Electrophysiological correlates of reading in children with attention deficit hyperactivity disorder

Pedro A. González-Pérez, Sergio Hernández-Expósito, Jhoanna Pérez, Gustavo Ramírez, Alberto Domínguez

Aims. To investigate whether or not the deficits in executive functions in the attention deficit hyperactivity disorder (ADHD) affect reading comprehension and identify a potential biological marker of this neuropsychological endophenotype through event-related potentials (ERP). The phenotypic association between reading comprehension and the specific functions of inhibition and working memory is studied.

Subjects and methods. The sample consisted of 52 children with ADHD (8-13 years) divided in two groups according to the presence (TDAH–; n = 27; percentile < 30) or the absence (TDAH+; n = 25; percentile > 50) of reading comprehension deficits and a control group (n = 27). The executive functions were evaluated. The ERPs were assessed during a task in which anaphoric sentences of different lengths were presented, recording the ERP in the last adjective of the sentence that required a gender agreement.

Results. Working memory and inhibition were associated to reading comprehension performance. The ADHD+ group and the control group seem to detect the disagreement at 100 ms, while the ADHD– group does not activate its working memory until 250 ms.

Conclusions. The delay in the implementation of the working memory mechanisms helps us to understand the deficits in reading comprehension of the ADHD– group.

Key words. ADHD. Child neuropsychology. Event-related potentials. Executive functions. Gender agreement. Grammatical gender violation. Reading comprehension. Working memory.

Departamento de Psicología Clínica, Psicobiología y Metodología, Sección Psicología y Logopedia, Facultad de Ciencias de la Salud (P.A. González-Pérez, S. Hernández-Expósito, G. Ramírez); Departamento de Psicología Cognitiva, Social y Organizacional, Sección Psicología y Logopedia, Facultad de Ciencias de la Salud (A. Domínguez); Instituto Universitario de Neurociencia, IUNE (P.A. González-Pérez, S. Hernández-Expósito, A. Domínguez); Universidad de La Laguna; Santa Cruz de Tenerife, Spain. Centro de Neurociencias de Cuba; La Habana, Cuba (J. Pérez).

Corresponding author:
Dr. Sergio Hernández Expósito. Facultad de Psicología. Campus de Guajara. Universidad de La Laguna. E-38205 Santa Cruz de Tenerife (Spain).

E-mail:
sexposit@ull.edu.es

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Introduction

Attention deficit hyperactivity disorder (ADHD) is one of the more frequently diagnosed disorders of neurodevelopment in childhood [1]. The clinical and pathological profile of ADHD presents deficits in executive functions and occasionally in reading [2]. The influence of executive functions on reading comprehension [3-4] contributes to the building of inferences, construction of mental models (i.e., abstraction), maintenance of previous structures (i.e., working memory), integration of ideas (i.e., cognitive flexibility) and removal of irrelevant information (i.e., inhibition). Working memory, in particular, is essential for reading sentences, because noun and verb phrases tend to be situated apart from each other and need to be maintained and attached in the proper order to be comprehended. This is the case, for example, with anaphoric phrases, in which the gender of a subject and its pronoun are the only clues to achieving their agreement and therefore their syntactic attachment [5,6]. Gender or number disagreement in anaphoric sentences affects certain components of the electrophysiological recording, such as ELAN (early left anterior negativity), LAN (left anterior negativity) and P600. ELAN is an early negativity that emerges 200 ms after stimulus presentation, whereas LAN evolves from 350 ms to 550 ms. Both have a left frontal or fronto-central distribution [7,8] and have been interpreted as representing the first syntactic parsing of the sentences using lexical information. P600, on the contrary, is a later component that develops between 500 and 900 ms that is also caused by agreement violations but reflects 'garden path' processes and syntactic reanalyzes to repair incorrect previous attachment [7-10].

Brandeis et al [11] observed that N400 peak latencies in non-plausible sentences were delayed in dyslexic children, and Helenius et al [12] found a similar delay in dyslexic adults. Rispens et al [13] also found also a delay of the P600 in response to agreement violations in a group of dyslexics, and Sabish et al [14] found that ELAN was delayed until 300-600 ms for dyslexic children and even later, until 700-1000 ms, in children diagnosed with Specific Language Impairment. Also, they saw an enhanced and more distributed N400, revealing an attempt to solve the syntactic incongruity with the use of lexical-

Table I. Mean and standard deviation (SD) of chronological age in months and intelligence quotient. A non-significant *F* for chronological age shows no differences in chronological age between groups, whereas a significant *F* for and intelligence quotient show that the control group is significantly more intelligent than the two ADHD groups.

	ADHD–		ADHD+		Control		*F*	*p*
	Mean	SD	Mean	SD	Mean	SD		
Chronological age	121.44	20.68	126.80	20.81	128.96	16.39	1.075	0.346
Intelligence quotient	100.59	10.68	102.32	10.86	118.41	7.63	26.813	0.001

Table II. Tasks presenting significant differences between the three groups in the multivariate analyses of covariance. Working memory and inhibition are, among others, significant factors in a posterior discriminant analysis.

	Variable	$F_{(1)}$	*p*	$F_{(2)}$	*p*
Attention	CPT-omissions	5.722	0.005	3.351	0.040
	CPT-variability	4.788	0.011	3.842	0.026
Processing speed	CPT-reaction time	8.902	0.001	4.915	0.010
Working memory	Phrase memory	20.575	0.001	7.934	0.001
	Reverse verbal span	9.502	0.001	3.758	0.028
Cognitive flexibility	CPT-perseverations	4.253	0.018	3.147	0.049
	WCST-perseverative errors	5.603	0.005	3.452	0.037
	WCST-perseverative answers	3.902	0.024	2.699	0.074
Abstraction and formation of concepts	WCST-categories	13.264	0.001	5.626	0.005
Inhibition	Stroop word-color	15.801	0.001	8.702	0.001

$F_{(1)}$ is the variance before including the intelligence quotient factor and $F_{(2)}$ is the variance after the inclusion.

semantic information to avoid the working memory load required by the agreement operations.

The goal of this study was to observe, using ERP measures, the brain signatures produced by differences in the executive functions required to read a sentence, such as working memory or inhibitory processes. A group of ADHD children with reading comprehension deficit was compared with a group of ADHD children without reading comprehension deficit and a healthy control group by means of a task in which the participants read a sentence that included a gender agreement violation. Specifically we trying to identify of there are specific cognitive predictors for reading comprehension difficulties in children with ADHD. The three groups were set up by applying diagnostic criteria for ADHD, reading comprehension tasks, neuropsychological tests, and intelligence scales.

Subjects and methods

Participants

For the selection of the sample, we used the diagnostic criteria of the DSM-IV-TR [15] for ADHD, with participants showing no symptomatology allocated to the control. For this purpose, parents and teachers completed the ADHD Rating Scale IV: Home Version [16]; the SDQ-Cas [17]; and the Family History and Health Scales [18]. A psychiatrist specializing in child assessment conducted the identification of children who met ADHD criteria. An additional condition was that participants must have an intelligence quotient (IQ) of 85 or higher as measured by the Spanish version of the Cattell scales [19]. Children with a neurological or psychopathological disorder other than ADHD were excluded. All children were between 8 and 13 years old. The sample was also classified according their ability to comprehend texts with the PROLEC and PROLEC-SE tests [20,21]. Good or 'normal' comprehenders were those with a reading comprehension above the 50th percentile and less efficient or 'poor' comprehenders were those with a percentile under 35th in these tasks. Three groups of children were formed: ADHD+, normal reading comprehension (percentile > 50): 25 participants; ADHD–, poor reading comprehension (percentile < 35): 27 participants; controls, normal reading comprehension (percentile > 50): 27 participants. Age and IQ are shown in table I.

A second step for the selection of the executive function of interest was to isolate the modulating effect of intelligence. For this purpose, intelligence was introduced as a covariate in a MANCOVA with the neuropsychological measures to see which of these measures were still significant in the differentiation between groups (Table II). Then, a discriminant analysis was carried out with the significant variables of table II, whereby two functions were obtained: the first showed differences between Controls and the two pathological groups, and the second presented significant differences between the ADHD+ (normal reading comprehension) and the ADHD– (poor reading comprehension) groups (F_1 = 0.615). Individual analyses of the results of these two groups showed that they differ in inhibition and working memory abilities, among others; these, therefore, were the variables manipulated in an experimental lexical decision reading task. This ERP experiment was completed by a sample of 23 ADHD– participants, 18 ADHD+ participants, and 25 controls, after some participant exclusions due to excessive noise in the record, abandonment of the task and desertion of participants (Table II).

Design and procedure

A 2 × 2 design was prepared with the variables length (short vs. long sentences) by agreement (gender agreement vs. disagreement). All sentences included a first person doing an action with a second person: '*Pedro besó a María*' ('Pedro kissed Mary'), and then a pronominal anaphora followed by a verb and an adjective referring to the first character: '*él se fue contento*' ('he left happy'). The long sentences included three words between the second verb and the adjective ('*por la calle*,' 'in the street') and the sentences with gender disagreement substituted the gender suffix to the adjective agreeing with the anaphora and the subject with that of the opposite gender ('*él se fue contenta*'). One hundred and twenty sentences were drafted, with four versions (short vs. long sentences; gender agreement vs. disagreement) prepared of each. The sentences included animal names, proper names and professions and were balanced across conditions and presented in a random order. The procedure started with the presentation of an asterisk in the center of the screen during 500 ms as a fixation point. Then, the first part of the sentence '*Pedro besó a María*' appeared on the screen and remained for 1200 ms, after which the anaphoric pronoun was presented for 1000 ms, followed by the three filler words if the sentence was being presented in the long version. Finally, the adjective showing agreement or disagreement with the pronoun appeared for 1500 ms. Ten questions, randomly presented, were also introduced with the aim of maintaining participants' attention. The participants responded by pressing yes/no keys. Each question was referred to the last sentence presented. During the experiment, participants remained comfortably seated in a soundproof room at a distance of 60 cm from the screen. The experiment was carried out in two blocks of 60 sentences each, with a break for participants in between. This break was announced by the word '*descanso*' ('break') on the screen. Pressing a key restarted the experiment. The stimuli were presented on a 24" computer screen with white characters in a 28 pt Courier font on a black background, using Presentation v. 16.2 software (Neurobehavioral Systems).

Table III. Significant factors and interactions at the 100-250 ms period.

		df	*F*	*p*	η_p^2	Power
Length × agreement × group		2.63	4.11	0.021	0.116	0.709
Agreement × region × group		2.63	3.511	0.036	0.100	0.635
Anterior	Length × agreement in ADHD+	1.16	6.99	0.018	0.304	0.699
	Agreement in long sentences in ADHD+	1.16	7.16	0.017	0.309	0.710
	Length in control	1.27	5.36	0.028	0.166	0.608
Posterior	Agreement × group	2.64	3.40	0.039	0.096	0.620
	Length × electrode × group	38.1216	2.01	0.040	0.059	0.845
	Agreement in ADHD–	1.20	3.98	0.060	0.166	0.476
	Agreement × electrode in control	19.532	2.75	0.050	0.839	0.761
	Length × electrode in control	19.5322	2.92	0.027	0.094	0.751

df: degrees of freedom; *F*: variance; *p*: probability; η_p^2: partial eta-squared, effect size.

Recording and pre-processing

EEG and EOG signals were recorded using 64 Ag/AgCl electrodes mounted in an elastic quick-cap according to the 10/20 system. A cephalic reference was taken (all electrodes were referenced to vertex), and two other electrodes were placed on mastoid bones. The EEG signal was re-referenced off-line to the mean activity in these two mastoid electrodes in keeping with the montage most typically used to evaluate N400 and LPC components. To monitor ocular movements and blinks, additional electrodes were placed on the external canthus of both eyes and on the left infra-orbital and supraorbital cantus. The inter-electrodes impedance was kept below 10 kΩ. EEG and EOG signals were amplified and digitized at a 500 Hz sampling rate using a SynAmps2 amplifier. High and low pass filters were set at 0.05 and 100 Hz, respectively. An additional 50 Hz Notch filter was applied. EEG data pre-processing was conducted using Brain Vision Analyser (Brain Products, Munich, Germany). EEG data epochs between –100 to 1000 ms post-stimulus onset were extracted and submitted to the following artifact rejection procedure: first, epochs showing amplitude values exceeding ±70 LV in vertical and

Figure 1. Contrasts between agreement (black line) and disagreement (red line) sentences at anterior (AF3 and F5 electrodes) and posterior regions (POz and P2 electrodes) for ADHD–, ADHD+ and control groups. The vertical lines show the boundaries between the analyzed windows.

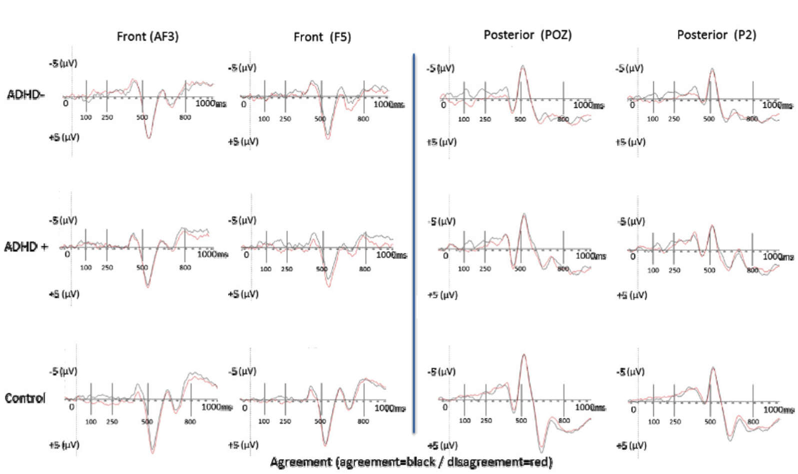
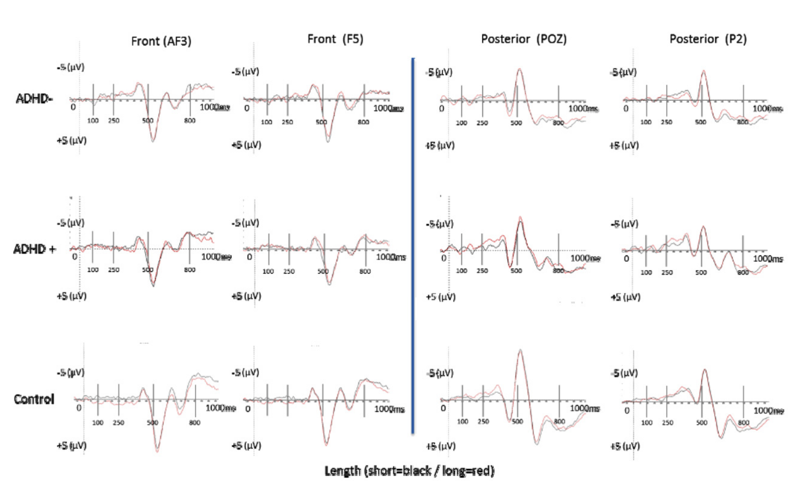


Figure 2. Contrasts between short (black line) and long (red line) sentences at anterior (AF3 and F5 electrodes) and posterior regions (POz and P2 electrodes) for ADHD–, ADHD+ and control groups. The vertical lines show the boundaries between the analyzed windows.



horizontal EOG channels were automatically removed. Further, a manual cleaning was carried out to ensure the complete removal of all artifacts. ERPs were then computed by averaging remaining epochs per subject and condition. Baseline correction was carried out using the 100 ms period preceding stimulus onset.

Statistical analyses

Three time windows were selected attending to the main components affected by this kind of manipulation: 100-250, 250-500, and 500-800 ms. Analyses included sentence length, gender agreement, and the electrodes as within-participant factors and the group as the between-participant factor. The antero-posterior factor was introduced in a subsequent analysis when these electrodes interacted with some of the other variables. This factor included two levels: anterior electrodes (Fp1, Fpz, Fp2, AF3, AF4, F7, F5, F3, F1, Fz, F2, F4, F6, F8, FT7, FC5, FC3, FC1, FCz, FC2) and posterior electrodes (TP8, P7, P5, P3, P1, Pz, P2, P4, P6, P8, PO7, PO5, PO3, POz, PO4, PO6, PO8, O1, Oz, O2). No laterality effects were observed, so the differences between left and right were not analyzed. The Greenhouse-Geisser correction was applied when a variable interacted with the electrodes or an analysis was the consequence of this type of interaction, so when heterogeneity was observed.

Results

100-250 ms window

Table III shows the significant factors found at this early window. The effects seem to be different as a modulation of the group and the antero-posterior axis.

The ADHD+ group shows a significant anterior effect of agreement in the long sentences, with the wave for non-agreement sentences being more positive. The ADHD– group shows only a marginal posterior effect, and the Control group shows the effect of both length, at anterior and posterior electrodes, and agreement, in the posterior electrodes only (Figs. 1 and 2).

250-500 ms window

All groups show the effect of length at the anterior and posterior regions (Table IV), but the interaction with the factor group at the anterior region supports a different impact of this variable for the pathological groups with respect to the control group, with the latter showing smaller differences in amplitude (Figs. 1 and 2).

500-800 ms window

The effects of length remain very extended at this window for all three groups and all regions (Table V;

Figs. 1 and 2). The agreement factor introduces only small differences at the posterior electrodes for the ADHD+ and the ADHD– groups, and none for the control.

Discussion

The neuropsychological factors revealed a pattern of abilities that are weakened in ADHD children (Table II), in particular cognitive flexibility, working memory and the capacity for abstraction [22]. These cognitive resources must be used for the sentences employed in the experiment to be understood efficiently. The results indicate that at the earlier window, between the 100 ms and the 250 ms marks, the ADHD– group only showed a tendency toward significance in the agreement variable, but no differences with respect to length. However, the ADHD+ group, characterized by normal reading comprehension, presented differences both in agreement and in length. Meanwhile, the children in the Control group presented similar significance at the main variables to that shown by the ADHD+ children, albeit more extended at posterior and anterior sites. These results indicate that the groups with normal reading comprehension start their morphosynctactic agreement using memory resources in the first 100 ms after appearance of the target (e.g. an adjective), in this case the last word of the sentence. In the same sense, Epstein et al [23] found differences at the LAN component in a group of children with specific language disorder with low cognitive resource capacity, implying a greater effort of working memory. The effects of enhancing the length of the sentence are well documented in adults and support an anterior effect of working memory. Our ADHD+ and control groups showed an anterior effect of the length variable, even though the children in the control group also presented the effect at the posterior sites. Some other studies emphasize a more distributed and widespread effect in children, because it is well known that frontal areas develop more slowly than other cerebral areas [24-26].

The activation of posterior areas to detect gender agreement in the control and ADHD– group could be suggesting a similar neural source. However, even when both groups activate similar areas with a similar time-course, why is it that the ADHD– group does not comprehend efficiently? Perhaps, the answer lies in the low working memory capacity of these participants, the only group with no effect of length at this window. ADHD– children do not reserve enough memory resources at frontal areas to perform the task. The slow activation of syntactic processes that require the attachment and agreement of two separated words diminishes the comprehension of the sentence. The detection of disagreement in children may be very distributed at seven years of age, and even more so at an earlier age [27]; the anterior topography of working memory is thus an effect associated with the linguistic maturity that ADHD– children do not seem to have.

Later on, at the 250-500 ms window, there is a clear effect of length on all the groups, in both anterior and posterior regions. However, this effect at the frontal region is similar in amplitude for both ADHD groups but different for the controls. The differences between short and long sentences are greater in the ADHD groups than in the controls, perhaps as a consequence of the greater demands on cognitive resources in the pathological groups. The most significant result at the last window (500-800 ms) was the significant effect of agreement for the ADHD– group, indicating a late attempt to repair the disagreement. Another remarkable effect is

Table IV. Significant factors and interactions at the 250-500 ms period.

		df	*F*	*p*	η_p^2	Power
Length		1.63	658.89	0.001	0.913	1
Region × group		2.63	6.11	0.004	0.162	0.873
Region × electrodes		19.1197	13.141	0.001	0.173	1
Length × region × group		2.63	4.42	0.016	0.123	0.742
Length × region × electrode		19.1197	10.959	0.001	0.148	1
Anterior	Length	1.63	222.44	0.001	0.779	1
	Length in ADHD–	1.63	85.97	0.001	0.811	1
	Length in ADHD+	1.63	91.58	0.001	0.851	1
	Length in control	1.27	53.16	0.001	0.663	1
	Length × electrode in control	19.513	2.74	0.032	0.092	0.742
	Length contrast ADHD+/ADHD–	1.36	0.001	0.990	0.001	0.05
	Length contrast ADHD–/control	1.47	5.61	0.022	0.107	0.641
	Length contrast ADHD+/control	1.43	5.48	0.024	0.113	0.629
Posterior	Length	1.63	375.32	0.001	0.856	1

df: degrees of freedom; *F*: variance; *p*: probability; η_p^2: partial eta-squared, effect size.

Table V. Significant factors and interactions at the 500-800 ms period.

		df	*F*	*p*	η_p^2	Power
Length		1.63	218.97	0.001	0.777	1
Length × region		1.63	5.49	0.022	0.080	0.636
Anterior	Length	1.63	90.72	0.001	0.590	1
	Length × electrode	19.1197	3.44	0.021	0.052	0.739
Posterior	Length	1.64	223.23	0.001	0.777	1
	Length × electrode	19.1216	12.27	0.001	0.161	1
	Length in ADHD–	1.20	53.81	0.001	0.729	1
	Agreement in ADHD–	1.20	4.26	0.050	0.729	0.502
	Length × electrode	16.320	3.082	0.029	0.134	0.724
	Length in ADHD+	1.16	58.91	0.001	0.786	1
	Length × electrode in ADHD+	19.304	4.519	0.001	0.786	1
	Agreement × electrode in ADHD+	19.304	3.22	0.025	0.168	0.747
	Length in control	1.28	122.48	0.001	0.814	1
	Length × electrode in control	19.532	7.56	0.001	0.213	1

df: degrees of freedom; *F*: variance; *p*: probability; η_p^2: partial eta-squared, effect size.

the transfer of the agreement effect from anterior to posterior regions at this late window. The time-course of these effects matches the P600, a component reported in adults associated with centro-parietal areas when gender or number agreement is manipulated, although some other syntactic ambiguities (e.g. garden path) also produce the P600, albeit with an anterior localization [28].

In sum, some important differences were observed between groups at different levels. The first, observed at the anterior sites, is a difference in cognitive effort between the two ADHD groups and the controls in the intermediate window. Also, in the last window, both pathological groups continue to perform operations relating to agreement, probably in an attempt to repair the effects of an adjective in disagreement with the initial anaphoric pronoun, whereas the healthy children do not show this effect. These differences support a general deficit of processing in ADHD children; however, they do not explain the differences in comprehension between the groups. These differences are situated at the first milliseconds of processing, where the clue seems to lie in the early use of working memory resources: these are not activated until 250 ms in the ADHD– group, whereas the ADHD+ group shows working memory effects from 100 ms. In addition, the agreement effect is anterior in the ADHD+ group and posterior in the ADHD– group.

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Correlatos electrofisiológicos de la lectura en niños con trastorno por déficit de atención/hiperactividad

Objetivos. Investigar si los déficits en las funciones ejecutivas en el trastorno por déficit de atención/hiperactividad (TDAH) afectan a su compresión lectora e identificar un potencial marcador biológico de este endofenotipo neuropsicológico a través de potenciales relacionados con eventos. Específicamente, hipotetizar si las diferencias en memoria de trabajo e inhibición mantienen una asociación fenotípica con la comprensión lectora en el TDAH.

Sujetos y métodos. La muestra estuvo constituida por 52 niños con TDAH (8-13 años) divididos en dos grupos según la presencia (TDAH–; $n = 27$; percentil < 30) o ausencia (TDAH+; $n = 25$; percentil > 50) de déficit en compresión lectora y un grupo control ($n = 27$). Se evaluaron las funciones ejecutivas y se realizó un experimento de potenciales relacionados con eventos en el que se presentaron oraciones anafóricas de diferentes longitudes, y se registraron los potenciales relacionados con eventos en el último adjetivo de la oración que requiere acuerdo de género.

Resultados. Se encontró una relación entre memoria de trabajo e inhibición con el rendimiento en compresión lectora. Mientras que los grupos de TDAH+ y control mostraron signos de detección de no concordancia sintáctica a los 100 ms, el grupo de TDAH– no activó la memoria de trabajo hasta los 250 ms.

Conclusiones. La lentitud en la puesta en marcha de los mecanismos de memoria de trabajo nos ayuda a entender los déficits en comprensión lectora del grupo de TDAH–.

Palabras clave. Comprensión lectora. Concordancia de género. Funciones ejecutivas. Memoria de trabajo. Neuropsicología infantil. Potenciales relacionados con eventos. TDAH. Violación de género gramatical.