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Hyperventilation during electroencephalography: Safety and efficacy

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ABSTRACT

Purpose.: To determine safety and efficacy of hyperventilation (HV) during electroencephalography (EEG).
Methods: We report the findings of a prospective multicentre National Service Evaluation of the occurrence of adverse events, seizures and interictal epileptiform discharges seen in association with HV during EEG, in a relatively unselected, largely out patient population of 3475 being investigated predominantly for possible epileptic seizures.
Results: Adverse events occurred rarely, and there were no reported significant cerebrovascular, cardiovascular or respiratory events. Of the 3170 patients suspected of 'epilepsy or possible epilepsy' 69 patients (2.2%) had seizures provoked by HV, but only one (0.03%) had a generalised tonic clonic seizure. The elicitation or increase of interictal epileptiform discharges (IEDs) was seen in 387 (12.2%) of the total 3170 patients with suspected epilepsy who hyperventilated. Furthermore 31 patients (0.9%) had psychogenic non-epileptic seizures.
Conclusion: HV is rarely associated with adverse events, but contributes to the diagnosis and classification of seizure disorders in an appreciable proportion of patients with epilepsy and non-epileptic attacks. These findings confirm that HV in selected patients is a valid activation technique in diagnostic EEG, where the potential benefits out weigh the risks, and also provide information that may assist the informed consent process.

1. Introduction

Voluntary hyperventilation (HV) was known to provoke epileptic seizures[1,2] prior to the advent of electroencephalography (EEG) as a clinical investigation. It is no surprise then that HV provided the first EEG 'activation procedure'.[3] However, in spite of its widespread use, surprisingly little is known about the risk of adverse events during voluntary HV, the incidence of epileptic seizure provocation, and its diagnostic efficacy in terms of eliciting or increasing interictal epileptiform discharges (IEDs). There is a single centre retrospective analysis reviewing 1000 EEG investigations, which gives some indication of the occurrence of both seizures and IEDs during activation procedures.[4] Twelve seizures (2.1%) were reported occurring in the 580 relatively unselected patients who were hyperventilated for 3 min, and an increase in IEDs in another 60 of their patients (10.3%).[4]

A review of the literature on HV as an activating procedure noted that it is considerably more effective in generalised epilepsies than in focal epilepsy syndromes.[5] Indeed the early exponents of HV identified that children with 'petit mal epilepsy' (Childhood Absence Epilepsy) were the most sensitive to its effects; 77% of patients with that diagnosis (from 1107 with epilepsy) had "three-per-second wave and spike pattern" in the resting record, but an additional 8% were only revealed by over-ventilation (HV).[6] The role of HV in Childhood Absence Epilepsy was secured by an extensive study which found that HV provoked 3 per second generalised spike and wave in 88% of 234 patients.[7] What is less clear is how efficacious it is in focal (or partial) epilepsies, although it has recently been pointed out that because focal IEDs, and sometimes seizures, can be activated by HV it should not be neglected in patients with focal epilepsy.[8] Early work is confounded by the exact interpretation of paroxysmal abnormalities in the EEG during HV; but in the modern era rates of IED activation have been reported between 6.6% of 255 patients and 3.4% of 383 patients, diagnosed with focal or partial epilepsy.[9,10] However, the induction of partial seizures appears to be more variable in patients diagnosed with focal epilepsies; with rates ranging from either none in 159 patients[11] or as low as 0.46%[10] up

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to 4.4% [9] in standard recordings. In medically intractable focal epilepsies 17.5% of 80 patients[12] and 24.7% of 97 patients[13] had seizures with repeated HV and anticonvulsant drug reduction in patients during prolonged video EEG monitoring.

The American EEG Society (AEEGS, 2004),[14] International League Against Epilepsy[15] and National Institute for Health and Clinical Excellence (NICE, 2012)[16] all recommend that HV is performed as part of a standard EEG. The AEEGS provides contraindications to HV including recent subarachnoid haemorrhage, intracranial haemorrhage, or significant cardio-pulmonary disease. NICE (CG 137) recommends that "the child, young person or adult and family and/or carer should be made aware that such activation procedures may induce a seizure and they have a right to refuse". In order to provide informed consent it is necessary to quantify these risks in an unselected population, reflecting actual clinical referral practice, and to place them in the context of the potential benefits of increased diagnostic sensitivity of the standard EEG. Patients should not only be advised of the risk of epileptic seizures but also potential non-epileptic events, as well as the likely positive outcomes in terms of diagnostic information. Useful diagnostic information includes eliciting generalised absence seizures, an increase in IEDs, and perhaps even psychogenic non-epileptic seizures. This prospective multicentre National Service Evaluation, organised by two professional organisations in the UK (the Association of Neurophysiological Scientists and the British Society for Clinical Neurophysiology), attempts to address this relative deficiency in the EEG literature.

2. Methods and patients

In line with the UK NHS National Research Ethics Service's guidelines Ethical approval was not deemed necessary for this service evaluation of routine clinical practice. However, all the patients in this service evaluation were given informed consent and provided with the option not to hyperventilate during their EEG recording. Data was collected prospectively by the professionally trained recording Clinical Physiologist in 56 participating UK Departments of Clinical Neurophysiology (see Acknowledgement) from 6242 consecutive patients referred for a standard EEG between beginning October and end December 2011 (see Appendix: Questionnaire). A total of 3475 (56%) patients could be hyperventilated, for periods ranging from 1 to 7 min (with a median of 3 min in 83% of patients). Some 2767 (44%) did not hyperventilate; either because it was against department protocol (46%), the patient could not co-operate (29%), was too young (19%), refused (1%), or some other reason not specifically defined (5%). There were 3129 females (50.1%) and 3113 males (49.9%) with an age range of 3 months to 97 years (mean 33.1 years). In terms of the provisional primary clinical diagnosis of those who hyperventilated 3170 patients (91%) were referred with 'epilepsy or possible epilepsy', 102 (3%) with possible psychogenic non-epileptic seizures, and 203 (6%) with some other diagnosis which was not defined.

Adverse Events are defined by the General Medical Council as "any unintended or unexpected event which could or did lead to harm of one or more patients". Such Events that were deemed to be caused by or temporally associated with HV were identified by the recording Clinical Physiologist, and classified as either a cardiovascular, respiratory or cerebrovascular event, a psychogenic non-epileptic seizure or an epileptic seizure. Predictable side effects of hyperventilation, such as dizziness, light headedness, paraesthesias and headaches, were not recorded. Any activated epileptic seizures were broadly classified by their electro-clinical characteristics as either focal or generalised, with a clinical description of seizure type where possible, along with spontaneous seizures occurring during the resting record (i.e. not activated). In order to determine efficacy the recording Physiologist identified if HV produced unequivocal epileptiform activity or IEDs (defined as 'sharp waves, spikes with or without slow waves') not seen in the resting record, or if HV exacerbated epileptiform activity seen in the resting record. All the information was submitted anonymously into a Microsoft Access database to the Organising Committee for analysis.

3. Results

Of the 3475 patients who were able and willing to HV there were only two reported symptomatic cardiovascular, respiratory or cerebrovascular adverse events. A known asthmatic complained of wheeziness and a second patient experienced symptomatic tachycardia (130 bpm from 100 bpm) during a non-epileptic seizure, both of which were self-limiting and stopped on cessation of HV. Non-epileptic attacks or psychogenic non-epileptic seizures were reported in 31 patients (including 'disorientation, jerks, twitching, eyelid flickering and other abnormal rhythmic movements involving the limbs or torso'), where there were no accompanying abnormal EEG changes.

Epileptic seizures were precipitated by HV in 69 patients (2.2%), with 59 (85%) identified as generalised, 8 (12%) as focal, and 2 (3%) as undetermined or unspecified. The 59 generalised seizures were classified as absences in 54, generalised tonic clonic seizure in 1, eyelid myoclonia in 1 and not specified in 3. The mean age of patients with generalised seizures was 10.3 years (range 3–33 years), and 29 (54%) of these patients had spontaneous seizures (all absences) during the resting record as well (i.e. not activated). This suggests that HV gives a nearly twofold increase in generalised absence seizures (although of course HV typically only accounts for around 3 min of a standard 20 min recording). The 8 focal seizures

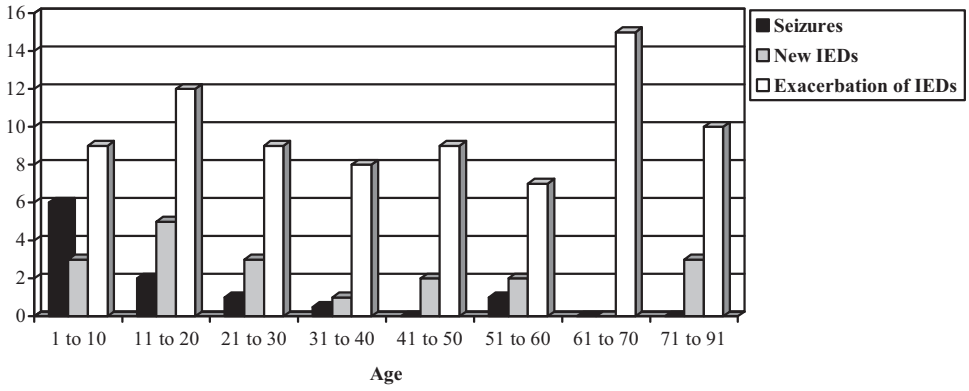

Fig. 1. Percentage hyperventilation activation of seizures and new interictal epileptiform discharges (IEDs) or their exacerbation by 10 year age groups.