SINGULAR VALUE DECOMPOSITION AND DIPOLE MODELLING APPLIED TO OBSERVE BACKGROUND ACTIVITY ORIGINATING FROM SAME AREA AS EPILEPTIFORM EVENTS IN THE EEG OF PAEDIATRIC PATIENTS WITH FOCAL EPILEPSY

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Abstract: The aim of this study was to investigate the presence and characteristics of apparent non-epileptiform activity arising in the same brain area as epileptiform activity in the EEG of paediatric patients with focal epilepsy. The EEG from eight patients was analyzed by an automated method which detects epochs with a single underlying source having a dipolar potential distribution. The EEG with the highlighted detections was then rated by a clinical neurophysiologist (EEGer) with respect to epileptiform activity. Although EEGer-marked events and computer detections often coincided, in five out of the eight patients a substantial number of other detections were found to arise from the same area as the marked events. The morphology of a high proportion of these other detections did not resemble typical epileptiform activity and had a frequency content mainly in the delta and theta ranges. This is the first study to use an automated technique to demonstrate the presence of non-epileptiform activity arising from the same area as the epileptiform activity in the EEG of paediatric patients with focal epilepsy. This slow wave activity is likely to be related to the underlying epileptogenic process.

Keywords: Paediatric patients; Focal epilepsy; EEG dipole modelling; Singular value decomposition; Epileptiform activity.

INTRODUCTION

The background EEG in patients with focal epilepsy often shows focal or localised delta activity ($<$4 Hz) related to the disorder [1].

Intermittent delta activity in the EEG of patients with focal epileptogenic brain lesions has been reported to be a marker for the existence of an epileptogenic focus [2]. Similarly, Huppertz et al. [3] used dipole localization to show delta activity coming from cortical regions close to the brain lesion.

Gallen et al. [4] selected epochs showing abnormal low-frequency activity in the magnetoencephalogram (MEG). The underlying equivalent current dipole of this activity was found to be useful in the presurgical evaluation of patients with epilepsy.

In the above studies, the epochs were visually selected by EEGer and related to abnormal activity in the delta range. In a group of patients with cerebral tumors de Jongh et al. [5] automatically examined the MEG for dipolar activity . They found that dipoles describing delta and theta activity were located ipsilateral to lesions.

Preliminary observations from our own comparisons of transient events detected by computer algorithm with those of an EEGer have led us to the study reported here. We applied a method that automatically detected dominant events with a dipolar scalp potential distribution in 19-channel EEG of pediatric patients with focal epilepsy. In addition, the algorithm provided the dipole location (within a spherical 3-shell model) associated with each detection. The EEGer was asked to identify all epileptiform events after being given the EEG recording with all computer detections already high-lighted. A region of interest (ROI) was than identified based on the epileptiform-events computer-detected.

PATIENTS AND EEG

Nineteen-channel EEGs (10-20 international electrode placement, 1-30 Hz band-pass filtered, sampled at 256 Hz, common referenced) of eight paediatric patients with focal epilepsy were recorded. The patients had been selected out of a pool of available data. The EEG recordings ranged from 12.4 to 21.2 minutes. The patients had an average age of 5.5 years (range 3-10 years). The EEG findings for each patient are summarized in Table 1.

METHODS

The method comprised applying a computer detection algorithm to the 19-channel EEG, having the EEGer categorize the EEG within which computer detections were highlighted, and constructing a region of interest based on the dipoles of epileptiform-events computer-detected.

Detection method

The detection algorithm was based on a novel method developed for detection of epileptiform activity in multichannel EEG recordings [6, 7]. Fig. 1 shows a flowchart of the method. The 19-channel EEG was first transformed from common referencing to average referencing. It was then divided into overlapping epochs of 250 ms (64

	Sex/Age	EEG Summary
1	F/3	Diffuse excess of fast activity and frequent discharges in left occipital region
2	F/4	Discharges predominantly from right parietal region plus slower background from same region
3	F/5	Right central and midtemporal discharges
4	M/5	Occipital sharp waves typical of benign occipital epilepsy
5	M/6	Drug induced beta, right antero-temporal to midtemporal sharp wave discharges
6	M/7	Right centro-temporal sharp wave discharges
7	M/4	Parasagittal epileptiform discharges prominent from the left central region
8	F/10	Slowing in right anterior quadrant and epileptiform discharges

Table 1: Summary of the EEG for the 8 patients

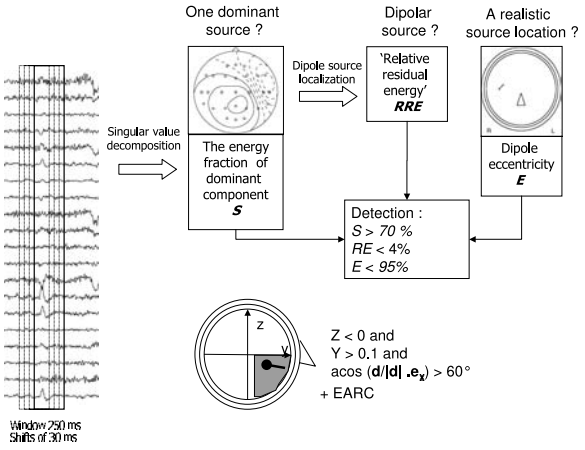


Fig. 1: A flowchart of the method for detecting focal sources in the EEG.

samples). Each epoch was shifted in time from the previous one by 31.25 ms (8 samples). The epochs were processed in two steps. The first step involved singular value decomposition (SVD) [8] to inspect the number of generators active in the epoch. The EEG epoch $\mathbf{V} \in \mathcal{R}^{19\times 64}$ was decomposed by SVD into $\mathbf{U}\cdot\mathbf{s}\cdot\mathbf{W}^T$ (^{T} transpose operator) with 19 'potential distributions' found in the columns of $\mathbf{U} \in \mathcal{R}^{19\times 19}$, 19 corresponding time courses in the columns of $\mathbf{W} \in \mathcal{R}^{64\times 19}$ and the singular values s_i found on the diagonal entries of diagonal matrix $\mathbf{s} \in \mathcal{R}^{19\times 19}$. The s_i values, representing the square-root of the energy contribution of component i, were ordered such that the one with the largest value had the smallest index i. SVD was used to inspect the number of generators active in the epoch. A detection was said to have occurred when only one generator was predominantly active in the epoch. The measure

$$S = \frac{s_1^2}{\sum_{i=1}^{19} s_i^2}, \tag{1}$$

was used for this purpose, where S is the fraction of energy contained in the first component. If S was higher than 70%, a dominant generator was assumed.

In the second step, EEG dipole source analysis was applied to the potential distribution $\mathbf{U}_{*1}$ (the left eigenvector corresponding to the first singular value) of the dominant generator. A three-shell spherical head model was used with the radii for the brain, skull and scalp compartment being 80 mm, 85 mm and 92 mm respectively. The relative conductivities with respect to the skull conductivity of the three compartments were 16, 1 and 16 respectively. The optimum dipole was found by changing the dipole parameters until a minimum was found in the cost-function given by the relative residual energy (RRE),

$$RRE = \frac{\|\mathbf{U}_{*1} - \mathbf{V}_{model}\|^2}{\|\mathbf{U}_{*1}\|^2}, \tag{2}$$

with $\mathbf{V}_{model}$ being the potentials generated by the fitted dipole in the three-shell spherical model. The RRE gives the fraction of energy which cannot be explained by a dipolar field. The smaller the RRE the better the dominant potentials obtained from the SVD represent a dipolar source and, hence, a focal source. Dipolar field distributions can also be generated by more extended sources [9] but the spatial extent of these sources is difficult to estimate. The detection algorithm triggered an EEG epoch when SVD indicated a dominant source and the RRE was lower than 4%.

Certain artifacts were subsequently removed by applying rejection rules based on the dipole model in the three-shell spherical head model [10]. First, the relative eccentricity (ECC) of the dipole position was calculated with respect to the radius of the inner shell. If the ECC was found to exceed 95%, the dipole was rejected on the grounds of being either an eye-blink or electrode artifact. A further eye-blink artifact removal criterion ($EARC$) was introduced to reject epochs from a dipole

located in the lower frontal area. A dipole with position $\mathbf{r}[r_x\ r_y\ r_z]$, normalized to the radius of the outer shell, (x-axis: left to right ear, y-axis: anterior to posterior, z-axis: vertical through Cz and origin in the center of the spheres) and orientation $\mathbf{d}[d_x\ d_y\ d_z]$ was removed when $(r_z < 0) \wedge (r_y > 0.1) \wedge (\arccos(\frac{\mathbf{d}}{\|\mathbf{d}\|} \cdot \mathbf{e}_x) > 60°)$ was true, with $\|\ \|$ the euclidian norm, $\cdot$ the inner-product and $\mathbf{e}_x$ the unity vector along the x-axis; that is, the detection was rejected if the computed dipole was located in the lower frontal area and its dipole moment vector made an angle of a least 60° with the x-axis.

In summary, an epoch was detected when four conditions were fulfilled: $S > 70\%$ indicating a dominant generator in the epoch, $RRE < 4\%$ demonstrating that a dipole was a good model for that generator, $ECC < 95\%$ indicating removal of electrode or eye-blink artifacts and the $EARC$ not being met, providing further support that the epoch was not due to an eye-blink artifact. Importantly, this method detects focal activity regardless of the morphology of the activity and the amount of total power in the epoch.

As the EEG is segmented into overlapping epochs, it is possible for a single event to be detected more than once. Detected epochs were therefore clustered into a *detection*. Two consecutive detected epochs were clustered if they both started within 250 ms of each other and had their associated dipole positions $\mathbf{r}_1$ and $\mathbf{r}_2$ located in the same region (i.e., $\|\mathbf{r}_1 - \mathbf{r}_2\| < 0.2$ or 18.4 mm). This was done to prevent activity in different brain regions being clustered as one detection. The dipole parameters associated with the detection were then obtained by averaging the dipole parameters associated with the detected epochs within it.

The thresholds for S, RRE and ECC were chosen as follows. The EEG of patient 7 was marked for epileptiform events by the EEGer before being re-marked with the automatic detections highlighted. For a given set of thresholds of these properties, a sensitivity (#detections also marked by the EEGer / #EEGer marked events) and selectivity (#detections also marked by the EEGer / #detections) to epileptiform events was obtained. The selectivity was then plotted versus sensitivity for a large number of threshold sets. The envelope curve, also called the receiver operator characteristic (ROC) curve, represented the best possible combinations of sensitivity and selectivity. The thresholds mentioned above were associated with a position on the ROC with a sensitivity and selectivity of 78% and 13%, respectively, in patient 7. The same thresholds were used for the other patients. The parameters associated with the $EARC$ were kept fixed in this preprocessing step.

Categorising the EEG

The EEGs with the detections highlighted were then presented to the EEGer who was asked to indicate all events which he considered to be definitely epileptiform or questionably epileptiform. Epileptiform patterns were defined in Chatrain et al. [11] as : 'Applies to distinctive waves or complexes, distinguished from background activity, and resembling those recorded in proportion of human subjects suffering from epileptic disorders and in animals rendered epileptic experimentally. Epileptiform patterns include spikes and sharp wave, alone or accompanied by slow waves, occurring singly or in bursts lasting at most a few seconds'. (In what follows we use epileptiform events and epileptiform activity as synonyms of epileptiform patterns.) Detections not marked by the EEGer were, in his opinion, *Non-Epileptiform-patterns computer-Detected* (NEDs).

Definite and questionable epileptiform events (marked by the EEGer) which coincided with computer detections were termed *Definite-Epileptiform-patterns computer-Detected* (DEDs) and *Questionable-Epileptiform-patterns computer-Detected* (QEDs) respectively.

Construction of a region of interest

To further process the NEDs, a spherical ROI was established to indicate the origin of the epileptiform patterns. Ideally, one would construct this region based only on DEDs as they are, in the EEGers' opinion, unequivocally epileptiform. However, when the number of DEDs is too small (less than 3), QEDs were also utilized to construct the ROI; this was the case in 4 of the 8 EEGs (see Table 2). The centre of the region was obtained by averaging the dipole positions of the DEDs or, if <3, DEDs and QEDs. The maximum of the standard deviations from that average along the cartesian axes ($\max(\sigma_x\ \sigma_y\ \sigma_z)$) ranged from 0.08-0.23 relative to the outer radius of the head model in the eight patients. A radius of 0.2 (i.e., 18.4 mm) was then chosen to establish a volume around the centre of the sphere. NEDs located in that spherical ROI were termed *Non-Epileptiform-patterns computer-Detected In Region of interest* (NEDIRs).

RESULTS

Table 2 shows the computer detections in each EEG divided into definite, questionable and non-epileptiform patterns according to the EEGer. The total number of definite or questionable epileptiform events marked by the EEGer are also shown. Note that in patients other than 7, the number of DEDs and QEDs are only a small subset of the definite and questionable epileptiform events marked by the EEGer, indicating that the method with the thresholds (fine-tuned for patient 7) fixed over the entire patient group performed suboptimally. Nevertheless, for our purposes, this number was sufficient to obtain a reasonable estimate of the epileptogenic region.

For patient 2 no DEDs were available. Hence, for this patient the QEDs were used to define the ROI from where the epileptiform activity originates. As the numbers of DEDs were too small for patient 3, 5 and 6, both the DEDs and QEDs were used to define the ROI.

The numbers of NEDIRs are also given in Table 2. For a uniform distribution of NEDs, the propor-

	#DEDs	#QEDs	#NEDs	#NEDIRs
1	24 (65)	21 (97)	93	30 (32%)
2	0 (6)	32 (92)	83	30 (36%)
3	1 (1)	87 (105)	243	120 (49%)
4	27 (96)	22 (88)	89	1 (1.1%)
5	1 (16)	2 (159)	5	0 (0%)
6	1 (7)	11 (31)	100	3 (3%)
7	17 (19)	40 (66)	47	21 (44.6%)
8	22 (102)	84 (167)	595	105 (17.6%)

Table 2: Computer detections categorized by EEGer into definite, questionable or non epileptiform patterns. #DEDs is number of definite-epileptiform-patterns computer-detected. #QEDs is number of questionable-epileptiform-patterns computer-detected. Figures in parentheses give the total number of definite/questionable epileptiform patterns marked by the EEGer. #NEDs is number of non-epileptiform-patterns computer-detected. #NEDIRs is number of NEDs located in the region of interest; the values in parentheses give the percentage of NEDs which are NEDIRs.

tion of NEDIRs (given in parenthesis) would be 1.22% ($(\frac{0.2}{80/92})^3 100$). For patients 4, 5 and 6 the proportion is of this order indicating that there were no strong association between NEDs and the epileptiform activity in these 3 patients. Conversely, for the remaining 5 patients this percentage was substantially higher, indicating a close-proximity link between the NEDs and the epileptiform activity.

The dipoles of DEDs for patients 1 and 4 are shown in Fig. 2(a). A frontal-, top- and side view of the same group of dipoles is illustrated to give a better understanding of the 3D position of the dipoles in the head model. The dipoles of the QEDs are given in Fig. 2(b). These dipoles are clustered in brain regions which correspond with the areas in which the EEGer detected epileptiform events as given in Table 1. Note that most dipole orientations tend to be in the same direction.

Fig. 2(c) shows dipole positions of the NEDs. The dipole orientations have been omitted to make the plots easier to read. The ROI encapsulating the NEDIRs is also shown. For patients 1, 2, 3, 7 and 8, a large number of dipoles are located in the same area (both within and immediately outside the region of interest) as the dipoles associated with the detections marked by the EEGer. Hence, it is clear that the dipoles of the NEDs are not randomly distributed in the spherical head model and their strong predominance in the same region as the detected epileptiform events has not occurred by chance. For patients 4 and 6 a large number of dipoles did not cluster in the region where the epileptiform activity originates. Looking at the EEG of all NEDs, alpha activity and eye-blink artifacts were associated with these detections in these patients. For patient 5 only a small number of NEDs was observed due to the small number of detections obtained by the algorithm.

Finally, Fig. 2(d) shows the dipole positions of the

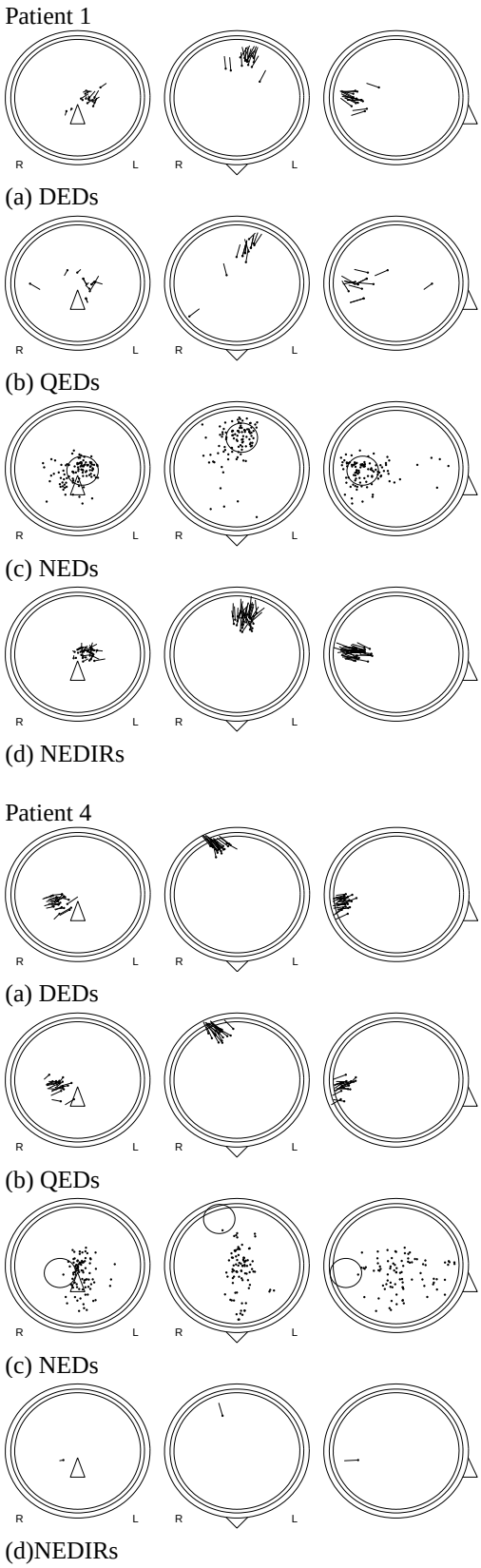


Fig. 2: For patients 1 and 4 the dipoles are presented for DEDs (a), QEDs (b), NEDs with ROI (c) and NEDIRs(d). The dipoles are shown in frontal-, top- and side view, respectively.

NEDIRs. It is striking for patient 1 that these orientations are very similar to those of the dipoles for the DEDs and QEDs.

Fig. 3 shows examples of NEDIRs with predominantly delta (a) and theta (b) activity.

DISCUSSION

For 5 of the 8 patients (patients 1, 2, 3, 7 and 8) the NEDs were clearly from the same region as DEDs and QEDs, as indicated in Fig. 2(c). Furthermore, the morphology of UFEs contained no epileptiform patterns as defined by Chatrain et al. [11].

In patients 4 and 6, the NED were found to be more spread out, as shown in Fig. 2(c), with no strong cluster in the same area as the DEDs and QEDs. This indicates that the detection method has by chance detected NEDs in the DED/QED zone which are probably not related to the underlying epilepsy. In patient 5, only 8 computer detections were found. Drug-induced beta activity [12] was superimposed on the background EEG leaving the S measure below the threshold of 70%. No single dominant source could be observed.

The NED clusters for patients 1, 2, 3, 7 and 8 are in quite different brain regions (Fig. 2(c)), indicating that the detection algorithm has no obvious bias regarding preferential brain region.

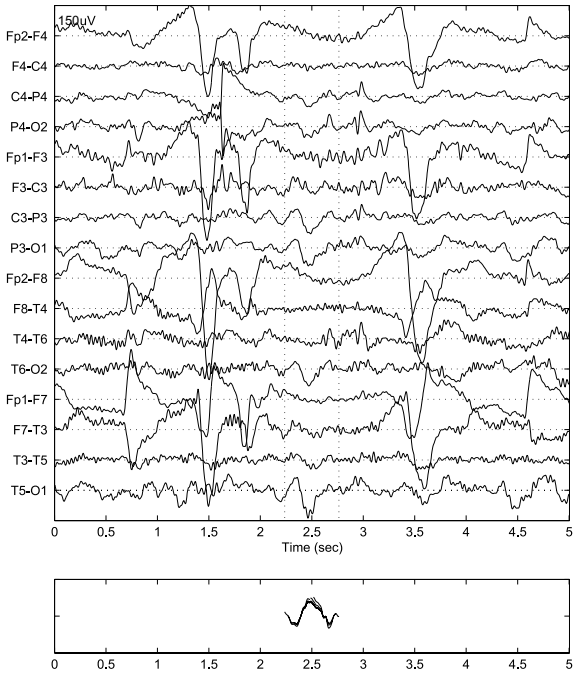
Importantly, the method is not sensitive to the waveform of the events, in contrast to mimetic detection methods [13, 14]. This would be a disadvantage if the algorithm was used to detect epileptiform patterns but is an advantage in the current study as it enables focal events to be detected, independent of morphology. The S measure looks at relative energy levels and, hence, the method can still work with relatively low absolute energy levels, in contrast to the method used by [15] which uses thresholds based on the absolute energy levels.

To automate the grouping of the detections, clustering algorithms based on the dipole coordinates, reported by Ossadtchi et al. [16] and, on the potential distribution, reported by van 't Ent et al. [17], could also be applied in the future.

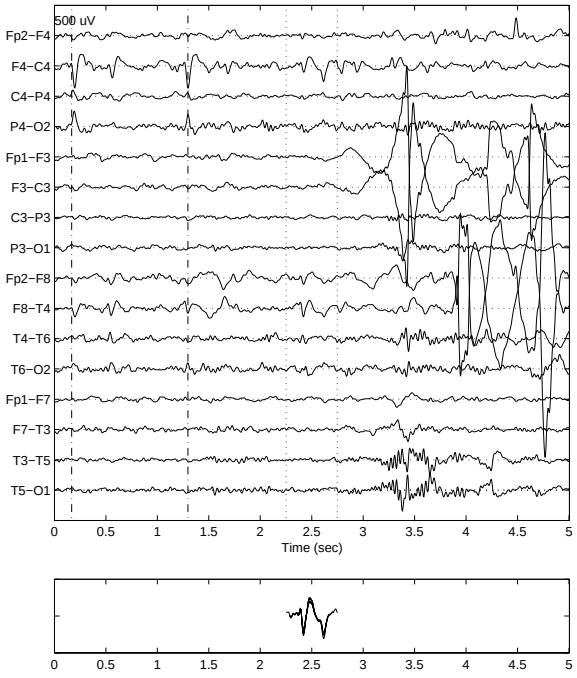
We have demonstrated a dominant presence of non-epileptiform patterns in the EEG from the same region as the epileptiform focus in the majority of a group of paediatric patients with focal epilepsy. Although it is difficult to distinguish visually between NEDIRs and other background activity, it nevertheless raises a possible need to extend the definition of epileptiform patterns to include activity characteristic to NEDIRs.

Although our results show the NEDIRs to be originating from the same area as the epileptogenic focus, their origin and morphology need to be confirmed by depth-electrodes as was done in a study by [18]. Depth-electrode studies would also allow investigations of the role which NEDIRs have in the epileptogenic process.

It would also be of interest to undertake further studies to determine whether the presence and characteristics of the NEDIRs in focal epilepsy are any different in adult



(a)



(b)

Fig. 3: The EEG is shown of NEDIRs with predominant delta (<4 Hz) activity in (a) (patient 1) and, with mainly theta activity (4-8 Hz) in (b) (patient 3). The EEG between the dotted lines represents the detection. The temporal vector of the first SVD component for each epoch in the detection is given below the EEG. The dot-dashed lines represent EEGer-marked event.

patients.

Finally, EEG recordings between seizures may contain no epileptiform patterns in approximately 20-40% of patients with a history of seizures [19]. By applying our approach it may be possible to demonstrate focal interictal 'non-epileptiform' activity in the EEG of these patients which correlates with their clinical history of seizures.

ACKNOWLEDGMENTS

Bart Vanrumste was a Postdoctoral Fellow funded by the University of Canterbury, Christchurch, New Zealand, until November 2003. Since then he is postdoctoral fellow at K. U. Leuven in Belgium. Currently, he is funded by the 'Programmatorische Federale Overheidsdienst Wetenschapsbeleid' of the Belgian Government.

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