Table 1 Clinical information for healthy controls and TLE patients.

Variables	Controls ($n=20$)			TLE patients ($n=20$)			
	Mean	(SD)	Range	Mean	(SD)	Range	
Age (years)	34.0	(7.8)	23–50	33.9	(10.0)	20–50	NS
Education (years)	16.6	(3.3)	12–22	14.5	(1.7)	12–16	NS
Gender (male/female)	10/10			12/8			
Duration of epilepsy (years)	NA			13.7	(9.8)	3–33	
Age of onset (years)	NA			20.1	(11.4)	0–45	
Side of epileptic focus (left/right/bilateral or undetermined)	NA			9/4/7			
Seizure status (intractable/remission)	NA			12/8			
Number of AED	NA			1.8	(1.0)	1–4	

AED, antiepileptic drug; NA, not applicable; NS, no significant difference.

(Commission on Classification and Terminology of the International League Against Epilepsy, 1989). Diagnoses were based on a combination of clinical symptoms, EEG, and structural/functional imaging data. Exclusion criteria for both groups included comorbid psychiatric disease, substance abuse or dependence, and reports of hearing or vision problems at the time of the experiment. Additional exclusion criteria for the control group included a history of psychiatric disease, history of traumatic brain injury with any known cognitive consequences or loss of consciousness, history of convulsions other than simple febrile seizures, and psychiatric disease or epileptic disorder in first-degree relatives.

Table 1 summarizes the subjects' clinical characteristics. Patients were divided into two subgroups, an intractable subgroup and a remission subgroup. The intractable subgroup experienced at least one seizure within a 20-month period prior to the experiment, while the remission subgroup was completely seizure-free during this time. All patients were treated with at least one anti-epileptic drug (AED), e.g., carbamazepine or phenytoin, for seizure control.

The study was approved by the Ethics Committee at Tokyo Medical and Dental University. Written informed consent was obtained from each participant after thoroughly describing the experiment.

Procedure

Subjects were presented with auditory stimulus sequences consisting of 600 standard stimuli and 150 deviant stimuli delivered in random order. Fifty deviant stimuli were presented to each subject in a single block, and each subject completed three blocks. The experimental conditions were designed to elicit MMN in response to changes in frequency of pure tones. To this end, stimuli consisted of pure tones presented for 100 ms each, with a rise/fall time of 5 ms and a stimulus onset asynchrony (SOA) of 500 ms. Standard stimuli (1000 Hz) comprised 80% of all trials, while deviant stimuli (1050 Hz) comprised 20%. The standard pure tone frequency of 1000 Hz is commonly used in psychoacoustic and electrophysiological studies, and was chosen because it does not directly correspond to the fundamental of any musical note. Stimuli were delivered binaurally via earphones at 90 dB as subjects watched a silent film while seated and were instructed to ignore auditory stimuli.

ERP recording

EEG was recorded using a portable bio-amplifier recording device (Polymate AP-1532 with silver/silver chloride electrodes, or Polymate AP-216 with active electrodes, TEAC Corporation, Japan) from the midline (Fz, Cz, Pz, and Oz) and bilateral mastoids. The tip of the nose served as the reference for all electrodes. Two electrodes were placed above the left eye and below the right eye to monitor the electrooculogram (EOG). Impedance between the electrodes and skin did not exceed 5 kΩ. The sampling rate was 1000 Hz for each channel and the recording bandwidth was between 0.05 Hz and 300 Hz.

Data analysis

Data analysis focused on a 600 ms time window ranging from 100 ms pre-stimulus to 500 ms post-stimulus onset. The pre-stimulus baseline was corrected separately for each channel according to the mean EEG amplitude over the 100 ms period. Averaging and artifact rejection were performed off-line. Trials with excessive movement activity or with EOG activity exceeding 100 μV peak-to-peak were excluded from analysis. Average waveforms were obtained separately for deviant and standard stimuli, with a minimum of 100 deviant trials for each subject.

Because MMN is known to show inverted polarity at mastoid locations, the term 'mismatch positivity' (MMP) has been adopted to describe the mismatch component at this location (Baldeweg et al., 1999). For this reason, we use the term MMP when describing mastoid findings, and MMN for findings at all other electrode locations.

Statistical analyses

The mean amplitudes of standard and deviant waveforms were defined as the average amplitude for each waveform 100–250 ms post-stimulus onset (the range in which MMN/P is typically found). MMN/P peak latency was defined as the latency of the peak showing maximal negativity/positivity 100–250 ms post-stimulus onset for the deviant – standard difference waveform.

Mean amplitudes for standard and deviant waveforms were first analyzed using three-way repeated-measures analyses of variance (ANOVA), with separate ANOVAs conducted for sites with negative and positive polarity. For both ANOVAs, factors included the between-subjects factor GROUP (TLE and control), and two within-subject factors STIMULUS (standard and deviant) and SITE (for sites with negative polarity: Fz and Cz; for sites with positive polarity: left and right mastoid). Additional two-way ANOVAs with one between-subject factor GROUP (TLE and control), and one within-subject factor SITE (for sites with negative polarity: Fz and Cz; for sites with positive polarity: left and right mastoid) followed separately for standard and deviant waveforms.

MMN/P peak latencies based on the difference waveform were examined using two-way repeated-measures ANOVAs with one between-subject factor GROUP (TLE and control), and one within-

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Table 2 Mean amplitudes of standard, deviant and difference (MMN) waveforms as well as MMN peak latencies in controls and TLE patients.

Variables	Site		Controls ($n = 20$)		TLE patients ($n = 20$)	
			Mean	(SD)	Mean	(SD)
Mean amplitude (μV)						
Standard	Frontocentral	Fz	0.17	(0.70)	0.17	(1.31)
		Cz	0.15	(0.69)	0.07	(1.12)
	Mastoid	L	−0.22	(0.66)	0.43	(0.56)
		R	−0.31	(0.67)	0.42	(0.59)
Deviant	Frontocentral	Fz	0.11	(0.73)	−0.56	(1.59)
		Cz	0.24	(1.07)	−0.55	(1.39)
	Mastoid	L	0.13	(0.60)	0.49	(0.98)
		R	0.16	(0.56)	0.45	(1.20)
MMN	Frontocentral	Fz	−0.05	(0.73)	−0.75	(0.84)
		Cz	−0.10	(1.19)	−0.64	(0.93)
	Mastoid	L	0.35	(0.51)	0.06	(0.91)
		R	0.47	(0.58)	0.02	(0.63)
Peak latency (ms)						
MMN	Frontocentral	Fz	133	(28)	179	(36)
		Cz	141	(42)	171	(41)
	Mastoid	L	145	(31)	157	(53)
		R	150	(33)	185	(39)

subject factor SITE (for sites with negative polarity: Fz and Cz; for sites with positive polarity: left and right mastoid).

Finally, to explore whether potential abnormalities in TLE patients were associated with epileptic seizures, the TLE group was divided into two subgroups, an intractable subgroup and a remission subgroup. Mean amplitudes for standard and deviant waveforms were first analyzed using three-way ANOVAs with one between-subjects factor SUBGROUP (intractable and remission), and two within-subject factors STIMULUS (standard and deviant) and SITE (for sites with negative polarity: Fz and Cz; for sites with positive polarity: left and right mastoid). When a three-way ANOVA yielded a significant interaction or trend for an interaction between factors, a two-way ANOVA was performed for the relevant factors. MMN/P peak latencies based on the difference waveform were examined using two-way repeated-measures ANOVAs with one between-subjects factor SUBGROUP (intractable and remission), and one within-subject factor SITE (for sites with negative polarity: Fz and Cz; for sites with positive polarity: left and right mastoid).

With respect to all analyses, statistics for sites showing a negative mismatch component were limited to Fz and Cz because MMN typically is largest at midline frontocentral sites. As anticipated, visual inspection of difference waveforms at Pz and Oz revealed small and obscure mismatch signals such that it was difficult to determine individual peaks. MMN typically reverses polarity at nose-referenced mastoid sites. To this end, evaluation of waveforms at mastoid sites enabled comparison of polarity with waveforms at Fz and Cz, providing additional assurance that the observed negativity at these sites was a "true" mismatch response (Näätänen et al., 2007).

Results

Fig. 1 presents grand-averaged ERP waveforms for standard and deviant stimuli in TLE patients and controls at Fz, Cz, and left and right mastoids, with associated mean amplitudes presented in Table 2. Although statistical analyses

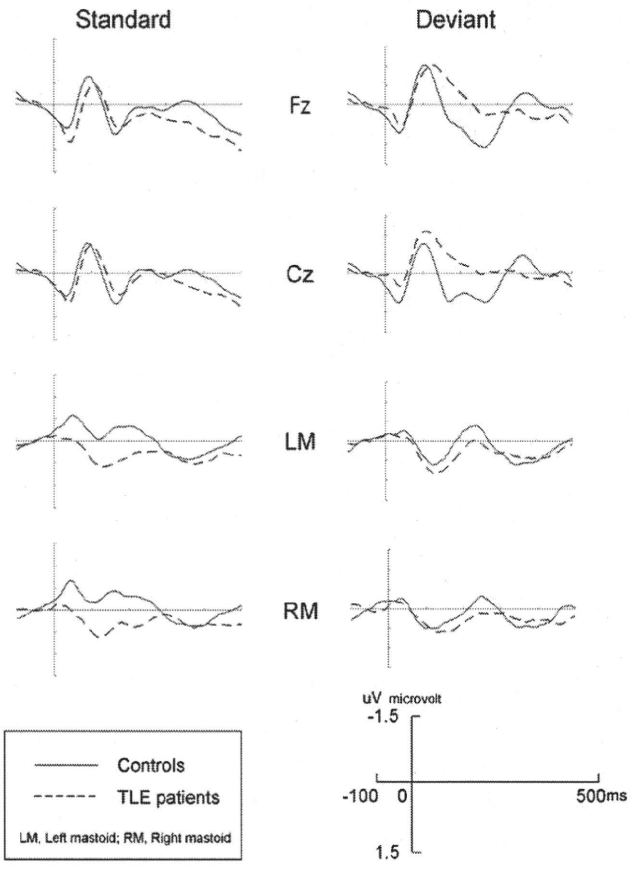

Figure 1 Comparison between grand-averaged ERPs for standard and deviant stimuli in controls and TLE patients. Solid line, control group; striped line, epilepsy group.

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Table 3 Mean amplitudes of standard deviant and difference (MMN) waveforms as well as MMN peak latencies in TLE intractable and remission subgroups.

Variables	Site		Intractable ($n = 12$)		Remission ($n = 8$)	
			Mean	(SD)	Mean	(SD)
Mean amplitude (μV)						
Standard	Frontocentral	Fz	0.23	(0.64)	0.08	(0.61)
		Cz	0.12	(1.46)	−0.01	(0.53)
	Mastoid	L	0.45	(0.68)	0.40	(0.36)
		R	0.43	(0.70)	0.43	(0.39)
Deviant	Frontocentral	Fz	−0.60	(1.91)	−0.51	(1.06)
		Cz	−0.66	(1.50)	−0.38	(1.29)
	Mastoid	L	0.36	(1.09)	0.70	(0.82)
		R	0.36	(1.06)	0.57	(0.53)
MMN	Frontocentral	Fz	−0.82	(0.84)	−0.63	(0.87)
		Cz	−0.78	(0.85)	−0.38	(1.03)
	Mastoid	L	−0.10	(0.96)	0.09	(0.90)
		R	−0.06	(0.73)	0.02	(0.58)
Peak latency (ms)						
MMN	Frontocentral	Fz	183	(34)	149	(72)
		Cz	172	(43)	148	(73)
	Mastoid	L	165	(64)	126	(59)
		R	193	(45)	147	(64)

for mean amplitude were performed based upon standard and deviant waveforms, we also present grand-averaged MMN/P waveforms (i.e., difference waveforms) in Fig. 2 for ease of comparing mismatch signals across groups. For the same reason, MMN/P mean amplitudes also are presented in Table 2, with mean amplitude defined as the average amplitude of the deviant − standard difference waveform 100–250 ms post-stimulus onset. Peak latencies for the difference waveform are also reported in Table 2. Finally, Table 3 presents data relevant to the TLE subgroup analysis, including mean amplitudes of standard, deviant and difference (MMN/P) waveforms, as well as peak latencies of the MMN/P waveform.

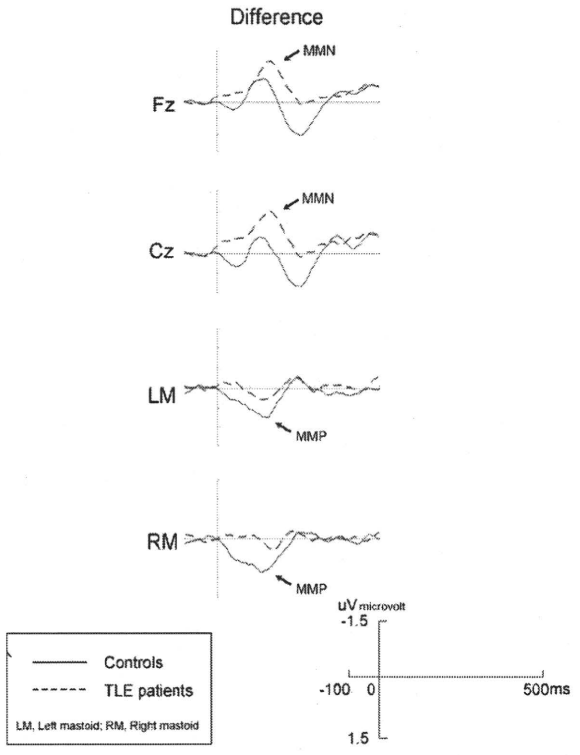

Figure 2 Deviant minus standard difference waveforms in controls and TLE patients. Solid line, control group; striped line, epilepsy group.

Frontocentral sites

A 2 (GROUP: TLE vs. control) × 2 (STIMULUS: standard vs. deviant) × 2 (SITE: Fz vs. Cz) repeated-measures ANOVA examining mean amplitudes for standard and deviant stimuli in the range of 100–250 ms revealed a significant main effect of STIMULUS [$F(1, 38) = 5.05$, $p < 0.05$], such that deviant amplitudes were greater than standard amplitudes. A significant interaction between STIMULUS and GROUP was also found [$F(1, 38) = 5.74$, $p < 0.05$], indicating that the difference between deviant and standard amplitudes in TLE patients was greater than that in controls. Stated another way, MMN was enhanced in TLE patients relative to controls (see Figs. 1 and 2 and Table 2). Separate 2 (SITE: Fz vs. Cz) × 2 (GROUP: TLE vs. control) repeated-measures ANOVAs for deviant and standard mean amplitudes showed no significant main effects or interactions. Additionally, visual inspection of waveforms revealed that deviant waveforms in TLE patients were still negative at a latency of 200 ms, whereas in controls deviant waveforms shifted from negative to positive around 150 ms, effectively leading to prolonged MMN duration in TLE patients (see Fig. 1 and Table 2).

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With respect to MMN peak latency (based on the deviant – standard difference waveform), a two-way repeated measures ANOVA revealed a significant main effect of GROUP [$F(1, 38) = 12.45$, $p < 0.01$], such that MMN peak latency was delayed in patients compared with controls. No significant main effect of SITE or interaction between GROUP and SITE was observed.

Mastoid sites

A three-way repeated-measures ANOVA examining mean amplitudes for standard and deviant stimuli revealed significant main effects of both GROUP [$F(1, 38) = 7.14$, $p < 0.05$] and STIMULUS [$F(1, 38) = 5.08$, $p < 0.05$]. Collapsed across stimulus type and site, mean amplitudes were greater in TLE patients than controls; collapsed across group and site, deviant amplitudes were greater than standard amplitudes. No significant interaction between factors was observed. In addition, separate two-way repeated-measures ANOVAs were performed for deviant and standard mean amplitudes. No significant main effects of GROUP or SITE or an interaction between factors were found for deviant stimuli. Conversely, for standard stimuli a main effect of GROUP was found [$F(1, 38) = 13.65$, $p < 0.001$], with TLE patients showing greater mean amplitudes than controls (see Fig. 1 and Table 2). No main effect of SITE or an interaction between GROUP and SITE was found for standard stimuli.

A two-way repeated measures ANOVA for MMP peak latency based on the difference waveform revealed a significant main effect of GROUP ($F(1, 38) = 4.39$, $p < 0.05$) and SITE ($F(1, 38) = 7.65$, $p < 0.01$), indicating that MMP peak latency was delayed in TLE patients relative to controls, and that both groups displayed delayed MMP peak latencies in the right relative to left mastoid (see Fig. 2 and Table 2). There was a trend toward a significant interaction between GROUP and SITE [$F(1, 38) = 3.88$, $p = 0.056$], although the difference did not reach a significant level.

MMN/P and epileptic seizures

At frontocentral sites, a 2 (STIMULUS: standard vs. deviant) × 2 (SITE: Fz vs. Cz) × 2 (SUBGROUP: intractable vs. remission) repeated-measures ANOVA for mean amplitudes of standard and deviant waveforms in the range of 100–250 ms revealed a significant main effect of STIMULUS [$F(1, 38) = 9.44$, $p < 0.01$], such that deviant amplitudes were greater than standard amplitudes (see Table 3). No main effect of GROUP or interaction between STIMULUS and SUBGROUP was observed. For MMN peak latency, a 2 (SITE: Fz vs. Cz) × 2 (SUBGROUP: intractable vs. remission) repeated measures ANOVA revealed no significant main effects or interactions.

At mastoid sites, a three-way repeated measures ANOVA for mean amplitudes of standard and deviant stimuli revealed no significant main effects or interactions between factors. With respect to MMP peak latency, a two-way repeated measures ANOVA revealed a significant main effect of SITE [$F(1, 18) = 7.06$, $p < 0.05$], reflecting longer latencies in both groups for right than left mastoid (see Table 3). No main effect of SUBGROUP or interaction between SITE and SUBGROUP was observed.

Discussion

In response to a passive auditory oddball task, patients with TLE exhibited patterns of cortical activity that differed from control subjects in several ways. First, at frontocentral sites, MMN was enhanced in TLE patients relative to controls, as revealed by a significant GROUP by STIMULUS interaction for mean amplitude. Secondly, at mastoid sites, TLE patients showed greater standard waveform amplitudes than controls. Finally, in addition to amplitude differences between groups, analyses revealed longer MMN/P peak latencies in TLE patients relative to controls at both frontocentral and mastoid sites.

A number of researchers have noted that mismatch potentials recorded from mastoid electrodes may exhibit characteristics different from those of MMN recorded from frontal electrodes (Baldeweg et al., 2002; Sato et al., 2002). Early studies of MMN identified a single dipole generator within the bilateral superior temporal gyri (STG) in the vicinity of Heschl's gyri (Scherg et al., 1989). Toward the mastoids, an inversion of polarity is typically observed and has been considered evidence for the generation of MMN in the temporal lobe (Sams et al., 1985). However, more recently it has been suggested that the single dipole model may not account for all the data, and that more than one source may contribute to the scalp MMN (Giard et al., 1994). To this end, multichannel MEG and EEG studies (Rinne et al., 2000) as well as intracranial recordings (Rosburg et al., 2005) have identified additional generators in the frontal cortex. In the latter study, MMN was observed in two patients at electrode contacts over lateral inferior frontal cortex and in one patient in a frontal interhemispheric electrode strip, providing evidence for the participation of frontal gyri in MMN generation. Recent observations have led to the view that temporal electrodes mainly detect mismatch sources in the superior temporal lobe, including perhaps its lateral surface, while electrodes over the frontal scalp may detect signals from putative frontal generators (Escera et al., 2003; Näätänen et al., 2007).

In addition to debate surrounding the number of MMN generators, the specific neural mechanisms underlying MMN generation also remain controversial. Two major competing hypotheses, the model adjustment hypothesis and the adaptation hypothesis, are considered below in relation to the current findings.

To date, the most commonly suggested mechanism underlying MMN generation is a pre-attentive sensory memory mechanism (Tiitinen et al., 1994) posited to automatically compare present auditory input and memory traces of previous sounds (Näätänen et al., 2007). More specifically, it has been suggested that MMN may reflect on-line modifications of a perceptual model that is updated when auditory input does not match its predictions (Näätänen and Winkler, 1999), a hypothesis known as the model-adjustment hypothesis. Based on this model, MMN is thought to result from two underlying functional processes: a sensory memory mechanism arising from temporal generators and an automatic attention-switching process arising from frontal generators (Giard et al., 1990). Providing support for this model, Escera et al. (2003) demonstrated evidence for prefrontal cortex involvement in providing top-down modulation of a deviance detection system in the temporal cortex. With respect to

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the current study, findings of enhanced MMN at frontocentral sites in TLE patients might thus be interpreted as frontal lobe hyperexcitability to compensate for temporal lobe dysfunction. That is, a larger number of synchronously activated frontal neurons may be required for successful automatic attention-switching in TLE patients than in controls, due to impairment of a initial sensory memory mechanism in the temporal lobe.

An alternative mechanism recently proposed by Jääskeläinen et al. (2004) suggests that MMN results from a much simpler mechanism of local neuronal adaptation in the auditory cortex. According to the adaptation hypothesis, reduced responsiveness in the auditory cortex during continuous stimulation is sufficient to explain the generation of an apparent MMN. In the current study, although deviant – standard differences (i.e., MMP) at mastoid sites did not significantly differ between the two groups, greater standard waveform amplitudes were observed in patients than in controls. With respect to the adaptation hypothesis, such findings may reflect poor neuronal adaptation in the temporal lobe such that repeated presentation of standard stimuli does not lead to reduced responses. In other words, processing resources may continue to be allocated in TLE patients despite the repetitive nature of the standard stimuli (Myatchin et al., 2009). TLE may be characterized by excitability of the temporal lobe despite stimulus repetition, which might be related to epileptogenesis of the temporal cortex. The current results suggest that adaptation mechanism of the temporal cortex for stimuli that are subsequently repeated may be impaired in TLE.

It also bears noting that longer latency components such as P3a may have affected the pre-stimulus baseline period, in turn affecting MMN/P amplitudes given that epochs were baseline-corrected. Specifically, because we chose a short SOA (500 ms), standard trials preceded by a deviant trial may have had different pre-stimulus baseline periods than those preceded by another standard trial. Although P300 abnormalities in TLE are controversial, studies in chronic TLE patients typically report trends toward lower P300 amplitudes relative to controls (e.g., Drake et al., 1986; Tuunainen et al., 1995; Abubakr and Wambacq, 2003). To avoid potential confounds related to P3a, future studies should exclude standard trials preceded by deviant trials from averaging.

In addition to amplitude differences between TLE patients and controls, a second key difference was an increase in MMN/P latency in TLE patients, consistent with previous reports (Lin et al., 2007; though see Duncan et al., 2009, for reports of normal auditory P300 latencies in patients with complex partial seizures). Because ERPs provide a chronological measure of brain function and ERP latencies are thought to indicate timing of covert neuronal events in which certain subroutines in the brain are activated (Kok, 1997), increased MMN/P latencies in TLE patients in the current study may be the result of an early but not later slowing in auditory information processing speed.

Furthermore, in TLE patients the MMN component persisted longer at frontocentral sites than in controls, consistent with previous findings by Gene-Cos et al. (2005). The authors argue that prolonged MMN duration might point to difficulty mainly in ''the closure mechanism of the MMN process''. They suggest that this information processing dysfunction could be related to concentration and memory difficulties observed in TLE patients, given that patients may spend more time evaluating stimulus novelty than controls and may experience difficulty switching attention from one stimulus to another difficult (Piazzini et al., 2006). Such findings in epilepsy patients are in agreement with previous studies in which barely discriminable tones elicited delayed MMN peaks (Näätänen and Alho, 1995; Inouchi et al., 2004) with delays increasing as the magnitude of deviation decreased (Yabe et al., 2001; Inouchi et al., 2004).

Interestingly, collapsed across subject groups, MMP was delayed in the right mastoid compared with the left. Because of the small number of patients whose epileptic focus was clearly lateralized, statistical analyses could not be conducted to evaluate the relationship between MMP latency and laterality of epileptic focus. Furthermore, given that laterality effects have not been reported previously with respect to MMP latency in healthy adults, further investigation is warranted before drawing strong conclusions about this finding.

Finally, our patient subgroup analysis investigating the relationship between seizures and MMN/P did not reveal any significant differences between groups, suggesting that the occurrence or absence of seizures in the months leading up to the experiment did not significantly affect MMN/P.

Because all patients were being treated with AEDs at the time of data collection, it bears noting that use of AEDs may have affected MMN/P amplitudes and latencies. It has been shown, for example, that anti-epileptic medication can have an effect on motor reaction times and on latencies in ERP studies (Lagae, 2006; Myatchin et al., 2009), as well as an overall dampening effect on amplitudes (Rosburg et al., 2005). Benzodiazepines, which are also used as AEDs, have been found to reduce MMN amplitude (Rosburg et al., 2004). To this end, the current finding of enhanced MMN amplitudes in TLE patients cannot be explained as a simple dampening effect of AEDs, though further studies will be required to better address the effects of AEDs on MMN. Finally, although all patients reported normal hearing levels, it is possible that MMN/P was affected by subclinical differences in auditory discriminative abilities between patients and controls.

Taken together, results from the present study reveal clear cortical abnormalities in TLE patients that have not been well-characterized previously by conventional EEG. In TLE patients, enhanced MMN at frontocentral sites and greater positivity at mastoid sites of standard waveforms may be interpreted in terms of increased activation of the same neuronal population as in controls, or activation of extra neuronal circuits. In conclusion, the current study extends previous findings of impaired short and long-term memory in TLE patients (Butler and Zeman, 2008; McCagh et al., 2009) by revealing that initial sensory memory is impaired in TLE as well. Our findings indicate that MMN/P can be useful as a physiological probe of pre-attentitve sensory memory for tones in TLE.

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■原著

動かしているが使えない
—両手動作時に左手の空振りを呈した一症例—

早川裕子[*,**]　岩崎奈緒[***]　穴水幸子[****]
三村　將[*****]　加藤元一郎[****]

要旨：両手動作時の左手に特異な障害を呈した症例を報告した。症例はくも膜下出血後脳梗塞を併発し，右頭頂葉病変を認めた。左半側空間無視や運動消去はなかったが，視・聴・触覚の左の消去現象を呈した。左手は高次体性感覚障害と拙劣に加え，両手動作の際，あたかも対象を操作しているかのように動作を継続するものの，実際には対象を把持せず，空振りのような動作が観察された。4年後，両手動作時の左手の障害と消去現象は並行して消失したが，左手の高次体性感覚障害と拙劣は残存した。これまで高次体性感覚障害を伴う病巣対側上肢の拙劣症の報告はあるが，両手動作時の異常の記載はない。また本例は左半側空間無視や運動消去は呈していない。本例の障害は，4年後にともに消失した多様式消去現象と関連し，能動的動作時に内発的に生じる体性感覚に対する消去現象により説明できる可能性が考えられ，右頭頂皮質病巣が関与しているものと思われた。

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Key Words：高次体性感覚障害，拙劣，消去現象，頭頂葉
higher somatosensory disturbance，clumsiness，extinction phenomenon，parietal lobe

はじめに

頭頂葉は，中心後回の一次体性感覚野に入力された情報を階層的に処理し，さらには同側の視覚情報や聴覚情報のみならず，対側からの情報も統合する「連合野の連合野」として知られている。またこの後方連合野は前頭連合野と連絡し，運動出力とも密接に関係している。そのため，頭頂葉が損傷されるとさまざまな症状を呈する。たとえば，皮質性感覚障害，肢節運動失行（運動拙劣症），把握障害，視覚性運動失調，自己身体定位障害が出現し，とくに右半球損傷では半側空間無視，半身無視，着衣失行などが認められる（平山ら2009）。

今回われわれは，右頭頂葉の梗塞後にこれまで報告のない特異な両手動作時の左手の障害を呈した症例を報告する。本報告にあたり，記載内容，画像の使用，報告内容について，症例本人に口頭と文書で説明を行い，署名による同意を得た。

Ⅰ．症　例

40歳代後半，右利き男性。大学卒。特記すべき既往歴はなかった。

現病歴：右内頸動脈瘤破裂によりくも膜下出血を発症，当日開頭動脈瘤頸部クリッピング術が施行された。第10病日，血管攣縮により右中大脳動脈・後大脳動脈境界領域に脳梗塞を発症し，第31病日に水頭症に対し脳室腹腔短絡術が施行された。第70病日，明らかな運動麻痺や感覚障害などもなく，自宅退院となった。その後，発症から8ヵ月後に，「左手がうまく使えない」と訴えがあり，外来を再診した。その後，心筋梗塞のため他院で加

*横浜市立脳血管医療センター リハビリテーション部
**山形大学大学院 医学系研究科 高次脳機能障害学　〒990-9585 山形市飯田西2-2-2
***ソフィア訪問看護ステーション
****慶應義塾大学 医学部 精神神経科
*****昭和大学医学部 精神医学教室

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療することとなり通院は中断していたが，復職を前に発症4年後に再度外来受診した。

Ⅱ．発症8ヵ月後の所見

1．神経学的所見

脳神経・小脳系の異常は認めず，視力・視野・眼球運動も問題なかった。随意運動は，左右ともに良好で麻痺は認めなかった。握力は右40kg・左20kgで，左上肢の筋力低下を認めた。体性感覚は「左手がちょっと鈍い」という日もあれば，「左右差はない」という日もあり，症例の表現は一定しなかったが，筆で軽く触れられた刺激の有無の判断は常に可能であった。また痛覚・温度覚も正常であった。深部感覚は，母指探しテストでは左上肢でごくわずかなずれを認めたが，運動覚に問題はなかった。

2．神経心理学的所見（表1・表2・表3）

神経心理学的検査結果を**表1**に，消去検査結果を**表2**に，高次体性感覚検査の結果を**表3**に示す。

意識は清明で，見当識，コミュニケーションに問題はなく，検査にも協力的であった。記憶は日常生活上，問題はなかった。視覚による物品の弁別・呼称，形・色・奥行きの認知は問題なく，図形模写や構成にも問題はなかった。星抹消検査では少数の見落としを認めたが左右に偏りはなく，線分二等分や図形模写でも半側空間無視は確認されなかった。日常生活でも左身体をどこかにぶつけることや髭のそり残しなどのエピソードもなかった。一方で，視覚・触覚・聴覚の左消去現象を認めた（**表2**）。動作時の運動無視，両手同時の上肢挙上や交互運動での運動消去は認めなかった。行為については，日常生活や訓練場面での物品操作の誤りはなく，模倣・言語指示からのジェスチャーや手指パターン模倣も両手とも問題なかった。着衣も可能であった。また，注視下でも周辺視野でも上肢の到達運動障害はなく，プレシェーピン

表1 神経心理学的検査所見（発症8ヵ月後）

MMSE		27/30
RCPM		29/36
WAIS-R	4下位検査による推定IQ	96～101
	知識	（評価点）10
	数唱	10
	理解	8
	類似	8
	絵画完成	10
	積み木模様	5
	符号	10
Ray-Osterrieth 複雑図形	模写	36/36
	遅延再生（5分後）	17/36
星抹消検査		31/36
RBMD	標準プロフィール点	19/24
	スクリーニング点	8/12
Word Fluency	カテゴリー（動物・果物・乗物）	19・10・10
	語頭音（し・い・れ）	7・8・7

MMSE：Mini-Mental State Examination
RCPM：Raven's Coloured Progressive Matrices
WAIS-R：Wechsler Adult Intelligence Scale-Revised
RBMT：Rivermead Behavioral Memory Test

グにも問題なかった。しかし，後述する左手の拙劣を認めた。

症例自身は検査を実施するまで明らかな感覚障害の自覚はなかったが，左手の二点識別覚・書字知覚・触点定位・皮膚運動方向覚（Benderら1982）・立体覚の障害を認めた（**表3**）。二点識別覚は左手で示指指先・手掌面ともに右手に比べ識別可能な距離が延長し，とくに手掌では7cmでも困難であった。書字知覚では1から5の数字を手掌面にペン先で書いて検査したが，左手ではまったく判別できなかった。触点定位は上肢の任意の部位を検者が指で軽く触れ，触れられた反対側の手で同じ場所を示させた。皮膚運動方向覚は，手掌面にペン先で縦・横・斜めの線を描き，その方向を口頭で答えてもらった。立体覚の検査は立方体や球など一辺が2.5～4cmの5種類の木製の積木を2セット準備し，1セットを机上に並べ，手に持たせたものと同じ物を選択させた。同様に日用物品はブラシ・鉛筆・鍵などの5つについて実施した。日用物品の立体覚検査で正答した物品は，「冷たいから金属…スプーン」など，材質や大きさの質感などから推測した回答であった。

表2　消去検査時の正答数

		8ヵ月後	4年後
視覚	左一側	10/10	10/10
	右一側	10/10	10/10
	両側同時	3/10	10/10
触覚	左一側	10/10	10/10
	右一側	10/10	10/10
	両側同時	3/10	10/10
聴覚	左一側	10/10	10/10
	右一側	10/10	10/10
	両側同時	4/10	10/10

各感覚様式について，一側刺激と両側同時刺激をランダムにそれぞれ10回提示した。触覚では手掌面を軽く触った。触覚・聴覚の検査は閉眼で実施した。

3. 左手の拙劣

日常生活で「左手がうまく使えない」場面を症例にたずねると，自宅で赤ん坊を両手で抱きあげる時，左手で持っているはずの赤ん坊の頭がはずれていて落としそうになったことや，またそれに気をつけすぎて赤ん坊だけでなく座っていた椅子まで一緒に左手が持ち上げていたことなどのエピソードを述べた。また，洗濯物をたたもうとしても，どうしてもうまくたためないと述べた。

診療場面で観察した左手の拙劣は，手袋を左手にはめようとすると一つの穴に2本の指を入れることや，左手を手探りでポケットに入れられないことであり，肢節運動失行様であった。これらの症状は視覚による代償で改善した。左手一側の動作は，キャッチボールなどの粗大運動，目視下でペグを穴に差し込むなどの比較的容易な巧緻動作は問題なく可能であった。しかし，指先だけでペグを回転させるなどのより巧緻な作業はやや拙劣であった。

一方，両手動作では，目視下であっても左手で押さえる，つまむなどの動作が不良で，作業が進まないことが観察された。症例の左手は動作が停滞することなく合目的的に動いており，右手に合わせて協調的に動きを継続しているが，いつの間にか左手が対象から離れていることや，適切な位

表3　高次体性感覚検査結果

		右手	左手（8ヵ月後）	左手（4年後）
二点識別覚	示指の識別閾値	0.3cm	1.0cm	1.2cm
	手掌の識別閾値	1.0cm	7cm以上	4cm
書字知覚（数字）	正答数	5/5	0/5	3/5
触点定位（上肢）	ずれの距離	0～1cm以内	5～10cm	3～10cm
皮膚運動方向覚（手掌面）	正答数	6/6	1/6	1/6
立体覚 積み木	正答数（正答率）	7/7（100%）	4/7（57%）	8/10（80%）
日用物品	正答数（正答率）	10/10（100%）	6/10（60%）	4/10（40%）

置を保っていないことに気づかずに動作を続けることが観察された。たとえば洋服やタオルをたたむ動作では，タオルの端を持つ動きをしているものの，左手はタオルを持たずに空振りしたまま動作を続けることや，端だけでなくほかの部分も一緒に持ったまま動作を続けることがあった（**図1**）。また，ボルトとナットを組み合わせる作業でも，目視による代償が可能な眼前で行っているにも関わらず，左手はボルトを把持した形でひねる動作をしているが，指はボルトからはなれていることがあった。症例は「うまくいかない」とは述べたが，左手の空振りや不適切な把持が原因であることには気づいていなかった。また，左手を見ながら動作を行うよう指示し，適切な位置を把持させて作業を再開しても，作業経過中に不適切な把持

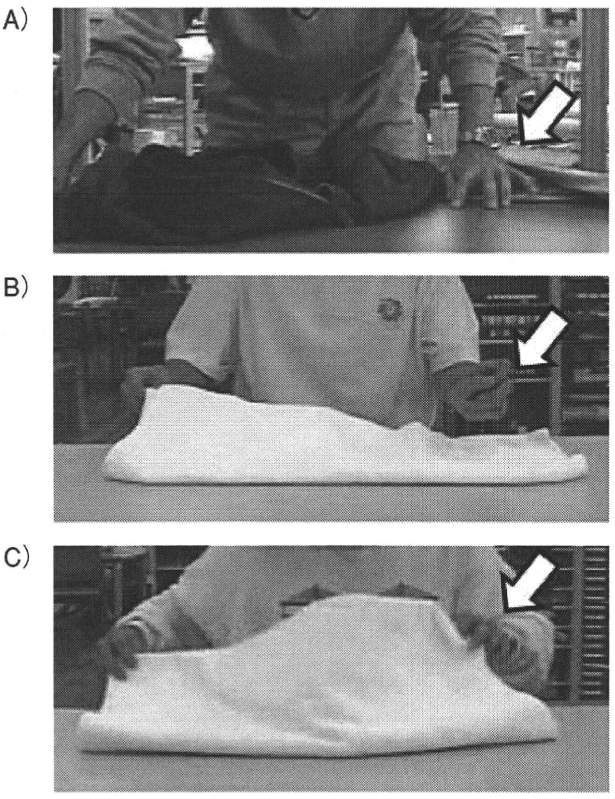

図1 発症8ヵ月後の両手動作時の左手の異常（動画から抽出）

A) 衣服（黒色）を机上に広げようと左手を動かしているが左手は衣服を捉えておらず，空振りした。
B) タオルをたたむ際，左手はタオルを把持せず作業を継続した。
C) タオルをたたむ際，端ではない部分も把持しているが持ち直すことなく作業を継続した。

になり，改善しなかった。

Ⅲ．発症4年後の所見

1．神経学的所見

左手の握力が8ヵ月後の20kgから29kgへと改善していた。その他は特記すべき変化を認めなかった。

2．神経心理学的所見

発症後8ヵ月後に認めた左側の視覚・聴覚・触覚の消去現象は消失していた（**表2**）。また，両手動作時の左手の使用障害も消失していた。日常生活においても，とくに困ることはないとのことであった。

一方，左上肢の高次体性感覚障害は，書字知覚と立体覚は多少改善していたものの，右手と比較すると成績は不良で，障害は残存していた（**表3**）。また，ポケットや手袋に手を入れることや巧緻動作は視覚の代償が必要で，片手使用時の拙劣は残存していた。

Ⅳ．脳画像所見

1．頭部CT（図2）

頭部CTでは，右半球に上側頭回から下・上頭頂小葉，側脳室前角外側の低吸収域を認めた。左半球では，前方のシャントチューブに加え，角回にも淡い低吸収域を認めた。発症後4年の時点でも，8ヵ月後と比較して低吸収域に著明な変化はなかった。

2．脳血流SPECT（図3）

脳血流SPECTでは，頭部CTで認めた低吸収領域の周囲を含む広範な右頭頂側頭葉と，右前頭葉下部の血流低下を認めた。また左角回にも血流低下を認めた。8ヵ月後と4年後を比較すると，両側側頭葉底面，右中前頭回，左頭頂側頭移行部，左前頭前野，両側帯状回，両側小脳の血流に軽度の改善があったが，右頭頂側頭部の血流低下は残存しており，大きな変化はなかった。

Ⅴ．考　察

1．高次体性感覚障害を伴う拙劣症について

求心性の体性感覚障害の関与する病巣対側上肢の肢節運動失行や拙劣症は，中心後回を含む一側

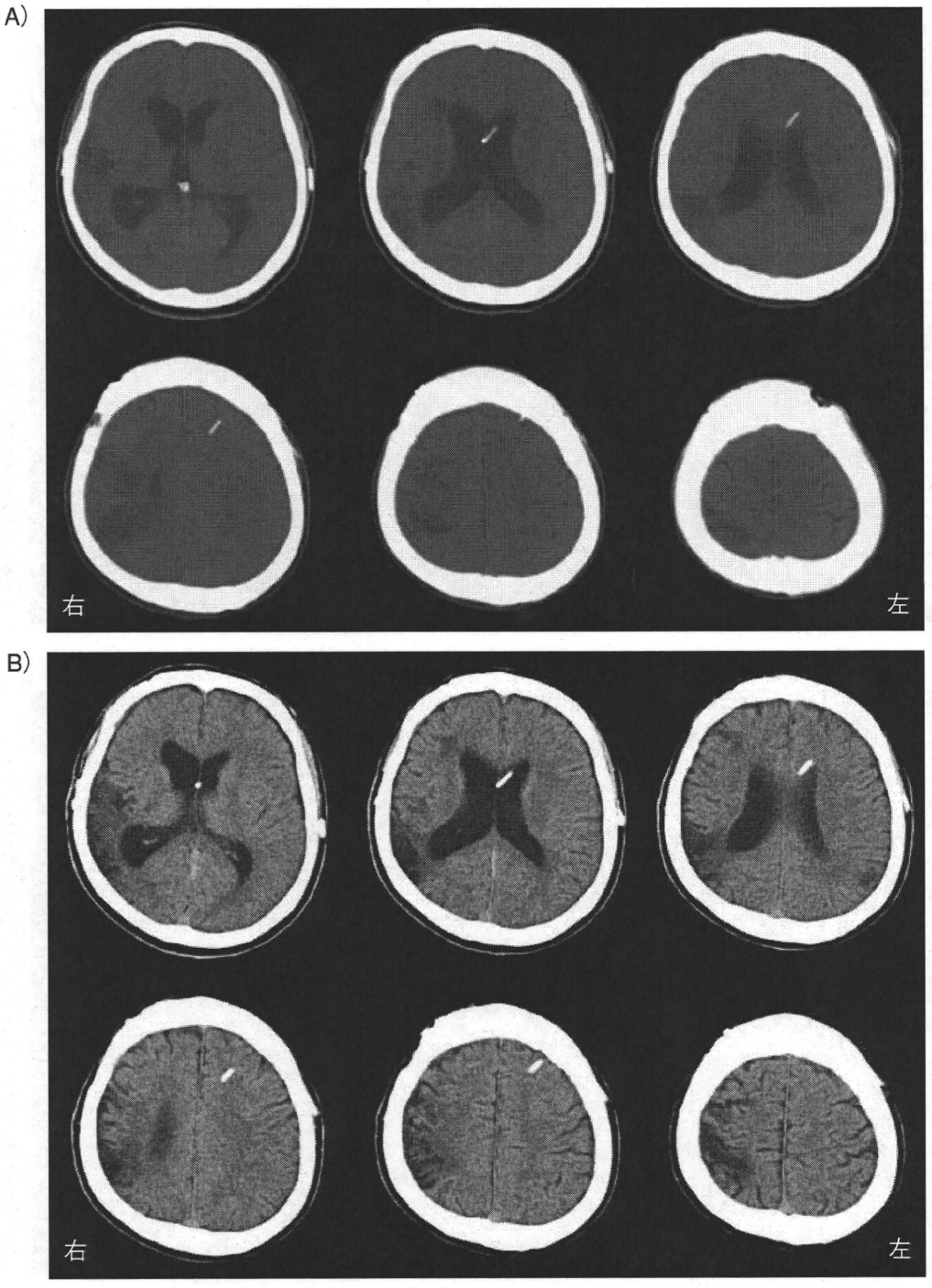

図2　CT画像
A）発症8ヵ月後，B）発症4年後

の頭頂葉病変を有する症例で報告されている（Yamadori 1982，河村ら 1986，下村ら 1988，Motomuraら 1990，Binkofskiら 2001，Valenzaら 2001，鈴木ら 2003）。また，頭頂葉損傷による高次の触覚認知障害例でも，病巣と反対側上肢の拙劣が報告されている（Bohlhalterら 2002）。これらの症例の特徴は，病巣の反対側上肢の筋力・分離運動や表在知覚・位置覚に問題がないにもかかわらず，対象の操作が拙劣になること，二点識別や立体覚などの高次体性感覚障害を伴うことである。拙劣は視覚により手指動作の補正が可能だが，病巣が後方に伸展し拙劣も重度であった症例では，

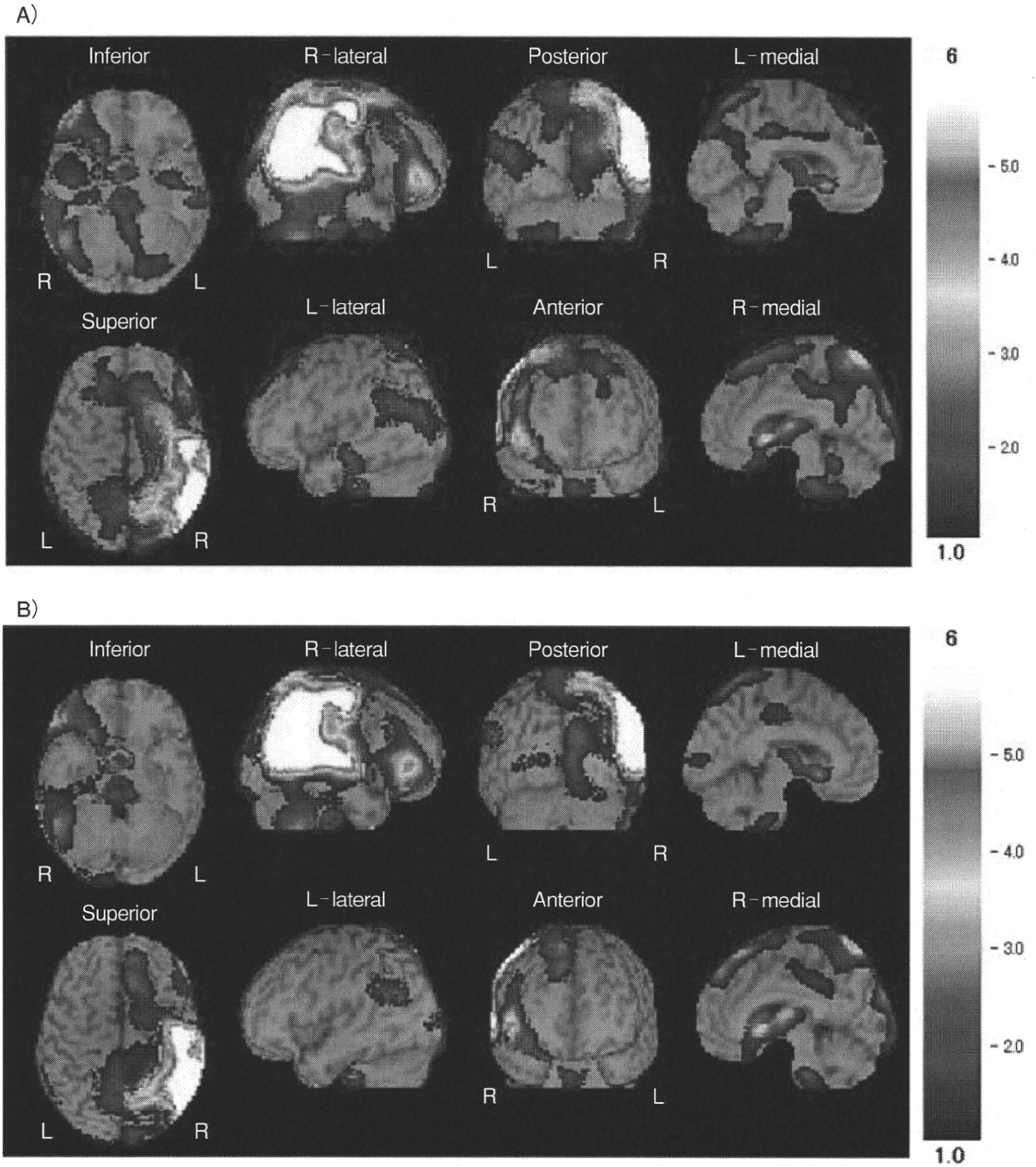

図3 99mTc-ECD SPECT e-ZIS解析
A）発症8ヵ月後，B）発症4年後

視覚補正の効果がなかったとの報告もある（細見ら 2005）。

本例は，発症後8ヵ月・4年の両時点において，左手は，表在知覚や位置覚にはほとんど問題はなかったが，立体覚を含む高次の体性感覚障害を呈していた。また運動機能が保存されていたにもかかわらず，手袋やポケットに手を入れることが不良で，巧緻動作もやや拙劣であった。よって本例の左手は，高次体性感覚障害を伴う肢節運動失行あるいは拙劣症であったと考えて矛盾はないと思われる。しかし，変性疾患を除く中心領域後方病変による拙劣症の報告では，両手動作時における

一側肢の障害や拙劣の悪化などの記載はない。また本例は，当初より左手一側でもペグ操作が可能なほど運動機能は保存されており，かつ視覚補正による改善も認めたことから，症例の両手動作時の障害は拙劣症だけでは説明できないと考えられる。

2. 本例の両手動作時の左手の障害について

本例の障害のもっとも特異な点は，左手はあたかも対象を操作しているかのように動かすものの，実際には対象を把持せず動作を続けていたことである。

Ghikaら（1998）は，頭頂葉に限局病変のある発症後1～3週の脳卒中症例32名について，運動に関する症候を検討した結果，全例に両手動作障害を認めたとしている。しかし，その内容は病巣対側上肢の不使用傾向であり，本例の呈した障害とは異なる。

本例は，図形模写や抹消検査で検出されるような左半側空間無視は認めず，日常生活でも身体の左側をぶつけるといったエピソードもなかった。また，左手の不使用や運動無視も認めず，両手動作中も左手の動きは減弱することなく，動きそのものも途切れなかった。つまり本例の両手動作時の左手の障害は，半側空間無視，半側身体無視，運動無視，運動消去により説明できる障害ではなく，これらとは異なる障害であると考えられる。

一方で，本例は両手動作中に左手が適切に対象を把持していないことを指摘しても改善しなかった。また，4年後における両手動作時の左手の障害の回復と並行して，視覚・触覚・聴覚の消去現象が消失していた。これらの現象からは，本例の左手の障害に，左側に対する何らかの注意の障害が関係している可能性が考えられる。

感覚性の消去現象は，臨床的には比較的急性期に生じる現象で，半側空間無視とともに観察されることが多いが，それぞれが独立して観察されることもある（Cocchiniら 1999）。よって，発症8ヵ月後に本例で半側空間無視は認めなかったものの左の消去現象が陽性であったことは珍しいこととは言えない。しかし，消去現象を認めた症例のうち，消去側の手の両手動作時の障害の記述は，われわれが検索した限りでは見つけられず，特異な現象であると思われる。

本例の呈した両手動作時の障害は，運動自体は継続されており，その際に生じる体性感覚の入力を無視しているかのようであった。われわれはこの障害を，これまで報告のない，運動時に生じる能動的で内発的な感覚に対する消去現象（active touch neglect）であったと考える。一般に，消去現象は，被験者に対し受動的な感覚刺激を与え，その刺激を感じた側を答えさせることで検査する。よって，検査では被験者にとって外部から受動的に入力された感覚に対する消去しか検出することはできない。一方，通常能動的な動作を行うときは，運動によって生じる内発的な体性感覚の入力を伴う。それは触覚系に加え，運動感覚や固有感覚であり，自分で運動をすることでしか得られない特殊な感覚である（Gibson 1983，岩村 2001）。この能動的な動作に伴う内発的な体性感覚の消去は，他の感覚消去と同様の方法では検出できない。この消去現象は，入力される感覚の問題であって，運動消去のように出力そのものが減弱することとはまったく異なる現象である。おそらく，臨床場面では，本例の呈したような左手の障害を観察し，推察する以外，発見する方法はないものと思われる。

本例の左手の障害に関するもう一つの説明として，単に多様式感覚の消去現象と高次体性感覚障害が重複して生じた現象である可能性も考えられる。本例では多様式の消去現象と高次体性感覚障害を随伴しているため，両者の関係性を検証することはできない。今後同様の障害を呈する症例を発見し，詳細に検討することで，何らかの示唆が得られる可能性があると思われる。

3. 病巣との関係

本例の病巣は，CT上両側性で，右側は頭頂-側頭皮質と前頭葉皮質下，左側は頭頂領域に低吸収域を認め，SPECTでも複数領域の血流低下を認めている。そのため，本例の呈した障害はこれらの複合した病変による偶発的な現象であった可能性もある。しかし，現症として左半球病変による症状は呈していないこと，上頭頂小葉病変で生じる可能性が高い視覚運動失調も認めなかったこと，観察された障害は高次感覚障害，拙劣，感覚消去，

両手動作時の左手の障害のみであったことを考えると，本例の障害を生じさせた主たる病巣は中心後回と下頭頂小葉を中心とする右頭頂葉領域であると考えられる。しかし，明らかな半側空間無視，半身無視は認めていない。

Bartolomeoら（2007），Doricchiら（2008）は，半側空間無視を脳内ネットワークの離断症候群として再考し，皮質下線維束の重要性を強調している。彼らは，皮質領域に生じた病変では，その領域そのものと，線維連絡のある遠隔皮質の機能のみが障害されるが，皮質下病変では密に隣り合った線維束まで影響を受けるため，その線維と連絡のある皮質領域すべての機能障害を引き起こすこととなり，結果としてより重篤な障害を呈するとしている。本例の右頭頂病変は皮質に限局していたため，左側への注意の障害が比較的軽度で，運動と感覚を統合する頭頂葉の機能の中でも，体性感覚に関連した障害だけが顕著に発現した可能性が考えられる。

頭頂葉後方に病変を有し，触覚性の消去現象を呈した症例では，両側同時刺激時も病巣側の一次感覚領域の賦活があることがfMRIで確認されている（Kobayashiら 2005, Sarriら 2006）。これは，感覚自体は入力されているが，それに対する注意を向ける機構が頭頂葉後方にあることを示している。本例ではおそらく，頭頂葉後方病変により，物体の弁別や認知，それに関わる運動感覚の処理そのものの障害も存在していたが，体性感覚に対する注意も同様に障害されていた可能性がある。本例においては，両者が脳内でどのように処理されていたのかは明らかではない。今後，頭頂葉損傷例のさらなる神経心理学的検討と脳機能画像研究により，これらの脳内メカニズムが解明されることを期待したい。

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Abstract

Moving but not Using
— a case with missing object due to inattention to moving left hand during bimanual movements —

Yuko Hayakawa*, ** Nao Iwasaki*** Sachiko Anamizu****
Masaru Mimura***** Motoichiro Kato****

We reported a unique patient who showed inattention to the left hand during bimanual movements following a right parietal lobe lesion despite absence of unilateral neglect and motor extinction. The patient was a man in his late forties who suffered from cerebral infarction at watershed area of the right middle and posterior cerebral arteries, which was followed by subsequent subarachnoid hemorrhage secondary to a ruptured right internal carotid artery aneurysm. Eight months after the onset, neuropsychological examination disclosed that he had left side visual/auditory/tactile extinction, left hand clumsiness, and impairments of higher somotosensory functions including two-point discrimination and stereognosis, while his touch, pain, temperature and position senses on the left hand were intact. The patient presented with a unique failure on his left hand during bimanual movements despite absence of unilateral neglect and motor extinction. Although he performed as if his left hand could manipulate an object, the left hand caught only the air and missed the object. Re-examination following 4 years demonstrated that higher somatosensory disturbances and left hand clumsiness remained unchanged. However, his left hand movements during bimanual activities improved and multimodal extinctions dissolved as well. Although limb-kinetic apraxia following a deficit in the higher order sensory system is well known, there has been no report that the apraxia coincided with deterioration of contralesional hand clumsiness during bimanual activities. We conclude that his multimodal extinctions affected bimanual movements. Furthermore, we suggest that his unique left hand failure is accounted by inattention to somatosensory information that could arise intrinsically or spontaneously within active and voluntary bimanual movements, resulting from lesions involving the right parietal lobe posterior to primary sensory area.

* Department of Rehabilitation, Yokohama Stroke and Brain Center
** Department of Clinical Neuroscience, Yamagata University Graduate School of Medicine. 2-2-2 Iidanisi, Yamagata 990-9585, Japan
*** Sofia Home visit Nursing Care Station
**** Department of Neuropsychiatry, Keio University School of Medicine
***** Department of Neuropsychiatry, Showa University School of Medicine

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ORIGINAL ARTICLE

Unmet supportive needs of cancer patients in an acute care hospital in Japan—a census study

Daisuke Fujisawa · Sunre Park · Rieko Kimura · Ikuko Suyama · Yurie Koyama · Mari Takeuchi · Hiroka Yoshikawa · Saori Hashiguchi · Joichiro Shirahase · Motoichiro Kato · Junzo Takeda · Haruo Kashima

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Abstract
Purpose Little research has been done on supportive needs of cancer patients in acute hospitals in Japan. This study aims to comprehensively assess the unmet supportive needs of hospitalized cancer patients, as well as literacy and utilization of appropriate professional care.
Methods All cancer patients (aged 20 to 80 years) who were hospitalized in a university hospital in Tokyo during the designated 3-day period between September 1 and October 31, 2007 were recruited for participation in the study. The M.D. Anderson Symptom Inventory, Brief Cancer-Related Worry Inventory, and Hospital Anxiety and Depression Scale were administered. Patients' knowledge and use of relevant services were evaluated. The results were compared with those of non-cancer patients in the same treatment settings.
Results A total of 125 cancer patients and 59 non-cancer patients were enrolled. Cancer patients and non-cancer patients equally suffered from physical symptoms (15–26% had severe appetite loss, 18–19% had severe dry mouth, and 16–22% had severe pain); however, psychological distress of cancer patients exceeded that of non-cancer patients (28.0% vs 8.5%; $p \leq 0.05$). Severe psychological distress was associated with severe worry about future prospects or interpersonal and social issues and presence of two or more severe symptoms. Two thirds of the patients with severe psychological distress knew about the psychiatric division, but only one third actually sought treatment.
Conclusions Needs related to psychological issues were more prevalent among cancer patients than among non-cancer patients, despite a similar level of physical distress. Special attention should be paid to cancer patients who worry over future prospects or interpersonal and social issues, and those who have two or more severe symptoms.

Keywords Unmet supportive needs · Psychological distress · Worry · Predictive factors · Service use

D. Fujisawa (✉) · M. Takeuchi · J. Shirahase · M. Kato · H. Kashima
Department of Neuropsychiatry, School of Medicine, Keio University,
35 Shinanomachi, Shinjuku-ku,
Tokyo 160-8582, Japan
e-mail: dai_fujisawa@yahoo.co.jp

D. Fujisawa · S. Park · R. Kimura · I. Suyama · M. Takeuchi · H. Yoshikawa · S. Hashiguchi · J. Shirahase
Division of Palliative Care, Keio University Hospital,
35 Shinanomachi, Shinjuku-ku,
Tokyo 160-8582, Japan

S. Park
Faculty of Nursing and Medicine Care, Keio University,
35 Shinanomachi, Shinjuku-ku,
Tokyo 160-8582, Japan

Y. Koyama
National College of Nursing, Japan,
1-2-1, Umezono, Kiyose-shi,
Tokyo 204-8575, Japan

H. Yoshikawa · S. Hashiguchi · J. Takeda
Department of Anesthesiology, School of Medicine, Keio University,
35 Shinanomachi, Shinjuku-ku,
Tokyo 160-8582, Japan

Introduction

Cancer patients have diverse needs throughout the course of their illness. Identification and management of supportive needs is an essential component of comprehensive health care

for people with cancer, because unmet supportive needs have a detrimental effect on patients' well-being [32]. The most frequently reported unmet needs were those related to physical, psychological, informational, psychosocial, and daily living issues. Spiritual, communication, and sexuality issues have also been sporadically investigated [13].

Supportive needs of cancer patients differ between individuals and across time. Increased level of needs have been identified among patients who are young, female, unmarried, living in a rural location, or those who have a low income. Poor physical condition, advanced stage of illness at diagnosis, and current and/or past psychiatric problems are also associated with more complex needs [18]. Prevalence trends and predictors of unmet needs were highly variable in all domains and across the phases of illness [13]. During the newly diagnosed phase, patients were more likely to have unmet psychosocial (6–69%) and physical (44%) needs, compared with needs related to activities of daily living (5–10%), economic (11%), information (10–24%), or psychological (12–17%) [9, 21, 51, 60]. During the treatment phase, the prevalence of unmet needs for each domain had the largest variation compared with any other time over the course of the cancer. Unmet needs appear to be highest during the treatment and post-treatment phase [19, 20, 44]. High level of psychosocial needs is reported throughout the trajectory, especially during advanced/palliative phase [22, 37, 49, 58], with a gap between needs and service provision [5, 7].

Rigorous and systemic assessment of needs is the first critical step in supportive care that leads to the delivery and development of appropriate services [31]; however, very little research about cancer patients' needs has been done in Japan. Thus far, the research has been limited to ambulatory patients with specific types of cancer [29, 33], or the selected assessment tools were not validated for use with Japanese patients with cancer [29].

A study of unmet needs in an acute hospital setting is important in Japan, because 80% of the Japanese general population die in hospitals [23], and approximately 50% even prefer to spend the end-of-life period in a hospital rather than at home [45]. This is presumably because they may not cause burden to their family [15]. A nationwide survey demonstrated that 14–25% of the patients are reluctant to discuss end-of-life issues with physicians, which may be a barrier to introduction of quality palliative care [30]. Negative attitude towards palliative care among patients, their family members, and even physicians is one of the barriers against proper referral to palliative care and subsequent delay in terminating active anti-cancer treatment [27]. Misbelief and negative attitude about opioids hamper proper use of opioids [30, 38] and a substantial number of patients and families are currently dissatisfied with the available palliative care services [48].

The present study was conducted in a university hospital in central Tokyo. Survey in a university hospital has the following significance: in the Japanese medical system, patients are allowed to visit any hospital of their choice without paying extra money; the national health insurance covers 70–80% of the medical fee. Regardless of type of illness, health condition, or socioeconomic background, any patient can be seen at university hospitals. Approximately half of all Japanese physicians are initially trained at university hospitals; therefore, development of viable palliative care in university hospital settings is important for the overall progress of palliative care in Japan [28]. At the time of this study, even though a nationwide campaign to promote palliative care had been initiated, the hospital was not equipped with palliative care services. Unfortunately, this lack of services is not unusual in university hospitals in Japan.

First, we sought a validated needs-assessment scale; however, none of the psychometrically reliable scales, identified in a recent review [42], had been validated among Japanese subjects at the time of our survey. Therefore, we used a combination of several validated assessment scales as a substitute for a single needs-assessment scale. We aimed to comprehensively cover the domains that may contribute to the satisfaction and quality of life of the patients. Those domains are generally categorized into physical, psychological, psychosocial, informational, and spiritual issues and problems related to daily living, communication, and sexuality [13, 61]. We used the Japanese version of the M. D. Anderson Symptom Inventory (MDASI) [8, 35] to assess physical needs and daily living issues; the Brief Cancer Worry Inventory (BCWI) [16] to evaluate psychosocial, informational, communication, and sexuality issues; and the Japanese version of Hospital Anxiety and Depression Scale (HADS) [26] to assess undertreated psychological distress. We also attempted to identify factors associated with psychological distress, because psychological distress is highly influenced by unmet needs in other domains [63].

We compared cancer patients with non-cancer patients who were hospitalized in the same ward during the same study period. In the study-site hospital, as is usually the case with most hospitals in Japan, place of admission is determined by the site of primary illness and not by type of illness. For example, patients with chronic lung disease and patients with lung cancer are admitted to the same "pulmonary ward" and are cared for by the same nursing team and often seen by the same physician. Therefore, the non-cancer patients in the same ward served as a comparison group to identify areas that require further support among cancer patients.

In brief, this study aims to assess the unmet supportive needs of hospitalized cancer patients in a university hospital setting in Japan. All types of cancer sites and all stages of illness were included, and needs of cancer patients were

compared with non-cancer patients in the same treatment setting.

Patients and methods

Participants

This study was conducted in a 1,000-bed private general tertiary medical facility affiliated to a medical university located in the central Tokyo. The candidates for participation included all patients who were hospitalized during the study period and undergoing treatment or diagnostic testing for cancer in the medical, surgical, or radiological departments of the abovementioned hospital. Participants were recruited during the designated 3-day period between September 1 and October 31, 2007 (dates were determined by each department). Those who were aged 20 to 80 years and were able to complete a written questionnaire were eligible. Patients were excluded for surgical procedures within the week before the survey or if they were incapable of understanding and consenting to participation in the study (based on the judgment of the physician in charge). All patients who were not diagnosed with cancer and were hospitalized during the same period were approached for participation in the comparison group.

Procedure

Eligible patients who gave written consent were asked to fill out three self-report questionnaires: the MDASI, BCWI, and HADS. The measures used in this study do not literally assess unmet needs; alternatively, we attempted to supplement this by directly asking about awareness and utilization of relevant services. The relevant services included the pain clinic, psychiatric division, social services, rehabilitation medicine, and clinical nurse specialists. Research assistants provided support to participants who required help in filling out the questionnaires. These assistants were physicians or registered nurses who were not involved in the care of the participants. Participants' demographic and clinical data, including Eastern Cooperative Oncology Group performance status, were collected from the medical records.

This study was approved by the institutional review committee of Keio University School of Medicine and was registered in the national clinical trial registry, the UMIN-CTR (register number: UMIN000000811).

Measures

All the measures used in this study were previously standardized among Japanese cancer patients. The Japanese version of the MDASI is a 19-item self-report questionnaire scored on an 11-point Likert scale (0–10). It is designed to assess the severity and impact of cancer-related physical and psychological symptoms within the past 24 h. The BCWI is a 15-item self-report questionnaire designed to assess cancer-related worries on a numeric scale (0–100). Severity of worry is calculated by totaling the scores for each item. The inventory consists of three factors: future prospects, physical problems, and social and interpersonal problems [16]. When assessing non-cancer patients, the item regarding "worry about cancer" was modified to "worry about your current illness". The Japanese version of HADS is a 14-item self-report questionnaire designed to assess depression and anxiety. Each question is answered by choosing a score from 0 to 3. HADS total score of 20 or more or HADS depression subscale score of 11 or more indicates that the respondent is highly likely to have major depression. HADS total score of 11 or more, HADS depression subscale score of 5 or more, or HADS anxiety subscale score of 8 or more indicates that the respondent is highly likely to have an adjustment disorder or a major depressive disorder [26].

Statistical analysis

Cancer patients' data were compared with the non-cancer patients' data by using chi-square test for categorical variables, Mann–Whitney U test for non-parametric variables, and unpaired t test for continuous variables. Significance was set at $p<0.05$. Mantel test was used to compare prevalence of moderate and severe symptoms on MDASI between cancer and non-cancer patients.

Stepwise logistic regression analysis (forward selection) was performed to explore for factors that predicted severe psychological distress. Major depression based on the results of the HADS was entered into the analysis as the dependent variable, and the following variables were entered as predictor variables: patients' demographic factors (age, gender, and performance status), presence of severe symptoms according to the MDASI, number of severe symptoms, and presence of severe worry in each BCWI domain. Predictor variables were dichotomized, according to age, into categories of 65 years or over and others, performance status into categories of three or over and others, MDASI symptoms (items 1 to 13) into categories of severe (score of 8 or over) and others, and mean score of BCWI domains into categories of 80 or over and others.

Results

Participants

Of the 287 patients who were approached, 215 (74.9%) met the inclusion criteria. The reasons for exclusion were