Peri-ictal responsiveness to the social environment is greater in psychogenic non-epileptic than epileptic seizures

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Abstract

OBJECTIVE: To look for evidence of peri-ictal social interaction in psychogenic non-epileptic seizures (PNES) and epileptic seizures exploring the notion of PNES as form of nonverbal communication.

METHODS: Video recordings of typical seizures experienced by patients with epilepsy and PNES were obtained in a naturalistic social setting (residential epilepsy monitoring unit). Video analysis by three non-expert clinicians identified 18 predefined semiological and interactional features indicative of apparent impairment of consciousness or of peri-ictal responsiveness to the social environment with assessment of inter-rater reliability using Fleiss' κ. Features were compared between epileptic seizures and PNES.

RESULTS: 189 seizures from 50 participants (24 epilepsy, 18 PNES, 8 combined) were analysed. At least fair (κ>0.20) inter-rater agreement was achieved for 14 features. The PNES and epileptic seizures compared were of similar severity in terms of ictal impairment of consciousness (κ=0.34; OR = 1.11 [0.62-1.96]) or responsiveness (κ=0.52; OR = 1.01 [0.55-1.86]). PNES were more likely to: be preceded by attempts to alert others (κ=0.52; odds ratio (OR) = 12.4 [95%CI 3.2-47.7, *p*<0.001]); show intensity affected by the presence of others (κ=0.44; OR = 199.4 [12.0-3309.9, *p*<0.001]); and display post-ictal behaviour affected by the presence of others (κ=0.35; OR = 91.1 [17.2-482.1, *p*<0.001]).

SIGNIFICANCE: Non-expert raters can, with fair to moderate reliability, rate features characterising ictal impairment of consciousness and responsivity in video recordings of seizures. PNES are associated with greater peri-ictal responsiveness to the social environment than epileptic seizures. These findings are consistent with a potential communicative function of PNES and could be of differential diagnostic significance.

KEYWORDS: Non-epileptic seizures; communication; dissociative disorders; psychology

1. Introduction

Psychogenic nonepileptic seizures are defined by their superficially similar phenomenology to epileptic seizures although these two seizure types have markedly different aetiologies. Whereas the manifestations of epileptic seizures are caused by epileptic activity in the brain, most psychogenic nonepileptic seizures (PNES) are interpreted as an automatic experiential and behavioural response to internal or external stimuli interpreted as aversive.[1]

The ICD-11 classifies most PNES as a form of dissociative disorder, while in the DSM-5[2] most presentations would fit the diagnostic criteria of functional neurological symptom (conversion) disorder.[3] These putative mechanisms suggest an important role for social interaction in the aetiology of PNES: The dissociative interpretation highlights that PNES are often a consequence of traumas or dilemmas, many of which are of an interpersonal nature,[4] while the conversion hypothesis suggests that PNES can be understood in part as a nonverbal means of communication. Research exploring the aetiology of PNES, however, has largely focussed on subjective or objective characteristics observable in patients themselves. Only a small number of observations suggest important contributions of the social environment to the occurrence of PNES. For instance, it has been reported that certain environments may make PNES more likely: PNES appear to occur more commonly than epileptic seizures during clinic attendances[5] (and show greater response to suggestion when patients have experienced seizures in clinical settings[6]). PNES are also more likely than epileptic seizures to happen in interpersonally challenging situations such as during psychotherapy sessions.[7] One previous study examined the influence of social environment on ictal phenomena, finding that the intensification or alleviation of seizures by the presence of others is a specific marker of PNES.[8] A case report suggests that prolonged PNES can be stopped by talking to patients.[9]

In addition, a small number of studies have compared families of patients with epilepsy and PNES, but these studies have not specifically examined the role or effects of the seizures themselves in patients' social environment.[10–13] At least a subgroup of patients with PNES is characterised by insecure attachment and particular anxieties about interpersonal relationships.[14,15] There is also evidence that carers differ in affective expression and that they experience their relationships with patients with seizures disorders differently, depending on whether the seizures are epileptic or nonepileptic.[16,17]

This exploratory study looks for evidence that – unlike epileptic seizures – PNES may arise as a consequence of objectively identifiable interpersonal constellations or whether the interactional consequences of PNES support the notion of PNES as a nonverbal form of communication.

To this end independent raters examined video recordings of peri-ictal behaviour from a residential video-EEG (vEEG) monitoring unit, in which people who experience seizures may move freely around a shared monitored living environment (including living room, kitchen and garden). This environment permits more natural social interactions than the traditional ward-based epilepsy monitoring unit (EMU), as residents, visitors, and staff can engage in typical daily and leisure activities while still undergoing vEEG monitoring. We hypothesise that people experiencing PNES will display greater responsiveness to those around them ictally and peri-ictally.

2. Methods

2.1. Participants and setting

We invited a consecutive sample of adult patients referred to the Scottish Epilepsy Centre (Glasgow, United Kingdom), a residential EMU specialising in the evaluation and medical treatment of seizure disorders, to participate in this study. This unit differs from conventional EMUs in that, instead of patients being confined to their bed or bedroom during the monitoring period, time-locked video-EEG recording takes place in a much more home-like environment, in which patients inhabit a communal living space. Video recording is available throughout the building and permits continuous monitoring of seizure activity in a less artificial setting and enable recording of seizures in a wider variety of different social situations.

All participants were given information about intended teaching and research uses of seizures recorded while resident in the EMU and gave written consent for the use of their videos for these purposes.

All diagnoses of individual seizures and patients' seizure disorders were made by an experienced epileptologist on the basis of all available clinical information including vEEG capture of episodes typical of the patient's reported episodes. The epileptologist classified all individual seizures as epileptic, non-epileptic, or (for patients with comorbid epilepsy and PNES) mixed or indeterminate based on semiology and vEEG (if occurring while on EEG monitoring). Seizures were also diagnosed and included in this analysis if they were captured only on video but if semiologically similar seizures had previously or subsequently been recorded during vEEG monitoring allowing the epileptologist to make a definite diagnosis. No "indeterminate" seizures or seizures thought to contain mixed elements of epileptic and nonepileptic seizures were included in our comparisons of characteristic associations of these two seizure types.

2.2. Sample

An epileptologist identified the first five recorded seizures for all participants (or all recorded seizures for those with fewer than five recorded events) and manually selected the cut-off points for start and end of recording, allowing the viewer to see the full event, as well as proceedings immediately pre- and post-ictally. Given the exploratory nature of this study and the lack of previous work permitting us to estimate a clinically-important difference we did not undertake a formal sample size calculation. Instead, we specified *a priori* a target of at least 100 epileptic seizures, with a matching number of PNES to capture the variety of semiologies of both seizure disorders and a range of different social settings.

2.3. Video analysis

From anecdotal reports and review of previous literature we identified 18 peri-ictal semiological and interactional features of interest potentially indicative of conscious impairment or of peri-ictal responsiveness to the patient's social environment (see Table 2 below). Three non-expert clinicians (two Core Psychiatric Trainees [postgraduate year three]; one Foundation Year 2 doctor [postgraduate year two]) reviewed each seizure recording and classified each feature of interest as present or absent. The raters were blinded to all clinical information regarding the participants including diagnosis and EEG findings; they were also blinded to the scores assigned by the other raters. Presence or absence of each feature in each seizure was determined by majority rating.

2.4. Statistical analysis

We evaluated the inter-rater reliability of the determination of presence/absence of features of interest by Fleiss' κ. Using conventional thresholds,[18] we performed further analysis on only those features displaying at least fair ($\kappa>0.20$) inter-rater agreement. We compared differences in each feature between epileptic seizures and PNES (two-tailed Fisher's exact test). We defined statistical significance using the Bonferroni correction for multiple comparisons with family-wise error rate $\alpha = 0.05$. We estimated odds ratios (ORs) for PNES and 95% confidence intervals (CIs) using Gart's logit interval.[19,20] As patients with PNES and intellectual disabilities (ID) are sometimes thought to represent an aetiologically distinct group, with greater emphasis on environmental or social interaction in both explanation and treatment,[21,22] we tested whether between-group differences persisted after controlling for intellectual disability by conducting hierarchical logistic regression, and compared differences in interactional features in PNES in participants with and without ID (two-tailed Fisher's exact test). We performed statistical analysis using MATLAB R2017b (The Mathworks Inc, Natick MA), except for logistic regression, which was performed using SPSS v26.0 (IBM Corp., Armonk NY).

3. Results

3.1. Descriptive analysis

50 patients consented to participation, with ages ranging from 16-79 years. 24 had diagnoses of epilepsy, 12 PNES, and 14 comorbid epilepsy and PNES (see Table 1 for demographic details). Age did not differ significantly between groups (one-way ANOVA, p = 0.365). Sex distribution differed significantly between groups, with more women in the PNES and combined groups than in the epilepsy group ($\chi^2(2) = 6.124$, $p = 0.047$). Significantly

more participants in the epilepsy group had some degree of intellectual disability ($\chi^2(2)$ = 10.506, p = 0.033).

Participants with epileptic seizures had diagnoses of idiopathic generalised (6 participants), or focal epilepsy (22 participants: 16 with purely focal aware or impaired awareness seizures, 6 with focal to generalised seizures). The epilepsy type could not be clearly specified in 10 participants.

We reviewed a total of 193 seizures (100 epilepsy, 89 PNES, 4 combined or indeterminate). Those that could not be clearly diagnosed as either epileptic seizures or PNES were excluded from further analysis. We did not have ratings from all raters for two episodes; these were also excluded from analysis.

3.2. Comparison of seizure characteristics

At least fair interrater agreement was achieved for 14 of the 18 features examined: substantial agreement was seen in two (0.60<κ≤0.80), moderate in seven (0.40<κ≤0.60) and fair in five (0.20<κ≤0.40). The raters did not reliably agree on the presence of four features (pre-ictal behaviour change, post-ictal agitation or behavioural difficulty, autonomic features, and evident injury). The PNES and epileptic seizures compared were of similar severity in terms of ratings of apparent ictal impairment of consciousness (κ=0.34; odds ratio [OR] = 1.11 [95% CI 0.62-1.96]) and responsiveness (κ=0.52; OR = 1.01 [0.55-1.86]).

Several features indicating peri-ictal responsiveness to social cues were more prominent in PNES than in epilepsy. PNES were more likely to: be preceded by attempts to alert others (κ=0.52; OR = 12.4 [95%CI 3.2-47.7, p<0.001]); show intensity affected by the presence of others (κ=0.44; OR = 199.4 [12.0-3309.9, p<0.001]); and display post-ictal behaviour affected by the presence of others (κ=0.35; OR = 91.1 [17.2-482.1, p<0.001]). The intensity of 51% of

PNES (but none of the epileptic seizures) were judged to be influenced by the presence of others; post-ictally only 1% of epileptic seizures were thought to show behaviour influenced by others compared to 58% of PNES. Differences in peri-ictal responsiveness remained statistically significant after controlling for ID. There were no significant differences in peri-ictal responsiveness in PNES in participants with and without ID.

Inter-rater reliability for all variables studied is displayed in Table 2. For those variables with at least fair inter-rater agreement, the table also displays corrected ORs with 95% CIs and proportion of patients with epilepsy and PNES displaying each feature. ORs with 95% CIs are displayed graphically in Fig.1.

4. Discussion

4.1. Ictal consciousness and social responsiveness

Our results demonstrate that, when in an environment permitting normal social interactions, PNES differ systematically from epileptic seizures in the degree of peri-ictal responsiveness to the social environment they are associated with. The presence of others affected people before, during, and after PNES significantly more than in epileptic seizures; in no epileptic seizure did the presence of others affect ictal intensity, compared with over half of PNES.

One previous study also identified the ability of others to alleviate or intensify PNES but not epileptic seizures; however, in that study all video recordings were from seizures recorded in traditional EMUs, and thus represent a more artificial setting less representative of people's usual social environments. Furthermore, raters in that study were all expert epileptologists, who may have been more likely to identify the underlying diagnosis correctly and thus be biased in their identification of particular features. Indeed, only 18% of lay eyewitnesses agreed with epileptologists' assessment of this form of ictal social responsiveness.[8] By contrast, we show that in a more naturalistic social environment the influence of others on ictal intensity clearly distinguishes PNES from ES, and can be identified by non-expert clinicians. This finding has potential diagnostic and therapeutic implications, as well as providing evidence for the communicative function of PNES discussed in the introduction.

Diagnostically, we demonstrate that video-documented peri-ictal social responsiveness can be identified with fair to moderate reliability by non-expert observers and that this is a highly specific sign for PNES compared with epilepsy (with just 1% of epileptic seizures demonstrating post-ictal responsiveness to others, and none showing ictal responsiveness). Thus ictal social responsiveness could be considered as a candidate criterion for diagnostic tools to assist in the differential diagnosis of seizures[23–28], although it is important to stress that our study evaluated social responsiveness objectively, by video analysis, rather than relying on carer- or family-reported responsiveness. There is some evidence from a previous study that attending to the communicative dimensions of ictal phenomena may aid diagnosis, with psychiatrists identifying socially-responsive ictal features such as 'putting oneself at the centre of attention' or 'mirror movements imitating the examiner' in video recordings of seizures as suggestive of PNES. However, in contrast to this previous study, the observations described here all achieved at least fair levels of inter-rater reliability.[29] Given the general consensus that no semiological feature is pathognomonic of PNES and that individual features are of limited diagnostic value,[8,28,30–32] it is particularly striking to observe that a noticable increase in seizure intensity in response to the presence of others was observed in over one half of all PNES studied here, whereas this was not identified in a single epileptic seizure. In view of the increasing importance of home video recordings in the diagnostic process, our findings therefore suggest that the observation of ictal social responsiveness may be very helpful in clinical practice.

Therapeutically, our observations have immediate relevance to the information patients and families should be given when the diagnosis of PNES is communicated and advice is provided on the management acute management of PNES by any caregivers. These individuals should be made aware that their interaction with the patient during the PNES can potentially make these seizures worse and that they should carefully monitor the effects of their actions on the patient's seizures.[33] Our observations are also relevant for psychological therapies which are considered the standard of care for further treatment of PNES.[34–37] Typical CBT approaches for PNES utilise a fear-avoidance model. A central feature of this approach is the identification of stimuli that may provoke an avoidant response, and helping those with PNES to understand the role their attacks can play in such responses.[38] Our study suggests that, in the search for potentially relevant stimuli, particular attention should be paid to potential interpersonal and social triggers. This approach will fit naturally into Psychodynamic Interpersonal Treatment approaches which have also been proposed for PNES.[39]

As discussed above, the putative communicative function of PNES (for instance as an expression of distress or other emotions, in some cases as a nonverbal representation of an unspeakable dilemma or traumatic memory) is a feature of multiple aetiological accounts of the mechanisms underlying PNES. Our findings of social responsiveness intra- and peri-ictally in PNES could be interpreted as behavioural, dissociative, or conversion responses to varying social stimuli. Indeed, it is likely that our PNES participants represented an aetiologically heterogeneous group; the fact that our findings were, nonetheless, robust (and that there were not significant semiological differences between the participants with and without ID) support efforts to develop integrated models of PNES that can incorporate distinct psychological mechanisms into understanding the phenomenon.[1,40]

4.2. Seizure semiology

Our results also demonstrate that non-expert raters could identify significant differences in other (not necessarily interaction-associated) features between video recordings of PNES or epileptic seizures and immediately peri-ictal scenarios. We found that a fluctuating intensity of ictal phenomena was highly predictive of PNES (OR 39.5, 95% CI 10.5-148.3, sensitivity 95.7% and specificity 69.1%); these figures are consistent with those found for expert rating of video recordings by Syed et al,[8] and broadly match those reported in other studies evaluating video-EEG recordings,[30] though they are better than those reported by Azar et al., whose findings were based on questionnaire data.[41] We found that sudden seizure onset and post-ictal confusion were more common in epilepsy than PNES (OR 0.925 [0.146-0.599]), associations with conflicting support in the previous literature.[8,30] Our other findings were broadly consistent with older reports, and would also support the conclusion of other authors that non-expert assessors can be supported in identifying semiological features to aid the differential diagnosis of seizures.[42]

Four features showed low inter-rater reliability in identification: pre-ictal behaviour change, post-ictal agitation or behavioural difficulty, autonomic features, and evident injury. The nature of the study (review of video recordings from cameras sometimes at some distance from the patient) may explain the lack of agreement on presence of autonomic features or injury, as both of these would normally be evaluated by closer assessment (e.g. physical examination for features of autonomic arousal or evidence of injury). The other two features, meanwhile, refer to immediate pre- or post-ictal behaviour change; disagreement here may relate to differing assessment of when the ictal period proper starts and finishes (and thus which behaviours are considered seizure phenomena, and which pre- or post-ictal).

4.3. Limitations

There are several limitations of note to this study. Most prominently, while the raters were not experts in seizure disorders, they were all qualified medical professionals. The reliability of seizure classification by healthcare professionals varies throughout training,[43] and differs from that of lay witnesses.[44] Thus our results do not necessarily generalise to other groups (especially non-expert carer), and despite their lack of epileptological expertise raters may have been able to identify the underlying diagnosis from the semiology alone. This could have influenced their determination regarding the presence/absence of features of interest. Furthermore, we found at least some disagreement between raters in their evaluation of all variables of interest, highlighting that simple reports of the presence/absence of particular features in clinic (in the absence of video documentation) do not unambiguously indicate that the feature was actually present in any seizure. None of the features examined showed more than substantial inter-rater agreement, highlighting that even witness reports from healthcare professionals or video interpretations by non-experts cannot serve as completely unambiguous guides to seizure semiology and that diagnoses always need to consider the full semiological, clinical and social context.

Importantly, our findings are based on the interpretation of high quality video recordings of seizures including the scenario before and after the ictal event. This means that the findings cannot be directly generalised to the interpretation of videos only capturing parts of seizures (most commonly the seizure ending) or to situations in which seizures are directly observed but not recorded. Furthermore we acknowledge that the nature of the peri-ictal behaviour of patients may have been influenced by which people were present (rather than only by whether others were present or not). Unfortunately, we did not collect information on the status of third parties visible in the seizure videos (e.g. whether others were visitors, members of staff or other patients. Finally, our comparisons between PNES and epilepsy are based on seizures of similar severity in terms of ictal awareness and responsiveness as rated by our non-expert observers. We acknowledge that, in the absence of patient self-report, this assessment of consciousness has significant limitations: There is evidence from previous studies that subjective and objective measures of ictal consciousness can discriminate between groups of patients with epilepsy and PNES. For instance, in one study patients with PNES displayed a higher level and content of consciousness than those with epilepsy on the Ictal Consciousness Inventory (ICI),[45] and in others patients with epilepsy and PNES were shown to differ in self- and witness-report in response to several questions regarding ictal awareness and responsiveness.[23,24,46] Differences have also been observed in the characterisation of PNES-related impairment of consciousness of patients themselves and eye witnesses.[47] What is more, patients with PNES report that degrees of loss of awareness – the absence of subjective experience – and loss of responsiveness – interaction with the surrounding environment – vary considerably (intra- and intersubjectively) across different seizures, with many describing one phenomenon occurring independently of the other.[46] Overall, our results suggest a relative preservation of some functions of consciousness (responsiveness to social stimuli) in contexts of ostensible loss of awareness within PNES.

5. Conclusions

We demonstrate exploratory evidence that PNES show greater peri-ictal responsiveness to the social environment than epileptic seizures, and that non-expert raters can, with at least fair reliability, identify a range of features suggestive of this, with over half of PNES showing ictal intensity influenced by the presence of others, a phenomenon not seen in epileptic seizures. This provides support and stimulus for further investigation into potential communicative functions of PNES. It shows that the observation of social interaction may serve as a diagnostic criterion in the diagnostic interpretation of ictal video recordings and suggests also has implications for the treatment of PNES. Correlating the subjective experience and objective manifestations of conscious behaviour in epilepsy and PNES with physiological and psychological differences may contribute to understanding better the functions and mechanisms of human consciousness.

Key points

- Psychogenic non-epileptic seizures (PNES) are more likely to show intra- and peri-ictal responsiveness to the presence of others than epileptic seizures.
- Over half of PNES, but no epileptic seizures, could be alleviated or intensified by the presence of others.
- Non-expert clinicians can identify these interactional features of PNES in video recordings with at least fair inter-rater reliability.
- PNES may serve a communicative function for those who experience them.

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Tables

	N (% female)	Mean age (SD)	Intellectual disability (*N*, %)
Epilepsy	24 (37.5)	33.9 (13.4)	13 (54.2)
PNES	12 (58.3)	41 (16.9)	2 (16.7)
Epilepsy+PNES	14 (78.6)	39 (11.1)	2 (14.3)

Table 1. Participant demographics

Feature	**Inter-rater agreement (Fleiss' κ)**	**Proportion patients displaying feature (%)**		**OR for PNES (95% CI)**
		Epilepsy	**PNES**	
Fall to ground/sideways	0.74	21.2	23.3	1.13 (0.57-2.23)
Interacting with others at onset	0.68	33.0	45.6	1.69 (0.94-3.03)
Cluster of seizures	0.57	1.0	8.9	6.83 (1.18-39.7)
Ictal emotional outburst (crying, laughter)	0.53	19.2	14.4	0.72 (0.34-1.54)
Apparent impaired responsiveness	0.52	68.4	68.5	1.01 (0.55-1.86)
Apparent attempts to alert others at onset	0.52	2.0	23.9	**12.4 (3.23-47.7)**
Apparent pre-ictal warning/aura	0.52	2.0	21.3	**10.9 (2.82-42.1)**
Post-ictal confusion	0.45	30.3	12.6	0.343 (0.161-0.727)
Seizure intensity affected by presence of others	0.44	0.0	50.6	**199 (12.0-3309)**
Fluctuating intensity of signs	0.39	2.0	50.1	**39.5 (10.5-148.3)**
Post-ictal behaviour affected by presence of others	0.35	1.0	58.0	**91.1 (17.2-482.1)**
Apparent impairment of consciousness	0.34	42.9	45.5	1.11 (0.624-1.98)
Sudden onset	0.33	86.0	65.5	**0.295 (0.146-0.599)**
Apparent attempt to take safety precautions	0.30	5.0	13.5	2.80 (0.983-7.98)
Apparent pre-ictal behaviour change	0.17	11.7	30.3	**3.19 (1.49-6.85)**
Evident injury	0.16	1.0	0.0	0.366 (0.015-9.11)
Evident post-ictal agitation	0.08	3.0	1.1	0.478 (0.069-3.30)
Autonomic features (flushing, pallor, sweating)	-0.02	1.1	2.3	1.82 (0.235-14.1)

Table 2. Inter-rater agreement and ORs for PNES of seizure variables. Statistically significant results are highlighted in ***bold*** *(FWER=0.05, Bonferroni correction)*

Figures

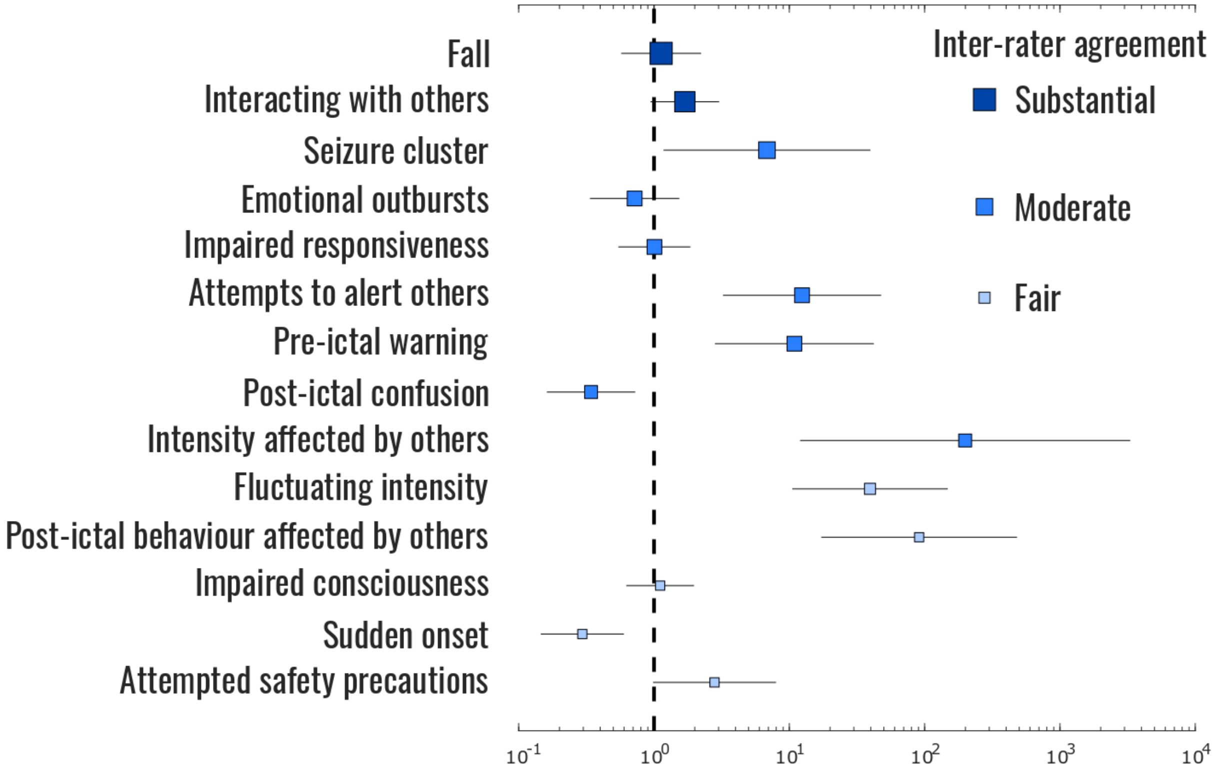

Figure 1. ORs for PNES of selected variables. Bars represent 95% CIs. Marker size is proportional to inter-rater agreement (Fleiss' kappa)