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Biomarkers in the Diagnosis and Study of Psychogenic Nonepileptic Seizures

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Introduction

Psychogenic nonepileptic seizures are a type of conversion disorder characterised by paroxysmal episodes that resemble epileptic seizures but lack electroencephalographic correlation. PNES diagnostic methods have evolved over time, but video electroencephalography is now considered the best diagnostic option for determining ES from PNES. Nonetheless, this methodology is expensive, only available in a few clinical settings, and is only useful for a review of the diagnostic and investigational utility of all candidate PNES biomarkers to date. We felt compelled to review this from both clinical and investigational perspectives as a field update in order to begin prioritising diagnostic, treatment, and research imperatives related to PNES. Many studies are being conducted that focus on the neuroimaging or other biological aspects of PNES.

Description

Initially, studies published between 1980 and 2015 were screened, and additional articles were found through references. The studies included ES and PNES patients with or without healthy controls (HC). Case reports with pertinent findings were also included. Other types of conversion disorder (including functional movement disorders), review articles, meta-analyses, and articles written in languages other than English were excluded. We did not include electrographic studies such as EEG/vEEG or single photon emission CT (SPECT) because these are neurophysiological tests currently considered to be the most robust or best available approaches to assessing ES versus PNES; vEEG in particular is considered the gold-standard of seizure diagnosis, whereas SPECT is less commonly used [1].

Studies published between 1980 and 2015 were initially screened, and additional articles were discovered through references. Patients with ES and PNES were included in the studies, along with or without healthy controls. Case studies with relevant findings were also included. Other types of conversion disorders (including functional movement disorders), review articles, meta analyses, and articles written in languages other than English were not considered. We did not include electrographic studies like EEG/vEEG or single photon emission CT because these are neurophysiological tests that are currently thought to be the most robust or best available approaches to assessing ES versus PNES; vEEG, in particular, is considered the gold standard of seizure diagnosis, whereas SPECT is less commonly used.

PNES patients have been studied using fMRI techniques in at least seven studies. Ding et al. found increased functional connectivity between various cortical areas as well as a "lattice-like" organisation in functional and structural connectivity networks in PNES subjects when compared to HC in two studies involving the same subjects (n = 17). Using the same cohort as Ding et al., Li et al. discovered hyperlinked functional connectivity in PNES insular subregions. van der Kruijs et al. discovered increased coactivation of cingulate and insular cortices in PNES compared to HC, and discovered a link between such coactivation and both dissociation and emotional dysregulation.

Heart rate (HR) and heart rate variability responses to seizure events in ES and PNES groups were compared in studies. One study found that maximal ictal HR above 130 beats per minute (BPM) distinguished ES from PNES with an 83% sensitivity, 96% specificity, and 97% positive predictive value. Oliveira et al. found ictal tachycardia in 100% of ES (complex partial) patients but not in PNES subjects; the authors replicated this finding in another cohort, finding ictal and postictal HR elevations in ES (complex partial seizures; CPS) but not in PNES groups. Reinsberger et al. discovered that ES (complex partial) had significantly higher preictal and postictal HR (but not ictal HR) than PNES [2-5].

Conclusion

In conclusion, biomarkers have provided limited benefit in the diagnostic and research needs surrounding PNES; specifically, PRL levels provide only negative predictive value. Until more research is conducted, the complex psychosocial dimensions inherent in PNES will continue to prevent the sole or meaningful use of cellular, hormonal, autonomic, or neuroimaging findings in clinical care. Clinically, vEEG is still the preferred modality for distinguishing ES from PNES, but in the absence of this diagnostic modality, multidimensional biopsychosocial assessments are the most useful to the practising clinician.

Acknowledgement

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Conflict of Interest

There are no conflicts of interest by author.

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