Methods to interrupt focal sensorimotor seizures

Self-reports of patients with central lobe epilepsy

Lydia van der Sman

University Medical Centre Utrecht (UMCU), Department of Neurology and Neurosurgery, Utrecht, The Netherlands - 2022

ABSTRACT

Objective: To collect and evaluate self-suppression methods used by patients with seizures arising from the primary sensorimotor cortex, so-called central lobe epilepsy (CLE), to estimate their efficacy in suppressing focal sensory-motor seizures.

Methods: We interviewed 11 patients with well-established CLE from a presurgical cohort. We determined self-suppression methods of the participants by using a VAS-score questionnaire, a semi-structured interview, and video-recordings of the methods. The descriptions were sorted by theme, with focus on sensory stimulation methods.

Results: 9 of the 11 patients could influence their attacks with empirical methods and 6 of the participants did so by applying some form of sensory stimulation early during the seizure.

Conclusion: Patients' accounts testify that peripheral stimulation methods can modulate sensorimotor seizures. These non-invasive stimulation methods are a way for patients to manage their disease when other therapeutic measures such as surgery or medication fail. This may open new therapeutic avenues such as the development of a peripheral sensory stimulation device.

Keywords: Epilepsy, Central Lobe Epilepsy (CLE), Self-suppression methods, Patients' perception of efficacy of sensory stimulation

Introduction:

Patients with central lobe epilepsy (CLE), or Jacksonian epilepsy, suffer from a rare focal form of epilepsy of sensorimotor nature. Clinically, CLE manifests itself as local tonic-clonic activity in a specific part of the body. Seizures easily spread and become uncontrollable and refractory in nature, sometimes with loss of consciousness, and with seizures both during the day and the night. These patients have focal seizures that originate in the precentral and postcentral gyrus, also known as the primary motor and somatosensory cortex (Brodmann areas 1-4), where motor and sensory information is processed [1-2].

The pericentral gyri are known for their somatotopic organization: the motor and sensory homunculus. In the homunculi the sensation and motor function of a specific body part is represented contralaterally. Some parts of the body, such as the fingers and perioral face, encompass larger areas for better sensual and motor acuity [3-6].

The mapping of this area is historically linked to the understanding of CLE. Typical seizures have the clinical feature of spreading in a specific body pattern or '"march" according to these maps [2]. Tonic-clonic seizures in the hand can for example spread to the arm and then to the leg and foot, or from the hand to the face. In fact, it was this marching of the seizure activity up and down the body (Jacksonian March), that allowed John Hughlings Jackson (1835-1911) to hypothesize the existence of a somatotopic organization, which later allowed the conception of the homunculi by Penfield and Boldrey in 1937 [3,6].

This area of the brain is considered unamenable for surgery because it will leave permanent sensorimotor deficits, particularly with relation to planned movement and motor learning [7]. Unfortunately, these patients rarely respond to antiseizure medication (ASM), which makes focal epilepsy in the central lobe a therapeutic challenge [8-9,1]. The effectivity of alternative treatment options such as vagal nerve or deep brain stimulation are unknown in this specific type of epilepsy. Thus, prospects for most patients with central lobe epilepsy have not changed since the reports of this condition by John Hughlings Jackson in 1861.

Although most patients with CLE suffer from lifelong seizures, new therapeutic avenues may lay hidden in ancient treatment methods. It has been observed early on that these patients themselves stop or prevent their attacks by applying sensory stimulation to the part in which the convulsion first manifests itself, often their hand or foot. Clinical evidence on peripheral sensory stimulation for suppression of focal epileptic discharges can be traced back to the ancient Greeks [10]. In the 19th century physicians such as Théodore Herpin (1799-1865), John Hughlings Jackson (1835-1911) and William Gowers (1845 – 1915)

suggested the use of methods such as: 1) the application of a ligature proximal to the convulsion site, 2) forcible prevention of spasm (stretching), 3) other cutaneous stimulation (pinching, rubbing, pricking, squeezing, cold water) and 4) muscular exertion (e.g., quickly walking around the room) [11-14]. Since the rise of ASM in the early twentieth century the issue of (self)suppression has been largely ignored [15], but still this could be a basis for novel therapies which use sensory stimulation of the limb in which seizures begin, to arrest the attack.

Theoretically, peripheral sensory stimulation of the place where the motor seizure starts might inhibit the motor neurons of the epileptogenic site via stimulation of already existing inhibitory pathways [16]. Sensory stimulation as a potential means of suppressing seizures seems to be especially suited for CLE and Jacksonian seizures, because sensory input is directly linked to the corresponding motor output. These two areas are tightly interconnected for fine-tuning of movement. Peripheral sensory input to the primary sensory cortex may provoke inhibition of impulses in the adjacent primary motor cortex.

We wanted to see if such methods are still used by patients with CLE and therefore decided to ask them.

Methods:

We collected information by means of (semi)structured interviews and a VAS questionnaire with patients suffering from central lobe epilepsy (CLE). Due to another study (METC 19-336, an intervention trial in CLE patients) many CLE patients had been sent to the PI over several years for exploration of surgical options [16]. The PI accumulated around 40 patients with well-defined CLE, as established by best clinical practice, confirmed by EEG and MRI. To be eligible to participate in this study, the subject had to meet all the following criteria: age 16 or older, ability to be interviewed, having proper understanding and expression of Dutch language and mental capability. A potential subject who had no access to online communication was excluded from participation in this study. The characteristics of the patients were collected in a baseline table (Table 1).

Gender (M/F)	Age	Medications	Epilepsy characteristics	Onset of epilepsy	Differential diagnosis	MRI	Function limbs
F (pt1)	31	Midazolam, Levetricetam, Folic Acid	Right central epilepsy (high in gyrus post-centralis). Tingling left side of the back, progression to left leg and shoulder, usually around falling asleep or waking up, 2x month	2006	(Neuro-)oncological history 2006: Symptomatic epilepsy (tingling in left back, spreading to left leg and shoulder, usually around falling asleep or waking up. Twice a month) 2013: DNET resection high in the postcentral gyrus R.	Parietal resection cavity right, with in surrounding elevated T2 signal, probably gliosis. Further in depth in the subcortical white matter a small more cystic round lesion.	(1) a central sensory disturbance in the L lower leg following surgery and (2) residual basic sensorimotor seizures in the L postcentral gyrus.
M (pt2)	47	Brivaracetam	Central right epilepsy. Focal-onset sensory seizures with intact perception, symptomatic, with birth defect Right hemisphere. Slight hemipiramidal syndrome Left and hemisensibility disorder Left.	peri/pre-natal	Birth trauma. 2004 Focal-onset sensory seizures with intact sensation, symptomatic in right hemisphere congenital anomaly. Minor hemipiramidal syndrome on the left and hemisensibility disorder on the left.		Minor hemipiramidal syndrome on the left and hemisensibility disorder on the left.
M (pt3)	26	Levetiracetam, Tegretol	Left central epilepsy. Epileptic seizures with cramping Right leg, treatment resistant epilepsy, 2020 REC2STIM implantation.	2001	Drug-resistant focal epilepsy, manifested by focal seizures with intact or reduced sensation and sometimes bilateral tonic-clonic seizures, on MRI with no explanatory abnormality. 1.Focal with intact/impaired sensation: often preceded by cramping of the entire right leg, the attack consists of a scream, spreading of arms and legs and a few seconds of cramping. Duration: 30 seconds. Frequency: almost every night. 2. Focal to bilateral tonic-clonic: A shriek at night, is found with generalized twitching. Duration: 2-3 minutes. Onset SMA left	No abnormalities	No abnormalities
M (pt4)	25	Midazolam, Lamotrigine, Pantoprazole	Left central epilepsy. Treatment-resistant epilepsy with left frontal cortical dysplasia, also Left cerebellar small focal abnormality with minimal staining on the MRI vw DD a pilocytic or low-grade glioma is considered. Since 2005 epilepsy with presentation: feeling Right throat as if he needs to vomit; then motor attacks with cramping and twitching in Right face, with extension to rest of the body, usually intact hearing.	2005	Treatment-resistant epilepsy due to left frontal cortical dysplasia. Also small focal left cerebellar abnormality with minimal enhancement on MRI, with differential diagnosis: pilocytic or low-grade glioma.	Left frontal focal cortical dysplasia at the location of the precentral gyrus. Also left cerebellar lesion.	No abnormalities
M (pt5)	25	Zorisamide, Tegretol, Paracetamol, Midazolam	Right central epilepsy. refractory epilepsy from the motor leg area, demonstrated with grid registration. Is in RE2STIM trial with closed loop cortical stimulation.	2014	Focal epilepsy with a source in the central gyri at the site of the Left leg. focal epilepsy with a source in the central turns at the representation of the Left leg.	Multiple small white matter abnormalities. Furthermore, no abnormalities were found in the brain parenchyma, in particular in the right pre-central no evidence of cortical dysplasia.	No abnormalities
F (pt6)	61	Nitroglycerine, Carbamaepine, Clonazepam, Peridopril, Metoprolol, Acetylslicylzuur, Pantoprazole, Rosuvastatin, Ezetimib, Napafenac, Dorzulamide	Left central epilepsy. Focal structural epiplesia with clonic seizures R in face and hand caused by anti-Hu encephalitis in 2010. Status after radiotherapy and lobectomy left lower lobe by pTaN0M0 high-grade neuroendocrine carcinoma with also small cell component (radically removed in April 2015) Muscle weakness in thigh (undiagnosed); LEMS excluded with EMG; REC2STIM implantation 2020.	2010	Focal structural epilepsy with clonic seizures in right face and hand due to anti-Hu encephalitis due to small cell lung carcinoma.	T2 increased signal intensity in the hippocampal region on the right, pons on the left, periventricular and subcortical.	Muscle weakness in upper legs for which there is no proper diagnosis. But epilepsy is elsewhere.
F (pt7)	53	Midazolam, Tegregol, Omeprazole, Cholecalfirerol, Ciclipirox	Right central epilepsy. Focal epilepsy, manifesting itself in motor seizures with cramping and twitching in the left leg, with varying expansion, usually intact sensation. Is in RE2STIM trial with closed loop cortical stimulation.	.	Focal epilepsy, manifested by motor seizures with left leg spasms and twitches, with variable progression.	No focal abnormalities on the brain parenchyma.	Left leg function is fine between attacks
F (pt8)	33	Carbamazepine, Clobazam, Escitalopram, Calciumcarbonate	Right central epilepsy. Seizures: Left arm with alternating expansion to the upper leg, calf or foot (cramps inwards). More at night than during the day. Starts with heaviness in limbs. This feeling can last for days. There are sometimes clusters.	2003	DD juvenile myoclonus epilepsy or focal epilepsy with focus in lower leg/foot representation on motor cortex Right. Generalized ton.cl. attacks and jerks especially in the morning but always in Left leg.	No abnormalities on MRI.	No abnormalities
F (pt9)	41	Lacosamide, Lamotrigine, Midazolam	Right central epilepsy for which grid implantation in 2020; is in REC2STIM study with pacemaker and intercranial strips for sensing/stimulation. Seizures: Right central focal epilepsy, tingling Left hand, then cramping, pulls up to arm, trunk and sometimes Left facial side. Apart from seizures: decreased coordination Left hand; speech over years with more stuttering/slurping; sometimes word-finding disorders.	2006	Focal epilepsy from the central gyri with a source in the Right hand area and Jacksonian seizures in the Left arm and hand	In the right thalamus a T2/FLAIR hyperintense lesion.	Complaints of the Left hand when tired and then have slightly less 'feeling' in the Left hand: for example, not feeling a cup in their hand properly and shaking.

Gender (M/F)	Age	Medications	Epilepsy characteristics	Onset of epilepsy	Differential diagnosis	MRI	Function limbs
M (pt10)	34	Pregabaline, Pantoprazole, Fenytoine, Oxcarbazepine, Paroxetine, Midazolam, Clobazam	Left central epilepsy. Current seizures in right hand/arm, Left central windings, is in REC2STIM trial in which closed-loop cortical stimulation is applied in case of seizures.	1988	Focal cortical displasia.	Left frontal and subinsular white matter abnormalities.	Less strength/motor skills in right arm.
M (pt11)	56	Levetiracetam, Lacosamide	Left central epilepsy. Seizures: start in right upper arm (right hand clawed and goes above the shoulder, elbow in flexion), possible extension to leg in more severe attacks. Subconscious; with no possibility to talk.	1998	Seizures: feeling in the head, then 'speech paralysis' ('I couldn't think of words when I wanted to say') and movement of Right arm. After his meningioma operation in 1999, he only had seizures with 'hiccups' in the head followed by movement Right arm, or only 'hiccups' in the head that did not progress to anything motor. The Right arm wants to move backwards and upwards; the head remains upright; he feels that his face is cramped. Thigh does not participate according to itself, but his partner says that the Right leg tends to stretch. No feeling in the throat. No rhythmic clones. 'Hiccup' is a feeling he can't describe. It is not visible externally. Frequency is 1-8x daily. Duration <30 s, usually 5-10 s. He is back to normal within 2 s of a seizure; no residual symptoms. Attacks are provoked by exertion, e.g. cycling. No attacks at night or in the morning. Medication has an influence: makes attacks 'smaller', e.g. leg participates less.	Unchanged postoperative image of resection of the Left frontal area with surrounding gliosis. No evidence of recurrent meningioma. (Resectional cavity Left, high frontally in front of the precentral gyrus.)	The function of the hand is good, but his handwriting has changed. No complaints from the Right arm apart from seizures. In the past sore feeling side Right upper arm. After surgery 1999 change in handwriting: more cock's feet. Had to put new signature at bank for identification.

Table 1 Baseline table.

This specific group of patients was preferentially referred to the principal investigator (PI) and gave informed consent to participate in the study, before being approached via telephone and email. We asked patients to consent to an online interview that included a semi-structured interview and a VAS questionnaire. Of the 40 patients, 11 patients consented to the study. Since there is no statistical element in the study, sample size calculation was not performed. A collection of 11 patients with CLE is already considerable in the literature. The VAS questionnaire was sent before the interview to the participants and consisted of 13 questions about the nature and perceived control of the seizures (Appendix A). To best assess the experience of patients a rating scale was used, The Symptomatology and Perceived Free Will Rating Scale (SAPF) [17]. This type of questionnaire was originally developed to explore the perception of free will in movement disorders, but we modified it to capture both the perception of the nature of the attacks and the measure of control patients with CLE experience over motor seizures. Answers to all questions were given on a Visual Analogue Scale (VAS scale), ranging from 0 (never) to 100 (always).

After completion of the questionnaire an interview was conducted to elucidate the answers and provide further information. See Appendix B, for the individual questions.

The interview consisted of two parts. In the first part, we asked questions on the symptomatology and nature of their attacks. In the second part of the interview, questions addressed whether patients could suppress their seizures and how they would do this. The questions we used were based on a literature study and patients reports, in which it became apparent that it is especially important to understand in detail the nature of the attacks to understand the suppression methods and their efficacy.

The interview was conducted in a semi-standardized way. The interviews were conducted online through WebEx (Cisco) within the UMC Utrecht environment, using VPN, a secure server connection. The choice of a semi-structured questionnaire as a format for the interviews accounted for the fact that many methods used by patients are instinctive. The use of a structured questionnaire would not have been as effective, for many patients need the space and freedom to think though their actions and reconstruct their self-suppression behaviors. To gain even more insight into the exact methods patients used, we also recorded demonstrations of their self-suppression methods. We thus made video recordings of the interview; the video was stored on a research server. During the recording, patients were asked, if applicable, to show how they try to stop a seizure, by showing what manipulation they use. The interview was then transcribed word by word and this document was added to the patient's electronic clinical file as well as the recording of the method. We subsequently sorted the intervention descriptions by theme.

The research data thus consisted of the transcribed interview, the short demonstration video, some general patient characteristics, and the VAS questionnaire.

Results:

The results of my research fall into two main categories, namely the SAPF scores and the semi-structured interviews.

SAPF-scores

Of the 11 patients 9 patients submitted a fully completed SAPF questionnaire. Two patients felt uncomfortable submitting the form, but were willing to participate in the semi-structured interview.

The results of the SAPF questionnaire in which we used a visual analogue scale showed the following results when the mean and median value were calculated per question (Figure 1).

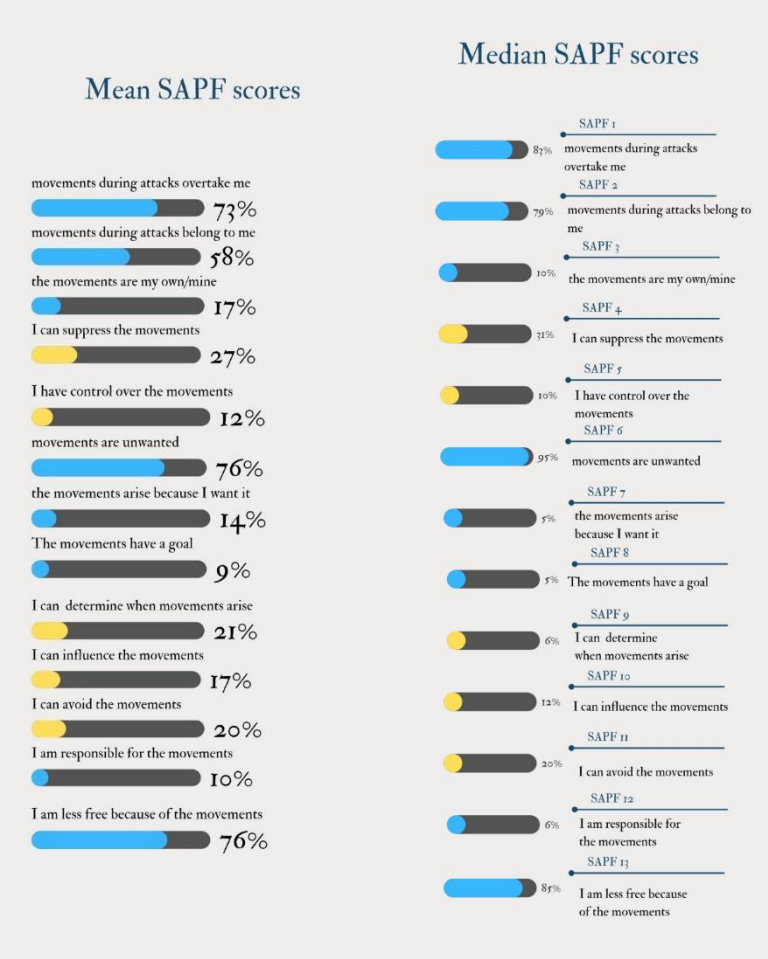

Figure 1 Mean and Median values SAPF-scores

The SAPF scores regarding the nature of the attacks (question 1,2,3,5,6,7,8,12,13) show that most patients feel no agency over motor seizures: the seizures overtake them, the movements are not felt as their own and are unwanted. Also, patients feel less free because of the seizures and feel a lack of control. Many of these questions are complementary to each other. There was one question patients had difficulty interpreting, viz. question 2 was either interpreted as movements are part of my disease or movements are of my own volition; this ambiguity produced mixed answers ranging from very negative, to very positive.

The SAPF scores regarding the perception of measures of control (question 4,5,9,10,11) show that the measure of control is certainly not to be neglected. Patients declared having a considerable degree of control when it comes to the ability to suppress the movements, determine when they arise and influence them or avoid them. It should be stressed that there are three patients who cannot do this at all (as confirmed by the semi-structured interviews, on which

more below), whereas other patients score much higher than 26%, more around 80%. There is variability in the answers, which we took into consideration by calculating the median score next to the mean score. As a result, there is a clear difference in scores between patients that can (group A) and cannot suppress (group B) their attacks (in question 4,10,11) (Figure 2).

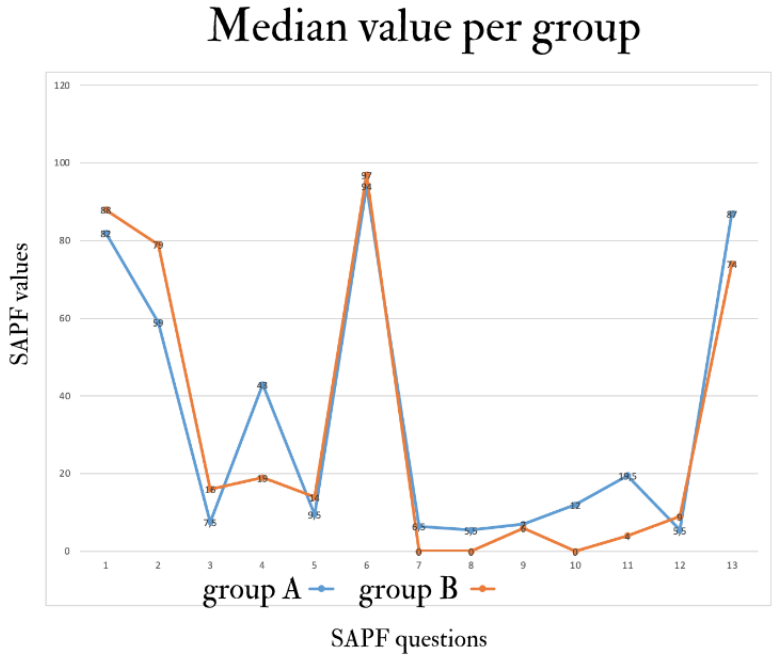

Figure 2 Median values per group.

Semi-structured interviews

The semi-structured interviews allow more specific insight into the symptomatology and the suppression methods of each patient (Appendix C-D). The questionnaire covers a wide range of aspects. The questions were largely based on my own literature study, in particular 19th and 20th-century patients' reports, in which it turned out especially important to describe the attacks in detail to understand the suppression methods and their efficacy [11-14]. For example, it is important to know if the patient experiences auras before an attack as a premonitory symptom or whether the patient has more seizures during the day or at night. In the second part of the interview, I asked whether patients could suppress their seizures and what they would exactly do. Patients who applied any type of suppression method were asked to demonstrate this before a camera, so that a video recording could be made for further clarification.

Among the 11 patients we encountered a considerable variety in the location of the onset of the attacks and their spreading, as visualized in the image below (Figure 3):

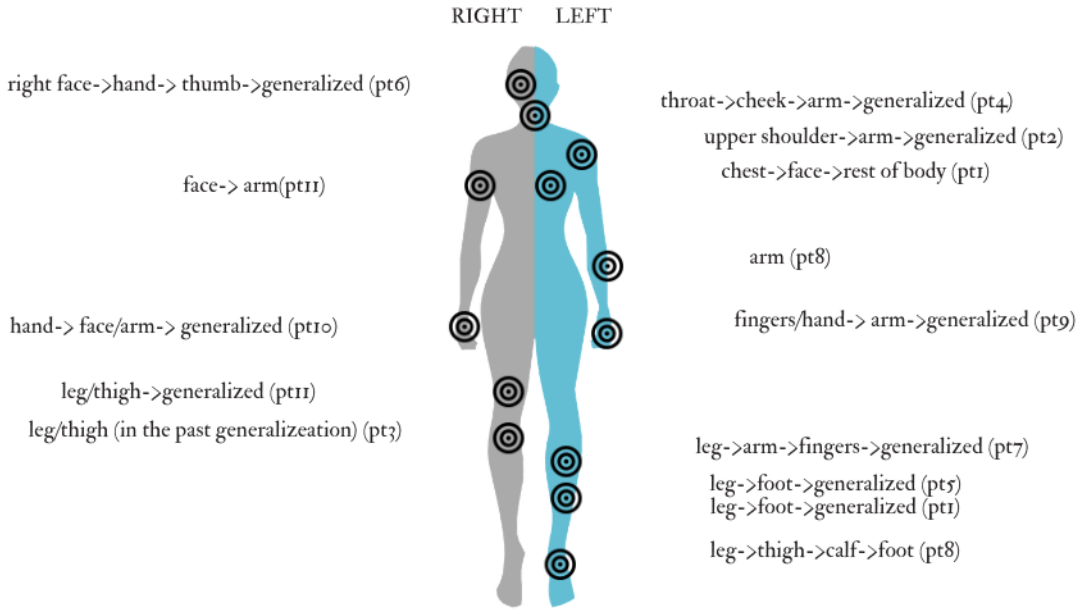

Figure 3 Localization of seizure onset and spread per patient.

In general, we found that approximately 60% of patients could sometimes stop attacks by either engaging in stimulation (4 out of 11), avoiding stimulation (2 out of 11) or with breathing techniques/meditation (2 out of 11). These patients could avoid their seizures spreading before becoming generalized and losing consciousness. This is especially important for patients with focal seizures, because it is the generalized tonic-clonic seizures that constitute the biggest risk and disease burden.

Based on a close (thematic) analysis of the interviews, I distinguished four major themes.

Firstly, I found a dichotomy between engaging and consciously avoiding stimulation. On the one hand, most patients engaged in stimulation such as stretching, squeezing, massaging, pressure, staying in motion with the hand for example. On the other hand, we saw that some patients choose to avoid any stimulation on the limb to avoid further triggering. It is striking that both methods can occur in the same patient. In patient 1 for example, the patient has attacks starting in either the upper or lower body. One type of attack commences in the chest, goes to the face, and then can become generalized. The other starts in the leg, goes to the foot and may generalize. The patient uses for each sort of attack a different method. For the first type of seizure, the patient stops talking

and avoids using the face. For the second, the patient engages in stimulation by moving the foot. The efficacy of the methods is different. When the patient is asked about her abatement methods, she says:

"I think that in 50% of the cases not talking prevents it (an attack commencing in the chest) from getting worse. And that foot, by continuing to move it, you really prevent a worse jerking or the attack in most cases. (…) I think it prevents it from becoming a big attack (a generalized one). I dare say it really prevents a big attack from happening 95% of the time".

Secondly, patients usually distinguish two types of focal seizures: smaller ones and bigger ones. The difference between minor and major focal attacks lies in timing, progression, and intensity. The larger attacks cover a bigger surface area, are described as faster and more intense. The minor attacks occur in a smaller area of the body and are often more manageable though abatement methods, slower, and less pronounced. Even though it is a smaller attack, a small attack might turn into a generalized seizure with loss of consciousness. This is crucial in understanding the distinction many patients make in efficacy of suppression methods. 60% of patients feel that the progression of a small attack into a generalized seizure can be prevented. Although the prevention of generalization of the attack isn't described by all patients, all patients with successful abatement methods describe a delay or weakening of the attack.

Thirdly, many patients experience warning signs of an attack that are of sensory or motor nature, such as a heavy feeling in the limb, numbness, tension or little muscle twitches. These signs can either be right before the attack or much earlier and of longer nature. The warning signs are mostly followed by attacks, but patients also describe instances where this is not the case, and the 'epileptic feeling' is not manifested. Patients report that the feeling has to "come out" or discharge before it goes away. One patient describes how he sometimes provokes an attack to get rid of the uncomfortable feeling; others say that after many consecutive attacks the feeling lessens and subsides. Patients who perceive warning signs are more likely to have influence on their attacks, especially if such signs are of longer duration than just a couple of seconds. The arrest or weakening of a seizure through sensory stimulation seems to heavily rely on the timeliness of the patient in applying the countermeasure. There appears to be a relationship between the timing of the spreading pattern and the possibly to intervene.

Finally, according to the patients, countermeasures only work during seizure onset and in the early stages of seizure activity. Once the seizure has progressed, stopping the seizure becomes impossible and unhelpful. Patients who have both

seizures during night and day describe this phenomenon by comparing their perceived difference in seizure control between night and day. While sensory stimulation may be successfully applied during the day at the commencement of the attack or during the warning signs, at night they wake up in the middle of the seizure and are incapable of exerting any control over the progression. Major control is only exerted during wakefulness.

Discussion:

There have been few systematic studies so far on the methods of self-suppression apart from isolated case reports. In this study, that comprised 11 patients with CLE, we combined SAPF-questionnaires and semi-structured interviews as research tools to complement each other.

The complementarity requires some explanation here. At the level of the individual patient the SAPF-scores and the interview largely correspond. The patients who scored relatively high in the SAPF scores regarding the measure of control (in particular questions 4,10,11), also describe having successful inhibitory strategies. As a trend, the SAPF-questionnaire paints a less positive picture than the interviews. This is because the patients, who were asked to fill in the SAPF-scores *before* the interview, were understandably cautious in their answers regarding self-control. Without further contextualization, they seemed to avoid being too optimistic towards us as caregivers. The interactive nature of the semi-structured interview permitted them instead to weigh their answers and explain their strategies, allowing them to be overall more positive. By offering the patient the space and freedom to think though their actions and reconstruct their self-suppression behaviors, we avoided the possibility of suggestion or putting words in their mouths. Furthermore, the making of video recordings added a concrete empirical dimension to the answers on their methods of suppression and avoided misinterpretation. For further research it is worth considering combining such video-recordings with corticographic registrations during the application of suppression methods.

The choice to use a narrative and descriptive means to understand the nature of the suppression methods was necessary to highlight the importance and existence of abatement methods within our population. Understanding the patients' needs, wishes and experiences is the first step towards the development of new therapeutic avenues. The relevance of these methods for the patients had to be clarified. All detailed information on these methods constituted essential means to understand which bedside-to-bench parameters were important.

One of the steps towards the use of abatement methods for future applications is quantitative. The methods should be quantified and solidified by corticographic evidence of seizure suppression and modulation. The measurement of seizure onset and suppression could provide a quantifiable means of measuring neuromodulation and a means to validate or falsify the perception of control. Although the interviews and the video recordings enabled us to somewhat quantify the methods the patients used, for example by asking patients about intensity of stimulation and measure of pressure used and its efficacy, other methods to quantify and measure the degree of stimulation and of resulting suppression should be considered. To rule out any misperception or distortion of agency measurement of modulation is required [17]. This also would also enable us to quantify the factors that predict the efficacy of the abatement methods.

From the data we collected it becomes clear that the efficacy of the abatement method relies on factors such as wakefulness, proper timing and intensity of the attack. Any method CLE-patients put into practice needs to be applied at the beginning of the fits and is useless once the attack has progressed. Patients need to be conscious and awake to be able to intervene. Smaller attacks seem to be easier to stop or suppress than large attacks. These findings may help to establish both the strengths and the limitations of the application of methods of self-suppression in general, and sensory stimulation in particular. For patients that successfully engage in stimulation we should explore the development of a device with the following characteristics: immediate application of stimuli on the limb onset location at the commencement of a fit, either when the patient has premonitory symptoms or at the very early stages of the attack before spreading. In an automated closed-loop scenario the device should be able to detect the commencement of a fit and apply stimulation accordingly. This detection part could imply chronic EEG recordings or heart rate, skin conduction or EMG sensors when autonomic changes accompany the aura phase [18]. This would also enable methodic application during the night as well as during the day.

These findings are in line with the latest insights into mechanisms of neuromodulation. Epilepsy is a network disease [19]. Within these networks one part of the brain can influence another. In this case the motor cortex is in a network with the somatosensory cortex and stimulation of the sensory cortex can suppress signals in the motor cortex. So, by peripheral sensory stimulation you can theoretically modulate epileptic activity in the motor cortex [20-21].

Perhaps the most important finding of our research is that patients with CLE have a very high disease burden and that the self-management of epileptic fits already constitutes a valuable resource in reducing the morbidity of the illness. The quality of life and the patient's agency can be increased by giving more control over

their seizures. There may be a neurophysiological substrate for such countermeasures, and the answer to finding new therapeutic possibilities still lays with the patients themselves. Systematically gathering firsthand information on these methods from the patients themselves is valuable and we recommend asking patients in the clinical setting not only about their triggers but also about their abatement strategies. One needs to characterize all processes related to the disease in the greatest detail through direct observation in order to be able to develop novel hypotheses and therapeutic strategies.

Conclusion:

The SAPF questionnaires and interviews testify that most patients with central lobe epilepsy have developed various forms of self-suppression strategies, particularly sensory stimulation methods. These methods are used to suppress or stop the seizures at the beginning of the attack at the place of onset. Thus, self-management strategies constitute a valuable asset to lower the morbidity of the disease and decrease perceived disease severity. We therefore advocate the further investigation and gathering of information on these phenomena on a larger scale with the prospect of developing new therapeutic avenues.

References

1. van Offen M, van Rijen PC, Leijten FS. Central lobe epilepsy surgery - (functional) results and how to evaluate them. Epilepsy Res [Internet]. 2017 Feb 1;130:37–46. Available from: https://pubmed.ncbi.nlm.nih.gov/28126646/
2. Jacksonian seizures | MedLink Neurology [Internet]. Available from: https://www.medlink.com/articles/jacksonian-seizures
3. Berkowitz A. You Can Observe a Lot by Watching: Hughlings Jackson's Underappreciated and Prescient Ideas about Brain Control of Movement. Neuroscientist [Internet]. 2018 Oct 1;24(5):448–55. Available from: https://pubmed.ncbi.nlm.nih.gov/29900803/
4. De Klerk CCJM, Johnson MH, Southgate V. An EEG study on the somatotopic organisation of sensorimotor cortex activation during action execution and observation in infancy. Dev Cogn Neurosci. 2015 Oct 1;15:1–10.
5. Schellekens W, Petridou N, Ramsey NF. Detailed somatotopy in primary motor and somatosensory cortex revealed by Gaussian population receptive fields. Neuroimage. 2018 Oct 1;179:337–47.

6. Penfield W, Boldrey E. Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. Brain. 1937 Dec;60(4):389–443.
7. Shorvon, S. Handbook Of Epilepsy Treatment. Oxford:Blackwell science;2000:1–15, 195–225.
8. Fisher RS, Acevedo C, Arzimanoglou A, *et al.* ILAE International league against epilepsy: a practical clinical definition of epilepsy. Epilepsia. 2014 Apr;55(4):475-82.
9. Heck CN, King-Stephens D, Massey AD *et al.* Two-year seizure reduction in adults with medically intractable partial onset epilepsy treated with responsive neurostimulation: final results of the RNS System Pivotal trial. Epilepsia,. 2014 Mar;55(3):432-41.
10. Temkin, O. The falling sickness: A history of epilepsy from the Greeks to the beginnings of modern neurology. Baltimore: Johns Hopkins Press;1945.
11. Herpin T. Du pronostic et du traitement curatif de l'épilepsie. Paris:Baillière;1852:74-5
12. Herpin T. Des Accès incomplets D'Épilepsie, Paris:Baillière;1867.
13. Hughlings Jackson J. National Hospital for the Epileptic and Paralysed. Case of convulsive attacks arrested by stopping the Aura. Lancet. 1868 May 10;91 (2333):618–9
14. Gowers RW. Epilepsy and other chronic convulsive disease: their causes, symptoms & treatment. New York: William Wood & Company;1885:236-7
15. Wolf P. Epileptic seizures and syndromes with some of their theoretical implications (= Current problems in epilepsy). London:Libbey;1994:668.
16. REC2Stim as a Treatment for Refractory Epilepsy in the Primary Sensorimotor Cortex. - Full Text View - ClinicalTrials.gov [Internet]. Available from: https://clinicaltrials.gov/ct2/show/NCT04158531
17. van Oudheusden, LJB, Draisma, S, van der Salm, S *et al.* Perceptions of free will in obsessive-compulsive disorder: a quantitative analysis. *BMC Psychiatry* 18,400 (2018). https://doi.org/10.1186/s12888-018-1985-3
18. Leijten, FSS, on behalf of the Dutch TeleEpilepsy Consortium. Multimodal seizure detection: A review. Epilepsia. 2018; 59(S1):42– 7. https://doi.org/10.1111/epi.14047)
19. Kramer MA, Cash SS. Epilepsy as a disorder of cortical network organization. Neuroscientist [Internet]. 2012 Aug;18(4):360–72. Available from: https://pubmed.ncbi.nlm.nih.gov/22235060/
20. Sisterson ND, Kokkinos V. Neuromodulation of Epilepsy Networks. Neurosurg Clin N Am. 2020 Jul;31(3):459-70. doi: 10.1016/j.nec.2020.03.009

21. Ryvlin P, Rheims S, Hirsch LJ, Sokolov A, Jehi L. Neuromodulation in epilepsy: state-of-the-art approved therapies. Lancet Neurol. 2021 Dec;20(12):1038-147. doi: 10.1016/S1474-4422(21)00300-8. Epub 2021 Oct 25.

Appendix:

Appendix A: SAPF score questionnaire.

Appendix B: Script for (semi-)structured interview.

Introduction:

Introduction, purpose of interview, approach, anonymity, duration, explanation.

Questions:

1. Can you describe your attacks? (how long, how often, when, course)
2. Do you have attacks at night, during the day, or both? Is there a difference between them?
3. Are attacks triggered by something? (movement, pressure, being startled etc.)
4. Do you have warning signs before the attacks? (description)
5. Do these warning signs immediately precede the attacks or do they also appear a few minutes to hours before the attack begins?
6. Have you had warning signs that were not followed by attacks?
7. Can you suppress your attacks intentionally? (estimation of percentage or categorically: never; occasionally; rarely; often)

If the answer to question 7 is positive:

8. Did you discover this yourself or was it pointed out to you by someone (such as your physician)?
9. How do you suppress the attacks? Do you do this yourself or with the help of someone else?
10. Can you describe the exact nature of your action(s)? What do you do exactly?
    for example: rubbing, friction, massaging; localization, timing, and frequency (on which part of the body, how long, one or more times)
11. If this intervention helps, what does this achieve? do these methods prevent or weaken the attack? And for how long?
12. When do you think your actions are most effective?
13. Can you describe what exactly the effect is of these methods?
14. Can you predict when they will be successful?
15. Does it also happen that the application of the method has a counterproductive effect? (for example: the attack ultimately gets worse than usual)
16. Are there circumstances or factors that negatively or positively influence the degree of success? (for example, fatigue, stress, use of alcohol, etc.)

17. Are there other things that have not been mentioned that you think are important to mention?
18. Do you have any questions for me?

If the answer to question 7 is negative:

8. If the answer is no, have you ever tried it? Has anyone ever advised you to try it?
9. Have you had negative experiences with trying to suppress your own attacks?
10. Do you have any questions for me?

Appendix C: Symptomatology.

	pt 1	pt 2	pt 3	pt 4	pt 5	pt 6
WHERE do they start?	(1) LEFT CHEST with progression to face or lower rest of the body (2) LEFT LEG/FOOT	*LEFT UPPER SCHOULDER*	RIGHT LEG/ THIGH	THROAT	LEFT LEG/FOOT; generalized at night	RIGHT FACE; HAND/THUMB
WHERE do they end?	(1) to the FACE or GENERALIZED (2) stays in LEG or GENERALIZED	goes down via ARM to the rest of the body GENERALIZED	In the past GENERALIZED	CHEEK->ARM-> GENERALIZED	RIGHT LEG OR ARM (never generalizes); THROAT=CHOCKING and GENERALIZED	GENERALIZED or local
HOW OFTEN do they occur?	1:3 generalized; 1 per week of smaller nature	Once a month (clusters); with meds once every 2-3 months	Around twice a day (6 in 3 days)	It changes: sometimes every month; sometimes 3 times a year.	(1) smaller ones: 5-10 times a day (2) big ones: 1 every 3 weeks	
WHEN? (nigth/ day/ both)	BOTH	DAY	BOTH (worse attacks at night)	BOTH	BOTH (worse attacks at night)	BOTH (worse attacks at night)
HOW LONG?	SMALLER ONES 1/2MIN (1)			10-20 sec and 3-5 min RECOVERY	10 sec (Right LEG)	5 min total
PROGRESSION	During seizures in bed, she lies still when she talks or moves, it shoots through to "the brain" (1); when she is lying down at the beautician, an attack occurs in the legs (2); when she does sports she gets a cramp in the leg (3)	Within a second or 60 in the whole body			Between sleep and wake in clusters onset 1-2, awake 3, alternating during the day	Also separate face or hand and thumb
CLUSTERS	NO	YES	YES		YES	
TRIGGERS	YES	YES	YES	YES	YES	YES
TRIGGERD BY	Formerly: touch navel on the left; Now: "rest"/not moving during the day (car or beautician (2)), fatigue, not taking the medication, movements (talking or moving; during a large attack in bed it marches to the place where the movement takes place (2)	Tension /fear, e.g. Efteling	Fatigue. stress. no medication. insomnia	Fever, stress, long illness	All activities on foot (running, rowing)	Writing
AURAS/ PRODROMES	YES	YES	YES	YES	YES	NO
HOW FAR AHEAD	HALF AN HOUR, HOURS (2)	RIGHT BEFORE	A COUPLE OF SECONDS BEFORE	A COUPLE OF SECONDS BEFORE	5MIN OR HOURS	
What is the AURA like?	Difficulty falling asleep, numb feeling back, not lying down well (major attacks) (2) ; small attacks (heavy leg) (1&2)	Tingling and getting busier in the head	Tingling, cramping, heaviness upper leg	Feeling like vomiting, right cheek	Tension in the leg/feeling of sleep/stress in the leg	
Are these auras always followed by attacks?	NO, but a spasm yes	Not sure, it is a notification that it will happen that day	No, sometimes I have it and then nothing happens at all	No, sometimes they do not continue, (stays with throat)	Yes, "it has to come out eventually"	
If yes, how often?	Once a week			The last period (2 wks) every day		

	pt 7	pt 8	pt 9	pt 10	pt 11
WHERE do they start?	LEFT LEG with progression to left arm (fingers)-> generalization	LEFT ARM/LEFT LEG (thigh, calf, foot)	LEFT FINGERS /HAND with progression arm and possible generalization	RIGHT HAND with progression to face and arm	RIGHT FACE/ ARM (when the attacks are generalized/more intense in the:) THIGH.
WHERE do they end?	GENERALIZED or local in leg	In the LEFT ARM	FACE or GENERALIZED	GENERALIZED or local	Bigger attacks in LEG and then GENERALIZED; the smaller ones local to ARM/FACE.
HOW OFTEN do they occur?	2-3-6 a day (in the past 1xmonth)	during the day: 1-2 x 2 weeks; at night: 1x week/1x 2 weeks		every night on bad periods; smaller ones: 1x week	3x week, some periods daily and other periods onces every 5-6 days.
WHEN? (nigth/ day/ both)		BOTH (worse attacks at night?)	BOTH	BOTH (worse attacks at night)	DAY
HOW LONG?		Sometimes 1-2 sec, sometimes clusters 1/2h	Clusters 1/2h		
PROGRESSION			Not sure	Choking during "generalized" attack (unimpaired vision)	Two ways: either to speech, or to arm (sometimes also leg and then generalized). The progression to the leg came later. The two modalities are mutually exclusive.
CLUSTERS	YES	YES	YES	YES	
TRIGGERS	YES	YES	YES	YES	YES
TRIGGERD BY	Menstruation/ hormones earlier; intestinal flora/fear of seizures	Stress, bump on leg or fright, sleep deprivation, around ovulation	Pressure, have a lot going on, a lot of stimuli; sitting quietly on the couch or in the car.	Stress and anxiety or thinking a lot about epilepsy	Poor sleep, at 8-9 kilometers cycling (within half an hour. It's flawless!) and talking about epilepsy
AURAS/ PRODROMES	NO	YES	YES	YES	YES
HOW FAR AHEAD		SOMETIMES HOURS	SOMETIMES DAYS	5 MIN BEFORE	AROUND 4 H
What is the AURA like?		Heaviness or warm feeling pubic area	Restlessness in arm or leg, jerks in hand	Persevering shocks in hands	3 varieties: (1)epileptic feeling: that you feel a bit insecure, an undercurrent. (2) before the operation: a kind of cramp/ as if that stock exchange were. (3) sensitive skin, especially in face and scar of tumor surgery
Are these auras always followed by attacks?			No, sometimes they aren't	No, not always	No, but certainly a big chance
If yes, how often?					

Appendix D: Suppression methods of each patient.

	Suppression Method(s)	What helps and what does this achieve?	Is it self-taught or not?	Circumastances that influence the effectiveness of the method.
pt1	Not moving the head, not talking / moving of the feet (at beautician)/ stretching of the muscle.	I think that in 50% of the cases not talking prevents it from getting worse, I dare say, in 50% of the cases it still shoots through, so you can also say it. And that foot, by continuing to move it, you really prevent a worse shock or perhaps an attack, in most the cases. Ik does not weaken, procrastinate the attack, I always get a jerk at the beautician, but it is not a big attack, it is just a kind of jerk/jolt. I think it prevents it from becoming a very big attack. I think you prevent that in 90 percent of the cases, because I had a couple of big attack there before I did this, well maybe it's in 95% of the cases that you really prevent a big attack.	Self-taught	During sleep you cannot prevent those attacks, they come anyway.
pt2	Staying calm. Staying in the moment.	You postpone it. You occasionally feel such an attack coming, half an hour or so. If the feeling stays you try to postpone it. How long do I manage to postpone it? I don't know, I sometimes managed to postpone it for half a day, but yes then I got the blow later.	Self-taught	
pt3	Squeezing hands/fists; Putting the jaws together; Focussing elsewhere.	It helps if I have a cramp to squeeze the hands and put my jaws together. "Then it is just gone". I just focus on the squeezing, not the attack. I squeeze as hard as I can. I only do it sometimes, because he wasn't sure if it was helping or maybe it was something I made up. I do it 6-7 times out of 10. Don't know if it's always successful, but I get the feeling it prevents some attacks.	Self-taught	
pt4	IT DOESN'T WORK: Contracting the muscles; Holding your breath.			
pt5	Squeezing feet together; continuously moving the feet "restless leg".	I can suppress the attacks to a certain extent. I think I do it partly subconsciously and partly consciously. So suppose there is a place where I really do not want to fall, the station, the supermarket, etc. Then I squeeze my foot together so I don't have it. Also, for example, on the bike I squeeze my feet together to prevent an attack. I might have tension in my limbs for so long (premonitory sign), but I still have to cycle, (often I choose to walk, but occasionally I take the bike) and then I squeeze my feet together. Now to the unconcious part. When I sit, and that is the unconscious part, I am constantly moving. I'm constantly moving my foot. I'm constantly tapping. I practically always do it (use the method), or well, almost always unless I'm in a nice/safe place. Very often I also want to have the attack, because after my attack I kind of have my complete freedom to do what I want. How successful am I at this? I think I would just get a passing grade, very often it still comes. To a certain extent, that tension still comes through. I think the longer I keep suppressing the more intense it becomes. It's a reprieve. How long I can put an aatck off varies day by day.	Self-taught	My cramps are always worse when I'm stressed, for example. If I have stress, if I have too little sleep, then the cramps and seizures are worse and also less success to do this. It is also very difficult to say when it will work and when it will not.
pt6	I CAN'T DO IT ; resting/ stoping with writing (for thumb/hand).			
pt7	Breathing techniques.	During the day when I'm sitting in the chair and my leg starts to jerk and I feel it coming, I can suppress it a bit with a certain breathing technique that I learned in the past. I sit upright you put a hand on my stomach under my diaphragm and feel my own breathing. If I feel that, then I have the focus on that and then the brain does not get the chance to disregulated because then your brain will focus on breathing. And that works for me. I can sometimes suppress seizures. Because then I am somewhere where it is not convenient to get a seiure, for example in the store or for example in the church, ; when the children were small, I would have had a number of moments when you would rather not take the chance, because that is just very annoying. I think it weakened it. Lately I've been using it to put the attack oof for a while. Maybe 10 min or so, not and half a day, that would be handy! I wish! It is more difficult at the moment to do, so I don't always use it anymore. I only do it 2 out of 10 times, that's not often at all. Of the 10 times I do it, it doesn't work 4 of the 10 times.	A neurologist suggested it to me, when I was a teenager, I spent half a year with some kind of physiotherapist, learning breathing techniques to suppress it. It helped me a lot at the time. And I've actually kept that trick with me all my life.	
pt8	Stretching of the limbs. Clamping themselves between two couches; Stretching the leg with other foot (while laying down); Asking a person to sit on the limb	I fixate the legs between two caouches at home. In bed I might ask my man to sit on the leg, stretch the foot/leg. At work I ask collegues to sit on my lap.	Self-taught	
pt9	Stretching and massaging of the hand; Stretching the wrist and fingers; Sitting on the hand (stretching and pressure).	What does it do? "If it's a small attack, I'll makes it calmer. With a violent attack it weakens it a bit; With the small attack I have the idea that it stops it. With the smaller ones it often works, say six out of ten times. If it is a bit more intense, it cannot be suppressed. I may try, but it doesn't work enough. With the small attacks, pretty much under control and I make sure that it stops then.	Self-taught	It is only affective in that very moment. But if I feel a certain "unrest" during the day I take the hand and then I smooth it (massage it) or I sit on my hand for a while. I also often do the kneading of the hand and fingers. I actually don't fully realize I am doing it half of the time. I have attacks both during day and night. At night I have less control over them. I wake up, when I'm further into the attack, even when it just at the start, but then it's also very intense right away, so I don't know if there have been any forebodings at night. Maybe I already unconsciously woke up and already grabbed that hand, because I know I'm lying on my side and if I wake up in such a violent attack that I actually already have queezed my hand, but then it's actually already too late.
pt10	IT DOESN'T WORK.			I tried many techniques without success. I tried breathing techniques, to get my breathing back on track as soon as possible during the beginning of the attack, get my heart rate down... Of course, a high heart rate also sometimes has an influence. before the attack, I try to breathe calmly, I have done many different techniques, I have also done hypoventilation, that also seems to be a method for some, but not for me.
pt11	IT DOESN'T WORK In the past, attacks stoped when lying on the bed.			