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Cognitive deficits' profiles of attention and executive functions in epilepsy versus psychogenic non-epileptic seizure patients: A preliminary cross-sectional study

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Abstract

Psychogenic non-epileptic seizures (PNES) resemble epileptic seizures (ES) but lack the associated brain electrical disruptions. Their underlying mechanism remains elusive, even though cognitive deficits are commonly reported in both ES and PNES patients. This preliminary cross-sectional study compared attention and executive functions in 20 patients with ES (ES group) and 18 with PNES or comorbid PNES and ES (PNES group) using the Stroop task and attentional network task (ANT). Both groups exhibited a significant Stroop effect, with no significant differences between them. In the ANT assessment, the ES group had significantly slower reaction times (RTs) in non-tone conditions compared to in-tone conditions ($P < 0.05$). Meanwhile, the PNES group displayed no significant difference in RTs between these conditions, indicating a more pronounced alerting effect in the ES compared to PNES group. No significant disparities emerged in executive control and orientation between the groups. The findings underscore differences in attentional processing between these groups, emphasizing the clinical significance of understanding these cognitive deficits for accurate diagnosis and tailored neuropsychological rehabilitation.

Keywords: Psychogenic non-epileptic seizures; Epileptic seizures; Attention; Executive functions; Alertness; Cognitive deficits

1. Introduction

Psychogenic non-epileptic seizures (PNES) are involuntary episodes of sensation, behavior, or movement that are very similar to epileptic seizures (ES) but lack the electrical activity disruption in the brain that characterizes epilepsy.[1] The accepted method for PNES diagnosis is prolonged video electroencephalography (vEEG) recording showing seizure-like behavior with no epileptic electrical correlates.[1] Estimations suggest that 25 – 30% of patients diagnosed with epilepsy each year may, in fact, have PNES instead of ES. During this delayed diagnostic period, patients often receive antiseizure medications (ASM), many of which are associated with negative side effects in both patients with ES and those with PNES.[2-4] Distinguishing between patients with ES and those with PNES poses a significant diagnostic challenge with important implications for quality of life and treatment.[5] Furthermore, PNES and ES may co-occur in 10 – 73% of PNES patients,[6] making the diagnosis even more challenging.

The etiology of PNES is complex and multidimensional. The Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) classifies PNES as a manifestation of functional neurological disorder, whereas the ICD-10 classifies it as a dissociative disorder.[7,8]

Numerous factors have been investigated as potential triggers for PNES.[9] According to the integrative cognitive model, overwhelming and distressing events or memories can destabilize cognitive and emotional systems. When this occurs, the brain may become unable to process the information, causing the sensory and motor systems to become reflexive, eventually leading to a seizure.[10]

Most of the published research has compared PNES and ES, often without contrasting these conditions with healthy controls. These studies have often found that both ES and PNES patients have cognitive deficits.[6,9] While such deficits are a consistent finding in both groups, getting into details presents a complicated picture. In some specific domains, studies noted superior performance in PNES patients,[11] whereas others observed comparable performance between the two groups.[12-14] Binder *et al.* showed that when testing memory and thinking skills using a specific set of tests (the Halstead–Reitan Battery), there were no performance differences between PNES and ES patients; however, both groups performed worse than healthy individuals, except in verbal IQ and certain tasks assessing problem-solving and flexibility.[15] Conversely, Çelik *et al.* reported more dominant attention and executive function problems in PNES patients when compared to ES patients.[16]

The cognitive deficits in patients with ES arise from a variety of organic brain conditions. The same changes in brain functioning that trigger seizures might also have a direct influence on cognition.[17] Structural damage or alterations due to events such as head injuries or infections and imbalanced electrical activity across the brain resulting from seizures.[18,19] Over time, some patients may develop malformations in different brain regions because of diverse causes; these malformations may disrupt the brain's regular communication and function, thereby leading to cognitive impairments.[20,21] Another influencing factor is the side effects of ASM. While crucial for seizure management, ASM may affect cognitive processes by either slowing neural transmission or modifying neurotransmitter levels.[22] In addition, cognitive functions such as memory and attention may also be affected by mood changes or mood disorders in these patients.[18] The cognitive deficits faced by ES patients can emerge from any single factor mentioned or a combination of them, among possible other causes.[6,19]

Studies suggest that the nature of cognitive impairment in epilepsy is intricately linked to the underlying pathophysiology of the seizure disorder.[23] Depending on the specific type of epilepsy, reduced activation is noticeable in different brain regions, such as the right occipital lobe, cerebellum, right frontal lobe, brainstem, and temporal lobe. These identified areas are thought to constitute the neural basis for attention deficits, particularly within the alerting network of temporal lobe epilepsy (TLE) patients.[24]

In cognitive evaluations encompassing areas such as attention, motor coordination, verbal/non-verbal fluency, and response inhibition, both TLE and frontal lobe epilepsy (FLE) patients significantly underperformed compared to healthy controls. Furthermore, results for FLE patients were notably worse than those for TLE patients.[25] Given the central role of the prefrontal cortex in attention and executive functions, this could explain the anticipated deficits in attentional performance in these patients.

An investigation that employed the Stroop task revealed that epilepsy patients are particularly hindered in conditions that evaluate response inhibition and shifting when contrasted with controls.[26] Interestingly, both FLE and TLE patients demonstrated "frontal-like" performances. This similarity may be due to the spread of neural disturbances in TLE patients.[27]

Similarly, major literature indicates that cognitive performance in individuals with PNES is generally poorer compared to healthy individuals.[6,28] However, current literature presents conflicting evidence on the extent to which PNES impacts cognition when compared to ES. Some studies have shown that patients with PNES may perform better than those with ES,[11] whereas others have found no significant differences in cognitive functions

between the two groups. Reported similarities include deficits in working memory, cognitive flexibility, and tasks requiring response inhibition and visuomotor coordination, suggesting that cognitive impairments in PNES patients can be as severe as in those with ES.[12] In addition, neuropsychological research often finds PNES individuals performing below normal levels,[11,29] especially in attention and executive functions, when compared to ES patients.[6,30] These variations in findings may stem from the diverse psychological and neurological profiles of PNES patients.[31]

According to the integrated cognitive-emotional approach,[28] cognitive impairments in PNES are influenced by a complex mix of factors due to the condition's heterogeneous nature. Dissociation, somatization, and post-traumatic stress disorder, which are common in PNES, negatively influence cognitive functioning. Studies comparing the prevalence of somatoform dissociation and compartmentalization in PNES and epilepsy patients show mixed results but generally indicate a higher prevalence of somatoform dissociation in PNES.[32] These psychopathological mechanisms affect cognition differently through their differential impacts on brain regions associated with memory, alertness, perception, and motor functions, illustrating the complex interplay between psychopathology and cognitive impairments in PNES.[28] In addition, patients with PNES exhibit mood disorders and other psychiatric diagnoses which negatively affect their cognitive profiles.[28,33] These patients frequently report significant cognitive concerns and tend to overestimate their cognitive impairments compared to those with epilepsy.[34]

Neurologically, some studies have found that PNES patients demonstrate prefrontal cortex atrophy and neurochemical changes, impacting cognitive function.[4,28] Specifically, there is evidence of substantial atrophy in their prefrontal cortex affecting their executive functions and emotional behavior.[35] In addition, neurochemical changes in the prefrontal cortex, anterior cingulate cortex, and thalamus are linked to attention deficits, inhibitory control problems, and general intelligence issues in these patients. By "general intelligence," we mean evaluating broad cognitive functions through the Wechsler Adult Intelligence Scale, encompassing verbal comprehension, perceptual reasoning, working memory, and processing speed.[36] It has been hypothesized that these structural changes are caused by a history of unnecessary antiepileptic drug treatments as well as high emotional stress.[28,35]

In summary, cognitive difficulties in both ES and PNES patients are multidimensional, stemming from psychological, emotional, neurological, and subjective factors.[18,28] This complexity necessitates a comprehensive approach in both research and clinical evaluation to fully understand and address the cognitive vulnerabilities in this population.

In this current preliminary cross-sectional study, we aimed to evaluate performance in two crucial frontal cognitive functions, attention, and executive control, which are considered essential for effective and adaptive behaviors. We focused on patients with PNES, with or without comorbid ES (categorized as PNES group), in comparison to patients with only ES (categorized as ES group). Smith and Jonides identified five executive functions: inhibition, coding, monitoring, planning, and task management.[37,38] We employed the attentional network test (ANT)[39,40] and the Stroop task[41] to measure these cognitive performances.

As reviewed, findings regarding attention and executive control in PNES patients compared to ES patients are heterogeneous and inconsistent. We hypothesize that adopting an integrated cognitive-emotional approach and the integrative cognitive model,[10] which examines seizures through a comprehensive, multidisciplinary lens – including biological, pathophysiological, neuropsychological, and cognitive-emotional aspects – will more effectively identify discrepancies in attention deficits and executive control between the two groups. Accordingly, we posit:

Patients in the PNES group will exhibit slower reaction times (RTs) on the Stroop index compared to those in the ES group.

(1) Patients in the PNES group will demonstrate slower RTs on the executive index of the ANT compared to those in the ES group.

2. Methods

2.1. Patients

We recruited 38 patients admitted to the neuropsychiatry unit and the epilepsy center at Hadassah Hebrew University Medical Center, Jerusalem, Israel, between January 2021 and June 2023. Inclusion criteria were age 18 – 65, confirmed diagnosis of ES/PNES both diagnoses and the ability to sign informed consent. Patients' diagnoses were verified through a neurological assessment performed by a qualified epileptologist and through ambulatory EEG or gold-standard vEEG monitoring as needed. All patients in the ES and PNES groups had stable or well-controlled ES.

Exclusion criteria included individuals outside the 18 – 65 age range, current psychotic state, active suicidality, current substance abuse, or any cognitive impairment that prevented them from giving informed consent. All medical information was obtained from the electronic medical records, which were then thoroughly reviewed and validated by a physician.

The study was approved by the Helsinki committee of Hadassah Hebrew University Medical Center (application HMO-0651-19), where all data were collected and stored.

2.2. Measures

2.2.1. Demographic clinical questionnaire

A self-report questionnaire, in Hebrew or Arabic, was administered to gather information on various demographic and clinical factors, including age (18 – 65 years), gender (male, female, or other), religion, native language (Arabic and Hebrew), psychiatric diagnosis, seizure severity, and seizure frequency. The severity scale section comprises levels of seizure severity (S-severity), where the severity level is influenced by the type of seizures, their impact on functioning, and the state of consciousness, among other factors. The score ranges from 1 to 6, with 6 indicating higher seizure severity. The frequency scale section includes four levels of seizure frequency, ranging from 0 to 4, with 4 being the highest score. Participants were needed to choose from each scale the option that best matched both the severity and frequency of the seizures experienced.

2.2.2. Psychiatric assessment: Diagnostic interview for anxiety, mood, and OCD and related neuropsychiatric disorders (DIAMOND)

The DIAMOND is a semi-structured psychiatric interview adjusted and aimed at providing psychiatric diagnosis according to the criteria outlined in The DSM-5. In this study, DIAMOND was administered by certified clinicians,[42] using the validated Arabic and Hebrew versions.

2.2.3. ANT

The ANT[40] is a computerized test that combines a flanker task (with arrows)[43] and a cued RT task[39] that measures participants' performance in three separate components of attention: alert, orientation, and executive control.

In this task, participants reacted to target arrows by quickly pressing the keyboard to indicate the target's direction. Participants fixated on a cross until the target appeared. Occasionally, participants received a cue (valid or invalid) hinting at the target, while in some trials, a tone sounded before the target, aiding in preparation. The target, a central arrow among five, pointed in congruent or incongruent directions. Participants quickly pressed "C" for left or "M" for right, indicating the target's direction. Dependent variables were overall RTs and three difference scores: Orientation ("invalid" RTs minus "valid" RTs), alertness ("no tone" RTs minus "tone" RTs), and executive control ("incongruent" RTs minus "congruent" RTs). The task's sequence of events is illustrated in Figure 1.

These three different scores represent three distinct attention networks: alertness, orientation, and executive control. The alertness network primes the brain for sensory input and sustains this heightened state of readiness. As such, it is essential for ongoing information processing. Moreover, alertness is significantly important in diagnosing, managing, and predicting ES.[44]

This task was translated into Arabic and Hebrew using a validated method and version.

2.2.4. The Stroop task

The Stroop task[41] is considered the gold standard of selective attention measurement. In this task, lexical-colored stimuli were presented on the screen one at a time in blue, green, red, and yellow. Participants were asked to respond to the color of the stimulus and to ignore the meaning of the word. The text color and meaning of the word could be either congruent (*e.g.*, the word RED appeared in red), incongruent (*e.g.*, the word RED appeared in yellow), or neutral (*e.g.*, a letter string XXXX appeared in red).

The interference effect, measured by the RT difference between incongruent and neutral stimuli, is large and reliable. In contrast, the facilitation effect, gauged by the RT difference between neutral and congruent stimuli, is small and less stable.[45]

This task was translated into Arabic and Hebrew using a validated method and version.

2.3. Procedure

Patients who met our inclusion criteria were approached when they arrived for their routine appointments at Hadassah Medical Center.

Each subject signed an informed consent form, followed by a computerized demographic questionnaire and a short survey regarding his or her seizures. Then, a computerized cognitive battery task was administered. The order of the cognitive tasks was randomized to rule out confounders. In addition, each patient without a prior psychiatric evaluation underwent a comprehensive assessment conducted by trained psychologists or master's degree psychology students, using a semi-structured interview.[42]

At the end of the session, patients exhibiting psychological distress were given the option to receive psychological treatment at the neuropsychiatric clinic. In addition, those diagnosed with a psychiatric disorder following their evaluation were informed about their diagnosis and were invited to follow up with the clinic's psychiatrist.

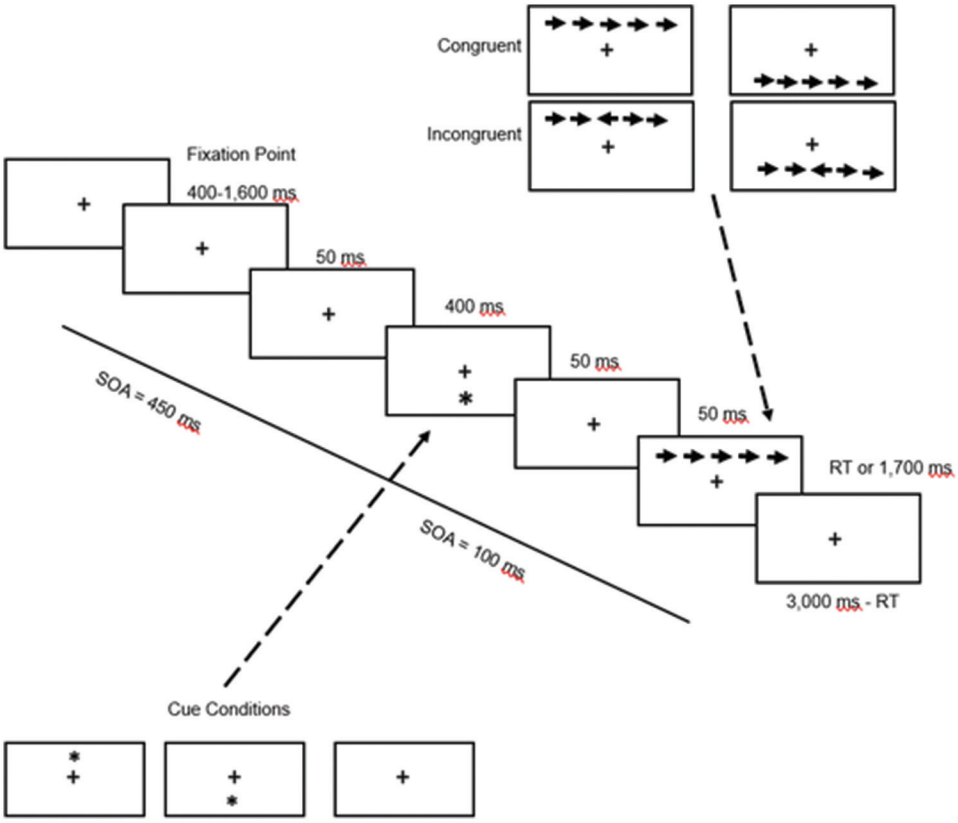

Figure 1. A schematic representation of the attentional network task. Each trial began with a fixation point displayed on-screen for 400 – 1600 ms. In half of the trials, a 50 ms alerting tone was followed. Subsequently, an asterisk cue, signaling the location of the target, appeared above or below the fixation for 50 ms in two-thirds of the trials. After a 50 ms gap, an arrow flanked by four distractor arrows was shown. These distractors were either congruent or incongruent to the central arrow's direction. Participants then indicated the central arrow's direction by pressing a key, followed by a fixation point that lasted up to 3000 ms.
Abbreviations: RT: Reaction time; SOA: Stimulus-onset. asynchrony.

2.4. Statistical analysis

We analyzed the demographic and clinical data using the International Business Machines Statistical Package for the Social Sciences version 26. The statistical analyses for the cognitive data were conducted using the R software. We reviewed the distribution of data to determine normality. Numerical data are expressed as mean±standard deviation (SD), whereas categorical data are presented as counts (percentages). Mann–Whitney *U* and Fisher's exact tests were employed to analyze the demographic and clinical data. Two-way analysis of variance (ANOVA) and four-way ANOVA were conducted for the Stroop and ANT tasks, respectively. The RTs served as the dependent variable for both groups in each task. A $P < 0.05$ was considered statistically significant.

3. Results

3.1. Sample description

The demographic and clinical data of the two clinical groups (the ES group and the PNES group) are summarized in Table 1. Eleven patients were diagnosed with PNES, seven with comorbid ES and PNES, and 20 with ES (ES group). Due to the small sample size, the first two groups were combined into one group, the PNES group (n = 18). No significant differences were found in age, gender, religion, and seizure frequency between the two groups. However, patients in the PNES group exhibited significantly higher instances of psychiatric diagnoses, and significantly greater seizure severity compared to those in the ES group (Table 1).

3.2. Usage of ASM

To present the use of ASM and enable effective comparison and analysis, we followed the approach of Çelik *et al.*,[16] categorizing patients into three subgroups based on the number of ASMs used: none, one ASM, and two or more ASM, as detailed in Table 2.

Considering the variety of ASM classes and instances of polytherapy, we have identified the most commonly

Table 1. Demographic and clinical characteristics (*n*=38)

	ES group (*n*=20)	PNES group (*n*=18)	*P*-value	
	Mean (SD)	Mean (SD)		
Age (years)	36.8 (14.07)	33.41 (13.04)	0.515	
Years of education	12.55 (3.53)	12.67 (3.86)	0.806	
Seizures frequency	1.8 (1.508)	2 (1.455)	0.696	
Seizures severity	3 (1.89)	4.44 (1.58)	0.02**	
	n (%)	*n* (%)	Z	*P*-value
Gender				
Male	11 (55)	6 (33.3)		
Female	9 (45)	12 (66.7)		
			1.79	0.21
Religion				
Muslim	6 (30)	8 (44.4)		
Jewish	12 (60)	10 (55.6)		
Christian	1 (5)	0 (0)		
Other	1 (5)	0 (0)		
			2.36	0.16
Comorbid psychiatric diagnosis				
With	3 (15)	15 (83.3)		
Depression	2	2		
Anxiety	1	4		
Conversion disorder	0	3		
Convulsive disorder	0	3		
Post-traumatic stress disorder	0	1		
BPD	0	2		
Without	17 (85)	3 (16.7)		
			17.74	<0.001**
	n (%)	*n* (%)		
Seizures localization				
Left Temporal	5 (25)	1 (14.2)		
Right Temporal	2 (10)	1 (14.2)		
Right Parietal	2 (10)	1 (14.2)		
Generalized/JME	6 (30)	1 (14.2)		
Frontal Lobe	5 (25)	3 (42.8)		

Notes: Values are presented as counts (percentages) and/or means±SD. The *P*-value indicates the level of significance for comparisons between groups. A $P<0.05$ is considered statistically significant **$P<0.05$.

Table 2. Antiseizure medication usage among ES and PNES groups

Number of ASMs used	ES group (*n*=20) *n* (%)	PNES group (*n*=18) *n* (%)
No ASM	1	7
One ASM	9	8
Two or more ASM	10	3

Abbreviations: ASM: Antiseizure medication; ES: Epileptic seizures; PNES: Psychogenic non-epileptic seizures.

used ASM and their median daily dose. In the ES group, the most frequently used drugs were lamotrigine (400 mg/day), carbamazepine (800 mg/day), and clobazam (10 – 20 mg/day); in the PNES group, the most common drugs were lamotrigine (400 mg/day) and carbamazepine (800 mg/day).

In addition, 13 patients (six with PNES only, three with ES, and four with both PNES and ES) received other medications, including, propranolol, mirabegron,

clonazepam, fluoxetine, quetiapine, hydrocortisone, clozapine, hydroxychloroquine, and sertraline.

3.3. Cognitive functions

From the initial 38 patients, 35 completed the Stroop task, and 34 completed the ANT. In the Stroop task, four patients (two patients with ES and two with PNES only) were excluded from the final analysis as outliers: three patients due to their mean accuracy being more than 2.5 SD from their group mean accuracy and one patient due to their mean RT being more than 2.5 SD compared to their group mean RT. Similarly, in the ANT, five patients (two patients with ES, two with PNES only, and one patient with PNES and ES) were removed from the final analysis for similar reasons: four due to their mean accuracy being more than 2.5 SD from their group mean accuracy and one due to their mean RT is more than 2.5 SD compared to their group mean RT. Consequently, a total of 31 patients remained for the final Stroop analysis, with 17 patients in the ES group and 14 in the PNES group. For the final ANT analysis, 29 patients were included, comprising 15 patients in the ES group and 14 in the PNES group.

3.3.1. Attention control (Stroop task)

Two-way ANOVA for RTs revealed a significant effect for condition (congruent, incongruent, and neutral) ($F[2, 58] = 26.45$, $P < 0.001$, $n_p^2 = 0.477$), and no significant effect for group ($F[1,29] = 0.00$, $P = 0.954$, $n_p^2 < 0.001$). The interaction between condition and group was found to be non-significant ($F[2, 58] = 2.61$, $P = 0.083$, $n_p^2 = 0.082$) (Figure 2). *Post hoc* contrast analysis revealed that patients in the ES group were significantly slower in the incongruent conditions than in the congruent conditions (Stroop effect) (congruent - incongruent; $t(29) = -5.276$, $P < 0.001$). In addition, they were significantly slower in the incongruent conditions compared to the neutral conditions (interference effect) (incongruent - neutral; $t(29) = 5.208$, $P < 0.001$). In contrast, patients in the PNES group were significantly slower in the incongruent conditions than in the congruent conditions (Stroop effect) (congruent - incongruent; $t(29) = -2.886$, $P = 0.019$). Patients in the PNES group showed no differences in RT between the incongruent and neutral conditions (incongruent - neutral; $t(29) = 2.258$, $P = 0.078$). Similarly, no difference was found in the interference effect between the two groups ($t[29] = 1.828$, $P = 0.078$).

3.3.2. Executive functions (ANT)

A four-way ANOVA was conducted with the group as a between-groups factor for each variable network index; (executive control; congruent and incongruent), (alerting; tone and non-tone) and (orienting; valid, no-cue, and invalid). Significant main effects were revealed for each attentional network index (executive control, alerting, and orienting): $F(1, 27) = 36.23$, $P < 0.001$, $n_p^2 < 0.001$; $F(1, 27) = 21.39$, $P < 0.001$, $n_p^2 = 0.442$; and $F(2, 54) = 11.52$, $P < 0.001$, $n_p^2 = 0.299$, respectively. The group × tone interaction was significant, $F(1, 27) = 5.67$, $P = 0.025$, $n_p^2 = 0.174$, reflecting the alerting network (Figure 3). In contrast, no significant interaction was found for group × flanker's congruency interaction in the executive function comparison $F(1, 27) = 1.04$, $P = 0.316$ $n_p^2 = 0.037$. Similarly, the orienting comparison yielded a non-significant effect for group × cue validity interaction $F(2, 54) = 0.19$, $P = 0.825$, $n_p^2 = 0.007$. The three-way and four-way interactions were not significant ($P > 0.05$).

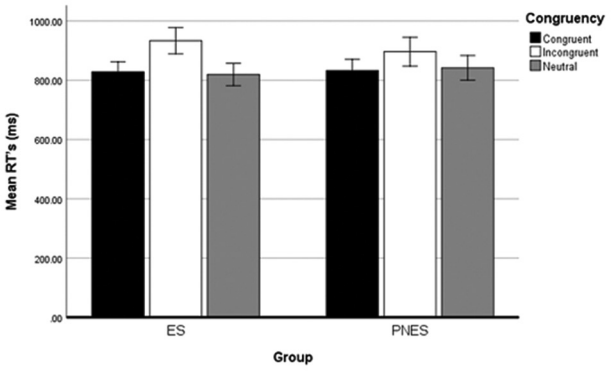

Figure 2. Results of Stroop task: reaction time indexes of the three congruency conditions
Note: Error bars represent standard errors of the mean (error bars ± 1 standard error).
Abbreviations: ES: Epileptic seizures; PNES: Psychogenic nonepileptic seizures; RT: Reaction time.

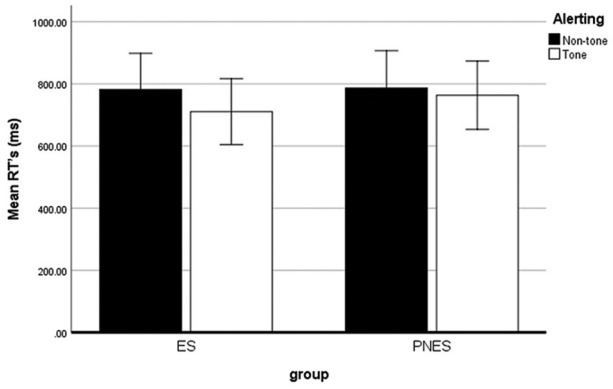

Figure 3. Results of attentional network task, with reaction time indexes of the two alerting conditions as a function of seizure. Error bars represent standard errors of the mean (error bars ± 2 standard error).
Abbreviations: ES: Epileptic seizures; PNES: Psychogenic non-epileptic seizures; RT: Reaction time.

These results suggest that while there were no significant differences between the groups in terms of executive control and orienting; differences were observed in alerting. Specifically, patients in the ES group displayed significantly slower RTs in the non-tone conditions compared to the tone conditions. In contrast, for the PNES group, no significant difference in RTs between the tone and non-tone conditions was found.

3.4. Effect of antiepileptic drug on cognitive assessment

To examine the effect of ASM usage on cognitive processing, data were analyzed using analysis of covariance. The interaction between ASM usage and Stroop task congruency, $F(4, 54) = 1.48$, $P = 0.221$, was not statistically significant, indicating that ASM usage did not significantly affect cognitive interference as measured by the Stroop task. Furthermore, there were no significant interactions between ASM usage and the attentional network indices of executive control, alerting, and orienting: $F(2, 25) = 1.89$, $P = 0.172$, $F(2, 25) = 1.95$, $P = 0.164$, and $F(4, 50) = 0.62$, $P = 0.653$, respectively. This suggests that ASM load – whether participants were on none, one, or multiple ASM – did not significantly influence RT variability across different cognitive task conditions.

4. Discussion

The current preliminary cross-sectional study aims to evaluate the cognitive deficit profiles in ES and PNES patients as assessed by the ANT and the Stroop task.

Our results primarily show a more pronounced alerting effect in the ES group compared to the PNES group, indicating marked differences in attentional processing between the groups. This was a significant observation we did not initially hypothesize. ES patients seem to be more responsive to warning cues, allowing them to achieve and maintain heightened alertness more efficiently than patients with PNES. This may imply that the alerting network in the PNES group is less efficient or sensitive compared to the ES group. However, drawing from prior research in this domain, the difference in the alerting effect might indicate a state of hyper-alertness to the presence of tones in the task among the ES group and not necessarily a deficit in the capacity of the PNES group to initiate and maintain an alert state in response to warning cues.[46,47]

According to the integrative cognitive model mentioned above, the first stage of PNES is marked by a sharp rise in sympathetic arousal. However, following a seizure event, there is a change in the patient's experience as the initial sympathetic response is interrupted, resulting in decreased arousal.[10] This alteration in arousal state may be associated with changes in alertness levels in response to external, non-emotional stimuli. This could explain why the alerting network in the PNES group is less efficient or sensitive compared to the ES group, according to the integrative cognitive model.

Contrary to our hypothesis, the executive score from the ANT revealed no significant difference in executive control between the ES and PNES groups. Similarly, the orienting score showed no notable difference between the two groups. It is possible that these effects were not significant because of the small sample size and the mixture of PNES + ES in the PNES group, which could have increased variability in the sample and interfered with the detection of these effects.

Regarding the Stroop task,[41] a significant Stroop effect was observed in both seizure groups. However, there was no difference in the interference effect among patients in the ES group compared to those in the PNES group, meaning that deficits in selective attention and cognitive control in the ES group may not differ significantly from those in the PNES group.

In addition, the cognitive performance observed in the ANT and the Stroop task is not differentially affected by the quantity of ASM consumed by the patients. This finding is inconsistent with previous studies that found cognitive deterioration in children with epilepsy after using carbamazepine.[48,49] This may be due to the fact that in the current study, participants were adults, part with comorbid PNES, and that we analyzed all kinds of ASMs together and used different cognitive assessment methods. However, this issue should be explored in further studies.

Given the small number of participants and other potential confounding factors that could influence the outcomes, we present these findings with considerable caution. Overall, our findings may indicate more severe cognitive deficits, especially in alertness, among patients with ES, compared to those with PNES and comorbid cases. However, this does not negate the presence of attentional cognitive impairments in PNES patients, which have been documented in previous studies.[28,50]

In our research, we identified a significantly higher rate of comorbid psychiatric diagnoses and greater seizure severity among patients in the PNES group compared to those in the ES group. This is notable, considering that previous studies in this field have consistently established a positive correlation between these factors and attention deficits, which may be significant confounding factors.[44,51] Given the high percentage of comorbid psychiatric diagnoses and the establishment of attentional control

theory,[52] future research can delve deeper into the emotional aspects of patients with ES and PNES.

This preliminary cross-sectional study expands the currently limited body of research, specifically designed to measure attention in patients with PNES and those with comorbid diagnoses (both PNES and ES), comparing them to matched patients with only ES. Our findings enhance our understanding of some cognitive deficits' profiles underlying PNES and ES. Further research is pivotal to validate these findings. Such insights could bolster the validity of diagnosis in ambiguous cases, pave the way for more effective and tailored treatments, and promote intervention programs and strategies to mitigate and manage seizures in these patients.

One of the primary limitations of our research was the small sample size. While smaller groups can offer preliminary insights and highlight potential trends or patterns, they often lack the statistical power necessary to draw broad, generalizable conclusions. For these reasons, while our findings provide a valuable starting point, they should be interpreted with caution until larger more comprehensive studies can validate or refine our conclusions. In addition, it is important to recognize that during the neuropsychological testing, most patients with ES and PNES are on ASM, psychiatric, or other neurological drugs. These medications can lead to several side effects, such as drowsiness or psychomotor slowing, which can adversely impact their performance on the tests.[6] Due to ongoing changes in the administration of antiepileptic or neurological drugs for our participants, we could not account for them in our research, which may be a potential confounder of our results. Psychotherapy use also varied in existence, length, and approach between participants along their medical course, which can also alleviate symptoms and affect results accordingly. Moreover, the cross-sectional nature of our study prevents us from drawing causal conclusions. In addition, the version of the ANT used might not be sensitive enough to detect differences in the attention networks between the ES group and the PNES group. Finally, due to the small sample size, we grouped participants to preserve statistical power. Incorporating patients with dual diagnoses (both PNES and ES) into the PNES group introduced additional variability, complicating the derivation of PNES-specific conclusions. Nonetheless, we recommend that future studies investigate these issues in separate groups to yield more definitive conclusions.

5. Conclusion

In our endeavor to understand the cognitive deficit profiles of patients with ES and PNES, our preliminary cross-sectional study highlighted subtle differences in attentional processing, particularly in alertness and selective attention, between these two groups. A more pronounced alerting effect in the ES group compared to the PNES group indicates differences in attentional processing between the groups. Future investigations should utilize larger participant cohorts and include more comprehensive assessments covering both emotional and cognitive domains. By doing so, they can provide insights into the complex interplay between cognitive deficits and emotional dysregulation. Exploring these underlying mechanisms is crucial for enabling earlier, tailored diagnoses and personalized treatment approaches, ultimately enhancing patients' quality of life.

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Conflict of interest

The authors declare that they have no competing interests.

Author contributions

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Ethics approval and consent to participate

The study was approved by the Helsinki committee of Hadassah Hebrew University Medical Center (ethics committee number: HMO-0651-19), where all data were collected and stored. Informed consent from the participants has been obtained before their participation. The consent was acquired through written means, ensuring that participants were fully informed about the study's purpose, procedures, risks, and their right to withdraw at any time.

Consent for publication

Informed consent for the publication of anonymous data was acquired through writing.

Availability of data

Data are available from the corresponding author upon reasonable request.

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