



## BLAST paradigm: A new test to assess brief attentional fluctuations in children with epilepsy, ADHD, and normally developing children

Marine Thieux<sup>a,b,\*</sup>, Julien Jung<sup>a,c</sup>, Romain Bouet<sup>a</sup>, Daniel Gerard<sup>d</sup>, Prisca R. Bauer<sup>a</sup>, Olivier Bertrand<sup>a</sup>, Marcela Perrone-Bertolotti<sup>e</sup>, Alexis Arzimanoglou<sup>a,b</sup>, Philippe Kahane<sup>f,g</sup>, Jean-Philippe Lachaux<sup>a,1</sup>, Julitta De Bellescize<sup>b,1</sup>, Vania Herbillon<sup>a,b,1</sup>

<sup>a</sup> INSERM, U1028, CNRS, UMR5292, Lyon Neuroscience Research Center, Lyon, France

<sup>b</sup> Department of Paediatric Clinical Epileptology, Sleep Disorders and Functional Neurology, Member of the European Reference Network on Rare and Complex Epilepsies EpicARE, Hospices Civils de Lyon and University Lyon, Lyon, France

<sup>c</sup> Department of Functional Neurology and Epileptology, Member of the European Reference Network on Rare and Complex Epilepsies EpicARE, Hospices Civils de Lyon and University Lyon, Lyon, France

<sup>d</sup> Department of Developmental Psychopathology of Child, Hospices Civils de Lyon, Lyon, France

<sup>e</sup> University Grenoble Alpes, CNRS, LPNC, Grenoble, France

<sup>f</sup> University Grenoble Alpes, Inserm, CHU Grenoble Alpes, GIN, Grenoble, France

<sup>g</sup> Department of Neurology, CHU Grenoble-Alpes, Grenoble, France

### ARTICLE INFO

#### Article history:

Received 18 June 2019

Revised 18 July 2019

Accepted 26 July 2019

Available online 17 August 2019

#### Keywords:

Childhood epilepsy

Attention-deficit hyperactivity disorder (ADHD)

Attentional stability

Neuropsychological

BLAST

### ABSTRACT

**Background:** Pure attentional deficits are still underdiagnosed in children with epilepsy. While attention-deficit hyperactivity disorder (ADHD) is historically the most studied cause of attentional disorders, an important number of children with epilepsy and attentional complaints do not fully meet the DSM-V (Diagnostic and Statistical Manual of Mental Disorders - Fifth Edition) criteria for ADHD and may be excluded from specific care. Clinical tools currently available are insufficient to detect more subtle but clinically relevant attentional fluctuations.

**Objective/methods:** The recently developed Bron–Lyon Attention Stability Test (BLAST) was used to evaluate brief attentional fluctuations with a high temporal precision. Drawing on two new attentional indices, we evaluated spontaneous fluctuations of response accuracy and timing, underlying attentional stability. The main objective was to assess attentional stability in children with i) epilepsy with comorbid ADHD, ii) epilepsy without comorbid ADHD, iii) ADHD not medicated and without epilepsy, and iv) normal development. Further objectives were to assess the main determinants of attentional stability in those groups, including the effect of factors related to the epileptic condition.

**Results:** In 122 children with epilepsy (67 with comorbid ADHD), 52 children with ADHD, and 53 healthy controls, we demonstrated lower attentional stability in both the groups with epilepsy and ADHD compared with healthy children. In children with epilepsy, BLAST scores were negatively associated with earlier seizure onset and AED (antiepileptic drug) polytherapy, while the seizure frequency, epilepsy duration, or type did not influence BLAST scores.

**Conclusions:** This study demonstrates that attentional stability is impaired in children with epilepsy and/or ADHD. Bron–Lyon Attention Stability Test seems to be a sensitive test to detect attentional stability deficit in children with epilepsy and with attentional complaints who did not meet all criteria of ADHD.

We propose that BLAST could be a useful clinical neuropsychological tool to assess attentional disorders in children.

© 2019 Elsevier Inc. All rights reserved.

\* Corresponding author at: INSERM, U1028, CNRS, UMR5292, Lyon Neuroscience Research Center, Lyon, France.

E-mail address: [marine.thieux@live.fr](mailto:marine.thieux@live.fr) (M. Thieux).

<sup>1</sup> These authors contributed equally to this work.

### 1. Introduction

Attention is a core executive function supported by structural and functional networks which mature throughout childhood and adulthood [1,2]. Substantial deficits in all or some attentional subdomains were shown to significantly impair academic achievement, social, and professional integration [3–5].

Epidemiological studies show that attentional deficits are common in the general population and the most frequent comorbidity in children with epilepsy (CWE) [6]. Attention-deficit hyperactivity disorder (ADHD) is the best characterized attentional disorder [7]. Attention-deficit hyperactivity disorder occurs in 5 to 7% of children, more commonly in boys than girls, and the mixed subtype (i.e., inattention plus hyperactivity) is overrepresented [7]. In CWE, ADHD is diagnosed in 30 to 40% of both girls and boys, and the inattentive subtype is more common [4,8–12].

There are qualitative and semi-quantitative consensus criteria for diagnosing ADHD, which are regularly updated [13]. These do, however, not cover all clinically relevant attentional deficits. A significant number of children with attentional complaints do not fulfill the criteria defined by DSM-V [7], leading to underdiagnoses [14,15].

To improve the detection of those deficits, behavioral performances on neuropsychological tests can be used to confirm clinical suspicion. Some children are suspected to have disturbances in sustained attention, which can be assessed by Continuous Performance Tests (CPT) [16]. There is an ongoing debate about conceptual and methodological approaches to measure “sustained attentional deficits” and their contribution to the ADHD phenotype. Traditional designs are well-adapted to study long lasting and slow drifts away from the ongoing task but brief fluctuations of attention within the task may go unnoticed, especially in tests in which only a subset of the stimuli requires attentive processing (e.g., CPT).

Other approaches use the global variability of reaction times (RT) – computed across the entire task – to measure attentional instability for the assessment of ADHD [17–19], in addition to more standard measures such as average RT and error rate. None of these measures alone, however, captures the fact that when individuals are more focused, they tend to react faster, with less errors and with more stable performance. Ideally, indices revealing attentional deficits should take all these elements into account. We suggest two measures with such properties, adapted from a task designed specifically to detect brief attentional fluctuations.

Given that in CWE, attentional deficits seem characterized by slow and fluctuating responses [10,15] and a significant number of children with attentional problems remain underdiagnosed [20], the International League Against Epilepsy (ILAE) and the American Academy of Pediatrics (AAP) advocate the urgent need for developing more objective and reliable clinical tools, taking into account the broad spectrum of attentional deficits [7,15].

The main objective of this study was to assess attentional stability in CWE with or without comorbid ADHD, ADHD only, and normally developing children. We used the recently developed BLAST (Bron–Lyon Attention Stability Test [21]) to assess the ability to “stay on task” on a second-to-second basis. This ability requires continuous and undivided attention, reflecting the duration of many task units in daily life (such as listening to an explanation integrally, reading one or two pages of a book, or remaining focused on the resolution of an arithmetical school task).

We aimed to assess the specific BLAST variables reflecting the dynamic aspects of responses as accuracy, regularity, and speed. They rely on reproducing series of fast and error-free responses and regular and error-free series and might be disturbed by brief attentional fluctuations.

Further objectives were to identify the most discriminating BLAST variables within the subgroups and to investigate factors related to epilepsy (i.e., seizure type and frequency, pharmacotherapy, age of onset, epilepsy duration) in order to better characterize the attentional components that are disturbed in children with attentional deficits.

We hypothesize that children with attentional deficits (i.e., CWE and ADHD and children with ADHD without epilepsy) show reduced attentional stability compared to healthy controls. We expect that the specific BLAST variables, *Intensity* and *Stability*, are more appropriate to detect these subtle attentional deficits than the

measures commonly used, like RT and error, allowing for better clinical management.

## 2. Materials and methods

### 2.1. Participants

We included the following four groups of children: 141 CWE (80 with comorbid ADHD and 61 without comorbid ADHD), 52 children with ADHD without epilepsy, and 60 children with a normal development. For all groups, inclusion criteria were as follows: (a) age between 6 to 18 years old, (b) ordinary school curriculum, (c) no major visual or auditory impairment, (d) no motor disability of the upper limbs, and (e) no epileptic seizure during the task. All children and both parents or caretakers signed an informed consent before participating.

The study protocol was approved by the Ethics Committee Sud-Est III (Lyon B) no. 2016-013B for healthy children and by the Ethics Committee Sud-Est V (COGNI-AIC-38RC14.374) for CWE and/or ADHD. This study has been approved by the CNIL (National Commission on Informatics and Liberty) (HCL [Hospices Civils de Lyon] CNIL register no.: 18-315) and by the Ethics Committee of HCL (no.: 19-19).

Children with epilepsy were recruited from the department of Paediatric Clinical Epileptology of the Femme-Mere-Enfant hospital (HFME), HCL, Lyon, France between 2015 and 2017. All CWE were included in this cross-sectional study of attentional disorders regardless of the evolution of their epilepsy, their epilepsy syndrome, type of epilepsy (i.e., focal or generalized, etiology), seizure frequency, or number of antiseizure drugs. The diagnosis and type of epilepsy were confirmed by two experienced neurologists according to ILAE criteria [22,23].

Children with ADHD were recruited from the department of child and adolescent psychopathology unit of the same hospital between 2015 and 2017. The diagnosis of ADHD (also in CWE) was confirmed by an experienced neuropsychiatrist and a neuropsychologist from the HFME using the ADHD rating scale (ADHD-RS) and the clinical questionnaire for ADHD from the DSM-V. None of the children was treated with a psychostimulant.

Healthy children without a history of seizures or clinical diagnosis of neurodevelopmental disorders were recruited between 2016 and 2017 through adverts in local newspapers and schools.

For all children, ADHD-RS scores and information on socioprofessional status of parents [24] were collected.

### 2.2. Procedure

#### 2.2.1. Task

For CWE and/or ADHD, the experiment was done during regular clinical follow-up requiring a video electroencephalogram (EEG). An EEG was also performed in healthy children for a separate study. For healthy controls, the task was conducted at the Lyon Neuroscience Research Center (CRNL). The paradigm was adapted for children from the original BLAST [21].

Participants were seated in front of a computer screen, in a quiet room with minimal distraction. They were informed that they were going to play a game, with the aim to find a balance between speed and accuracy. The experiment started after a 1-min training period: there were three blocks of 3 min interspersed by a 30-second (s) break. The complete experiment took approximately 15 min. Visual BLAST stimuli were presented on a computer running the Presentation® stimulus delivery software [25] synchronized with the EEG acquisition system. For each trial, the stimulus appeared in foveal vision, in black on a gray background.

Participants were instructed to find a target letter colored in red in an array of four letters. First, the target letter appeared on the screen during 200 milliseconds (ms), followed by a mask (#) during 300 ms, followed by a 2-by-2 array of four letters in which one of them was red in 50% of cases (Fig. 1). They had to provide their responses

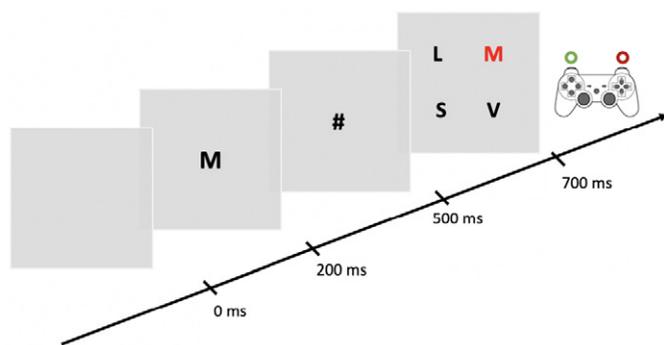


Fig. 1. Typical trial of the BLAST experimental paradigm.

manually using a joystick. The “Yes” responses were provided when one of the four letters was red using their nondominant hand. The “No” responses were provided when no red letter was presented and using their dominant hand. The first letter was always the same as the red target letter. We decided to maintain this design in the simplified version as a signal to focus on the task. The next trial started 800 ms after the array if a response was given and 3800 ms after the array in case of no response. No feedback was given after trials. This paradigm involved visual target detection, selection of response, and motor transformation, all dependent on attentional resources of the participant. Visual search is automatized by the saliency of the stimulus, producing a “pop-out” effect.

The BLAST has the following good psychometric properties [21]: *i*) a good test–retest reliability ( $r > 0.6$  for most measures), *ii*) a significant correlation between the subtest of processing speed index (e.g., CODE) from the Wechsler Intelligence Scale for children (WISC-IV) and the Wechsler Adult Intelligence Scale (WAIS-IV) [26,27] and most behavioral indices of the BLAST, and *iii*) a high sensitivity to the inattention component of the ADHD-RS (and more precisely with the observed inability to stay-on-task) for all the indices.

### 2.2.2. Behavioral measures

The following three standard measures were assessed: RT, error rate, and variability of RT.

The *RT* is the time (in ms) between the onset of the letter array and the motor response. The *Error* is the percentage of no response and false alarms. The *Variability* is the variance of the RT, computed over all trials.

The following two specific variables were computed: *Stability* and *Intensity*. These indices reveal momentary lapses of attention (MLA) to capture the moment-to-moment dynamics of attention.

*Intensity* was derived from the assumption that highly focused individuals tend to respond fast and with few errors. It quantifies the ability of individuals to produce long series of fast and accurate responses, and ranges from 0 and 100 (maximal performance). The computation of *Intensity* is fully described in Supplementary material.

*Stability* was derived from the assumption that task-irrelevant cognitive processes add “noise” to the RT [18]. It quantifies the ability of an individual to produce long series of correct responses with a stable RT, independently of its speed, and ranges from 0 and 40 (maximal performance). The *Stability* measure relies on the variation of RT without taking speed into account, focusing on regularity. The full details of *Stability* computation are provided in the Supplementary materials.

## 2.3. Statistical analysis

Statistical analyses were conducted using the R software [28].

### 2.3.1. Demographic analysis

Analysis of variance (ANOVA) and  $\chi^2$  tests were performed in order to compare socioprofessional status of parents and age between

the four groups and epilepsy type and duration, seizure frequency, and number of antiseizure drugs between CWE with and without comorbid ADHD. Statistical significance value was set to a *p*-value below .05 for each test.

### 2.3.2. Behavioral analysis

First, an ANOVA was conducted with a single explanatory factor (block factor) to assess the influence of the order of each block on BLAST measures (to rule out a potential influence of fatigue). Since no effect of the block factor was shown, we used trials from the three blocks for subsequent statistical analyses.

To assess the factors influencing the attentional performance during BLAST paradigm, we used an ANOVA applied on a linear mixed effect model (R-lme4 package) [29] taking into account the heterogeneity, heteroscedasticity, and nonnormality of data. These models were used because they take intersubject and interage heterogeneity into account. The choice of the best model was made according to criteria reflecting its parsimony (Akaike information criterion (AIC) and Bayesian information criterion (BIC) values). Type II variance analyses (car package version 3.0-2) [30] were performed using a Wald  $\chi^2$  test. Post hoc tests, adjusted for the number of comparisons, were performed using the Lsmeans package (Lsmean version 2.27-61) [31] with the Tukey method. The following two analyses were performed:

- the first analysis included the four groups (epilepsy with ADHD and without ADHD, ADHD, and controls) considering the group and the age as explanatory variable.
- the second analysis focused on the groups with epilepsy by taking the age of seizure onset, the seizure frequency during the last 12 months (none, 1–5 seizures, 5–12 seizures, 13–50 seizures, 1 seizure per week, or one seizure per day), the type of epilepsy (focal or generalized), the duration of epilepsy (duration in months between the age of the first seizure and the age at the test), and the number of antiseizure drugs (none, monotherapy, or polytherapy) as explanatory variables.

For each analysis, variables to be explained were RT, error rate, variability, *Stability*, and *Intensity*.

A complementary analysis was performed to describe behavioral responses of CWE with attentional complaints but who did not fully meet the DSM-V criteria (i.e., 4 to 5 inattention criteria and less than 6 hyperactivity criteria) ( $n = 17$ ). To this end, we established age-dependent normative values for the different BLAST scores in the control group using the R-lme4 package [29]. A polynomial fit was used to model the relationship between BLAST variables and age of the subject with a 95% confidence interval. A cutoff was established (95% confidence interval) and allowed to categorize the performance for each BLAST variable as pathological or not pathological as compared to the norm derived from the control group. The performance was considered as “pathological” when its attentional performance was out of the confidence interval of normative values established on control children.

## 3. Results

Six CWE with ADHD and 3 without ADHD who experienced a seizure during the EEG-BLAST session, 9 who were treated with methylphenidate (i.e., 7 CWE and ADHD and 2 CWE only), and 7 healthy subjects with practical problems during the experiment were excluded from the analysis. One CWE with a mean RT lower than 200 ms and error percentage higher than 40% was excluded from statistical analysis because of its outlier performances. After exclusion, the group with epilepsy included 122 children (67 with ADHD and 55 without ADHD); the group with ADHD included 52 children; and 53 healthy children formed the control group. Additional information about subjects are given in Table 1.

**Table 1**  
Demographic and clinical characteristics of the study sample.

	Epilepsy with ADHD	Epilepsy without ADHD	ADHD	Control
N	67	55	52	53
Demographic characteristics				
Age (months, mean, SD)	124 (39)	131 (40)	133 (25)	139 (42)
Gender (male/female)	33/34	23/32	43/9	33/20
Epilepsy				
Age of seizure onset (months, mean, SD)	64 (41)	78 (39)	-	-
Type of epilepsy (n, percentage)				
Focal	26 (39%)	27 (49%)	-	-
Generalized	41 (61%)	28 (51%)	-	-
Seizure frequency (last 12 months) (n, percentage)				
None	26 (39%)	16 (29%)	-	-
1–5 seizures	16 (24%)	17 (31%)	-	-
5–12 seizures	3 (5%)	2 (4%)	-	-
13–50 seizures	6 (9%)	4 (7%)	-	-
1 seizure per week	3 (5%)	6 (11%)	-	-
1 seizure per day	12 (18%)	10 (18%)	-	-
Number of antiseizure drugs (n, percentage)				
None	21 (31%)	15 (27%)	52 (100%)	53 (100%)
Monotherapy	29 (43%)	26 (47%)	0	0
Polytherapy	17 (26%)	14 (26%)	0	0
ADHD - mean (SD)				
ADHD-RS				
Global	29 (9)	12 (6)	31 (9)	8 (6)
Inattention	16 (6)	8 (4)	21 (4)	5 (4)
Hyperactivity	12 (7)	5 (4)	10 (7)	4 (3)

### 3.1. Participant demographics

The four groups were not different in terms of age ( $F(3, 223) = 1.691; p > .05$ ) and socioprofessional status of parents ( $\chi^2(15) = 13.398; p > .05$ ).

The two groups of CWE were not different in terms of duration of epilepsy ( $F(1, 120) = 1.049; p > .05$ ), type of epilepsy ( $\chi^2(1) = 0.915; p > .05$ ), seizure frequency ( $\chi^2(5) = 3.219; p > .05$ ), number of antiseizure drugs ( $\chi^2(2) = 0.276; p > .05$ ), and the age of first seizure ( $F(1, 120) = 3.719; p > .05$ ).

### 3.2. Attentional performances

First, we performed an ANOVA on the “block” factor for each score of the BLAST, to check for a possible learning and/or fatigue effects during the experiment. This analysis showed no significant effect ( $F(2, 672) < 2; p > .05$ ).

Regardless of the group, attentional performances assessed by BLAST improved with age. Reaction time and error rate decreased significantly (RT:  $Wald \chi^2(3, 45,906) = 130.67, p < .0001$ ; error percentage:  $Wald \chi^2(3, 45,906) = 50.88, p < .0001$ ) while *Intensity* and *Stability* increased significantly with age (*Stability*:  $Wald \chi^2(3, 45,906) = 104.68, p < .0001$ ; *Intensity*:  $Wald \chi^2(3, 45,906) = 161.31, p < .0001$ ).

Type II variance analyses performed with Wald's  $\chi^2$  showed that there was no significant difference between the groups for the RT (Fig. 2-a), the error percentage (Fig. 2-b), and the variability (Fig. 2-e). There were significant differences between groups for the *Stability* ( $Wald \chi^2(3, 45,906) = 28.369; p < .0001$ ) (Fig. 2-c) and *Intensity* ( $Wald \chi^2(3, 45,906) = 9.084; p < .05$ ) (Fig. 2-d). Post hoc analyses showed that CWE with and without ADHD and children with ADHD performed worse than the control group. Controls had a higher *Stability* than CWE with ADHD ( $t(220) = 4.383; p < .0001$ ) and than children

with ADHD ( $t(219) = 4.806; p < .0001$ ) (Fig. 2-c). The control group also had a higher *Intensity* than CWE with ADHD ( $t(218) = 2.738; p < .05$ ) (Fig. 2-d). Mean scores for each group are shown in Table 2.

There was no significant interaction between age and groups: thus, difference between groups appears independently of the age effect.

### 3.3. Relationship between characteristics of epilepsy and attentional performances

In CWE (with and without ADHD), earlier age of the seizure onset was associated with a higher RT ( $Wald \chi^2(1, 23,453) = 22.399; p < .0001$ ) (Fig. 3-a), a higher error percentage ( $Wald \chi^2(1, 23,453) = 5.269; p < .05$ ) (Fig. 3-d), and lower *Stability* ( $Wald \chi^2(1, 23,453) = 9.469; p < .01$ ) (Fig. 3-c) and *Intensity* ( $Wald \chi^2(1, 23,453) = 9.904; p < .01$ ) (Fig. 3-b).

In these children, a higher number of antiseizure drugs were correlated with lower performances. It was significant for the RT ( $Wald \chi^2(2, 23,453) = 11.727; p < .001$ ) and the error rate ( $Wald \chi^2(2, 23,453) = 7.394; p < .01$ ) and not significant for *Stability* and *Intensity* ( $p > .05$ ). Post hoc analyses demonstrated that children with polytherapy had a higher RT ( $t(81) = 2.979; p < .05$ ) and error percentage ( $t(94) = 2.712; p < .05$ ) than children with monotherapy. There was no significant difference in performances between children without antiseizure drugs and children with monotherapy ( $p > .05$ ).

Neither epilepsy type, groups (with and without ADHD), seizure frequency, nor epilepsy duration were related to the BLAST outcome measures (RT, error percentage, *Intensity*, and *Stability*) ( $p > .05$ ).

### 3.4. Relationships between attentional performances on BLAST and ADHD criteria

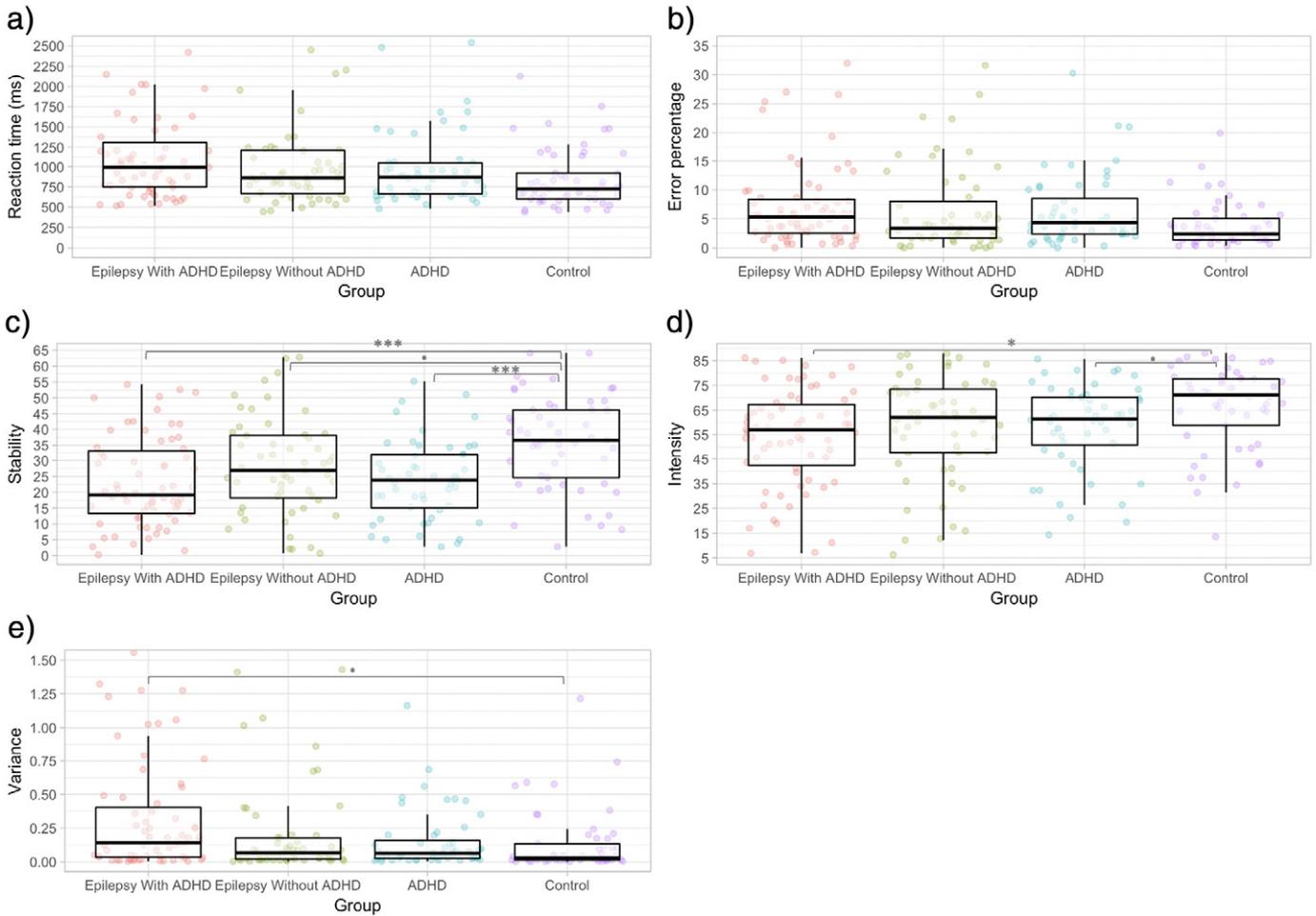
There were 17 CWE without ADHD who did not fully meet DSM-V criteria for ADHD and who did not have pathological scores on the ADHD-RS. The BLAST highlighted difficulties in attentional stability in six of those children using the RT, in eight using error rates, in 16 using *Stability*, and in 13 using *Intensity* (see Table 3).

## 4. Discussion

The recently described BLAST paradigm evaluates the ability to stay on-task by assessing the dynamics of brief attentional fluctuations. Our study aimed at evaluating the clinical utility of a simplified BLAST version in children with high prevalence of attentional deficits: children with ADHD and children with a broad range of epileptic disorders. Few studies have been performed to better characterize the nature of attentional complaints in those populations and focused mostly on sustained attention [32]. To the best of our knowledge, none specifically measured the influence of very brief attentional fluctuations on attentional stability.

We compared the impact of intratask attentional fluctuations on attentional stability between CWE with and without comorbid ADHD, children with ADHD without epilepsy, and in typical developing children. We found that CWE and/or ADHD performed worse on the BLAST than healthy controls. Two new specific measures, *Stability* and *Intensity*, showed deficits in attentional functioning that are not captured by classical variables such as RT, error rate, or the global variability of RT across trials. In line with our hypothesis, *Stability* differentiated controls from the three disease groups (ADHD, CWE with and without ADHD). *Intensity* distinguished the children with an ADHD component (i.e., CWE with ADHD or children with ADHD only) from controls.

These results indicate that standard measures such as RT, error rates, or variability alone are insufficient to detect fluctuations in attentional stability, which is an essential component of cognitive functioning in everyday life. Traditional attention tests (e.g., CPT) that assess performance over the entire test do not capture intratask dynamics, which can lead to an incomplete assessment of attentional deficits. These



**Fig. 2.** Each point represents the median reaction time (a), the error rate (b), the Stability (c), the Intensity (d), and the variability (e) for each subject according to the groups (red: epilepsy with ADHD, green: epilepsy without ADHD, blue: ADHD, purple: control). The central line of the boxplot corresponds to the median of each score, the upper and lower parts corresponds to the first and third quartiles. Difference between groups is represented by star: \*\*\*:  $p < .001$ ; \*:  $p < .05$ ; . :  $p < .1$ .

very brief attentional fluctuations can be explained by MLA lasting a few moments (seconds or less) during which cognitive resources are side tracked towards processes unrelated to the task [33]. Previous studies suggested that MLA manifest by isolated errors or a transient increase in RT [34,35]. With its high temporal resolution and its new specific variables, the BLAST captures the dynamics of attentional performances throughout the task and allows to compare the fluctuations of speed and quality of response underlying attentional stability.

The *Stability* measure relies on the variation of RT without taking speed into account, focusing on regularity. It differentiated controls from the three disease groups and interestingly revealed lower

performances in CWE without ADHD, despite normal speed. This result shows that slowness, which is frequently reported in previous studies, does not fully describe attentional disorders in those children [36]. In children who do not fully meet criteria of ADHD, but have problems at school or reported by parents, difficulties in attentional stability can be more easily identified by the BLAST than by conventional measures. We found that especially *Stability* was sensitive to attentional deficits that were not detected by the ADHD-RS. This new test may thus increase the diagnostic sensitivity for attentional disorders, as recommended by the ILAE and the AAP.

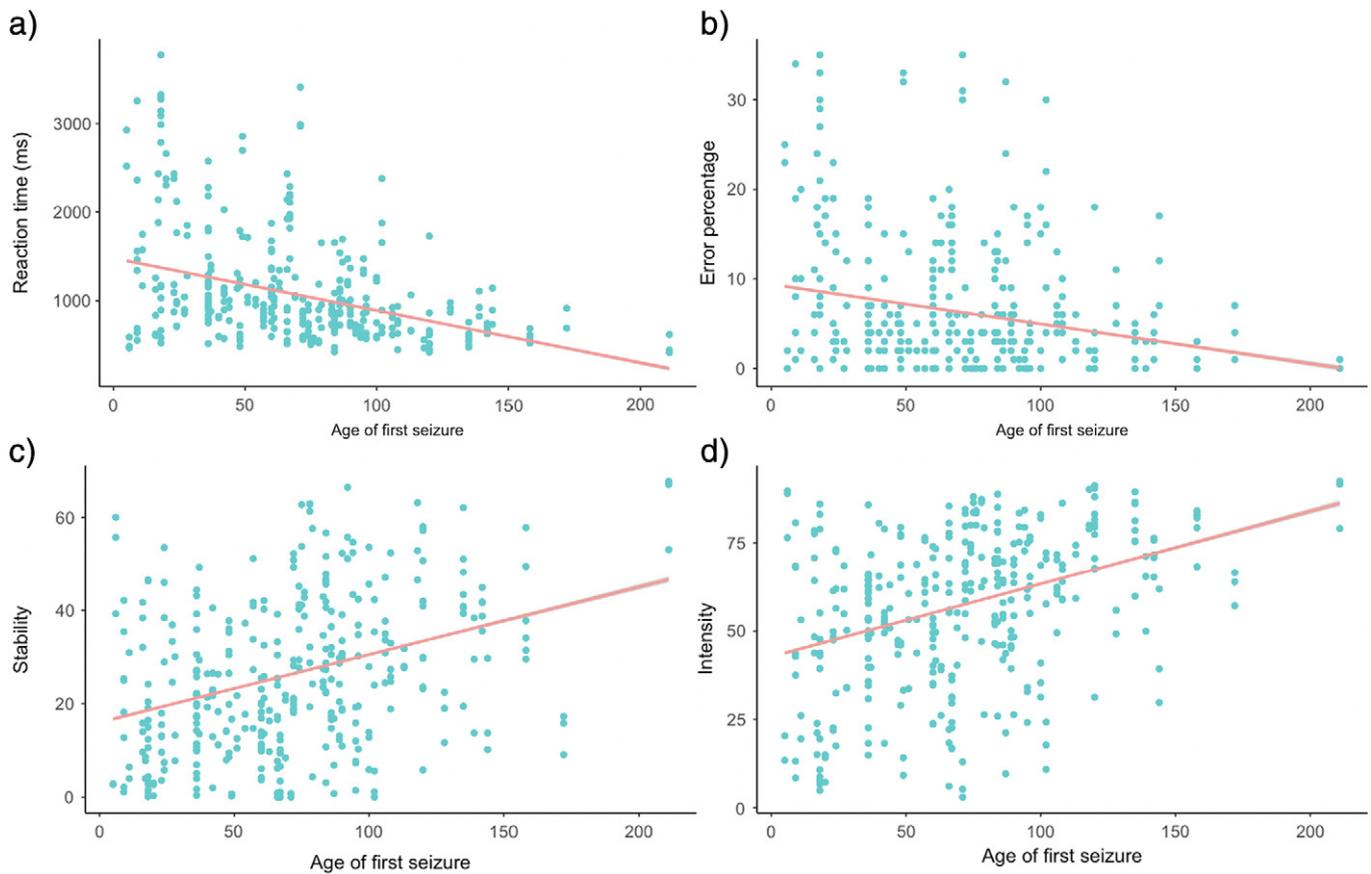
The *Intensity* measure of the BLAST distinguished children with an ADHD component (i.e., CWE with ADHD or children with ADHD only) from controls. This specific measure, which integrates processing speed and accuracy of the responses, seems to best reflect the core behavioral attentional disorders, shared by ADHD and CWE with ADHD.

As a whole, our results suggest that the BLAST highlights attentional difficulties that are not measured by conventional scales. Thus, BLAST can complement the assessment of attentional deficits to provide a better diagnosis of attentional disorders. The new specific measures, *Stability* and *Intensity*, may also be computed for other neuropsychological tests that measure RT and errors, such as the kiTAP battery [37].

In CWE (with and without ADHD), we found that an earlier seizure onset was associated with lower performances on RT, error percentage, *Stability*, and *Intensity*. As expected, the number of antiseizure drugs also impacted performances [38,39]. Children with epilepsy with polytherapy had higher RT and error percentages and tended to have

**Table 2**  
Mean scores on BLAST test for each group.

	Epilepsy with ADHD	Epilepsy without ADHD	ADHD	Control
N	67	55	52	53
BLAST - mean (SD)				
Reaction time (seconds)	0.75 (0.26)	0.71 (0.28)	0.65 (0.19)	0.63 (0.18)
Error rate (percentage)	7 (7)	6 (7)	6 (6)	4 (4)
Variability	0.31 (0.4)	0.21 (0.35)	0.15 (0.22)	0.13 (0.23)
Stability	23 (14)	28 (16)	24 (13)	36 (15)
Intensity	54 (20)	58 (21)	58 (18)	66 (17)



**Fig. 3.** Each point represents the median reaction time (a), Intensity (b), Stability (c), and rate of error (d) for each subject according to the age of the first seizure (in months).

lower *Stability* and *Intensity* than CWE with monotherapy or without treatment. *Stability* and *Intensity* were thus less impacted by the number of antiseizure drugs than classical measures.

In line with earlier results showing that fluctuations in attention were associated with an earlier age at diagnosis [9,10,35], our results show that the age of the first seizure had an impact on attentional stability, independent from the duration of epilepsy. In addition, attentional deficits were not linked to epilepsy-related clinical characteristics such as seizure frequency or epilepsy type. These results suggest that early seizure onset impacts attentional skill development at crucial developmental milestones in childhood. On the contrary, it appears that the diagnosis of focal versus generalized epilepsy was not a major determinant of attentional deficits, within the limits of our relatively small cohort of patients regarding epilepsy types.

The capacity to maintain attention focused matures in childhood [40, 41]. The neuroanatomical network involved in the BLAST was recently described [21]. It involves the Dorsal Attentional Network (DAN) [42], a network at the interface of the premotor areas and the anterior cingulate gyrus involved in maintaining attention throughout time. This activation pattern was also associated with a deactivation of the Default Mode Network (DMN), in line with previous studies showing deactivation of the DMN in active tasks [43]. Studies using intracranial EEG,

however, show a brief reactivation of this network between each trial [21]. Good BLAST performance seems to depend on the interplay between the DAN and the DMN. We suggest that children with reduced attentional stability may have an imbalance between these two networks, resulting in the intermittent reactivation of the DMN or limited activation of the DAN.

Limitations of our study include the recruitment of CWE from a tertiary epilepsy center, potentially leading to a high prevalence of comorbid disorders such as cognitive difficulties and a high heterogeneity of the population. Moreover, CWE and/or ADHD were investigated at different stages of the disease in a cross-sectional design. More large-scale studies are thus needed to evaluate attentional performance in different epilepsy syndromes, and longitudinal studies may be performed to evaluate the influence of epilepsy duration. In CWE, we excluded the impact of potential seizures on task results, but interictal epileptiform discharges were not considered. This will be the aim of future studies.

## 5. Conclusion

Attentional deficits are a major concern in CWE and/or ADHD. Using a novel test, we demonstrate that attentional stability is altered by brief attentional fluctuations in CWE with or without ADHD and in children with ADHD only, compared to controls.

The BLAST improved the detection of deficits in attentional stability in CWE and attentional complaints, who did not meet all criteria for ADHD. The BLAST identified differences in attentional functioning in children with ADHD, with or without epilepsy compared to controls. This test could also show the cognitive impact of a polytherapy with antiseizure drugs.

The BLAST with its innovative specific attentional indices should be included in neuropsychological assessments of attentional disorders, particularly in syndromes with a high prevalence of pure attentional

**Table 3**  
BLAST performance scores in children with epilepsy.

BLAST							
Reaction time		Rate of errors		Stability		Intensity	
Deficit	Normal	Deficit	Normal	Deficit	Normal	Deficit	Normal
<b>6</b>	11	<b>8</b>	9	<b>16</b>	1	<b>13</b>	4

The number of subjects with pathological performances on BLAST is reported in bold font.

deficits. This ergonomic test lasts 15 min and can be easily performed in the setting of standard follow-up. It is well adapted to children and may thus be evaluated in a broad range of neurodevelopmental disorders impacting cognitive skills.

### Funding

This study was conducted without a specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

### Declaration of competing interest

None.

### Acknowledgments

We thank all children and their parents for their participation in the study and gratefully acknowledge the following medical staff and fellows involved in this project for their help in recruiting participants: Dr. P. Keo-Kosal, Dr. K. Ostrowsky-Coste, Dr. E. Panagiotakaki, Dr. A. Montavont, Dr. J. Toulouse, Dr. C. Milleret, Dr. Z. Gokce, Mrs. F. Ilisky-Lecoanet, and Mrs. A. Marcastel.

### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.yebeh.2019.106470>.

### References

- Rueda MR, Rothbart MK, McCandliss BD, Saccomanno L, Posner MI. Training, maturation, and genetic influences on the development of executive attention. *Proc Natl Acad Sci* 2005;102(41):14931–6.
- Shaw P, Eckstrand K, Sharp W, Blumenthal J, Lerch JP, Greenstein DEEA, et al. Attention-deficit/hyperactivity disorder is characterized by a delay in cortical maturation. *Proc Natl Acad Sci* 2007;104(49):19649–54.
- Barry TD, Lyman RD, Klinger LG. Academic underachievement and attention-deficit/hyperactivity disorder: the negative impact of symptom severity on school performance. *J Sch Psychol* 2002;40(3):259–83.
- MacAllister WS, Vasserman M, Rosenthal J, Sherman E. Attention and executive functions in children with epilepsy: what, why, and what to do. *Appl Neuropsychol Child* 2014;3(3):215–25.
- Schubert R. Attention deficit disorder and epilepsy. *Pediatr Neurol* 2005;32(1):1–10.
- Dunn DW, Austin JK. Differential diagnosis and treatment of psychiatric disorders in children and adolescents with epilepsy. *Epilepsy Behav* 2004;5:10–7.
- American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Pub; 2013.
- Salpekar JA, Mishra G. Key issues in addressing the comorbidity of attention deficit hyperactivity disorder and pediatric epilepsy. *Epilepsy Behav* 2014;37:310–5.
- Berl MM, Terwilliger V, Scheller A, Sepeta L, Walkowiak J, Gaillard WD. Speed and complexity characterize attention problems in children with localization-related epilepsy. *Epilepsia* 2015;56(6):833–40.
- Williams AE, Giust JM, Kronenberger WG, Dunn DW. Epilepsy and attention-deficit hyperactivity disorder: links, risks, and challenges. *Neuropsychiatr Dis Treat* 2016;12:287.
- Brikell I, Chen Q, Kuja-Halkola R, D'Onofrio BM, Wiggs KK, Lichtenstein P, et al. Medication treatment for attention-deficit/hyperactivity disorder and the risk of acute seizures in individuals with epilepsy. *Epilepsia* 2019;60:284–93. <https://doi.org/10.1111/epi.146407>.
- Mercier C, Roche S, Gaillard S, Kassai B, Arzimanoglou A, Herbillon V, et al. Partial validation of a French version of the ADHD-rating scale IV on a French population of children with ADHD and epilepsy. Factorial structure, reliability, and responsiveness. *Epilepsy Behav* 2016;58:1–6.
- American Academy of Pediatrics, Committee on Quality Improvement, Subcommittee on Attention-Deficit/Hyperactivity Disorder. ADHD: clinical practice guideline for the diagnosis, evaluation and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics* 2011;128:1007.
- Sherman EMS, Brooks BL, Akdag S, Connolly MB, Wiebe S. Parents report more ADHD symptoms than do teachers in children with epilepsy. *Epilepsy Behav* 2010;19(3):428–35 [Internet]. Available from: <https://doi.org/10.1016/j.yebeh.2010.08.015>.
- Auvin S, Wirrell E, Donald KA, Berl M, Hartmann H, Valente KD, et al. Systematic review of the screening, diagnosis, and management of ADHD in children with epilepsy. Consensus paper of the Task Force on Comorbidities of the ILAE Pediatric Commission. *Epilepsia* 2018;59(10):1867–80.
- Semrud-Clikeman M, Wical B. Components of attention in children with complex partial seizures with and without ADHD. *Epilepsia* 1999;40(2):211–5.
- Kofler MJ, Rapport MD, Sarver DE, Raiker JS, Orban SA, Friedman LM, et al. Reaction time variability in ADHD: a meta-analytic review of 319 studies. *Clin Psychol Rev* 2013;33(6):795–811.
- Gmehlin D, Fuermaier AB, Walther S, Tucha L, Koerts J, Lange KW, et al. Attentional lapses of adults with attention deficit hyperactivity disorder in tasks of sustained attention. *Arch Clin Neuropsychol* 2016;31(4):343–57.
- Tamm L, Narad ME, Antonini TN, O'Brien KM, Hawk LW, Epstein JN. Reaction time variability in ADHD: a review. *Neurotherapeutics* 2012;9(3):500–8.
- Ekinci O, Okuyaz Ç, Erdoğan S, Gunes S, Ekinci N, Kalinli M, et al. Attention-deficit hyperactivity disorder (ADHD) in epilepsy and primary ADHD: differences in symptom dimensions and quality of life. *J Child Neurol* 2017;32(14):1083–91.
- Petton M, Perrone-Bertolotti M, Mac-Auliffe D, Bertrand O, Aguera PE, Sipp F, et al. BLAST: a short computerized test to measure the ability to stay on task. Normative behavioral data and detailed cortical dynamics. *bioRxiv* 2018:498691 Available at: <https://doi.org/10.1101/498691>.
- Berg AT, Berkovic SF, Brodie MJ, Buchhalter J, Cross JH, van Emde Boas W, et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005–2009. *Epilepsia* 2010;51(4):676–85.
- Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, et al. ILAE classification of the epilepsies: position paper of the ILAE Commission on Classification and Terminology. *Epilepsia* 2017;58(4):512–21.
- Insee. Nomenclatures des Professions et Catégories Socioprofessionnelles (PCS). Paris: INSEE; 2003 Available at: [www.insee.fr/fr/metadonnees/pcs2003/categorieSocioprofessionnelleAgregree/1?champRecherche=true](http://www.insee.fr/fr/metadonnees/pcs2003/categorieSocioprofessionnelleAgregree/1?champRecherche=true).
- Presentation software. Berkeley, CA: NeurobehavioralSystems, Inc.; 2012 version 16.3. Internet: [www.neurobs.com](http://www.neurobs.com).
- Wechsler D. Wechsler intelligence scale for children-fourth edition (WISC-IV). [Internet] San Antonio, TX: Psychol. Corp.; 2003 Available from: <https://www.pearsonassessments.com/HAIWEB/Cultures/en-us/Productdetail.htm?Pid=015-8979-044&Mode=resource%5Cnhttp://www.pearsonclinical.com/psychology/products/100000310/wechsler-intelligence-scale-for-children-fourth-edition-wisciv.html?Pid=015-8979-044&Mo>.
- Wechsler D. Wechsler adult intelligence scale-fourth edition (WAIS-IV). [Internet] San Antonio, TX: NCS Pearson; 2008 Available from: <http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:Wechsler+Adult+Intelligence+Scale++3rd+edition#3%0Ahttp://www.statisticssolutions.com/academic-solutions/resources/directoryof-survey-instruments/wechsler-adult-intelligence-scale-fourth-edition>.
- RDevelopment, C. O. R. E. TEAM 2009: R: a language and environment for statistical computing. Vienna, Austria. Internet: <http://www.R-project.org>; 2012.
- Bates D, Maechler M, Bolker B, Walker S. lme4: linear mixed-effects models using Eigen and S4. R package version 1.1–7. 2014; 2015.
- Fox J, Weisberg S. Multivariate linear models in R. An R companion to applied regression. Los Angeles: Thousand Oaks; 2011.
- Lenth R, Lenth MR. Package 'lsmeans'. *Am Stat* 2018;34(4):216–21.
- Sánchez-Carpintero R, Neville BG. Attentional ability in children with epilepsy. *Epilepsia* 2003;44(10):1340–9.
- Weissman DH, Roberts KC, Visscher KM, Woldorff MG. The neural bases of momentary lapses in attention. *Nat Neurosci* 2006;9(7):971.
- Dunn DW, Austin JK, Harezlak J, Ambrosius WT. ADHD and epilepsy in childhood. *Dev Med Child Neurol* 2003;45(1):50–4.
- Lin JJ, Mula M, Hermann BP. Uncovering the neurobehavioural comorbidities of epilepsy over the lifespan. *Lancet* 2012;380(9848):1180–92.
- Smka K, Seidenberg M, Hermann B, Jones J. Intraindividual variability in attentional vigilance in children with epilepsy. *Epilepsy Behav* 2018;79:42–5.
- Zimmermann P, Gondan M, Fimm B. kiTAP. Test d'évaluation de l'attention, version pour enfants. Psytest; 2005.
- Kerr MP, Mensah S, Besag F, De Toffol B, Ettinger A, Kanemoto K, et al. International consensus clinical practice statements for the treatment of neuropsychiatric conditions associated with epilepsy. *Epilepsia* 2011;52(11):2133–8.
- Meador KJ. Cognitive outcomes and predictive factors in epilepsy. *Neurology* 2002;58(8 suppl 5):S21–6.
- Ruff HA, Lawson KR. Development of sustained, focused attention in young children during free play. *Dev Psychol* 1990;26(1):85.
- Richards JE. Attention in young infants: a developmental psychophysiological perspective. *Handbook of developmental cognitive neuroscience*; 2001. p. 321–38.
- Corbetta M, Shulman GL. Control of goal-directed and stimulus-driven attention in the brain. *Nat Rev Neurosci* 2002;3(3):201.
- Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA, Shulman GL. A default mode of brain function. *Proc Natl Acad Sci* 2001;98(2):676–82.