

Visual ERPs and cortical function

Shozo Tobimatsu¹, Yoshinobu Goto², Takao Yamasaki¹,
Taisuke Nakashima¹, Yasuko Tomoda³, Akihisa Mitsudome⁴

¹ Department of Clinical Neurophysiology, Graduate School
of Medical Sciences, Neurological Institute, Faculty of Medicine,
Kyushu University

² Department of Occupational Therapy, Faculty of Rehabilitation,
International University of Health and Welfare,
Okawa, Japan

³ Department of Pediatrics, Faculty of Medicine, Fukuoka University

⁴ International University of Health and Welfare, Fukuoka, Japan

■ Parallel visual pathways

Anatomy and physiology of the visual pathways

The human visual system is made up of multiple, parallel channels which process different information, and each channel is made up of a set of the sequential processing centers [1, 2]. Light increments (ON) and decrements (OFF), motion, stereoscopic depth, color, shape, and other parameters of visual stimuli are processed separately and simultaneously (Figure 1). There are two major parallel pathways in humans; the parvocellular (P) and magnocellular (M) pathways. The former is responsible for carrying information on the form and color of an object because of its ability to detect stimuli with high spatial frequencies and color while the latter plays an important role in detecting motion due to its ability to respond to high temporal stimuli [1, 2].

The elementary components of visual stimuli such as luminance, contrast, color, spatial frequency, and temporal frequency are important for parallel processing (Figure 2). Surprisingly, even a picture of a face can be decomposed into its spatial frequency components. We have been studying the functions of the P- and M-pathways with evoked potentials and event-related potentials (ERPs) elicited by visual stimuli whose characteristics have been altered [2-5]. This approach has enabled us to explore the functions of the retina and primary visual cortex (V1). Thus, information on the characteristics of a face is first processed in the fusiform gyrus (V4), and the information is carried by the P-pathway [6]. Information on the motion of an object is processed in MT/V5 and the information is carried by the M-pathway [7].

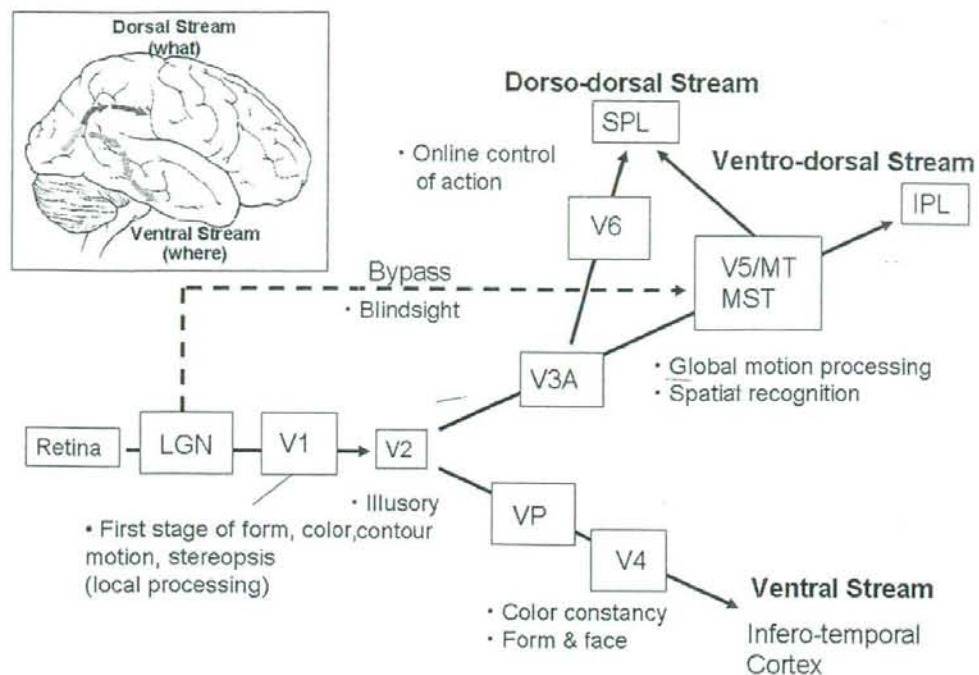


Figure 1. Recent concepts of parallel visual pathways.

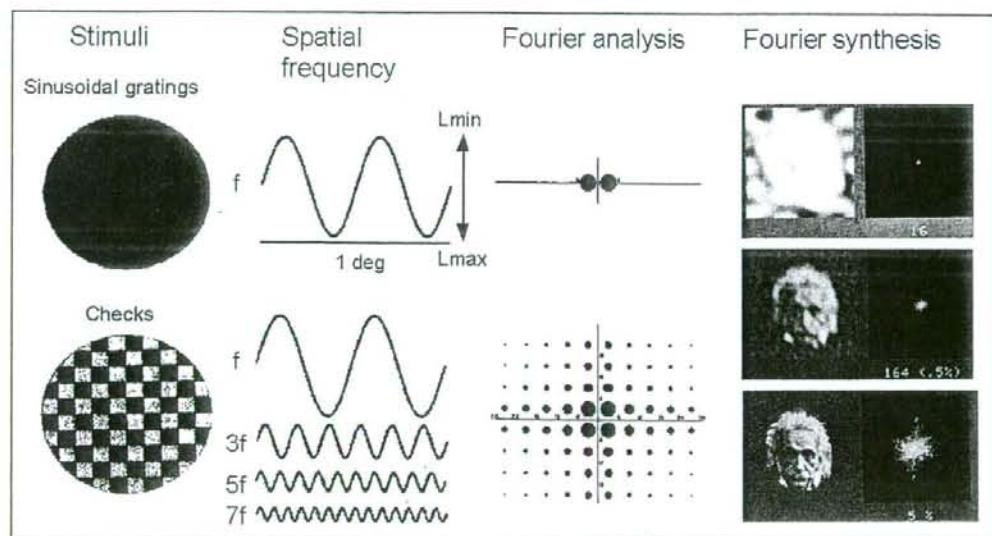


Figure 2. Importance of the elementary components (luminance, contrast, color, spatial frequency and temporal frequency) of the visual images. Regarding spatial frequency, a checkerboard pattern is rather complex compared with sinusoidal gratings (left). A photograph of a face is decomposed into several spatial frequencies (right).

Face perception

ERPs elicited by facial and motion stimuli were recorded at multiple scalp sites in normal subjects. A photograph of a face was filtered in the spatial domain to alter its spatial frequency components, and the resulting images were used to investigate how the low-spatial-frequency (LSF) and high-spatial-frequency (HSF) components of the face contributed to the identification and facial expressions of the face. Faces and houses for the LSF and HSF stimuli were created by image engineering techniques with two-dimensional fast Fourier transformation [8]. Broad-band spatial frequency (BSF) stimuli were original photographs and unfiltered. The cut-off frequencies (< 2.5 to 4.0 cycles/face for LSF; and > 30.0 to 50.0 cycles/face for HSF) were determined by measuring the psychophysical threshold for the recognition of facial expressions prior to the ERP recordings. The mean luminance and contrast were controlled by normalizing the mean and standard deviation (SD) of the gray values of the entire stimulus [8]. Representative examples of the stimuli (fearful expression) are shown in Figure 3.

The ERPs evoked by faces, objects, and facial expressions under the three conditions of spatial frequency are shown in Figures 4 and 5. The grand-averaged P100 waveforms at O_z for each stimulus are shown in Figure 4 (upper panel). The P100 amplitudes were significantly enhanced by the LSF information of faces, but not by that of objects, regardless of the facial expressions.

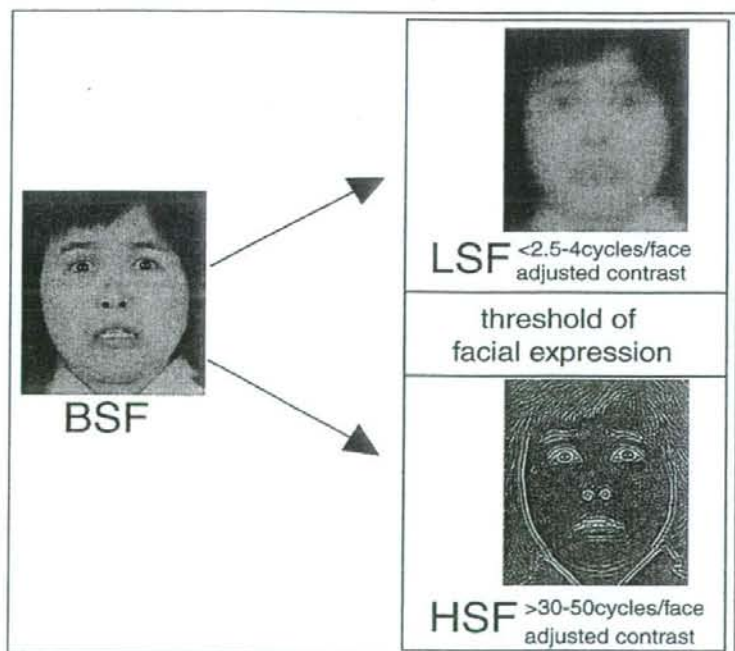


Figure 3. Representative examples of the face stimuli used in this study. BSF is an original non-filtered image (left), which contains broad spatial frequency components. LSF and HSF faces are filtered by fast Fourier transformation. The LSF face consists of information with low spatial frequencies ($< 2.5-4$ cycles/face width) and preserves the holistic facial image (right). The HSF face extracts information with high spatial frequencies ($> 30-50$ cycles/face width) and emphasizes the detailed features of the facial components.

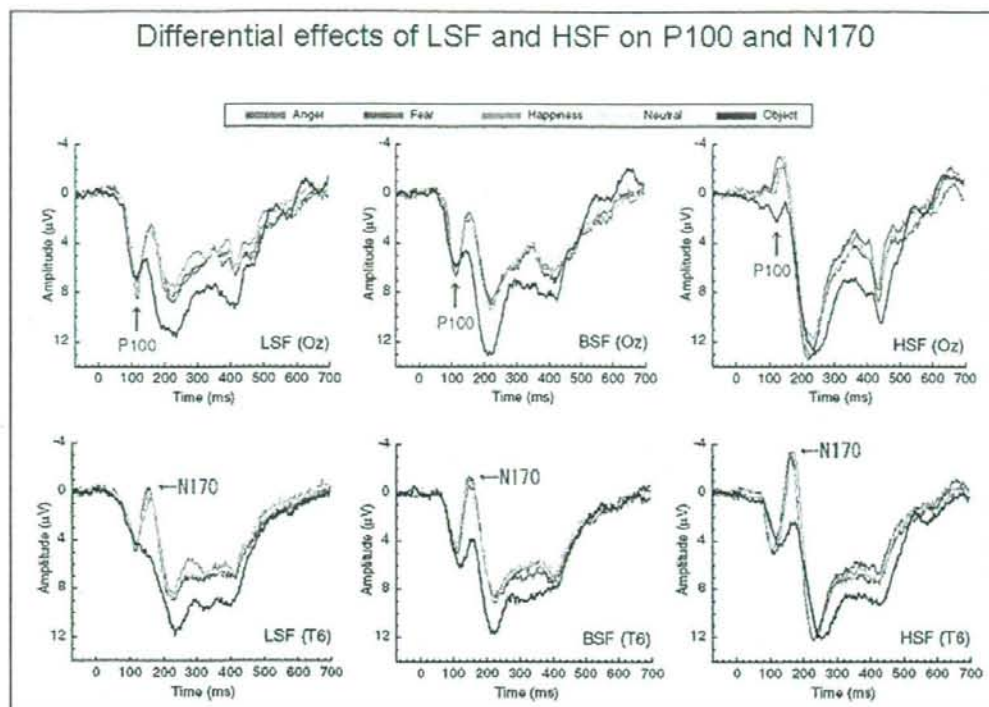


Figure 4. P100 responses to each stimulus recorded at the mid-occipital region (Oz). The grand-averaged P100 is specifically larger for LSF faces (left) than for BSF (middle) and HSF (right) faces. The N170 responses to each stimulus at the temporo-occipital electrodes (T5 and T6). The grand-averaged N170 for HSF faces is clearly larger than those for BSF and LSF faces with right hemisphere predominance.

The grand-averaged N170 waveforms at the T5 and T6 electrodes are shown in Figure 4 (lower panel). The N170 amplitudes in the right hemisphere were significantly augmented by HSF information of faces, but not by that of objects, irrespective of the facial expressions. Enlarged waveforms of the late components for LSF, BSF and HSF faces at the T5 and T6 electrodes for the time window of 200-450 ms are shown in Figure 5. The LSF images elicit different responses for "positive and negative" expressions in the relatively early phase of the late components, while HSF images induced different responses for "negative and negative" expressions in the late phase of the late components.

Information of different components of the face is transmitted mainly by the P-pathway and processed in the fusiform gyrus (V4) [6]. Direct recordings from human V4 demonstrated that a surface-negative potential (N200) was evoked by faces but not by the other types of stimuli [9]. Scalp-recorded ERPs showed that the N170 component was a face-specific potential, and that it was predominant in the posterior temporal cortex [10]. More specifically, it was most likely generated in the occipitotemporal sulcus lateral to V4 [10]. Our results suggested that P100 reflects holistic processing of faces, whereas N170 analyzes their features. Consequently, N270-310 is involved in the discrimination between positive and negative expressions, whereas N330-390 separates detailed information among the negative expressions. Therefore, faces and facial expressions are sequentially processed in parallel based on the LSF and HSF information.

Differential effects of LSF and HSF on late negative potentials (250-400 ms)

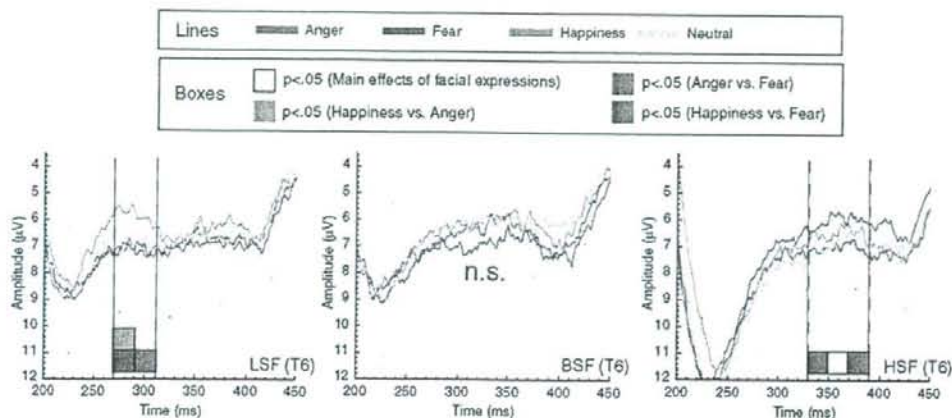


Figure 5. Waveform of the late components for each facial expression. The original waveforms in Figure 4 in the time window of 200-450 ms are enlarged for comparison. The white square boxes on the abscissa indicate the main effects of facial expressions, while the colored boxes show statistically significant differences revealed by paired comparisons (Bonferroni correction). Under the LSF condition, there are significant differences in amplitudes between positive (happiness) and negative (anger and fear) expressions during the time window of 270-310 ms, regardless of the hemisphere. In contrast, a significant difference is found only for negative expressions (anger vs. fear) during the time window of 330-390 ms under the HSF condition.

Motion perception

To study motion perception, stimuli with coherent horizontal (HO) movements and stimuli with radial optic flow (OF) motion were used (Figure 6, left). First, the thresholds for detecting HO and OF movements were determined psychophysically in young and elderly healthy subjects. Second, the motion coherence thresholds for HO and radial OF motions were determined using a left/right two-alternative forced-choice discrimination technique [11]. The perceptual threshold was defined by the percentage of coherent motion in the stimuli ($[\text{coherently moving dots}]/[\text{coherently moving dots} + \text{random dots}] * 100$) yielding 82.5% correct responses. The thresholds were related to the Weibull fit to psychophysical responses [11]. From these results, the coherence level eliciting 90% correct responses was used to elicit ERPs in normal subjects.

In the ERP study, there were two major components elicited by motion stimuli; an N170 component and a P200 component (Figure 6, right). In the parietal area, the N170 component was evoked by HO motion and N170 was less marked by OF motion and showed an adaptational effect for random motion [12]. The P200 component, on the other hand, was elicited by only the OF motion and did not show an adaptational effect.

Functional magnetic resonance images (fMRI) were recorded measured while normal subjects viewed the motion stimuli. A box-car design was employed and statistical analysis was performed with SPM99. The HO and OF motion stimuli activated the dorsal pathway differentially (Figure 7) [12]. Interestingly, the inferior parietal lobule (IPL) was activated by OF motion while the superior parietal lobule (SPL) was activated by HO motion.

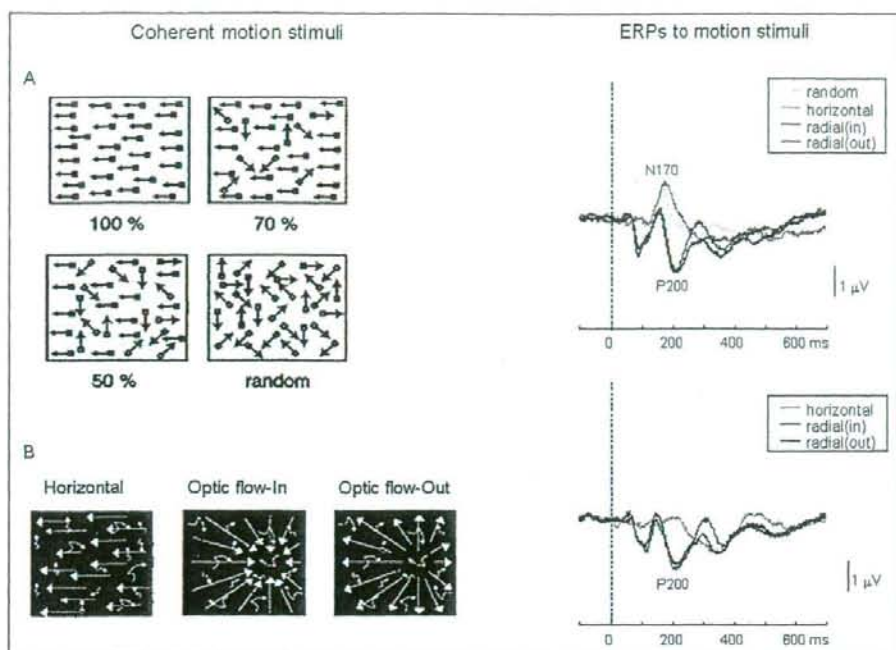


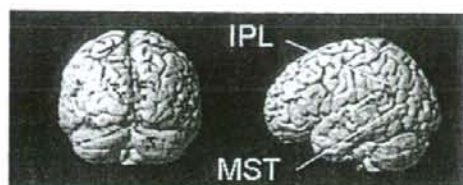
Figure 6. Horizontal and radial optic flow stimuli were used to evoke motion perception (left A, B). Four hundred white dots on a dark background were animated at a 60 Hz frame rate. The horizontal motion stimuli consisted of leftward or rightward movement of the dots. Radial motion consisted of dots moving in a radial pattern out from a focus of expansion on the horizontal meridian, 5 deg to the left or right of center. Motion stimuli also evoke N170 but this component is maximal over the parietal region (P3 or P4) (right). The N170 component is much larger to horizontal motion than to radial optic flow. In contrast, the later component, P200, is only recorded by radial optic flow.

Information about a moving stimulus is carried by the M-pathway and is processed in MT/V5 [7]. A recent magnetoencephalographic study has shown that the human V5 is activated by HO motion made up of random dot kinematograms [13]. Our results showed that HO motion elicited an N170 component in the parietal area and had an adaptational effect for random motion while a P200 component was elicited by OF without an adaptational effect. Our observations suggest that the perception of HO and OF are segregated and sequentially processed. In agreement with this suggestion, fMRI studies showed that both HO and OF motion stimuli activated MT/V5 with the superior parietal lobule was activated by only HO motion. These findings are in accord with the recent view on the importance of the parietal lobe for OF motion perception [14]. The differential effects of adaptation on OF and HO are evident, which suggest that OF perception, especially OF (out), is related to the ventro-dorsal pathway while HO perception is related to the dorso-dorsal pathway.

■ Mechanism of photosensitive epilepsy

Photosensitive epilepsy (PSE) occurs in approximately one out of 4000 individuals from the general population and tends to be most prevalent in adolescence [15]. PSE can be caused by flickering light and/or high contrast patterned stimuli. Patients with PSE usually show a photoparoxysmal response (PPR) to intermittent photic stimulation (IPS) in their EEGs. Apparently, the ON-OFF pathway [2] is responsible for PSE.

OF minus HO



HO minus OF



RM minus OF

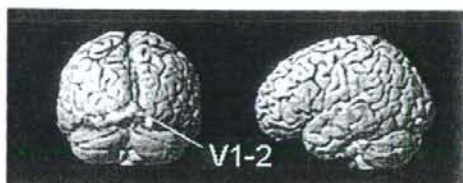


Figure 7. fMRI results under different conditions of motion. Subtracting the response to HO from that to OF (out) shows activation of IPL, MST, STS, cerebellum for OF (out; upper) while subtracting OF (out) from HO shows activation of SPL (middle). Random motion only activated V1/V2 (lower).

"Pocket monsters" seizures

On December 16, 1997 at around 18:50 hours, 685 Japanese children and some adults suffered generalized convulsions and a loss of consciousness suggesting epileptic seizures, while watching a popular animated TV program called Pocket Monsters [16, 17]. The probable cause was PSE because an unusually large number of children developed similar symptoms at exactly the same time in a similar situation when watching a scene consisting of flashing lights and rapid color changes in the cartoon. However, it was not clear why so many children without any previous seizures were affected or exactly which components of the cartoon were the provocative stimuli. We reported that rapid changes of blue and red (B/R) color frames were the provoking factor for these seizures.

Clinical findings

Twenty children (11 boys and 9 girls, aged 5-17 years) with seizures provoked by a cartoon which was broadcast on December 16, 1997 were referred to the Department of Pediatrics of Fukuoka University (Table I). All patients underwent a comprehensive EEG investigation including hyperventilation. Intermittent photic stimulation (IPS) was performed using a photostimulator (NEC San-ei or Nihon Kohden) placed at a distance of 30 cm from the patient's eyes. In addition, EEG recordings were made from four male children (aged 8-13 years) who were recruited from the 20 cases and were watching the critical sequences of the cartoon that had induced the seizures. The patient sat 1.3 m from the

Table I. Summary of clinical findings

Case	Age	Gender	Seizure type	Febrile convulsion	CT or MRI	Time
1.	11	M	GTC	-	N	6:51
2.	9	M	GTC	-	N	6:51
3.	14	M	GTC	-	N	6:50
4.	8	M	GTC	+	N	?
5.	13	M	GTC	-	ND	6:51
6.	10	M	GTC	-	N	6:51
7.	11	M	GTC	+	N	6:51
8.	15	F	GTC	+	N	6:40
9.	15	F	GTC	-	N	6:45
10.	16	F	GTC	-	N	6:50
11.	17	F	GTC	-	N	6:51
12.	11	F	GTC	-	N	6:51
13.	12	M	GTC	-	N	6:51
14.	5	F	UNCONCIOUSNESS	+	N	6:51
15.	6	F	VISUAL	+	N	6:51
16.	8	F	GTC	-	ND	6:51
17.	8	M	GTC	-	N	6:51
18.	12	M	GTC	-	N	6:51
19.	14	M	GTC	-	N	6:51
20.	12	F	GTC	-	ND	6:50

Abbreviations: GTC = generalized tonic convulsions, + = present, - = absent, N = normal, ND = not done.

video monitor which subtended a visual angle of 23.1 degree horizontally and 17.4 degree vertically. Rapidly changing blue and red (B/R) color frames and monochromatic gray and black (G/B) frames were presented at different stimulus frequencies of 3, 6, 8.57, 10, 12, and 15 Hz in 2 patients, because the committee had determined that the background of the colored cartoon frames consisted of rapid changes of red and blue frames at 12 Hz. The mean luminances of the red, blue, gray, and black were 120 cd/m², 160 cd/m², 160 cd/m² and 20 cd/m², respectively.

EEG findings

All four boys had photoparoxysmal responses (PPRs), *i.e.*, bursts of 3 Hz spike and wave complex, when exposed to the colored cartoon frames, and the PPRs were less frequent while watching a monochromatic version of the same cartoon (Figures 8, 9). The effect of the stimulus frequency on the EEG is shown in Figure 9 for one subject. This subject had a PPR to B/R color stimulus at 6 Hz and at 12 Hz and did not show the PPR to G/B stimuli up to 12 Hz (Figure 9) [17]. The other patient showed a PPR to B/R color stimulus at 10 Hz and did not show a PPR up to 12 Hz with G/B stimuli (data not shown).

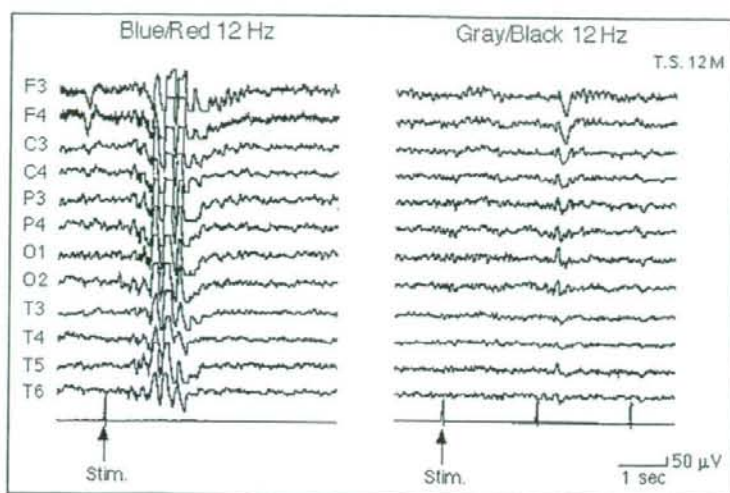


Figure 8. Photoparoxysmal response induced by the cartoon frames (blue/red) and monochromatic version (gray/black) of the same cartoon in a representative case. This patient was more sensitive to chromatic changes than monochromatic changes. Adopted from Tobimatsu *et al.* (1999) [17].

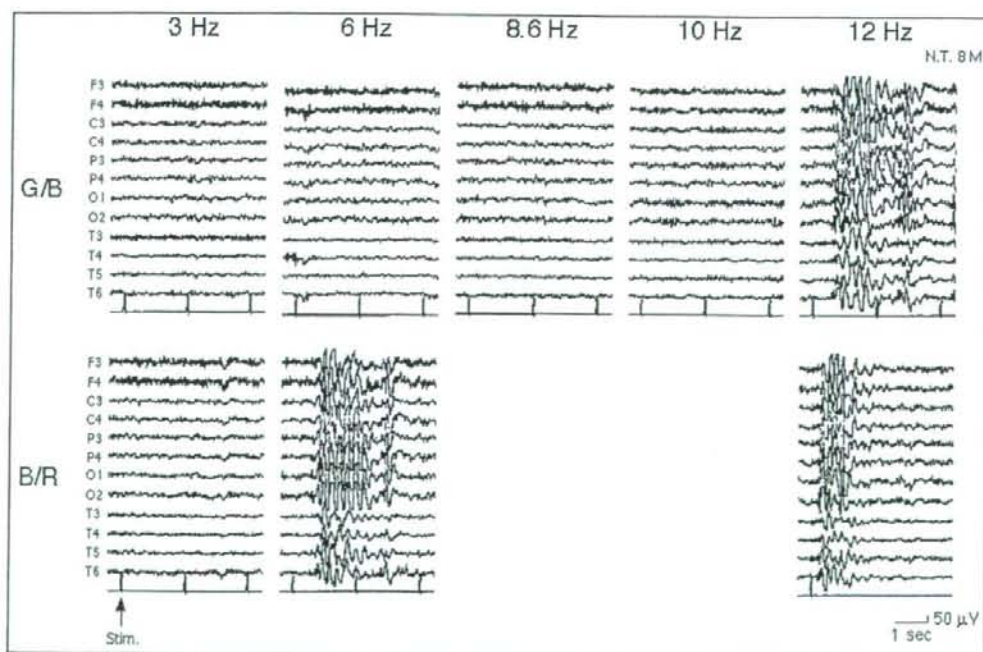


Figure 9. Effect of stimulus frequency on photoparoxysmal response (PPR) in another patient. Note that not only blue/red (B/R) chromatic changes at a rate of 12 Hz but also that of 6 Hz provoked a PPR. In contrast, a gray/black (G/B) flicker induced a PPR only at 12 Hz. Adopted from Tobimatsu *et al.* (1999) [17].

Chromatic sensitivity

Four patients without history of seizures were more sensitive to rapid color changes than to monochromatic ones. Similarly, five of six British PSE patients had a PPR after viewing colored (B/R) cartoon frames but not after watching monochromatic (G/B) ones [16]. We also found that B/R stimuli provoked a PPR at even lower stimulus frequencies than that with achromatic stimuli. These findings suggest that the rapid color changes in the cartoon provoked the seizures. The long wavelength red light from the red frame stimulates red cones while short wavelength blue light stimulates blue cones [2]. It was thus postulated that no antagonistic relationship existed between the red and blue cone impulses in the visual cortical neurons [18]. No matching inhibitory signals were elicited by stimulating with these two colors, which thus resulted in a maximal stimulation of the visual cortex, and seizures in photosensitive individuals. It remains controversial, however, as to whether red light is more provocative than white light [16, 19-22]. Takahashi and Tsukahara [19, 20] claimed that red flickering light was more epileptogenic than white or other colors while other studies found no consistent difference between red and green stimuli. These findings suggest that a combination of colors without any antagonistic relationship in the visual cortex such as red and blue is apparently more provocative than red alone.

Revised concept of photosensitive epilepsy

From all of these observations, we would like to revise the overall concept of photosensitive epilepsy. We propose that four factors play important roles in the generation of a PSE: 1) photosensitivity, 2) pattern sensitivity, 3) chromatic sensitivity and 4) stimulus frequency [17]. Photosensitivity to IPS is well-known to be essential for diagnosing PSE [22-24]. Pattern sensitivity is already known to play an important role in TV game epilepsy [15, 25, 26]. High contrast black and white square-wave grating patterns at spatial frequencies between 0.5 and 6 cycles/degree are recommended for laboratory tests of pattern sensitivity [15]. Chromatic sensitivity is also important as observed in this study, especially a combination of colors without any antagonistic relation in the visual cortex such as red and blue. Finally, stimulus frequency is another important factor. PSE patients are most sensitive to a frequency range of 10 to 30 Hz of the IPS [15]. Similarly, the induction of PPRs was highly dependent on the stimulus frequency for B/R or G/B as shown in the present study. Taken together, investigators should thus recognize that each PSE patient has a different susceptibility to these four factors. These findings suggest that testing for chromatic sensitivity as well as IPS sensitivity during routine EEG tests is required when physicians suspect chromatic sensitivity in patients. In sum, our patients were all considered to have PSE. However, chromatic sensitivity also played an important role in the generation of seizures. Therefore, we propose that chromatic sensitive epilepsy should be considered a variant of PSE, and a substantial population of children are affected by it.

■ Conclusions

We have outlined the functions of the major parallel pathways of the visual system to understand the mechanism of visual reflex epilepsy such as PSE. The results of our study clearly suggest that visual stimuli should be tailored to answer specific clinical and/or research questions.

Acknowledgments

This study was supported in part by Grant-in-Aid for the 21st Century COE Program.

References

1. Livingstone M, Hubel D. Segregation of form, color, movement, and depth: anatomy, physiology, and perception. *Science* 1988; 240: 740-9.
2. Tobimatsu S, Celesia GG. Studies of human visual pathophysiology with visual evoked potentials. *Clin Neurophysiol* 2006; 117: 1414-33.
3. Tobimatsu S, Tomoda H, Kato M. Parvocellular and magnocellular contributions to visual evoked potentials in humans: Stimulation with chromatic and achromatic gratings and apparent motion. *J Neurol Sci* 1995; 134: 73-82.
4. Arakawa K, Tobimatsu S, Kato M, Kira J. Parvocellular and magnocellular visual processing in spinocerebellar degeneration and Parkinson's disease: An event-related potential study. *Clin Neurophysiol* 1999; 110: 1048-57.
5. Tobimatsu S, Celesia GG, Haug BA, Onofrij M, Sartucci F, Porciatti V. Recent advances in clinical neurophysiology of vision. *Electroenceph Clin Neurophysiol* 2000; S53: 312-22.
6. Vuilleumier P, Armony JL, Driver J, Dolna RJ. Distinct spatial frequency sensitivities for processing faces and emotional expressions. *Nat Neurosci* 2003; 6: 624-31.
7. Rizzolatti G, Matelli M. Two different streams from the dorsal visual system: anatomy and functions. *Exp Brain Res* 2003; 153: 146-57.
8. Nakashima T, Goto Y, Abe T, Kaneko K, Saito T, Makinouchi A *et al.* Dual route model for recognition of faces and facial expressions: An event-related potential study with spatially filtered images. *Clin Neurophysiol* 2006; 117: S302.
9. Allison T, Ginter H, McCarthy G, Nobre AC, Puce A, Luby M, Spencer DD. Face-recognition in human extrastriate cortex. *J Neurophysiol* 1994; 71: 821-5.
10. Bentin S, Allison T, Puce A, Perez E, McCarthy G. Electrophysiological studies of face perception in humans. *J Cogn Neurosci* 1996; 8: 551-65.
11. Mapstone M, Steffenella TM, Duffy CJ. A visuospatial variant of mild cognitive impairment. Getting lost between aging and AD. *Neurology* 2003; 60: 802-8.
12. Tobimatsu S, Goto Y, Yamasaki T, Tsurusawa R, Taniwaki T. An integrated approach to face and motion perception in humans. *Clin Neurophysiol* 2006; S59: 41-6.
13. Nakamura H, Kashii S, Nagamine T, Matsui Y, Hashimoto T, Honda Y *et al.* Human V5 demonstrated by magnetoencephalography using random dot kinematograms of different coherence levels. *Neurosci Res* 2003; 46: 423-33.
14. Prito M, Kupers R, Faubert J, Gjedde A. Cortical representation of inward and outward radial motion in man. *Neuroimage* 2001; 14: 1409-15.
15. Harding GFA, Jeavons PM, Edson AS. Video material and epilepsy. *Epilepsia* 1994; 35: 1208-16.
16. Harding GFA. TV can be bad for your health. *Nature Med* 1998; 4: 265-7.
17. Tobimatsu S, Zhang Y-M, Tomoda Y, Mitsudome A, Kato M. Chromatic sensitive epilepsy - A variant of photosensitive epilepsy. *Ann Neurol* 1999; 45: 790-3.
18. Livingstone MS, Hubel DH. Anatomy and physiology of a color system in the primate visual cortex. *J Neurosci* 1984; 4: 309-56.
19. Takahashi T, Tsukahara Y. Influence of color on the photoconvulsive response. *Electroencephalogr Clin Neurophysiol* 1976; 41: 124-36.
20. Takahashi T, Tsukahara Y. Usefulness of blue sunglasses in photosensitive epilepsy. *Epilepsia* 1992; 33: 517-21.
21. Binnie CD, Estevez O, Kasteleijn-Nolst Trenité DGA, Peters A. Colour and photosensitive epilepsy. *Electroencephalogr Clin Neurophysiol* 1984; 58: 387-91.
22. Harding GFA, Pearce K, Dimitrakoudi M, Jeavons PM. The effect of coloured intermittent photic stimulation (IPS) on the photoconvulsive response (PCR). *Electroencephalogr Clin Neurophysiol* 1975; 39: 428.

23. Panayiotopoulos CP, Jeavons PM, Harding GFA. Occipital spikes and their relation to visually evoked responses in epilepsy, with particular reference to photosensitive epilepsy. *Electroencephalogr Clin Neurophysiol* 1972; 32: 179-90.
24. Jeavons PM, Harding GFA, Panayiotopoulos CP, Drasdo N. The effect of geometric patterns combined with intermittent photic stimulation in photosensitive epilepsy. *Electroencephalogr Clin Neurophysiol* 1972; 33: 221-4.
25. Wilkins AJ, Darby CE, Binnie CD, Stefansson SB, Jeavons PM, Harding GF. Television epilepsy-The role of pattern. *Electroencephalogr Clin Neurophysiol* 1979; 47: 163-71.
26. Fylan F, Harding GFA. The effect of television frame rate on EEG abnormalities in photosensitive and pattern-sensitive epilepsy. *Epilepsia* 1997; 38: 1124-31.

lumière

専門医のための
精神科臨床
リュミエール

2

精神疾患と脳画像

【責任編集】 福田正人

中山書店

1. MRI

精神科における画像検査

精神科の一般診療においては、まず脳器質性疾患を念頭におき、見落とさないことがいちばん重要である。身体所見（体温、脈拍）、神経学的所見（局在所見の有無）、意識障害の有無に常に注意を払う必要がある。本書では、精神疾患の脳画像の基礎から多少進んだ研究的な所見まで幅広く記述されているが、本項では精神疾患の画像診断のうちでも特に磁気共鳴映像法（magnetic resonance imaging：MRI）についての基礎知識および症例を紹介することにより、精神科一般診療に役立つ内容を目指すことにする。

精神科において必要となる画像検査は、頭部のCT、MRI、SPECT、PETなどである。CTとMRIは形態学検査で、SPECTとPETは機能的検査であり、患者の病態に応じてこれらの検査を使い分けて検査を進めていく。脳器質性疾患を除外するためにやみくもに検査を行えばよいというのではなく、限られた医療経済のなかでは、必要な検査を効率良く行うことが重要であり、そのために各検査の原理や特性を把握しておく必要がある。本項では、最初にMRIの基礎知識について述べた後に、実際の診療の参考になるよう症例を提示する。

MRIの基礎事項

MRIの基礎事項として、その特徴を以下に列挙する。

- ① mm単位の空間分解能をもつため、病変の発見が比較的容易である。
- ② 体中のどのような部位においても任意の断面が撮影可能である。
- ③ 造影剤を使用せずに血管撮影やミエログラフィーを行うことも可能である。
- ④ 撮像方法を変えることで、機能的MRI（fMRI）として脳機能を画像化することが可能である。
- ⑤ X線を使うX線撮影法やCTのようなX線被曝はない。
- ⑥ 骨や脂肪組織の影響を比較的受けにくい。

MRI の原理

MRI は NMR (nuclear magnetic resonance ; 核磁気共鳴) を利用した画像診断法であり, NMR に位置情報を加えることにより, その信号の強度を画像化する方法である。つまり, MRI は強力な磁力と電波 (高周波) によって人体を撮影する画像であり, 強い磁場の中に患者を入れて外から電波を与えると, 体の中の水素原子が共鳴し, 電波を止めると共鳴した水素原子から微弱な電波が出るが, この微弱な電波を受信してコンピュータにより画像化するというものである¹⁾。理論上は, 水素以外の原子からの電波を受信することも可能であるが, 画像診断法として役立つのは現在のところ水素原子のみである。

MRI 撮像の実際

電波や磁場の人体への影響は, まだはっきりしないといわれており, 原則として妊婦は検査しないことになっている。またペースメーカーや金属が体内にある患者は原則として検査禁忌である。検査前に体内の金属の有無は患者や家族に必ず確認しなければならない。検査時間は撮影条件や撮影機種にもよるが, 20 ~ 40 分かかることが多く, この間の数分間, 被検者はまったく動かずにいることが必要である。理解力のない患者はこの数分間の安静が保てず, 検査ができないことがある。

次にいくつかの撮像方法を説明する。

T1 強調画像

スピンエコー法では repetition time (TR), echo time (TE) が信号強度と関係しており, 撮像条件で TR, TE をともに短く設定すると, 各組織の T1 (縦緩和時間) の差が強く出る画像が得られる (T1 強調画像 <T1 weighted image : T1WI>)。T1 値の長い水が低信号 (黒色), T1 値の短い脂肪が高信号 (白色) となる。脳灰白質は白質に比べてやや低信号を呈する¹⁾。

T2 強調画像

撮像条件で TR, TE をともに長く設定すると, 各組織の T2 (横緩和時間) の差が強く出る画像が得られる (T2 強調画像 <T2 weighted image : T2WI>)。T2 値の長い水が高信号 (白色) を呈する。一方, 白質は低信号を呈する¹⁾。

T2 star (T2*)

自由誘導減衰の磁気緩和定数のことを T2* と呼ぶ。T2* は原子核位置で

の磁場の不均一性に依存するので、臨床的には症状を伴わない微小な出血の同定に役立つとされている。

拡散強調画像

拡散強調画像 (diffusion weighted image ; DWI) は、強い双極傾斜磁場を付加して、水分子の拡散 (Brown 運動) を画像に反映する方法である。拡散が激しいほど信号強度は低く、拡散が低下した部分が高信号になる²⁾。DWI は T2WI での高信号の影響を受けるため (T2 shine through)、ADC (apparent diffusion coefficient ; 見かけの拡散係数) map を作製し、拡散低下を評価することが望ましい。

FLAIR 法

FLAIR (fluid attenuated inversion recovery) 法は、自由水 (細胞内外を自由に移動できる水) の信号を抑制する撮像方法で、T2WI では病変も脳脊髄液も高信号になり区別しづらいことが多いが、この撮像方法では脳脊髄液が低信号となるため、脳溝や脳室に接する病変の診断に有効である³⁾。てんかん患者の検査では FLAIR 画像を撮影することが望ましい。

BOLD 法

BOLD (blood oxygenation level dependent) 法は、脳活動に伴う神経代謝や脳血流の変化を間接的にとらえる方法である。酸素が消費されると、酸素化ヘモグロビンが常磁性体である脱酸素化ヘモグロビンに変化する。脱酸素化ヘモグロビンは磁化率効果により局所の信号強度を低下させるが、脱酸素化ヘモグロビンの増加に比べ不相应な局所血流増加が生じるため、脱酸素化ヘモグロビン密度は低下し、結果として局所の信号強度が上昇する³⁾。つまり信号強度の上昇が脳の機能を反映することになる。図 1 に BOLD 法による fMRI 画像の一例を示す。

MRI の解析方法

MRI を含めた脳画像検査では、初期の病態になればなるほど画像上の変化は軽微であるため、画像の評価には一定の経験が必要なうえに、評価者の主観に左右されることがしばしばある。このような問題点を克服するために、画像統計解析法という手法をとることもある。MRI による脳構造解析では、主に statistical parametric mapping (SPM) で voxel-based morphometry (VBM) を用いて検索する方法と、手書きにより関心領域の体積を測定する方法がある。詳細は項末の Further reading を参照されたい。また、SPM や VBM を応用して、各患者個人の脳情報を正常データベースと比較する Alzheimer 型認知症の診断支援ソフト (VSRAD) も開発されている。

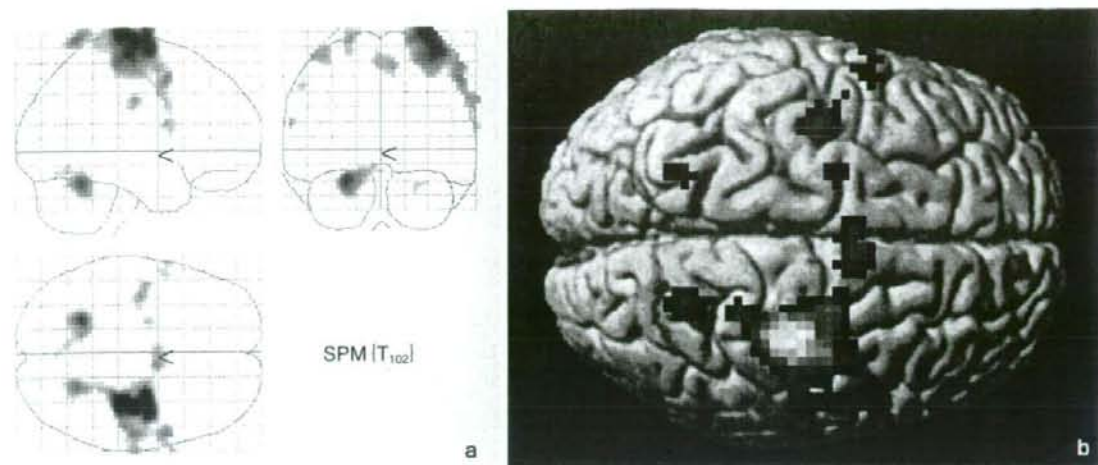


図1 fMRI (24歳, 健常男性)

左手の複雑運動時記録から安静時記録を差し引いた信号をSPMにて処理(a)した後に、標準脳3D画像にその信号を重ねて表示した(b)。

る⁴⁾、このような手法を用いることで、健常者と比較してどの部位がどの程度変化しているかが視覚的・客観的に判定可能となり、画像診断の豊富な経験をもっていなくても状態評価が可能となることが期待されている。

MRI 診断の実際

はじめに述べたように、一般診療においては、脳器質性疾患を見落とさないことが重要である。ここでは、脳器質性疾患を鑑別するにあたり参考となる症例のMRI画像を列記する。

症例1

56歳, 女性。

20歳の頃、徐々にしゃべるのが遅くなり、上肢で何かしようとするときに手が震えるようになったため受診。臨床症状と採血結果から診断した。以後、30年以上通院・服薬を行っている。

診断：Wilson病(図2)。

解説：Wilson病は銅輸送遺伝子異常のため銅が脳、角膜、肝臓などに沈着する。大脳基底核に銅が沈着するため、基底核障害としてパーキンソン症状が出現する。肝臓への沈着のため肝機能障害を、角膜への沈着のためKayser-Fleischer角膜炎を生じる。若年で、話が下手になってきた、動きが硬く表情が無くなってきた、振戦やジストニアなどの不随意運動が出てきたというパーキンソン症状を呈する場合には、Wilson病を鑑別する必要がある。治療として銅キレート薬を投与するが、障害された脳組織が完全には回復しないこともあるので、早期発見、早期治療が重要である。

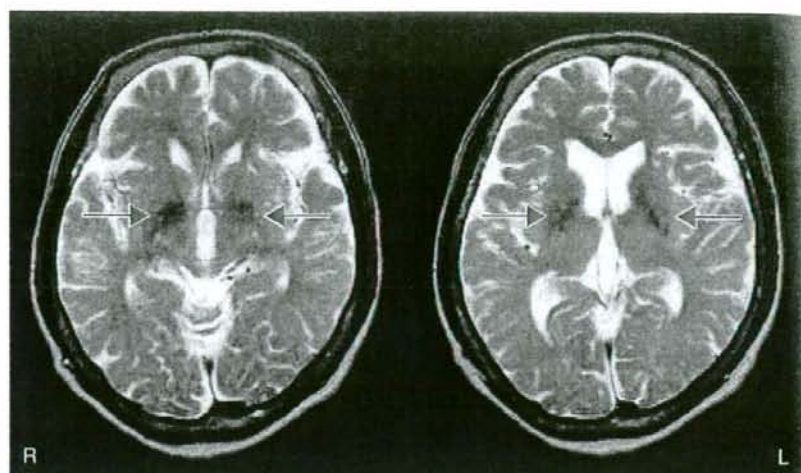


図2 症例1: Wilson病のT2WI

銅の沈着による基底核のT2短縮(低信号)と被殻の組織障害によるT2延長(高信号)を認める(矢印)。

症例2

71歳, 男性.

記憶力が低下して, 時に失禁をするようになった. 半年前から歩幅が狭くなり, ころびやすくなっていた.

診断: 正常圧水頭症(図3).

解説: 記憶障害や反応性の低下が主訴の場合には, 水頭症を鑑別しなければならない. 髄液の吸収障害以外に, 中脳水道の狭窄が原因となることがあり, 画像で確かめる必要がある. この場合, 脳MRI矢状断撮影を行うことが望ましい. 実際には水頭症と脳萎縮の鑑別が困難なことがあり, その場合は髄液の動きをとらえたシネMRIで髄液の流れを調べたり, 髄液を大量に排除して症状の改善があるかどうかCSFタップテストを行う必要がある.

症例3

34歳, 女性.

1か月前から不眠があり, 微熱と頭痛もあるため近医受診したが, 頭部CTで異常なく帰宅した. 会話はできるが短期記憶が著明に障害されていたため, 精神科を受診. 前夜以後の記憶がなくなっていた. ストレスによるものとして抗不安薬を処方されたが, 翌日, 不穏状態となった.

診断: 傍腫瘍性辺縁系脳炎(図4).

解説: 辺縁系脳炎は記憶障害や精神症状を呈するため, 精神疾患との鑑別が困難なことが多い. 画像や髄液検査をする必要があるが, それらの検査でも異常が出ないこともしばしばである. この症例では腫瘍を検索した結果, 卵巣腫瘍が見つかった. 腫瘍, 特に乳腺腫瘍や卵巣腫瘍に起因する免

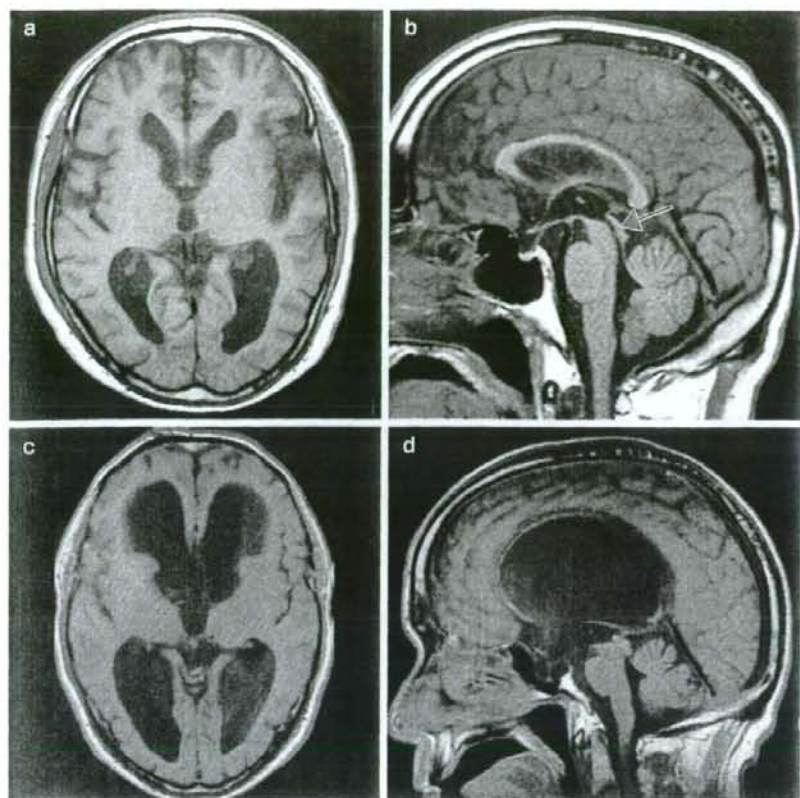


図3 正常圧水頭症のMRI

- a, b: 症例2. 脳室の拡大を認める. 矢状断では中脳水道には狭窄がないことがわかる(矢印). 脳室以外にも Sylvius 裂の開大や軽度の脳溝の狭小化を認める.
 c, d: 中脳水道の狭窄があり水頭症を呈している別の症例. 側脳室, 第三脳室の著明な拡大を認める.

疫関連性の辺縁系脳炎を生じることがあり, 精神症状をきたす場合, 特にそれが女性の場合は腫瘍が潜在しうることを知っておく必要がある. 腫瘍を摘出しても, 脳に不可逆的な障害が残ることも多い. DWIで高信号であっても T2WIの高信号が透けて見える場合があり (T2 shine through), ADC map で確かめる必要がある. ADCで高信号・等信号のときは血管性浮腫 (vasogenic edema), 低信号のときは細胞毒性浮腫 (cytotoxic edema) を示唆し, 前者の場合は可逆的であるが, 後者の場合は細胞破壊が起こっているため障害が不可逆になる可能性が高い.

症例4

50歳, 女性.

発熱と咳が出現し, その2日後に軽度意識障害, けいれんが出現し搬送された. 30歳から全身性エリテマトーデス (SLE) の診断でステロイド内服を行っていたが, 自己中止することも多かった.

診断: CNS (中枢神経系) ループス (図5).

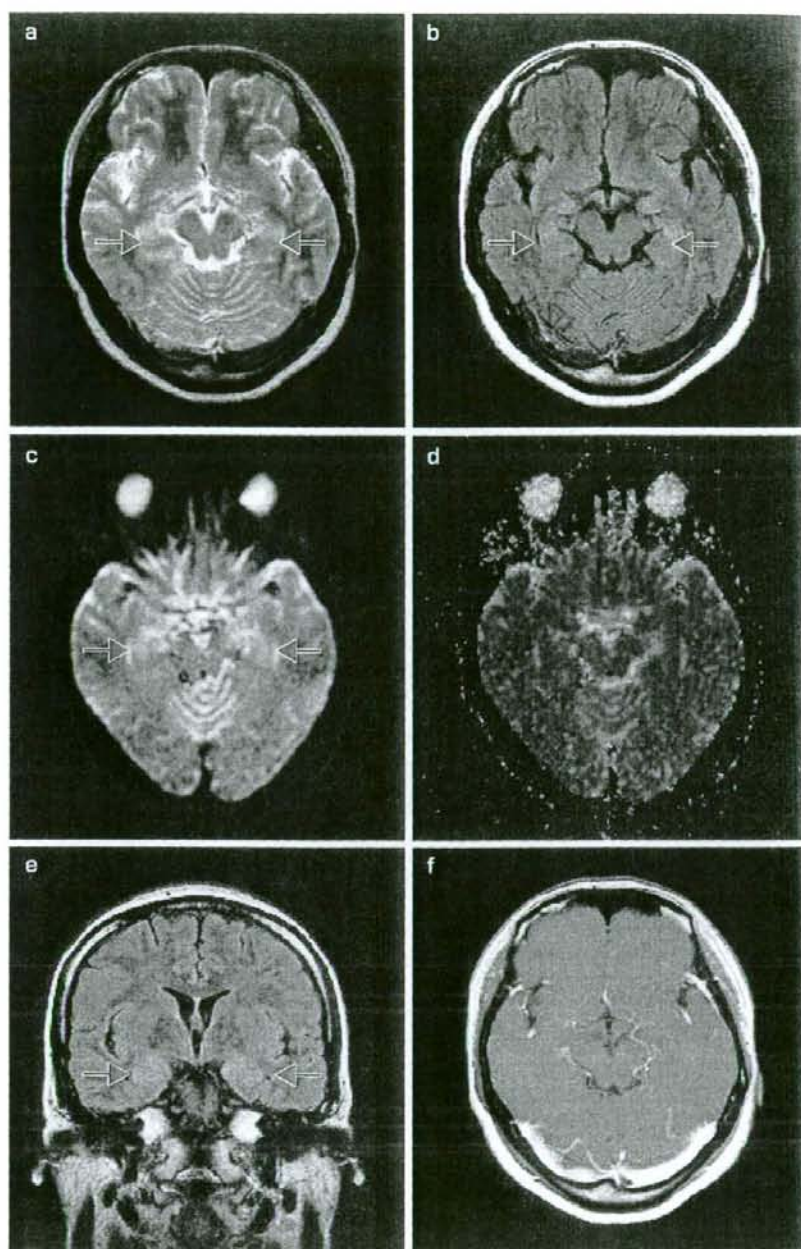


図4 症例3：傍腫瘍性辺縁系脳炎

海馬が腫大し T2WI (a)、FLAIR 画像 (b) で高信号を呈する。DWI (c) では高信号だが、ADC (d) では信号低下はみられず、血管性浮腫であることを示唆する。海馬部冠状断像 (e)、造影効果はなかった (f)。

解説：脳炎の鑑別としては、ウイルス性、細菌性、結核性、自己免疫性、傍腫瘍性などがあげられる。辺縁系脳炎で発作が重積している場合は、海馬・辺縁系は DWI で高信号をきたすため、病変なのか、神経過剰興奮による二次的な変化なのか、鑑別困難な場合がある。