vs 1-back Coef.† (95% CI)	2-back Coef.‡ (95% CI)	2-back vs 1-back Coef.§ (95% CI)
Extracurricular physical activity (ref. high)					
All	Accuracy	-0.95 (-2.81 to 0.92)	-1.71 (-3.14 to -0.28) [¶]	-4.22 (-8.05 to -0.39) [¶]	-1.26 (-3.16 to 0.64)
	<i>d'</i>	-0.06 (-0.22 to 0.10)	-0.19 (-0.34 to -0.03) [¶]	-0.53 (-1.09 to 0.03)	-0.30 (-0.56 to -0.04) [¶]
Girls	Accuracy	-2.25 (-4.76 to 0.26)	-2.23 (-4.29 to -0.17) [¶]	-3.25 (-8.59 to 2.10)	-0.44 (-3.00 to 2.12)
	<i>d'</i>	-0.19 (-0.41 to 0.03)	-0.23 (-0.46 to -0.01) [¶]	-0.28 (-1.05 to 0.49)	-0.24 (-0.60 to 0.13)
Boys	Accuracy	0.34 (-2.41 to 3.10)	-1.28 (-3.29 to 0.73)	-4.76 (-10.21 to 0.69)	-2.08 (-4.92 to 0.75)
	<i>d'</i>	0.07 (-0.15 to 0.29)	-0.15 (-0.37 to 0.06)	-0.76 (-1.57 to 0.05)	-0.38 (-0.75 to -0.01) [¶]
TV watching (ref. low)					
All	Accuracy	0.21 (-1.70 to 2.11)	0.10 (-1.37 to 1.56)	-0.01 (-3.37 to 3.35)	-0.44 (-2.16 to 1.29)
	<i>d'</i>	0.04 (-0.12 to 0.20)	0.02 (-0.14 to 0.18)	-0.07 (-0.58 to 0.45)	-0.09 (-0.34 to 0.16)
Girls	Accuracy	0.49 (-2.07 to 3.05)	0.69 (-1.41 to 2.79)	1.33 (-3.47 to 6.13)	0.15 (-2.21 to 2.51)
	<i>d'</i>	0.11 (-0.12 to 0.33)	0.09 (-0.14 to 0.33)	0.10 (-0.61 to 0.82)	-0.04 (-0.38 to 0.31)
Boys	Accuracy	-0.12 (-2.93 to 2.69)	-0.48 (-2.54 to 1.58)	-1.06 (-5.72 to 3.60)	-0.98 (-3.53 to 1.56)
	<i>d'</i>	-0.02 (-0.25 to 0.20)	-0.05 (-0.27 to 0.17)	-0.12 (-0.86 to 0.62)	-0.11 (-0.46 to 0.25)
Other sedentary behaviors (ref. low)					
All	Accuracy	0.08 (-1.81 to 1.97)	-0.25 (-1.72 to 1.21)	-2.20 (-5.46 to 1.05)	-0.54 (-2.23 to 1.15)
	<i>d'</i>	0.06 (-0.10 to 0.22)	0.05 (-0.11 to 0.21)	-0.33 (-0.83 to 0.17)	-0.09 (-0.33 to 0.15)
Girls	Accuracy	-0.65 (-3.16 to 1.87)	-0.87 (-2.92 to 1.19)	0.29 (-4.20 to 4.77)	0.64 (-1.60 to 2.88)
	<i>d'</i>	-0.02 (-0.24 to 0.20)	-0.02 (-0.25 to 0.21)	0.03 (-0.65 to 0.71)	0.17 (-0.17 to 0.50)
Boys	Accuracy	0.86 (-1.96 to 3.68)	0.37 (-1.73 to 2.46)	-5.07 (-9.68 to -0.46) [¶]	-2.00 (-4.57 to 0.57)
	<i>d'</i>	0.14 (-0.09 to 0.37)	0.12 (-0.10 to 0.34)	-0.70 (-1.43 to 0.03)	-0.38 (-0.73 to -0.02) [¶]

Coef., coefficient.

*Tobit models adjusted for age, sex, maternal education, and subcohort.

†Linear regression models adjusted for age, sex, maternal education, and subcohort.

‡Tobit models adjusted for age, sex, and maternal education.

§Linear regression models adjusted for age, sex, and maternal education.

¶*P* < .05.

activity at 4 years of age showed reductions in 2-back performance in relation to 1-back at age 7 years of age, compared with those with high levels of extracurricular physical activity (accuracy $P = .019$; $d'P = .018$). The stratified models showed that the associations were statistically significant only in girls (accuracy $P = .034$; $d'P = .046$), but there was no interaction by sex (accuracy P for interaction = .516; $d'P$ for interaction = .636). TV watching and other sedentary behaviors were not associated with working memory performance.

In the older subcohort, we observed poorer 2-back performance in adolescents who were less active at 6 years of age compared with those who were more active, with a significant association between physical activity and accuracy ($P = .031$; **Table III**). We also found a more pronounced reduction in 2-back performance (d') in relation to 1-back in adolescents who were less active at 6 years of age compared with those who were more active ($P = .024$). The stratified analyses showed a clear association in boys ($P = .042$) but did not in girls (P for interaction = .761). We also observed reductions in 2-back accuracy ($P = .032$; P for interaction = .136) and in 2-back vs 1-back d' change in adolescent boys who were more sedentary when they were 6 years of age ($P = .037$; P for interaction = .044). There were no significant associations between TV watching and working memory at either age or for either sex.

Discussion

We evaluated the role of extracurricular physical activity and sedentary behavior on cognitive function in schoolchildren using a prospective study design. Low levels of extracurricular physical activity at 4 years of age were associated with poorer cognitive performance in terms of working memory at 7 years of age. Similar associations were observed in adolescents with low physical activity levels at 6 years of age in a separate study population. No associations were observed between TV watching and working memory performance. Other sedentary behaviors at 6 years of age were associated with deteriorated working memory at 14 years of age in boys.

Many studies have observed the positive cross-sectional relationship between physical activity and cognitive functions in children, especially executive functions.^{4,10,20} Physical activity may enhance working memory through different mechanisms at multiple levels, from cells to social interaction. Cognitive skills acquired during physical activity may transfer to cognitive functioning in other situations.² Chronic physical activity has been associated with larger brain volume in regions supporting memory and executive functions,^{21,22} improvement in the connectivity of brain networks,^{23,24} higher levels of brain-derived neurotrophic factor,^{25,26} and enhanced cerebrovascular function.²⁷

We found a positive association between extracurricular physical activity levels at 4 years of age and working memory performance at 7 years of age. The question included different types of physical activity, such as playing, walking, cycling, and sports. A previous study based on measured physical

activity using accelerometers has supported the idea that any type of physical activity is associated with better cognitive capacities.¹⁰ This is particularly true for younger children, who may benefit more from unstructured forms of physical activity than older children.² The longitudinal approach of our study highlights the importance of early physical activity habits for maximizing cognitive development of children. Interestingly, in line with previous studies,^{28,29} the positive association between physical activity and working memory performance was stronger in girls. This finding could be explained, at least in part, by different levels and types of physical activity between boys and girls.²⁸ In animals, brain-derived neurotrophic factor mediated the relationship between long-term stress and depression in females but not in males,³⁰ suggesting that different metabolic pathways between boys and girls could also explain this findings.

Regarding older children, our results indicated that time spent in extracurricular physical activity at 6 years of age predicted working memory performance 8 years later. In this subcohort, the variable of extracurricular physical activity included mainly structured physical activity, such as sports. Although physical activity levels start to decrease through late childhood,¹² it is known that sports participation increases at school age, because preschool children do not normally participate regularly in organized physical activity.³¹ Children engaged in sports are more likely to be physically active during adolescence and adulthood.³² Thus, this study showed that structured physical activity during childhood might have long-term positive impacts on cognitive development. In this sample, the associations were stronger in boys and did not reach statistical significance in girls. It is possible that the intensity of the structured physical activity at school age was higher in boys than in girls, which could be more beneficial for later working memory development.

Regarding TV watching, the inclusion of the younger participants did not represent an important contribution to the weak negative associations between TV viewing and working memory reported in a previous study performed only in the older subcohort.⁹ Nevertheless, the variables "TV watching" and "other sedentary behaviors" were probably too general. We had no information about the content of the TV programs, which might be detrimental or beneficial for cognitive functions. For instance, early exposure to age-appropriate programs designed around an educational curriculum is associated with academic enhancement, whereas exposure to violent content is associated with poorer cognitive development.³³ We observed a negative association between sedentary behavior and working memory only in adolescent boys, with a statistically significant sex interaction. The different types of sedentary activities between boys and girls could be an explanation for this finding; however, we were not able to test this hypothesis based on our data. The variable "other sedentary behaviors" included a large variety of behaviors, such as solving puzzles, reading, playing with dolls, doing homework, or playing video games, which could affect cognitive development in different ways.¹⁰ Our observed lack of associations between sedentary behavior and working memory in the younger

subcohorts could be due to the heterogeneity of activities included in this question.

Our study has some limitations. First, some questions were not identical between subcohorts. In Valencia, the question about extracurricular physical activity included only 1 activity per day, whereas in Sabadell and in Gipuzkoa this question included up to 3 different activities per day. To account for these differences by region, we used dichotomous variables split by subcohort-specific medians. The limited question in Valencia could have led to misclassification, whereas the use of dichotomous instead of continuous variables could have reduced the precision of the results obtained. Second, one-half of the initial sample was lost to follow-up, which could have made selection bias possible. Our sample might have been more predisposed to participate in activities than the general population, leading to an underestimation of effects. Third, the reduced sample size in the sex-stratified analyses restricted the interpretation of our results. Fourth, residual confounding by unmeasured variables, such as household income, could explain, in part, the associations found in this study. Fifth, we did not have data on the TV program content, which is key for the cognitive consequences of screen time in children. Moreover, the general questions regarding sedentary behavior (ie, TV program content, type of sedentary activity) might have diluted possible longitudinal associations between specific sedentary activities and working memory. Furthermore, we did not explore whether current levels of physical activity mediated the associations or, on the contrary, the effects were independent of these levels. Finally, our measures of lifestyle habits were not objective, which might have resulted in misclassification, recall bias, or perceived desirability of responses. The use of objective measurements, such as accelerometers, could provide information on the intensity of physical activity, which has a key role in the potential to cause changes in the brain through cerebral oxygenation.

The main strength of this study was its prospective design with a long period between exposure and outcome measurements. The different ages of the samples in this study allowed us to compare different developmental periods. Our sample is part of a population-based birth cohort including different Spanish regions with diverse cultural and lifestyle habits. This diversity could increase the external validity of the study. Furthermore, this cohort allows studying the longitudinal effects of healthy lifestyles with longer time lapses, because the follow-ups assessing different health and cognitive outcomes were carried out consecutively. The cognitive instrument used to measure working memory in our study was validated in the Spanish general population.¹⁵ Although less comprehensive than formal neuropsychological assessment, the computerized tests provided an objective tool to characterize cognitive function.³⁴

In conclusion, this study showed that low physical activity levels at preschool age may be associated with poorer working memory performance at primary school age and that low physical activity levels at primary school age relate to lesser working memory in adolescents. These data indicate that physical activity habits at early ages may influence academic achievement. Our findings also suggest that highly intense and

structured physical activities are especially relevant for working memory development in adolescence. According to our results, early sedentary behavior may negatively influence later cognitive maturation at adolescence, but only in boys. These findings highlight the importance of promoting physical activity habits and reducing sedentary behaviors early in life for increasing the cognitive potential of children. Further studies should include larger sample sizes to compare the effects by sex at different ages, longer time periods between the exposure and the cognitive outcomes, and specific sedentary behavior questions and/or objective measurements of physical activity. A mediation analysis would be interesting to disentangle whether current physical activity levels mediated the associations found in this study or these habits at early ages have a permanent impact on the nervous system development. ■

We thank all the participants and collaborators of the INMA project and Raquel Garcia-Esteban (ISGlobal) for statistical support.

Submitted for publication Jan 19, 2017; last revision received Apr 17, 2017; accepted May 31, 2017

Reprint requests: Mónica López-Vicente, PhD, ISGlobal, C. Doctor Aiguader 88, 08003 Barcelona, Spain. E-mail: monica.lopez@isglobal.org

References

- World Health Organization (WHO). Physical activity strategy for the WHO European Region 2016-2025; 2015.
- Best JR. Effects of physical activity on children's executive function: contributions of experimental research on aerobic exercise. *Dev Rev* 2010;30:331-551.
- Best JR, Miller PH. A developmental perspective on executive function. *Child Dev* 2010;81:1641-60.
- Kamijo K, Pontifex MB, O'Leary KC, Scudder MR, Wu C-T, Castelli DM, et al. The effects of an afterschool physical activity program on working memory in preadolescent children. *Dev Sci* 2011;14:1046-58.
- Guiney H, Machado L. Benefits of regular aerobic exercise for executive functioning in healthy populations. *Psychon Bull Rev* 2013;20:73-86.
- Verburgh L, Königs M, Scherder EJA, Oosterlaan J. Physical exercise and executive functions in preadolescent children, adolescents and young adults: a meta-analysis. *Br J Sports Med* 2014;48:973-9.
- van der Niet AG, Smith J, Scherder EJA, Oosterlaan J, Hartman E, Visscher C. Associations between daily physical activity and executive functioning in primary school-aged children. *J Sci Med Sport* 2015;18:673-7.
- López-Vicente M, Fornis J, Esnaola M, Suades-González E, Álvarez-Pedrerol M, Robinson O, et al. Physical activity and cognitive trajectories in schoolchildren. *Pediatr Exerc Sci* 2016;28:431-8.
- O'Connor G, Piñero Casas M, Basagaña X, López-Vicente M, Dadvand P, Torrent M, et al. Television viewing duration during childhood and long-term association with adolescent neuropsychological outcomes. *Prev Med Rep* 2016;4:447-52.
- Syväoja HJ, Tammelin TH, Ahonen T, Kankaanpää A, Kantamaa MT. The associations of objectively measured physical activity and sedentary time with cognitive functions in school-aged children. *PLoS ONE* 2014;9:e103559.
- Pujol J, Fenoll R, Fornis J, Harrison BJ, Martínez-Vilavella G, Macià D, et al. Video gaming in school children: how much is enough? *Ann Neurol* 2016;80:424-33.
- Ortega FB, Konstabel K, Pasquali E, Ruiz JR, Hurtig-Wennlöf A, Mäestu J, et al. Objectively measured physical activity and sedentary time during childhood, adolescence and young adulthood: a cohort study. *PLoS ONE* 2013;8:e60871.
- Guxens M, Ballester F, Espada M, Fernández MF, Grimalt JO, Ibarluzea J, et al. Cohort profile: the INMA-Infancia y Medio Ambiente- (Environment and Childhood) project. *Int J Epidemiol* 2012;41:930-40.

14. Vuontela V, Steenari M-R, Carlson S, Koivisto J, Fjällberg M, Aronen ET. Audiospatial and visuospatial working memory in 6-13 year old school children. *Learn Mem* 2003;10:74-81.
15. Fornis J, Esnaola M, López-Vicente M, Suades-González E, Alvarez-Pedrerol M, Julvez J, et al. The n-back test and the attentional network task as measures of child neuropsychological development in epidemiological studies. *Neuropsychology* 2014;28:519-29.
16. López-Vicente M, Fornis J, Suades-González E, Esnaola M, García-Esteban R, Álvarez-Pedrerol M, et al. Developmental trajectories in primary schoolchildren using n- back task. *Front Psychol* 2016;7:716.
17. Moisala M, Salmela V, Hietajärvi L, Carlson S, Vuontela V, Lonka K, et al. Gaming is related to enhanced working memory performance and task-related cortical activity. *Brain Res* 2017;1655:204-15.
18. McDonald JF, Moffitt RA. The uses of tobit analysis. *Rev Econ Stat* 1980;62:318-21.
19. Verloigne M, Van Lippevelde W, Maes L, Yıldırım M, Chinapaw M, Manios Y, et al. Levels of physical activity and sedentary time among 10- to 12-year-old boys and girls across 5 European countries using accelerometers: an observational study within the ENERGY- project. *Int J Behav Nutr Phys Act* 2012;9:34.
20. Chaddock-Heyman L, Erickson KI, Voss MW, Knecht AM, Pontifex MB, Castelli DM, et al. The effects of physical activity on functional MRI activation associated with cognitive control in children: a randomized controlled intervention. *Front Hum Neurosci* 2013;7:72.
21. Chaddock L, Erickson KI, Prakash RS, Kim JS, Voss MW, Vanpatter M, et al. A neuroimaging investigation of the association between aerobic fitness, hippocampal volume, and memory performance in preadolescent children. *Brain Res* 2010;1358:172-83.
22. Weinstein AM, Voss MW, Prakash RS, Chaddock L, Szabo A, White SM, et al. The association between aerobic fitness and executive function is mediated by prefrontal cortex volume. *Brain Behav Immun* 2012;26:811-9.
23. Schaeffer DJ, Krafft CE, Schwarz NF, Chi L, Rodrigue AL, Pierce JE, et al. An 8- month exercise intervention alters frontotemporal white matter integrity in overweight children. *Psychophysiology* 2014;51:728-33.
24. Krafft CE, Schaeffer DJ, Schwarz NF, Chi L, Weinberger AL, Pierce JE, et al. Improved frontoparietal white matter integrity in overweight children is associated with attendance at an after-school exercise program. *Dev Neurosci* 2014;36:1-9.
25. Vaynman S, Gomez-Pinilla F. Revenge of the “sit”: how lifestyle impacts neuronal and cognitive health through molecular systems that interface energy metabolism with neuronal plasticity. *J Neurosci Res* 2006;84:699-715.
26. Leckie RL, Oberlin LE, Voss MW, Prakash RS, Szabo-Reed A, Chaddock-Heyman L, et al. BDNF mediates improvements in executive function following a 1-year exercise intervention. *Front Hum Neurosci* 2014;8:985.
27. Brown AD, McMorris CA, Longman RS, Leigh R, Hill MD, Friedenreich CM, et al. Effects of cardiorespiratory fitness and cerebral blood flow on cognitive outcomes in older women. *Neurobiol Aging* 2010;31:2047-57.
28. Martínez-Gómez D, Ruiz JR, Gómez-Martínez S, Chillón P, Rey-López JP, Díaz LE, et al. Active commuting to school and cognitive performance in adolescents: the AVENA study. *Arch Pediatr Adolesc Med* 2011;165:300-5.
29. Kwak L, Kremers SPJ, Bergman P, Ruiz JR, Rizzo NS, Sjöström M. Associations between physical activity, fitness, and academic achievement. *J Pediatr* 2009;155:914-8, e1.
30. Autry AE, Adachi M, Cheng P, Monteggia LM. Gender-specific impact of brain- derived neurotrophic factor signaling on stress-induced depression-like behavior. *Biol Psychiatry* 2009;66:84-90.
31. Santaliestra-Pasías AM, Mouratidou T, Verbestel V, Bammann K, Molnar D, Sieri S, et al. Physical activity and sedentary behaviour in European children: the IDEFICS study. *Public Health Nutr* 2013;1-12.
32. Hallal PC, Wells JCK, Reichert FF, Anselmi L, Victora CG. Early determinants of physical activity in adolescence: prospective birth cohort study. *BMJ* 2006;332:1002-7.
33. Schmidt ME, Vandewater EA. Media and attention, cognition, and school achievement. *Future Child* 2008;18:63-85.
34. Letz R. Use of computerized test batteries for quantifying neurobehavioral outcomes. *Environ Health Perspect* 1991;90:195-8.

Extracurricular physical activity

Menorca:

In his/her free time, including extracurricular sport activities, how long does your child spend exercising or playing sports?

Less than ½ hour/day, ½ to 1 hour/day, 1 hour/day, 2 hours/day, 3 hours/day, 4 or more hours/day^a

Gipuzkoa and Sabadell:

During a typical week, how long does your child usually practice extracurricular physical activity in each day, (eg, dance/swim lessons) or simply play, run, cycle, skate, swim, etc (to exclude Wii and trip to school). Specify the activities.

Valencia:

How long does your child usually practice extracurricular organized physical activity (eg, dance/swim lessons) or non-organized as playing outdoors, cycle, run, jump, skate, swim, gym, etc (to exclude Wii and trip to school).

TV watching

Menorca:

How many hours does your child watch TV per week?

Gipuzkoa and Sabadell:

How many hours does your child watch TV/videos per day?

a. During week days: hours and minutes

b. Weekends: hours and minutes

Valencia:

How many hours does your child watch TV/videos per day?

a. During week days: never or almost never, less than ½ hour per day, between ½ and less than 1 hour/day, 1 hour/day, 2 hours/day, 3 hours/day, 4 or more hours/day^bb. Weekends: never or almost never, less than ½ hour per day, between ½ and less than 1 hour/day, 1 hour/day, 2 hours/day, 3 hours/day, 4 or more hours/day^b**Other sedentary behaviors**

Menorca:

In his/her free time, how long he/she spend watching TV, videos, sedentary games, reading or playing in the computer?

Less than 1 hour/day, 1 hour/day, 2 hours/day, 3 hours/day, 4 hours/day, 5 hours/day, 6 or more hours/day^c

Gipuzkoa and Sabadell:

Out of school, how long per day does your child spend in sedentary games or activities (eg, puzzles, books, dolls, homework, computer/video games)?

Exclude TV/videos and Wii-sports.

a. During week days: hours and minutes

b. During weekend: hours and minutes

Valencia:

Out of school, how long per day does your child spend in sedentary games or activities (eg, puzzles, books, dolls, homework, computer/video games)?

Exclude TV/videos and Wii-sports.

a. During week days: almost never, 1 hour/day, 2 hours/day, 3 hours/day, 4 hours/day, 5 hours/day, 6 or more hours/day^db. Weekends: almost never, 1 hour/day, 2 hours/day, 3 hours/day, 4 hours/day, 5 hours/day, 6 or more hours/day^d

Transformations of categorical variables to continuous variables:

^a Less than ½ hour/day	20 min/d
½ to 1 hour/day	45 min/d
1 hour/day	1 h/d
2 hours/day	2 h/d
3 hours/day	3 h/d
4 or more hours/day	4 h/d
^b Never or almost never	0.1 h/d
Less than ½ hour per day	20 min/d
Between ½ and less than 1 hour/day	45 min/d
1 hour/day	1 h/d
2 hours/day	2 h/d
3 hours/day	3 h/d
4 or more hours/day	4 h/d
^c Less than 1 hour/day	30 min/d
1 hour/day	1 h/d
2 hours/day	2 h/d
3 hours/day	3 h/d
4 hours/day	4 h/d
5 hours/day	5 h/d
6 or more hours/day	6 h/d
^d Almost never	0.1 h/d
1 hour/day	1 h/d
2 hours/day	2 h/d
3 hours/day	3 h/d
4 hours/day	4 h/d
5 hours/day	5 h/d
6 or more hours/day	6 h/d

Appendix. Questionnaires.