ORIGINAL ARTICLE

Recognition of Psychogenic Versus Epileptic Seizures Based on Videos

Veronica Birca, Mark R. Keezer, Laury Chamelian, Anne Lortie, Dang K. Nguyen

ABSTRACT ***Objective:*** Ictal semiology interpretation for differentiating psychogenic nonepileptic seizures (PNESs) and epileptic seizures (ESs) is important for the institution of appropriate treatment. Our objective was to assess the ability of different health care professionals (HCPs) or students to distinguish PNES from ES based on video-recorded seizure semiology. ***Methods:*** This study was designed following the Standards for Reporting of Diagnostic Accuracy Studies (STARD) guidelines. We showed in a random mix 36 videos of PNES or ES (18 each) and asked 558 participants to classify each seizure. The diagnostic accuracy of various groups of HCPs or students for PNES versus ES was assessed, as well as the effect of patient age and sex. Measures of diagnostic accuracy included sensitivity, specificity, and area under the curve (AUC). ***Results:*** The descending order of diagnostic accuracy (AUC) was the following ($p \leq 0.001$): (1) neurologists and epileptologists; (2) neurology residents; (3) other specialists and nurses with experience in epilepsy; and (4) undergraduate medical students. Although there was a strong trend toward statistical difference, with AUC 95% confidence intervals (CIs) that were not overlapping, between epileptologists (95% CI 93, 97) compared to neurologists (95% CI 88, 91), and neurologists compared to electroencephalography technicians (95% CI 82, 87), multiple pairwise comparisons with the conservative Tukey–Kramer honest significant difference test revealed no statistical difference ($p = 0.25$ and 0.1, respectively). Patient age and sex did not have an effect on diagnostic accuracy in neurology specialists. ***Conclusion:*** Visual recognition of PNES by HCPs or students varies overall proportionately with the level of expertise in the field of neurology/epilepsy.

RÉSUMÉ : Reconnaissance visuelle des crises psychogènes versus épileptiques sur vidéos. *Objectif* : La distinction de la sémiologie ictale des crises non-epileptiques psychogenes (CNEP) des crises epileptiques (CE) est importante pour l'amorce d'un traitement approprie. Notre objectif était d'évaluer la capacité de reconnaissance des CNEP versus CE de différents professionnels de la santé (PS) et étudiants, basée sur la sémiologie de crises enregistrées sur vidéo. ***Méthodes* :** Cette étude est conforme aux lignes directrices *Standards for Reporting of Diagnostic Accuracy Studies (STARD)*. 558 participants ont visionné un mélange aléatoire de 36 enregistrements vidéos de CNEP ou CE (18 pour chaque catégorie) et classifié chacune des crises. La precision diagnostique de différents groupes de PS ou étudiants pour les CNEP versus CE a été évaluée, ainsi que l'effet de l'âge et du sexe des patients. Les tests diagnostiques ont inclus la sensibilité, spécificité et aire sous la courbe (ASC). ***Résultats* :** L'ordre decroissant de précision diagnostique (en fonction de l'ASC) était le suivant ($p \leq 0{,}001$) : (1) neurologues et épileptologues ; (2) résidents en neurologie ; (3) autres spécialistes et infirmières avec expérience en épilepsie ; et (4) étudiants en médecine de premier cycle. Malgré une forte tendance pour une différence statistique, basée sur des ASC avec intervalles de confiance (IC) à 95% qui ne se chevauchent pas, entre les épileptologues (IC 95% = 93-97) comparés aux neurologues (IC 95% = 88-91), et neurologues comparés aux techniciens en électroencéphalographie (IC 95% = 82-87), le test conservatif de comparaison multiple par paires de Tukey-Kramer (honnête différence significative) n'a pas démontré de différence statistique ($p = 0{,}25$ et 0,1 respectivement). L'âge et le sexe des patients n'ont pas eu d'effet sur la précision diagnostique des spécialistes en neurologie. ***Conclusion* :** De façon générale, la reconnaissance visuelle des CNEP par les PS ou étudiants varie proportionnellement avec le niveau d'expertise dans les domaines de la neurologie/épilepsie.

Keywords: Psychogenic nonepileptic seizure, Functional neurological symptom disorder, Epileptic seizure, Misdiagnosis, Semiology, Diagnostic accuracy

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Introduction

Psychogenic nonepileptic seizures (PNESs) may semiologically resemble epileptic seizures (ESs) but are caused by a psychological process rather than abnormal electrical discharges in the brain.[1,2] They are classified as a conversion disorder/functional neurological symptom disorder in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).[3] The delay in diagnosis, averaging 7–10 years,[4–6] leads to unnecessary health care utilization and costs, iatrogenic complications, and worse prognosis.[5,7–11] A variety of health care professionals (HCPs) encounter patients presenting with PNES as they are heavy users

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of nonemergency and emergency health care,[12] where they sometimes even present in 'PNES status'.[13] Video-electroencephalography (EEG) monitoring is the gold standard for the differentiation of PNES versus ES,[14] but since it is an elective procedure, HCPs frequently depend on visual analysis of seizure semiology to make an initial diagnosis.[15,16] Furthermore, when analyzing video-EEG recordings, ictal semiology is as important as ictal EEG to make the correct diagnosis.[14]

Previous studies included participants from various countries and demonstrated that a HCP or student's ability to distinguish ES from PNES based on video-recorded semiology varies to a great degree according to the level of medical expertise, as well as the patient's seizure type; in some cases, it is no better than chance.[15–21] The training and scope of practice of the different HCPs or students may vary according to the health care model of a specific country. To our knowledge, there has not been a North American study comparing the performance in diagnosis between different groups of HCPs or students. Furthermore, the potential effect of patient sex and age in diagnosing PNES has not been investigated. It has been reported that 70% of PNES patients are between the ages of 20 and 40 years[22,23] and three-quarters are female.[23] However, this sex prevalence is only present starting from adolescence,[14,24,25] and some studies suggest a greater prevalence of PNES in preadolescent boys.[25,26]

The main objective of this study was to assess the ability of different Canadian HCPs and students to distinguish PNES from ES, based on video-recorded semiology. We hypothesized that the correct recognition of PNES would vary according to: (1) seizure type and semiology; (2) a HCP's or student's level of expertise in the field of neurology/epilepsy; and (3) the patient's age and sex.

Material and Methods

This study of diagnostic accuracy was conducted according to the Standards for Reporting of Diagnostic Accuracy (STARD) guideline.[27]

Video Selection

We retrospectively reviewed the medical charts and video-EEG recordings of approximately 400 patients with PNES and/or ES confirmed by video-EEG monitoring admitted to the epilepsy monitoring units of the Centre hospitalier de l'Université de Montréal (CHUM) and Centre hospitalier universitaire Sainte-Justine (CHUSJ) since 2002. Eighteen ESs and 18 PNESs were selected and classified according to the 2017 International League Against Epilepsy (ILAE) classification[28,29] and another proposed semiological classification,[30] respectively (Table 1). The selected videos represent a wide diversity of ES and PNES. For each seizure video, either the full event or only a short clip was selected (ranging from 6 s to < 30 s) that included the essential semiology allowing to categorize it as an ES or PNES. Examples were the Figure 4 sign (typical of ES) or asynchronous limb movements (typical of PNES). In order to have comparable PNES and ES video groups, 6 pediatric patients (older children and teenagers) and 12 adult patients, and an equal proportion of males and females were selected in each. An epileptologist reconfirmed the diagnosis previously established based on ictal EEG and semiology. Video clips were randomly assembled into a video montage using computer random number generation. The video montage included 7-s breaks between each seizure. All selected patients had given their written and informed consent to their videos being used for educational and research purposes. Additionally, videos were anonymized by blurring parts of the face which did not exhibit essential clues for diagnosis.

Study Population and Data Collection

Data were collected prospectively by organizing video viewing sessions where the video montage was shown only once. Participants were selected through convenience sampling in various hospitals in the province of Quebec, Canada, from 2017 to 2019. Although all types of HCPs or students were free to participate, targeted groups included neurologists, emergency physicians, psychiatrists, neurology residents, nurses, EEG technicians, and undergraduate medical students. After watching each seizure, participants were requested to individually mark the diagnosis as ES or PNES on an answer sheet. No additional information was provided. Participants already knowing the diagnosis of particular cases were required to indicate it on the answer sheet. We also collected information on participants' professions and their age category, as to maintain confidentiality.

Data Analysis

Seizure Diagnostic Difficulty

For each of the 36 seizures, the HCPs' and students' percent concordance with the gold standard (video-EEG) was calculated (i.e. total number of correct answers for each video/(total number of correct answers + total number of incorrect answers for each video)). This allowed ranking of all 36 seizure subtypes from most difficult to easiest to diagnose (Table 1). The mean percent concordance with the gold standard for PNES was then calculated and compared to the mean percent concordance with the gold standard for ES.

Diagnostic Accuracy Based on Level of Expertise

Participants' answers were pooled in 2 x 2 tables for each HCP or student group. For each group, the diagnostic accuracy for PNES (with people with ES as the negative result) was quantified by three different measures: mean sensitivity (Sn), mean specificity (Sp), and area under the curve (AUC) derived from summary receiver operating characteristic (SROC) curves. SROC summarize the diagnostic performance of a population of participants as a single number (AUC), allowing comparison of a single measure between groups of HCPs or students (e.g. AUC of neurologists compared to AUC of medical students). First, sensitivity (y-axis) is plotted against (1 – specificity) (x-axis) for each participant. Next, an SROC curve is placed over the data points to form a smooth curve, using a mathematic formula. The AUC is then calculated for the SROC of each group of HCPs or students.[31] A perfect diagnostic performance will result in an AUC of 1; an AUC of 0.5 represents diagnostic accuracies that are no better than chance, while an AUC less than 0.5 is worse than chance alone.[32] For each value, the confidence interval (CI) was calculated (with overdispersion correction in the case of Sn and Sp).

We further explored the effect of increased level of expertise in the field of neurology/epilepsy by comparing the diagnostic

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Table 1: Seizure characteristics and health care professionals' and students' percent concordance with the gold standard*[*]

Percent concordance with the gold standard (%)	Video no.	Patient characteristics (sex, age[†])	Classification of seizure[‡]	Key semiologic features
5.1	15	M, adult aged 33 years	Focal automatism ES	Bilateral symmetric automatisms of UL (repetitive flexion of shoulders and elbows) while holding an object in the right hand → attenuation and modification of automatisms while handing over the object to an examiner → resumption of automatisms in L UL only; accompanied by oral automatisms
37.7	3	F, adult aged 38 years	Focal hyperkinetic ES	Brief behavioral arrest → yelling → dystonic posture of L UL and hyperkinetic activity of L LL
40.0	20	M, adult aged 26 years	Focal automatism and impaired awareness ES	Oral automatisms, unresponsiveness, and hands and fingers in a dystonic positioning
47.4	2	F, adult aged 52 years	Rhythmic motor PNES	Asynchronous asymmetric rhythmic movements of UL (shaking-like with flaccid fingers) and LL (tremor-like)
48.1	19	F, adult aged 44 years	Focal automatism and impaired awareness ES	Behavioral arrest, oral automatisms, purposeless repositioning of body posture and objects, inadequate response to questions
48.2	18	M, adult aged 50 years	Focal automatism ES	Repetitive purposeless circular motion of R hand over L and R knee, head version to the R
51.8	33	F, child aged 11 years	Hyperkinetic ES	Abrupt onset from sleep, supine to seating position → dystonic position L arm/hand while rotating the trunk and head side to side
51.8	14	F, adult aged 18 years	Tonic ES	Sudden tonic flexion of four limbs → tonic extension of L UL; accompanied by a vocalisation (groan)
53.6	16	M, adult aged 36 years	Mixed PNES (rhythmic → complex motor PNES)	Rhythmic tremor-like movements of UL, LL, trunk, and head → violent back-arching causing a change of position from supine to prone at the edge of the bed without falling
55.9	1	M, adult aged 26 years	Tonic ES	Symmetric tonic flexion of UL and trunk
57.9	27	F, adult aged 33 years	Rhythmic PNES	Licking of lips with tongue → rhythmic flexion of trunk with L UL shaking
57.9	35	F, child aged 10 years	Mixed PNES (rhythmic and dialeptic[‖] PNES)	Eyelids closure while dropping of head and L UL to the L → voluntary-like salivation, trunk and LL asymmetric and asynchronous rhythmic tremor-like movements in various directions
59.7	36	M, child aged 16 years	Tonic ES	Eating while sitting on the bed → abrupt behavioral arrest → tonic positioning of UL and trunk while drifting backward
59.9	4	M, adult aged 17 years	Gelastic ES	Unnatural laughing
60.3	25	F, child 14 years	Rhythmic PNES	Careful positioning, rhythmic trunk, and hip flexion
60.3	11	F, adult 50 years	Rhythmic motor PNES	Abrupt onset of rhythmic trunk, then forearm and knees symmetric and synchronized flexion/extension
60.3	22	M, adult aged 37 years	Rhythmic PNES	Abrupt onset, short duration of rhythmic shaking-like movements of forearms, hands, and fingers
61.2	7	F, child aged 5 years	Tonic ES	Sudden behavioral arrest → tonic flexion of neck and upward deviation of gaze
61.3	23	F, child aged 15 years	Rhythmic PNES	Rhythmic oscillatory movement of R forearm; does not stop when examiner holds forearm, but rhythm becomes irregular
61.7	17	F[§], adult aged 20 years	Atonic ES	Patient in sitting position → loss of trunk and L UL tonus → backward fall to the L while hitting head on bedrail
62.7	31	M, child aged 8 years	Hypermotor PNES	Side to side back-arching and head rotation while holding on to bedrails with fingers
69.2	13	F, adult aged 30 years	Dialeptic[‖] PNES	Upward deviation of gaze, eyelids fluttering; accompanied by complex purposeless movements of left forearm with fingers in a fixed non-tonic position

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Table 1: *(Continued)*

Percent concordance with the gold standard (%)	Video no.	Patient characteristics (sex, age[†])	Classification of seizure[‡]	Key semiologic features
69.4	9	M, adult aged 66 years	Dialeptic[‖] PNES	Upward deviation of gaze, eyelids fluttering, and response to threat (blinking)
73.6	26	M, child aged 16 years	Focal to bilateral tonic–clonic ES	Eyes, head, trunk, and UL version to the R → dropping of electronic device to the floor → tonic–clonic seizure with vocalizations
74.3	32	M, adult aged 35 years	Focal to bilateral tonic–clonic ES	Head, R UL, and trunk deviation to the right, mouth opening → "sign of four" → tonic phase
74.7	12	F, adult aged 46 years	Focal to bilateral tonic–clonic ES	Head version, mouth opening and epileptic guttural sound → tonic R UL elevation → "sign of four" → bilateral tonic–clonic movements
77.4	21	M[§], adult aged 78 years	Rhythmic PNES	Rythmic tremor-like movements of R hand with direction change (flexion/extension → pronation/ supination)
80.3	34	F, adult aged 24 years	Hypermotor PNES	Violent back-arching and bilateral knees flexion/ extension repetitive movements with dramatic vocalizations
80.5	5	F, adult aged 41 years	Absence ES	Behavioral arrest (eating) → upward deviation of gaze and blinking → rapid offset and resumption of activity
81.8	29	M, child aged 14 years	Rhythmic PNES	Abrupt onset, R hand tremor-like movements with direction change (flexion/extension → pronation/ supination)
83.4	8	M, child aged 5 years	Tonic ES	Fencing posture (R UL extension), gaze deviation to the right, right-sided mouth myoclonias
84.1	6	M, child aged 12 years	Complex motor PNES	Complex and multifocal movements of head, trunk, and UL accompanied by heavy breathing
84.6	24	F, adult aged 20 years	Hypermotor PNES	Side-to-side repetitive movement of trunk and head → side to side trashing movements of head and UL shaking while temporarily holding on to examiner's hand
85.9	30	F[§], child aged 12 years	Tonic ES	Abrupt onset from sleep, tonic flexion of UL and LL, neck extension, and forced mouth opening
87.9	10	M[§], adult aged 60 years	Rhythmic motor PNES	Abrupt onset, rhythmic movements of UL (symmetric and synchronous), and LL (symmetric but asynchronous)
88.3	28	M, adult aged 21 years	Dialeptic[‖] PNES	Walking toward bed → lifting of R knee on the bed → loss of tonus and fall on bed

ES = epileptic seizure; PNES = psychogenic nonepileptic seizure; M = male; F = female; UL = upper limb; LL = lower limb; R = right; L = left; → = then

[*]Seizures are presented in order of health care professionals' and students' percent concordance with the gold standard (video-EEG)

[†]Child patients are ≤16 years old

[‡]Classified according to the 2017 International League Against Epilepsy (ILAE) classification (ES),[28,29] and another proposed semiological classification (PNES)[30]

[§]Seizure where video quality does not allow for sex identification

[‖]"Focal impaired awareness" replaces the older term 'dialeptic' in the 2017 International League Against Epilepsy (ILAE) classification

accuracy between groups of neurologists with increasing years of experience.

Diagnostic Accuracy of Neurology Specialists Based on Patient Age and Sex

Seizure videos were separated into age groups (adult patients versus pediatric patients) and sex groups (male versus female). Diagnostic accuracy for neurology specialists was calculated (using Sn, Sp, and AUC measures) for each one of these groups. Data were analyzed only for neurology specialists (neurologists and epileptologists), as they are more likely to have knowledge of the epidemiology of PNES, therefore most likely to take into account the age and sex in their diagnostic decision.

Statistical analyses were performed using the software Meta-DiSc,[33] IBM SPSS Statistics, and online softwares.[34,35] Diagnostic accuracy measures were reported with their standard deviation and 95% CIs and compared using the t-test or one-way ANOVA followed by Tukey–Kramer honest significant

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Table 2: Health care professionals or students' diagnostic accuracy of PNES versus ES diagnosis

Group	n	Age median (IQR) (years)	Sensitivity		Specificity		AUC	
			Mean ± SD (%)	95% CI (%)	Mean ± SD (%)	95% CI (%)	Mean ± SD (%)	95% CI (%)
Epileptologists	18	40–49 (30–39 – ≥ 50)	92 ± 6	90, 95	86 ± 9	82, 90	95 ± 4	93, 97
Neurologists	82	40–49 (30–39 – ≥ 50)	89 ± 10	87, 91	76 ± 13	73, 79	89 ± 6	88, 91
EEG technicians	34	30–49 (30–49 – 40–49)	83 ± 13	79, 88	73 ± 12	69, 77	84 ± 8	82, 87
Neurology residents	70	30–39 (< 30 – 30–39)	81 ± 15	77, 84	73 ± 13	70, 76	83 ± 8	82, 85
Emergency physicians	27	40–49 (30–39 – ≥ 50)	76 ± 14	71, 81	55 ± 15	49, 61	71 ± 9	67, 75
Nurses with experience in epilepsy	43	40–49 (30–39 – 40–49)	69 ± 21	63, 75	60 ± 19	55, 66	69 ± 10	66, 71
Residents (non-neurology)	31	< 30 (< 30 – < 30)	78 ± 14	73, 83	47 ± 17	41, 53	68 ± 10	65, 72
Psychiatrists	19	40–49 (40–49 – ≥ 50)	66 ± 11	61, 71	57 ± 18	49, 65	65 ± 10	61, 69
Nurses (varia)	90	40–49 (30–39 – ≥ 50)	53 ± 16	50, 57	45 ± 16	42, 48	49 ± 10	47, 51
Undergraduate medical students	77	< 30 (< 30 – < 30)	53 ± 19	48, 57	45 ± 16	42, 49	48 ± 10	46, 51

n = total number; IQR = interquartile range; SD = standard deviation; CI = confidence interval; AUC = area under the curve

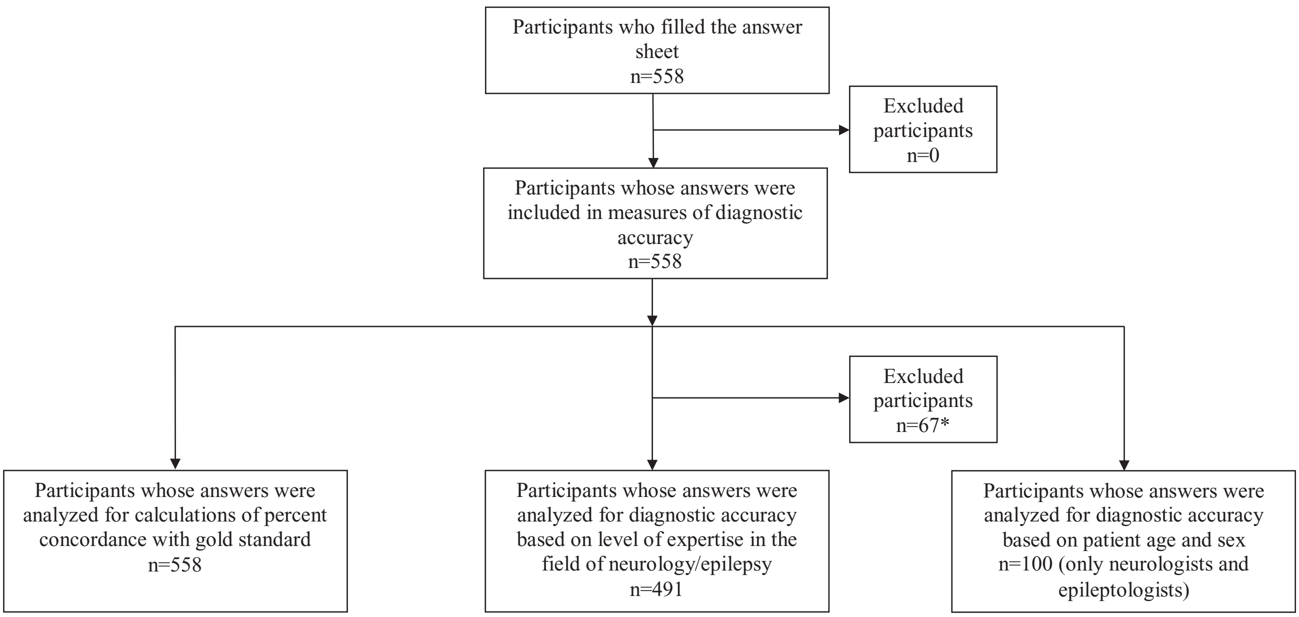

Figure 1: *Flow diagram of the study participants according to the Standards for Reporting of Diagnostic Accuracy (STARD) guideline. *Including 14 participants who did not identify their profession on the form, 32 participants whot were part of a wide variety of health care professional or student groups with few representants in each category (e.g. one pharmacist, two neuropsychologists, etc.), and 21 participants who identified themselves as working in research or administration (without significant direct patient care)*

difference (HSD) post hoc test. P-values < 0.05 were considered statistically significant. Of note, the few answers (174/20 088, 0.9%) where participants indicated that they already knew the diagnosis, or that were not adequately filled (e.g. no answer or both ES and PNES cases with a check mark), were considered as invalid and excluded from the analysis.

Ethical Considerations

This study was approved by the ethics committee of the CHUM and CHUSJ.

Results

Characteristics of HCPs

A total of 558 HCPs or students participated in the study (Figure 1). The number of participants and median age in each HCP or student group are indicated in Table 2. Within the epileptologists group, 13 participants identified themselves as working with adult patients, 4 with pediatric patients, and 1 with both adult and pediatric patients. The following participants were not classified into HCP or student groups, however were included in calculations of percent concordance with the gold standard:

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Table 3: Differences in AUC means among health care professional or student groups using Tukey–Kramer HSD test

Group	Neuro.	EEG tech.	Neuro. res.	Emerg.	Nur. epil.	Res. (non-neuro.)	Psych.	Nur. (var.)	Med. stud.
	Difference in AUC means (95% CI) (%)								
Epil.	6 (−1, 13) p = 0.25	11 (3, 19) *	12 (4, 19) *	24 (16, 33) *	27 (19, 34) *	27 (19, 35) *	30 (21, 39) *	46 (39, 54) *	47 (39, 54) *
Neuro.		5 (0, 11) p = 0.1	6 (2, 11) *	18 (12, 25) *	21 (16, 26) *	21 (15, 27) *	24 (17, 31) *	41 (37, 45) *	41 (37, 45) *
EEG tech.			1 (−5, 7) p = 1	13 (6, 20) *	16 (9, 22) *	16 (9, 23) *	19 (11, 27) *	35 (30, 41) *	36 (30, 41) *
Neuro. res.				12 (6, 19) *	15 (10, 20) *	15 (9, 21) *	18 (11, 26) *	35 (30, 39) *	35 (30, 40) *
Emerg.					2 (−4, 9) p = 0.98	3 (−4, 10) p = 0.97	5.9 (−2, 14) p = 0.4	22 (16, 28) *	23 (16, 29) *
Nur. epil.						0 (−6, 7) p = 1	4 (−4, 11) p = 0.9	20 (15, 25) *	20 (15, 25) *
Res. (non-neuro.)							3 (−5, 11) p = 0.96	20 (14, 25) *	20 (14, 26) *
Psych.								16 (9, 23) *	17 (10, 24) *
Nur. (var.)									0 (−4, 5) p = 1

Epil. = epileptologists; Neuro. = neurologists; EEG tech. = EEG technicians; Neuro. res. = neurology residents; Emerg. = emergency physicians; Nur. epil. = nurses with experience in epilepsy; Res. (non-neuro.) = residents (non-neurology); Psych. = psychiatrists; Nur. (var.) = Nurses (varia); Med. stud. = undergraduate medical students

*p-value ≤ 0.001

14 HCPs or students who did not identify their profession on the form, 32 participants who were part of a wide variety of HCP or student groups with few representants in each category (e.g. one pharmacist, two neuropsychologists, etc.), and 21 participants who identified themselves as working in research or administration (without significant direct patient care). Of note, the group "nurses with experience in epilepsy" includes neuroscience nurses or nurses working in video-EEG monitoring units. The group "nurses (varia)" includes all the remaining nurses who participated.

Seizure Diagnostic Difficulty

The mean HCPs' and students' percent concordance with the gold standard were not statistically significant between PNES (69.1 ± 12.9%) and ES (58.5 ± 19.6%) ($p = 0.06$) and varied between the 36 seizures from 5.1% to 88.3% (Table 1). The percent concordance with the gold standard was between 37.7% and 88.3% (inclusively) for the majority of seizures (35/36), whereas the percent concordance with the gold standard was only 5.1% for video no. 15 (focal automatism ES). Additionally, four out of five seizures that were easiest to diagnose (i.e. had the highest percent concordance with the gold standard) were PNES, whereas four out of five seizures that were the most difficult to diagnose were ES. The diagnostic difficulty varied according to the specific semiology of each type of PNES or ES: for example, the percent concordance with the gold standard for the nine rhythmic motor PNESs ranged from 57.9% to 87.9% and from 51.8% to 83.4% for the four tonic ES.

Diagnostic Accuracy Based on Level of Expertise

The mean sensitivity, specificity, and AUC of SROC for the groups of HCPs or students are summarized in Table 2. Diagnostic accuracies expressed as the AUC ranged from as high as 95% (epileptologists) to as low as 48% (medical students). An AUC of 48% is worse than luck; the wrong diagnosis is more likely to be chosen that the correct one. There was a statistically significant difference between groups of HCPs or students as determined by one-way ANOVA ($p \leq 0.001$). A Tukey–Kramer HSD post hoc test comparing the difference between each pair of group AUCs revealed statistical difference between most groups ($p \leq 0.001$), while there was no statistical difference between a few groups ($p \geq 0.1$) (Table 3).

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Table 4: Impact of years of experience on neurologists' diagnostic accuracy of PNES versus ES diagnosis

Group (years of experience)	n	Age median (IQR) (years)	Sensitivity		Specificity		AUC	
			Mean ± SD (%)	95% CI (%)	Mean ± SD (%)	95% CI (%)	Mean ± SD (%)	95% CI (%)
Neurologists < 10	31	30–39 (30–39 – 30–39)	90 ± 9	87, 94	77 ± 10	74, 81	91 ± 6	89, 93
Neurologists 10–20	18	40–49 (40–49 – ≥ 50)	87 ± 11	82, 93	78 ± 14	71, 84	90 ± 6	87, 93
Neurologists > 20	15	≥ 50 (≥ 50 – ≥ 50)	84 ± 11	79, 90	75 ± 14	68, 82	86 ± 7	82, 89

n = total number; IQR = interquartile range; CI = confidence interval; AUC = area under the curve

Table 5: Neurology specialists' (pediatric and adult epileptologists and neurologists) diagnostic accuracy of PNES versus ES diagnosis based on patient age and sex

Group	n	Sensitivity		Specificity		AUC	
		Mean ± SD (%)	95% CI (%)	Mean ± SD (%)	95% CI (%)	Mean ± SD (%)	95% CI (%)
Adult patients	24	91 ± 10	89, 93	78 ± 15	75, 81	90 ± 4	89, 92
Pediatric patients	12	87 ± 15	84, 90	77 ± 17	74, 81	87 ± 4	85, 90
Female patients	16	89 ± 14	86, 91	79 ± 18	76, 83	88 ± 4	86, 90
Male patients	16	88 ± 14	86, 91	76 ± 13	73, 78	88 ± 4	86, 90

n = total number; CI = confidence interval; AUC = area under the curve

The mean sensitivity, specificity, and AUC of SROC for groups of neurologists with increasing years of experience are summarized in Table 4. There was a statistically significant difference between the AUCs averaged for groups of neurologists with increasing years of experience as determined by one-way ANOVA ($p = 0.048$). A Tukey–Kramer HSD post hoc test revealed that the AUCs averaged for neurologists with < 10 years of experience (AUC = 91%) were significantly higher ($p = 0.04$) when compared to neurologists with > 20 years of experience (AUC = 86%). There was no statistically significant difference between the groups of neurologists < 10 years and 10–20 years ($p = 0.81$) and between groups of neurologists 10–20 years and > 20 years ($p = 0.20$) of experience.

Diagnostic Accuracy of Neurology Specialists Based on Patient Age and Sex

Due to video quality or anonymization-rendering distinction between male or female patients ambiguous, four seizure clips were excluded from this analysis (videos #10, 17, 21, and 30; Table 1). The diagnostic accuracy (Sn, Sp, and AUC) was similar in adult versus pediatric and female versus male patients (Table 5).

Discussion

Our results confirmed our hypotheses that the ability of Canadian HCPs or students to distinguish PNES from ES based on video-recorded semiology varied overall according to (1) seizure type and semiology, and (2) a HCP or student's level of expertise in the field of neurology/epilepsy. However, (3) we did not identify evidence that the patient's age and sex affect diagnostic performance in the group of neurology specialists.

Seizure Diagnostic Difficulty

Similar to Seneviratne et al. and Jin et al.,[15,16] we found that the HCPs' and students' percent concordance with the gold standard (video-EEG) varied greatly between the different seizure types and semiology. Additionally, we found that while percent concordance with the gold standard was similar between PNES and ES, the highest percent concordance was obtained for PNES types, whereas the lowest percent concordance was obtained for ES types. Participants might instinctively be prompted to choose PNES as a diagnosis when semiology appears intentional/voluntary or overly dramatic. Indeed, the four out of five easiest (PNES) and four out of five most difficult (ES) seizures to identify had features of partial obedience to the examiner's command, trashing, and violent or nonrhythmic motor signs, dramatic vocalizations, and abrupt onset of symptoms appearing to occur only at the most opportune moments. Recognition of features characteristic of ES is often not as instinctive. For example, typical oral automatisms were key semiological features for the correct diagnosis of the first, third, and fifth most missed seizures. In the first most missed seizure (with a percent concordance of 5.1%), only paying attention to the most prominent semiology (symmetric repetitive flexion of the upper limbs while still being able to hand over an object to the examiner) would not allow for a clear differential diagnosis.

Diagnostic Accuracy Based on Level of Expertise

The diagnostic accuracy of PNES versus ES based on video-recorded semiology varied overall proportionately with the caregiver's level of expertise in the field of neurology/epilepsy (Table 2): as expected, HCPs and students with more training performed better. Based on the results obtained, participants can

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be separated into three groups according to decreasing order of diagnostic performance (Table 3): (1) neurology specialists (epileptologists and neurologists), EEG technicians, and neurology residents all performed better than (2) emergency physicians, nurses with experience in epilepsy, residents (non-neurology), and psychiatrists. The latter group performed better than (3) nurses (varia) and undergraduate medical students. Within the first group, neurology specialists performed better than neurology residents. There was a strong trend toward statistical difference, with AUC 95% CIs that were not overlapping between epileptologists (95% CI 93, 97) compared to neurologists (95% CI 88, 91) and neurologists compared to EEG technicians (95% CI 82, 87). However, multiple pairwise comparisons with the conservative Tukey–Kramer HSD test revealed no statistical difference ($p = 0.25$ and 0.1, respectively). Neurology residents performed similarly to EEG technicians. HCP and students within group 2 and within group 3 performed similarly. These findings are overall consistent with previous studies[15–18,20] including smaller samples of groups of HCP or students, with a few differences to be noted. Seneviratne et al. found that neuroscience nurses performed similarly to undergraduate medical students, which could in part be explained by differences in HCP training/exposure between countries (Australia versus Canada).[16]

Increasing experience within the same field/scope of practice might not lead to a better ability to differentiate PNES form ES, as neurologists with 10–20 or > 20 years of experience did not have a better performance than neurologists with < 10 years of experience (Table 4). Furthermore, neurologists with < 10 years of experience performed better than neurologists with > 20 years of experience ($p = 0.04$). First, these results could indicate that the learning curve for visual distinction of PNES from ES might reach a plateau in HCPs with expertise in neurology/epilepsy, above which additional knowledge or experience does not lead to better performance. This 'learning plateau' might explain that seizure diagnosis solely on the basis of videos remains challenging, even when reaching high levels of expertise: more experienced neurologists and epileptologists did not attain a diagnostic accuracy of 100%. Similarly, Erba et al. found that in only about one-third of cases, neurologists could establish a confident diagnosis of PNES/ES based on video data alone.[21] Second, these results emphasize the need for continuing medical education, even among HCPs with the highest expertise.

These findings are of practical relevance. Awareness of the difficulty of PNES semiology differentiation from ES and the importance of early diagnosis in prognosis should prompt HCPs to consider this diagnosis earlier and to seek help from neurology specialists. Likewise, specialists should obtain video-EEG as a diagnostic aid in some cases. Diagnostic suspicion of PNES should remain high in patients with confirmed ES, since an estimated 10%–30% of patients with PNES have coexisting ES,[36] and epilepsy may be a risk factor for PNES. This is especially relevant for mental health professionals, since they are involved in the management of the highly prevalent psychiatric comorbidities in patients with epilepsy and PNES (that might be undiagnosed).[37,38] Additionally, short teaching sessions focusing on differentiating the non-stereotypical semiology of PNES from ES using videos could be an effective and time-efficient strategy to improve diagnostic accuracy in less experienced HCPs or students. Jin et al. showed that the diagnostic reliability can be improved by observing more seizures within the same viewing session, but only in the neurologists and other physicians groups, and not in the group of epileptologists.[15] Two recent studies showed that the accuracy of visual discrimination of seizures improved immediately after a 15-min teaching presentation[17] and 3 and 6 months after a targeted video-based training.[19]

Diagnostic Accuracy Based on Patient Age and Sex

We found that neurology specialists (including pediatric and adult neurologists and epileptologists) were as likely to diagnose PNES in adult versus pediatric, and female versus male patients. This goes against the conception that since PNESs are far more common in women, clinicians are likely to have a lower threshold to diagnose PNESs in women while having a higher threshold to diagnose PNESs in men, as suggested by Dworetzky et al.[37]

Limitations

Our study has certain limitations. First, the small sample sizes in some groups limit the interpretation of results, for example, when comparing the diagnostic accuracy of PNES versus ES diagnosis based on patient age (24 adult and 12 pediatric patients) and sex (16 female and 16 male patients), or the diagnostic accuracy of neurologists with > 20 years of experience ($n = 15$) compared to < 10 years of experience ($n = 31$). Second, despite the comparison of multiple groups, adjustment for multiple tests was not carried in our study. In exploratory analyses, multiple test adjustments are not strictly required, and it might be preferable that data should be analyzed without multiplicity adjustment.[39] Furthermore, in our study, significant findings in pairwise comparisons were quite strong ($p \leq 0.001$). Third, our results may underestimate the true diagnostic accuracy for seizure diagnosis, given that the participants were only shown portions of seizures and were unable to interact, question the patient, or consult the chart for additional clinical details. It must be noted, however, that in real clinical practice, physicians often rely solely on visual diagnosis in cases where obtaining a detailed history is not possible, such as a patient having a seizure in the emergency department. Also, we made sure that all selected video clips contained sufficient semiology information for making a diagnosis. Fourth, the suboptimal quality of some of the videos recorded at night, and the blurring of the eyes required for anonymization may have slightly hampered the interpretation, although we made sure sufficient clues were available for participants to render an informed diagnosis. Although videos where sex and age could not be discerned were excluded from analysis when analyzing potential bias, results might not be representative as this information is usually known without ambiguity to the HCP and student when taking care of a patient. Finally, some participants might not have appropriately identified their profession on the response form. For example, nurses with experience in epilepsy were required to check an additional box identifying themselves as such.

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Conflicts of Interest

MRK reports unrestricted educational grants from UCB and Eisai, and research grants from UCB and Eisai. The remaining authors have no conflicts of interest to declare.

Statement of Authorship

Study conceptualization and methodology (VB, MRK, AL, and DKN), including review and selection of seizure video-EEG clips (VB, AL, and DKN); data acquisition (VB and DKN); data analysis (VB, MRK, and DKN); drafting and revision of the manuscript (all authors); and study supervision and final correction (DKN).

References

1. Reuber M, House AO. Treating patients with psychogenic non-epileptic seizures. Curr Opin Neurol. 2002;15:207–11.
2. Reuber M, Jamnadas-Khoda J, Broadhurst M, et al. Psychogenic nonepileptic seizure manifestations reported by patients and witnesses. Epilepsia. 2011;52:2028–35.
3. American Psychiatric Association. Somatic symptom and related disorders. In: American Psychiatric Association, editor. Diagnostic and statistical manual of mental disorders, 5th ed. Arlington, VA: American Psychiatric Association; 2013, p. 318.
4. Reuber M, Fernandez G, Bauer J, Helmstaedter C, Elger CE. Diagnostic delay in psychogenic nonepileptic seizures. Neurology. 2002;58:493–5.
5. Seneviratne U, Briggs B, Lowenstern D, D'Souza W. The spectrum of psychogenic non-epileptic seizures and comorbidities seen in an epilepsy monitoring unit. J Clin Neurosci. 2011;18:361–3.
6. Carton S, Thompson PJ, Duncan JS. Non-epileptic seizures: patients' understanding and reaction to the diagnosis and impact on outcome. Seizure. 2003;12:287–94.
7. Holtkamp M, Othman J, Buchheim K, Meierkord H. Diagnosis of psychogenic nonepileptic status epilepticus in the emergency setting. Neurology. 2006;66:1727–9.
8. Howell SJ, Owen L, Chadwick DW. Pseudostatus epilepticus. Q J Med. 1989;71:507–19.
9. Martin RC, Gilliam FG, Kilgore M, Faught E, Kuzniecky R. Improved health care resource utilization following video-EEG-confirmed diagnosis of nonepileptic psychogenic seizures. Seizure. 1998;7:385–90.
10. LaFrance WC Jr, Benbadis SR. Avoiding the costs of unrecognized psychological nonepileptic seizures. Neurology. 2006;66: 1620–1.
11. Seneviratne U, Low ZM, Low ZX, et al. Medical health care utilization cost of patients presenting with psychogenic nonepileptic seizures. Epilepsia. 2019;60:349–57.
12. Razvi S, Mulhern S, Duncan R. Newly diagnosed psychogenic nonepileptic seizures: health care demand prior to and following diagnosis at a first seizure clinic. Epilepsy Behav. 2012;23:7–9.
13. Reuber M, Pukrop R, Mitchell AJ, Bauer J, Elger CE. Clinical significance of recurrent psychogenic nonepileptic seizure status. J Neurol. 2003;250:1355–62.
14. Benbadis SR. Nonepileptic behavioral disorders: diagnosis and treatment. Continuum. 2013;19:715–29.
15. Jin B, Wu H, Xu J, et al. Analyzing reliability of seizure diagnosis based on semiology. Epilepsy Behav. 2014;41:197–202.
16. Seneviratne U, Rajendran D, Brusco M, Phan TG. How good are we at diagnosing seizures based on semiology? Epilepsia. 2012;53: e63–6.
17. O'Sullivan SS, Redwood RI, Hunt D, McMahon EM, O'Sullivan S. Recognition of psychogenic non-epileptic seizures: a curable neurophobia? J Neurol Neurosurg Psychiatry. 2013;84:228–31.
18. Ristic AJ, Draskovic M, Bukumiric Z, Sokic D. Reliability of the witness descriptions of epileptic seizures and psychogenic non-epileptic attacks: a comparative analysis. Neurol Res. 2015;37: 560–2.
19. Seneviratne U, Ding C, Bower S, Craig S, Leech M, Phan TG. Video-based training improves the accuracy of seizure diagnosis. J Neurol Neurosurg Psychiatry. 2014;85:466–70.
20. Wasserman D, Herskovitz M. Epileptic vs psychogenic nonepileptic seizures: a video-based survey. Epilepsy Behav. 2017; 73:42–5.
21. Erba G, Giussani G, Juersivich A, et al. The semiology of psychogenic nonepileptic seizures revisited: can video alone predict the diagnosis? Preliminary data from a prospective feasibility study. Epilepsia. 2016;57:777–85.
22. Devinsky O, Gazzola D, LaFrance WC Jr. Differentiating between nonepileptic and epileptic seizures. Nat Rev Neurol. 2011;7: 210–20.
23. LaFrance WC Jr, Baker GA, Duncan R, Goldstein LH, Reuber M. Minimum requirements for the diagnosis of psychogenic nonepileptic seizures: a staged approach: a report from the international league against epilepsy nonepileptic seizures task force. Epilepsia. 2013;54:2005–18.
24. Reilly C, Menlove L, Fenton V, Das KB. Psychogenic nonepileptic seizures in children: a review. Epilepsia. 2013;54: 1715–24.
25. Sawchuk T, Buchhalter J. Psychogenic nonepileptic seizures in children – psychological presentation, treatment, and short-term outcomes. Epilepsy Behav. 2015;52:49–56.
26. Park EG, Lee J, Lee BL, Lee M, Lee J. Paroxysmal nonepileptic events in pediatric patients. Epilepsy Behav. 2015;48:83–7.
27. Cohen JF, Korevaar DA, Altman DG, et al. STARD 2015 guidelines for reporting diagnostic accuracy studies: explanation and elaboration. BMJ Open. 2016;6:e012799.
28. Fisher RS, Cross JH, D'Souza C, et al. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia. 2017;58:531–42.
29. Fisher RS, Cross JH, French JA, et al. Operational classification of seizure types by the international league against epilepsy: position paper of the ILAE commission for classification and terminology. Epilepsia. 2017;58:522–30.
30. Seneviratne U, Reutens D, D'Souza W. Stereotypy of psychogenic nonepileptic seizures: insights from video-EEG monitoring. Epilepsia. 2010;51:1159–68.
31. Jones CM, Athanasiou T. Summary receiver operating characteristic curve analysis techniques in the evaluation of diagnostic tests. Ann Thorac Surg. 2005;79:16–20.
32. Lee J, Kim KW, Choi SH, Huh J, Park SH. Systematic review and meta-analysis of studies evaluating diagnostic test accuracy: a practical review for clinical researchers-part II. Statistical methods of meta-analysis. Korean J Radiol. 2015;16:1188–96.
33. Zamora J, Abraira V, Muriel A, Khan K, Coomarasamy A. Meta-DiSc: a software for meta-analysis of test accuracy data. BMC Med Res Methodol. 2006;6:31.
34. StatPages. Analysis of variance from summary data [software]. 2020. Available at: https://acetabulum.dk/anova.html. Accessed 4 July 2021.
35. GraphPad. QuickCalcs t test calculator [software]. 2020. Available at: https://www.graphpad.com/quickcalcs/ttest1.cfm. Accessed 4 July 2021.
36. Benbadis SR, Agrawal V, Tatum WOT. How many patients with psychogenic nonepileptic seizures also have epilepsy? Neurology. 2001;57:915–7.
37. Dworetzky BA, Baslet G. Psychogenic nonepileptic seizures in women. Semin Neurol. 2017;37:624–31.
38. Hingray C, Biberon J, El-Hage W, de Toffol B. Psychogenic non-epileptic seizures (PNES). Rev Neurol (Paris). 2016;172: 263–9.
39. Bender R, Lange S. Adjusting for multiple testing–when and how? J Clin Epidemiol. 2001;54:343–9.

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