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CASE REPORT

Increase in seizure activity is associated with change to daylight savings time as identified by an implanted thalamic neurostimulator in bilateral thalamic centrum medianum nuclei

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ABSTRACT
This the first known case denoting the association with seizure activity on the morning after a change to daylight savings time in the United States recorded on an implanted neurostimulator (Neuropace Inc., RNS System ®)

Introduction

This is the first report which denotes and discusses the observation from the human brain electrocorticography from an implanted neurostimulator device (RNS System-Neuropace ®) which identified seizure activity after change to daylight savings time in the US in a patient who ultimately was well controlled for six (6) months prior to that event although previously exhibited intractable epilepsy. This case report highlights and speculates how the use of RNS technology may allow for further study of this issue in additional research, scenarios, and observations

Report of Case

A 28-year-old patient with intractable epilepsy had a responsive neurostimulator device (RNS System ®, Neuropace, Inc.) placed bilaterally into the centro-median nuclei due to the presence of a diffusely poorly localized frontal seizure disorder as the patient failed multiple medications, was not a cortical resection candidate, and nor were there 2 or fewer discrete cortical localization targets of seizure onsets identified that would allow practically placement of cortical neurostimulation according to its approved indications. This patient had failed multiple medications and was disabled by seizures that occurred several times weekly and generalized about monthly. The patient's neuroimaging and results of invasive EEG monitoring are noted below, identifying overall non lesional neuroimaging but diffuse but poorly localized seizures over the R>L frontal regions. After RNS implantation and device programming and adjustments with medication changes, the electrocorticogram noted significant reduction in seizure activity over multiple (6) months and ultimately the patient had cessation of clinical seizure activities along with cessation of long episodes (arbitrarily defined as >20 seconds of activity change from baseline), and experienced cessation of channel saturations, see figures. However, the night before the change to daylight savings time in the US, the patient experienced anxiety and that night of the time change, she experienced nonrestorative fragmented sleep, and she and family reported a seizure which involved right thalamic contacts the following morning subsequently to the time change, see the figures below.

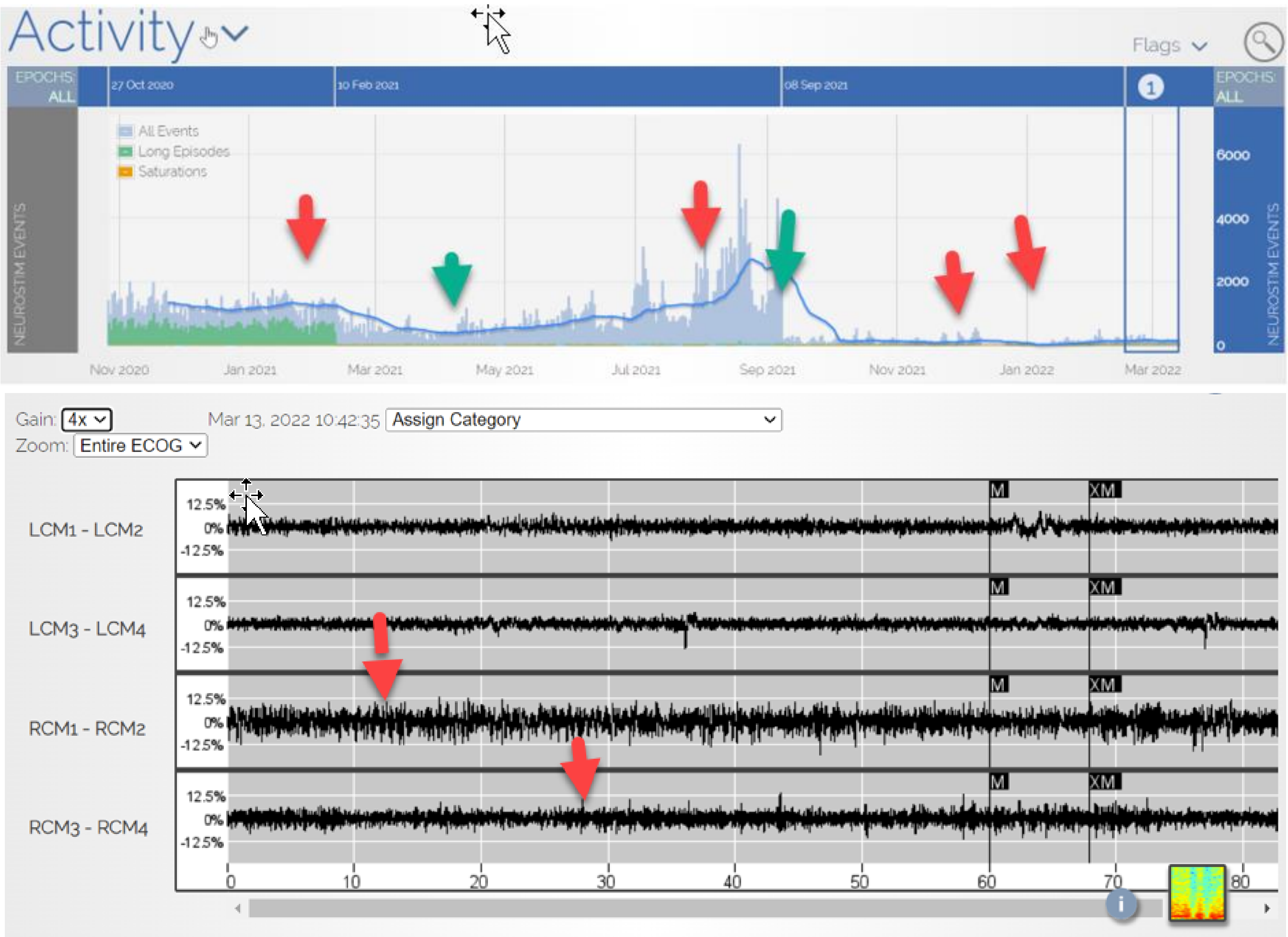
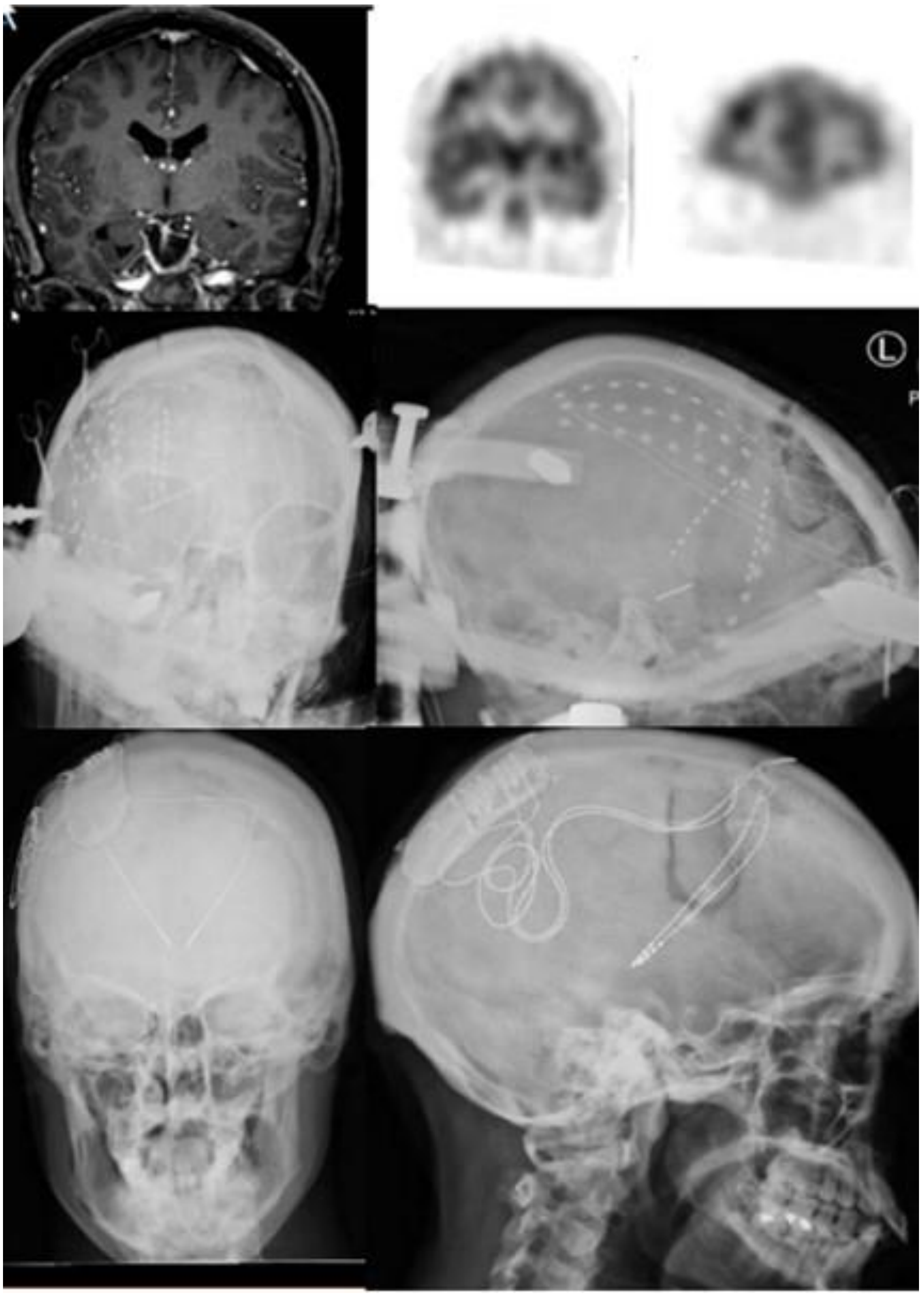


Image- Top: Histogram of Activity log from the patient data management system.
Note significant reduction in ictal and interictal discharges (From November 2020 to September 2021) and channel saturations inventoried on a histogram plot and recorded by the responsive neurostimulator device placed in bilateral thalamic Centro median nuclei over many months despite changes in medications and detection algorithms over time. Such quantitative and qualitative analyses are representative of the current literature on RNS[3-5]. Red arrows note the most recent times when detection algorithms were changed and green arrows denote where seizure medications were changed. Most recent RNS Detection algorithms changed 1/2022, 12/2021, 8/2021, 2/2021. Most recent medication changes were September 2021 and April 2021.
Bottom: Note seizure activity in predominantly the Right Centrum Medianum nuclei contacts(arrows) at the most distal end of the placed contacts of an implanted Neurostimulator device (RCM1 and 2) during the morning after change to daylight savings time and such activity was reported by the patient and her family with clinical correlation.

SELECTED IMAGING



Left top panel: T1 Coronal MRI with contrast delineating no areas of enhancement, although there is some volume loss around the right hippocampal formation which may be mal-rotated, with upper middle and right panels delineating coronal sections of ICTAL SPECT imaging delineating subtle right cortical and midline more than left frontal and sub frontal regions of Tc-99 uptake during a typical seizure. Middle panels delineate the placement of invasive electrodes placed over the cortical surface of the right hemisphere along with a right depth electrode, and ultimately diffuse multifocal right neocortical changes were noted in a broad distribution during seizure onsets. Bottom Panels identify ultimate position of the RNS Neuropace ™ in AP and Lateral views (Xray).

Discussion

There has been debate about potentially deleterious effects of switching to daylight savings time and the consensus statement of the American Academy of Sleep Medicine indicates that the seasonal time changes to and from daylight savings time and standard times exhibit potential deleterious effects on cardiovascular morbidity and other potential health issues potentially due to circadian effects as noted in earlier literature[1,2]. Although this is a solitary case report, this is the first known case of daylight savings time's association with a seizure on the morning after such change in the United States recorded on an implanted neurostimulator in bilateral centromedianum nuclei of the thalami in a case that was actually quite well controlled without any clinical or sub clinical seizure activity for 6 months prior to that event which supports that coincidental or spontaneous seizure was not likely for the observation although such might not be excluded.

Neurostimulation is a modality that may allow for significant future research as it can objectively quantitate seizure activity objectively under various conditions - and this observation indicates that electrocorticography review and quantification of presumed ictal and interictal discharges recorded on such devices may ultimately objectively identify the extent for which seasonal time changes as noted impact patients as in other conditions although confounding variables may bear exclusion as the literature also evolves for other indications, circumstances, and pathologies[3,4,5].

Exactly what brain structures or circuitry might control circadian physiology and relate to time changes or be involved in seizure activity associated with circadian effects in the setting of having an implanted neurostimulator are unknowns, although incremental understanding of neurological mechanisms involving neuronal networks and biology are noted [6,7,8]. The circadian system's importance from an evolutionary perspective in the orchestration of hibernation in animals is noted and how such related circadian biology might be involved in pathological conditions such as Kleine- Levin syndrome involving prolonged or aberrant manifestations of sleep with other concomitant abnormal behavioral disturbances are additional observations that are not yet fully understood [9,10,11] Scientific literature identifies how the effects of light and daylight hours involve the release or central production of melatonin during hours of darkness and involve the pineal gland and light sensing neural fibers from the eye or retina that connect with the pineal gland, but how such mechanisms might directly impact this case report due to changes in total daylight hour exposure remain unknown.[12] Literature that denotes circadian molecular biology within the suprachiasmatic nucleus and the hypothalamic regions has evolved over recent years that involves genetic mechanisms of the various proteins involved producing a centrally acting biological clock that modulates neural connectivity, but how the observation noted in this solitary case report relates to potentially disrupting this physiology remains unknown at this time although relationships among seizure occurrence, sleep disorders, and specifically circadian dysfunction exist. [13,14,15,16] Literature indicates that there is also a relationship among circadian clocks, sleep, and neurodegeneration and recent literature has identified that RNS or Neurostimulation may alter the circadian distribution of both interictal and ictal discharges over time. [17,18]

The specific circumstances and electrocorticogram dataset identified by the electrocorticography in this case report indicate that the patient's seizure was probably associated with the immediately preceding clinical event or circumstances that preceded the seizure as this patient objectively had complete eradication of clinical events along with subclinical discharges including volleys and trains of significant groups of discharges that included long episodes and channel saturations for a significant amount of time- namely 6 months prior to the breakthrough seizure. Although a coincidental seizure is possible, given this dataset, it seems that the seizure was unlikely a spontaneously occurring random event although seizures might however occur coincidentally or spontaneously and may not be completely excluded. Nonetheless, this unique report indicates that such an observation combined with an actual ability to tally quantification of both clinical and subclinical activities on RNS that may relate to time changes or circadian effects even with other confounding variables present may be the subject of further study.

Conclusion

The noted observation of seizure activity which is associated with time changes could yield further quantitative research or investigation which may elucidate what mechanisms or substrates are involved with the occurrence of seizure activity associated with seasonal time changes.

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