

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-attentive 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—

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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

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療することとなり通院は中断していたが、復職の前に発症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	模写	36/36
複雑図形	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。

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、またそれに気が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一つ一つの穴に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。

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%)

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

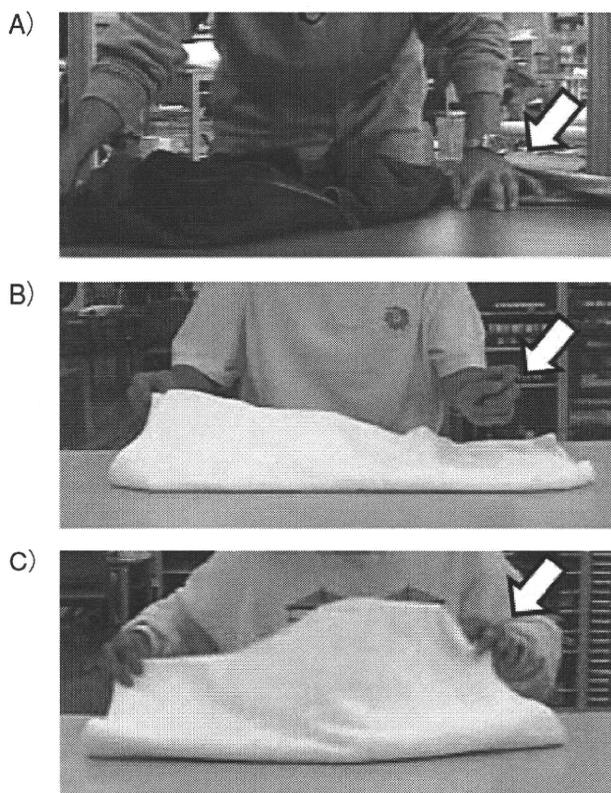


図1 発症8ヵ月後の両手動作時の左手の異常
(動画から抽出)

- 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、前方のシヤ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

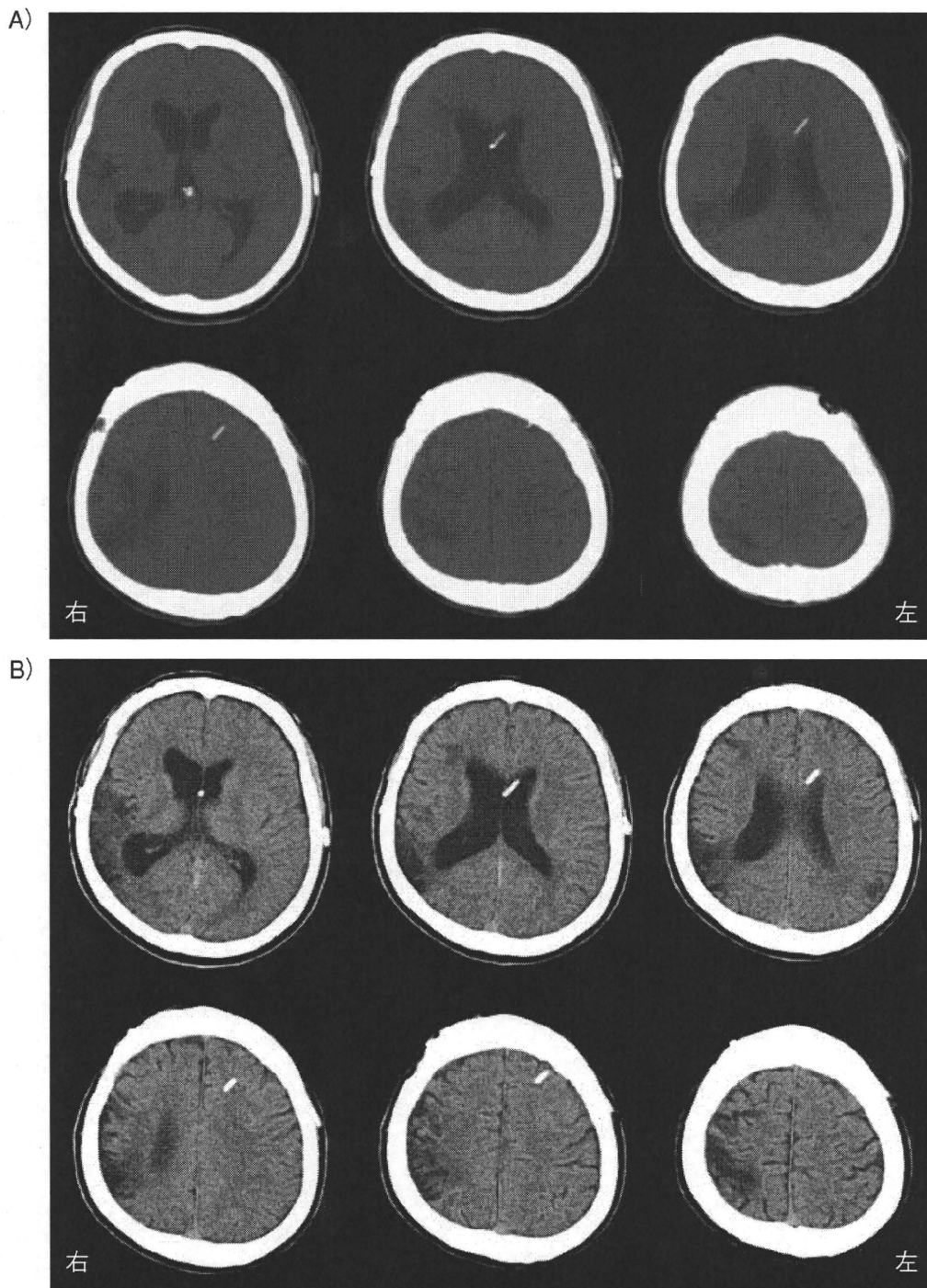


図2 CT画像

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,

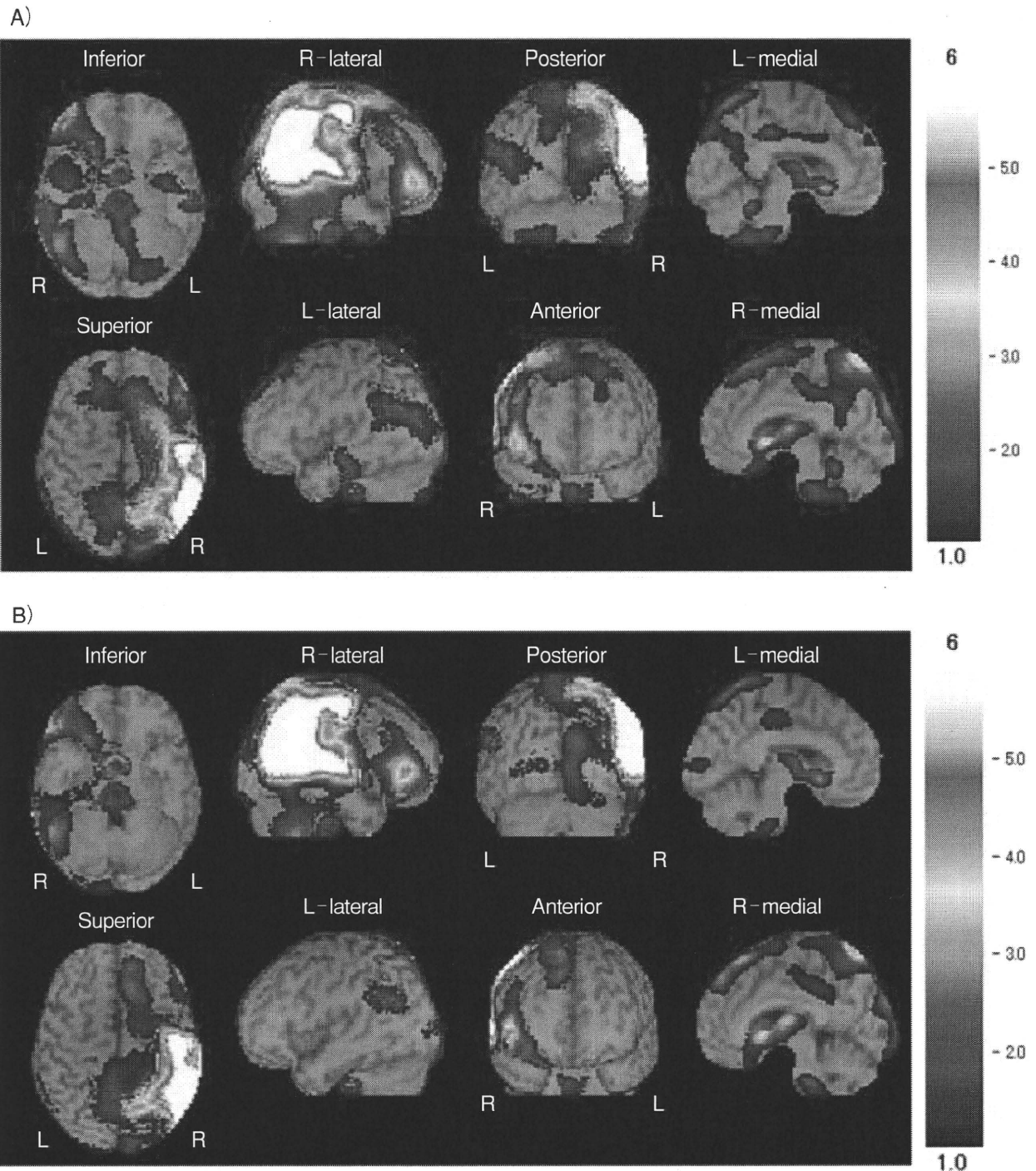


図3 99mTc-ECD SPECT e-ZIS解析

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ると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 —

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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 somatosensory 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.

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

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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.

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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

cognitive dysfunction (22 patients), severe physical condition (18 patients), decision of the physician in charge (four patients), and other unspecified reasons (38 patients). Of those, 184 patients (97 males and 87 females) gave written consent and were enrolled in the study (response rate, 85.6%). Differences in gender and age were not significant between those included and those excluded.

The demographic data of the participants are shown in Table 1. The participants consisted of 125 cancer patients with mean age of 58.9 years (SD=12.5) and 59 non-cancer patients with mean age of 61.2 years (SD=13.9). The majority of cancer and non-cancer patients were admitted for active treatment, and a few were admitted for evaluation and diagnosis. Few patients were admitted solely for palliative purpose; however, it should be noted that a large proportion of cancer patients have cancers that are considered unresectable or incurable; thus, even though the patients were admitted for active treatment, a substantial proportion of patients were implicitly at the stage of palliation. Opiates were prescribed for only 18 patients (12.1%).

Prevalence of physical and psychological symptoms

The mean number of severe symptoms was 1.9 (SD=2.6) in the cancer patient group and 1.7 (SD=2.5) in the non-cancer patient group, and the difference was not significant.

Figure 1 shows the results of the MDASI, listed in the order of prevalence. Symptoms related to psychological state outweighed physical symptoms. Cancer patients frequently (>20%) suffered from severe distress, lack of appetite, drowsiness, disturbed sleep, sad mood, and dry mouth, whereas the non-cancer patients frequently suffered from pain, disturbed sleep, numbness or tingling, and feelings of distress. There were no significant differences in the severity of any symptoms between cancer patients and non-cancer patients.

Severity of worries

Table 2 shows the severity of worries assessed by the BCWI. In all domains and for most items, worry was significantly more severe among cancer patients than among non-cancer patients. Worry was remarkable (mean score >50) among cancer patients with regards to treatment and prognosis, such as “the cancer itself”, “the cancer might get worse in the future”, “life and death”, “effect of current treatment”, “side effects of the treatment”, and “future of family members”. Cancer patients were significantly more worried about their “mental status” and “how to cope with the illness”.

The severity of worry was generally low with regards to physical symptoms and daily life issues, such as sexual problems, economic problems, relationships with family

members, and work or housework among cancer and non-cancer patients.

Age significantly correlated with the severity of all domains of worry, and the younger group had the most severe worries ($r=0.34$, $p<0.01$). Gender did not significantly correlate with the severity of worries. Performance status weakly correlated with the physical domain of worry, and worry became increasingly more severe as performance status declined ($r=0.15$, $p<0.05$).

Prevalence of psychological distress and predictive variables

As shown in Table 3, cancer patients had significantly higher total HADS scores and HADS anxiety subscale scores ($p<0.05$). Based on the cutoff scores recommended in a previous study [26], 93 (74.4%) of the 125 cancer patients suffered from psychological distress that corresponded to an adjustment disorder or major depression, and 35 (28.0%) suffered from severe psychological distress that corresponded to major depression. The prevalence of both was significantly higher in the cancer group. In the non-cancer group, 34 (57.6%) of 59 patients suffered from psychological distress that corresponded to an adjustment disorder or major depression, and only four (6.8%) suffered from severe psychological distress that corresponded to major depression.

Table 4 shows the results of a stepwise binary logistic regression analysis to identify factors associated with severe psychological distress. The analysis yielded a significant model (omnibus Chi-square=27.45, $df=3$, $p<0.001$), accounting for between 21.4% and 30.6% of the variance, with 76.3% of overall predictions being accurate. The future-prospects domain and social-and-interpersonal-problems domain of the BCWI and the presence of two or more severe symptoms according to the MDASI were significantly associated with severe psychological distress.

Literacy rate and rate of utilization of relevant services

Table 5 shows the percentage of patients who knew about (literacy rate) and who used (utilization rate) the relevant services. About two thirds of the patients knew about the psychiatric division, but less than 50% knew about social services, the pain clinic, and clinical nurse specialists. The literacy and utilization rates of cancer patients and non-cancer patients were not significantly different, except that the psychiatric division was more likely to be used by cancer patients.

Among the patients suspected of having major depression ($n=39$), 24 patients (61.5%) were aware of the psychiatric division, but only 11 patients (29.7%) actually used it; thus, 13 (33.3%) of the 39 patients who were

Table 1 Demographics of the participants

	Total (%)	Cancer (n=125)	Non-cancer (n=59)	<i>p</i> ^a
Male	97 (52.7)	68 (54.4)	29 (49.2)	0.53
Female	87 (47.3)	57 (45.6)	30 (50.8)	
Age (year)	59.6 (SD = 13.1)	58.9 (SD = 12.5)	61.2 (SD = 13.9)	0.27
Surgical ward	128 (69.57)	83 (66.4)	45 (76.3)	0.17
Medical ward	56 (30.43)	42 (33.6)	14 (23.7)	
ECOG performance status				
0	21 (11.5)	13 (10.5)	8 (13.6)	0.30
1	85 (56.5)	64 (51.6)	21 (35.6)	
2	47 (25.7)	29 (23.4)	18 (30.5)	
3	24 (13.1)	14 (11.3)	10 (17.0)	
4	6 (3.2)	4 (3.2)	2 (3.4)	
Cancer progression				
Curable/resectable		33 (26.4)		
Advanced		82 (65.6)		
Not identified		10 (8.0)		
Treatment phase				
Diagnostic (pretreatment)	8 (4.3)	6 (4.8)	2 (3.4)	
Active treatment	141 (76.6)	97 (77.6)	44 (74.6)	
Palliative	23 (12.5)	14 (11.2)	9 (15.3)	
Not identified	12 (6.5)	8 (6.4)	4 (6.8)	
Purpose of admission				
Examination/diagnosis	9 (4.9)	5 (4.0)	4 (6.8)	
Chemotherapy	64 (34.8)	64 (51.2)	0 (0.0)	
Other disease-targeted pharmacotherapy	23 (12.5)	0 (0.0)	23 (39.0)	
Radiotherapy	19 (10.3)	19 (15.2)	0 (0.0)	
Operation	53 (28.8)	33 (26.4)	20 (33.9)	
Local operation	1 (0.5)	0 (0.0)	1 (1.7)	
Rehabilitation	14 (7.6)	6 (4.8)	8 (13.6)	
Symptom control	34 (18.5)	22 (17.6)	12 (20.3)	
End-of-life care	3 (1.6)	3 (2.4)	0 (0.0)	
Others	8 (4.3)	6 (4.8)	2 (3.4)	
Use of opioids				
Yes	18 (9.8)	15 (12.0)	3 (5.1)	0.13
No	166 (90.2)	110 (88.0)	56 (94.9)	
Primary site of illness				
Gastrointestinal (surgical)	30 (16.3)	23 (18.4)	7 (11.9)	
Musculoskeletal	27 (14.7)	9 (7.2)	18 (30.5)	
Gastrointestinal (medical)	24 (13.0)	17 (13.6)	7 (11.9)	
Gynecological	20 (10.9)	20 (16.0)	0 (0.0)	
Hematological	18 (9.8)	18 (14.4)	0 (0.0)	
Head and neck	16 (8.7)	14 (11.2)	2 (3.4)	
Dermatological	10 (5.4)	3 (2.4)	7 (11.9)	
Urological	10 (5.4)	7 (5.6)	3 (5.1)	
Respiratory (medical)	7 (3.8)	3 (2.4)	4 (6.8)	
Neurosurgical	7 (3.8)	4 (3.2)	3 (5.1)	
Cardiovascular	4 (2.2)	0 (0.0)	4 (6.8)	
Respiratory (surgical)	4 (2.2)	3 (2.4)	1 (1.7)	
Radiological ^b	4 (2.2)	4 (3.2)	0 (0.0)	
Rehabilitation medicine ^c	3 (1.6)	0 (0.0)	3 (5.1)	

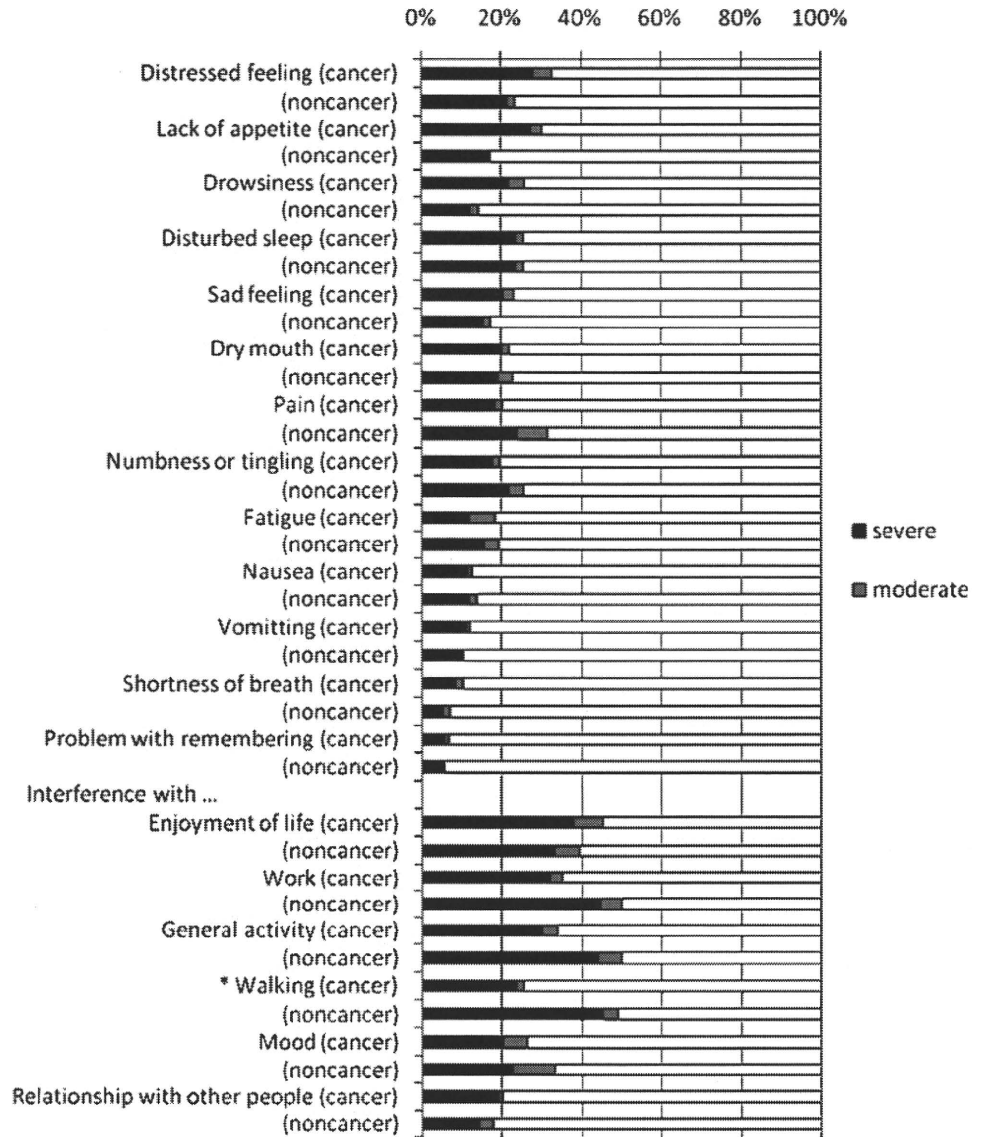
ECOG Eastern Cooperative Oncology Group

^a Chi-square test for gender, for whether medical or surgical division, for performance status and for use of opioids. Student's *t* test for age

^b Admitted for radiologic treatments, site unspecified

^c Admitted for multi-system rehabilitation therapy, site unspecified

Fig. 1 Distribution of severity for M.D. Anderson Symptom Inventory



suspected of having major depression did not consult the psychiatric division even though they knew it was available. Fifteen (38.5%) of the 39 patients did not know about the availability of psychiatric service.

Among the patients suspected of having an adjustment disorder ($n=127$), 87 patients (68.5%) knew of the availability of the psychiatric division, but only 17 patients (13.7%) actually used it; therefore, 70 (55.1%) of the 127 patients suspected of having an adjustment disorder did not consult the psychiatric division even though they knew about the availability of the service, and 40 (38.5%) of 127 patients did not know about the availability of psychiatric help. Only 15 (38.5%) of the patients with moderate-to-severe pain ($n=39$) knew about the services offered by the pain clinic, and only six patients (15.4%) actually used the clinic.

Discussion

The aim of our study was to comprehensively assess the unmet supportive needs of cancer patients who were hospitalized in an acute care hospital. Our results demonstrated that a substantial number of patients experience a wide range of symptoms and had worries that were undertreated. Detection and appropriate management of these symptoms and worries appear to be a pervasive problem.

Although there were no significant differences in the severity of each physical symptom between cancer patients and non-cancer patients, cancer patients are more likely to be psychologically distressed. These findings are consistent with other studies from Australia [46] and Finland [43], reporting that cancer patients have more needs in psychological domains than in physical domains. Our study

Table 2 Severity of worries

Item content and domains of worries	Cancer patients		Non-cancer patients		<i>p</i> ^a
	Mean	SD	Mean	SD	
Item content					
Current illness itself	71.0	26.2	54.2	34.3	<0.01
Illness might get worse in the future	66.9	29.6	43.5	35.3	<0.001
Life and death of self	56.5	33.1	31.0	34.3	<0.001
Ability to cope with the illness	55.5	29.8	38.0	31.5	<0.001
Effect of current treatment	53.4	30.1	38.7	30.9	<0.01
Side effects of the treatment	52.2	31.1	32.6	30.8	<0.0001
Future of family members	51.2	33.7	29.3	33.0	<0.0001
Mental status	49.1	27.6	33.7	29.9	<0.001
Physical symptom	46.5	29.5	40.7	30.5	0.22
Ability to do job or house work	41.3	33.7	39.3	35.0	0.71
Economic problems	39.8	32.4	32.7	33.3	0.17
Change of appearance	38.3	31.4	22.9	28.3	<0.001
Relationships with medical staff	25.6	26.9	15.0	23.9	<0.05
Relationships with family members	24.1	25.5	18.5	28.6	0.18
Sexual issues	16.3	24.6	13.3	24.4	0.46
Domains					
Future prospects	59.0	29.4	40.0	32.7	<0.0001
Physical problems	38.0	29.2	27.7	28.5	<0.01
Social and interpersonal problems	36.0	30.4	27.6	30.7	<0.05
Total	46.2	29.7	33.0	30.9	<0.0001

^a Student's *t* test

showed a higher rate of depression and anxiety than found in the Finnish study.

The distribution and frequency of each symptom were similar to the results of previous studies [4, 43]. Among the symptoms covered by the MDASI, feelings of distress, lack of appetite, disturbed sleep, drowsiness, and sad feelings were the most prevalent symptoms. Dry mouth was another frequent symptom among both cancer patients and non-cancer patients, suggesting another important area that requires care and attention. Tong et al. [54] reported that dry mouth was the most common oral symptom among medical oncology patients. Furthermore, they found that the symptom was associated with lower performance status and poorer quality of life.

Severe pain was present in 18.4% of our cancer group. Although the World Health Organization guidelines declare that 90% of cancer pain can be eliminated by proper analgesic use [62], our results showed a failure of the medical system in meeting this standard. It appeared that patients' pain is not adequately relieved even in a university hospital in the capital city. This unfortunate finding is evidenced by a low rate of opium usage and low rate of referrals to a pain specialist. The results of our study were

marginally better than those reported in the UK [14], Finland [43], and The Netherlands [56], but our findings replicate a series of previous reports showing the inadequacy of pain treatment in Japan [36, 52, 55].

Possible reasons of low opioid usage include (1) patients' cultural view of pain behaviors [17], (2) patients' beliefs and negative attitudes toward opioids, (3) under-detection of pain due to lack of routine screening, (4) insufficient knowledge and skills in prescribing opioids among physicians [38, 53], and (5) exclusion of severely ill patients from our sample. A nationwide survey showed that approximately 40% of the general population believes that cancer pain is not relievable, and approximately 30% believe that opioids cause addiction and shorten life [30, 38]. Further investigation into pain management is needed.

The results of the BCWI suggested that cancer patients had more severe worries and concerns about a larger range of issues compared with non-cancer patients. The severity of worry increases as their performance status declines. Their worry is more severe with regards to the course of illness and treatment, and issues related to mental status and coping with the illness. They worry less about social and interpersonal issues, including sexual and financial issues.