**TABLE IV. Amplitudes and latencies of major wave components in Type I responses**

| Stimulation | Recording | Latency ± SD (ms) | | | | Amplitude ± SD (μV) | | |
|---|---|---|---|---|---|---|---|---|
| | | Onset | P1 | N1 | P2 | P1 | N1 | P2 |
| f-MA | f-MA | 4.8 ± 0.7 | 11.9 ± 2.8 | 29.4 ± 2.0 | 56.0 ± 4.7 | 22.3 ± 7.5[a] | 119.7 ± 61.8[b] | 162.0 ± 73.9[b] |
| | nf-MA | | | | | | | |
| | SA | | | | | | | |
| | NEA | 4.9 ± 0.8 | 13.7 ± 3.6 | 29.9 ± 2.9 | 53.5 ± 9.3 | 14.6 ± 6.4 | 61.4 ± 31.6 | 83.2 ± 37.0 |
| nf-MA | f-MA | | | | | | | |
| | nf-MA | | | | | | | |
| | SA | | | | | | | |
| | NEA | | | | | | | |
| SA | f-MA | | | | | | | |
| | nf-MA | | | | | | | |
| | SA | | | | | | | |
| | NEA | 6.9 ± 0.5 | 17.7 ± 0.1 | 35.2 ± 0.3 | 70.4 ± 5.0 | 7.0 ± 1.4 | 30.5 ± 3.5 | 48.5 ± 0.7 |
| NEA | f-MA | | | | | | | |
| | nf-MA | | | | | | | |
| | SA | 6.2 | 10.1 | 27.1 | 55.4 | 5.0 | 15.0 | 40.0 |
| | NEA | 5.5 | 13.1 | 28.7 | 55.7 | 8.0 | 15.0 | 39.0 |

SD, standard deviation; f-MA, facial motor area; nf-MA, nonfacial motor area; SA, somatosensory area; NEA, noneloquent area.
[a]Significantly greater compared with other stimulation/recording patterns ($P < 0.01$).
[b]Significantly greater compared with other stimulation/recording patterns ($P < 0.05$).

The statistical analysis on the effect of the recording site demonstrated that the recording site was important for a positive contralateral CCEP response only for MA-MRI ($P < 0.05$) (Table III). For MA-MRI stimulation, a significant difference in positive CCEP response was found between MA-MRI and NEA-MRI recordings ($P < 0.01$). These data also suggested that MA stimulation tended to evoke contralateral CCEP responses at the MA.

### *Comparisons of latencies and amplitudes*

The latencies and the amplitudes were analyzed statistically using t-test, for each waveform type (Tables IV–VI). Because of the limited data available, not all comparisons were possible. Therefore, comparisons of waveform parameters were performed only between f-MA recording with contralateral f-MA stimulation (the most frequently

**TABLE V. Amplitudes and latencies of major wave components in Type 2 responses**

| Stimulation | Recording | Latency ± SD (ms) | | | Amplitude ± SD (μV) | |
|---|---|---|---|---|---|---|
| | | Onset | N1 | P2 | N1 | P2 |
| f-MA | f-MA | 7.8 ± 0.6[a] | 24.3 ± 1.9[a] | 47.6 ± 11.4 | 30.2 ± 23.0 | 56.0 ± 29.6 |
| | nf-MA | | | | | |
| | SA | 9.0 | 33.2 | 29.0 | 14.0 | 29.0 |
| | NEA | 12.1 ± 4.2 | 33.1 ± 2.9 | 58.7 ± 4.8 | 34.3 ± 19.9 | 54.6 ± 35.7 |
| nf-MA | f-MA | 11.3 ± 4.9 | 23.7 ± 2.4 | 44.4 ± 8.4 | 19.3 ± 16.2 | 55.0 ± 25.5 |
| | nf-MA | 9.5 | 22.3 | 37.0 | 16.0 | 18.0 |
| | SA | | | | | |
| | NEA | 13.5 ± 4.7 | 31.5 ± 5.9 | 49.3 ± 7.5 | 15.0 ± 1.4 | 40.0 ± 19.8 |
| SA | f-MA | | | | | |
| | nf-MA | | | | | |
| | SA | | | | | |
| | NEA | | | | | |
| NEA | f-MA | 9.6 | 26.6 | 50.6 | 18.0 | 36.0 |
| | nf-MA | | | | | |
| | SA | | | | | |
| | NEA | 11.8 ± 3.5 | 28.2 ± 5.0 | 52.9 ± 5.6 | 28.5 ± 4.9 | 42.8 ± 10.5 |

SD, standard deviation; f-MA, facial motor area; nf-MA, nonfacial motor area; SA, somatosensory area; NEA, noneloquent area.
[a]Significantly shorter compared with other stimulation/recording patterns ($P < 0.001$).

**TABLE VI. Amplitudes and latencies of major wave components in Type 3 responses**

| | | Latency ± SD (ms) | | | Amplitude ± SD (μV) | |
|---|---|---|---|---|---|---|
| Stimulation | Recording | Onset | P1′ | N1′ | P1′ | N1′ |
| f-MA | f-MA | 20.0 ± 4.5 | 31.6 ± 4.1 | 52.0 ± 5.6 | 20.0 ± 15.6 | 38.3 ± 27.5 |
| | nf-MA | 15.1 | 22.2 | 43.7 | 11.0 | 29.0 |
| | SA | | | | | |
| | NEA | | | | | |
| nf-MA | f-MA | 10.0 | 28.9 | 53.1 | 25.0 | 48.0 |
| | nf-MA | | | | | |
| | SA | | | | | |
| | NEA | | | | | |
| SA | f-MA | | | | | |
| | nf-MA | | | | | |
| | SA | | | | | |
| | NEA | | | | | |
| NEA | f-MA | 18.8 | 34.3 | 52.0 | 35.0 | 30.0 |
| | nf-MA | 21.7 | 29.4 | 50.9 | 16.0 | 30.0 |
| | SA | | | | | |
| | NEA | 7.6 | 25.7 | 39.8 | 20.0 | 25.0 |

SD, standard deviation; f-MA, facial motor area; nf-MA, nonfacial motor area; SA, somatosensory area; NEA, noneloquent area.

recorded and the most prominent waveforms obtained in this study) versus all other stimulation/recording patterns.

For Type 1 response, no significant differences in latencies such as latencies of onset, P1, N1, and P2 were observed in all comparisons. On the other hand, all amplitudes were significantly greater in the waveforms of f-MA recording with contralateral f-MA stimulation than other waveforms: from onset to P1 ($P < 0.01$), from P1 to N1 ($P < 0.05$), and from N1 to P2 ($P < 0.05$) (Table IV). For Type 2 response, the latencies of onset ($P < 0.001$) and N1 ($P < 0.001$) were shorter in the waveforms of f-MA recording with contralateral f-MA stimulation than other waveforms. However, no significant differences were detected in the comparisons of the latency of P2 and of all amplitudes (Table V). For Type 3, no significant differences were observed in all comparisons (Table VI).

## DISCUSSION

Consistent with our previous report [Terada et al., 2008], CCEP responses were recorded from the contralateral hemisphere in the current study. Compared with the previous study, this study investigated a larger number of patients, and furthermore succeeded to stimulate not only f-MA but also nf-MA and SA. The data obtained allowed us to clarify the characteristics of these interhemispheric connections more precisely. All patients in the current study had temporal lobe epilepsy. Therefore, we presume that all the CCEP responses observed in the present study may reflect normal physiological phenomena.

### Effect of Stimulation and Recording Sites

#### *Facial motor area stimulation*

CCEP responses were recorded from the contralateral hemisphere more frequently by stimulating f-MA (29.1%) than by stimulating SA (2.9%) or NEA (3.8%). And, f-MA stimulation evoked CCEP responses more frequently at the contralateral f-MA (55.6%) than at nf-MA (14.3%), SA (12.5%), or NEA (22.1%), although the differences were only significant when compared with SA or NEA recordings, probably because the number of data was too small. Furthermore, the amplitudes of all components in Type 1 response were significantly greater when stimulating f-MA and recording from contralateral f-MA. These data suggest that compared to other areas, the f-MA has denser interhemispheric connections with the contralateral f-MA. From the physiological point of view, these connections are supposed to play an important role to control facial movements, which are usually symmetric or not independent between both sides.

#### *Nonfacial motor area stimulation*

CCEP responses were recorded from the contralateral hemisphere more frequently by stimulating nf-MA (25.0%) than by stimulating SA (2.9%) or NEA (3.8%). Furthermore, nf-MA stimulation evoked CCEP responses more frequently at the contralateral f-MA (80.0%) than at nf-MA (25.0%), SA (0%), or NEA (12.5%), although the differences were only significant when compared with SA or NEA recordings. There were no apparent differences in amplitudes when compared with SA or NEA stimulation,

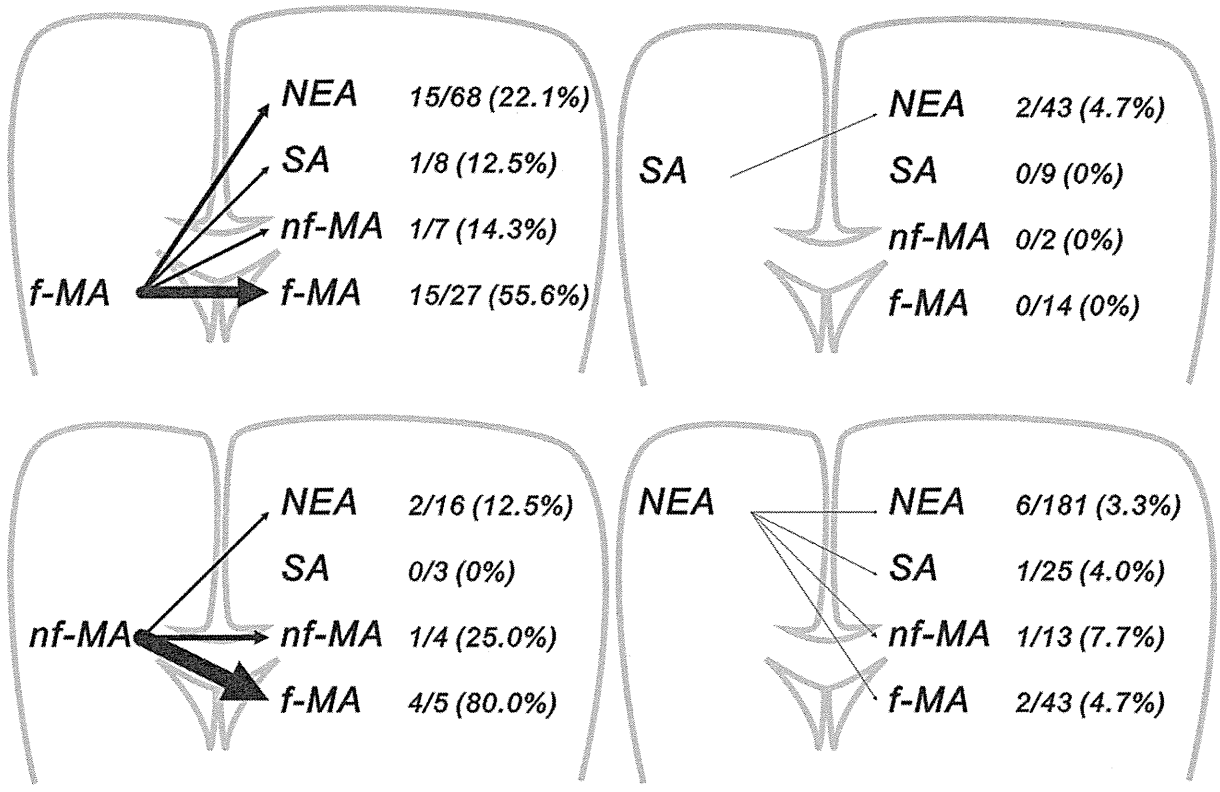


**Figure 7.**

Schematic presentation of the results. Arrows indicate the interhemispheric connections. The line thicknesses correspond to the positive rate of CCEP responses; i.e., the thicker the line is, the more frequently the interhemispheric responses can be recorded. It is demonstrated that both facial motor area (f-MA) and nonfacial motor area (nf-MA) send their neural connections to the contralateral f-MA rather than nf-MA or other areas. Furthermore, it is also seen that both somatosensory area (SA) and noneloquent area (NEA) send sparse connections to the contralateral hemisphere.

although statistical analysis could not be performed. These findings suggest that interhemispheric connections originating from the nf-MA extend to the contralateral f-MA more frequently than to other areas including the contralateral homologous nf-MA. From the physiological viewpoint, the relatively sparse connections between bilateral nf-MA may correspond to the fact that left and right hands are controlled separately and may move independently in humans.

In a previous electrophysiological study, Ugawa et al. [1993] demonstrated interhemispheric connections between strictly homotopic areas in left and right MA using transcranial magnetic stimulation. In an anatomical study conducted in humans, Aboitiz et al. [1992] also noticed that most fibers in the corpus callosum connect the corresponding areas of the left and right hemispheres. Furthermore, our previous report suggests that the interhemispheric connections are between bilateral homologous areas, although the data were limited only to f-MA stimulation [Terada et al., 2008]. In contrast, the current study demonstrated that the neural connections between left and right MA were uneven. Both f-MA and nf-MA send interhemispheric fibers to the contralateral f-MA more frequently than to the contralateral nf-MA (see Fig. 7). On the other hand, compared with nf-MA, f-MA tends to receive more interhemispheric connections from the contralateral MA, both f-MA and nf-MA. Anatomical analysis in animals demonstrated uneven transcallosal connections between left and right MA [Gould et al., 1986; Pandya and Vignolo, 1971). They reported that motor representation of the distal forelimb has no or greatly reduced callosal connections, as was also observed in the present human study.

### *Sensory area and noneloquent area stimulation*

Stimulation of SA or NEA evoked only rare CCEP responses that could be recorded from the contralateral hemisphere. Especially, SA stimulation never evoked any response at the contralateral MA or SA, even though both facial and nonfacial SA were examined. For both SA and

NEA stimulation, there were no significant differences in positive response rate among the recording sites. These findings indicate that there is no or only very sparse neural connection from the SA or NEA to the contralateral hemisphere in humans. There was no previous report on the interhemispheric connection between left and right SA in humans by any method. However, animal studies have demonstrated transcallosal connection between bilateral SA by anatomical investigations [Cusick et al., 1985; Jones and Powell, 1969; Pandya and Vignolo, 1968] and also by electrophysiological studies [Chang, 1953; Curtis, 1940a]. The discrepancy between this study and the previous reports may represent the difference in functional organization between humans and animals or the difference in methodology.

### *Analysis of MRI-defined eloquent areas*

Recently, 3D reconstruction MRI imaging is used to identify "motor area," "somatosensory area," or other eloquent areas. In this study, we also used the same method, although we could not differentiate between f-MA and nf-MA by MRI imaging. In the results, it was also demonstrated that MA-MRI (25.4%) more frequently sent the interhemispheric neural connections than SA-MRI (8.8%) or NEA-MRI (1.8%). It was also demonstrated that MA-MRI stimulation more frequently demonstrated the CCEP responses in the contralateral MA-MRI (35.8%) than SA-MRI (27.8%) or NEA-MRI (14.3%). These findings are concordant with the analysis mentioned above.

In this analysis, however, the statistically significant difference was also observed in comparison between SA-MRI stimulation (8.8%) and NEA-MRI stimulation (1.8%). In the analysis discussed above, there was no statistically significant difference between SA stimulation (2.9%) and NEA stimulation (3.8%). By stimulating SA-MRI, 13 of 147 trials demonstrated CCEP responses in the contralateral hemisphere. Of 13, six stimulations resulted in motor response in cortical stimulation, even the electrical stimuli were given on SA-MRI. It was most likely that these six stimulations might activate the adjacent MA, and, therefore, resulted in activation of the interhemispheric neural connections arising from the MA. This kind of phenomenon was called "distant response" by Penfield and Jasper [1954].

### *Waveform types*

In this study, three types of waveforms were recorded, which we designated Type 1, Type 2, and Type 3. Judged from the waveforms and peak latencies, the generators of N1 and P2 in Type 1 and Type 2 are most likely to be identical, while an additional generator may give rise to P1 in Type 1.

Type 1 responses were mainly recorded while stimulating f-MA (12 of 16 Type 1 responses) and while recording at f-MA (seven responses). Interestingly, this response was never recorded when nf-MA was stimulated. Therefore, we speculate that P1 in Type 1 response may be a relatively specific component generated by the contralateral f-MA.

In Type 1 response, one or two notches always superimpose on P1. As discussed in our previous report [Terada et al., 2008], this notch may represent the high frequency oscillation seen in somatosensory evoked potential [Hashimoto et al., 1996; Maegaki et al., 2000], or the d-wave and i-wave observed in transcranial magnetic stimulation [Hanajima et al., 2001], or the different latencies between anodal and cathodal stimuli. Further study is needed to specify the significance of the notches.

Judged from the peak latencies, P1′ and N1′ of Type 3 may correspond to the opposite tail of dipoles of N1 and P2. However, because of technical limitation (spatial sampling problem in subdural recording), we could not analyze their distributions and fields. Therefore, we could not confirm the presence of this dipole. Further study, including EEG or MEG studies, is necessary to clarify the relationship between N1-P2 in Type 1/2 response and P1′-N1′ in Type 3 responses.

### *Latencies*

In this study, the onset of P1 in Type 1 response was 3.6–7.2 ms, and the peak latency of P1 in Type 1 was 7.6–13.6 ms. The onset of N1 in Type 2 was 7.1–20.6 ms, the peak latency of N1 15.9–38.6 ms, the onset of P1′ in Type 3 7.6–24.2 ms, and the latency of P1′ 22.2–36.2 ms.

Shibasaki et al. [1978] demonstrated the latency difference of C reflexes in bilateral limbs in patients with cortical myoclonus, and suggested that the transit time between bilateral hemispheres is 9–11 ms. Brown et al. [1991] also demonstrated similar side-to-side difference of C reflexes in patients with cortical myoclonus. Their data suggested that the interhemispheric transit time is 10.1–15.6 ms. Transcranial magnetic stimulation also demonstrated transcallosal connections between bilateral MA. When the ipsilateral MA was stimulated as the conditioning stimulation, EMG responses evoked by contralateral MA stimulation was reduced significantly. This interhemispheric inhibition was maximal when the stimulus interval was approximately 8–9 ms [Ferbert et al., 1992]. Ugawa et al. [1993] reported that stimulation of the ipsilateral MA facilitated the response for the contralateral MA stimulation, and demonstrated that this effect was prominent when the conditioning stimulation was given 8 ms before the contralateral stimulation. Cracco et al. [1989] and Amassian and Cracco [1987] reported cortical responses similar to our results by transcranial electrical or magnetic stimulations. Their peak latencies of the initial positive peak were 8.8–12.2 and 9–14 ms, respectively. These studies suggest that the transcallosal transit time is approximately 8–14 ms for left and right MA, and are almost concordant with our result (the peak latency of P1 in Type 1, the onset of N1 in Type 2, or the onset of P1′ in Type 3).

Hanajima et al. [2001] showed the occurrence of interhemispheric facilitation 4–5 ms after contralateral MA stimulation, followed by late inhibition maximal at 11 ms. This facilitation occurred much earlier than our initial peak, but occurred with the similar timing with the onset of P1 in Type 1. Then, it is possible that the very early portion of our CCEP components (P1 in Type 1 response) corresponds to this facilitation.

In animal studies, the initial positive wave lasted approximately 15 ms and the second negative wave lasted approximately 75 ms in cat [Curtis, 1940b]. Cukiert and Timo-Iaria [1989] reported that the initial response started at 2–10 ms and the second peak at 10–25 ms. Single neuron recording in animals demonstrated that the initial unit arrived at 6–8 ms by stimulating the opposite pyramidal tract in cat [Asanuma and Okuda, 1962]. The latencies obtained in the present study are consistent with those of previous works.

Anatomically, Aboitiz [1992] reported the presence of fast-conducting, large-caliber fibers between bilateral MA and SA in human. Hofer and Frahm [2006] reported connecting fibers of larger diameters (>3 μm) between bilateral MA located posterior to the midbody of corpus callosum. The estimated conduction velocity of these fibers is 40 mm/ms, corresponding to a transcallosal transit time of 2.5–3.2 ms [Aboitiz et al., 1992]. This time lag is much shorter than the latency of our initial positive peak, and even shorter than the onset of the positive wave. This discrepancy may be explained by the time lag between the stimulation and volley generation at the stimulated site, as well as the time lag between the arrival time of the volley and the EPSP generation at the recording site. It is also possible that we might have missed the earliest potential of CCEP in the present study.

### *Generators*

As discussed above, we speculate that there are at least two independent generators for the current CCEP, corresponding to the initial (P1 in Type 1) and the following peaks. Curtis [1940b] reported that the initial positive and the second negative peaks responded differently to chemical agents. He, therefore, concluded that ascending fibers in the upper layers of the cortex give rise to the initial positive peak, and descending fibers, which reach the deeper cortical layers from interneuron in the upper layer, generate the next negative peak. Chang [1953] analyzed the effects of Novocaine and strychnine to these components, and compared the potentials between stimulation of contralateral hemisphere and direct stimulation on corpus callosum. He speculated that the initial positive wave is caused by the antidromic volley and the presynaptic orthodromic volley, and the second peak is the activity of the superficially placed callosal afferent and their postsynaptic neurons. The feline study of Cukiert and Timo-Iaria [1989] suggested that the early and late components reflect most probably the involvement of mono- and polysynaptic pathways, respectively, on account of the differences in latency, response to stimulus frequency, and the stability.

## CONCLUSION

As previously reported, we demonstrated interhemispheric connections between left and right MA in humans in this study. In addition, we also demonstrated that the interhemispheric connections were uneven. The f-MA has dense connections with the contralateral f-MA, and the nf-MA also has dense connections with the contralateral f-MA but less dense connections with the contralateral homologous nf-MA. The SA has no or only sparse connection with the contralateral MA or SA.

## ACKNOWLEDGMENTS

The authors thank Ms. Miyako Yamaguchi, Ms. Mariko Ishikawa, and Mr. Yuji Sakura for technical assistance. They also gratefully acknowledge the efforts and generous cooperation of the patients in this study.

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# Epilepsy surgery and employment

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The aim of epilepsy surgery is to stop or at least reduce the seizures while preserving daily and professional functions. Most patients receiving surgery have had a long history of medically refractory disabling seizures, which impair their daily and social life directly or indirectly through chronic fear of seizure occurrence. They often have neuropsychological or neuropsychiatric comorbidities, which also contribute to the disabling condition. As a consequence, they have endured long periods of burden and handicap.

Once the surgery has been performed, there is usually a dramatic effect on seizures. The patients have to adapt to the abrupt change from a condition with seizures to one without seizures, although the comorbities usually do not or minimally change, which may pose psychological conflicts as a function of expectation for surgery of the patients and related persons. When the surgical effect on seizures is insufficient, the patients may remain the same as before, or become worse if there is any complication.

Employment is an important domain of social life. It contributes to economic life, personal identity and self-worth. The unemployment rate of people with epilepsy has been shown to be two to four times higher than that of the general population, and 40% of those employed are underemployed; the employment problems in epilepsy are the result of a set of adverse internal (personal) and external (social) factors interacting with each other in a complex manner [1].

As early as 1984, Augustine *et al.* [2] investigated occupational adjustment of 32 patients 1 to 10 years after surgery and found an increase of the employed, a decrease of the underemployed and little change of the unemployed. Poor occupational adjustment was often associated with fair or poor seizure control and also related to the presence of pre-operative psychiatric disorders, a history of past unemployment, and cognitive disturbances.

An appropriate intervention program before and after surgery may help facilitate the social integration of patients. There are some practices and practical proposals of the relevant interventions in various phases of the pre/post-surgery process [3].

This article reviews the effect of surgery on employment condition, adding our personal experience and discussions about the necessary interventions.

## Epilepsy and employment

Employment rates vary widely according to the economic and social situations and between communities and countries. The rates among persons with epilepsy can also differ according to patient selection, definition of employment, and even treatment conditions. Moreover, the diagnosis of epilepsy was often hidden in the society. Surveys of members of Japan Epilepsy Association [4] found the employment rates of persons with epilepsy to be 51.6% in 1984, 40.2% in 2001 and 36.4% in 2007, although the members of the association changed and the socio-welfare system of Japan changed during these years. These figures suggest that employment rates reflect many factors in the society. Nevertheless, past studies clearly indicate that many people with epilepsy face difficulties in finding and maintaining employment.

Several factors have been suggested to contribute to lowered employment among persons with epilepsy [1]. Besides the actual risk of seizure-related injury and economic loss, many other factors are involved, such as stigma, perception of stigma, fear of seizure, low self-esteem, inappropriate work belief [5], anxiety and depression, as well as other psychopathologies. Some patients with epilepsy may have impaired sensorimotor or cognitive function due to organic, epilepsy-related or drug-related brain dysfunction. Growth with a chronic condition may hamper acquisition of interpersonal skills.

According to our study comparing the occupational performances and the results of work aptitude tests in 15 subsequently employed and 14 persistently unemployed patients, the unemployed showed significantly lower scores in volition and spontaneity for work habit, tendency of self-isolation in interpersonal relationship, and lower results in fine motor and motor coordination tasks, although the abilities to work and practice showed no differences. With regard to job maintenance, Fraser *et al.* [6] pointed that the best discriminators of keeping a job at 1 year post-employment are related to cognitive flexibility and motor speed. Furthermore, a literature review indicated that self-efficacy, self-directed activities, and active coping strategies are crucial in adapting to epilepsy and in finding and maintaining employment [1].

## Surgery effect on employment

In so far as surgery is an option of treatment for seizures, the employment situation after surgery may not differ from that after medical treatment, as long as both treatments are equally effective in controlling seizures. However, there are some, mainly quantitative, differences. First, most patients who underwent surgery had experienced disabling seizures and drug effects for a long period of time, which profoundly impaired their daily and psychosocial lives. They grew up with this burden often from early childhood. Second, patients treated by surgery often had detectable brain lesions that cause, apart from the epileptic seizures, more serious brain dysfunction than patients without lesion and responsive to medical treatment. Third, the surgical patients and their environment have high expectation for surgery, which may sometimes be unrealistic. During the process of psychodynamic development after surgery, this unrealistic expectation may prevent them from adopting and adapting to new roles. Fourth, surgery may cause new neurological and neuropsychological complications not present before surgery, although surgery may also relieve some preexisting neuropsychological dysfunctions.

The issue of employment after surgery should be addressed taking all these differences into consideration. Numerous studies were devoted to identify the effects of surgery on employment *(Tables I and II)*. Generally, employment increased, and underemployment and unemployment decreased after surgery, although often not dramatically. Sperling *et al.* [7] suggested that the employment gains came slowly: unemployed patients took up to 6 years to obtain work after surgery. Wilson *et al.* [8] suggested that factors leading to employment gains evolve over the first 2 years alongside improvements in areas such as family dynamics, social functioning, and driving.

## ■ Factors relating to social improvement after surgery

Because surgery primarily aims at stopping or reducing seizures, all studies first investigated the relation between seizure outcome and employment outcome. Indeed, seizure relief is the essential factor for improved employment in most studies. Comparisons between surgery patients and medically treated patients made this difference more clear *(Table II)*. Surgery patients with residual seizures show closer figures to the medically intractable patients. Sperling *et al.* [7] suggested that complete seizure freedom and not just reduction in seizure frequency may be the most important issue in gaining employment.

However, besides seizure reduction, other factors have been shown to be important for employment outcome. Guldvog *et al.* [9] stressed that surgery resulted in significant improvements in the actual working situation only for those in regular education or work before treatment, concluding the superiority of surgical treatment to traditional therapy in assuring maintenance of full-time employment. Thorbecke *et al.* [3] also suggested that postoperative employment status was best predicted by pre-operative work status.

As factors for postoperative employment, Lendt *et al.* [10] indicated the importance of successful seizure control, pre-operative employment, young age, and postoperative improvements in the neuropsychological status. Students who underwent surgery are more likely to achieve employment after graduation than older patients [11].

Wilson *et al.* [12] regarded early anxiety as a marker for poor psychosocial outcome, and no vocational changes in the first 12 months as indicator for poor employment outcome. Dulay *et al.* [13] suggested that the frequency of unemployment was directly related to IQ, which might be related to onset of epileptic seizures at an earlier age, or more severe epilepsy.

Wilson *et al.* [14] reported on the difficulties associated with the cessation of seizures after surgery, *i.e.*, burden of normality. This burden may be felt by the majority of the patients, but could reach a pathological level in some, spanning a minimum of 2 years. They show inability to cope with a new situation that entails less social constraints but at the same time makes new demands. According to Thorbecke *et al.* [3], patients with few resources for adaptation, *i.e.*, those with a dearth of social skills and cognitive impairments before surgery, especially with IQ in the range of learning disability, are more susceptible to develop these maladaptive reactions.

## ■ Experience at Shizuoka Epilepsy Center

The data of two studies conducted at Shizuoka Epilepsy Center where epilepsy surgery has been performed since 1983 will be shown here.

Fifty-four patients who underwent resection surgery at ages older than 16 years and followed for more than 2 years postoperatively were randomly selected for pre- and post-surgical evaluations according to the criteria proposed by Dodrill *et al.* [15]. The epileptogenic foci

**Table I. Employment outcome after surgery in the literature**

| Reference | Patients | Follow-up (mean) | Employment status and relevant findings |
|---|---|---|---|
| Taylor, 1968 [18] | 100 TLE | 2-12 years | Unemployment: pre 37%, post 21% (of which 81% unemployed before surgery) |
| Augustine, 1984 [2] | 32 focal epilepsy | 1-10 (3.9) years | Employed: pre 44%, post 72%<br>Underemployed: pre 25%, post 0<br>Unemployed: pre 31%, post 28%<br>Unemployment was related to seizure control, psychiatric disorder, past unemployment and cognitive disturbances |
| Bladin, 1992 [19] | 107 TLE | 1-10 (4) years | Full-time: pre 48%, post 59% |
| Sperling, 1995 [7] | 86 TLE | 3.5-8 years | Unemployed: pre 25%, post 11%<br>Improvement in occupational status was related to the degree of postoperative seizure relief<br>Employment gains came slowly<br>Unemployed patients tended to be older than patients who became employed |
| Lendt, 1997 [10] | 151 focal epilepsy | 1-5 (3) years | Unemployed: pre 33%, post 16%.<br>Improved 21%, unchanged 68%, deteriorated 11%<br>Important factors were successful seizure control, pre-operative employment, younger age and improvements in the neuropsychological status |
| Reeves, 1997 [17] | 134 TLE | 4.2 years | Full- and part-time: pre 75%, post 74%<br>Unemployed: pre 4%, post 7%<br>Work outcome was influenced by presurgical work experience, successful postsurgical seizure control to allow driving, and obtaining further education after surgery |
| Eliashiv, 1997 [20] | 49 TLE | 1-30 (8.4) years | Employed/unemployed: pre 45%/47%, post 76%/16%<br>A good seizure outcome was related to a good psychosocial outcome |
| Jarrar, 2002 [21] | 32 TLE operated at age 7-18 years | 4-27 (19) years | Employed 78%, part-time 3%, homemaker 9%, unemployed 3%<br>Good seizure outcome was associated with good psychosocial outcome |
| Dupont, 2006 [22] | 110 mesial TLE | 1-17 (7) years | Professional status improved in 53% of seizure-free (> 1 year) patients and in 25% of patients with persisting seizures; worsened in 11% and 22%, respectively<br>Employment status was not different for short- or long-term follow-up |
| Dulay, 2006 [13] | 90 TLE | 3-45 (11.3) months | Unemployment 46.7% before surgery and 35.6% after surgery<br>A trend where employment was associated with good seizure outcome |

| | | | |
|---|---|---|---|
| Asztely, 2007 [23] | 65 focal epilepsy | 2 years, and 8.6-16.2 (12.4) years | Presurgery: 74% full or part-time employed<br>2 years: 76% of seizure-free and 44% with seizures were full- or part-time employed<br>Long-term: 74% of seizure free and 30% with seizures were full- or part-time employed |
| Chin, 2007 [24] | 299 focal epilepsy | 2 years | Full-, part-time, disabled, unemployed: pre- 39.5%, 6.9%, 26.7%, 11.7%; 2 years 42.8%, 12.4%, 20.7%, 9.7%<br>Net employment gains were modest 2 years after surgery and higher with better seizure outcomes |
| Benifla, 2008 [25] | 42 TLE operated at 0-18 (12.5) years | 10-20 (12) years | More seizure-free patients (86%) than residual seizure patients (57%) were employed or in school |
| Tanriverdi, 2008 [26] | 63 TLE | 6 months, 2 years and 12 years | Full- or part-time job: pre 37.5%, 6 months 62.5%, 2 years 74.5%, 12 years 67%<br>Seizure free patients had higher employment rate than non-seizure free at short- and long-term follow-ups |
| Thorbecke, 2008 [3] | 115 TLE | 2 years | Unemployed: pre 20%, post 9%; improved in 22.5%<br>Work-related problems: pre- 59%. post 25%.<br>Postoperative employment status was best predicted by pre-operative work status<br>General improvement after surgery except frequency of social contact |

were in the temporal lobe in 49 patients, frontal lobe in 4, and temporo-occipital lobe in 1. The mean age at surgery was 30.9 years (16-55) and mean postoperative follow-up period was 3.2 (2-5) years. There were equal numbers of men and women. Resection side was the left in 18 and the right in 36. Seizure outcome was Engel class I (no seizure) in 47 patients, class II (rare disabling seizures) in 1, and class III (worthwhile improvement) in 6.

Vocational outcome is shown in *Table III*. One patient (Engel class I) in class 4 had a child so that she voluntarily reduced working hours, another patient (Engel class I) in class 4 was working part-time in a job that he wished to continue, hoping to become full-time in the near future. Two patients (Engel class I) in class 5 had psychiatric symptoms that continued or aggravated postoperatively (psychosis and severe anxiety-dissociative state). The remaining three patients (Engel class III in 1, and Engel class I in 2) in class 5 had mild aphasia, subjective memory decline or visual field defect.

Social outcome was evaluated for 6 domains (mobility, sports, leisure time activities, social contacts, living situation and financial situation) and the results are shown in *Table IV*. Two patients (Engel class I) in class 4 had memory disturbance or somatoform disorder, another patient (Engel class 1) became busy at work so that he had less time for leisure or sport activity. Two patients (Engel class I) in class 5 had psychosis or depression.

**Table II. Comparison of employment outcomes between surgically treated and medically treated patients**

| Author | Subjects (surgery) | Control | Follow-up (mean) | Results |
|---|---|---|---|---|
| Guldvog, 1991 [9] | 112 focal epilepsy | 92 focal epilepsy medically treated | 12-28 (17) years | Higher proportion of surgically (53.2%) than medically treated patients (24.2%) claimed that treatment had improved their "working ability", but this resulted in significant improvements in the actual working situation only for those in regular education or work before treatment |
| Vickrey, 1995 [27] | 202 focal epilepsy | 46 patients unfit for surgery | 1-17 (5.8) years | Changed from unemployed to employed (surgery *vs.* non-surgery): 29.2% *vs.* 25.7%, unchanged: 66.1% *vs.* 65.7%, changed from employed to unemployed: 4,8% *vs.* 8.6% (no difference) |
| Kellete, 1997 [28] | 94 focal epilepsy | 36 patients unfit for surgery | | 80% of seizure-free and 53% of patients having less than 10 seizures per year in gainful employment postoperatively, compared with 28% and 27% of patients having greater than 10 seizures per year or those who were unsuitable for surgery |
| Wiebe, 2001 [29] | 40 TLE | 40 TLE medically treated | 1 year | Employed/attending school: surgical group, 56.4%; non-surgical 38.5% (non-significant) |
| Jones, 2002 [30] | 61 TLE | 23 TLE unfit for surgery | 2-9 (5.8) years | Full-time employment: surgery group (pre 56%, post 69%), medical group (pre- 48%, post 39%)<br>Among surgery group with full-time employment, 69% were seizure-free |

**Table III. Experience at Shizuoka Epilepsy Center: vocational outcome after surgery (54 patients followed for > 2 years)**

| | | N |
|---|---|---|
| Class 1 | Marked improvement | 8 |
| Class 2 | Some improvement | 7 |
| Class 3 | No change | 25 (incl. 7 students) |
| Class 4 | Some deterioration | 2 |
| Class 5 | Marked deterioration | 5 |

In summary, for both vocational and social outcomes, no change was the most common outcome, followed by improvement and then deterioration. Patients with deterioration often had neurological, neuropsychological or neuropsychiatric complications that may explain their poor employment condition.

**Table IV. Experience at Shizuoka Epilepsy Center: Social outcome after surgery (54 patients followed for > 2 years)**

| | | N |
|---|---|---|
| Class 1 | Marked improvement | 7 |
| Class 2 | Some improvement | 5 |
| Class 3 | No change | 37 |
| Class 4 | Some deterioration | 3 |
| Class 5 | Marked deterioration | 2 |

We then looked at the long-term employment condition. Medical records of 170 patients who underwent resection surgery (temporal lobe in 142 and extratemporal lobe in 28) more than 15 years before were reviewed and their employment conditions were retrospectively investigated. The mean age at surgery was 25.5 years (4-55) and mean postoperative follow-up period was 18.6 (15-25) years. There were 102 males and 68 females. Resection side was the left in 79 and the right in 91. Seizure outcome was Engel class I in 129 patients (76%), class II in 16, class III in 8, and class IV in 16 (no worthwhile improvement) at the last follow-up. Seven patients died. Antiepileptic medication was discontinued in 78 patients, continued in 54, and unknown in 31. Most of the unknown cases were assumed not to be in a medically serious condition, otherwise they would have been under our care.

Employment outcome is shown in *Table V*. There is generally an increase of stable employment and a decrease of unemployment. Among 12 unemployed persons after long-term follow-up, only 6 were in Engel class I, 5 had neurologic complications (anomia, paresis, anopsia), and 9 had psychiatric symptoms. They were significantly younger at seizure onset, and were unemployed or unstably employed before surgery.

*Table VI* compares the employment status between patients who stopped medication and those who continued taking medication. Medication status of 31 patients was unknown. Reduction towards a cessation of medication was tailored to each patient with an extended period of tapering. A patient who has discontinued medication (also without seizure) is no longer regarded as a person with epilepsy. The number of unstable employment and unemployment was apparently higher in patients who continued to take medication.

## ■ Interventions and rehabilitation

Not all patients need intervention in the postoperative course. However, there are some who are more vulnerable in the ability to adapt to the postoperative situation and require support and interventions.

Horowitz *et al.* [16] described a five-phase model of psychosocial development after surgery, by which the patient detaches himself from his chronic disease: moratorium, reappraisal, great expectations, turbulent period within self, and gradual adaptation. The endpoint is an autonomic person or chronically ill person. This model can be applied to postoperative rehabilitation where appropriate interventions should be programmed according to

**Table V. Experience at Shizuoka Epilepsy Center: Long-term (> 15 years) employment outcome of 163 patients**

| | Pre | Post (> 15 years) |
|---|---|---|
| Employed stable | 41 | 67 |
| Employed unstable | 41 | 15 |
| Sheltered | 10 | 7 |
| On welfare | 1 | 7 |
| Unemployed | 27 | 12 |
| Housekeeping | 4 | 25 |
| Student | 39 | 0 |
| Unknown | 0 | 30 |

* Part-time was included in the unstable employment.

**Table IV. Experience at Shizuoka Epilepsy Center: Employment situation of patients who discontinued and patients who continued to take medication after surgery**

| | AED discontinued (N = 78) | AED continued (N = 54)* |
|---|---|---|
| Employed stable | 47 | 18 |
| Employed unstable | 4 | 9 |
| Sheltered | 3 | 4 |
| On welfare | 1 | 4 |
| Unemployed | 3 | 6 |
| Housekeeping | 11 | 12 |
| Student | 0 | 0 |
| Unknown | 9 | 1 |

* (Engel class I: 29, II: 10, III: 6, IV: 9); AED: antiepileptic drugs.

the phase of the patients. Thorbecke *et al.* [3] suggested that the first three phases are passed in the first 6-12 months after surgery and only in rare cases does it take longer, and it seems that the situation at 24 months after surgery can be taken as the outcome of surgery.

Smeets *et al.* [1] recommended specific training interventions that focus on increasing the self-efficacy and coping skills of people with epilepsy so that these individuals will be able to accept their disorder and make personal and health-related choices that help them achieving better employment positions in the society.

Reeves *et al.* [17] suggested the importance of further education after surgery in case of insufficient qualification before surgery.

Thorbecke *et al.* [3] indicated that postoperative improvements of the psychosocial situation depends strongly on pre-operative expectations or aims set in connection with the surgical intervention, and recommended rehabilitation to start before surgery in the form of working

out realistic expectations together with patient and family. Postoperatively, they proposed three occasions for considering rehabilitation support: 1) immediately after surgery if there is a high risk for psychosocial complications or complications have already occurred; 2) about 6 months after surgery when there are hints that the patient does not profit as much as would have been possible; and 3) when the seizure relapses after some time without seizures. Rehabilitation should be performed by a team composed of multidisciplinary professionals.

## ■ Conclusion

For patients with intractable epilepsy, surgery is more effective than medical treatment to achieve employment when there is complete control of seizures. Younger patients with pre-operative education or work experience have greater benefits, and employment integration needs time. Appropriate interventions and support as well as education help vulnerable patients integrate into employment life. Such interventions should be started before surgery and performed by a comprehensive team.

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Achevé d'imprimer par Corlet, Imprimeur, S.A.
14110 Condé-sur-Noireau
N° d'Imprimeur : 127343 - Dépôt légal : mai 2010
*Imprimé en France*

診　断

# Wadaテストによる言語・記憶機能検査
## ―てんかん外科の手術前検査における役割―

*The role of the Wada test in the surgical treatment of epilepsy*

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### はじめに

Wadaテストは内頚動脈アモバルビタール法とも呼ばれるものであり，言語優位半球の同定を可能にする有力な検査法として，1948年にJuhn Wada(和田淳)博士により開発された．この翌年，雑誌『医学生物学』に発表された論文[1]はすぐ英訳され，Wadaテストが世界中で実施されるようになった．その後，言語機能のみならず記憶機能検査においても使用されるようになり，今日に至っている[2,3]．てんかん外科における手術前検査としては，言語，記憶機能の評価だけではなく，てんかん原性領域の側方性の同定[4]や，術後発作転帰の予測[5]など，多様な脳機能検査に威力を発揮してきた．

Wadaテストは，現在，言語優位半球の同定法として最も信頼度の高い検査である．しかし，21世紀に入って，アモバルビタールが入手困難になったこと，ならびに磁気共鳴イメージング(magnetic resonance imaging；MRI)，脳磁図(magnetoencephalography；MEG)をはじめとする非侵襲的検査手法の技術向上による脳機能評価法の拡大によって，Wadaテストの位置付けあるいは意義に変化が生じ始めている．

本稿では，Wadaテストを主としてんかん外科治療の観点から，その実際の内容をやや詳細に概観するとともに，世界での使用状況と趨勢を展望する．さらにWadaテストの代替検査として行われている非侵襲的手法についても言及する．

### 一般的なテスト内容と主要な特長

概略としては，脳血管造影検査用に挿入されたカテーテル(通常，大腿動脈から挿入)を頭頚部まで進め，左または右内頚動脈から麻酔薬を注入して同側大脳半球を一過性に不活化することにより，脳機能局在の確

認を行う方法である．50年以上にわたって世界中で広く実施されている検査法であることから，共通の統一された実施手順が存在するものと思われがちであるが，実際には多くのバリエーションが存在する．言語優位半球の同定のみならず，記憶機能検査，さらにはてんかん外科手術前検査など多様な用途に使用されていることから，詳細な部分に関しては施設ごとに異なっている場合が多い．

紙面の制約を勘案し，ここではこれらの多様なバリエーションには言及せず，多くの施設で実施されている，言語と記憶機能検査としてのWadaテストの基本と共通的な技術について述べることにする．

## 1. Wadaテストの手順(表1)

### (1) ベースラインの確認

言語機能に関する検査であることから明らかなように，被験者の理解と協力が必須である．このため，精神症状や著しい知能障害など，検査遂行の妨げとなるような問題がないかを検査前に確認することがまず第1である．検査前日，または検査数時間前に手順の説明と，言語・記憶機能のベースライン確認のための言語・記憶検査課題項目の練習を実施しておく．

### (2) 麻酔薬注入による対側の一過性半身麻痺の確認

麻酔の効果は，注入直後に対側半身に一過性麻痺が生じることで確認される．検査は，両上肢を挙上した状態や，両手の指の反復運動を継続した状態で開始し，カテーテルから麻酔薬を3〜5秒かけて注入し，注入後に対側上肢が落下する，または，対側の指の反復運動が停止することで対側半身の麻痺を確認する．麻酔効果の持続時間は3〜5分程度とかなり短いため，この間に効率的に言語検査，記憶検査を実施する必要がある．

ただし，施術としては次項で述べる言語課題は麻酔薬注入前から開始することになる．

### (3) 言語機能検査における課題および評価

言語機能は，麻酔薬注入後の失語症状の有無により評価する．そのため，実際には麻酔薬注入前に，被験者に言語課題(数唱，1週間の曜日名を順番に言う，など)を開始するように指示する．そのうえで，課題継続中にカテーテルから麻酔薬を注入し，意識レベル，麻痺の状況を確認しつつ，言語機能検査を行う．このために使用される検査課題は，物品呼称，読字，音声提示言語の復唱，言語理解を評価するための簡単な口頭指示(開閉眼，挺舌など)などである．

麻酔薬注入により，なんらかの言語機能の阻害が出

表1　Wadaテストの手順

| | |
|---|---|
| 検査前日または数時間前 | |
| 0 | 被験者への検査課題・手順説明およびベースライン確認 |
| 検査当日 | |
| 1 | 内頸動脈へのカテーテル挿入を確認 |
| 2 | 言語課題(数唱など)開始 |
| 3 | 麻酔薬注入 |
| 4 | 対側半身麻痺の確認・意識状態の確認 |
| 5 | 言語課題(物品呼称，読字，聴覚言語理解など)継続 |
| 6 | 記憶課題も同時進行 |
| 7 | 半身麻痺の回復確認 |
| 8 | 言語機能回復確認 |
| 9 | 記憶課題再認検査 |
| 10 | 30分程度の間隔を空けて対側の検査(手順1〜9反復) |

言語・記憶課題はベースライン検査用と初回側用，対側用に異なるものを3セット用意する．

現する．言語優位側では全失語がみられる．麻酔薬注入前から継続していた数唱などの正常な言語表出が停止し，言語理解も不能となる．言語機能は数分で緩やかに回復するが，回復過程で，保続や錯語などの失語症状がみられることが多い．一方，非言語優位側では，一時的な言語停止が生じるが，全失語ではない．また，回復も早く(使用する麻酔薬や被験者の個人差はあるが，通常数十秒程度)，言語停止を認めない場合もある．回復過程で構音障害を認めることがあっても，物品呼称，読字，復唱，口頭命令遂行などは可能で，失語症状は認めない．

言語優位側の判定には，通常，言語停止持続時間の左右差を用い，麻酔薬注入後の言語停止の時間が長い側を言語優位側と判定する．錯語などの失語症状の有無も参考になる．ただし，言語停止の左右での時間差が30秒以内の場合，両側言語支配を疑う必要がある．言語優位側の判定について側性指数(laterality index)を使う施設も存在する[6]．

#### (4) 記憶機能検査における課題および評価

記憶機能の検査のみを目的とする課題を設定することはなく，通常は麻酔薬注入後の麻痺作用が持続している状態で実施される言語課題の項目が，記憶課題をかねる場合が多い．被験者に対して，あらかじめ検査中の特定の課題項目を覚えておくように指示しておく．記憶機能検査をかねる課題項目を提示するタイミングは施設により異なっており，実際には麻酔による半身麻痺出現直後に課題を開始する施設や，麻酔薬注入後に最初の言語反応が認められてから記憶課題を実施する施設などがある．

記憶課題項目の提示に関しては，視覚的に提示する場合と聴覚的に提示する場合がある．視覚提示項目としては，日常的に使用する物品(時計，ペンなど)またはその線画，動植物の線画，文字言語(単語)，無意味図形，写真(人物，物品，動植物)などがある．聴覚提示項目としては，音声言語(単語，語句，簡単な文章など)が用いられる．提示項目数は施設ごとに異なるが，麻酔効果の持続する数分間に提示可能な項目数は最大十数個程度である．

#### (5) 麻酔からの回復確認

一過性の半身麻痺と言語機能が回復したのを確認してから(通常，麻酔薬注入10～15分後)，記憶課題の再生，再認検査を実施する．既出の課題の自発的な再生とともに，新規項目を含む課題もあわせて実施し，正しく再認できたものも正解として結果を評価する．

### 2. 主要な特長

Wadaテストの当初からの目的であり，今日においても最も重要な役割のひとつは，言語優位半球の同定である．具体的な内容および手順を概観した前項においてみたように，言語機能は，麻酔薬注入後の失語の状態により判断されるため信頼性が高い．すなわち，言語優位側では全失語が観察されるのに対し，非言語優位側では，一時的な言語停止が生じても回復は早く，言語停止を認めない場合もある．この明確な相異により言語優位側を特定できる．

一方，てんかん外科治療における記憶機能の検査としての重要な目的は，一側の側頭葉切除による術後障害として記憶障害を生じる危険がないかどうかを評価することである．多くの施設において，患側の麻酔薬注入で記憶機能検査成績が67％(全記憶項目の3分の2)以上であれば，患側切除後に記憶障害の危険がなく，67％未満であれば術後記憶障害の危険がある，との判定がなされている[2]．Wadaテストのみにより術後の記憶障害のリスクを完全に特定できるわけではないが，術前評価法の第一選択としての重要性を有するものである．

## テストの実施および評価における留意点

### 1. 実施上の注意点

#### (1) リスク，合併症

Wadaテストは動脈穿刺，カテーテル挿入を伴う侵襲的検査である．脳血管造影検査と同等のリスクお

よび不快感を患者に与えることに留意しなくてはならない．生じうる危険としては，動脈壁損傷，血栓による末梢または脳血管の塞栓，動脈スパズム，薬剤アレルギーなどがある．若年の被験者に比べて比較的高齢(平均51.3歳)の被験者で，頚動脈解離の合併症がみられたとの報告もある[7]．多施設調査による合併症の発生率は，約1％である[8,9]．危険性については，十分に説明のうえ，文書による同意を得て実施する必要がある．

**(2) 脳血管造影検査**

脳血管造影検査は，血管の走行，異常の有無を確認すると同時に，Wadaテストの結果に影響を与える可能性のある血管走行の個人差，特に同側の後大脳動脈や対側の前大脳動脈への流入がないかを確認するためにも必要である．脳血管撮影検査とWadaテストの実施順序は施設によって異なっており，脳血管撮影実施後にWadaテストを実施する場合や，一側のWadaテスト実施後に脳血管撮影検査を実施し，最後に対側のWadaテストを実施する場合がある．

**(3) 麻酔薬の種類**

使用される麻酔薬は，前述のようにアモバルビタールが入手困難になったために，複数の代替薬が存在し，施設により使用薬は異なる．アモバルビタール以外に使用されている麻酔薬は，プロポフォール，ペントバルビタール，セコバルビタール，メトヘキシタールなどがある(メトヘキシタールはわが国では未承認)．使用する麻酔薬によって，使用量，麻酔からの回復時間が異なる．使用量は，注入半球の対側半身に一過性の麻痺を生じるのに十分な量で，施設ごとに使用量が定められている．当院は，プロポフォール(成人量で7 mg)を使用している．

**(4) 脳波の同時記録**

施設によっては，麻酔状態の評価のため脳波を測定しながらWadaテストを実施する．麻酔により同側半球に徐波が出現するのを確認して言語課題，記憶課題を実施し，徐波が消失してから記憶再生，再認検査を実施する．

**(5) 検査側の順序**

ほとんどの施設で両側の検査を実施している．左右どちら側から検査を開始するかは，施設ごと，また症例ごとに異なる．患側から検査を開始する施設，想定される言語非優位側から検査を開始する施設がある．通常，同日に両側の検査を実施するが，一側の検査を実施したあとに残存麻酔薬の影響を除外したうえで対側の検査を実施する必要がある．アモバルビタールを使用する場合，多くの施設では30分が麻酔薬の排出および効果消失に十分な時間と想定して検査を実施している．

## 2. 評価における注意点

言語優位半球同定に関して，信頼性，妥当性の高い検査であることは論を俟たないであろう．しかし，いかなる方法も万能ではなく，目的に応じて適切に使い分けることが肝要である．侵襲的検査であるために，複数回の検査で再現性を検討することは困難であるが，医療上の必要から再検査を実施した症例で，再現性をもって言語優位側が確認されたとの報告がある[10]．Wadaテストに代わる検査法について評価した研究も，言語優位側同定についてはWadaテストとの整合性をその検出感度の基準としている[11]．留意すべき点は，侵襲性の高い検査であることと，言語優位半球を同定する検査であり，個々の言語野の局在を同定するものではないということである．Broca野，Wernicke野などの言語野の同定には，皮質電気刺激検査，機能的MRI(functional MRI；fMRI)検査などを用いる必要がある．

記憶機能検査としてのWadaテストについては，その信頼性が十分であるとはいえない点を理解しておくことが必要である[12]．まず，海馬の血管支配は前部が内頚動脈系，後部が後大脳動脈であることから，内頚動脈に注入した麻酔薬で海馬全体を不活化することはできず，したがって，海馬を中心とした記憶機能の