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MEG-guided analysis of 7T-MRI in patients with epilepsy

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ABSTRACT

Purpose: To study possible detection of structural abnormalities on 7T MRI that were not detected on 3T MRI and estimate the added value of MEG-guidance. For abnormalities found, analysis of convergence between clinical, MEG and 7T MRI localization of suspected epileptogenic foci.
Methods: In adult patients with well-documented localization-related epilepsy in whom a previous 3T MRI did not demonstrate an epileptogenic lesion but MEG indicated a plausible epileptogenic focus, 7T MRI was performed. Based on semiologic data, visual analysis of the 7T images was performed as well as based on prior MEG results. Correlation with other data from the patient charts, for as far as these were available, was analysed. To establish the level of concordance between the three observers the generalized or Fleiss kappa was calculated.
Results: In 3/19 patients abnormalities that, based on semiology, could plausibly represent an epileptogenic lesion were detected using 7T MRI. In an additional 3/19 an abnormality was detected after MEG-guidance. However, in these later cases there was no concordance among the three observers with regard to the presence of a structural abnormality. In one of these three cases intracranial recording was performed, proving the possible abnormality on 7T MRI to be the epileptogenic focus.
Conclusions: In 32% of patients 7T MRI showed abnormalities that could indicate an epileptogenic lesion whereas previous 3T MRI did not, especially when visual inspection was guided by the presence of focal interictal MEG abnormalities.

1. Introduction

Epilepsy has an estimated prevalence of 0.4 to 1.4% [1]. At least 61% of the patients diagnosed with epilepsy suffer from localization-related epilepsies [2]. Approximately 30% of patients with localization-related seizures suffer from refractory epilepsy [3]. In up to 74% of patients with localization-related seizures, MRI shows no abnormalities [4]. In children with epilepsy this is about one-third [5]. Prognosis for seizure control following focal resection of the epileptogenic zone is excellent [6]. Identification of a lesion on MRI is a major predictive factor for surgical outcome [7,8]. The majority of patients suffering from focal seizures of unknown origin [9] probably have a small focal cortical dysplasia (FCD) [10,11]. FCD's often escape detection with present imaging techniques [12], may considerably vary in size and localization [13] and are likely to be located at the bottom of sulci [14]. Post-processing of the images using voxel-based morphometric techniques, like MAP07, can enhance detection rate [15,16]. Also, using higher field strength MRI more abnormalities can be visualized [17,18]. Therefor, 7 T MRI yields the promise of improving detection. In epilepsy patients, ex vivo [19] and in vivo 7T MRI examples of FCD in humans are available [20–22].

When an MRI is re-analysed with an a-priori hypothesis more lesions are detected [23,24]. Magnetoencephalography (MEG) is not only a reliable indicator of epilepsy [25] but also a powerful tool to determine a possible epileptogenic focus [26,27] and is of growing presurgical importance in combination with MRI (MRS, magnetic source imaging) [28]. In frontal lobe epilepsy interictal MEG might even be more predictive than ictal semiology in locating the epileptogenic zone [29].

The present study explores the possible role of visual and of MEG-guided visual 7T MRI analysis in improving detection of a possible epileptogenic lesion. The levels of convergence between clinical data,

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Table 1
Patient characteristics: gender, age, present semiology.

Patient	gender	Age	Semiology
1	F	45	Undefinable feeling, orofacial automatisms, motionless. Clusters.
2	M	36	Abrupt hyperkinetic movements of all extremities.
3	F	31	1) short lasting unresponsiveness and freezing 2) painful sensation stomach 3) clusters of staring and automatisms.
4	M	33	Headache, orofacial automatisms, lowered consciousness, inconsistent version.
5	M	23	Sometimes auditive aura. Gasping for breath and fast eye blinking. Late in seizure turning to left and lowered consciousness. Provocation by specific sounds possible but not mandatory
6	F	34	Tingling left hand, cramp left hand, hyperkinesias left arm
7	M	65	Shout, bilateralhypertonia changing to clonias. Postictal incoherent speech.
8	M	19	Arousal, clonias both arms, head turning to right
9	M	56	Head version to left, tonic left arm, then leg and face. Preserved consciousness
10	F	49	Arms hyperkinetic, vocalisation, inadequate responses
11	M	29	Tingling right hand, cramp right hand
12	M	27	1) Sensations left arm, than leg, then lowered consciousness and automatisms 2) cramps left arm, secondary generalisation
13	M	32	Feeling warm, dreamy, cramps hands, orofacial automatisms, inability to react, lowered consciousness, fists, stretching arms. Mainly during sleep.
14	F		Strange feeling stomach, feeling of falling through the floor, inability to react
15	F	21	Head version to right, tonic right hemi face
16	M	46	Right arm turns backward while trembling.
17	F	33	1) No grip on her own thoughts 2) clonic movements eyes (sometimes also head) to the right.
18	M	19	1) up to 30 s lowered conscience 2) nausea, loss of conscience, peri-oral cramps, making sounds, turning away eyes.
19	F	28	1) fear, turning red, incontinence. 2) Asymmetric cramp arms (L > R), torso flexed, tachypneu, followed by restlessness and manual automatisms
20	M	32	Pre-ictal hyperactive behaviour, then staring, perspiring, lowered conscience, restlessness. Sometimes leading to spastic movements, clonias, foaming mouth, hitting and kicking, tongue bite, grey skin.

MEG and 7T MRI findings are described.

2. Methods

Patients were prospectively recruited from the Academic Centre for Epileptology (ACE), location Kempenhaeghe, a tertiary epilepsy centre. Additionally, two patients were referred by another institution (SEIN) to participate in this study. Inclusion criteria included previously diagnosed focal epilepsy, MEG results showing epileptiform abnormalities concordant with semiology ("plausible"), and a 3T-MRI without showing abnormalities that could explain the seizures, despite availability of all other clinical data. Further inclusion criteria included age 18 or above and signed informed consent. Exclusion criteria included pregnancy and being incapacitated. Standard MRI-exclusion criteria applied, including body implants that are not (yet) proven safe at 7T MRI.

Although not an inclusion criterion, all but one patient were included during a period of pre-surgical analysis. Seizure description, MEG results and other auxiliary information on possible locations of the epileptic focus were gathered from the patient charts. If, after analysis of the 7T MRI, a patient was operated upon, data on results of surgery and histopathology were added to the database. The 7T MRI then was re-evaluated by two of the three observers.

Previously performed clinical MEG data (Neuromag 306, Elekta Oy, Helsinki, Finland) had been analysed in an experienced centre (VUmc, Amsterdam, Netherlands) and indicated a plausible epileptogenic focus in all patients. MEG recording time was at least one hour, including eye opening and closing, hyperventilation and rest. Obtaining a recording in sleep was not mandatory. No EEG co-registration was available. Used analysis methods included equivalent current dipole modelling and beamforming analysis [30,31].

The previously performed state-of-the-art 3T MRI (3.0 T Achieva, Philips, Best, The Netherlands) was analysed by an experienced neuroradiologist with special interest in epilepsy, aware of all available data including the MEG results. A voxel-based morphologic analysis program (MAP-07 [32,33]) was available during part of our study. During this time, patients were only included if MAP-07 did not indicate any abnormalities. In 14 out of the 19 included patients MAP-07 was applied prior to the 7T MRI. In the remaining 5 patients, MAP07 retrospectively performed on the original 3T MRI also did not show abnormalities. Used 3T MRI sequences included 3D-T1 (TR 8.1 ms, TE 3.7 ms, voxel $1 \times 1 \times 1$ mm), T2 (TR 3000 ms, TE 80 ms, voxel $0.5 \times 0.5 \times 5$ mm), T2* (TR 777 ms, TE 16 ms, voxel $0.9 \times 1.1 \times 5$ mm), IR (TR 120 ms, TE 10 ms, TI 400 ms, voxel $0.4 \times 0.6 \times 2$ mm) and 3D-FLAIR (TR 8000 ms, TE 50 ms, TI 2400 ms, voxel $1.1 \times 1.1 \times 0.5$ mm) No abnormalities that could account for the particular epilepsy were found.

7T MRI was applied well within the limits of the American Food and Drug Administration (FDA) guidelines. Images were acquired on a Philips 7.0 T Achieva (Philips, Best, The Netherlands) using a 32-channel receive head coil at Leiden University Medical Center (LUMC). The protocol included: 3D T1 (TR 4.2 ms, TE 1.88 ms, voxel $0.9 \times 0.9 \times 0.9$ mm), 3D FLAIR (TR 8000 ms, TE 300 ms, TI 2200 ms, voxel $0.80 \times 0.84 \times 0.80$ mm), T2TSE (TR 3000 ms, TE 58 ms, voxel $0.5 \times 0.5 \times 1$ mm) and T2* (TR 1764 ms, TE 25 ms, voxel $0.24 \times 0.24 \times 1$ mm). No specific correction or post-processing techniques were used.

The region of interest (ROI) was determined by semiological data and by localization of epileptiform abnormalities recorded during MEG, projected on a 3D T1 3T MRI.

Images were visually assessed by two experienced neuroradiologists and one neurologist specialized in epilepsy. The first assessment was done by these 3 specialists independently of each other, while taking semiologic data into account but without knowledge of the MEG-results. A second assessment was based on visual guidance by MEG. Presence and location of MRI abnormalities were noted and compared to the contralateral site. Finally conclusions by the individual specialists were compared. To establish the level of concordance the generalized or Fleiss kappa was calculated.

In this study, one patient in whom an SEEG recording [34,35] was performed before, and five patients in whom an SEEG recording was performed after the 7T MRI were included. In one patient intracranial recording using multiple subdural strips was carried out. Results of the intracranial recordings and results of surgery, when performed, were not available at the time of analysis of the MRI. However, surgical outcome and histological diagnosis were added in a later stage to the database in patients who underwent resective surgery. For patients without abnormalities on the first analysis of 7T MRI but a successful resection, two of the three observers re-evaluated the 7T MRI.

The medical ethical committee of LUMC approved the study protocol. All patients provided informed consent.