Spatially Fixed Patterns Account for the Spike and Wave Features in Absence Seizures

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Summary: Despite genetic, morphological and experimental *in vivo* data implying fixed abnormalities in patients with absence seizures, attempts to find highly consistent features in the 3-Hz spike-and-wave pattern recorded during sequential seizures from the same subject have been largely unsuccessful. We used a new data decomposition technique called Independent Component Analysis (ICA) to separate multiple spike-and-wave episodes in the EEG recorded from five subjects with absence seizures into multiple consistent components. Each component corresponded to a temporally-independent waveform and a fixed spatial distribution. Almost all components separated by the ICA algorithm had overlapping, largely frontal spatial distributions. The analysis unmasked 5-8 components from each subject that were consistently activated across all seizures, with no components detected that were selectively activated by one seizure and not another. The "spike" and "wave" features noted in the EEG of every subject were each separated by the ICA algorithm into two or more components. Other components were active only at the beginning of each seizure or were related to ongoing brain activity not directly related to the 3Hz spike-and-wave pattern. By contrast, randomly selected spatial patterns used for data decomposition resulted in components that were uninformative, similar to simply changing the montage for viewing the EEG. Our results suggest that despite previously described variability in the raw EEG, certain highly specific spatial distributions of activation are reproducible across seizures. These may reflect ictal and non-ictal brain activity consistently activating the same group of neurons.

Key words: Absence seizures; Independent component analysis; Data decomposition.

Introduction

Absence (petit mal) seizures are generalized seizures affecting predominately children, typically lasting 2-10 sec, occasionally longer, and patients may exhibit numerous seizures within a 24-hr period (Adams and Victor 1989). Awareness is lost slightly after the onset of electroencephalographic (EEG) abnormalities, and returns shortly after their cessation. The seizures usually start without warning, with the patient alert and no obvious discerning features noticeable in the EEG prior to seizure onset. The EEG features associated with absence seizures are classically described as a bilaterally synchronous spike-and-wave discharge pattern, starting at about 3.0-3.5 Hz at the beginning of the seizure, and tending to slow to 2.5-3Hz towards the end of the seizure. Maximum negativity during spike-and-wave bursts occurs symmetrically, usually on the frontal leads (e.g., F7 and F8) (Berkovic 1993).

Many diverse factors have been implicated in the pathogenesis of absence seizures (Berkovic 1993). There is a strong associative link between genetic factors and absence seizures; the concordance of seizures between monozygotic twins is about 75% (Lennox and Lennox 1960). Gibbs et al. first proposed that a diffuse cortical abnormality was largely responsible for the spike-and-wave discharges (Gibbs et al. 1939), and many features point to the cortex as the primary locus. Morphological studies have revealed diffuse abnormalities of the gray matter and specifically areas of microdysgenesis (Meencke and Janz 1984; Meencke 1985; Meencke and Janz 1985). A feline generalized peni-

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cillin epilepsy model (Gloor 1979; Gloor and Fariello 1988) suggested that a generalized increase in excitability of cortical neurons would make spike-and-wave discharges more likely when the cortical neurons are bombarded with thalamocortical trains of action potentials. However, experimental evidence implicates the thalamus as important not only in initiating the spike-and-wave discharges, but also in sustaining the cyclic firing (Avoli et al. 1983; Danober et al. 1998). This is a refinement of the original centroencephalic hypothesis, that generalized seizures originate from the upper brainstem and diencephalon driving the cortex to spike-and-wave discharges (Jasper 1991).

The cellular mechanisms underlying the spike-and-wave oscillations characteristic of absence seizures have been investigated with *in vitro* preparations of ferret thalamic slices and computational models. These studies suggest that 2-4 Hz oscillations may arise from the reciprocal interactions between thalamocortical (TC) and inhibitory thalamic and reticular (RE) cells (Destexhe et al. 1996). TC cells can elicit α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA)-mediated excitatory post-synaptic potentials (EPSPs) in RE cells, whereas RE cells can elicit γ-aminobutyric acid-A ($GABA_A$) and $GABA_B$ inhibitory postsynaptic potentials (IPSPs) in TC cells. At hyperpolarized membrane potentials, the network of RE and TC cells can exhibit oscillations, but usually in the sleep spindle frequency range of 9-11 Hz.

GABA responses may be involved in the conversion from physiological spindle-frequency oscillations in the thalamo-cortical network to pathologic 3-Hz spike-and-wave discharges. In ferret thalamic slices, if the $GABA_A$-mediated lateral inhibition between RE cells is removed with bicuculline, the resultant prolonged burst discharges in response to EPSPs from TC cells transforms oscillations in the spindle frequency range into slower, more globally synchronized oscillations in the 2-4 Hz absence seizure range (Destexhe et al. 1996). Either $GABA_B$ antagonists or $GABA_A$ agonists abolish these synchronized, lower-frequency oscillations. This is consistent with results obtained with the lethargic (lh/lh) mouse, which serves as an animal model of absence seizures, where $GABA_B$ antagonists prevent the development of spike-and-wave discharges (Hosford et al. 1992; Getova et al. 1997).

Although morphological studies have implicated a cortical abnormality in patients with absence seizures, the original model of Destexhe et al. (1996) did not include the effects of cortical inputs. However, they suggested that suitably stimulated cortico-thalamo cells could produce strong enough discharges to overcome intact intra-RE inhibition to evoke bursts in RE cells. The prolonged bursts in RE cells can result in powerful $GABA_B$ dominated IPSPs in TC cells. The rebound burst in TC cells then occurs after a period of ~300 ms. The TC rebound can re-excite strong cortical discharges, allowing the development of ~3-Hz oscillations in the entire thalamocortical circuit. A recent model of thalamocortical interaction shows how a reduction of the fast $GABA_A$ inhibition in the cortex could lead to a recruitment of the slow $GABA_B$ inhibition in the thalamus and contribute to runaway spike-and-wave seizures (Destexhe 1998).

Even with complementary evidence from genetic, modeling and morphological studies pointing to specific, fixed abnormalities in absence seizure patients, attempts to find consistent features in different spike-and-wave patterns both between patients and especially within patients have been largely unsuccessful. For example, Prevett et al. (1995) performed a PET study on patients with absence seizures and detected a focal increase in thalamic blood flow during absence seizures but no consistent cortical focus when the results were averaged over several subjects. These results suggest that the locus of the cortical abnormality may be different for each person, and hence no cortical area of abnormal activation would reach statistical significance when averaged over all subjects. Differing loci of abnormalities between subjects may also be why these seizures can be classified by their transverse as well as their anterio-posterior topology (Dondey 1983). However, if there were a specific cortical abnormality in each subject, then careful analysis of different seizures from the same subject might reveal a consistent pattern among different seizures.

Digital EEG recording and analysis has allowed more accurate descriptions of the electroencephalopathic features of ictal events than visual inspection alone (Koszer et al. 1996), and may therefore provide clues to the loci of possible abnormalities in a given subject. Several methods have used digital EEG to quantitatively analyze absence seizures, including a careful examination of the raw data across seizures (Rodin and Ancheta 1987; Lemieux and Blume 1986), frequency analysis of the periods just before seizures (Ferri et al. 1995) , and fitting the scalp electrode voltages during seizures as activity to a fixed dipole (Rodin et al. 1994). A detailed examination of the raw digital EEG, as pointed out by Rodin and Ancheta (1987), reveals that the classic 3-Hz spike-and-wave pattern is neither truly generalized, nor exactly bilaterally symmetrical nor entirely synchronous (Rodin and Ancheta 1987). This study, and other quantitative analyses of absence seizures (Lemieux and Blume 1986) observed maximum positivity and negativity quite consistently in broad frontal areas in different absence seizures within subjects; however, the way in which positivity was reached varied considerably. In fact, successive spike-and-wave complexes could vary even

within the same seizure, leading to the conclusion that observing the raw EEG (as opposed to some underlying components of the EEG) to discern a consistent locus of abnormality could be misleading (Rodin and Ancheta 1987). A dipole analysis of the multiple voltages across different electrodes also failed to demonstrate features that were exactly consistent within seizures (Rodin et al. 1994).

Although it is clear that there may be variability in the raw EEG between seizures of a given subject, this does not preclude the possibility that there may be some underlying components of the EEG that are, in fact, constant across seizures. For example, if less than the entire cortex is involved in a seizure, activity from the non-seizing cortical regions could introduce variability in the EEG even when the regions involved in the seizure may be highly consistent between seizures. This suggests that it may be informative to separate the EEG into different components, to determine if some features or components are unmasked that are highly consistent across seizures. Separation of the EEG into differing temporal components is possible with a new data decomposition technique, Independent Component Analysis.

Independent Component Analysis (ICA)

ICA takes linear combinations of the channels from a multi-channel EEG recording to produce a new set of waveforms, numbering the same as the number of recorded channels, with each waveform associated with a specific static spatial distribution. Knowing the spatial patterns and their associated waveforms allows one to reconstruct the original EEG exactly; transformations like ICA are therefore a different way to view the same data, analogous to changing the montage when viewing the EEG. ICA (Comon 1994; Bell and Sejnowski 1995) assumes that the EEG is composed of mixed, statistically independent components of different strengths and tries to determine how to "unmix" the data to recover the underlying components.

To implement ICA, the EEG data for a given segment of time, or epoch, is first digitized and stored in an n by p matrix $\boldsymbol{X}$, where n is the number of channels and p is the number of time points in the epoch. The time waveforms recorded from each of the EEG electrodes during the epoch can be combined into a new set of waveforms, $\boldsymbol{C}$, by taking linear combinations, defined by an n by n matrix $\boldsymbol{W}$, of the recordings from each channel. Thus,

$$\boldsymbol{C} = \boldsymbol{W}\boldsymbol{X} \tag{1}$$

where $\boldsymbol{C}$ is an n by p matrix of transformed waveforms, $\boldsymbol{W}$ is an n by n matrix containing combinations of channels, and $\boldsymbol{X}$ is the n by p data matrix. If $\boldsymbol{W}$ is an invertible matrix, we can define $\boldsymbol{M} = \boldsymbol{W}^{-1}$, so that:

$$\boldsymbol{X} = \boldsymbol{M}\,\boldsymbol{C} \tag{2}$$

The general ICA algorithm assumes that the data can be modeled accurately as implied by equation 2, i.e., the data, $\boldsymbol{X}$, consists of n independent components linearly mixed as specified by matrix $\boldsymbol{M}$, and tries to blindly "unmix" the data to recover the original components $\boldsymbol{C}$. When applied to EEG data (Makeig et al. 1996; McKeown, Humphries et al. 1998) , ICA determines the optimum combination of channels (specified by $\boldsymbol{W}$ in equation 1) via an iterative training process that separates the EEG into component waveforms that are as statistically independent as possible so that the component waveforms sum together to the original EEG. No strong assumptions about the spatial distributions of each waveform need to be made.

Note that equation 2 has the effect of separating the temporal and spatial information contained in the EEG data matrix, $\boldsymbol{X}$, into temporal waveforms, $\boldsymbol{C}$, and fixed spatial combinations of channels, $\boldsymbol{W}$. The ICA algorithm determines $\boldsymbol{W}$ (from which $\boldsymbol{C}$ can be determined) and is oblivious to the temporal sequence of information contained in $\boldsymbol{X}$. It tries to find the combinations of channels that over the whole epoch result in temporally independent waveforms contained in $\boldsymbol{C}$. It is this property of being insensitive to temporal order that allows the EEG to be divided into sections, so that many seizures can be concatenated together to look for features constant across seizures.

We report here use of the ICA algorithm to separate the seizure patterns from five subjects into temporally-independent components and demonstrate that although the raw EEG can vary between seizures, there are some components that are constant across all seizures in a given subject.

Methods

Data Acquisition

Five subjects with absence seizures were recorded, ranging from age from 6-38yrs. Patient 1 was a 34 year old male, with intractable absence seizures since childhood, treated with Valproic acid and a vagal nerve stimulator for 2.5 yrs. Patient 2 was a 20 year old male, treated with Valproic acid and primidone, with a seven year history of seizures. Patient 3 was a 6 year old female with a 1.5 month history of typical absence. She was not on medication at the time of the recordings. Patient 4 was a 23 year old female with combined tonic-clonic and absence seizures treated with Valproic acid, Carbamazepine, and a vagal nerve stimulator. Patient 5 was a 38 yr old male treated with phenytoin, gabapentin, and ethosuxamide. He was seizure-free except for occasional minor absences.

EEG data were collected on a Nicolet machine (Model Voyageur, Nicolet, Inc, Madison, WI, USA), sampled at 256 Hz, with bandpass setting set at 1-70Hz (-3dB). Standard gold cup electrodes were employed and applied with electrode paste using the standard 10/20-electrode placement. The electrode impedance was always less than 5KΩ.

The EEG was recorded while the subject was awake for at least 20 min. No psychological testing was performed during the spike-and-wave activity. Data were recorded onto optical disk for later retrieval and analysis.

Data Processing and Analysis

The EEG data were read off the proprietary optical disk using a 200 MHz Pentium PC running the FreeBSD UNIX operating system, and transferred to a hard drive for later analysis with the MATLAB program (Mathworks, Inc, Natick, MA, USA). Twenty EEG channels were used for analysis, all channels referenced to lead A_1. (Note that the ICA algorithm puts the EEG into a "montage independent" format, and the components extracted are independent of the reference lead used).

Periods of spike-and-wave activity from the raw digital EEG were determined by visual inspection for each subject. All spike-and-wave periods from each subject were then excised and concatenated together to form one long data set for analysis. The data set from each subject was separated using the extended infomax ICA algorithm (Lee et al. 1998) implemented in MATLAB.

Results

The five subjects had 5, 6, 3, 11, and 18 separate episodes of spike-and-wave activity for a total seizure activity of 94, 52, 53, 40 and 48 sec respectively.

An ICA decomposition of all seizure activity for a given subject took approximately 30 min for the longest duration of combined seizure activity (patient 1, 94-sec) on a DEC alpha 300 MHz computer.

With 20 channels, the ICA method determined 20 temporally-independent components, each with its own scalp distribution. Almost all components had highly overlapping, largely frontal distributions (figures 1-6). Each subject had at least 5-8 out of 20 components that showed a consistent activation across all seizures in that particular subject (figure 1-2). Most other components were related to EKG or muscle artifacts, or had small variance and irregular, random-like time courses resembling noise of unknown origin (figure 2a). Across all subjects, no seizure-related components were selectively activated during one seizure and not another. In order to explore the specificity of the calculated components, various random spatial patterns were used to decompose the data (i.e., by selecting random elements selected from a Gaussian distribution to create "W" in equation 1). In all cases, application of the random matrices resulted in similar-looking components, comparable to viewing the raw EEG under a different montage (figure 2b).

The seizure-related components from each subject corresponded to either the "spike" or "wave" portions of the spike-and-wave pattern observed in the EEG, or were active during only part of the seizure, either at the beginning or a few seconds after seizure onset. Typically, two components from each patient corresponded to the "wave" portion of the spike-and-wave discharge observed in the EEG (figure 3). These two "wave" components had predominately frontal and medial spatial distributions for all subjects.

The "spike" of the spike-and-wave pattern was isolated into component(s) separate from the "wave" components in all subjects (figure 4). These components were also quite focal, predominately localizing to one or two channels, and largely overlapping but more focussed than the spatial distributions of the "wave" components.

Patients 1-3 had components that appeared to follow the "wave" of the spike-and-wave pattern during the early part of the seizure and then decayed away as the seizure progressed (figures 1 and 5).

The decomposition from patient 1 revealed a small component (~2.6% of the total variance of the raw EEG) that was composed of multiple sharply contoured waves at the beginning of each seizure (figure 6). To localize this component further, we reconstructed the data using only this component (i.e., using equation 2 and setting all columns in M except the appropriate column associated with this component to zero). The reconstructed data were then used as raw data for the BESA program (Neuroscan, Inc, Herndon, VA, USA) to fit a single dipole. This method yielded a dipole in the deep left dorso-lateral frontal region. By selecting the appropriate row of W in equation 1, we created a filter based on this component that could be applied to the entire data set. This filter detected the beginning of all seizures, in addition to the occasional short sections of the EEG that appeared to be a "form fruste" of a full-blown seizure (figure 6c, top). In some cases, the filter produced sharply contoured waves, with minimal changes observed in the raw EEG (figure 6c, bottom).

A few components were not directly time-locked to the 3 Hz spike-and-wave activity, appeared unrelated to known artifacts, and seemed most like other brain activity (figure 7) in the theta range. Careful inspection of the raw EEG suggested that these components appeared to correspond to subtle "notches" in the spike-and-wave pattern (large arrows, figure 7).

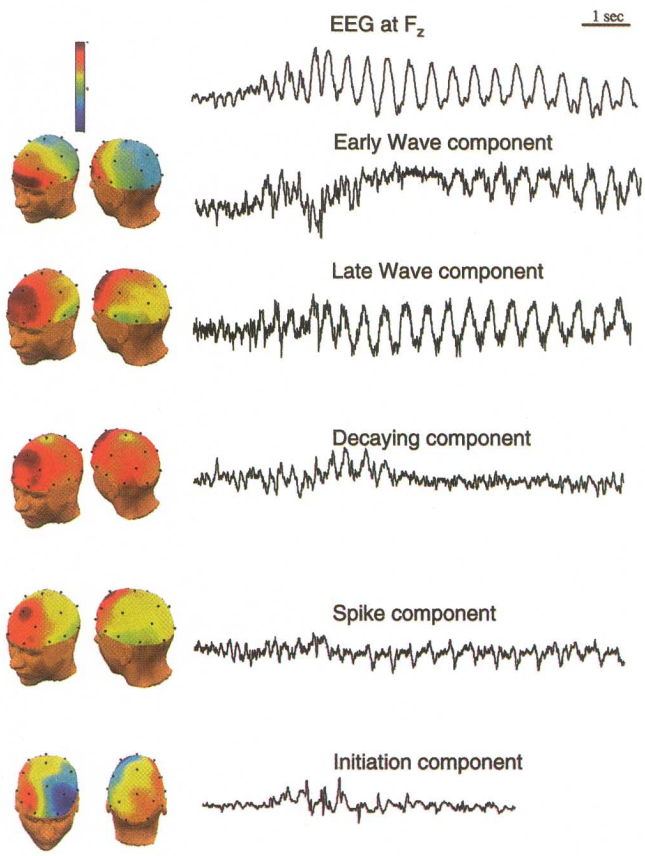

Figure 1. EEG components activated with each seizure. Some of the components from the first subject are shown, demonstrating the static spatial distributions and temporally independent waveforms. Dark values on the head figures show greater contribution (either positive or negative) of a channel to the given component spatial distribution. Although all waveforms were activated for each seizure, activity from one seizure is shown. The waveforms are not scaled to the size they would contribute to the original data for clarity. (a) The EEG recorded at lead Fz, (b) and (c) Components which appeared to follow the early and late parts of the "wave" of the spike-and-wave pattern, (d) A component whose activity appeared to decay as each seizure progressed, (e) A component corresponding to the subtle "spike" in the spike-and-wave pattern (compare to (a)), (f) A component that demonstrated sharply contoured waves at the start of each seizure.

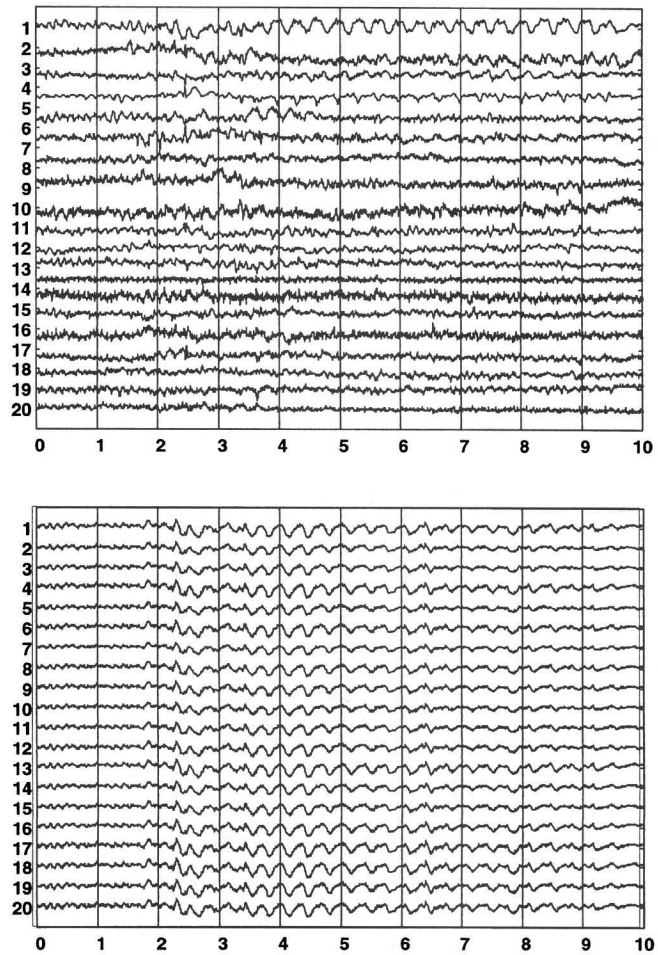

Figure 2. Specificity of computed ICA spatial patterns. (A - top) Application of spatial patterns determined with ICA resulted in 20 temporally independent waveforms corresponding to the "wave", "spike", artifacts and other features in the EEG. Ten seconds of data at the start of a seizure are shown. (B - bottom) Use of random spatial patterns to separate the same portion of the EEG into (dependent) temporal waveforms resulted in non-informative components that were similar to each other. Selection of other random patterns gave comparable results. Contrast with (a).

Discussion

The EEG is a complex mixture of signals from many sources and methods have been developed which attempt to decompose the EEG into different components. Principal Component Analysis (PCA), for example, that takes linear combinations of the channels from a multi-channel EEG recording to produce a new set of waveforms, equal to the number of recorded channels, with each waveform associated with a specific static spatial distribution (Lagerlund et al. 1997; Skrandies 1993). In PCA, the linear combinations are chosen so that the derived waveforms are uncorrelated. There are an infinite number of ways to separate the EEG into decorrelated waveforms or components, and PCA tries to find decorrelated waveforms that summarize the variability seen in all channels of the EEG in as few components as possible. However, if there is a small but consistent component across seizures, for example the "initiation component" that we describe, reducing

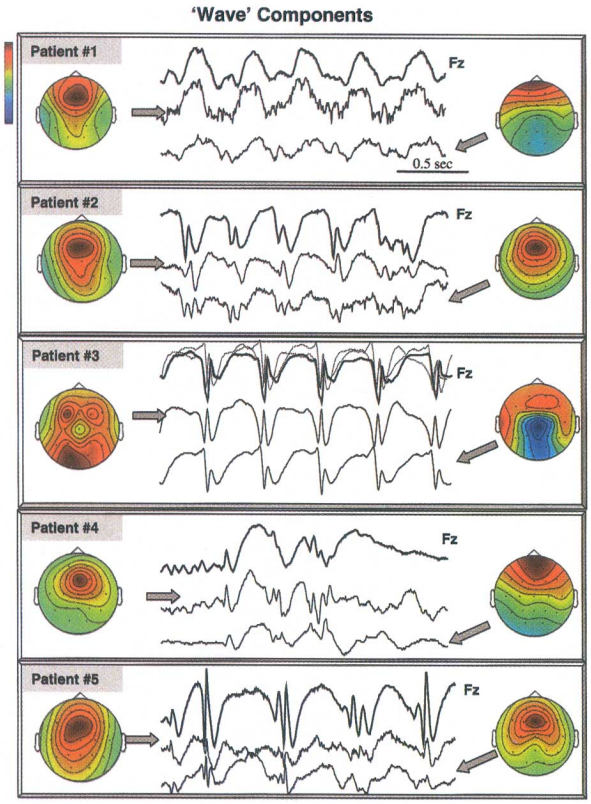

Figure 3. Wave independent components (ICs) of EEG from five subjects. Recording at F_z is shown above projections of two components onto F_z. Each subject has two components corresponding to the "wave" of the spike-and-wave complex. Note that the two components contributing to the raw data at Fz appear to account for different portions of the wave.

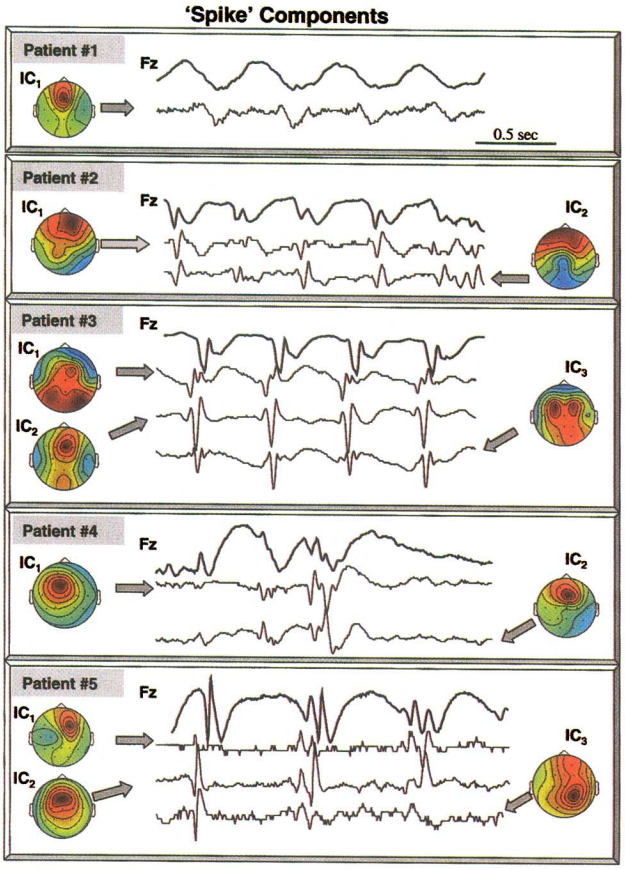

Figure 4. Spike independent components (ICs) of EEG from each subject. Recording at F_z is shown above projections of one to three components corresponded to the "spike" portion of the spike-and-wave complex noted in the EEG. Note the predominately focal, frontal spatial distributions of the components. Each waveform and associated scalp pattern represents a separate component.

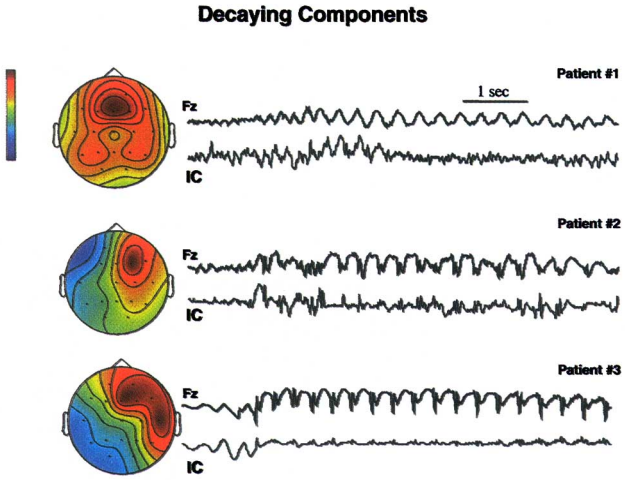

Figure 5. Components of EEG active only at the beginning of seizures. Recording at F_z shown above projection of decaying component. These components were activated at the beginning of each seizure and tended to decay as the seizure progressed.

the EEG to as few components as possible may be a poor criterion to detect such a component. In contrast, independent component analysis (ICA) (Comon 1994; Bell and Sejnowski 1995) assumes that the EEG is composed of mixed, statistically independent components of different strengths and tries to determine how to "unmix" the data to recover the underlying components.

By relaxing the requirement that the spatial patterns be orthogonal, ICA is more closely resembles the ad hoc procedure "promax" (Hendrickson and White 1964). However, ICA appears more successful than promax at unmixing test data sets composed of more than a few variables, and therefore may be more appropriate for EEG data composed of twenty or more channels. The heavily overlapping spatial distributions of the different spike, wave, and early components (figures 1-7) as well as the small relative size of the these components (figures

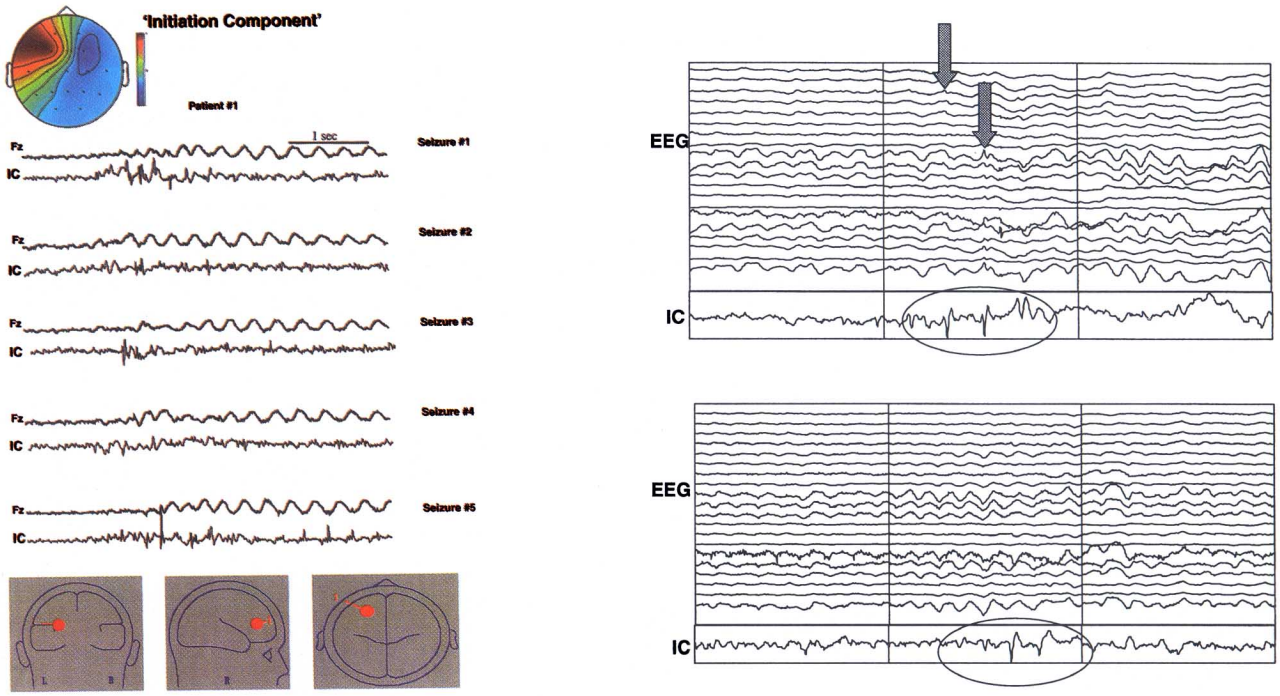

Figure 6. Initiation component of EEG. (A - top left) One component from the first subject demonstrated sharply contoured waves at the start of each of five seizures. (B - bottom left) fitting the fields from this component to the BESA program (Neuroscan, Inc, Herndon, VA, USA) revealed a single dipole localizing closely to the left thalamus. (C - right) Application of the initiation component (IC) scalp pattern to non-ictal data from the same subject demonstrated periods of activation of the initiation component, corresponding to inter-ictal spikes (large arrows, top) or with no apparent change in the EEG (bottom).

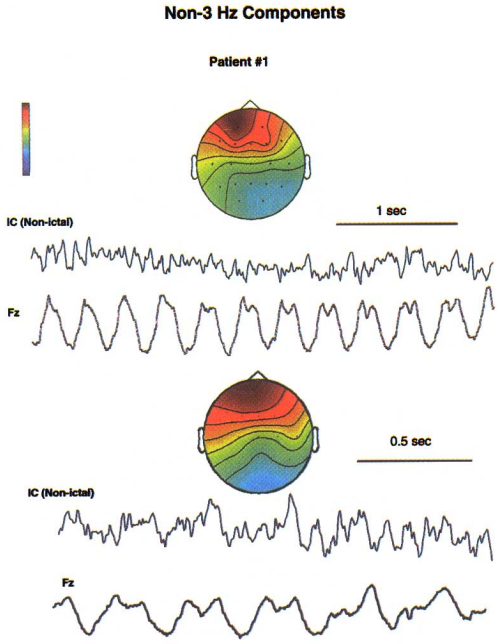

Figure 7. Non 3 Hz components. Two components from the first subject reflecting on-going, non-ictal activity (solid thin line) are shown (top and bottom). Some components appeared to reveal brain activity not entrained in the 3-Hz spike-and-wave pattern.

6-7) suggest that a decomposition technique looking for orthogonal scalp patterns explaining maximal variance (i.e., PCA) would be less robust for detecting consistent components of activation in absence seizures.

The ICA algorithm attempts to find fixed relationships between EEG electrodes that separate the EEG into waveforms that are as statistically independent as possible in the time domain. The assumption required by all linear models of the form expressed in equation 2, that the relationship between channels can be assumed to be constant over an entire epoch, may not be always valid in the EEG (McKeown, Humphries et al. 1998). Despite this, we found components that were consistently activated with each seizure for a given subject. Although we tested a relatively few number of patients, these results of consistent activation across all seizures within a subject contrast with previous studies of absence seizures that demonstrated that the raw EEG could vary significantly from seizure to seizure (Rodin and Ancheta 1987; Rodin et al. 1994; Lemieux and Blume 1986). The consistent activation was seen in all patients tested, regardless of age, despite that there may be differences in absences between children and adults (Michelucci et al. 1996). This apparent discrepancy between detecting consistent underlying components when the raw EEG varies between seizures can be explained by a

number of factors. First, some components decayed away early in the seizure (figure 1 and 5), so their presence could not contribute to the raw EEG spike-and-wave pattern as the seizure progressed. Second, we detected components that appeared to reflect brain activity (figure 7) not directly related to the spike-and-wave activity of the seizure. If the whole brain was not completely entrained in the spike-and-wave activity, on-going cortical activity from the non-seizing areas could contribute variability to the raw EEG, similar to the variability seen in optical recordings of evoked cortical responses caused by concurrent brain activity (Arieli et al. 1996). Third, careful inspection of components active during the entire seizure (figures 1-4) revealed subtle differences between successive spike or wave events. Each component is associated with a static spatial distribution, demonstrating that there are constant spatial distributions of activation even though there may be slight temporal variability between successive spike-and-wave complexes.

The ICA algorithm is well suited to separating temporally overlapping individual components, and we found multiple components contributing to the "spike" part of the spike-and-wave complex (figure 4). Kandel et al. (1997) did a careful study of the sources and sinks in response to VPL (ventero-posterolateral) thalamic stimulation and spontaneous spike-and-wave activity in the rat and found that although the largest sink was in layer IV, there were also smaller sinks in other layers (Kandel and Buzsaki 1997). Consequently, they concluded that the "spike" of field potential recordings (and EEG) was composed of the effects of three or more temporally overlapping dipoles. The major contributor to these time-shifted dipoles was activity along intracortical linkages, as opposed to thalamocortical activity. Because the different spike components consistently picked up the same portions of the spikes in successive spike-and-wave complexes (figure 4), the stationary spatial pattern associated with these "spike" components reflect consistent spatial patterns of activation among spike-and-wave complexes. Each time-shifted dipole determined by Kandel et al. (1997) may therefore reflect a group of neurons consistently activated by varying intra-cortical activity.

The ICA method separated the ongoing wave activity from the spike activity. The "wave" part of the spike-and-wave complex was associated with relative quiescence of firing of cortical neurons and possibly reflects inhibitory synaptic activity (Giaretta et al. 1987). The two ICA "wave" components we detected for each patient appeared similar, but shifted, suggesting a consistent propagation of activity from one spatial pattern to another as ICA tends to break up propagating activity into separate components, each activated at slightly different times (McKeown, Jung et al. 1998; McKeown, Makeig et al. 1998).

The small initiation component detected for the first subject (figure 6) demonstrated sharply contoured waves that were consistently activated at the beginning of each seizure. The fitted dipole associated with this component was in a deep left-frontal position. This component may perhaps reflect the small initiating activity from anterior thalamocortical cells bombarding possibly abnormal cortex that starts off the whole spike-and-wave cascade. This is consistent with the notion that the cortex, due to strong intra-cortical excitatory connections (Douglas et al. 1995), can be considered a powerful amplifier of thalamic inputs. Activation of this component did not always lead to full-blown seizure activity (figure 6c), suggesting that abnormal thalamocortical activity may have to be sufficiently powerful or sustained to progress to seizures. Once a seizure has started however, both cortex and thalamus are required to sustain spike-and-wave discharges (Danober et al. 1998) and the other spike components (figure 4) probably reflect combined thalamocortical and cortico-cortical activity.

The ability to detect inter-ictal spikes that are not obvious in the raw EEG (figure 6c, bottom) suggests that ICA may be a practical means to determine a patient-specific filter to monitor inter-ictal activity. Once a seizure has been recorded with digital EEG, an initiation component determined through an ICA decomposition of the seizure would then provide a way to inter-ictally monitor for stereotyped spatial patterns of activation.

Some components appeared to be consistently active during the early part of each seizure only (figure 5). These may be related to the observation that behaviorally, very short duration seizures (< 4 sec) are associated with minimal cognitive impairment (Giannakodimos et al. 1995), independent of motor activity (Provinciali et al. 1991). These early-activating components may represent the initial spreading cortical patterns of activation as more and more of the cortex gets entrained in the thalamocortical spike-and-wave activity. The anterior nuclei of the thalamus appears to play an important role in the continuation of seizures, as there is a high coherence between anterior thalamic nuclei recordings and the EEG in the rat (Sherman et al. 1997). The lag-time between the onset of spike-and-wave and actual cognitive impairment may reflect the load of greater cortical areas involved in the seizure, or perhaps the propagation of the spike-and-wave activity to other thalamic nuclei, such as intra-laminar nuclei, important for subserving consciousness (Bogen 1997). Correlation between ICA components determined from an analysis of the EEG and behavioral tasks recorded during seizures are needed to explore this further.

The stability of the spatial patterns during absence seizures is quite unlike that observed when ICA is used to analyze sleep spindles, where sequential spindles are

composed of differing combinations of spatial patterns (Humphries et al. 1998). This implies that the macroscopic properties of spindles and absence seizures may be quite different, despite reports suggesting similarities at the cellular level (Caderas et al. 1982; Contreras and Steriade 1995; Medvedev et al. 1996).

Our results suggest that although the raw EEG can vary between seizures within a given subject, there are some overlapping spatial distributions of activation that are highly consistent across seizures. Possibly these spatial patterns of activation reflect seizure and ongoing, non-seizure cortical activity recurring in the same brain areas.

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