Journal of Developmental & Behavioral Pediatrics

Sleeping, TV, Cognitively-stimulating Activities, Physical Activity, and ADHD Symptom Incidence in Children. A Prospective Study

--Manuscript Draft--

Manuscript Number:	JDBP17-140R2
Full Title:	Sleeping, TV, Cognitively-stimulating Activities, Physical Activity, and ADHD Symptom Incidence in Children. A Prospective Study
Short Title:	Lifestyle factors and ADHD incidence in children
Article Type:	Original Study
Corresponding Author:	Judith Garcia-Aymerich, PhD, MD Barcelona, Barcelona SPAIN
Corresponding Author Secondary Information:	
Corresponding Author's Institution:	
Corresponding Author's Secondary Institution:	
First Author:	Gabriela Prado Peralta, MSc
First Author Secondary Information:	
Order of Authors:	Gabriela Prado Peralta, MSc
	Joan Forns, PhD
	Manuela García de la Hera, MPH, PhD
	Llúcia González, MSc
	Mònica Guxens, MD, PhD
	Mónica López-Vicente, PhD
	Jordi Sunyer, MD, PhD
	Judith Garcia-Aymerich, MD, PhD
Order of Authors Secondary Information:	
Abstract:	Objective: To analyze associations between time spent sleeping, watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity, all at 4 years, and (i) attention-deficit/ hyperactivity disorder (ADHD) symptoms and (ii) behavior problems, both assessed at 7 years, in ADHD-free children at baseline. Method: In total, 817 participants of the INfancia y Medio Ambiente birth cohort, without ADHD at baseline, were included. At the 4-year follow-up, parents reported the time that their children spent sleeping, watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity. At the 7-year follow-up, parents completed the Conner's Parent Rating Scales and the Strengths and Difficulties Questionnaire, which measure ADHD symptoms and behavior problems, respectively. Negative binomial regression models were used to assess associations between the activities at 4 years and ADHD symptoms and behavior problems at 7 years. Results: Children (48% girls) spent a median (p25-p75) of 10 (10-11) h/day sleeping, 1.5 (0.9-2) h/day watching TV, 1.4 (0.9-1.9) h/day engaging in cognitively-stimulating activities, and 1.5 (0.4-2.3) h/day engaging in physical activity. Longer sleep duration (>10h/d) was associated with a lower ADHD symptom score (adjusted incidence rate ratio=0.97, 95% CI=0.95-1.00). Longer time spent in cognitively-stimulating activities (>1h/d) was associated with lower scores of both ADHD symptoms (0.96, 0.94-0.98) and behavior problems (0.89, 0.83-0.97). Time spent watching TV and engaging in physical activity were not associated with either outcome.

Powered by Editorial Manager® and ProduXion Manager® from Aries Systems Corporation

	Conclusions: A shorter sleep duration and less time spent in cognitively-stimulating activities were associated with an increased risk of developing ADHD symptoms and behavior problems.
Additional Information:	
Question	**Response**
This manuscript has been seen, reviewed, and approved by all contributing authors.	Yes
At least one author (e.g. the lead author) had complete access to all data in the study. He/she takes responsibility for the integrity of the data and the accuracy of any data analysis.	Yes
Are there any potential conflicts of interest?	No
Is the first author is eligible for the SDBP Young Investigator Manuscript Award? If the first author is a trainee, or has completed post-doctoral training within 3 years of the date of submission of the paper, the author is eligible for consideration for the Young Investigator Manuscript Award. For the purpose of this award, "trainee" is defined as an undergraduate or medical student, pediatric resident, fellow in pediatrics, or graduate student or post-graduate clinical trainee in psychology or an allied health profession (e.g., nursing, speech/language therapy, occupational or physical therapy).	Yes
Have the contents of the manuscript, in any form, been published elsewhere? Copies of any closely related publications should be provided at the time of manuscript submission.	No
Is the manuscript currently submitted elsewhere?	No
Please provide the WORD COUNT (not character count) of the text of your manuscript, excluding abstract and references.	3163
Was the first author a trainee during this project?	Yes, the first author was a Masters Student

Barcelona, November 7th, 2017

Dear Editor,

Thank you for your letter accepting the manuscript entitled "Sleeping, TV, Cognitively-stimulating Activities, Physical Activity, and ADHD Symptom Incidence in Children. A Prospective Study". The comments and suggestions that the Editors and Reviewers provided are very much appreciated, and have improved the manuscript substantially.

We have made all the changes that Editors and Reviewers have suggested, which are appropriately specified in the response to Reviewers form and in the highlighted version of the manuscript. We would be willing to make further changes if you felt them necessary to improve the manuscript.

We certify that this submission is an original work and is not under consideration at any other journal. Principle and corresponding authors have full access to all of the data in the study and have the right to publish such data. All authors have participated in a meaningful way in the preparation of this revised version of the manuscript and have approved its submission to the Journal of Developmental and Behavioral Pediatrics. All authors declare that they do not have any conflict of interest.

Sincerely, on behalf of the authors,

Judith Garcia-Aymerich, MD, PhD
ISGlobal, Centre for Research in Environmental Epidemiology (CREAL)
Doctor Aiguader 88, 08003 Barcelona, Spain
Email: judith.garcia@isglobal.org
Tel. (+34) 93 214 73 40

Title: Sleeping, TV, Cognitively-Stimulating Activities, Physical Activity, and ADHD Symptom Incidence in Children. A Prospective Study

Running Head: Lifestyle factors and ADHD incidence in children

Authors: Gabriela P Peralta, MSc [1,2,3], Joan Forns, PhD [1,2,3], Manuela García de la Hera, MPH, PhD [3,4], Llúcia González, MSc [5,6], Mònica Guxens, MD [1,2,3,7], Mónica López-Vicente, PhD [1,2,3,8], Jordi Sunyer, MD, PhD [1,2,3,8], and Judith Garcia-Aymerich, MD, PhD [1,2,3]

Authors' Affiliations:

[1] ISGlobal, Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain.

[2] Universitat Pompeu Fabra (UPF), Barcelona, Spain.

[3] CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain

[4] Department of Public Health, Miguel Hernandez University, Campus San Juan, Alicante, Spain

[5] Universitat Jaume I de Castelló, Castelló, Spain

[6] Unidad Mixta de Investigación en Epidemiología, Ambiente y Salud FISABIO-Universitat Jaume I -Universitat de València, Valencia, Spain

[7] Department of Child and Adolescent Psychiatry/Psychology, Erasmus University Medical Centre–Sophia Children's Hospital, Rotterdam, The Netherlands

[8] IMIM (Hospital del Mar Medical Research Institute), Barcelona, Spain

Corresponding Author: Judith Garcia-Aymerich. ISGlobal, Centre for Research in Environmental Epidemiology (CREAL), Doctor Aiguader, 88, 08003 Barcelona, Spain. E-mail address: judith.garcia@isglobal.org, Tel.: (+34) 93 214 73 40,
Fax: (+34) 93 217 73 02

Conflicts of Interest and Source of Funding: The authors have no conflicts of interest to disclose

Acknowledgements: The authors would particularly like to thank all INMA cohort participants for their generous collaboration. A full roster of the INMA Project Investigators can be found at http://www.proyectoinma.org/presentacion-inma/listado-investigadores/en_listado-investigadores.html

Funding: This study was funded by grants from EU Commission (FP7-ENV-2011 cod 282957, HEALTH.2010.2.4.5-1, and 261357), and from Spain: Instituto de Salud

Carlos III (Red INMA G03/176, CB06/02/0041, PI041436, PI081151 incl. FEDER funds; FIS-FEDER 03/1615, 04/1509, 04/1112, 04/1931, 05/1079, 05/1052, 06/1213, 07/0314, 09/02647, 11/0178, 11/01007, 11/02591, 11/02038, 13/1944, 13/2032, 14/0891, 14/1687, and MS13/00054), CIBERESP, Generalitat de Catalunya-CIRIT 1999SGR 00241, Generalitat de Catalunya-AGAUR 2009 SGR 501, Fundació La marató de TV3 (090430), and the Conselleria de Sanitat, Generalitat Valenciana.

Title: Sleeping, TV, Cognitively-stimulating Activities, Physical Activity, and ADHD Symptom Incidence in Children. A Prospective Study

Conflicts of Interest and Source of Funding: The authors have no conflicts of interest to disclose

Sleeping, TV, Cognitively-stimulating Activities, Physical Activity, and ADHD Symptom Incidence in Children. A Prospective Study
JDBP17-140R2

Response to Reviewers Instructions:
Please use the table below to document the Response to Reviewers. Copy and paste the editor and reviewers' comments verbatim into the "Comments" column and insert your responses to the specific comment in the corresponding "Response" column. Please use one row per question. Make sure to list the page and line reference where your change can be found, if changes were made to the manuscript. Please also highlight the changes in the Highlighted Manuscript file. If no change was made, please make sure to note this in your response, including your reasoning. You may delete the example row and insert or delete rows to these tables as needed.

Responses to Editor Comments

COMMENTS	RESPONSE	LOCATION OF CHANGE	CHANGES APPROVED? For Editorial Use Only
1. In addition to addressing the Reviewer's comments, please also justify the rationale for using generalized additive models for determining if variables should be categorical or continuous (…)	We thank the Editor for their comment. First, we would like to clarify that the decision to use the predictor variables as categorical variables was not based only on the results of the generalized additive models (GAMs). Rather, we first considered the existing recommendations for children and the fact that the use of categorical variables would facilitate the interpretation of our results. This has been clarified in the revised version of the manuscript. GAMs are powerful models for estimating the relationship between continuous predictor variables and outcomes with no need to make any assumptions about the shape of this relationship [1]. These models plot a relationship graphically, which allows an analyst to examine the shape of the relationship and decide whether two variables may be linearly related (and thus can be used as continuous variables) or whether there is a cut-off point at which the relationship between the variables changes (and then it is better to use categorical variables). With the aim of keeping the manuscript clear, we would prefer not to provide these details relating to the GAM models in the Statistical Analysis section. However, we would be happy to add this information if the Editor thinks the revised version is not sufficiently clear. We have modified the manuscript as follows: *Statistical Analysis* *A priori to any modeling, we decided to use all exposure variables as categorical variables in the main analysis and as continuous variables in sensitivity analyses. This decision was primarily based on existing recommendations [1–3] (which facilitates the interpretation of the results in terms of public health relevance) and is supported by the results of the generalized additive models (GAMs). The GAMs*	Page 5, lines 132-143	

	suggested generally linear trends between time spent watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity with the CPRS ADHD Index and the SDQ Total Difficulties Score. However, the GAM for the association between time spent sleeping and the CPRS ADHD Index and the SDQ Total Difficulties Score showed an inflection point at 10 hours per day, which suggests that entering time spent sleeping as a continuous variable into the models for our outcome variables could hide potential true associations. Response reference: 1. Hastie T, Tibshirani R. Generalized Additive Models. London: Chapman & Hall; 1990.		
2. (…) and the use of negative binomial regression in the analyses	We used negative binomial regression models because both the CPRS ADHD index score and the SDQ total difficulties score are over-dispersed count variables. The Editors and Reviewers can see the distribution of these variables at the end of this document (Annex 1). Poisson regression models are commonly used with count variables, but these models cannot be used with over-dispersed count variables. With this latter type of variable, negative binomial regression models are needed, which can be considered as a generalization of Poisson regression but with an extra parameter to model over-dispersion [1,2]. We tested the goodness of fit of our models using the likelihood-ratio test, which compares the negative binomial regression model to a Poisson regression model. In all analyses, this test confirmed that the use of the negative binomial regression was preferred. The reason for the use of negative binomial regression models was mentioned in the Statistical Analysis section of the previous version of the manuscript, however we have made small changes to make this point clearer. Also, we have added a new reference to the manuscript that explains why negative regression models should be used with over-dispersed count variables. <u>Statistical Analysis</u> *Negative binomial regression models were used to assess the association between each exposure variable and ADHD symptoms (CPRS scores) and behavior problems (SDQ scores), because the outcome variables were over-dispersed count variables [23].* <u>References:</u> *23. Gardner W, Mulvey EP, Shaw EC. Regression Analyses of Counts and Rates: Poisson, Overdispersed Poisson, and Negative Binomial Models. Psychol Bull. 1995;118(3):392-404*	Page 6, lines 154-155 Page 13, lines 361-363	

	Response reference: 1. Negative binomial regression. Stata data analysis examples. UCLA: Statistical Consulting Group. Available at: https://stats.idre.ucla.edu/stata/dae/negative-binomial-regression/. Accessed October 31, 2017 2. Gardner W, Mulvey EP, Shaw EC. Regression Analyses of Counts and Rates: Poisson, Overdispersed Poisson, and Negative Binomial Models. *Psychol Bull*. 1995;118(3):392-404		

Responses to Reviewer 1

COMMENTS	RESPONSE	LOCATION OF CHANGE	CHANGES APPROVED? For Editorial Use Only
1. The authors are to be commended for their close attention to the concerns raised by the reviewers and their detailed response with quite significant changes in the revised manuscript, including "toning down" the conclusion. The use of the term "cognitively stimulating activities" is much more accurately descriptive than the previous "sedentary activities." I still have some concern about the difference between statistical significance and clinical relevance but the authors have added extensive justification for the potentially large effects at the population level.	We thank Reviewer 1 for their positive appraisal.		

Responses to Reviewer 2

COMMENTS	RESPONSE	LOCATION OF CHANGE	CHANGES APPROVED? For Editorial Use Only
1. The manuscript is significantly improved from the earlier version and the authors have done a good job of addressing most of the reviewers concerns.	We thank Reviewer 2 for their positive comment.		
2. I appreciate that the authors now adjust the analysis for the age 4 ADHD symptoms, but exactly how they do that is not completely clear. They don't	We agree with the Reviewer that this point was not clear in the manuscript. For model adjustment, we used the number of ADHD symptoms reported by the teacher at the assessment done at age 4 years.		

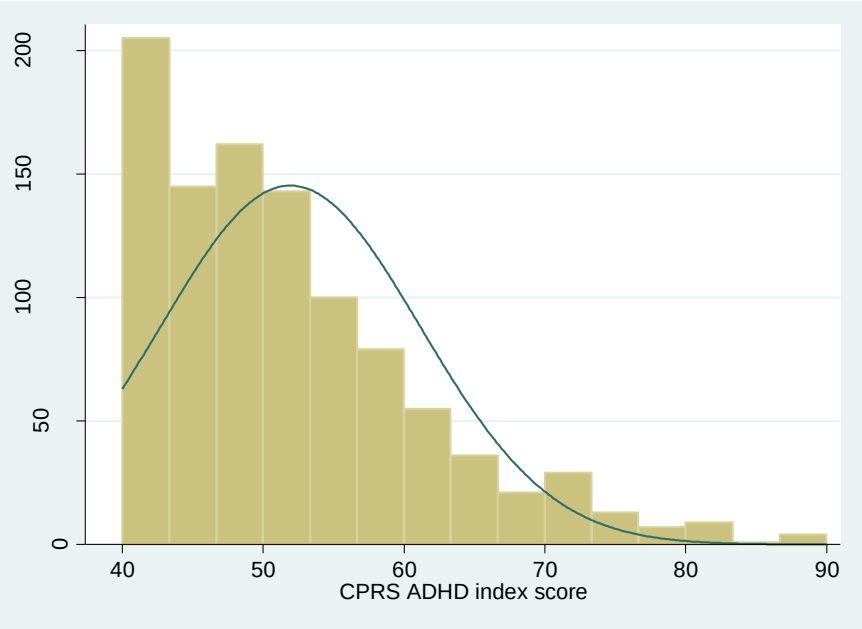
state in the manuscript whether they use the number of teacher reported ADHD symptoms, total score on an DSM ADHD rating scale, or a standardized score on the rating scale at age 4.	We have clarified this point in several parts of the manuscript: *Behavior assessment* We used the number of symptoms reported in the ADHD-DSM-IV form by each child's teacher as a key covariate in the final models to account for potential reverse causation. *Statistical Analysis* All models were additionally adjusted for the number of symptoms reported in the ADHD-DSM-IV form by each child's teacher at baseline to account for potential reverse causation. *Results* After adjustment for child sex, duration of breastfeeding, maternal smoking during pregnancy, maternal smoking when the child was 4 years, maternal education, maternal IQ, maternal mental health, paternal education, child daycare/nursery attendance before school, baseline child neuropsychological conditions, number of ADHD-DSM-IV symptoms at baseline, and region, the association between time spent sleeping and ADHD symptoms, as well as between time spent engaging in cognitively-stimulating activities and ADHD symptoms and behavior problems remained statistically significant (Table 3). We have also clarified this information in Table 1, footnotes of Table 3 and in the supplemental digital content (footnotes of Tables 3 to 7)	Page 4, lines 95-96 Page 6, lines 168-169 Page7, lines 196-197	
3. One reviewer comment that is not sufficiently addressed in the manuscript is the response to comment #5 from Reviewer 2. In the response to the reviewer the authors note that 97% of children are enrolled in preschool with a fairly standardized curriculum. This is not mentioned in the paper, but seems like an important point as the impact of low levels of cognitively stimulating activities or physical activity might be different in an environment in which children were not attending preschool. This limit on the generalizability of the findings needs to be included in the discussion.	We agree with the Reviewer that the characteristics of our study setting may limit the broad generalizability of our findings. However, the Authors' opinion is that although our results may not be applicable everywhere, they are likely to be relevant to developed countries with right rates of preschool attendance. Of note, in 2012, 93.9% of children aged between 4 years and the starting age of compulsory education attended preschool programs in the European Union Member States [1]. We have included the following in the manuscript: *Discussion (limitations)* *Fourth, although attendance to school at age 4 years is not compulsory in our study area, it is very common and the educational programs are fairly standardized. This may limit the broad generalizability of our findings to other geographical areas with different educational norms and programs.*	Page 9-10, lines 280-284	

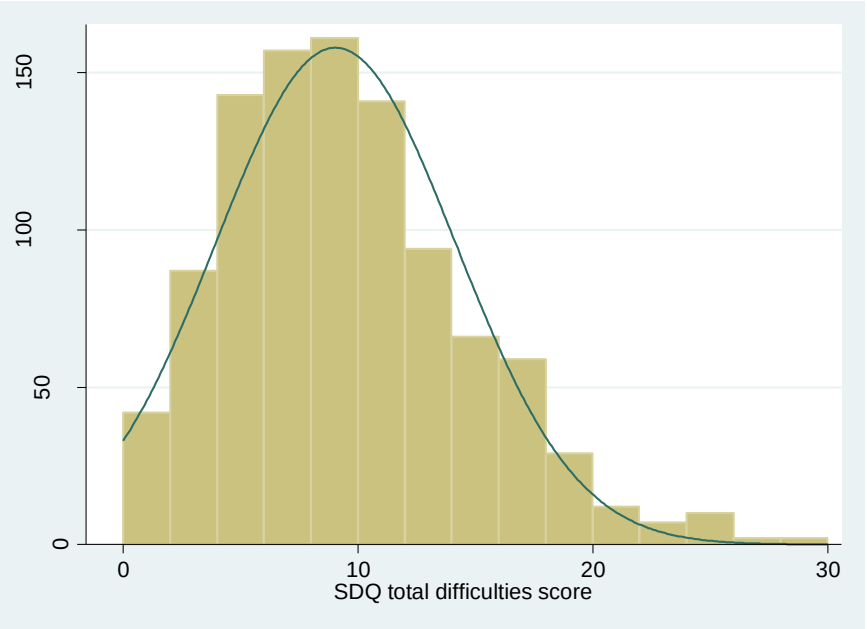
	Response reference: 1. Being young in Europe today - education - Statistics Explained. Available at: http://ec.europa.eu/eurostat/statistics-explained/index.php/Being_young_in_Europe_today_-_education#Further_Eurostat_information. Accessed October 31, 2017		
4. I found the authors description of their measure of ADHD as a measure of "symptom incidence" confusing. This is a measure from the CPRS which combines both the presence of symptoms and the severity of symptoms (and thus is not solely a measure of incidence). I would prefer the term "ADHD symptom score" or something similar.	We agree with the Reviewer. The description of the ADHD measure has been modified in several parts of the manuscript: *Abstract* *Objective: To analyze associations between time spent sleeping, watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity, all at 4 years, and (i) attention-deficit/ hyperactivity disorder (ADHD) symptoms and (ii) behavior problems, both assessed at 7 years, in ADHD-free children at baseline.* *Results: (…) Longer sleep duration (>10h/d) was associated with a lower ADHD symptom score (adjusted incidence rate ratio=0.97, 95% CI=0.95-1.00). Longer time spent in cognitively-stimulating activities (>1h/d) was associated with lower scores of both ADHD symptoms (0.96, 0.94-0.98) and behavior problems (0.89, 0.83-0.97).* *Introduction (objective)* *To analyze associations between time spent sleeping, watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity, all at 4 years, and (i) ADHD symptoms and (ii) behavior problems, both assessed at 7 years, in ADHD-free children at baseline* *Results* *A shorter sleep duration and a shorter time spent engaging in cognitively-stimulating activities at age 4 years were associated with a higher ADHD symptom score at age 7 years.* *Discussion* *This study is the first to demonstrate associations between a longer time spent engaging in cognitively-stimulating activities and lower scores of both ADHD symptoms and behavior problems, in ADHD-free children at baseline. We also found that sleeping longer was associated with a lower ADHD symptom score. In contrast, time spent watching TV and time spent engaging in physical activity at age 4 years were not associated with ADHD symptoms or behavior problems at age 7 years, nor was there any evidence of interactions between the several exposures considered.* *(…)* *The associations between higher time spent in cognitively-stimulating activities and lowers scores of both ADHD symptoms and behavior problems are supported by previous studies which reported*	Page 1, lines 4-5 Page1, lines 17 and 19 Page 2, lines 52-53 Page 7, line 190 Page 7-8, lines 212-218 Page 8, lines 219-220	

	associations between playing, reading or being read to, and positive cognitive development[9,24]. *(…)* *The association we observed between a longer sleep duration and a lower ADHD symptom score is in concordance with previous similar longitudinal studies, which included children of diverse age ranges (from 3 to 11 years)[6,26], thereby adding to the consistency of the findings.* *(…)* *We found no association between time spent watching TV during early childhood and scores of either ADHD symptoms or behavior problems by school age.* *(…)* *Our study is the first to assess the longitudinal association between physical activity (at 4 years) and scores of ADHD symptoms and behavior problems (at 7 years), and we found no indication of an existing association.*	Page 8, lines 232-233 Page 9, lines 252-253 Page 9, lines 260-261	
5. I would recommend that in the discussion the authors remind the reader that the results apply to a very specific hypothesis that exposures at age 4 are associated with symptoms at age 7. For example in the first paragraph of the discussion the authors could clarify their results by saying, "In contrast, time spent watching TV and time spent engaging in physical activity at age 4 were not associated with ADHD symptoms or behavior problems at age 7, nor was there…." Similar clarification might be helpful in the discussion of the results related to physical activity as there study does not address the question of whether activity and sports participation at age 7 is associated with decreased ADHD symptoms or behavior problems in 7 year olds.	We thank the Reviewer for their recommendation. The discussion has been modified as follows: <u>Discussion</u> *In contrast, time spent watching TV and time spent engaging in physical activity at age 4 years were not associated with ADHD symptoms or behavior problems at age 7 years, nor was there any evidence of interactions between the several exposures considered.* *(…)* *Our study is the first to assess the longitudinal association between physical activity (at 4 years) and scores of ADHD symptoms and behavior problems (at 7 years), and we found no indication of an existing association.*	Pages 7-8, lines 216-217 Page 9, lines 260-261	
6. Page 9 line 271-274: I am not sure what evidence there is that parents of children with ADHD are more likely to misclassify their children as sleeping less or being more physically active. If this is true it needs a reference.	We understand the Reviewer's concern about this statement since there is no published evidence that parents of children with ADHD are more likely to misclassify their children as sleeping less or being more physically active. However, the general opinion of the Authors' is that because ADHD is characterized by a pattern of hyperactivity-impulsivity, in addition to inattention, parents may be more likely to associate these symptoms to being more physically active in non-structured activities, such as running or jumping. Also, these symptoms		

	could make parents think that their children have more problems going to bed, and consequently, sleep less. To clarify that this point is only the hypothesis of the Authors', we have modified this statement as follows: *<u>Discussion (limitations)</u>* *Furthermore, the misclassification may be differential for ADHD symptoms as parents of children with ADHD symptoms may be more likely to report that their children sleep less hours or are more physically active.*	Page 9, lines 273-274	

Annex 1. Distribution of the CPRS ADHD index score and the SDQ total difficulties score.





ABSTRACT

Objective: To analyze associations between time spent sleeping, watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity, all at 4 years, and (i) attention-deficit/ hyperactivity disorder (ADHD) symptoms and (ii) behavior problems, both assessed at 7 years, in ADHD-free children at baseline.

Method: In total, 817 participants of the INfancia y Medio Ambiente birth cohort, without ADHD at baseline, were included. At the 4-year follow-up, parents reported the time that their children spent sleeping, watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity. At the 7-year follow-up, parents completed the Conner's Parent Rating Scales and the Strengths and Difficulties Questionnaire, which measure ADHD symptoms and behavior problems, respectively. Negative binomial regression models were used to assess associations between the activities at 4 years and ADHD symptoms and behavior problems at 7 years.

Results: Children (48% girls) spent a median (p25-p75) of 10 (10-11) h/day sleeping, 1.5 (0.9-2) h/day watching TV, 1.4 (0.9-1.9) h/day engaging in cognitively-stimulating activities, and 1.5 (0.4-2.3) h/day engaging in physical activity. Longer sleep duration (>10h/d) was associated with a lower ADHD symptom score (adjusted incidence rate ratio=0.97, 95% CI=0.95-1.00). Longer time spent in cognitively-stimulating activities (>1h/d) was associated with lower scores of both ADHD symptoms (0.96, 0.94-0.98) and behavior problems (0.89, 0.83-0.97). Time spent watching TV and engaging in physical activity were not associated with either outcome.

Conclusions: A shorter sleep duration and less time spent in cognitively-stimulating activities were associated with an increased risk of developing ADHD symptoms and behavior problems.

Keywords: ADHD**;** behavior problems; physical activity; sleep; cognitively-stimulating activities

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is considered the most common childhood neurobehavioral disorder, with a worldwide prevalence of 5% in children and adolescents[1]. It is characterized by an age-inappropriate pattern of inattention and/or hyperactivity–impulsivity[2]. ADHD symptoms are associated with academic difficulties[3] and with an increased risk of other comorbid behavior problems[4]. The etiology of ADHD is complex as it is influenced by both genetic and non-genetic factors, such as smoking during pregnancy or duration of breastfeeding, as well as their interplay[5]. Moreover, some lifestyle factors have been associated with ADHD symptoms. Sleeping less than 9 hours at 2.5 years of age was related to a higher risk of ADHD symptoms at 6 years[6]. Continued high TV exposure was also associated with the incidence of ADHD-related symptoms in both preschool and school-aged children in studies with 1-year follow-ups[7,8]. However, there is a lack of knowledge regarding the role of other relevant lifestyle factors on the incidence of ADHD symptoms. Cognitively-stimulating activities, such as reading or doing puzzles, have not yet been studied, despite the fact that these are common childhood activities and that they might have positive effects on child development [9]. Similarly, although exercise interventions have been found to be effective at mitigating ADHD symptoms in children with this disorder[10], and involvement in sports has been cross-sectionally related to fewer behavior problems[11], no study has longitudinally analyzed the role of physical activity on the incidence of ADHD symptoms. Furthermore, the joint effect of such lifestyle factors has not yet been assessed, despite their close relation, e.g., a higher time spent watching TV may come at the cost of less sleep[12].

The objective of the current study was to analyze associations between time spent sleeping, watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity, all at 4 years, and (i) ADHD symptoms and (ii) behavior problems, both assessed at 7 years, in ADHD-free children at baseline.

METHOD

Study Design and Participants

We used data from two regions of the Spanish longitudinal birth cohort INMA - INfancia y Medio Ambiente [Environment and Childhood]

(http://www.proyectoinma.org). The criteria for inclusion and details of the data collection have been described elsewhere [13]. Briefly, between November 2003 and July 2006, pregnant women were recruited while attending antenatal care and eventually, their children were included in the study. The children were followed-up at 1.5, 4, 7 and 9 years of age. The present study includes information covering age 4 years (set as our baseline visit) to 7 years (follow-up visit). Out of the 1147 children that attended the baseline visit at 4-years, we excluded: 4 prevalent ADHD cases (children with a doctor diagnosis of ADHD), 49 children without exposure data, 151 children without information about baseline ADHD symptoms, 108 children lost to follow-up by age 7 years, and 18 children without outcome data at the follow-up visit. Ultimately, 817 children (71% of the original sample) were included in the present analysis (see figure, Supplemental Digital Content 1, which illustrates the selection of study participants). The Ethics Committee of participating hospitals approved the study and all parents provided informed consent.

Measures

Lifestyle Factors Assessment

At age 4 years, we assessed the time children spent sleeping, watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity using a parent-completed questionnaire. Time spent sleeping was assessed with the question "How many hours per day does your child spend sleeping? Include nap time". Time spent watching TV was assessed with the question "How many hours per day does your child spend watching TV/videos?" Time spent engaging in cognitively-stimulating activities was assessed with the question "Outside school, how many hours per day does your child spend with games or other sedentary activities (for example: jigsaw puzzles, books, dolls, homework, or computer/videogames)? Exclude TV/videos and Wii sports". Finally, time spent engaging in physical activity was assessed with the question "How many hours per day does your child spend with structured extracurricular activities (as dance, swimming, etc.) or with non-structured activities (playing in the playground/park, cycling, running, jumping, skating, swimming, etc.). Exclude Wii sports and commute to school".

Behavior Assessment

Data on behavior problems, including ADHD, were collected at both age periods. At age 4 years, we used medical histories to assess a clinical diagnosis of ADHD (used to exclude prevalent ADHD cases at baseline). Additionally, each child's teacher completed the ADHD *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) (ADHD-DSM-IV) form[14]. This form is an internationally recognized list of 18 items designed to evaluate attention deficit, hyperactivity, and impulsivity symptoms in children. We used the number of symptoms reported in the ADHD-DSM-IV form by each child's teacher as a key covariate in the final models to account for potential reverse causation.

At age 7 years, we measured ADHD symptoms with the short form of the Conners' Parent Rating Scales (CPRS)[15], which assesses problematic behavior in children. The CPRS consists of 27 items that result into scores for three subscales (oppositional, cognitive problems/inattention, and hyperactivity) and an ADHD Index. The raw scores are transformed (T-Scores) to have a mean of 50 and a standard deviation of 10. A higher ADHD Index score indicates higher ADHD symptoms and a score above 65 is usually indicative of a clinically significant problem[16]. For the present study, the ADHD Index, as a continuous variable, was used as the main measure of ADHD symptoms. The subscales were used in secondary analyses.

The behavior development of the children was also assessed at 7 years using the parental version of the Strengths and Difficulties Questionnaire (SDQ)[17]. The SDQ consists of 25 items, which translate into individual scores for five subscales (emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems, and prosocial behavior) that range from 0 to 10 and a Total Difficulties Score that ranges from 0 to 40. The Total Difficulties Score is obtained by summing four of the five scales (emotional symptoms, conduct problems, hyperactivity/inattention, and peer relationship problems; prosocial behavior is excluded because it is a positive subscale), and a higher score is indicative of more behavior problems. A score of ≥17 is indicative of abnormal behavior problems[17]. For the present study, we used the Total Difficulties Score, as a continuous variable, as the main measure of behavior problems. The five subscales were used in secondary analyses.

Covariates

During pregnancy, at birth, and at age 1 year questionnaires or medical records were used to collect data on maternal and paternal education, maternal and paternal social class, any maternal smoking during pregnancy, any maternal alcohol use during pregnancy, child's sex, gestational age at birth, birth weight, and duration of any breastfeeding. The following information was also obtained by questionnaire when the children were 4 years: maternal smoking habits, maternal intelligence (using the similarities subtest of the Wechsler Adult Intelligence Scales 3rd edition (WAIS-III)[18] as a proxy of intelligence quotient (IQ)), maternal mental health (using the Symptom Check List- 90-R (SCL-90-R)[19]), child daycare/nursery attendance before school, and child neuropsychological conditions (defined as seeing a psychologist and/or having a neuropsychological diagnosis other than ADHD).

Statistical Analysis

A priori to any modeling, we decided to use all exposure variables as categorical variables in the main analysis and as continuous variables in sensitivity analyses. This decision was primarily based on existing recommendations [20–22] (which facilitates the interpretation of the results in terms of public health relevance) and is supported by the results of the generalized additive models (GAMs). The GAMs suggested generally linear trends between time spent watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity with the CPRS ADHD Index and the SDQ Total Difficulties Score. However, the GAM for the association between time spent sleeping and the CPRS ADHD Index and the SDQ Total Difficulties Score showed an inflection point at 10 hours per day, which suggests that entering time spent sleeping as a continuous variable into the models for our outcome variables could hide potential true associations. Thus, the cut-offs for time spent sleeping and watching TV were 10 h/day and 1h/day, respectively, according to recommendations set for preschoolers[20–22]. Time spent engaging in cognitively-stimulating activities was categorized as ≤1h/day and >1h/day, according to the data distribution. Finally, time spent engaging in physical activity was categorized as low, moderate, and high according to region-specific tertiles, as the data distribution for this variable differed by region.

We analyzed the differences in the distribution of the outcomes (ADHD symptoms and behavior problems) at age 7 years according to the exposures (sleep, TV, cognitively-stimulating activities, and physical activity) at age 4 years using U-Mann Whitney or

Kruskal-Wallis tests. Negative binomial regression models were used to assess the association between each exposure variable and ADHD symptoms (CPRS scores) and behavior problems (SDQ scores), because the outcome variables were over-dispersed count variables [23]. We performed a complete case analysis. Effect estimates are presented as incidence rate ratios (IRR) and their corresponding 95% confidence intervals. The IRR indicates the number of times that the CPRS ADHD Index/SDQ Total Difficulties Score is lower (IRR<1) or higher (IRR>1) than that of the reference group.

Based on the previous literature, we initially considered the following variables as potential confounders: children age, sex, birth weight, gestational age, duration of any breastfeeding, parents' social class, educational level, maternal IQ, maternal mental health, any maternal alcohol intake during pregnancy, any maternal smoking during pregnancy, maternal smoking when the child was 4 years, child daycare/nursery attendance before school, and child neuropsychological conditions at 4 years. Covariates were retained in the final model if they were statistically related to the outcome or modified the coefficient of any other covariate >10%. All models were additionally adjusted for the number of symptoms reported in the ADHD-DSM-IV form by each child's teacher at baseline to account for potential reverse causation. We tested goodness of fit of the models using the likelihood-ratio test.

We tested potential interactions between the exposure variables in the final models by using interaction terms. We performed several sensitivity analyses to assess the robustness of the results: the exposures were entered into the models as continuous variables, children with extreme exposure values were excluded, and children beyond the established cut-offs for ADHD symptoms and behavior problems were excluded. All statistical analyses were conducted with Stata 12.0 (Stata Corporation, College Station, Texas).

RESULTS

There were no differences in birth weight or gestational age between participants and non-participants. Non-participants had a lower duration of breastfeeding, maternal IQ, and parental educational level compared to participants (see table, Supplemental Digital Content 1, which compares the characteristics of participants and non-participants). The study population consisted of 817 children (418 boys and 399 girls). Children spent a median (p25-p75) of 10 (10-11) h/day sleeping, 1.5 (0.9-2) h/day watching TV, 1.4

(0.9-1.9) h/day engaging in cognitively-stimulating activities, and 1.5 (0.4-2.3) h/day engaging in physical activity (Table 1). The median score (p25-p75) of the ADHD Index and the Total Difficulties Score was 49 (45-56) and 8 (5-12), respectively (Table 1).

A shorter sleep duration and a shorter time spent engaging in cognitively-stimulating activities at age 4 years were associated with a higher ADHD symptom score at age 7 years. A longer time spent watching TV and a shorter time spent engaging in cognitively-stimulating activities were related to more behavior problems (Table 2). After adjustment for child sex, duration of breastfeeding, maternal smoking during pregnancy, maternal smoking when the child was 4 years, maternal education, maternal IQ, maternal mental health, paternal education, child daycare/nursery attendance before school, baseline child neuropsychological conditions, number of ADHD-DSM-IV symptoms at baseline, and region, the association between time spent sleeping and ADHD symptoms, as well as between time spent engaging in cognitively-stimulating activities and ADHD symptoms and behavior problems remained statistically significant (Table 3). However, time spent watching TV and engaging in physical activity at were no longer associated with either outcome.

Additional analyses using the CPRS and SDQ subscales indicated that a longer sleep duration was associated with a lower CPRS cognitive score, and a longer time spent engaging in cognitively-stimulating activities was associated with lower CPRS cognitive, CPRS hyperactivity, SDQ conduct problem, and hyperactivity/inattention problem scores (see tables, Supplemental Digital Content 2 and 3, which show results for all subscales of CPRS and SDQ).

We did not find statistically significant interactions between any of the exposure variables. Sensitivity analyses showed very similar estimates (see tables, Supplemental Digital Content 4 to 6, which show the results of each sensitivity analysis).

DISCUSSION

This study is the first to demonstrate associations between a longer time spent engaging in cognitively-stimulating activities and lower scores of both ADHD symptoms and behavior problems, in ADHD-free children at baseline. We also found that sleeping longer was associated with a lower ADHD symptom score. In contrast, time spent watching TV and time spent engaging in physical activity at age 4 years were not

associated with ADHD symptoms or behavior problems at age 7 years, nor was there any evidence of interactions between the several exposures considered.

The associations between higher time spent in cognitively-stimulating activities and lowers scores of both ADHD symptoms and behavior problems are supported by previous studies which reported associations between playing, reading or being read to, and positive cognitive development[9,24]. Although the mechanisms for these associations are still unclear, the context in which these activities occur may be important. Playing, reading or being read to may increase interactions with other children and/or with the parents, which in turn, have been related to a better cognitive development in school-aged children[25]. Unfortunately, as the original question about cognitively-stimulating activities included different kinds of activities, it is not possible to decipher which activity may be most important. Moreover, time reading a book may not be equal to time spent playing video games. Thus, the current findings need to be interpreted with caution and future research with detailed assessments of time spent in each of the cognitively-stimulating activities may provide more conclusive evidence.

The association we observed between a longer sleep duration and a lower ADHD symptom score is in concordance with previous similar longitudinal studies, which included children of diverse age ranges (from 3 to 11 years)[6,26], thereby adding to the consistency of the findings. The benefits of more sleep may be explained in part by the fact that sleeping improves the development of executive functions[27], whose deficits are key neuropsychological features of ADHD. On the other hand, our results show no association between sleeping time and behavior problems, which is in discordance with previous evidence[28]. This apparent discrepancy may be explained by the fact that previous studies that report an association between short sleep and behavior problems define a short sleep as having less than 9 hours per night, a level achieved by less than 5% of our sample.

It could be argued that, both for sleep duration and time spent engaging in cognitively-stimulating activities, the magnitude of the association with ADHD symptoms and behavior problems is relatively small and therefore, the clinical significance of our findings may be questionable. However, in population-based research, it is common that small differences (e.g., in CPRS ADHD Index score) at the individual level result in large differences at the population level (e.g., prevalence of ADHD disorder)[29]. Given

that ADHD is currently considered the most common neurobehavioral disorder in childhood, even a small effect of lifestyle factors on this disorder could result in important and measurable health and societal impacts at the population level.

We found no association between time spent watching TV during early childhood and scores of either ADHD symptoms or behavior problems by school age. This finding is also not in line with previous work. Longitudinal studies have found positive associations between time spent watching TV and ADHD symptoms [7,8] as well as with an increased risk of behavior problems in children [30,31]. Reasons for this inconsistency may be that our TV exposure variable was less detailed than that used in previous studies, and that the age distribution of our study is different from that used in other studies, as the effect of TV exposure may differ by stage of development.

Our study is the first to assess the longitudinal association between physical activity (at 4 years) and scores of ADHD symptoms and behavior problems (at 7 years), and we found no indication of an existing association. Exercise interventions in children with ADHD have shown to be effective for mitigating ADHD symptoms[10] and involvement in sports has been associated with fewer behavior problems and more prosocial behaviors[11]. The fact that we found no associations may be due to a lack of any real effect of physical activity on the development of ADHD or behavior problems, or because of misclassification in the physical activity variable due to the use of a questionnaire.

The present research is subject to some limitations. First, we used a parental questionnaire to assess time spent sleeping, watching TV, engaging in cognitive-stimulating activities, and engaging in physical activity. Misclassification for all of these exposures is thus possible. Furthermore, the misclassification may be differential for ADHD symptoms as parents of children with ADHD symptoms may be more likely to report that their children sleep less hours or are more physically active. Second, ADHD symptoms and behavior problems were also measured using questionnaires completed by the parents, and therefore, some misclassification of the outcome is also possible. Third, the children who participated in the study had longer breastfeeding, higher maternal IQ, and higher parental education levels than those who did not participate. Because these are all risk factors for ADHD symptoms and behavior problems, our associations may be underestimated. Fourth, although attendance to

school at age 4 years is not compulsory in our study area, it is very common and the educational programs are fairly standardized. This may limit the broad generalizability of our findings to other geographical areas with different educational norms and programs. Finally, as we did not collect information on pharmacological or non-pharmacological treatment of children with comorbidities, genetic factors, or all potentially relevant parental factors (e.g. paternal history of ADHD), our results may be subject to some residual confounding.

This research nonetheless has several strengths. First, the longitudinal study design and the adjustment for baseline ADHD symptoms and neuropsychological conditions of the children reduced the possibility of reverse causation. Second, we had detailed information of many relevant potential confounders, such as socioeconomic and environmental factors. Third, the population-based sampling improves the generalizability of the findings. Finally, to our knowledge, this is the first study to analyze the effect of cognitively-stimulating activities, like reading, doing puzzles, and playing games, on the risk of developing ADHD symptoms and behavior problems.

Conclusion

A shorter sleep duration and less time spent in cognitively-stimulating activities were associated with an increased risk of developing ADHD symptoms and behavior problems. These results have important public health implications since an adequate sleep schedule and an appropriate distribution of leisure-time activities during preschool life could affect future ADHD and behavior development. Further research in other geographical areas with different distributions of the investigated lifestyle factors is warranted to better design and test health promotion strategies.

REFERENCES

1. Polanczyk G, De Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: A systematic review and metaregression analysis. *Am J Psychiatry*. 2007;164(6):942-948.

2. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4 th. Washington, DC: American Psychiatric Association; 1994.

3. Barbaresi WJ, Katusic SK, Colligan RC, Weaver AL, Jacobsen SJ. Long-Term School Outcomes for Children with Attention-Deficit/Hyperactivity Disorder: A Population-Based Perspective. *J Dev Behav Pediatr*. 2007;28(4):265-273.

4. Jensen CM, Steinhausen H-C. Comorbid mental disorders in children and adolescents with attention-deficit/hyperactivity disorder in a large nationwide study. *ADHD Atten Deficit Hyperact Disord*. 2015;7(1):27-38.

5. Thapar A, Cooper M, Jefferies R, Stergiakouli E. What causes attention deficit hyperactivity disorder? *Arch Dis Child*. 2012;97(3):260-265.

6. Touchette E, Petit D, Séguin JR, et al. Associations between sleep duration patterns and behavioral/cognitive functioning at school entry. *Sleep*. 2007;30(9):1213-1219.

7. Verlinden M, Tiemeier H, Hudziak JJ, et al. Television viewing and externalizing problems in preschool children: the Generation R Study. *Arch Pediatr Adolesc Med*. 2012;166(10):919-25.

8. Swing EL, Gentile DA, Anderson CA, et al. Television and video game exposure and the development of attention problems. *Pediatrics*. 2010;126(2):214-21.

9. Carson V, Kuzik N, Hunter S, et al. Systematic review of sedentary behavior and cognitive development in early childhood. *Prev Med (Baltim)*. 2015;78:115-122.

10. Cerrillo-Urbina AJ, García-Hermoso A, Sánchez-López M, et al. The effects of physical exercise in children with attention deficit hyperactivity disorder: a systematic review and meta-analysis of randomized control trials. *Child Care Health Dev*. 2015 Nov;41(6):779-88.

11. Griffiths LJ, Dowda M, Dezateux C, et al. Associations between sport and screen-entertainment with mental health problems in 5-year-old children. *Int J Behav Nutr Phys Act*. 2010;7:30.

12. Marinelli M, Sunyer J, Alvarez-Pedrerol M, et al. Hours of Television Viewing and Sleep Duration in Children: A Multicenter Birth Cohort Study. *JAMA Pediatr*. 2014;168(5):1-7.

13. Guxens M, Ballester F, Espada M, et al. Cohort Profile: The INMA-INfancia y Medio Ambiente-(Environment and Childhood) Project. *Int J Epidemiol*. 2012;41(4):930-940.

14. American Psychiatric Association. *Manual Diagnóstico Y Estadístico de Los Trastornos Mentales*. Barcelona: Masson; 2002.

15. Gianarris WJ, Golden CJ, Greene L. The Conner's Parent rating Scales: A critical review of the litearature. *Clin Psychol Rev*. 2001;21(7):1061-1093.

16. Conners CK. *Conners' Rating Scales—Revised*. Toronto: ON: Multi-Health Systems Inc.; 1997.

17. Goodman R. The Strengths and Difficulties Questionnaire: a research note. *J Child Psychol Psychiatry*. 1997;38(5):581-6.

18. WechslerD, Kaufman A.*WAIS-III: Escala de Inteligencia de Wechsler para Adultos (III)*. Madrid, Spain: Tea Ediciones; 2001.

19. González de Rivera JL, Derogatis LR, De Las Cuevas C, et al. The Spanish

Version of the SCL-90-R: Normative Data in the General Population. Towson, MD: Clinical Psychometric Research; 1989.

20. Hirshkowitz M, Whiton K, Albert SM, et al. National sleep foundation's sleep time duration recommendations: Methodology and results summary. *Sleep Heal*. 2015;1(1):40-43.

21. American Academy of Pediatrics. Children, Adolescents, and Television. *Pediatrics*. 2001;107(1):423.

22. American Academy of Pediatrics Policy Statement. Children, Adolescents, and the Media. *Pediatrics*. 2013;132:958–961.

23. Gardner W, Mulvey EP, Shaw EC. Regression Analyses of Counts and Rates: Poisson, Overdispersed Poisson, and Negative Binomial Models. *Psychol Bull*. 1995;118(3):392-404.

24. Ginsburg KR. The Importance of Play in Promoting Healthy Child Development and Maintaining Strong Parent-Child Bond : Focus on Children in Poverty abstract. *Pediatrics*. 2007;119(1):182-188.

25. Sills J, Rowse G, Emerson L-M. The role of collaboration in the cognitive development of young children: a systematic review. *Child Care Health Dev*. 2016;42(3):313-324.

26. Lehto JE, Uusitalo-Malmivaara L. Sleep-related factors: Associations with poor attention and depressive symptoms. *Child Care Health Dev*. 2014;40(3):419-425.

27. Turnbull K, Reid GJ, Morton JB. Behavioral Sleep Problems and their Potential Impact on Developing Executive Function in Children. *Sleep*. 2013;36(7):1077-1084.

28. Astill RG, Van der Heijden KB, Van IJzendoorn MH, et al. Sleep, cognition, and

behavioral problems in school-age children: A century of research meta-analyzed. *Psychol Bull*. 2012;138(6):1109-1138.

29. Künzli N, Ackermann-Liebrich U, Brändli O, et al. Clinically "small" effects of air pollution on FVC have a large public health impact. *Eur Respir J*. 2000;15(1):131-136.

30. Cheng S, Maeda T, Yoichi S, et al. Early Television Exposure and Children's Behavioral and Social Outcomes at Age 30 Months. *J Epidemiol*. 2010;20(Suppl 2):S485-S489.

31. Parkes A, Sweeting H, Wight D, et al. Do television and electronic games predict children's psychosocial adjustment? Longitudinal research using the UK Millennium Cohort Study. *Arch Dis Child*. 2013;98(5):341-8.

LIST OF SUPPLEMENTAL DIGITAL CONTENT

ABSTRACT

Objective: To analyze associations between time spent sleeping, watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity, all at 4 years, and (i) attention-deficit/ hyperactivity disorder (ADHD) symptoms and (ii) behavior problems, both assessed at 7 years, in ADHD-free children at baseline.

Method: In total, 817 participants of the INfancia y Medio Ambiente birth cohort, without ADHD at baseline, were included. At the 4-year follow-up, parents reported the time that their children spent sleeping, watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity. At the 7-year follow-up, parents completed the Conner's Parent Rating Scales and the Strengths and Difficulties Questionnaire, which measure ADHD symptoms and behavior problems, respectively. Negative binomial regression models were used to assess associations between the activities at 4 years and ADHD symptoms and behavior problems at 7 years.

Results: Children (48% girls) spent a median (p25-p75) of 10 (10-11) h/day sleeping, 1.5 (0.9-2) h/day watching TV, 1.4 (0.9-1.9) h/day engaging in cognitively-stimulating activities, and 1.5 (0.4-2.3) h/day engaging in physical activity. Longer sleep duration (>10h/d) was associated with a lower ADHD symptom score (adjusted incidence rate ratio=0.97, 95% CI=0.95-1.00). Longer time spent in cognitively-stimulating activities (>1h/d) was associated with lower scores of both ADHD symptoms (0.96, 0.94-0.98) and behavior problems (0.89, 0.83-0.97). Time spent watching TV and engaging in physical activity were not associated with either outcome.

Conclusions: A shorter sleep duration and less time spent in cognitively-stimulating activities were associated with an increased risk of developing ADHD symptoms and behavior problems.

Keywords: ADHD**;** behavior problems; physical activity; sleep; cognitively-stimulating activities

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is considered the most common childhood neurobehavioral disorder, with a worldwide prevalence of 5% in children and adolescents[1]. It is characterized by an age-inappropriate pattern of inattention and/or hyperactivity–impulsivity[2]. ADHD symptoms are associated with academic difficulties[3] and with an increased risk of other comorbid behavior problems[4]. The etiology of ADHD is complex as it is influenced by both genetic and non-genetic factors, such as smoking during pregnancy or duration of breastfeeding, as well as their interplay[5]. Moreover, some lifestyle factors have been associated with ADHD symptoms. Sleeping less than 9 hours at 2.5 years of age was related to a higher risk of ADHD symptoms at 6 years[6]. Continued high TV exposure was also associated with the incidence of ADHD-related symptoms in both preschool and school-aged children in studies with 1-year follow-ups[7,8]. However, there is a lack of knowledge regarding the role of other relevant lifestyle factors on the incidence of ADHD symptoms. Cognitively-stimulating activities, such as reading or doing puzzles, have not yet been studied, despite the fact that these are common childhood activities and that they might have positive effects on child development [9]. Similarly, although exercise interventions have been found to be effective at mitigating ADHD symptoms in children with this disorder[10], and involvement in sports has been cross-sectionally related to fewer behavior problems[11], no study has longitudinally analyzed the role of physical activity on the incidence of ADHD symptoms. Furthermore, the joint effect of such lifestyle factors has not yet been assessed, despite their close relation, e.g., a higher time spent watching TV may come at the cost of less sleep[12].

The objective of the current study was to analyze associations between time spent sleeping, watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity, all at 4 years, and (i) ADHD symptoms and (ii) behavior problems, both assessed at 7 years, in ADHD-free children at baseline.

METHOD

Study Design and Participants

We used data from two regions of the Spanish longitudinal birth cohort INMA - INfancia y Medio Ambiente [Environment and Childhood]

(http://www.proyectoinma.org). The criteria for inclusion and details of the data collection have been described elsewhere [13]. Briefly, between November 2003 and July 2006, pregnant women were recruited while attending antenatal care and eventually, their children were included in the study. The children were followed-up at 1.5, 4, 7 and 9 years of age. The present study includes information covering age 4 years (set as our baseline visit) to 7 years (follow-up visit). Out of the 1147 children that attended the baseline visit at 4-years, we excluded: 4 prevalent ADHD cases (children with a doctor diagnosis of ADHD), 49 children without exposure data, 151 children without information about baseline ADHD symptoms, 108 children lost to follow-up by age 7 years, and 18 children without outcome data at the follow-up visit. Ultimately, 817 children (71% of the original sample) were included in the present analysis (see figure, Supplemental Digital Content 1, which illustrates the selection of study participants). The Ethics Committee of participating hospitals approved the study and all parents provided informed consent.

Measures

Lifestyle Factors Assessment

At age 4 years, we assessed the time children spent sleeping, watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity using a parent-completed questionnaire. Time spent sleeping was assessed with the question "How many hours per day does your child spend sleeping? Include nap time". Time spent watching TV was assessed with the question "How many hours per day does your child spend watching TV/videos?" Time spent engaging in cognitively-stimulating activities was assessed with the question "Outside school, how many hours per day does your child spend with games or other sedentary activities (for example: jigsaw puzzles, books, dolls, homework, or computer/videogames)? Exclude TV/videos and Wii sports". Finally, time spent engaging in physical activity was assessed with the question "How many hours per day does your child spend with structured extracurricular activities (as dance, swimming, etc.) or with non-structured activities (playing in the playground/park, cycling, running, jumping, skating, swimming, etc.). Exclude Wii sports and commute to school".

Behavior Assessment

Data on behavior problems, including ADHD, were collected at both age periods. At age 4 years, we used medical histories to assess a clinical diagnosis of ADHD (used to exclude prevalent ADHD cases at baseline). Additionally, each child's teacher completed the ADHD *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) (ADHD-DSM-IV) form[14]. This form is an internationally recognized list of 18 items designed to evaluate attention deficit, hyperactivity, and impulsivity symptoms in children. We used the number of symptoms reported in the ADHD-DSM-IV form by each child's teacher as a key covariate in the final models to account for potential reverse causation.

At age 7 years, we measured ADHD symptoms with the short form of the Conners' Parent Rating Scales (CPRS)[15], which assesses problematic behavior in children. The CPRS consists of 27 items that result into scores for three subscales (oppositional, cognitive problems/inattention, and hyperactivity) and an ADHD Index. The raw scores are transformed (T-Scores) to have a mean of 50 and a standard deviation of 10. A higher ADHD Index score indicates higher ADHD symptoms and a score above 65 is usually indicative of a clinically significant problem[16]. For the present study, the ADHD Index, as a continuous variable, was used as the main measure of ADHD symptoms. The subscales were used in secondary analyses.

The behavior development of the children was also assessed at 7 years using the parental version of the Strengths and Difficulties Questionnaire (SDQ)[17]. The SDQ consists of 25 items, which translate into individual scores for five subscales (emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems, and prosocial behavior) that range from 0 to 10 and a Total Difficulties Score that ranges from 0 to 40. The Total Difficulties Score is obtained by summing four of the five scales (emotional symptoms, conduct problems, hyperactivity/inattention, and peer relationship problems; prosocial behavior is excluded because it is a positive subscale), and a higher score is indicative of more behavior problems. A score of ≥17 is indicative of abnormal behavior problems[17]. For the present study, we used the Total Difficulties Score, as a continuous variable, as the main measure of behavior problems. The five subscales were used in secondary analyses.

Covariates

During pregnancy, at birth, and at age 1 year questionnaires or medical records were used to collect data on maternal and paternal education, maternal and paternal social class, any maternal smoking during pregnancy, any maternal alcohol use during pregnancy, child's sex, gestational age at birth, birth weight, and duration of any breastfeeding. The following information was also obtained by questionnaire when the children were 4 years: maternal smoking habits, maternal intelligence (using the similarities subtest of the Wechsler Adult Intelligence Scales 3rd edition (WAIS-III)[18] as a proxy of intelligence quotient (IQ)), maternal mental health (using the Symptom Check List- 90-R (SCL-90-R)[19]), child daycare/nursery attendance before school, and child neuropsychological conditions (defined as seeing a psychologist and/or having a neuropsychological diagnosis other than ADHD).

Statistical Analysis

A priori to any modeling, we decided to use all exposure variables as categorical variables in the main analysis and as continuous variables in sensitivity analyses. This decision was primarily based on existing recommendations [20–22] (which facilitates the interpretation of the results in terms of public health relevance) and is supported by the results of the generalized additive models (GAMs). The GAMs suggested generally linear trends between time spent watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity with the CPRS ADHD Index and the SDQ Total Difficulties Score. However, the GAM for the association between time spent sleeping and the CPRS ADHD Index and the SDQ Total Difficulties Score showed an inflection point at 10 hours per day, which suggests that entering time spent sleeping as a continuous variable into the models for our outcome variables could hide potential true associations. Thus, the cut-offs for time spent sleeping and watching TV were 10 h/day and 1h/day, respectively, according to recommendations set for preschoolers[20–22]. Time spent engaging in cognitively-stimulating activities was categorized as ≤1h/day and >1h/day, according to the data distribution. Finally, time spent engaging in physical activity was categorized as low, moderate, and high according to region-specific tertiles, as the data distribution for this variable differed by region.

We analyzed the differences in the distribution of the outcomes (ADHD symptoms and behavior problems) at age 7 years according to the exposures (sleep, TV, cognitively-stimulating activities, and physical activity) at age 4 years using U-Mann Whitney or

Kruskal-Wallis tests. Negative binomial regression models were used to assess the association between each exposure variable and ADHD symptoms (CPRS scores) and behavior problems (SDQ scores), because the outcome variables were over-dispersed count variables [23]. We performed a complete case analysis. Effect estimates are presented as incidence rate ratios (IRR) and their corresponding 95% confidence intervals. The IRR indicates the number of times that the CPRS ADHD Index/SDQ Total Difficulties Score is lower (IRR<1) or higher (IRR>1) than that of the reference group.

Based on the previous literature, we initially considered the following variables as potential confounders: children age, sex, birth weight, gestational age, duration of any breastfeeding, parents' social class, educational level, maternal IQ, maternal mental health, any maternal alcohol intake during pregnancy, any maternal smoking during pregnancy, maternal smoking when the child was 4 years, child daycare/nursery attendance before school, and child neuropsychological conditions at 4 years. Covariates were retained in the final model if they were statistically related to the outcome or modified the coefficient of any other covariate >10%. All models were additionally adjusted for the number of symptoms reported in the ADHD-DSM-IV form by each child's teacher at baseline to account for potential reverse causation. We tested goodness of fit of the models using the likelihood-ratio test.

We tested potential interactions between the exposure variables in the final models by using interaction terms. We performed several sensitivity analyses to assess the robustness of the results: the exposures were entered into the models as continuous variables, children with extreme exposure values were excluded, and children beyond the established cut-offs for ADHD symptoms and behavior problems were excluded. All statistical analyses were conducted with Stata 12.0 (Stata Corporation, College Station, Texas).

RESULTS

There were no differences in birth weight or gestational age between participants and non-participants. Non-participants had a lower duration of breastfeeding, maternal IQ, and parental educational level compared to participants (see table, Supplemental Digital Content 1, which compares the characteristics of participants and non-participants). The study population consisted of 817 children (418 boys and 399 girls). Children spent a median (p25-p75) of 10 (10-11) h/day sleeping, 1.5 (0.9-2) h/day watching TV, 1.4

(0.9-1.9) h/day engaging in cognitively-stimulating activities, and 1.5 (0.4-2.3) h/day engaging in physical activity (Table 1). The median score (p25-p75) of the ADHD Index and the Total Difficulties Score was 49 (45-56) and 8 (5-12), respectively (Table 1).

A shorter sleep duration and a shorter time spent engaging in cognitively-stimulating activities at age 4 years were associated with a higher ADHD symptom score at age 7 years. A longer time spent watching TV and a shorter time spent engaging in cognitively-stimulating activities were related to more behavior problems (Table 2). After adjustment for child sex, duration of breastfeeding, maternal smoking during pregnancy, maternal smoking when the child was 4 years, maternal education, maternal IQ, maternal mental health, paternal education, child daycare/nursery attendance before school, baseline child neuropsychological conditions, number of ADHD-DSM-IV symptoms at baseline, and region, the association between time spent sleeping and ADHD symptoms, as well as between time spent engaging in cognitively-stimulating activities and ADHD symptoms and behavior problems remained statistically significant (Table 3). However, time spent watching TV and engaging in physical activity at were no longer associated with either outcome.

Additional analyses using the CPRS and SDQ subscales indicated that a longer sleep duration was associated with a lower CPRS cognitive score, and a longer time spent engaging in cognitively-stimulating activities was associated with lower CPRS cognitive, CPRS hyperactivity, SDQ conduct problem, and hyperactivity/inattention problem scores (see tables, Supplemental Digital Content 2 and 3, which show results for all subscales of CPRS and SDQ).

We did not find statistically significant interactions between any of the exposure variables. Sensitivity analyses showed very similar estimates (see tables, Supplemental Digital Content 4 to 6, which show the results of each sensitivity analysis).

DISCUSSION

This study is the first to demonstrate associations between a longer time spent engaging in cognitively-stimulating activities and lower scores of both ADHD symptoms and behavior problems, in ADHD-free children at baseline. We also found that sleeping longer was associated with a lower ADHD symptom score. In contrast, time spent watching TV and time spent engaging in physical activity at age 4 years were not

associated with ADHD symptoms or behavior problems at age 7 years, nor was there any evidence of interactions between the several exposures considered.

The associations between higher time spent in cognitively-stimulating activities and lowers scores of both ADHD symptoms and behavior problems are supported by previous studies which reported associations between playing, reading or being read to, and positive cognitive development[9,24]. Although the mechanisms for these associations are still unclear, the context in which these activities occur may be important. Playing, reading or being read to may increase interactions with other children and/or with the parents, which in turn, have been related to a better cognitive development in school-aged children[25]. Unfortunately, as the original question about cognitively-stimulating activities included different kinds of activities, it is not possible to decipher which activity may be most important. Moreover, time reading a book may not be equal to time spent playing video games. Thus, the current findings need to be interpreted with caution and future research with detailed assessments of time spent in each of the cognitively-stimulating activities may provide more conclusive evidence.

The association we observed between a longer sleep duration and a lower ADHD symptom score is in concordance with previous similar longitudinal studies, which included children of diverse age ranges (from 3 to 11 years)[6,26], thereby adding to the consistency of the findings. The benefits of more sleep may be explained in part by the fact that sleeping improves the development of executive functions[27], whose deficits are key neuropsychological features of ADHD. On the other hand, our results show no association between sleeping time and behavior problems, which is in discordance with previous evidence[28]. This apparent discrepancy may be explained by the fact that previous studies that report an association between short sleep and behavior problems define a short sleep as having less than 9 hours per night, a level achieved by less than 5% of our sample.

It could be argued that, both for sleep duration and time spent engaging in cognitively-stimulating activities, the magnitude of the association with ADHD symptoms and behavior problems is relatively small and therefore, the clinical significance of our findings may be questionable. However, in population-based research, it is common that small differences (e.g., in CPRS ADHD Index score) at the individual level result in large differences at the population level (e.g., prevalence of ADHD disorder)[29]. Given

that ADHD is currently considered the most common neurobehavioral disorder in childhood, even a small effect of lifestyle factors on this disorder could result in important and measurable health and societal impacts at the population level.

We found no association between time spent watching TV during early childhood and scores of either ADHD symptoms or behavior problems by school age. This finding is also not in line with previous work. Longitudinal studies have found positive associations between time spent watching TV and ADHD symptoms [7,8] as well as with an increased risk of behavior problems in children [30,31]. Reasons for this inconsistency may be that our TV exposure variable was less detailed than that used in previous studies, and that the age distribution of our study is different from that used in other studies, as the effect of TV exposure may differ by stage of development.

Our study is the first to assess the longitudinal association between physical activity (at 4 years) and scores of ADHD symptoms and behavior problems (at 7 years), and we found no indication of an existing association. Exercise interventions in children with ADHD have shown to be effective for mitigating ADHD symptoms[10] and involvement in sports has been associated with fewer behavior problems and more prosocial behaviors[11]. The fact that we found no associations may be due to a lack of any real effect of physical activity on the development of ADHD or behavior problems, or because of misclassification in the physical activity variable due to the use of a questionnaire.

The present research is subject to some limitations. First, we used a parental questionnaire to assess time spent sleeping, watching TV, engaging in cognitive-stimulating activities, and engaging in physical activity. Misclassification for all of these exposures is thus possible. Furthermore, the misclassification may be differential for ADHD symptoms as parents of children with ADHD symptoms may be more likely to report that their children sleep less hours or are more physically active. Second, ADHD symptoms and behavior problems were also measured using questionnaires completed by the parents, and therefore, some misclassification of the outcome is also possible. Third, the children who participated in the study had longer breastfeeding, higher maternal IQ, and higher parental education levels than those who did not participate. Because these are all risk factors for ADHD symptoms and behavior problems, our associations may be underestimated. Fourth, although attendance to

school at age 4 years is not compulsory in our study area, it is very common and the educational programs are fairly standardized. This may limit the broad generalizability of our findings to other geographical areas with different educational norms and programs. Finally, as we did not collect information on pharmacological or non-pharmacological treatment of children with comorbidities, genetic factors, or all potentially relevant parental factors (e.g. paternal history of ADHD), our results may be subject to some residual confounding.

This research nonetheless has several strengths. First, the longitudinal study design and the adjustment for baseline ADHD symptoms and neuropsychological conditions of the children reduced the possibility of reverse causation. Second, we had detailed information of many relevant potential confounders, such as socioeconomic and environmental factors. Third, the population-based sampling improves the generalizability of the findings. Finally, to our knowledge, this is the first study to analyze the effect of cognitively-stimulating activities, like reading, doing puzzles, and playing games, on the risk of developing ADHD symptoms and behavior problems.

Conclusion

A shorter sleep duration and less time spent in cognitively-stimulating activities were associated with an increased risk of developing ADHD symptoms and behavior problems. These results have important public health implications since an adequate sleep schedule and an appropriate distribution of leisure-time activities during preschool life could affect future ADHD and behavior development. Further research in other geographical areas with different distributions of the investigated lifestyle factors is warranted to better design and test health promotion strategies.

REFERENCES

1. Polanczyk G, De Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: A systematic review and metaregression analysis. *Am J Psychiatry*. 2007;164(6):942-948.

2. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4 th. Washington, DC: American Psychiatric Association; 1994.

3. Barbaresi WJ, Katusic SK, Colligan RC, Weaver AL, Jacobsen SJ. Long-Term School Outcomes for Children with Attention-Deficit/Hyperactivity Disorder: A Population-Based Perspective. *J Dev Behav Pediatr*. 2007;28(4):265-273.

4. Jensen CM, Steinhausen H-C. Comorbid mental disorders in children and adolescents with attention-deficit/hyperactivity disorder in a large nationwide study. *ADHD Atten Deficit Hyperact Disord*. 2015;7(1):27-38.

5. Thapar A, Cooper M, Jefferies R, Stergiakouli E. What causes attention deficit hyperactivity disorder? *Arch Dis Child*. 2012;97(3):260-265.

6. Touchette E, Petit D, Séguin JR, et al. Associations between sleep duration patterns and behavioral/cognitive functioning at school entry. *Sleep*. 2007;30(9):1213-1219.

7. Verlinden M, Tiemeier H, Hudziak JJ, et al. Television viewing and externalizing problems in preschool children: the Generation R Study. *Arch Pediatr Adolesc Med*. 2012;166(10):919-25.

8. Swing EL, Gentile DA, Anderson CA, et al. Television and video game exposure and the development of attention problems. *Pediatrics*. 2010;126(2):214-21.

9. Carson V, Kuzik N, Hunter S, et al. Systematic review of sedentary behavior and cognitive development in early childhood. *Prev Med (Baltim)*. 2015;78:115-122.

10. Cerrillo-Urbina AJ, García-Hermoso A, Sánchez-López M, et al. The effects of physical exercise in children with attention deficit hyperactivity disorder: a systematic review and meta-analysis of randomized control trials. *Child Care Health Dev*. 2015 Nov;41(6):779-88.

11. Griffiths LJ, Dowda M, Dezateux C, et al. Associations between sport and screen-entertainment with mental health problems in 5-year-old children. *Int J Behav Nutr Phys Act*. 2010;7:30.

12. Marinelli M, Sunyer J, Alvarez-Pedrerol M, et al. Hours of Television Viewing and Sleep Duration in Children: A Multicenter Birth Cohort Study. *JAMA Pediatr*. 2014;168(5):1-7.

13. Guxens M, Ballester F, Espada M, et al. Cohort Profile: The INMA-INfancia y Medio Ambiente-(Environment and Childhood) Project. *Int J Epidemiol*. 2012;41(4):930-940.

14. American Psychiatric Association. *Manual Diagnóstico Y Estadístico de Los Trastornos Mentales*. Barcelona: Masson; 2002.

15. Gianarris WJ, Golden CJ, Greene L. The Conner's Parent rating Scales: A critical review of the litearature. *Clin Psychol Rev*. 2001;21(7):1061-1093.

16. Conners CK. *Conners' Rating Scales—Revised*. Toronto: ON: Multi-Health Systems Inc.; 1997.

17. Goodman R. The Strengths and Difficulties Questionnaire: a research note. *J Child Psychol Psychiatry*. 1997;38(5):581-6.

18. WechslerD, Kaufman A.*WAIS-III: Escala de Inteligencia de Wechsler para Adultos (III)*. Madrid, Spain: Tea Ediciones; 2001.

19. González de Rivera JL, Derogatis LR, De Las Cuevas C, et al. The Spanish

Version of the SCL-90-R: Normative Data in the General Population. Towson, MD: Clinical Psychometric Research; 1989.

20. Hirshkowitz M, Whiton K, Albert SM, et al. National sleep foundation's sleep time duration recommendations: Methodology and results summary. *Sleep Heal*. 2015;1(1):40-43.

21. American Academy of Pediatrics. Children, Adolescents, and Television. *Pediatrics*. 2001;107(1):423.

22. American Academy of Pediatrics Policy Statement. Children, Adolescents, and the Media. *Pediatrics*. 2013;132:958–961.

23. Gardner W, Mulvey EP, Shaw EC. Regression Analyses of Counts and Rates: Poisson, Overdispersed Poisson, and Negative Binomial Models. *Psychol Bull*. 1995;118(3):392-404.

24. Ginsburg KR. The Importance of Play in Promoting Healthy Child Development and Maintaining Strong Parent-Child Bond : Focus on Children in Poverty abstract. *Pediatrics*. 2007;119(1):182-188.

25. Sills J, Rowse G, Emerson L-M. The role of collaboration in the cognitive development of young children: a systematic review. *Child Care Health Dev*. 2016;42(3):313-324.

26. Lehto JE, Uusitalo-Malmivaara L. Sleep-related factors: Associations with poor attention and depressive symptoms. *Child Care Health Dev*. 2014;40(3):419-425.

27. Turnbull K, Reid GJ, Morton JB. Behavioral Sleep Problems and their Potential Impact on Developing Executive Function in Children. *Sleep*. 2013;36(7):1077-1084.

28. Astill RG, Van der Heijden KB, Van IJzendoorn MH, et al. Sleep, cognition, and

behavioral problems in school-age children: A century of research meta-analyzed. *Psychol Bull*. 2012;138(6):1109-1138.

29. Künzli N, Ackermann-Liebrich U, Brändli O, et al. Clinically "small" effects of air pollution on FVC have a large public health impact. *Eur Respir J*. 2000;15(1):131-136.

30. Cheng S, Maeda T, Yoichi S, et al. Early Television Exposure and Children's Behavioral and Social Outcomes at Age 30 Months. *J Epidemiol*. 2010;20(Suppl 2):S485-S489.

31. Parkes A, Sweeting H, Wight D, et al. Do television and electronic games predict children's psychosocial adjustment? Longitudinal research using the UK Millennium Cohort Study. *Arch Dis Child*. 2013;98(5):341-8.

LIST OF SUPPLEMENTAL DIGITAL CONTENT

Table

Table 1
Description of the study population

	n (N=817)	n(%)/mean(sd)/ median (p25-p75)
Mothers Characteristics		
Age at child birth	812	30.6 (4.1)
Social class	755	
High skilled/ skilled (I+II)		162 (21.5)
Partly skilled (III)		231 (30.6)
Unskilled / unemployed (IV+V)		362 (47.9)
Educational level	803	
Primary or less		184 (22.1)
Secondary		355 (44.2)
University		264 (32.9)
Smoking during pregnancy	808	256 (31.7)
Smoking when child was 4 years	814	249 (30.6)
Alcohol intake during pregnancy	745	79 (10.6)
Maternal IQ (WAIS-III score)	806	10.4 (3.1)
Maternal mental health (SCL-90-R score)	810	0.7 (0.4-1)
Fathers Characteristics		
Age at child birth	813	32.5 (29-35)
Social class	730	
High skilled/ skilled (I+II)		151 (20.7)
Partly skilled (III)		140 (19.2)
Unskilled / unemployed (IV+V)		439 (60.1)
Educational level	803	
Primary or less		299 (36.9)
Secondary		332 (41)
University		179 (22.1)
Children Characteristics		
Age at baseline visit	817	4.4 (4.3-4.5)
Age at follow-up visit	817	7 (6.5-7.1)
Sex	817	
Male		418 (51.2)
Female		399 (48.8)
Low birth weight (<2.5kg)	817	43 (5.3)
Gestational age at birth (weeks)	817	39.9 (38.9-40.7)
Duration of any breastfeeding (weeks)	816	25.9 (8.9-39.4)
Daycare/nursery attendance before school	742	
Yes		635 (85.6)
No		107 (14.4)
Baseline neuropsychological conditions*	815	
Yes		59 (7.2)
No		756 (92.8)
Number of ADHD-DSM-IV symptoms at baseline	817	0 (0-1)

Table 1
Description of the study population (continued)

	n (N=817)	n(%)/mean(sd)/ median (p25-p75)
Sleep, sedentary activities, and physical activity at age 4 years		
Sleeping (h/day)	817	10 (10-11)
Watching TV (h/day)	817	1.5 (0.9-2)
Cognitively-stimulating activities (h/day)	817	1.4 (0.9-1.9)
Physical activity (h/day)	817	1.5 (0.4-2.3)
Behavior assessment at age 7 years		
CPRS (T-Scores)		
ADHD Index	817	49 (45-56)
Oppositional/Inattention subscale	817	48 (43-54)
Cognitive subscale	817	50 (44-56)
Hyperactivity subscale	817	51 (45-60)
SDQ		
Total difficulties score (0-40)	817	8 (5-12)
Emotional subscale (0-10)	817	2 (1-3)
Conduct subscale (0-10)	817	1 (1-3)
Hyperactivity/ Inattention subscale (0-10)	817	4 (2-5)
Peer relationship subscale (0-10)	817	1 (0-2)
Prosocial behavior subscale (0-10)	817	9 (7-10)

Note: CPRS: Conner's Parent Rating Scale; DSM-IV: Diagnostic and Statistical Manual of mental disorders- 4th edition; IQ: Intelligence Quotient; SCL-90-R: Symptom Check List- 90-R: SDQ: Strengths and Difficulties Questionnaire; WAIS-III: Wechsler Adult Intelligence-Third Edition

* Defined as seeing a psychologist and/or having a neuropsychological diagnosis different than ADHD

Table 2
Distribution of ADHD symptom and behavior problem scores at age 7 years, according to the length of time spent sleeping, watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity at age 4 years

	n	ADHD symptoms (CPRS ADHD Index)		Behavior problems (SDQ Total Difficulties Score)	
		Median (p25-p75)	p-value[§]	Median (p25-p75)	p-value[§]
Sleeping					
≤10 h/day	418	51 (45-58)	0.006	8 (6-12)	0.111
>10 h/day	399	48 (45-55)		8 (5-11)	
Watching TV					
≤1 h/day	297	49 (45-56)	0.044	7 (5-11)	0.001
>1 h/day	520	51 (45-57)		9 (5-12)	
Cognitively-stimulating activities					
≤1 h/day	364	51.5 (45-58)	0.004	9 (6-12)	0.001
>1 h/day	453	49 (45-55)		8 (5-11)	
Physical activity					
Low	308	49 (45-58)	0.219	8 (5-11)	0.650
Moderate	243	51 (45-56)		8 (5-13)	
High	266	49 (45-55)		8 (6-11)	

Note: CPRS: Conner's Parent Rating Scale; SDQ: Strengths and Difficulties Questionnaire.
[§] U-Mann Whitney or Kruskal-Wallis according to variable type

Table 3

Adjusted associations between time spent sleeping, watching TV, engaging in cognitively-stimulating activities, and engaging in physical activity at age 4 years, and ADHD symptoms and behavior problems at age 7 years (negative binomial regression)

	n	ADHD symptoms (CPRS ADHD Index) Adjusted ǂ IRR (95% CI)	p-value	Behavior problems (SDQ Total Difficulties Score) Adjusted ǂ IRR (95% CI)	p-value
Sleeping					
≤10 h/day	363	1[reference]		1 [reference]	
>10 h/day	348	0.97 (0.95 to 1.00)	0.035	0.97 (0.89 to 1.04)	0.380
Watching TV					
≤1 h/day	268	1 [reference]		1 [reference]	
>1 h/day	443	1.01 (0.99 to 1.04)	0.338	1.07 (0.99 to 1.16)	0.106
Cognitively-stimulating activities					
≤1 h/day	320	1 [reference]		1 [reference]	
>1 h/day	391	0.96 (0.94 to 0.98)	<0.001	0.89 (0.83 to 0.97)	0.005
Physical activity					
Low	283	1 [reference]		1 [reference]	
Moderate	208	1.01 (0.98 to 1.04)	0.607	1.01 (0.92 to 1.11)	0.769
High	220	0.99 (0.96 to 1.02)	0.471	1.03 (0.94 to 1.13)	0.480

Note: CI: confidence interval; CPRS: Conner's Parent Rating Scale; IRR: incidence rate ratio; SDQ: Strengths and Difficulties Questionnaire.

ǂ All models are adjusted for child sex (male/female), any breastfeeding (continuous in weeks), maternal smoking during pregnancy (yes/no), maternal smoking when child was 4 years (yes/no), maternal education (primary or less, secondary, and university), maternal intelligence quotient (continuous), maternal mental health (continuous), paternal education (primary or less, secondary, and university), child daycare/nursery attendance before school (yes/no), baseline neuropsychological conditions (yes/no), number of ADHD-DSM-IV symptoms at baseline (continuous), and region.

The IRR indicates the number of times that the CPRS ADHD Index/SDQ Total Difficulties Score is lower (IRR<1) or higher (IRR>1) than the reference group. For example, children sleeping more than 10h/day have a CPRS ADHD Index score 0.97 times lower than children sleeping ≤10h/day. In other words, if the children sleeping ≤10h/day have a median CPRS ADHD Index of 51, then the children sleeping >10h/day will have 1.53 (51 – 0.97*51) points less in the CPRS ADHD Index after adjusting for the effect of confounders. Hence, these latter children sleeping >10h/day will have a median score of 49.47

LWW Editorial Manager
Mandatory Manuscript Submission Checklist

YES	NO	ITEM
☒	☐	This manuscript has been seen, reviewed, and approved by all contributing authors.
☐	☒	Are there any potential conflicts of interest? **If yes**, please supply full disclosure of financial arrangement between any author and any company whose product or competing product plays a prominent role in the manuscript in the space provided below.
☒	☐	At least one author (e.g. the lead author) had complete access to all data in the study. He/she takes responsibility for the integrity of the data and the accuracy of any data analysis.
☒	☐	The first author is eligible for the SDBP Young Investigator Manuscript Award If the first author is a trainee, or has completed post-doctoral training within 3 years of the date of submission of the paper, the author is eligible for consideration for the Young Investigator Manuscript Award. For the purpose of this award, "trainee" is defined as an undergraduate or medical student, pediatric resident, fellow in pediatrics, or graduate student or post-graduate clinical trainee in psychology or an allied health profession (e.g., nursing, speech/language therapy, occupational or physical therapy).

The questions below do not apply to abstracts or posters published in conjunction with a scientific meeting.

YES	NO	ITEM
☐	☒	Have the contents of the manuscript, in any form, been published elsewhere? Copies of any closely related publications should be provided at the time of manuscript submission.
☐	☒	Is the manuscript currently submitted elsewhere?
☒	☐	Copyright Transfer form completed and signed by all indicated parties.

Copyright © 2002 - All rights reserved
LIPPINCOTT WILLIAMS & WILKINS
Copyright/Legal Disclaimer • Privacy Policy

Copyright © 2002 - All rights reserved
LIPPINCOTT WILLIAMS & WILKINS
Copyright/Legal Disclaimer • Privacy Policy

Click here to access/download
Supplemental Digital Content
Supplemental Digital Content_JDBP17-140R2.docx