Case Report

Neck atonia with a focal stimulation-induced seizure arising from the SMA: Pathophysiological considerations

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ABSTRACT

A 28-year-old patient with pharmacoresistant non-lesional right frontal epilepsy underwent extra-operative intracranial EEG recordings and electrical cortical stimulation (ECS) to map eloquent cortex. Right supplementary motor area (SMA) ECS induced a brief seizure with habitual symptoms involving neck tingling followed by asymmetric tonic posturing. An additional feature was neck atonia. During atonia and sensory aura, discharges were seen in the mesial frontal electrodes and precentral gyrus. Besides motor signs, atonia, although rare and not described in the neck muscles, and sensations have been reported with SMA stimulation. The mechanisms underlying neck atonia in seizures arising from the SMA can be explained by supplementary negative motor area (SNMA) – though this was not mapped in electrodes overlying the ictal onset zone in our patient – or primary sensorimotor cortex activation through rapid propagation. Given the broad spectrum of signs elicited by SMA stimulation and rapid spread of seizures arising from the SMA, caution should be taken to not diagnose these as non-epileptic, as had previously occurred in this patient.

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1. Introduction

Negative motor phenomena and particularly atonia as a clinical manifestation of seizures are a rare, though well-recognized phenomenon [1]. Some of the reports presenting atonia as a seizure phenomenon have demonstrated scalp ictal activity during these episodes. However, only a few reports presented intracranial recordings during these events, further delineating the anatomical area involved in atonia seen in spontaneous seizures [2]. Atonia in focal seizures presents usually with limb atonia, and there are no detailed reports about isolated neck atonia in focal seizures [3]. Unlike focal atonic seizures, generalized atonic seizures often involve trunk muscles, and head nodding as the clinical correlate of neck atonia has been observed in myoclonic astatic epilepsy of childhood [4]. However, in symptomatic generalized epilepsy, focal seizure activity might underlie neck atonia. Focal atonic seizures, as a manifestation of focal epilepsy, have been described in epilepsies arising from the central region or mesial frontal lobe [3,5].

Activation of the negative motor areas has been identified as one mechanism underlying focal atonic seizures. Insight into these mechanisms comes mainly from electrical cortical stimulation performed extra- or intra-operatively prior to resection in eloquent cortical areas. Pioneering studies showed that electrical stimulation of the cortex not only elicits positive motor phenomena but also is capable of disrupting muscle activity as seen in atonia [6]. Subsequently, two non-continuous cortical areas on the lateral and mesial frontal cortices that generate such responses were discovered and labeled primary and supplementary negative motor area (PNMA/SNMA). The PNMA was identified anterior to the primary motor face area, and the SMNA lies anterior to the face region of the supplementary sensorimotor area of the mesial frontal lobe (SMA; [7]).

Here we present a patient with seizures arising from the SMA. Extra-operative electrical cortical stimulation of the mapped seizure onset zone and adjacent cortex within the mesial cortex reproduced the habitual seizures with sensory symptoms followed by asymmetric tonic motor seizure. An additional feature of the stimulation-induced seizure was neck atonia that has not been described previously in focal seizures. Detailed analysis of the stimulation-induced seizure provides insight into the pathophysiology of neck atonia in focal seizures. Knowledge about the spectrum of clinical signs that can arise from SMA stimulation is important in order to avoid misdiagnosis of these as non-epileptic attacks, as had occurred in this patient in the past.

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2. Case study

A 28-year-old right-handed woman underwent presurgical evaluation for seizures with initial paresthesia or a strange feeling localized in the left posterior aspect of the neck, a feeling of heaviness of her head followed by a bilateral asymmetric tonic–clonic posture with the left arm more extended than the right arm. These episodes started when the patient was 10 years old, and the episodes have been refractory to treatment since. At some point in the past, these were diagnosed as non-epileptic, resulting in discontinuation of treatment and exacerbation of seizure frequency. At the time of admission, she suffered daily from ~1–3 seizures, mostly during the night, and rare generalized tonic-clonic seizures (~1/month). There were no risk factors for epilepsy in the past medical history. High-resolution magnetic resonance imaging at 3 T was normal. Scalp video-EEG telemetry was performed twice, revealing midline fast activity on EEG, but failed to capture conclusive lateralizing interictal and ictal activity despite recording many seizures. Clinical semiology included hyperkinetic, generalized tonic and asymmetric tonic seizures. Repeated non-invasive video-telemetry evaluation, however, showed left arm or left leg clonic movements in some of the seizures, and a few of the 28 seizures captured showed a right frontocentral maximum on ictal EEG, concordant with right hemispheric focal epilepsy. Fluorodeoxyglucose-positron emission tomography was normal. Ictal SPECT showed hyperperfusion

in the right mesial frontal cortex. The patient underwent invasive recordings covering the right mesial frontal cortex with high-density electrodes (5-mm-inter contact spacing, center to center). Due to bridging veins, one high-density electrode grid of 16 contacts (4×4) was placed on either side of the vein. A third 8×8 contact electrode grid with 1 cm spacing of contacts was placed over the right lateral convexity (Figs. 1A and B). 12 habitual seizures, consisting of a tingling sensation of the neck and bilateral arm posturing, were captured during invasive monitoring (Supplementary video 2; Supplementary Fig.). Ictal EEG showed an initial spike, followed by fast activity, and was restricted initially to a few mesial electrodes (Fig. 1C) with propagation to the lateral convexity (Fig. 1D) or to adjacent anterior mesial contacts. Interictally, constant runs of spikes, polyspikes, and fast activity were seen in the contacts implicated in ictal onset (contacts B1, B2, B3, B5, B6, and B7).

To map eloquent cortex in this area, we performed bipolar cortical stimulation by delivering biphasic pulse stimuli at 50 Hz in trains lasting up to 5 s to adjacent electrodes.

Stimulation of three contact pairs within the mesial electrode array induced the habitual aura and seizure (B1–B2; B5–B6; and B9–B10). Bipolar stimulation of a contact pair within the seizure onset zone (B1–B2) reproduced the sensory aura observed with habitual seizures and induced afterdischarges in the electrodes involved in the immediate seizure onset zone (B1, B2, B5, and B6), quickly
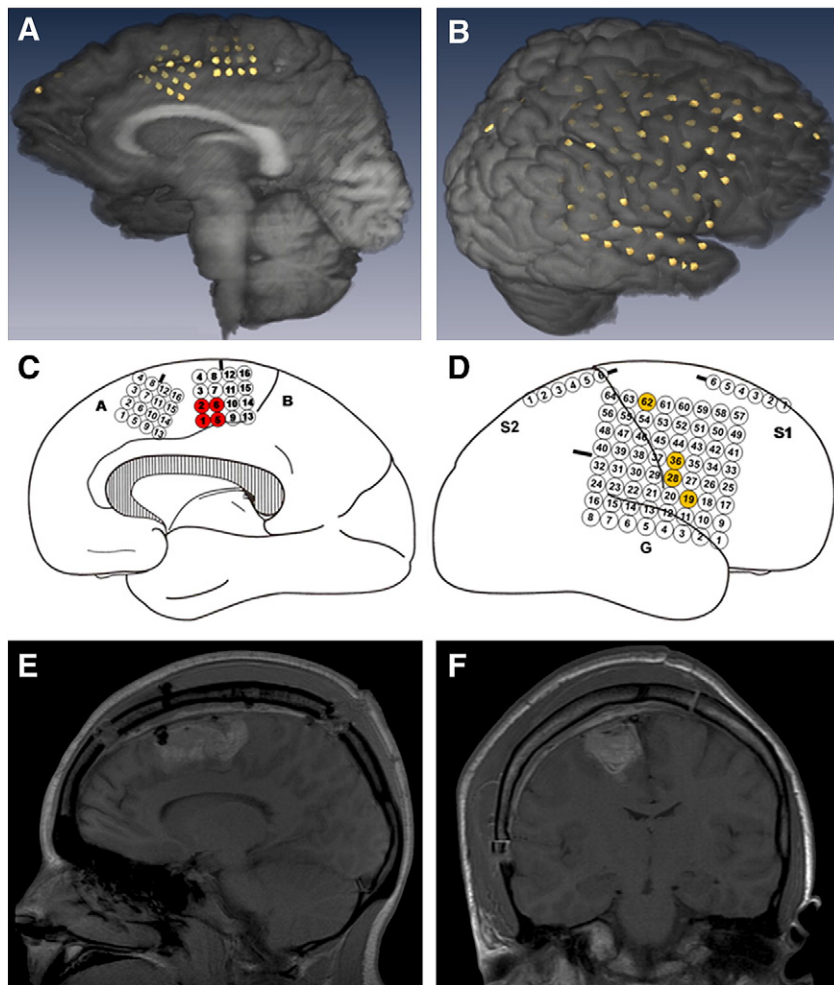

Fig. 1. Subdural electrode placement, seizure onset zone, and surgical resection. The MRI coregistration images show subdural electrode placement on the right lateral and mesial frontal lobe cortices. Note the higher density array (5 mm interelectrode distance) that covers the mesial frontal surface (A and B). Schematic drawing of subdural electrode placement. Electrodes involved in seizure onset (red) are on the mesial surface (C). Seizure spread was seen within 2 s to cortical areas on the lateral convexity (yellow; D). Postoperative MRI images (FLAIR) show a hyperintensity indicating edema from the resection and a small area of hypointensity, indicating the extent of tissue resected (sagittal view E; coronal view F).

involving all contacts of electrode array B. Stimulation of another contact pair within the seizure onset zone (B5–B6) produced the sensory aura and tonic posturing. Stimulation of adjacent contacts (B9–B10) induced a habitual seizure. Interestingly, an additional feature was a marked atonia of the neck muscles that preceded the asymmetric tonic posturing (Supplementary video 1). This atonia may be also present in the patient's habitual seizures, as she described a "heaviness of the head" as part of her habitual semiology. During atonia and sensory aura, discharges were seen in the mesial frontal electrodes (contacts B1 and B2; red asterisk in Fig. 2A) and on the two contiguous contacts on the precentral gyrus on the lateral frontal convexity. These contacts, when stimulated, evoked a combined trunk and left proximal arm movement. Surprisingly, cortical stimulation of the mesial frontal cortex outside the setting of the stimulation induced seizures was not able to reproduce the neck atonia (Fig. 2C).

The patient underwent resection of the seizure onset zone within the SMA (Figs. 1E and F). Pathological examination of the tissue resected showed a focal cortical dysplasia Type IIB, despite normal MRI. Postoperatively, the patient suffered from a minor left upper and lower extremity weakness that resolved within a few days. The patient was seizure-free at 6 months after the operation (ILAE class 1).

3. Discussion

Atonia as an effect of cortical stimulation mapping of the SMA has been reported before, and the responses were observed in the limb muscles and in the tongue [8]. We report a patient in whom atonia of the neck was triggered during an induced seizure by stimulating electrodes on the mesial frontal cortex. The preceding sensory phenomenon of tingling in the neck may indicate SMA activation [7].
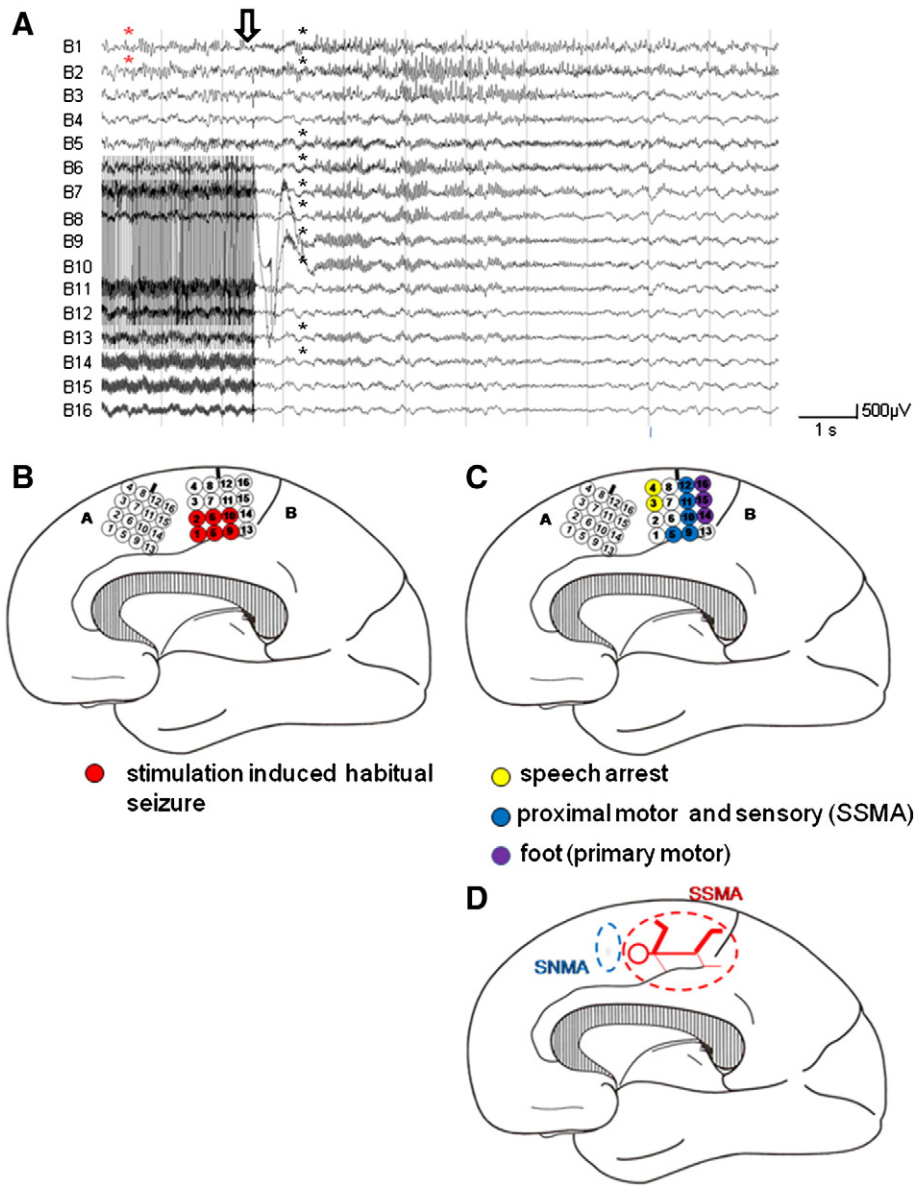
Fig. 2. Cortical stimulation results and stimulation-induced habitual seizures. Electroencephalography recordings during bipolar cortical stimulation of contacts B9 and B10 within the electrode array B that covers the mesial surface (A). The cortical stimulation artifact is seen in adjacent electrodes and is most prominent in the electrodes that are stimulated (B9 and B10). The open arrow indicates the end of the stimulation. Note that afterdischarges (indicated with the red and black asterisks) are seen first in electrodes involved in the seizure onset zone (B1 and B2) with spread to other electrodes (black asterisks) within the electrode array B. Schematic drawing of the electrode stimulations that evoked a habitual seizure (red; B). Panel (C) shows the functional responses that were evoked by cortical stimulation within the electrode array B. (D) Schematic drawing of the somatotopic organization of the SSMA (modified after [8]) and the SMNA representation within the mesial frontal cortex. Note that there is bilateral limb presentation though the contralateral limb is represented on a larger cortical area; SSMA: supplementary sensorimotor area; SNMA: supplementary negative motor area.

It is important to distinguish direct effects of cortical stimulation performed to map eloquent cortex prior to resection in eloquent cortical areas and phenomena observed during stimulation-induced seizures that may be a by-product of cortical stimulation. In the first setting, the cortex underlying the stimulated contacts largely accounts for the clinical sign that is observed during the stimulation procedure. Activation remains relatively restricted to the stimulated electrodes, and clinical activation discontinues after the stimulation current is withdrawn. In the case of stimulation-induced seizures, the clinical signs observed cannot necessarily be attributed to activation of the cortex underlying the electrodes, as there may be spread of ictal activity to distant brain areas that may continue independently of the current applied. Electrographically, this additional activation is represented by afterdischarges (Fig. 2A) which may be seen during cortical stimulation and may occur with or without stimulation-induced seizures [9]. This spread to distant brain areas can be visualized if the area of cortex that is involved by the propagated activity is also covered with recording electrodes. This explains why a stimulation-induced seizure resembles a situation in between a coordinated cortical stimulation and a spontaneous seizure.

To our knowledge, this is the first detailed documentation of focal isolated neck atonia in the setting of a seizure arising from the SMA. A previous study reported two cases of axial atonia with focal seizures. One of their patients showed initial atonia of the neck before atonia of the trunk and presented with a left central seizure pattern [10]. Zhao et al. also reported a case with frontal lobe seizures presenting with facial grimacing and neck atonia [11]. In none of these patients were intracranial recordings available to further elucidate the precise seizure onset zone. Atonic seizures, focal inhibitory seizures, akinetic seizures, epileptic negative myoclonus, and drop attacks are different manifestations of ictal atonia [3]. Luders and Noachtar reported three patients with atonic seizures that manifested as limb atonia. One of their patients underwent intracranial recordings, and the seizure onset zone was mapped to the mesial frontal cortex [2]. They concluded that the ictal semiology in this patient was caused by epileptic activity involving the negative motor area of the SMA (SNMA). Activation of the SNMA may be one mechanism to explain the neck atonia in our patient. However, a previous study showed that activation of the primary sensorimotor area (MI-SI) by a single pulse (0.3 ms duration and 1 Hz) stimulation elicited a silent period in the contralateral hand muscles [12]. This implies that primary sensorimotor area activation may underlie brief negative atonia and challenges the view that negative motor phenomena can only be evoked by activation of the negative motor areas. It is important to note that the cutaneous silent period does not represent an epileptic seizure; however, similar mechanisms might apply to atonic seizures. Further evidence for a pivotal role of the primary sensorimotor areas in atonia comes from a case that presented with seizures manifesting as atonia of the left arm. Intracranial recordings during these episodes revealed discharges in the right precentral gyrus, with sparing of the negative motor areas that were also covered by the intracranial electrodes [13]. During the brief neck atonia seen in our patient, afterdischarges were observed not only in the electrodes overlying the mesial frontal cortex but also in a few contacts overlying the precentral gyrus, implying that primary sensorimotor cortex was activated during atonia. Therefore, an alternative explanation of the neck atonia seen in our

patient might be primary sensorimotor area activation in keeping with the findings of Matsumoto et al. and Ikeda, A et al. [12,13]. This hypothesis is further supported by the fact that atonia was only seen during the cortical stimulation-induced seizure and not by stimulation of the mesial frontal contacts, implying that atonia was not due to mesial frontal/SNMA activation but rather a result of spread to a distant area.

Another important point illustrated here is that in the patient's past, the seizures had been diagnosed as non-epileptic. This is most likely due to the unusual semiology in our patient, with sensory aura, "heaviness of the head" that might represent the neck atonia and bilateral tonic posturing. Compared to the primary motor cortex that extends over the frontal convexity, the SMA is a small cortical area on the mesial surface of the frontal lobe [14]. Stimulation of this area can produce a variety of symptoms including positive and negative motor and sensory symptoms [8]. Non-epileptologists might not be familiar with such signs, and therefore, insight into the semiology of seizures arising from or spreading rapidly into the SMA might prevent these events being misdiagnosed as non-epileptic, as had previously occurred in our patient.

Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.yebeh.2012.05.012.

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