Artikel Asli/*Original Article*

Observation of Auditory Perceptual and Visuo-Spatial Characteristic of a Patient with Hemangiopericytoma in Occipital Lobe: A Magnetoencephalography (MEG) Study
(Pemerhatian Persepsi dan Visual-ruang Pesakit dengan Tumor pada Lobus Oksipital: Satu Kajian Magnetoensefalografi (MEG))

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ABSTRACT

The present study discussed functional reorganization and alteration in respond to the slow-growing tumour, hemangiopericytoma in the occipital cortex. Visual evoked field (VEF) and auditory evoked field (AEF) using magnetoencephalography (MEG) was used to evaluate the source localization and brain activity. Results of VEF source localization show a typical brain waves. Brain activity of the occipital lobe demonstrate low activation in the ipsilateral to the tumour. However, result shows the activation on the contralateral hemisphere was high and bigger in activation volume. AEF result shows an identical source localization and both side of the temporal lobe are activated. This result suggests that there is a positive plasticity in auditory cortex and slow-growing tumour can induce functional reorganization and alteration to the brain.

Keywords: Visual evoked field (VEF); auditory evoked field (AEF); magnetoencephalography (MEG); hemangiopericytoma; occipital cortex

ABSTRAK

Kajian ini membincangkan terdapatnya proses penyusunan semula dan perubahan kefungsian bagi tindak balas terhadap tumor yang lambat membesar, hemangiopericytoma yang terletak pada bahagian korteks osipital. Kajian ini menggunakan bidang visual yang ditimbulkan (VEF) dan bidang auditori yang ditimbulkan (AEF) menggunakan magnetoencephalografi (MEG) untuk menilai penyetempatan sumber dan pengaktifan otak peserta. Hasil penyetempatan sumber VEF menunjukkan gelombang otak yang tidak sejajar di antara kedua-dua belah hemisfera. Pengaktifan otak juga menunjukkan pengaktifan yang rendah pada lobus oksipital di ipsilateral tumor manakala, hemisfera kontralateral diaktifkan dengan intensiti tinggi dan jumlah pengaktifan yang lebih besar. Hasil AEF menunjukkan penyetempatan sumber yang sama pada kedua-dua belah hemisfera dan kedua-dua belah lobus temporal diaktifkan. Hasil ini menunjukkan bahawa terdapatnya keplastikan positif pada kawasan korteks auditori dan tumor yang lambat membesar dapat mendorong penyusunan semula dan menyebabkan perubahan pada fungsi otak.

Kata kunci: Bidang visual yang ditimbulkan (VEF); bidang auditori yang ditimbulkan (AEF); magnetoencephalography (MEG); hemangiopericytoma; korteks oksipital

INTRODUCTION

Visual cortex is a part of the cerebral cortex that processes visual information and it is located in the occipital lobe. Damage to visual cortex is a common incidence in cases of brain tumour, stroke or trauma (Young et al. 2007). The damage of visual cortex can cause alteration in the brain function and lead to the changes of vision abilities (Lau et al. 2017). In the case of brain tumour, as a tumour grows, it puts pressure on surrounding tissues. Therefore, affecting the function, process and part of the cortex that controlled the area of the brain. In slow-growing tumour e.g. hemangiopericytoma, a positive functional reorganization can occur (Restani & Caleo 2016). During the process of functional reorganization, new cortical regions can be recruited to participate in the visual cortex network, aiding in the recovery of function of the visual areas (Boldt et al. 2014).

Previously, there are suggestions that functional reorganization and plasticity in visual cortex that is induced by the tumour growth might be limited to an early critical period of the development (Hubel & Wiesel 1969; 1979; 1998). Any changes after the early critical period will not lead to significant response which led to the common assumption that all cortical connections in visual cortex are fixed (Hubel et al. 1977). However, this assumption

has been challenged by evidence of plasticity in early visual cortex evoked by changes in normal experience (Abe et al. 2015; Liang et al. 2017) and by damage to peripheral visual pathways (Abe et al. 2015; Gilbert & Li 2012). However, the endpoint of functional reorganization and alteration is not always beneficial and can lead to significant maladaptive outcomes (Schumacher et al. 2008). The effects are related to the nature and extent of the neuropathogenic process. The stage of neurodevelopment during which the insult occurs is also play an important role (Sabbah et al. 2017).

The present study will discuss the functional reorganization and alteration of the brain in respond to the hemangiopericytoma occurring within the occipital cortex. Hemangiopericytoma is an uncommon tumour that only accounts for 1% of all central nervous system tumour (Joo et al. 2016). It is characterised by histopathological finding of abnormal pericytes around the capillaries. The mass effect from this lesion can manifest as a gradual increase in intracranial pressure, or more localized symptoms such as hemiparesis, aphasia, gait unsteadiness and loss of vision (Zweckberger et al. 2011). The aim of this study is to observe and report the functional and structural reorganization that has been made by the brain in response to the tumour growth.

The present study recorded visual evoked field (VEF) and auditory evoked field (AEF) of magnetoencephalography (MEG) to evaluate the function of auditory and visual processing. The tumour not only invades the occipital area but also extended to the posterior temporal lobe. The observation of the tumour induced structural and functional reorganization will be discussed based on the MEG assessment using VEF and AEF (peak and latency).

MATERIALS AND METHODS

PARTICIPANTS

A 30-year-old, right handed male participant complaining of worsening headaches, tinnitus and bilateral blurring of vision for 2 months. The participant had an uneventful medical and social history. There is no previous seizure, recurrent vomiting or trauma. On clinical examination, the participant was fully conscious but impaired visual acuity. Fundoscopy examination found bilateral papilloedema with optic atrophy. MRI of the brain showed lobulated extra-axial lesion measuring $6 \times 5 \times 7$ cm at left occipital region crossing to the right, attached to falx. The lesion was hypointense in T1 view, hyperintense in T2 view, and vividly enhanced by contrast. No hydrocephalus was seen. Histopathological examination from the lesion sample showed closely packed moderately pleomorphic cells interlacing with blood vessels exhibiting staghorn pattern, oval to round nuclei, fine chromatin pattern and indistinct cell borders which was consistent with Anaplastic Hemangiopericytoma (WHO Grade III). After a full explanation of the nature and risks of the study, informed consent was obtained according to the protocol approved by the Institutional Ethics Committee (IEC) of Universiti Sains Malaysia.

MAGNETOENCEPHALOGRAPHY AND DATA PROCESSING

Magnetoencephalogram (MEG) data were recorded continuously during the performance of a visual (checkerboard pattern) and auditory (two and three syllabus words presented) stimulus, as shown in Figure 1 (A), (B) and (C). MEG data were collected using a 306-channel Vectorview system (ElektaNeuromag, Helsinki) in a light Elekta-Neuromag magnetically-shielded room. A magnetometer and two orthogonal planar gradiometers were located at each of 102 positions. Vertical and horizontal eye movements were recorded using paired EOG electrodes. Four head position indicator (HPI) coils were used to monitor the head position. A 3D digitizer (Fastrak Polhemus Inc., Colchester, VA) was used to record the three-dimensional locations of the HPI coils and approximately 200 'head points' across the scalp, and three anatomical fiducials (the nasion and left and right pre-auricular points). Data were sampled 1000 Hz and pre-processed using Max Filter software (Elekta-Neuromag, Helsinki) with movement compensation. Software Brain Electrical Source Analysis (BESA version 6.0, GmbH, Graefelfing, Germany) was used to process for source analysis of the waveforms of the visual processing area. An MRI image was also collected using 3-Tesla magnetic resonance imaging (MRI) (Philips Achieva 3.0T X-series, Philips, *Netherlands*).

SOURCE ANALYSIS OF VISUAL EVOKED FIELD (VEF) AND AUDITORY EVOKED FIELD (AEF)

To provide the precise spatial localizations compared to distributed source models for both visual evoked field (VEF) and auditory evoked field (AEF): minimum norm approaches and equivalent current dipole approach was used. For maximization of algorithm (EM), the algorithm iteratively shifts dipole sources at the at specific brain location with a specific dipole orientation is used. The source dipole solutions for the N100 component were determined.

Data were filtered using high pass filter (>1 Hz, Butterworth filter 6 dB/oct with no added padding) and the artefact rejection threshold was set to 2500 fT for magnetometers and 900 fT for gradiometers. Using adaptive artefact correction, eye-blinks were corrected and modelled in the source analysis with one fixed source. Epochs were low pass filtered to 200 Hz (Butterworth filter 24 dB/oct), time locked to the tone onset, baseline corrected (- 50 to 200 ms). Source analysis of evoked responses from the gradiometer MEG channels, was performed on the visual and auditory processing response. The forward model topography (leadfield) was estimated using a realistic head model, co-registered by fiducial and digitised scalp

loci. The inverse of this leadfield matrix was applied to the gradiometer data to estimate the source waveforms, varying source location and orientation iteratively until the residual difference between scalp and model waveforms was minimized. The data were fitted to two bilateral equivalent current dipoles (regional sources). The fits were constrained by imposing symmetry on the two sources, but not constrained by location or orientation, and with regularisation constant 1% to stabilise source fitting in the presence of noise.

For the N100 (50 –150 ms) produced in a two-source solution that was most likely fundamental the generation of scalp recorded potential in these time windows. Two source dipoles were fitted distinctly with the constraint of having symmetrical sources in each hemisphere. Using different starting locations, these symmetric dipoles were allocated consistently to the occipital cortex for VEF and temporal cortex for AEF for the N100. Dipoles were fitted sequentially in the right and left occipital and temporal activation at over 50–150 ms.
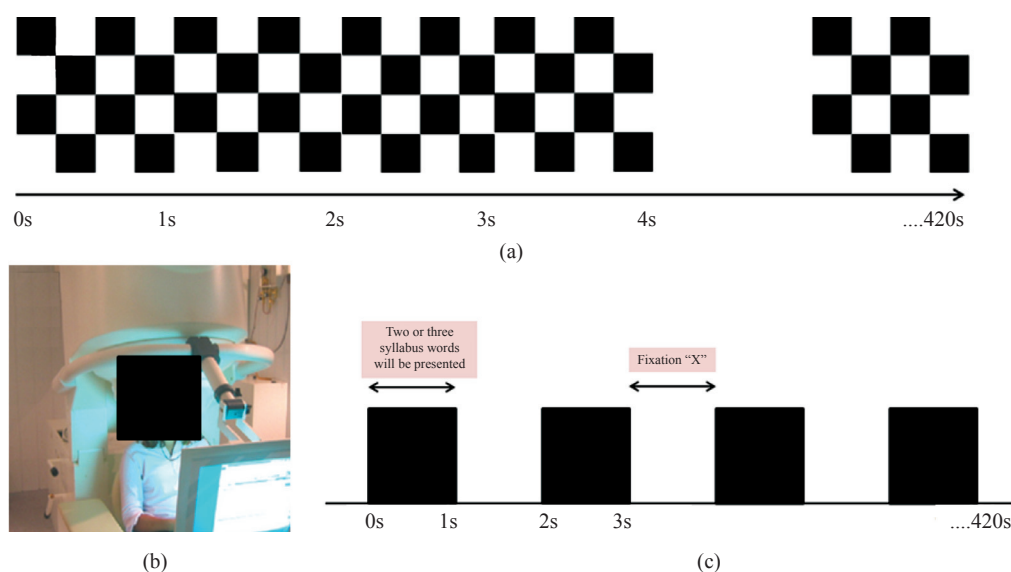

FIGURE 1. Sequence of checkerboard used during the study. The stimulus was presented continuously for about 7 minutes. Participant need to focus to the stimulus presented, not to think about anything, to stay awake and must not fall asleep during the scan (a). This is how participant was position during the study. The screen was positioned in front of the participant (b). Auditory stimulus was used in the study; the stimulus was presented using earphone which are compatible with MEG. The stimulus was presented for 7 minutes (c)

RESULTS

Figure 2(a) and (b) demonstrate a sagittal and transverse view of MRI brain depicting a solid tumour at the bilateral occipital region, in the red circle. MRI result indicate the tumour mass are greater in the left hemisphere. The tumour not only invades the occipital area but also extended to the posterior temporal lobe. Figure 2(c) shows the brain wave of source analysis including amplitude and latency using BESA Software. Comparing between right and left hemisphere of N100 visual evoked field (VEF) signal; right hemisphere component of N100 is corresponding in time. Whilst, the left hemisphere, ipsilateral to the tumour, signal shows prolonged in N100 latency and the signal peak is in the opposite direction. Furthermore, left hemisphere brain wave shows lower wave amplitude that could indicates a dysfunction of the visual pathway. Figure 2(d) shows 3D images and transverse view of source localization. Results indicate that both hemispheres were activated but the left hemisphere (ipsilateral to the tumour) was activated with low intensity and small activation volume.

Figure 3(a) demonstrate N100 auditory evoked field (AEF) wave signal comparing between right and left hemisphere. For both hemispheres, the component of N100 is corresponding in time to the AEF. However, result indicates that the left hemisphere shows lower wave amplitude. The auditory task used activated both temporal area of the brain, as in Figure 3(b). Comparing between hemispheres, left hemisphere (ipsilateral to the tumour) shows higher activation intensity. Source activity results demonstrated that both source localization and brain activity is matched.

DISCUSSION

In the present study, we observed tumour-induced functional reorganization and changes in the brain particularly in the occipital area. Temporal area was also included as a region of interest. This is due to the tumour have also occupied a small area in the posterior part of the left temporal lobe. Brain activation and source localization were used to
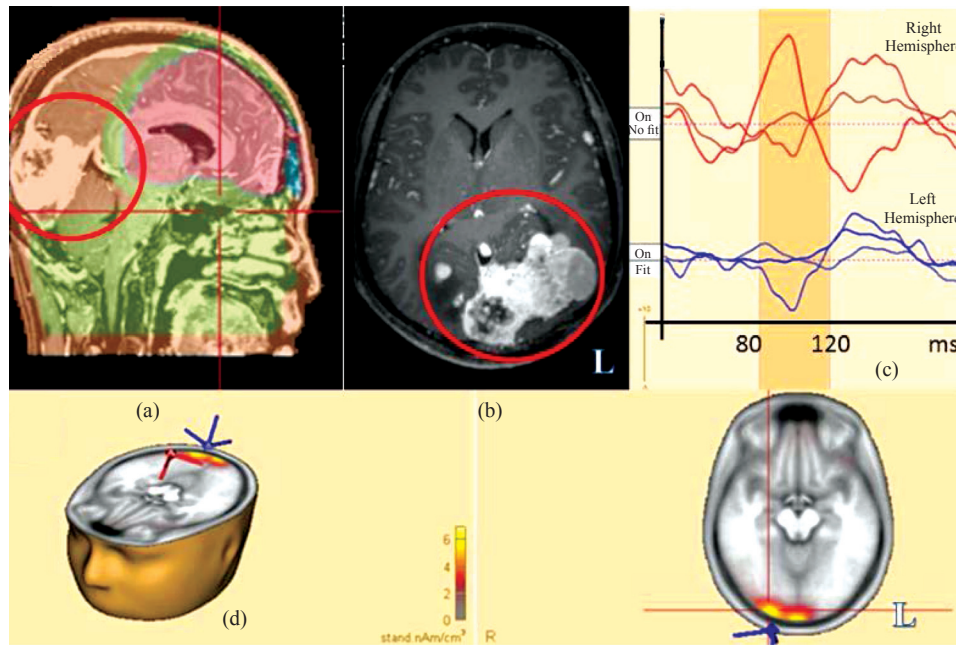
FIGURE 2. Sagittal (a) and transverse view of MRI brain depicting a solid tumour at the bilateral occipital region (red circle). MRI result indicate the tumour mass are greater in the left hemisphere (b). Comparing between right and left hemisphere of N100 VEF signal, right hemisphere component of N100 is corresponding in time whilst the left hemisphere signal shows prolonged in N100 latency and lower wave amplitude which might indicate a dysfunction of the visual pathway (c). Shows source localization analyzed using BESA source analysis. It shows activation on both sides of occipital region but with low activation intensity in the left (d). R: right side of brain; L: left side of the brain.
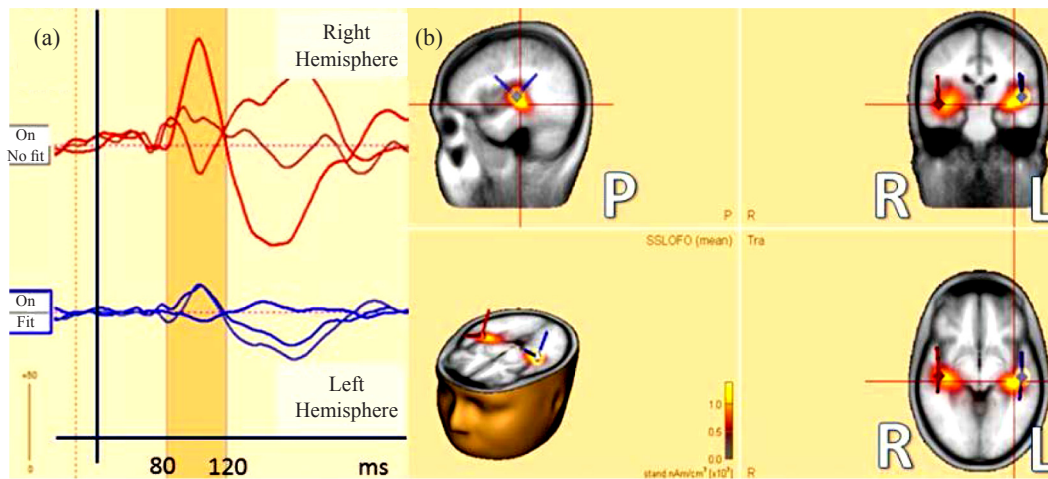

FIGURE 3. N100 wave signal of AEF comparing between right and left hemisphere. Both hemisphere component of N100 is corresponding in time to the AEF. Comparing to the right, left hemisphere shows lower wave amplitude (a). Shows source localization analysed using BESA source analysis. Both side of the brain are activated but with different intensity (b). R: rightside of brain; L: left side of the brain

measure the functional localization during both visual (VEF) and auditory (AEF) tasks. As a result, we found that atypical N100 VEF wave signal and brain activation. However, for N100 AEF, the wave signals are corresponding in time and brain activation is identical with previous published study (Kim et al. 2014; Korostenskaja et al. 2013).

N100 VEF

The present data on continuous prolonged recording of VEF suggest that complaints of visual disturbances are associated with marked functional lability and prolonged in N100 VEF latency in the ipsilateral hemisphere to the tumour. The present study further suggests that the presented

symptoms are also associated with atypical wave signal. The amplitude of the brain wave is in the opposite direction to the N100 amplitude. Our observation is in agreement with the previous studies. The studies reported that brain tumour interfere with normal brain wave and function by disrupting their wave signal of the brain network (Inoue et al. 2004; Morrison et al. 2016). Comparing between hemispheres, left hemisphere brain wave shows lower wave amplitude which might indicate a dysfunction of the visual pathway. This present study proposed that the tumour has suppressed the functional visual processing areas. Therefore, disrupts the propagation of the brain waves. This situation is expected as the tumour provoking loss of associated fibers or changes in synaptic efficiency. This may alter the communication between neuronal networks and may underlie neurological disturbances (Jarosiewicz et al. 2008; Jutzeler et al. 2015; Manan et al. 2015). It has been shown that patients with brain tumor experience cognitive deficits. These cognitive deficits are probably primarily due to the tumor itself, and not to adverse effects of radiotherapy because only high fraction doses (exceeding 2Gy) are likely to affect cognition. Patients experience attention deficits, working memory problems, reduced psychomotor speed, and problems with executive functions. The origin of the cognitive deficits in low-grade glioma patients is incompletely understood.

Brain activation result reveals that bilateral hemispheres of occipital areas are activated. However, result demonstrates that left hemisphere (ipsilateral to the tumour) activated with low intensity and smaller activation volume compared to the right hemisphere. The present observation proposed that the contralateral area of the functional lesion-visual would take place in response to the brain insult (in this case brain tumour). This is shows by the increased of activation of contralateral and reduced ipsilateral activity. Similar pattern of brain behaviour was also found in a previous study where a series of activation shifts took place involving an early recruitment of contralesional homologous brain regions after a brain insult (Chen et al. 2010). Similar pattern of results was found in stroke-induced aphasia suggesting an increased activation in the contralateral area of the lesion-language network, followed by re-shifting of main activation to left hemisphere language areas (Duffau 2005). The present result is also supported by the source localization analysis. The component of N100 in the left hemisphere is not corresponding in time to those of the VEP are identified and the recording of VEP shows the localization of the two dipoles is in the right occipital region. Therefore, we proposed that the cortical reorganization occurs in brain and right occipital area take over the functional processing that previously performed by the left hemisphere of the brain in response to the brain insult.

N100 AEF

AEF examination was performed to the patient to observe the effect of the tumour to the auditory processing. The latency and the location of equivalent current dipole of N100 AEF for both hemispheres are match. However, the brain wave signal in the ipsilateral to the tumour shows lower in amplitude but higher in brain activation intensity. This result indicates that there are alterations and changes in the brain wave and activation intensity even though the posterior part of the temporal lobe involved is small. This brain alterations and changes are proposed to be related to the mechanism of survival of the tumour tissues. Previous studies suggest that the phenomenon of higher brain activity and intensity in the tumour area is due to the high metabolism rate (Sontheimer 2015). This is a common phenomenon for the tumour tissue to have higher activity compared to normal cells. This phenomenon is known as Warburg Effect, which postulated the changes in metabolism as the fundamental cause of cancer (Weber 2016) .

In summary, the neuroimaging result of the VEF and AEF demonstrate a brain changes and alteration. This changes and alteration to the brain anatomy and function are due to the brain tumours invaded the functional areas of the brain. The present study suggests that the mechanisms of the tumour-induced plasticity are based on the intrinsic reorganisation within the lesion area. Consequently, this mechanism leads to the recruitment of other regions implicated in the original functional network, which is contralateral area to the tumour.

CONCLUSION

In the present study, the effect of a local brain lesion (brain tumour) in the occipital area to the source localization and brain activity using VEF and AEF of MEG signals were identified. The main observations were that patient with brain tumours have atypical brain waves and activation ipsilateral to the tumour. This interference in the brain signals and activation were not only confined to the tumour areas but also areas close to the tumour. We also observed that the contralateral hemisphere activated with high intensity and bigger activation volume. This is proposed due to mechanism of neural plasticity in respond to the tumour. The concept of neural plasticity is certainly appealing. However, unequivocal proofs that plastic changes following the changes of environmental factors such as tumour, better adaptation remain to be provided. Thus, future study related to this issue is suggested.

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