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Quantitative Analysis of Ictal Head Movements in Temporal Lobe Epilepsy

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1 INTRODUCTION

The accurate evaluation of epileptic seizures plays a vital role in the localization of the symptomatogenic zone. The symptoms that occur in a seizure may vary greatly and depend on which areas of the cortex are stimulated (Lüders et al., 1995). The analysis of seizure symptoms is a well established method in pre-surgical evaluation of patients considered for resective epilepsy surgery (Noachtar et al., 2003b; Rosenow and Luders, 2001).

However there are discrepancies between the lateralizing values of differing symptoms for different epilepsy syndromes. For example, in temporal lobe epilepsy post-ictal aphasia lateralizes seizure onset to the left (speech dominant) hemisphere, and automatisms while the patient is fully conscious suggest a seizure onset to the right (speech non-dominant) hemisphere (Gabr et al., 1989) (Ebner et al., 1995). Other symptoms, such as dystonic posturing of upper limbs show repeatedly to be of high and reliable lateralizing value (Kotagal et al., 1989) (Steinhoff et al., 1998). The lateralizing value of versive head movement has not been without controversy. If defined as forced and involuntary head movement resulting in unnatural positioning (Wyllie et al., 1986a), versive head movement displays a high positive predictive value for localization of a contralateral seizure onset. Although this has been confirmed (Bleasel et al., 1997; Chee et al., 1993; Steinhoff et al., 1998), some have debated its lateralizing value (Newton et al., 1992; Ochs et al., 1984; Robillard et al., 1983). It is recognized that the qualitative nature of the definition of version may lead to a questionable reliability of the observer (Javakar et al., 1992; McLachlan, 1987) explaining the contradictory data. The interobserver reliability for several lateralizing signs was poor (Bleasel et al. 1997). This observation asks for a more objective way of analysis. In an attempt to reconcile such discrepancies, this study with the combined use of established EEG-video monitoring technology (Penry et al., 1975) and recently introduced video tracking technology (Li et al., 2002)Cunha SJP, 2003), establishes an interobserver independent method of versive movement analysis.

1.1 <u>Temporal Lobe Epilepsy</u>

The term temporal lobe epilepsy (TLE) is given to those patients whose seizure onset arises from the temporal lobe and adjoining structures (Noachtar and Lüders, 1997). TLE is the most prevalent focal epilepsy syndrome in adults and is also the syndrome that is most frequently treated by resective surgery (Rasmussen, 1987; Sander et al., 1995). The seizures are usually characterized by manual and oral automatisms (automotor seizure) as opposed to more proximal motor automatisms (hypermotor seizure) as seen predominantly in frontal lobe epilepsy, often proceeded by a distinctive epigastric, psychic or vegetative aura (Henkel et al., 2002; Kotagal et al., 1988; Wieser, 1983). Secondary generalized tonic-clonic seizures are also not uncommon and seizures often occur in clusters. EEG seizure patterns can display either unilateral or bilateral epileptiform discharges, in the presence of bitemporal ictal EEG patterns invasive electrodes may identify a unitemporal seizure onset (So et al., 1989a; So et al., 1989b). EEG patterns between

seizures may be identified through typical epileptiform discharges in the temporal regions (Jasper et al., 1951).

1.2 Seizure Classification

1.2.1 Definition of Symptomatogenic and Epileptogenic Zones

The symptomatogenic zone is defined as the area of cortex which, when activated by an epileptiform discharge, produces ictal symptoms (Rosenow and Luders, 2001). For this area of cortex to produce symptoms, the stimulus must have the appropriate frequency and be of sufficient duration and intensity. If the stimulus does not fulfill all these criteria, this zone will not elicit a response (Lüders and Awad, 1992).

The epileptogenic zone is the area of cortex that is indispensable for the generation of epileptic seizures. The seizure onset zone is the area of cortex that actually generates clinical seizures. If the epileptogenic zone is smaller than the seizure onset zone, partial resection of the seizure onset zone may render the patient seizure-free, as the remaining seizure onset zone is incapable of generating a seizure. However, if the epileptogenic zone is larger than the seizure onset zone, total resection of the seizure onset zone will not lead to seizure-freedom. A seizure onset zone of a higher threshold within the epileptogenic zone may replace the resected zone and become clinically evident (Lüders and Awad, 1992).

It is important to note that there is frequently no overlap between symptomatogenic and the epileptogenic zones. With the aid of EEG and neuroimaging, it is known that the epileptogenic discharge is generated in the epileptogenic zone and then spreads to the syptomatogenic zone usually some distance form the epileptogenic zone.

1.2.2 A Brief History of Epilepsy Classification

Since the pioneering days of John Hughlings Jackson in the nineteenth century, seizure semiology has played a central role in the classification of epilepsy syndromes. Hughlings Jackson in 1863 first proposed the involvement of the cortex in generating motor seizures (Jackson, 1863). The experimental work of Fritsch and Hitzig showed that the stimulation of the dog's frontal cortex produced movement in the body on the opposite side (Fritsch and Hitzig, 1870). Ferrier performed similar work on monkeys, paving the way for Foerster, Penfield and Rasmussen to map the motor cortex in the early twentieth century, and also added weight to Hughlings Jackson's theory (Ferrier, 1893). Victor Horsley, worked with Hughlings Jackson and Ferrier, resecting tissue based on the localization from observed symptoms (Horsley, 1886). At this time it was the accepted view that the epileptogenic zone was synonymous with the symptomatogenic zone.

With the arrival of electroencephalographic technology came a great revolution in the thinking of epileptologists. In 1929 Hans Berger published his work on scalp recordings of the human EEG (Berger, 1929) and in 1933 presented his findings on interictal EEG activity (Berger, 1933). Epileptologists were able to identify the seizure onset zone. EEG- patterns and changes were noted in conjunction with certain ictal events, as well as interictally. For example, recorded epileptiform discharges occurring in the anterior temporal lobe interictally were often followed by seizures characterized by oral and maual automatisms (Gibbs et al., 1948). Foerster and Altenburger first reported in 1935 the measurement of electrical activity directly from the human cortex (Foerster, 1931). By the early 1950s electrocorticography played an essential role in the surgical treatment of TLE. Ajmone-Marsan and Van Buren introduced the use of chronic intracranial electrodes allowing ictal EEG potentials to be recorded without skull artifact (Ajmone-Marsan and Goldhammer, 1973; Ajmone-Marsan and VanBuren, 1958). These technological advances influenced the classification of seizures, which were now seen as electroclinical syndromes and lead to a classification based solely on EEG findings (Comission on Classification & Terminology of the League Against Epilepsy, 1981).

In 1962 Goldensohn introduced a system in which the patient was simultaneously monitored by a closed-circuit television and EEG was recorded (Goldensohn, 1966). This new technique allowed for the systematic analysis of seizure semiology in respect to EEG recordings, paving the way for a new evaluation of seizure classification (Lüders et al., 1998; Noachtar et al., 1998b; Noachtar et al., 1997). Video-monitoring has become a vital part of pre-surgical evaluation of focal epilepsies. In the pre-surgical evaluation candidates undergo a wide range of studies, including EEG-video monitoring, MRI, fMRI, SPECT and PET scans, to verify the location of the seizure onset zone as well as the epileptogenic zone. A more accurate localization is found when there is greater concordance between the different methods (Noachtar et al., 1996).

1.3 Clinical Seizure Lateralization in Temporal Lobe Epilepsy

Lateralizing signs during seizures are used in the identification of the sympatogenic zone in focal epilepsies. It has been reported that 78% of patients studied, presented with lateralizing signs during seizures with a positive predictive value (PPV) of 94% (Chee et al., 1993). In a more recent study it was shown that lateralizing signs occur significantly more frequent in unitemporal epilepsy as opposed to bitemporal epilepsy (Serles et al., 1998). The following is a brief list of important lateralizing signs in TLE, and not to be understood as conclusive. These lateralizing signs were chosen as they were seen in conjunction with or as part of a developing evolution of symptoms including seizure head movements in this study. Head movements will be discussed separately in more detail in Section 1.4.

1.3.1 Auras

Auras are epileptic seizures that present with subjective symptoms only. They can last a few seconds or as long as a few minutes. They can present as isolated incidences or may evolve into other types of epileptic seizures. They may be identified by epileptiform discharges in EEG.

Epigastric auras are the most frequent auras in TLE (Kotagal, 1991; Noachtar et al., 1992; Rosenow and Luders, 2001; Wieser, 1983), followed by psychic

and olfactory auras in occurrence. It has been reported that psychic and vegetative auras occur more frequently in right TLE (Gupta et al., 1983), this has been disputed by others, however (Palmini and Gloor, 1992; Wieser, 1983; Wieser and Williamson, 1993). Epigastric auras are reported to occur statistically more frequently in right than in left TLE, with an incidence of 21% and 57% respectively (Steinhoff et al., 1998).

1.3.2 Focal Clonic Movement

Focal clonic movement has been found to lateralize the sympatogenic zone to the contralateral side of the movement (Rosenow et al., 2001). Focal clonic movement has been noted to be more frequent in general and occurs earlier in the seizure evolution in FLE as opposed to TLE (Noachtar and Arnold, 2000) and has been reported to be more common in left TLE (Fakhoury et al., 1994).

1.3.3 Unilateral Motor Automatisms and Dystonia

Several authors have reported unilateral motor automatisms to be of ipsilateral lateralizing value (O'Brien et al., 1996; Wada, 1982). Some authors however, postulate that the unilateral nature of this movement is a result of associated contralateral dystonic posturing (Chee et al., 1993; Kotagal et al., 2000). The occurrence of motor automatisms in conjunction with dystonic posturing has been attributed to a specific primary spread of seizure discharges and not to the seizure onset (Dupont et al., 1999; Kotagal et al., 1989; Newton et al., 1992). The progression of ipsilateral motor automatisms to contralateral dystonic posturing occurs more frequently in mesial than in neocortical TLE (Saygi et al., 1994), while another study showed early contralateral dystonic posturing to occur more frequently in neocortical TLE (Gil-Nagel and Risinger, 1997). This progression has subsequently been shown to be common in mesial TLE (Dupont et al., 1999; Williamson et al., 1998) and has been suggested as a criterion to distinguish between mesial and neocortical TLE (Dupont et al., 1999). The progression of ipsilateral motor automatisms to contralateral dystonic posturing occurs less frequently in neocortical TLE than in mesial TLE.

1.3.4 Immobile Limb

It has been described that during seizures of patients with TLE one limb is not moved (Oestreich et al., 1995). This has been labeled ictal paresis. However, the patients were not responsive and it was not tested whether they had paresis or just did not move one limb. Probably this description is related to the observations of unilateral automatisms (O'Brien et al., 1996; Oestreich et al., 1995). Since paresis was not proven and rather assumed in clinical practice the term "immobile limb" should be preferred (Noachtar et al., 1994; Noachtar et al., 1998b). It lateralizes to the contralateral side and has been found to occur in 12% of TLE patients (Bleasel et al., 1997).

1.3.5 Dystonia

Dystonic posturing of limbs is regarded of high lateralizing value in TLE, lateralizing to a syptomatogenic zone contralaterally (Kotagal et al., 1989), and has been confirmed in several studies on numerous occasions (Dupont et al., 1999; Noachtar et al., 1994; Noachtar et al., 1998b; Williamson et al., 1998).

1.3.6 Asymmetric Tonic Limb Posturing (figure 4 sign")

In a recent publication, the lateralizing value of asymmetric limb posturing has been presented (Kotagal et al., 2000). During the tonic phase of a secondary generalized tonic-clonic seizure the patient extends one elbow while flexing the other forming what appears to be a "figure 4 sign". The extended elbow is contralateral to the seizure onset zone.

1.4 Clinically Relevant Head Movements

1.4.1 Introduction

Versive head movement has been reported in 15 – 35% of patients with TLE (Bleasel et al., 1997; Kotagal et al., 1989). A study basing data on gathered information from history taken, reported a high incidence of 61% in TLE patients for versive head movements (Bleasel et al., 1997). John Hughlings Jackson first recognized the potential clinical value of the head turning "to one side and then to the other" during an epileptic seizure over a hundred years ago (Jackson, 1879). Ferrier electrically stimulated the posterior half of the superior and middle frontal gyri of monkeys inducing conjugate eye turning, and if the stimulation was of an adequate intensity, induced contralateral head turning in seizures (Ferrier, 1874; Ferrier, 1886). Further work by Foerster, Rasmussen and Penfield confirmed Ferrier's observations in humans (Foerster, 1931; Penfield and Rasmussen, 1950). They noted that the cortex area responsible for eye movements, called the 'frontal eye field', was guite restricted but not separated from motor representation (Penfield and Jasper, 1954). It was later reported that adversive, i.e. away from the focus, head movements were induced after the spread of epileptiform discharges through the 'frontal eye field', which lies anterior to the precentral gyrus, thus the coining of the term adversive head deviation (Rasmussen and Penfield, 1947). These findings were later confirmed (Godov et al., 1990), however, the differentiation between head turning and versive head movement posed many difficulties, from which a great controversy arose.

1.4.2 Versive Head movements

A more neutral term for versive head movement was adopted when it was recognized that there were conflicting reports of "ipsilateral adversion" and "contralateral adversion", the former appearing absurd in meaning (Gastaut, 1964). Versive head movements were found to have a high lateralizing value to the contralateral side of the seizure onset, if defined as tonic or clonic head turning "unquestionably forced and involuntary, resulting in sustained unnatural positioning of the head" (Wyllie et al., 1986a). This has been repeatedly confirmed by other studies, showing contralateral versive head movements to have a PPV of over 95% (Bleasel et al., 1997; Chee et al.,

1993; Ebner et al., 1995; Kotagal et al., 2000; McLachlan, 1987; Steinhoff et al., 1998)).

However, the lateralizing value of versive head movements has been disputed (Newton et al., 1992; Ochs et al., 1984; Robillard et al., 1983; Wada, 1982) and found to be of no clinical value. It should be noted that none of these studies adhered to the strict definition as proposed by the study above (Wyllie et al., 1986a). One definition used for versive movement was, "a smooth, seemingly involuntary turning of the head to one side" (Ochs et al., 1984), allowing more ambiguous head movement to be considered as versive. Two other studies (Newton et al., 1992; Robillard et al., 1983) divided head movement into major and minor head deviation and slight, moderate and marked head deviation respectively, using even more subjective criteria for defining versive head movement.

Sustained ictal head deviation is due to activation of the ipsilateral sternocleidomastoid muscle, resulting in three possible head turning patterns: ipsiversive head tilt, contraversive face rotation or a combined ipsilateral tilt – contralateral rotation (Jayakar et al., 1992). By assessing the head movement in context of the activation of the sternomastoid and cleidomastoid muscle divisions, it was shown that contraversive face rotation and combined tilt-rotation accurately lateralized the seizure onset (Jayakar et al., 1992). In both of these movements the neck is extended, a characteristic of versive head movements that ensures unnatural positioning of the head and is in keeping with Wyllie's definition.

For the purpose of this study, versive head movement was defined as forced and involuntary head movement resulting in sustained and unnatural positioning of the head to one side.

1.4.2.1 Incidence of Versive Movements

A higher incidence of contralateral versive head movements in left TLE (22%) as in comparison to right TLE (6%) was reported (Fakhoury et al., 1994). These findings were confirmed, showing that contralateral versive head movements also have a higher sensitivity for left TLE (51%) than right TLE (7%) (Steinhoff et al., 1998).

1.4.3 Head Movement Occurring Early and Late in Seizure

There are conflicting reports about the lateralizing value of head movements occurring during seizures (Chee et al., 1993; Kernan et al., 1993a; Ochs et al., 1984; Robillard et al., 1983; Wyllie et al., 1986a). The head movement maybe divided into three groups: versive movements; non-versive head deviation and non-versive head deviation followed by versive head movement.

1.4.3.1 Early and Late Versive Movement

It has been observed that versive head movements may occur more than once in a seizure (Wyllie et al., 1986b). When versive movement occurs directly before secondary generalization, it is found to lateralize to the contralateral side of the seizure onset (Kernan et al., 1993a; Kotagal et al., 1989; Williamson et al., 1998; Wyllie et al., 1986b) (Williamson et al., 1998). If this movement is sustained through the generalization, it is often followed by a later versive movement to the ipsilateral direction (Wyllie et al., 1986b) during the generalization. The mechanism of the initial and late versive movements may be similar as both movements resemble movement elicited by stimulation of Brodman's area 6 (Foerster, 1931; Penfield and Rasmussen, 1950). The initial versive movement, though frequently ipsilateral, was of no reliable lateralizing value (Wyllie et al., 1986b).

1.4.4 Non-Versive Head Movement

Non-versive head movement has been defined as not forced or sustained enough to be considered versive and appearing voluntary in nature (Fakhoury and Abou Khalil, 1995). It has been suggested that it may be voluntary as a response to an aura (Godoy et al., 1990), due to the "purposeful" nature of the movement. A parallel has been made between ipsilateral conjugate eye deviation in stroke involving the parietal cortex and ipsilateral non-versive head turning in partial seizures (Chee et al., 1993). There is consensus that non-versive head movement occurs early in the seizure and before versive movements (Chee et al., 1993; Kotagal et al., 1989; Serles et al., 1998; Williamson et al., 1998; Wyllie et al., 1986a; Wyllie et al., 1986b) sometimes even occurring repeatedly. However, while all agree that early non-versive head movement is predominantly in the ipsilateral direction (Fakhoury and Abou Khalil, 1995), it has been denoted of unreliable lateralizing value unless followed by a contralateral versive head movement (Kernan et al., 1993a; Wyllie et al., 1986a; Wyllie et al., 1986b). Non-versive head turning has a shorter mean latency during a seizure in comparison to contralateral head turning. It has been reported to occur on occasion co-comittantly with contralateral dystonic posturing (Fakhoury and Abou Khalil, 1995).

1.4.4.1 Sequence : Non-Versive Followed by Versive Head Movement

The observed sequence starting with a non-versive turning of the head to the ipsilateral direction during automatisms, followed by versive head turning in the contralateral direction as the seizure begins to generalize, has been reported (Serles et al., 1998; Williamson et al., 1998; Wyllie et al., 1986a). This sequence does not occur as frequently as contralateral versive movement without such an accompaniment, and unfortunately is not reported consistently as a sequence, making it impossible to determine its incidence. For the purposes of this study the versive head movements occurring only in this sequence were analyzed.

1.4.4.2 Sequence : Versive Head Movement Followed by "Figure 4 Sign"

It has recently been shown that asymmetric tonic limb posturing (ATLP), popularly known as the "Figure 4 sign" has been shown to lateralize in concordance with versive head movements contralaterally (Kotagal et al., 2000). Versive head movement preceding ATLP has been attributed as one of its characteristics, and occurred when the head was in the midline position or returning to the midline position after a versive movement and before the seizure generalized secondarily.

1.5 Interobserver Reliability of Versive Head Movements

In a recent study on lateralizing motor phenomena during seizures in TLE and extratemporal epilepsies, only dystonic hand posturing in TLE had a good inter-observer reliability (Bleasel et al., 1997). It has been recognized that the qualitative nature of the definition for versive head movement may lead to a questionable reliability of the observer (Chee et al., 1993; Jayakar et al., 1992; McLachlan, 1987). The different interpretations of versive head movements may explain the presence of contradictory data (Bleasel et al., 1997; Chee et al., 1993; Newton et al., 1992; Ochs et al., 1984; Robillard et al., 1983; Steinhoff et al., 1998; Wyllie et al., 1986a). Objective methods are required to quantify versive head movements during epileptic seizures, as shown by its poor inter-observer reliability. This study proposes a new objective, observer independent method on quantifying versive head movements that could overcome observer dependent differences.

1.6 Quantification of Movement in Epileptic Seizures

In other areas of neurology such as movement disorders, methods to further quantify movement in order to gain further clinical information have been established (Altiparmak et al., 2006; Bowers et al., 2006; Jobbagy et al., 1997).

The unpredictable nature of movements seen in epileptic seizures may be the reason that quantitative analysis has not been performed so far. With the use of video-EEG technology, movement can be subjectively analyzed, although it is always dependent on the clinician's observations and experience. Li *et al.* proposed a new movement quantification system, QMovES that attempted to extract information from seizures that had been monitored using video-EEG technology (Li et al., 2002), taking advantage of new compression software by saving video data in M-JPEG format, allowing minimum loss of image information. Blobs with reflective material were placed on the patient's body at 22 predefined landmark points (MPS22). Using previously proposed algorithms (Jobbagy, 1997; Jobbagy et al., 1997); these blobs were tracked for each frame. The movement was then colour-coded according to intensity and could be reproduced in an animated colour-coded video.

It has been shown that this technology could be utilized in a typical Epilepsy Monitoring Unit (EMU) with high precision. The maximum movement error was 8% (Cuhna et al., 2003). The set-up used was more in keeping with a typical EMU set-up, in which the camera position was perpendicular to the head of the patient facing the camera in an upright position. This system has been used successfully to differentiate between hypermotor and automotor seizures, by measuring movement of the wrist relative to that of the trunk (Meier et al., 2004).

2 OBJECTIVE

We aimed to quantitatively investigate the head movements during epileptic seizures of patients with TLE in order to avoid poor inter-observer reliability and contribute to the debate of the lateralization significance of head movements. By studying quantitatively ictal head movements in both directions with regard to seizure evolution, we wished to identify objective criteria that allow versive head movements to be distinguished from non-versive head movements and evaluate their lateralizing significance.

3 METHODS

3.1 Patients

Patients were collected from the video archives of the Epilepsy Monitoring Units (EMUs) at the University of Munich, (n=13), Cleveland Clinic Foundation, Ohio (n=13) and Bethel Epilepsy Monitoring Unit, Bielefeld (n=6). A data base search was performed in each centre for the terms: temporal lobe epilepsy, version, versive seizure and versive head movement. Patients found in these archives were referred to special out-patient clinics in the named centres by their respective neurologists from January 1992 to March 2004 for various reasons including pharamcoresistancy. Patients were then submitted to the respective EMUs for epilepsy syndrome classification and evaluation for surgical resection.

Pre-surgical evaluation included non-evasive video-EEG monitoring (for further details see section 3.2), magnetic resonance imaging (MRI) and neuropyschological testing. MRI included proton density weighted, T1-weighted and T2-weighted images in axial, coronal and saggital planes (5mm slices) (1.0 Telsa/Siemens). If the MRI was normal or surgical planning required additional testing, high resolution (1-3 mm slices) MRI with inversion recovery (IR), 3D- fast low angle shot (FLASH) images, fluid attenuated inversion recovery (FLAIR) and /or magnetization prepared rapid attenuated gradient echo (MPRAGE) was performed (1.5 Telsa/Siemens) (Jackson et al., 1990; Laxer and Garcia, 1993). Further imaging studies undertaken in selected patients, included interictal [¹⁸F] fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) and ictal ^{99m}Tc-ethyl-cysteinate-dimer single photon emission computerized tomography (ECD-SPECT) following established protocols (Noachtar et al., 1998a).

The epilepsy syndrome was defined in a patient management meeting attended by epileptologists, neuroradiologists, neurosurgeons and neuropsychologists. The classification of TLE was based on localizing evidence found in interictal and ictal EEG, as well as in the above mentioned neuroimaging diagnostics (Noachtar et al., 2003b).

3.2 Video-EEG Monitoring

Patients were monitored with a video-EEG monitoring system in which EEG and video findings were simultaneously recorded. Patients spent from 3 to 14 days in the respective EMUs. The continuous surveillance of the patients was performed by nurses and specially trained neurophysiological technical assistants.

The video-recording system allowed the transmission of coloured pictures in the presence of daylight and with the aid of an infrared system, black and white pictures during the night. An infrared sensitive CCD camera, with 720 x 576 pixels resolution (PAL), was used. A 6mm lens, providing 56 x 41 degrees of horizontal and vertical field of vision (FOV) angles was mounted and adjusted to include the bed in the image.

The EEG was continually measured by 36-64 channel EEG-machines (Vangard System, Cleveland/Ohio). The EEG-signal was amplified (Schwarzer, Munich and Lamont, Sydney) and then digitalized (200Hz for 12bit) and archived. Surface electrodes were placed according to the standardized 10-20-system; additional electrodes placed at half the distance between electrodes were added (10-10-system) (American Electrocephalographic Society 1991). All patients underwent non-invasive monitoring with the use of surface electrodes. These electrodes consisted of gold-coated silver "saucers" with a diameter of 7mm, which were stuck to the scalp with the aid of collodium.

Some patients underwent semi-invasive monitoring in which epidural electrodes were used or electrodes were placed in the oval foramen (Noachtar et al., 1991), while others underwent invasive monitoring in which subdural electrodes were placed stereotactically according to the individual diagnostic requirements. Subdural electrodes were also used for electrical stimulation to identify eloquent cortex, in TLE particularly speech areas (Noachtar et al., 2003b).

3.2.1 Clinical Video Set-up

The video set-up is based on the International Federation of Clinical Neurophysiology (IFCN) recommendations on long-term monitoring of epilepsy (van Emde Boas and Parra, 2001). **Figure 1** presents a geometrical model for the set-up, in which the patient is sitting facing the camera; see Section 3.3.4 for desired positioning of patient. It is assumed that the patient's upper body is perpendicular to the camera incidence angle, allowing the tilting angle (T) of the camera and bed to be equal. Distance R was defined as the distance from the camera to the patient's trunk centre; D and H were defined as the respective horizontal and vertical distances. In previous work (Cuhna et al., 2003) these distances could be measured with a 1.3% error, giving a horizontal and vertical sampling resolution of 3.8 x 5.4mm with the specified lens.

3.2.2 Video Selection

All videos of the recorded seizures were analyzed independently of the appropriate EEG findings in accordance with the Semiological Seizure Classification (SSC) (Lüders and Noachtar, 2001; Noachtar et al., 1998c). A diary of the clinical events, including EEG findings, seizure evolutions and lateralizing phenomena, was kept for each patient. A daily discussion of the diary entries lead to the prospective classification of the seizures. The state of consciousness of the patient during the seizure was systematically tested with respect to the patient's reaction to certain questions, following an established protocol (Noachtar, 1993; Noachtar et al., 1992).

Videos were then selected with respect to the inclusion and exclusion criteria, as described in Section 3.3.4, for the study. Selected videos were digitized with a 700×525 pixels resolution and compressed into MPEG-4 format according to the Overview of the MPEG-4 Standard, with key frame distance of one second and 2048 kbps data rate for a crispness factor of 75%.

3.3 Movement Analysis

3.3.1 Initial Movement Analysis

Two points on the patient were chosen for each seizure, a nostril (Point 1) and an easily identifiable point on the patient's thorax (Point 2), such as a button. Point 1 represented the movement of the head, and Point 2 served as a reference point. Despite the ability of the software to track the movement of the head independently, a reference point was necessary to ensure accurate measurement of head movement. Without the use of a reference point, movement of the body without turning of the head would have been incorrectly measured as head movement as depicted by **Figure 2**. The choice of a reference point on the trunk allows only the angular distance traveled between the head and the body in the plane perpendicular to the camera to be measured.

Each point using MaxTraQ × 2 (Innovision Systems Inc.) was tracked for each video frame (25/s), generating the respective two dimensional positions (x,y). These positions were then connected and superimposed on the video recording, allowing the movement pattern to be better visualized, as depicted in **Figure 3**. Due to the limitations of 2-dimensional analysis and based on a geometric model recently published elsewhere (Cunha et al. 2003), only head movement during which both eyes could be seen was further used for angular analysis. For each frame i, the angle α was computed (α_i) and a movement tracing was generated, as shown in Figure 2. From these tracings ipsilateral and contralateral angular speed and duration were extracted.

3.3.2 Duration Analysis

The video and movement tracing were inspected. The frame number at the beginning (f_l) and at the end of movement (f_e) in either direction was noted in the video and verified on the tracing allowing the duration to be calculated. As the duration did not require active tracking of two points, the entire duration of the movement, including movement in which both eyes could not be seen, was measured. The duration was calculated as follows:

 $(f_e - f_l) / 25$

3.3.3 Angular Speed Analysis

The movement tracing was inspected and head turning in each direction was identified. The frame numbers at the beginning and end of each head turning (**Figure 4**) were noted. These frame numbers were then verified by repeated observation of the video recording. Movement containing artefacts and/or not fluid in nature (e.g. head extension, rocking of trunk) was identified from the tracing and verified in the video, excluding it from evaluation. The slope of the remaining tracing (as shown in **Figure 5**) which depicted head movement in which both eyes could be seen, was used to determine the angular speed. This ensured that movement could be accurately analysed despite two-dimensional restrictions.

3.3.4 Inclusion and Exclusion Criteria

The seizures were first analyzed visually by at least two senior epileptologists and classified according to a recently published seizure classification (Noachtar, 2001; Noachtar et al., 1998c; Pfänder et al., 2002). All patients met the following inclusion criteria:

- Diagnosis of TLE
- Contralateral version and additional head turning in both directions lasting at least 1.25 seconds (31 frames)
- Camera position was perpendicular to the head facing the camera in an upright position, complying with geometric model as previously defined (Cuhna et al., 2003) due reduce limitations of 2-dimensional movement analysis.
- Versive head movement was identified through visual analysis by at least two senior epileptologists and defined as contralateral or ipsilateral according to EEG ictal patterns.

The following criteria excluded the patients from the study:

- head movement was in response to external stimuli
- head or reference point were hidden for longer than 5 seconds
- head and trunk left the plane perpendicular to the camera.

3.3.5 Statistical Analysis

Statistical analysis was performed using the SPSS for Windows (Version 10.0) software. Intersubject and intrasubject analysis was executed. To obtain normal distribution the natural logarithm of each value was calculated, where appropriate these values were used. The mean, median and standard deviation were calculated for angular speed (deg/s) and duration (s) in both directions. The drop out rate was calculated with respect to the total number of patients screened and the number of patients included in the study.

3.3.5.1 Positive Predictive Value (PPV)

To examine the reliability of versive head movements in lateralizing seizure onset, the positive predictive value was calculated. Ictal EEG records and other diagnostic findings were consulted when deciding if the versive head movement correctly lateralized the seizure onset contralaterally. The number of patients whose versive head movement lateralized correctly was divided by the total number of patients included in the study; this value was then multiplied by 100 to give the PPV as a percentage. A higher the PPV denotes a higher reliability of the clinical phenomena in predicting a correct lateralization.

3.3.5.2 Non-parametric Tests

Non-parametric tests are of use when the number of subjects to be analyzed is small. These tests do not require an estimation of the mean or variance and

assumptions about the probability distribution are unnecessary. A p-value smaller than 0.05 was defined to be significant.

The Wilcoxon Paired Comparison Test was used because, as the name suggests, it allowed a comparison between ipsilateral and contralateral movements to be made. The angular speed in the ispilateral direction was paired with the contralateral angular speed for each seizure. The same was done for duration. When analyzing the angular speed the Null and Alternative Hypotheses were thus stated:

 H_0 = Contralateral and ipsilateral angular speeds belong to the same group H_1 = Contralateral and ipsilateral angular speeds belong to different groups

The Null and Alternative Hypotheses were thus stated for duration analysis: H_0 = The duration of contralateral and ipsilateral movements are the same H_1 = The duration of contralateral and ipsilateral movements are different

Similar hypotheses were stated for angular speed. The Wilcoxon table was used to determine if S_ fell in the critical region, if it did the Null Hypothesis was rejected.

3.3.5.2 Box-and-Whisker Plots

Box-and-whisker plots were used to represent the differences in duration and angular speed for ipsilateral and contralateral head movements. Using the conventions proposed by Tukey (Tukey, 1977), a box was drawn for each parameter, i.e. ipsilateral angular speed, contralateral angular speed, ipsilateral duration, contralateral duration, with ends at quartiles Q_1 and Q_3 . The statistical median was calculated for each and then drawn as a horizontal line in the box. "Whiskers" were then drawn to the farthest values that were not outliers, i.e. lay within 3/2 times the interquartile range of Q_1 and Q_3 . For every value that lay outside 3/2 times the interquartile range a dot was drawn. This historgram-like representation was also completed for the natural logarithm values of the above named parameters.

3.3.5.4 Pearson's Product Moment Correlation

The Pearson's product moment correlation was performed to determine if there is a linear relationship between the angular speed and the duration of versive head movements. A scattergram for movement in either direction was constructed, the x-axis was defined by the natural logarithm of angular speed and the y-axis was defined by natural logarithm of duration. The correlation coefficient is a quantity that gives the quality of a least squares fitting to the original data.

Pearson's correlation coefficient (or r) can range from -1 to +1. No other value is possible. A value of zero (0.0) indicates that the variables are not related or perhaps more complex or nonlinear relationships. Values close to -1 or +1 indicate strong predicative relationships. The sign indicates the direction of the relationship (or its slope). Negative correlations come from relationships with a negative slope, and vice versa for positive correlations. The correlation

coefficients were tested for significance, to ensure obtained values did not occur by chance.

4 RESULTS

The following is an overview of all obtained results. Attention was drawn to the role versive head movements played in the seizure's evolution and to their lateralizing significance. The results of the quantitative analysis are then described, firstly as an overall result of the three centres and then individually listed for each centre. Each seizure was given an identification number according to which centre it came from. Seizures obtained from the archive at the Epilepsy Monitoring Unit at the Klinikum Grosshadern of the University of Munich, were given the letter "G". Seizures obtained from the Cleveland Clinic Foundation, Ohio were given the letter "C" and likewise the seizures obtained from the letter "B". More than one seizure can arise from one patient.

4.1 Patient Collective

From the three above mentioned centers 256 patients diagnosed with TLE and displaying versive head movements during recorded seizures were reviewed.

186 patients showed versive movements in the contralateral direction unaccompanied by a preceding ipsilateral head movement. 70 patients displayed the sequence of head turning to the ipsilateral side followed by versive head movement in the contralateral direction. However only 32 of these patients could be included in the study, as in 38 patients head movement was either blocked for longer than five seconds, the patient was incorrectly positioned or moved out of the desired plane for analysis. An overview of each center's patient collective and the final patient collective is depicted in **Figures 6a-d**.

Fourteen women and 17 men were included in the study. The average age of the patients was 33 years, with a range from 11 years to 58 years. Twentynine patients were diagnosed with unilateral TLE and two patients with bitemporal lobe epilepsy. Sixteen patients had right TLE whereas 7 had left TLE, a further patient had right mesial TLE and five patients had left mesial TLE. The MRI findings and ictal EEG results were also noted. Four patients had normal MRI findings, the predominant finding, however, occurring in 14 patients was mesial temporal sclerosis. Six patients were not surgically resected, of the remaining 35 all had an excellent surgery outcome (Engel Classification Ia-d) with the exception of one patient (IIIa). (**Table 1**)

4.2 Seizure Evolution

4.2.1 Sequence: Ipsilateral Followed by Contralateral Head Movement

The sequence ipsilateral head turning followed by versive head movement in the contralateral direction occurred late and before secondary generalization in all seizures. With use of movement tracings this sequence could be divided into three phases (**Figure 4-5**): 1: head movement in the ipsilateral direction, 2: a "plateau phase" in which the head remained relatively still and 3: head movement in the contralateral direction.

4.2.2 Occurrence in Seizure

The average onset time of the ipsilateral movement after the clinical beginning of the seizure was 26s from a range of 2s-92s. It should be noted that the following observations were unable to be made for five seizures due to poor video quality or unfavourable positioning of the patient, for example the patient's extremities remained hidden under a blanket. Automatisms were seen in 26 seizures preceding and/or during head movement in the ipsilateral direction. The automatisms were mainly observed in the ipsilateral upper extremity; however oral automatisms were also seen in 10 seizures. In seizure 28 from patient C6, it was noted that the patient at the beginning of the seizure turned their head in the ipsilateral direction three times, returning each time to the center in an alternating manner.

These automatisms usually came to an end either at the end of the ipsilateral head movement or during the plateau phase when the head remains still. Versive head movement in the contralateral direction followed the ipsilateral head turning and automatisms. It should be noted that automatisms and versive head movements were rarely observed to occur simultaneously. Dystonic posturing of the upper extremities during and/or directly after versive head movement was observed in 26 seizures, however in some seizures the movement could not be accurately observed due to re-positioning of the patient onto his side before secondary generalization. Dystonic posturing sometimes began during the plateau phase. When the dystonic posturing was unilateral in nature, it always occurred on the contralateral side to the seizure onset zone. Seven patients displayed the "figure of 4 sign" and two displayed the "fencing position". Versive head movement and dystonic posturing was followed directly by secondary tonic-clonic generalization in all seizures.

The described above sequence occurs late in the seizure and directly before secondary tonic-clonic generalization.

4.3 Lateralizing Significance of Versive Head Movement

The seizure onset zone was defined in patient management meetings as described in Section 3 with regard to EEG seizure patterns. Both head movements in the ipsilateral and the contralateral direction were found to correctly lateralize the seizure onset zone in all patients. The sequence of ipsilateral head turning followed by contralateral versive head movement was found to have a positive predictive value of 100% when occurring late in the seizure and before secondary generalization.

4.3.1 Identification of Head Tilting and Neck Extension

It should be noted that the following findings were observed for contralateral versive head movements only. The combination of ipsiversive tilting of the head and contraversive rotation of the face can occur throughout the versive movement. With the aid of movement tracings, however, ipsiversive head tilting was identified to occur sometimes in isolation at the beginning of the versive movement, followed by face rotation or occur at the end of the face rotation. This was verified by visual analysis of the seizures. Extension of the neck was also identified, positioning the face upwards with or without a

rotational component occurring predominantly at the beginning or the end of the versive movement. Neck extension was identified in 25 seizures visually, on review of the movement tracings, extension of the neck could be identified in 21 seizures by noting an abrupt change in each tracing's slope. Movement tracings helped identify different components of versive head movement that often appear visually as a single fluid movement, either occurring in combination with rotation of the head or alone causing the head to tilt upwards.

4.4 Duration of Head Movement

The average duration of head movements in each direction was calculated (**Table 2**). The quantitative analysis showed that contralateral head movement lasts significantly longer than ipsilateral head movements $(3.9\pm3.1 \text{ s} \text$

Contralateral movements had a longer duration in 32 seizures while 6 seizures presented with a longer ipsilateral movement. In all three centers, the majority of seizures had longer contralateral movements (**Table 2a**).

4.5 Angular Speed of Head Movement

The average angular speed of head movements in each direction was calculated (**Table 3**). Ipsilateral and contralateral head movements displayed similar angular speeds (15.5 ± 12.1 deg/s vs. 17.3 ± 13.0 deg/s), the quantitative analysis could not show a significant difference (p= 0.26).

In 20 seizures the contralateral head movement had a greater speed than the movement in the ipsilateral direction, whereas in 18 seizures the speed of the ipsilateral movement was greater than the contralateral movement.

There was poor agreement between the three centres in respect to the angular speed of head movements. In eight out of 14 seizures from Clinic Gross Hadern the ipsilateral movement had greater speed, this was also shown in four seizures out of six at the Bethel Epilepsy Center, however neither of these findings showed significance. Thirteen seizures out of 18 at the Cleveland Clinic Foundation had contralateral movements of greater speeds than in the ipsilateral direction; again however, this finding was not significant. The exact same speed in both directions during one seizure was never recorded (**Table 3a**).

4.6 Correlations between Duration & Speed

Two significant correlations could be drawn from the data. There was a correlation between the angular speed in one direction and the speed in the other direction (p<0.001). If the ipsilateral head movement was of a slower speed, it was more likely that the following contralateral movement would also be of a slower speed. The equivalent is true for movements of higher speeds.

There was also a correlation for movements in the contralateral direction between angular speed and duration (p<0.05). If the speed of the movement is of a higher speed, it is more likely that the movement will have a shorter duration. The equivalent is true for movements of slower speeds, which have longer durations (**Table 4**).

4.7 Overview of Results

The table on the following page (**Table 5**) is an overview of all variables measured and results obtained from the study. The table lists the results according to patient and seizure number.

Automatisms were also noted, although only in the context of to which side of the seizure onset zone they occurred. Where automatisms occurred on both sides, they were loosely classified such as "oral" or "ipsilateral limb". Automatisms which could not be properly observed e.g. the patient's hands were under a blanket, were noted under "unable to be analysed" as the movement seen suggested automatisms but could not be verified.

Dystonia was also noted on observation. Neck extension played an important role in distinguishing versive from non-versive movement and hence was noted separately. Dystonia was also loosely classified; dystonia involving both upper limbs was noted as "upper limbs". Patients who displayed the 'Figure of 4 Sign" were noted. In three patients, their dystonic movements were disrupted before they had ended and were so noted.

Neck extension was identified on observation and with use of movement tracings. If neck extension could be identified through observation and with the movement tracing it was donated "yes, identified", if it was observed but could not be identified in the movement tracing it was donated, "yes, unable to identify".

The angular speed was noted in each direction in degrees per second, and the duration of head movement in each direction was noted in seconds.

5 DISCUSSION

5.1 Introduction

This study shows that head movement in temporal lobe epilepsy (TLE) occurring early in a seizure differs from that which occurs later in the course of the seizure. Ipsilateral head movements followed by contralateral versive head movements and occurring before secondary generalization have a positive predictive value (PPV) of 100% for lateralization of the seizure onset zone. There are controversies regarding the lateralizing significance of head movements (Abou Khalil and Fakhoury, 1996). It has been emphasized that correct distinction between versive and non-versive head movement is important for the correct lateralization of the seizure onset zone (Wyllie et al., 1986a). Versive head movement is distinguished from non-versive head movement by gualitative criteria, such as forced, sustained and unnatural contralateral positioning of the head (Wyllie et al., 1986a). Contralateral head version typically occurs prior to secondary generalization and thus late in the seizure evolution (Wyllie et al., 1986b). Non-versive head movement is defined as being not forced and appearing voluntary in nature (Fakhoury and Abou Khalil, 1995; Wyllie et al., 1986a). However, the lateralizing significance of head version has been debated by others (Ochs et al., 1984; Robillard et al., 1983). This may be related to the observation that in many patients in addition to contralateral head version, there is also ipsilateral head turning. There is a lack of objective criteria allowing versive head movement to be distinguished from non-versive, resulting in poor interobserver reliability (Bleasel et al., 1997). Therefore, we applied a new method that defined new quantitative aspects of head movement TLE independent of observer bias.

5.2 Versive Head Movement

The value of versive head movements in correctly lateralizing the seizure onset zone has been for many years accompanied by great controversy. It has been previously reported to have a high lateralizing significance, directing to a contralateral seizure onset in patients with TLE (Bleasel et al., 1997; Chee et al., 1997; Kernan et al., 1993a; Kernan et al., 1993b; Wyllie et al., 1986a). Others, however, could not confirm this (Newton et al., 1992; Ochs et al., 1984; Robillard et al., 1983), although versive head movement was also defined as forced. In the latter studies, however, attention was not paid to the unnatural positioning of the head or to the occurrence of head movement in relation to the seizure evolution. For correct lateralization of versive head movements, head movement must be considered with regard seizure evolution. Versive head movement occurs with respect to the duration of the seizure, significantly earlier in extra-temporal than in TLE, although always occurring late in the respective seizure evolution (Chee et al., 1993). It may occur after non-versive head turning in the opposite direction or as the first ictal head movement, however, it usually occurs directly before or accompanied by secondary generalization (Chee et al., 1993; Kernan et al., 1993a; Kernan et al., 1993b; Wyllie et al., 1986a).

5.2.1 Versive Head Movements as Part of Sequence

Often versive head movements occur as part of a sequence with other seizure phenomena. There has been some disagreement of the usefulness of

unilateral automatisms of the upper limbs when lateralizing the seizure onset zone. Often automatisms begin bilaterally and then become unilateral. These unilateral automatisms have been reported to lateralize ipsilaterally (O'Brien et al., 1996; Saygi et al., 1994; Wada, 1982); however, these could be the result of dystonic posturing of the contralateral limb (Kotagal et al., 1995). The breakthrough of bilateral automatisms must not only result in dystonic posturing, it can lead to an "immobile limb" as a muted expression of tonic posturing (Bleasel et al., 1997).

When occurring in tandem with dystonic posturing, versive head movement has high lateralizing reliability (Bleasel et al., 1997; Chee et al., 1993; Kotagal et al., 1989; Wyllie et al., 1986b), lateralizing to the contralateral side. Our study confirmed this. The "Figure of 4 Sign" and the "fencing position" have also been noted to follow versive head movements (Kotagal et al., 2000), whereby the head has returned to or is returning to midline. Although this did not occur as often as dystonic posturing, the extended elbow of those patients who did display a "Figure of 4 Sign", as well as the direction of versive head movements did in all instances correctly lateralize to the contralateral side (Kotagal et al., 2000).

Versive head movement, as with all seizure semiology, when occurring in tandem with other lateralizing signs, has a higher reliability (Noachtar et al., 2003a). The seizure evolution and sequence of lateralizing signs should be considered when attempting to identify versive head movements correctly. The following sequence was frequently observed among our patients:

bilateral upper limb automatisms \rightarrow ipsilateral upper limb automatisms \rightarrow ipsilateral head turning \rightarrow dystonic posturing of contralateral upper limb \rightarrow contralateral versive head turning \rightarrow generalized tonic-clonic seizure.

Although all components of this evolution were not always present, the order in which the seizure evolved remained the same. For example, bilateral upper limb automatisms never occurred during or after versive head movements. Non-versive head movement has been reported to occur in tandem with dystonic posturing (Fakhoury and Abou Khalil, 1995). It would be useful to further study with which other lateralizing signs non-versive movement occurs as an aid to correctly identify it

5.3 Non-Versive Head Movement

Non-versive head movement is described as appearing voluntary and "purposeful" in nature (Godoy et al., 1990; Serles et al., 1998). If occurring early in the seizure and before versive head movement, it is often in the ipsilateral direction to the seizure onset (Kernan et al., 1993a; Kernan et al., 1993b; Kotagal et al., 2000; Williamson et al., 1998; Wyllie et al., 1986a), if occurring within the first 10 seconds of clinical onset the head movement is of no lateralizing significance (Kernan et al., 1993b). Therefore, we excluded those seizures from further evaluation in which the patient turned the head in response to external stimuli, such as an EEG technician approaching the

patient and excluded head movement that had a shorter duration than 1.25 seconds. Thus, non-versive movement is of unreliable lateralizing value unless followed by a contralateral versive head movement (Kernan et al., 1993a; Kernan et al., 1993b; Wyllie et al., 1986a; Wyllie et al., 1986b).

Ipsilateral head turning has been associated with three sequences of head turning in TLE (Abou Khalil and Fakhoury, 1996). In seizures without focal jerking or secondary generalization: [1a] a single ipsilateral head turn or [1b] two or more turns, with the first two turns in the ipsilateral direction. In seizures with secondary generalization: [2] a non-tonic ipsilateral head turn followed by a tonic contralateral head turn (Abou Khalil and Fakhoury, 1996). It has also been demonstrated that non-versive head turning occurring within 30s of seizure onset and with concomitant dystonic posturing lateralizes to the ipsilateral side (Fakhoury and Abou Khalil, 1995). Although cluster analysis of seizures was not applied, in the screening process for appropriate seizures, often a progression through consecutive seizures was seen as how the seizure evolved:

Seizure 1: alternating non-versive head turning ipsilaterally **Seizure 2**: a single non-versive head turn ipsilaterally accompanied by dystonic posturing of the contralateral arm **Seizure 3**: a single non-versive head turn ipsilaterally accompanied by dystonic posturing of the contralateral arm \rightarrow contralateral versive head turning \rightarrow secondary tonic-clonic generalization.

It is possible that the confusion in distinguishing versive and non-versive head movements stems from two factors: [1] the use of equivocal qualitative definitions that are used to identify these movements, [2] the failure to take the sequence of head movement into consideration.

5.4 New Objective Method

There is a poor inter-observer reliability for versive head movement particularly in extra-temporal lobe epilepsy (kappa 0.54), although it is more reliable for TLE (kappa 0.77) (Bleasel et al., 1997). These movements often occur in sequence with a non-versive head turn followed by head version, however both types of head turning have also been associated with many different lateralizing signs while also occurring in an isolated fashion (Sections 5.2 and 5.3). In the absence of a quantitative definition such information can further add to the confusion. Identification of these versive head movements often relies on clinical experience and higher inter-observer reliability is found amongst close working colleagues (Parra et al., 2001). To improve interobserver reliability and improve correct lateralization, head movements need to be quantitatively reviewed utilizing an objective method. By studying ictal head movements in both directions with regard seizure evolution, we could objectively quantify head movements while also identifying new criteria that allow versive head movements to be distinguished from non-versive head movements.

5.5 Quantitative Movement Analysis

We use a new objective method in quantifying versive head movements overcoming observer dependent differences. This method, based on previously quantitative movement analysis in seizures (Cuhna et al., 2003), is easily applicable to a normal epilepsy monitoring unit (EMU) environment. The archives of three independent epilepsy centres were used without installation of new hardware or further adjustments to the established monitoring set-up. There were negligible differences in quantitative results obtained from the three different centres. There was only one incidence where results did not concur between the three centres, the duration of contralateral head movements were not found to last significantly longer than in the ipsilateral direction. It should be noted however, that in five of the seizures taken, the contralateral head movement did last longer. The number of seizures taken from the Bethel Epilepsy Centre is small, allowing one unconventional seizure to have a greater effect on the overall statistics of the group.

Careful and constant selection criteria were applied, ensuring that the patient's position during version was kept similar in all cases. Two points were chosen, one on the nose and the other on the thorax of the patient, allowing the movement of the head relative to the trunk to be traced. With the interpretation of movement tracings in conjunction with recorded seizures much additional information about versive head movements can be gained. Movement tracings offer many advantages. They can be interpreted independent of any clinical experience. Each movement produces a pattern, allowing the observer to analyse the movement without any other distractions, such as clonic movement of limbs, which may influence his analysis of the head movement. The tracings also displayed movement patterns which were endemic to a particular movement tracing. It should be noted that the tracings from different seizures taken from the same patient after appropriate scaling looked similar (**Figure 7**).

The two-dimensional analysis bears several drawbacks, however. As figures 4 - 5 show that from 70 seizures displaying the desired sequence of head movement, over half (57%) were rejected and only 31 seizures cold be used for further analysis. Many were rejected due to the patient's head not being positioned perpendicular to and facing the camera. Head movement that was hidden from the camera for whatever reason or which did not allow both eves to be seen was rejected for angular analysis, as this movement could not be accurately measured due to the planar confinements of two-dimensional geometry. Absolute angular rotational measurements could not be made and angular speed measurements were confined to head movement in which both eyes were seen, ensuring that movement occurring only in the plane perpendicular to the camera was analysed (Figure 1 and 3). These confinements only allowed a small proportion of the entire movement to be measured with regard to angular speed. A three-dimensional method, however, could overcome these planar restrictions and allow absolute rotational distances to be further investigated.

5.6 Duration

Our study shows that the duration of contralateral versive head movement is significantly longer (p<0.001) than preceding ipsilateral head movement; an important criterion for the correct identification of versive movement when ictal head movement occurs as a sequence in both directions. However, this finding should be treated with care, as this difference while significant for the group of patients, is not always present in single cases. The overlap between the duration of head movement to be defined according to a definitive length of time. **Figure 8**, by means of a Box-and-Whisker Plot displays the significantly longer duration of the versive head movement in the contralateal direction (median 5.8s) in comparison to the ipsilateral head movement (median 2.9s) (p<0.001).

5.7 Angular Speed

Angular speeds of versive head movements are objectively faster for frontal lobe epilepsy than for TLE using this method (Wagner et al., 2004). Significant differences in the angular speeds of movement in either direction could not be found for TLE. **Figure 9** by means of a Box-and-Whisker Plot displays the similarity between the ipsilateral absolute angular speed (median 13.4 deg/s) and the contralateral absolute angular speed (median 12.3 deg/s). This finding fits well with the fact that we found ipsilateral movement to last significantly longer than contralateral movement. If there is no difference in angular speed than it will naturally take the head longer to turn contralaterally, as it must return to the midline after turning ipsilaterally before completing the contralateral turn. Again, however due to the 2-dimensional confinements, it should be noted that only a small proportion of the head turning was measured for angular speed and it is possible that the head accelerates later in the turn.

Figure 10 shows the correlation (r = 0.595) between angular speeds in either direction. It appears that fast movements in one direction are accompanied by fast movements in the other direction, likewise for slow movements. This confirms that there is no significant difference in the angular speed in either direction or in versive / non-versive head movement. In the contralateral direction, however, angular speed correlates significantly to the duration of the versive movement (r = -0.384) (**Figure 11**). Contralateral versive movements have a longer duration, which is a logical finding, only if a constant distance is being travelled with each versive movement. This significant correlation suggests, with regard to the pathophysiology of the seizure, that the rotational distance plays the defining role and not speed or duration of the versive movement. Another characteristic which differentiates versive head movement from non-versive movement.

5.8 Head Tilting

It is known from previous studies that stimulation of Brodman's area 6 elicits versive movements of the head, eyes and trunk to the opposite side (Godoy

et al., 1990). Upon stimulation, versive movement of the head always begins after the eye movement has started and occurs only with full-range eye deviations (Godov et al., 1990). Versive head movements are complex in nature, arising from the contraction of the ipsilateral sternocleidomastoid muscle. Three possible versive head turning patterns are described (Jayakar et al., 1992): contraversive rotation of face, ipsiversive tilting of the head or a combination of both (Jayakar et al., 1992). These patterns were observed with use of movement tracings, although we were unable to further quantify them, as this would require the evaluation of three-dimensional rotational distances. Ipsiversive tilting was noted to occur only in contralateral versive movements and not in ipsilateral head movements. The combination of ipsiversive tilting of the head and contraversive rotation of the face can occur throughout the versive movement. With the aid of movement tracings, however, ipsiversive head tilting was observed to occur sometimes in isolation at the beginning of the versive movement, followed by face rotation. Extension of the neck and positioning of the face upwards without a rotational component occurred at any time during the versive movement. Movement tracings shed interesting light on Javakar's findings and help greatly in identifying different components of versive head movement. These intricate components often appear visually as a single fluid movement, unfortunately however our two-dimensional model cannot further define or identify them reliably. Further three-dimensional analysis would be of great value in investigating these components in greater detail

5.9 Further work

We have established a new observer independent method to quantify ictal head movements in TLE. We have shown that this method can be easily applied in a normal EMU setting. This new method has innumerable applications in further investigations of seizure semiology. It has already been used to distinguish hypermotor from automotor seizures, by quantifying wrist and trunk movements (Meier et al., 2004). However due to the constraints of two-dimensional geometry, further studies of head turning should involve a three-dimensional method, in which the entire head movement could be measured.

We found there was a correlation between the duration and the angular speed of head movement in the contralateral direction. We could infer that the rotational distance travelled by the head is the defining parameter and neither duration nor angular speed. Analysis using three-dimensional technology could prove this. It would allow not only the angular speed of the entire head movement to be measured but also the rotational distance turned by the head, perhaps allowing a determinant angle to be defined.

Another great advantage to three-dimensional technology would be a smaller drop-out rate of seizures due to inappropriate positioning of the patient. The strict planar confinements of two-dimensional technology would not have to be considered and allow more seizures to be included in further investigations. A greater number of seizures with less strict inclusion criteria would allow cluster analysis of seizures to be more readily performed. This could allow our investigations to include a greater number of patients with a greater variety of head movement. For example, seizures in which patients displayed the sequence of a non-forced ipsilateral head turn followed by a versive head turn would be included. However preceding seizures, where perhaps the patient only displays alternating head turning in the ipsilateral direction could also be included and compared with head movement of other seizures, giving further information about the ipsilateral head turn in relation to versive head movement.

With a greater pool of available seizures the possibilities of further investigation are endless. This method could be used to define dystonic posturing as well as head tilting more accurately. The presence of correlations between the frequency of cloni and other movements could be investigated. With the use of synchronous EEG spread patterns and their clinical correlates could be easily visualized simultaneously.

Future investigations could compare how different lateralizing signs distinguish themselves among epilepsies of different foci. In a recent publication, gyratory seizures were reported to occur more frequently in FLE (Dobesberger et al., 2005). These seizures were divided into two types with regard their lateralization. Those rotations initiated by a versive head movement lateralized to the contralateral side, whereas those not preceded by a forced head movement lateralized to the ipsilateral side. With the ability to quantify absolute rotational distances, tilting and tonic posturing of the head, differences particular to a certain focus could be identified in different types of head movement and used not only to correctly lateralize a seizure but also to identify a possible focus.

5.10 Conclusions

The sequence of non-versive ipsilateral head movement followed by versive contralateral head movement has a high lateralizing value (PPV 100%) in TLE. Our analysis shows the importance of evaluating head movement quantitatively with regard to seizure evolution. The quantitative analysis of versive head movements provides additional information about duration and angular speed in an interobserver independent manner. Future studies should utilize three-dimensional technology, allowing further aspects of versive head movement to be objectively evaluated.

6 SUMMARY

6.1 English Version

The analysis of seizure semiology is a clinically well-established method in localization of the seizure onset zone of patients undergoing evaluation for epilepsy surgery. Lateralizing seizure phenomena are frequently observed. Some motor phenomena, such as dystonic posturing of the upper limbs show repeatedly to be of high and reliable lateralizing value (PPV 100%). The lateralizing value of versive head movements in TLE, however, has been subject to debate.

If defined as forced and involuntary head movement resulting in unnatural positioning, versive head movement displays a high PPV for localization of a contralateral seizure onset. Some have debated its lateralizing value. Non-forced head movement is not a lateralizing sign unless ending before generalization or followed by contralateral forced head movement, lateralizing to the ipsilateral side of the seizure onset zone. It is recognized that the qualitative nature of the definition of version may lead to its' questionable lateralizing reliability. The different interpretations of versive head movements may explain the presence of contradictory data.

In this situation, observer independent quantitative methods may help to resolve the problem. Therefore, we quantitatively analysed versive head movements with the application of a proposed method in a typical clinical EMU setting in three different EMUs using recently introduced video tracking technology for clinical application. We selected patients who displayed the precise seizure evolution of a head turn in one direction followed by a tonic head turn in the other direction. We investigated EEG-video recorded seizures of patients with TLE, in which the camera position was perpendicular to the head facing the camera in an upright position and bilateral head movement was recorded. Thirty-eight seizures (32 patients) with head movement in both directions were further investigated. Ipsilateral and contralateral head movement were defined according to ictal EEG. Using new tracking technology head movements were quantified by selecting the movement of the nose in relation to a defined point on the thorax, from which a movement tracing was generated and used for all subsequent analyses. The duration of the head version was determined independently of the camera angle. Due to the limitations of 2-dimensional geometry, only head movement in which both eyes could be seen in the video were used for analysizing angular speed. This ensured that the same plane in relation to the camera was always measured.

Ipsilateral movement always preceded contralateral movement. The positive predictive value (PPV) was 100% for movement in both directions. The duration of contralateral head version was significantly longer than ipsilateral head movement ($6.4s \pm 4.1s vs. 3.9s \pm 3.1s$, p<0.001). The angular speed of both movements was similar ($15.5deg/s \pm 12.1 deg/s vs. 17.3 deg/s \pm 13.0 deg/s$). In the contralateral direction, versive movements with higher speed had a shorter duration than versive movements with slower speeds. We infer from this finding that the absolute angle, through which the head turns, plays the defining role in versive head movements. This rotational distance possibly

remains constant for each particular head movement, however 3-dimensional analysis would be required to prove this.

This new method has many advantages. It has been applied without difficulty to three different EMUs, without further adjustments required to the established clinical set-up. The investigations in the three centres showed relatively homogenous results, adding to the validity of this method. This method is observer independent and requires little experience to correctly identify movement patterns form movement tracings. However, there are some disadvantages to this method, the most important being the constraints of 2-dimensional measurements. Only a limited portion of the head movement could be accurately measured with regard angular speed. Hundreds of seizures were initially reviewed but could not be further investigated due to inappropriate positioning of the patient, or the head could not be seen for more than five seconds. Head tilting during head turning could be identified in some instances. This was than verified in the videos; however, 2-dimensional geometry did not allow this movement to be further quantified.

Future studies using 3-dimensional technology could overcome the problems and limitations of our method. The intricacies and subtleties of all movement such as the absolute rotational distance or the degree of head tilting could be objectively and quantitatively defined. Our analysis shows the importance of evaluating head movement quantitatively with regard to seizure evolution, for the correct lateralization of versive head movements. We show that contralateral versive head movements have a longer duration than ipsilateral head movement in either direction. We establish a new observer independent method that can objectively quantify movement and show the lateralizing importance of ictal head movements.

6.2 Zusammenfassung

Die Analyse der Anfallssemiologie ist eine klinisch gut etablierte Methode zur Lokalisation der Anfallsursprungszone bei Patienten, bei denen eine prächirurgische Epilepsiediagnostik erfolgt. Lateralisierende Anfallsphänomene werden oft beobachtet. Manche Anfallsphänomene wie zum Beispiel unilaterale Handdystonien weisen zuverlässig auf die Ursprungshemisphäre (PPV = 100%) hin. Eine Kontroverse besteht jedoch in der Frage der korrekten Lateralisierung durch versive Kopfwendung.

Unter der Bedingung, dass als versive Kopfwendung nur heftige, anhaltende und unnatürlich anmutende Bewegungen gewertet werden, zeigte sich eine hohe Übereinstimmung mit einem kontrallateralen Anfallsursprung. Obwohl dieses Ergebnis mehrfach bestätigt werden konnten, wird es von manchen Autoren angezweifelt. Weniger heftige Bewegungen können nicht als Lateralisierungsphänome gewertet werden, es sei denn sie enden vor der Anfallsgeneralisierung oder werden von einer heftigen Bewegung gefolgt, die zur betroffenen Anfallsursprungsseite lateralisiert. Die Diskrepanz in der Literatur bezüglich der Wertigkeit von versiven Kopfwendungen zur Anfallslateralisation liegt vermutlich darin, dass von manchen Autoren keine Unterscheidung bezüglich Charakter oder Heftigkeit der Wendung getroffen wurde. Einfache und versive Kopfwendungen wurden gleichermaßen gewertet.

Vor dem Hintergrund diese Kontroverse, verwendeten wir eine neue quantitative Methode, wobei iktale Kopfwendungen unabhängig vom Beobachter analysiert wurden. Wir verwendeten zur Video Tracking Methode Anfallsvideos von drei verschiedenen typischen Epilepsie Monitoring Units (EMU). Zur Beobachtung wählten wir Patienten aus, die die bestimmte Anfallsevolution - von Kopfwendung auf die eine Seite, gefolgt von einer tonischen Kopfwendung in die andere Richtung - zeigten. Wir analysierten anschließend die EEG-gesteuerten Videoaufnahmen der Anfälle dieser TLE-Patienten. Dabei saßen die Patienten aufrecht im Bett, während die Kamera senkrecht zum Kopf des Patienten angebracht war. Die Kopfwendungen in beide Richtungen konnten dabei auf Video festgehalten werden. Von 32 Patienten wurden 38 Anfälle weiter analysiert. Die ipsilateralen und kontralateralen Bewegungen wurden nach der Anfallsursprungszone, die sich im EEG zeigte, definiert. Mittels neuer Tracking-Technologie konnte die Kopfbewegungen guantifiziert werden, indem die Bewegung der Nase in Bezug zu einem Fixpunkt auf dem Thorax des Patienten gesetzt wurde. Dadurch konnte die Bewegung auf dem Computer nachberechnet werden und die Daten standen weiteren Untersuchungen zur Verfügung. Die Analyse der Bewegungsdauer wurde unabhängig vom Kamerawinkel durchgeführt. Aufgrund der Zweidimensionalität des Kamerabildes wurden nur die Aufnahmen zur Errechung der Winkelgeschwindigkeit verwendet, bei denen beide Augen des Patienten zu sehen waren. So stellten wir sicher, dass immer nur dieselbe Fläche im Verhältnis zum Kamerawinkel gemessen wurde.

Die ipsilaterale Bewegung ging der kontralateralen jeweils immer voraus. Der PPV befand sich jeweils bei 100% für die Bewegungen in beide Richtungen. Die kontralateralen Kopfbewegung dauerte signifikant länger als die ipsilaterale ($6,4s \pm 4,1s vs. 3,9s \pm 3,1s, p < 0,001$). Die Winkelgeschwindigkeit beider Bewegungen war ähnlich ($15,5 \text{ deg/s} \pm 12,1 \text{ deg/s} vs. 17,3 \text{ deg/s} \pm 13,0 \text{ deg/s}$). In der kontralateralen Richtung zeigten die versiven Bewegungen eine höhere Geschwindigkeit und waren auch schneller beendet. Wir folgern daraus, dass der absolute Winkel durch den der Kopf dreht eine entscheidende Rolle für Definition versiver Kopfwendungen spielt. Wahrscheinlich bleibt die Drehung für die entsprechende Wendung konstant, allerdings bräuchte man weitere dreidimensionale Analysen um den absoluten Wert dieser Drehung zu beweisen.

Die angewandte neue Analysemethode weist viele Vorteile auf. Ohne jegliche Schwierigkeiten konnte sie in drei verschiedenen EMUs angewandt werden. Der klinische Alltag wurde durch keinerlei weitere Veränderung gestört und die Untersuchungen an den drei verschieden Zentren zeigten relativ homogene Resultate, was die Validität der Methode weiter erhärtet. Die Methode ist Beobachter-unabhängig durchzuführen und bedarf nur wenig Erfahrung um die zu untersuchenden Bewegungsmuster richtig zu erkennen. Trotzdem wurden in der Anwendung ein paar Nachteile offenbar. Am schwerwiegendsten war wohl die Tatsache, dass, wie bereits erwähnt, nur zweidimensionale Daten gewonnen werden konnten, so dass nur wenige Videos schließlich weiter analysiert werden konnten. Einige Hundert Anfälle wurden aufgenommen und schienen initial verwendbar, konnten dann aber im Verlauf nicht mehr weiter untersucht werden, aufgrund einer für die Kamera ungünstigen Kopfhaltung des Patienten während des Anfalls, oder weil der Kopf des Patienten für nur weniger als fünf Sekunden zu sehen war. Manchmal konnte ein Abkippen des Kopfes während der Drehung festgestellt werden. Dies wurde dann mit Hilfe der Videos verifiziert, konnte aber in Folge der Zweidimensionalität nicht weiter guantifiziert werden.

Zukünftige dreidimensionale Untersuchungen könnten die Probleme und Eingrenzungen der von uns angewandten Methode überwinden. Die Feinheiten aller Bewegungen, wie zum Beispiel die absolute Kopfdrehung oder der Winkel der Kopfkippung könnten dann objektiviert und quantifiziert werden. Unsere Analyse zeigt, wie wichtig es ist, die Kopfbewegungen in Hinsicht auf die Anfallsentwicklung zu evaluieren, um versive Kopfbewegungen richtig zuordnen zu können. Wir konnten zeigen, dass versive kontralaterale Kopfwendungen länger dauern, als ipsilaterale. Dabei machten wir keinen signifikanten Unterschied in der Winkelgeschindigkeit in beide Richtungen aus. Wir etablierten eine neue Methode, die unabhängig vom Beobachter ausgeübt werden kann, die es erlaubt die Bewegungen objektiv zu quantifizieren und die eine große Bedeutung für die korrekte Seitenzuordung iktaler Bewegungen für die epilepsiechirurgische Diagnostik hat.

7 FIGURES AND TABLES

7.1 Legend to Figures

Figure 1: Geometrical Set-up in typical clinical setting; T = tilting angle, F= FOV angle.

Figure 2: Shows the use of a reference pointing a defined clinical set-up accurately allows angle α i to be measured and reflects the real movement of the head.

Figure 3: Ipsilateral movement of nose in relation to a defined point on the trunk is measured in a defined clinical set-up.

Figure 4: Movement tracing used to define different components of sequence of movements.

Figure 5: Movement tracing showing movement appropriate for analysis.

Figure 6a-d: Overview of Patient Collective for all patients reviewed in three different epilepsy centres.

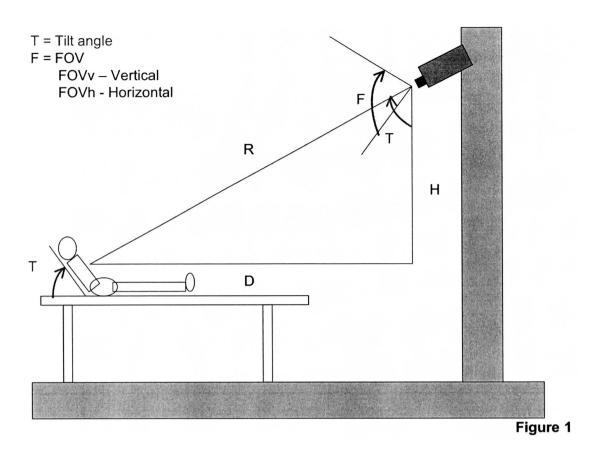
Figure 7: Movement tracings taken from two consecutive seizures showing similar movement pattern, especially in the ipsilateral turning of the head.

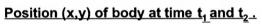
Figure 8: Box & Whisker Plot displaying significantly longer duration of the contraversion (median 5.8s) in comparison to the ipsiversion (median 2.9s) (p<0.001).

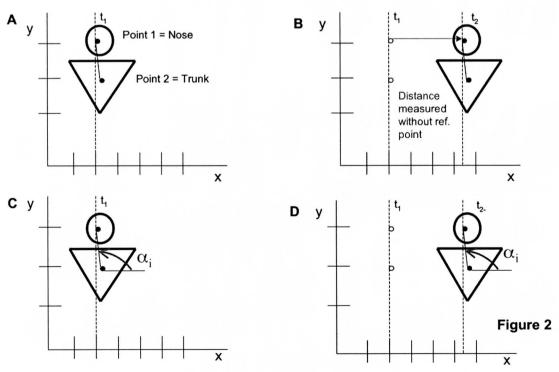
Figure 9: Box & Whisker Plot displaying the similarity between the ipsilateral absolute angular speed (median 13.4 deg/s) and the contralateral absolute angular speed (median 12.3 deg/s).

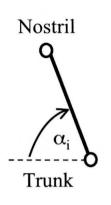
Figure 10: Displays the correlation between angular speeds in either direction, fast ipsilateral speeds are more likely to be followed by fast contralateral speeds. (r = 0.595, p<0.001).

Figure 11: Displays the correlation between angular speed in the contralateral direction and its duration (r = -0.384, p = 0.01).



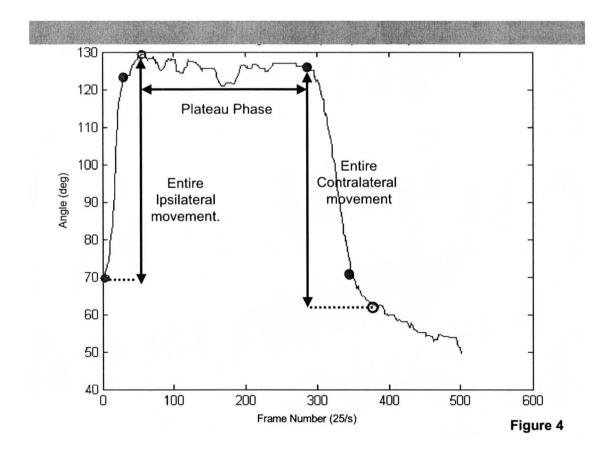












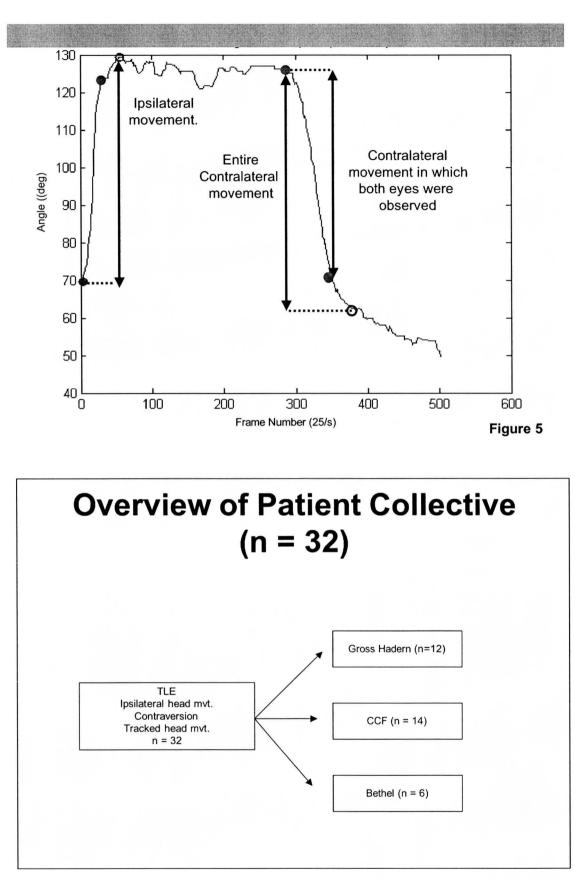


Figure 6a

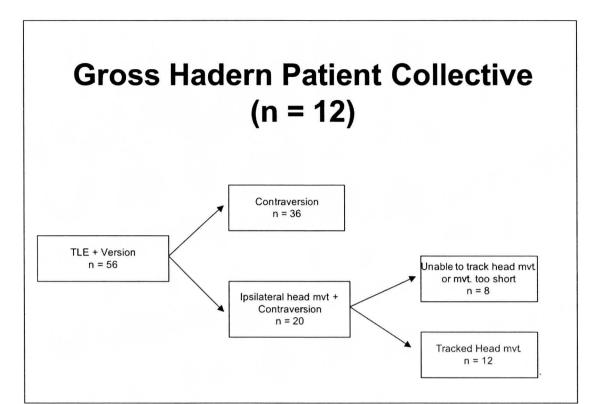
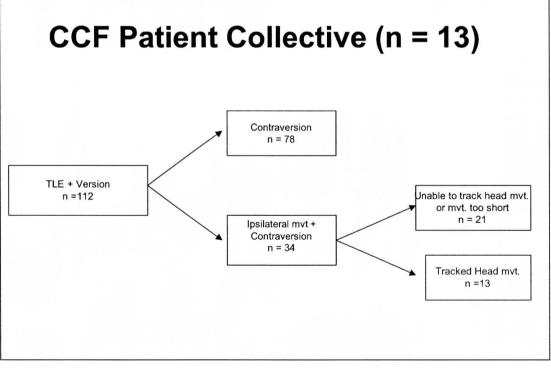


Figure 6b





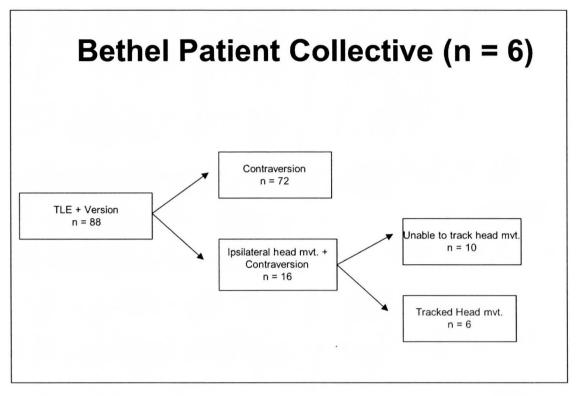
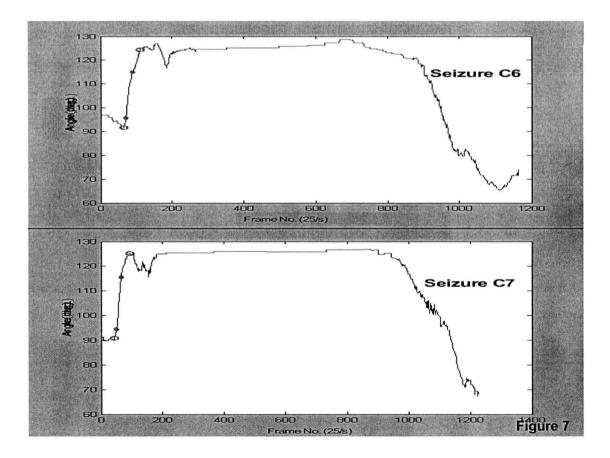
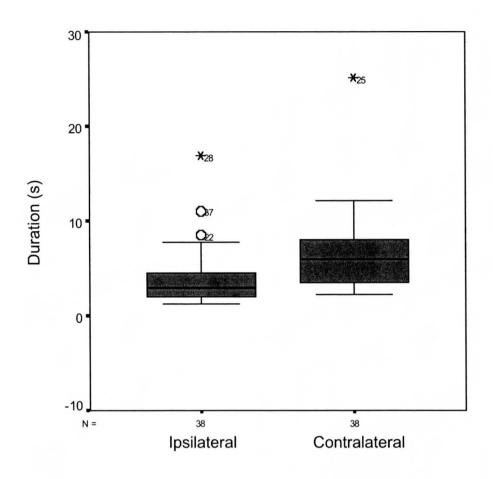
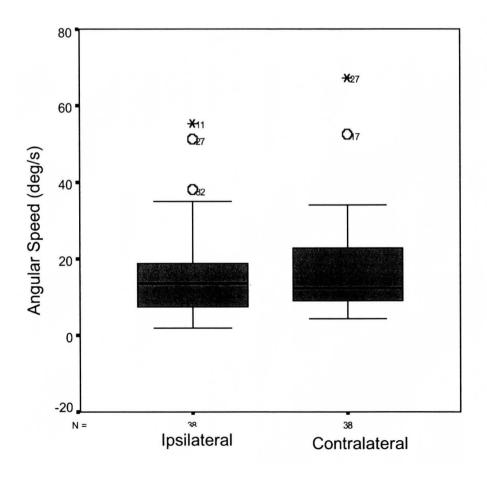


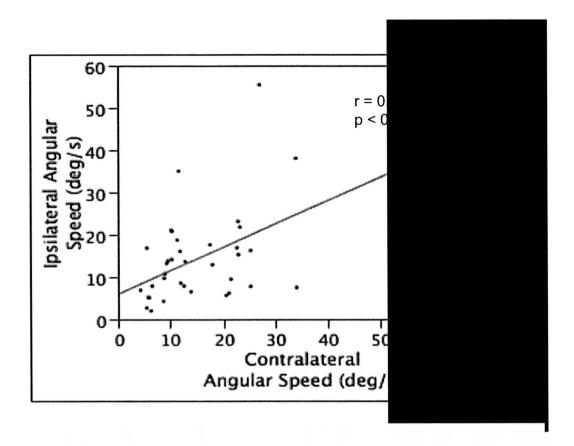
Figure 6d











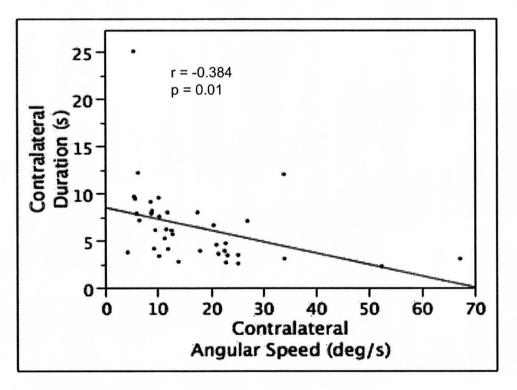


Figure 11

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7.2 Tables

Table 1: Patient data including seizure semiology, MRI findings and surgery outcome.

Pat. #	Sz. #	TLE	Age [years] (gender)	Age at onset	MRI findings	Seizure semiology	lctal EEG	Surgery Outcome (Engel et al., 1993)
G1	1	Bilateral	41 (m)	21	nl	Abdominal aura \rightarrow automotor sz. \rightarrow GTC sz.	Right temporal	No surgery
G2	2	Right	28 (f)	9	nl Automotor sz. \rightarrow GTC sz.		Right temporal	IC
G3	3	Left	39 (m)	5	Post Left temporal astrocytoma Aura \rightarrow automotor sz. \rightarrow GTC sz.		Left temporal	IC
G4	4	Right	58 (f)	23	nl	Abdominal aura \rightarrow automotor sz. \rightarrow GTC sz.	Right temporal	No surgery
G6	5	Left	43 (f)	2	Left mesial temporal sclerosis	Automotor sz. \rightarrow GTC sz.	Left temporal	ID
G7	6	Left	29 (f)	6	Left mesial temporal sclerosis	Automotor sz. \rightarrow GTC sz.	Left temporal	IC
G8	7	Right	27 (m)	16	nl	Aura \rightarrow automotor sz \rightarrow GTC sz.	Right temporal	IA
G9	8	Left	34 (m)	1	Bilateral mesial temporal sclerosis	Aura \rightarrow automotor sz \rightarrow GTC sz.	Left temporal	IA
G10	9	Right	42 (m)	21	nl	Abdominal aura \rightarrow automotor sz. \rightarrow GTC sz.	Right temporal	IA
G11	10	Right	39 (f)	5 R	Right mesial temporal sclerosis	Automotor sz. → GTC sz.	Right temporal	IA
GII	11	Right	39(1)	5	Right mesial temporal scierosis		Right temporal	IA
G12	12	Bilateral	36 (m)	30	Bilateral parahippocampal	Automotor sz. \rightarrow GTC sz.	Right temporal	No ourgony
GIZ	13	Dilateral	30 (III)	30	edema	Automotor sz. \rightarrow GTC sz.	Left temporal	No surgery
B1	14	Left	24 (m)	7	Left mesial temporal sclerosis	Aura \rightarrow automotor sz. \rightarrow GTC sz.	Left temporal	IA
B2	15	Right	35 (f)	2	Right mesial temporal sclerosis	Aura \rightarrow automotor sz. \rightarrow GTC sz.	Right temporal	No surgery
B3	16	Right	34 (m)	30	Right mesial temporal sclerosis	Abdominal aura \rightarrow automotor sz. \rightarrow GTC sz.	Right temporal	IB
B4	17	Left	57 (m)	18	Left temporal pole hamartoma	Aura \rightarrow automotor sz. \rightarrow GTC sz.	Left temporal	No surgery
B5	18	Right	39 (f)	6	Right mesial temporal sclerosis	nporal sclerosis Aura \rightarrow automotor sz. \rightarrow GTC sz.		IA
B6	19	Left	15 (f)	7	nl Aura \rightarrow automotor sz. \rightarrow GTC sz.		Left temporal	IA
C1	20	Right	27 (m)	20	nl	Automotor sz. \rightarrow GTC sz.	Right temporal	IIIA
01	21	. ugin	27 (11)	20		Automotor sz. → GTC sz.	Right temporal	

			1					
C2	22	Left	42 (m)	29	Left mesial temporal sclerosis	Automotor sz. \rightarrow GTC sz.	Left temporal	IA
02	23		20		Automotor sz. \rightarrow GTC sz.	Left temporal		
C3	24	Left 10 (m)		1	Left mesial temporal sclerosis	Aura \rightarrow automotor sz. \rightarrow GTC sz.	Left temporal	IA
0.5	25	Len	10 (11)	1		Aura \rightarrow automotor sz. \rightarrow GTC sz.	Left temporal	IA
C4	26	Right	52 (m)	21	Right mesial temporal sclerosis	Aura \rightarrow automotor sz. \rightarrow GTC sz.	Right temporal	IA
C5	27	Right	21 (m)	4	Right temporo-parietal encephalomalaciaAutomotor sz. \rightarrow GTC sz.F		Right temporal	IC
C6	28	Right	33 (m)	18	Right amygdala hamartoma	Automotor sz. \rightarrow GTC sz.	Right temporal	IA
C7	29	Left	11 (f)	3	Left temporal focal cortical dysplasia	Aura \rightarrow automotor sz \rightarrow GTC sz.	Left temporal	IA
C8	30	Right	27 (m)	4	Right mesial temporal sclerosis	Aura \rightarrow automotor sz \rightarrow GTC sz.	Right temporal	IC
C9	31	Left	32 (f)	10	Left mesial temporal sclerosis	eft mesial temporal sclerosis Aura \rightarrow automotor sz \rightarrow GTC sz.		IA
C10	32	Left	34 (f)	5	Left mesial temporal sclerosis	Abdominal aura \rightarrow automotor sz. \rightarrow GTC sz.	Left temporal	No surgery
C11	33	Right	53 (f)	12	Right mesial temporal sclerosis	Automotor sz. \rightarrow GTC sz.	Right temporal	IA
C12	34	Loft	11 (F)	10	Loft modial temporal coloradia	Aura \rightarrow automotor sz. \rightarrow GTC sz.	Left temporal	IA
012	35	Left 44 (f) 19		19	Left mesial temporal sclerosis	Aura \rightarrow automotor sz. \rightarrow GTC sz.	Left temporal	IA
C13	36 Diabt 10 (m)		10 (~l	Aura \rightarrow automotor sz. \rightarrow GTC sz.	Right temporal	IA	
	37	Right	16 (m)	9	nl	Aura \rightarrow automotor sz. \rightarrow GTC sz.	Right temporal	IA
C14	38	Left	15 (f)	6	Left parahippocampal hamartoma	Automotor sz. \rightarrow GTC sz.	Left temporal	IB

nl= normal; sz. = seizure; GTC = generalized tonic-clonic

Duration (s)							
	Ipsilateral	Contralateral	Difference				
Mean	3.9	6.4					
SD	3.1	4.1	p<0.001				
Median	2.9	5.8					

Table 2: Duration of Head Movements in both Directions.

Table 2a: Duration of Head Movements in each Centre.

Duration (s)							
	Ipsilateral Contralateral						
Großhadern							
Mean	3.85	6.17	p=0.01				
SD	1.98	1.79					
CCF							
Mean	3.42	3.64	p=0.01				
SD	6.37	5.40					
Bethel							
Mean	5.40	3.48	n.s.				
SD	6.97	3.27					

Angular Speed (deg/s)							
	Ipsilateral	Contralateral	Difference				
Mean	15.5	17.3					
SD	12.1	13.0	n.s.				
Median	13.4	12.3					

Table 3: Angular Speed of Head Movements in both Directions.

Table 3a: Angular Speed of Head Movements in each Centre.

Angular Speed (deg/s)						
	Ipsilateral Contralateral					
<u>Großhadern</u>						
Mean	17.72	14.54	n.s.			
SD	13.97	6.92				
CCF						
Mean	15.43	12.23	n.s.			
SD	21.28	16.45				
<u>Bethel</u>						
Mean	10.81	6.30	n.s.			
SD	10.68	5.57				

		Ipsilateral	Contralateral	Ipsilateral	Contralateral
		Speed	Speed	Duration	Duration
Ipsilateral	Correlation	1	0.595	-0.265	-0.135
Speed	P value		0.001	0.108	0.419
Contralateral	Correlation	0.595	1	-0.189	-0.384
Speed	P value	0.001		0.256	0.01

Table 4: Correlation of Angular Speed and Duration of Head Movements.

Table 5: Review of further variables.

Pat.	Sz.	. Automatisms	Dystonic	Neck Extension /	Angular Spe	eed (degrees/s)	Duration (s)	
#	#	Automatisms	Posturing	identified through tracing	Ipsilateral	Contralateral	lpsilateral	Contralateral
G1	1	Bilateral hand	Upper limbs	-	13.2	9.37	3.4	4.12
G2	2	Ipsilateral limbs	Upper limbs	-	16.86	22.66	3.72	3.88
G3	3	Ipsilateral limbs	Sign of 4	yes / not identified	34.99	11.67	1.28	6.16
G4	4	Oral & ipsilateral hand	Disrupted	-	12.88	17.96	2	3.88
G6	5	Ipsilateral limbs	Disrupted	yes / identified	18.72	11.37	5.64	5.2
G7	6	Bilateral hand	Disrupted	yes / identified	5.13	5.82	3.88	9.4
G8	7	None	Upper limbs, Sign of 4	yes / not identified	13.61	12.85	3.48	5.64
G9	8	None	Contralateral upper limb, Sign of 4	yes / identified	16.05	11.9	7.76	7.96
G10	9	Ipsilateral limbs	Upper limbs	-	23.11	22.87	1.48	4.68
014	10	Dilatarakkanak	Contralateral		9.7	8.88	4.24	7.84
G11	11	Bilateral hand	upper limb	yes / identified	5.07	6.05	4.2	7.84
G12	12	Oral & ipsilateral	Cian of 4		55.41	27.07	2.12	7.04
GIZ	13	limbs	Sign of 4	-	5.6	20.55	6.88	6.6
B1	14	None	Upper limbs	yes / identified	10.7	9.01	4.8	8.12
B2	15	Oral	-	yes / not identified	14.11	10.33	2.32	3.32
B3	16	Hidden	-	yes / identified	7.84	6.6	6.16	7.12
B4	17	Hidden	-	-	1.97	6.36	6.76	12.16
B5	18	Bilateral hand	-	-	9.45	21.48	11.04	3.56
B6	19	lpsilateral hand	Contralateral limbs	-	20.76	10.35	1.32	7.52

C1	20	Bilateral hand	Sign of 4	yes / identified	21.06	10.25	2.12	9.52
	21				16.83	5.59	2.04	9.64
C2	22	Hidden	-	yes / identified	23.56	52.41	1.36	2.24
02	23	Thaten	-	yes / identified	13.79	9.61	1.24	6.08
C3	24	Oral	Sign of 4	yes / not identified	8.52	12	2.84	4.08
00	25	Orar	Oigh of 4	yes / not identified	6.5	13.94	3.32	2.72
C4	26	Oral	-	yes / identified	4.23	8.75	4.52	9.08
C5	27	lpsilateral limbs	Fencing position	yes / identified	7.83	12.64	8.44	6.04
C6	28	Oral	Upper limbs	yes / identified	6.14	21.11	1.36	4.52
C7	29	-	-	yes / identified	7.48	34.1	2.88	3.04
C8	30	Hidden	-	yes / identified	2.68	5.53	3.76	25.08
C9	31	Hidden	Upper limbs	yes / identified	21.79	23.22	2.24	3.4
C10	32	lpsilateral hand and head	Upper limbs	-	51.21	67.26	2.2	3.04
C11	33	-	Fencing position	-	17.61	17.49	16.84	7.96
C12	34	Oral	Upper	yes / identified	16.25	25.29	1.4	3.44
012	35	Orai	limbs/Sign of 4	yes / identified	14.96	21.44	2.28	2.96
012	36	Incilatoral	Linnerlimbe	veo / identified	6.88	4.37	2.44	3.72
C13	37	lpsilateral	Upper limbs	yes / identified	38.02	34	1.36	12
C14	38	Oral	Sign of 4	yes / identified	7.74	25.28	2.32	2.52

8 REFERENCES

- 1. Abou Khalil B, Fakhoury T. Significance of head turn sequences in temporal lobe onset seizures. 1996; 23: 245-250.
- 2. Ajmone-Marsan C, Goldhammer L. Clinical ictal patterns and electrographic data in cases of partial seizures of fronto-central-parietal origin. In: Brazier MAB, editor. Epilepsy: its phenomena in man. New York: Academic Press, 1973: 235-258.
- 3. Ajmone-Marsan C, VanBuren J. Epileptiform activity in cortical and subcortical structures in the temporal lobe of man. Springfiled, 1958.
- 4. Altiparmak U, Eggenberger E, Coleman A, K C. The ratio of square wave jerk rates to blink rates distinguishes progressive supranuclear palsy from Parkinson disease. J Neuroophthalmol. 2006; 26: 257-9.
- 5. Berger H. Über das Elektrenkephalogramm des Menschen. Arch Psychiat Nervkrankh 1929; 87: 527-70.
- 6. Berger H. Über das Electrenkephalogramm des Menschen. Arch Psychiat Nervkrankh 1933; 100: 301-20.
- 7. Bleasel A, Kotagal P, Kankirawatana P, Rybicki L. Lateralizing value and semiology of ictal limb posturing and version in temporal lobe and extratemporal epilepsy. Epilepsia 1997; 38: 168-174.
- Bowers D, Miller K, Bosch W, Gokcay D, Pedraza O, Springer U, et al. Faces of emotion in Parkinsons disease: micro-expressivity and bradykinesia during voluntary facial expressions. J Int Neuropsychol Soc. 2006; 12: 6.
- 9. Chee MW, Kotagal P, Van Ness PC, Gragg L, Murphy D, Lüders HO. Lateralizing signs in intractable partial epilepsy: blinded multiple-observer analysis. Neurology 1993; 43: 2519-2525.
- 10. Chee MW, So NK, Dinner DS. Speech and the dominant superior frontal gyrus: correlation of ictal symptoms, EEG, and results of surgical resection. 1997; 14: 226-229.
- 11. Cuhna JP, Vollmar C, Li Z, Fernandes J, Feddersen B, Noachtar S. Movement quantification during epileptic seizures: a new technical contribution to the evaluation of the seizure semiology. 25th Annual International Conference of the IEEE EMBS. Cancun, Mexico, 2003.
- 12. Dobesberger J, Walser G, Embacher N, Unterberger I, Luef G, Bauer G, et al. Gyratory seizures revisited. Neurology 2005; 56: 1884-1887.

- 13. Dupont S, Semah F, Boon PA, Saint-Hilaire JM, Adam C, Broglin D, et al. Association of ipsilateral motor automatisms and contralateral dystonic posturing: a clinical feature differentiating medial from neocortical temporal lobe epilepsy. Arch Neurol 1999; 56: 927-932.
- 14. Ebner A, Dinner DS, Noachtar S, Lüders H. Automatisms with preserved responsiveness: a lateralizing sign in psychomotor seizures. Neurology 1995; 45: 61-4.
- 15. Engel JJ, Van Ness PC, Rasmussen TB, Ojemann LM. Outcome with respect to epileptic seizure. In: Engel JJ, editor. Surgical treatment of the epilepsies. New York: Raven Press, 1993: 609-621.
- 16. Fakhoury T, Abou Khalil B. Association of ipsilateral head turning and dystonia in temporal lobe seizures. Epilepsia 1995; 36: 1065-1070.
- 17. Fakhoury T, Abou-Khalil B, Peguero E. Differentiating clinical features of right and left temporal lobe seizures. Epilepsia 1994; 35: 1038-1044.
- 18. Ferrier D. The localization of function in the brain. Proc Roy Soc Lond Vol 22. London, 1874: 229-67.
- 19. Ferrier D. Functions of the Brain. New York: GP Putnam & Sons, 1886.
- 20. Ferrier D. Experimental researches in cerebral physiology and pathology. Rep West Riding Lunatic Asylum 1893: 30-96.
- 21. Foerster O. The cerebral cortex in man. Lancet 1931; 2: 309-312.
- 22. Fritsch G, Hitzig E. ∫ber elektrische Erregbarkeit des Grosshirns. Arch Anat Physiol Med Wiss 1870; 37: 300-332.
- 23. Gabr M, Lüders H, Dinner D, Morris H, Wyllie E. Speech manifestations in lateralization of temporal lobe seizures. Ann Neurol 1989; 25: 82-87.
- 24. Gastaut H. Certain Basic Concepts Concerning the Treatment of the Epilepsies. Br J Clin Pract. 1964; 18: 463-8.
- 25. Gibbs EL, Gibbs FA, Fuster B. Psychomotor epilepsy. Arch Neurol Psychiatry 1948; 60: 331-339.
- 26. Gil-Nagel A, Risinger MW. Ictal semiology in hippocampal versus extrahippocampal temporal lobe epilepsy. Brain 1997; 120: 183-192.
- 27. Godoy J, Lüders H, Dinner DS, Morris HH, Wyllie E. Versive eye movements elicited by cortical stimulation of the human brain. Neurology 1990; 40: 296-299.

- Goldensohn E. Simultaneous recording of EEG and clinical seizures using the kineoscope [abstract]. Electreoencephaolgr Clin Neurophysiol 1966; 21: 623.
- 29. Gupta AK, Jeavons PM, Hughes RC, Covanis A. Aura in temporal lobe epilepsy: clinical and electroenecephalographic correlation. J Neurol Neurosurg Psychiatry 1983; 46: 1083.
- 30. Henkel A, Noachtar S, Pfänder M, Lüders HO. The localizing value of the abdominal aura and its evolution: a study in focal epilepsies. Neurology 2002; 58: 271-6.
- 31. Horsley V. Brain-surgery. Br Med J 1886; 2: 670-675.
- Jackson G, Berkovic S, Tress B, Kalnins R, Fabinyi G, Bladin P. Hippocampal sclerosis may be reliably detected by MRI. Neurology 1990; 40: 1869-1875.
- 33. Jackson JH. Epileptiform seizures, aura from the thumb, attacks of coloured visions. Medical Times and Gazette 1863; 1: 589-590.
- 34. Jackson JH. Lectures on the diagnosis of epilepsy. Lecture III. Medical Times and Gazette 1879; 1: 141-143.
- 35. Jasper H, Pertuisset B, Flanigin H. EEG and cortical electrograms in patients with temporal lobe seizures. Arch Neurol Psychiatry 1951; 65: 272-290.
- Jayakar P, Duchowny M, Resnick T, Alvarez L. Ictal head deviation: lateralizing significance of the pattern of head movement. Neurology 1992; 42: 1989-1992.
- Jobbagy A. Fault diagnosis in biomedical engineering application. Dept. Meas. Inform. Syst. Budapest, Tech. Univ. Budapest. Budapest: Technical University Budapest, 1997.
- 38. Jobbagy A, Furnee EH, Harcos P, Tarczy M. Analysis of movement patterns aids rhe early detection of Parkinson's disease. 19th IEEE/EMBS. Chocago, IL, 1997: 81-8.
- 39. Kernan J, Devinsky O, Luciano D, Vazquez B, Perrine K. Lateralizing significance of head and eye deviation in secondary generalized tonic-clonic seizures. Neurology 1993a; 43: 1308-1310.
- 40. Kernan JC, Devinsky O, Luciano DJ, Vazquez B, Perrine K. Lateralizing significance of head and eye deviation in secondary generalized tonic-clonic seizures. Neurology 1993b; 43: 1308-1310.

- 41. Kotagal P. Seizure symptomatology of temporal lobe epilepsy. In: L∞ders HO, editor. Epilepsy Surgery. New York: Raven Press, 1991: 143-156.
- 42. Kotagal P, Bleasel A, Geller E, Kankirawatana P, Moorjani BI, Rybicki L. Lateralizing value of asymmetric tonic limb posturing observed in secondarily generalized tonic-clonic seizures. Epilepsia 2000; 41: 457-462.
- 43. Kotagal P, Lüders H, Williams G, Wyllie E, NIchols T, McPherson J. Temporal lobe complex partial seizures: analysis of symptom clusters and sequences. Epilepsia 1988; 29: 661.
- 44. Kotagal P, Lüders H, Morris HH, Dinner DS, Wyllie E, Godoy J, et al. Dystonic posturing in complex partial seizures of temporal lobe onset: a new lateralizing sign. Neurology 1989; 39: 196-201.
- 45. Kotagal P, Lüders HO, Williams G, Nichols TR, McPherson J. Psychomotor seizures of temporal lobe onset: analysis of symptom clusters and sequences. Epilepsy Res 1995; 20: 49-67.
- 46. Laxer KD, Garcia PA. Imaging criteria to identify the epileptic focus. Magnetic resonance imaging, magnetic resonance spectroscopy, positron emission tomography scanning, and single photon emission computed tomography. Neurosurg Clin N AM 1993; 4: 199-209.
- 47. Li Z, Martins da Silva A, Cunha JP. Movement quantification in epileptic seizures: a new approach to video-EEG analysis. IEEE Trans Biomed Eng 2002; 49: 565-73.
- 48. Lüders H, Acharya J, Baumgartner C, Benbadis S, Bleasel A, Burgess R, et al. Semiological seizure classification. Epilepsia 1998; 39: 1006-13.
- 49. Lüders HO, Awad IA. Conceptual considerations. In: Lüders HO, editor. Epilepsy surgery. New York: Raven Press, 1992: 51-62.
- 50. Lüders HO, Dinner DS, Morris HH, Wyllie E, Comair YG. Cortical electrical stimulation in humans. The negative motor areas. Adv Neurol 1995; 67: 115-129.
- 51. Lüders HO, Noachtar S. Atlas of epileptic seizures and syndromes. Philadelphia: Saunders, 2001.
- 52. McLachlan RS. The significance of head and eye turning in seizures. Neurology 1987; 37: 1617-1619.
- 53. Meier A, Cuhna JP, Mauerer C, Feddersen B, Noachtar S. Quantified analysis of wrist and trunk movements differentiates between hypermotor and automotor seizures. Epilepsia 2004; 45: 83.

- 54. Newton MR, Berkovic SF, Austin MC, Reutens DC, McKay WJ, Bladin PF. Dystonia, clinical lateralization, and regional blood flow changes in temporal lobe seizures. Neurology 1992; 42: 371-377.
- 55. Noachtar S. Der Klicker-Test: eine einfache Methode zur Überprüfung und Dokumentation der Bewusstseinslage im EEG. EEG Labor 1993; 15: 41-46.
- 56. Noachtar S. Seizure semiology. In: Lüders HO, editor. Epilepsy: comprehensive review and case discussions. London: Martin Dunitz Publishers, 2001: 127-140.
- 57. Noachtar S, Arnold S. Clonic seizures. In: Lüders HO and Noachtar S, editors. Epileptic seizures: pathophysiology and clincal semiology. New York: Churchill Livingstone, 2000: 412-424.
- 58. Noachtar S, Arnold S, Yousry TA, Bartenstein P, Werhahn KJ, Tatsch K. Ictal technetium-99m ethyl cysteinate dimer single-photon emission tomographic findings and propagation of epileptic seizure activity in patients with extratemporal epilepsies. Eur J Nucl Med 1998a; 25: 166-172.
- 59. Noachtar S, Burgess RC, Lüders H, Wyllie E, Awad I. Die epidurale "Peg"-Elektrode: eine neue semi-invasive Elektrode in der epilepsiechirurgischen Diagnostik. In: Scheffner D, editor. Epilepsie 90. Reinbek: Einhorn-Presse Verlag, 1991: 342-347.
- 60. Noachtar S, Ebner A, Dinner DS. Das Auftreten von Automatismen bei erhaltenem Bewusstsein. Zur Frage der Bewusstseinsst"rung bei komplexfokalen Anf, Ilen. In: Scheffner D, editor. Epilepsie 91. Reinbek: Einhorn-Presse Verlag, 1992: 82-87.
- 61. Noachtar S, Hufnagel A, Winkler PA. Chirurgische Behandlung der Epilepsien. In: Brandt T, Dichgans J and Diener J, editors. Therapie neurologischer Erkrankungen. München: Kohlhammer, 2003a: 236-251.
- 62. Noachtar S, Lüders HO, Holthausen H, May T, Chee M. Subdural and surface recordings of focal negative motor phenomena in epileptic seizures. Epilepsia 1994; 35: 123.
- 63. Noachtar S, Lüders HO. Classification of epileptic seizures and epileptic syndromes. In: Gildenberg PL and Taxer RR, editors. Textbook of stereotactic and functional neurosurgery. New York: McGraw-Hill, 1997: 1763-1774.
- 64. Noachtar S, Lüders HO, Bromfield EB. Surgical therapy of epilepsy. In: Brandt T, Caplan C, Dichgans J, Diener J and Kennard C, editors.

Neurological disorders: course and treatment. San Diego: Academic Press, 1996: 183-191.

- 65. Noachtar S, Pfänder M, Arnold S, Werhahn KJ, Müller A, Winkler PA, et al. Different seizure patterns in frontal and temporal lobe epilepsy. Epilepsia 1998b; 39: 113.
- 66. Noachtar S, Pfänder M, Arnold S, Werhahn K, Müller A, Ebner A, et al. Frequency and significance of lateralizing ictal signs and symptoms in temporal lobe epilepsies. J Neurol 1997; 244: S30.
- 67. Noachtar S, Rosenow F, Arnold S, Baumgartner C, Ebner A, Hamer H, et al. Die semiologische Klassifikation epileptischer Anfälle. Nervenarzt 1998c; 69: 117-126.
- Noachtar S, Winkler PA, Lüders HO. Surgical therapy of epilepsy. In: Brandt T, Caplan C, Dichgans J, Diener J and Kennard C, editors. Neurological disorders: course and treatment. San Diego: Academic Press, 2003b: 235-244.
- 69. O'Brien TJ, Kilpatrick C, Murrie V, Vogrin S, Morris K, Cook MJ. Temporal lobe epilepsy caused by mesial temporal sclerosis and temporal neocortical lesions. A clinical and electroencephalographic study of 46 pathologically proven cases. Brain 1996; 119: 2133-2141.
- Ochs R, Gloor P, Quesney F, Ives J, Olivier A. Does head-turning during a seizure have lateralizing or localizing significance? Neurology 1984; 34: 884-890.
- Oestreich LJ, Berg MJ, Bachmann DL, Burchfiel J, Erba G. Ictal contralateral paresis in complex partial seizures. Epilepsia 1995; 36: 671-5.
- 72. Palmini A, Gloor P. The localizing value of auras in partial epilepsies. Neurology 1992; 42: 801-808.
- 73. Parra J, Augustijn PB, Geerts Y, van Emde Boas W. Classification of epileptic seizures: a comparison of two systems. Epilepsia 2001; 42: 476-82.
- 74. Penfield W, Jasper H. Epilepsy and the functional anatomy of the human brain. Boston: Brown Little & Co, 1954.
- 75. Penfield WG, Rasmussen TB. The Cerebral Cortex of Man. New York: Macmillan, 1950.

- 76. Penry JK, Porter RJ, Dreifuss FE. Simultaneous recording of absence seizures with videotape and electroencephalography: a study of 374 seizures in 48 patients. Brain 1975; 98: 427-440.
- 77. Pfänder M, Arnold S, Henkel A, Weil S, Werhahn KJ, Eisensehr I, et al. Clinical features and EEG findings differentiating mesial from neocortical temporal lobe epilepsy. Epileptic Disord 2002; 4: 189-95.
- Rasmussen T. Focal epilepsies of nontemporal and nonfrontal origin. In: Wieser HG and Elger C, editors. Presurgical evaluation of the epileptics. Berlin: Springer Verlag, 1987: 300-305.
- 79. Rasmussen T, Penfield W. Movement of head and eyes from stimulation of the human frontal cortex. Res Publ Ass Nerv Ment Dis 1947; 27: 346-61.
- 80. Robillard A, Saint-Hilaire JM, Mercier M, Bouvier G. The lateralizing and localizing value of adversion in epileptic seizures. Neurology 1983; 33: 1241-1242.
- 81. Rosenow F, Hamer HM, Knake S, Katsarou N, Fritsch B, Oertel WH, et al. Lateralisierende und lokalisierende Anfallssymptome: Bedeutung und Anwendung in der klinischen Praxis. Nervenarzt 2001; 72: 743-9.
- 82. Rosenow F, Lüders H. Presurgical evaluation of epilepsy. Brain 2001; 124: 1683-1700.
- 83. Sander T, Hildmann T, Janz D, Wienker TF, Neitzel H, Bianchi A, et al. The phenotypic spectrum related to the human epilepsy susceptibility gene "EJM1". Annals of Neurology 1995; 38: 210-217.
- 84. Saygi S, Spencer SS, Scheyer R, Katz A, Mattson R, Spencer DD. Differentiation of temporal lobe ictal behavior associated with hippocampal sclerosis and tumors of temporal lobe. Epilepsia 1994; 35: 737-742.
- 85. Serles W, Pataraia E, Bacher J, Olbrich A, Aull S, Lehrner J, et al. Clinical seizure lateralization in mesial temporal lobe epilepsy: Differences between patients with unitemporal and bitemporal interictal spikes. Neurology 1998; 50: 742-747.
- So N, Berkovic S, Andermann F, Kuzniecky R, Gendron D, Quesney LF. Myoclonus epilepsy and ragged-red fibres (MERRF). 2. Electrophysiological studies and comparison with other progressive myoclonus epilepsies. Brain 1989a; 112 (Pt 5): 1261-76.
- So N, Gloor P, Quesney LF, Jones-Gotman M, Olivier A, Andermann F. Depth electrode investigations in patients with bitemporal epileptiform abnormalities. Ann Neurol 1989b; 25: 423-31.

- Steinhoff BJ, Schindler M, Herrendorf G, Kurth C, Bittermann HJ, Paulus W. The lateralizing value of ictal clinical symptoms in uniregional temporal lobe epilepsy. 1998; 39: 72-79.
- 89. Tukey JW. Box-and-Whisker Plots. MA: Addison-Wesley, 1977.
- van Emde Boas W, Parra J. Long-term Noninvasive Video-Electroencephalographic Monitoring in Temporal Lobe Epilepsy. In: Lüders H and Comair Y, editors. Epilepsy Surgery. New York: Lippincott Williams & Wilkins, 2001: 413-429.
- Wada JA. Cerebral lateralization and epileptic manifestations. In: Akimoto H, Kazamatsuri H, Seino M and Ward A, editors. Advances in epileptology: XIII Epilepsy International Symposium. New York: Raven Press, 1982: 365-372.
- 92. Wagner P, Cuhna JP, Mauerer C, Vollmar C, Feddersen B, Noachtar S. Comparison of quantified ipsilateral and contralateral head movements in patients with frontal and temporal lobe epilepsies. Epilepsia 2004; 45: 269.
- 93. Wieser HG. Electroclinical features of the psychomotor seizure. Stuttgart: Fischer, 1983.
- 94. Wieser HG, Williamson P. Ictal semiology. In: Engel JJ, editor. Surgical treatment of the epilepsies. New York: Raven Press, 1993: 161-171.
- 95. Williamson P, Thadani VM, French JA, Darcey TM, Mattson RH, Spencer SS, et al. Medial Temporal Lobe Epilepsy: Video Analysis of Objective Clinical Seizure Characteristics. Epilepsia 1998; 39.
- 96. Wyllie E, Lüders H, Morris HH, Lesser RP, Dinner DS. The lateralizing significance of versive head and eye movements during epileptic seizures. Neurology 1986a; 36: 606-611.
- 97. Wyllie E, Lüders H, Morris HH, Lesser RP, Dinner DS, Goldstick L. Ipsilateral forced head and eye turning at the end of the generalized tonicclonic phase of versive seizures. Neurology 1986b; 36: 1212-1217.

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