

較すると恐怖条件でN200成分の振幅が高い。これは、ダミー条件で見られた親近性向上時のN200成分と共通性があると考えられる。つまり、想起率も示唆するように恐怖条件の映像+セリフ条件は他の条件に比しより想起しやすい(記憶に残っている)事を示唆している。本研究で見られるN200は従来NA (Negative Activity) と呼ばれている、刺激弁別過程を反映した活動(Chope M et al., 1994)にきわめて類似していると考えられる。特に記憶想起を活性化する刺激に対してはこのN200成分が強く現れ、経験的記憶を同定するきっかけを示すと考えられる。N350成分は、主に海馬活動を反映していると報告されており、記憶が確かであるほど本活動は強く記録されるとされ、本研究でも側頭近傍電極で強く観察されており、親近性が高いことを裏付けている(Klaver P et al., 2005)。

恐怖条件における映像のみ条件ではP300成分の振幅が有意に低下している。この所見は本研究ではこの条件でのみ観察される特異的所見といえる。一般的に、P300成分は刺激に注意を向けると発生する事が知られており(Muller-Gass A & Campbell K, 2002)、これが減少する要因としては、わざと注意をそらす場合と、処理資源の減少がよく知られている。統合失調症やうつ病ではこの、処理資源の減少によりP300の減衰が指摘されており(McCarley RW et al., 1991; Gangadhar BN et al., 1993)、その後の認知処理に大きく影響を与える認知成分である事が指摘されている(Yang CL et al., 2007)。つまり、P300を引き出すような注意配分があると、その後の処理が促進される。本研究では、言語音声刺激に注意を向けるように指示をしているにもかかわらず、恐怖条件における映像のみ条件ではこの要素の減少が見られた。これは、無意識的に注意をそらしている可能性が示唆される。前述のN200成分の減衰も共にこの条件では認められることから、本条件では、無意識的に想起を避けているような反応を示している可能性が推測される。中性条件では対照的に映像のみ条件でN200,P300成分ともに強く惹起されているにもかかわらず、恐怖、中性条件間に想起率に差がないことから、強く記録されているが、能動的か受動的か不明であるが意識下でブロックするような反応であることが想定される。

映像のみ条件は、記録刺激と想起刺激が異なるクロスモダル特性を持っており、言語化過程を含んでいることをすでに考察した。また、情動情報の減少が言語化過程による情報量低下に関連している可能性も考えられる。しかし、神経生理学特性をみると中性刺激ではN200,P300ともむしろ活動が大きく、恐怖条件とは正反対の特性を示していることから、他の記録-想起に関する制御機能が働いている可能性が強く示唆される。

【引用文献】

- Hamm AO, Weike AI. The neuropsychology of fear learning and fear regulation. *Int J Psychophysiol* 57: 5-14. 2005.
- Strange BA, Dolan RJ. Anterior medial temporal lobe in human cognition: memory for fear and the unexpected. *Cogn Neuropsychiatry* 11: 198-218. 2006.
- Schooler JW, Engstler-Schooler TY. Verbal overshadowing of visual memories: some things are better left unsaid. *Cogn Psychol* 22: 36-71. 1990.
- Folmer RL, Yingling CD. Auditory P3 responses to name stimuli. *Brain and Language* 56, 306-311. 1997.
- Spironelli C, Angrilli A. Influence of Phonological, Semantic and Orthographic tasks on the early linguistic components N150 and N350. *Int J Psychophysiol* 64: 190-198. 2007.
- Chope M, Metz-Lutz MN, Wioland N, Rumbach L, Kurtz D. Event-related potentials and language processing. *Neurophysiol Clin* 24: 275-300. 1994.
- Klaver P, Fell J, Dietl T, Schür S, Schaller C, Elger CE, Fernández G. Word imageability affects the hippocampus in recognition memory. *Hippocampus* 15: 704-12. 2005.
- Muller-Gass A, Campbell K. Event-related potential measures of the inhibition of information processing: I. Selective attention in the waking state. *Int J Psychophysiol* 46: 177-195. 2002.
- McCarley RW, Faux SF, Shenton ME, Nestor PG, Adams J. Event-related potentials in schizophrenia: their biological and clinical correlates and a new model of schizophrenic pathophysiology. *Schizophr Res* 4: 209-231. 1991.
- Gangadhar BN, Ancy J, Janakiramaiah N, Umapathy C. P300 amplitude in non-bipolar, melancholic depression. *J Affect Disord* 28: 57-60. 1993.
- Yang CL, Perfetti CA, Schmalhofer F. Event-related potential indicators of text integration across sentence boundaries. *J Exp Psychol Learn Mem Cogn* 33: 55-89. 2007.

E. 結論

本研究では、PTSDの基盤病態を構成する恐怖記憶の想起に関する基礎的特性を検討した。恐怖記憶の意図的想起に関する脳内神経基盤に関しては様々な研究で報告されており、扁桃核、島皮質、帯状回

を含む辺縁構造および側頭、前頭新皮質がこれに関与することは良く知られている。しかし、PTSDにおける侵入性想起症状やフラッシュバルブ記憶と呼ばれる意図に反する自動的な想起過程に関しては全く調べられていない。今回我々は、このメカニズムの一端に迫ることができた。言語化プロセスを経て想起される恐怖記憶に関しては、一般記憶の想起とは全く異なる抑制的な神経生理学特性を示すことが明らかとなった。今後さらにNIRSにて計測した皮質血流動態との関連を解析し、さらなる検討を行う予定である。

F. 健康危険情報

なし

G. 研究発表

1. 論文発表

なし

2. 学会発表

なし

H. 知的財産権の出願・登録状況

なし

III. 研究成果の刊行に関する一覧表

< 書籍 >

金吉晴, 小西聖子監訳, E. B. フォア, E. A. ヘンブリー, B. O. ロスバウム著 : PTSD の持続エクスポージャー療法. 星和書店, 東京. 2009

小西聖子編: 犯罪被害者のメンタルヘルス. 誠信書房, 東京. 2008

松岡豊, 袴田優子: PTSD. 精神疾患の脳画像解析・診断学 (平安良雄・笠井清登編集). 南山堂, 東京, pp112-113, 2008

中島聡美: 被害者等の受ける精神的・心理的影響と治療. 犯罪被害者支援必携 (特定非営利法人 全国被害者支援ネットワーク編集). 東京法令出版, 東京, pp32-42, 2008

中島聡美: 精神医療現場での治療と対応. 犯罪被害者のメンタルヘルス (小西聖子編著). 誠信書房, 東京, pp21-31, 2008

中島聡美: 犯罪被害者治療の実践的組み立てと連携. 犯罪被害者のメンタルヘルス (小西聖子編著). 誠信書房, 東京, pp64-81, 2008

Suzuki Y, Tsutsumi A, Izutsu T, Kim Y.: Psychological consequences more than half a century after the Nagasaki atomic bombing. Radiation Health Risk Sciences. Nakashima M, et al (Eds.) pp277-282. Springer, Tokyo, 2008

< 雑誌 >

Nagamitsu et al.: Characteristic perfrontal blood volume patterns when imagining body type, high-calorie food, and mother-child attachment in childhood anorexia nervosa: a near infrared spectroscopy study. Brain and Development (2009 in press)

Matsumoto T, Imamura F, Katsumata Y, Kitani M, Takeshima T: Analgesia during self-cutting: clinical implications and the association with suicidal ideation. Psychiatry and clinical neurosciences 62: 355-358, 2008

Nishi D, Matsuoka Y, Nakajima S, Noguchi H, Kim Y, Kanba S, Schnyder U: Are patients following severe injury who drop out in a longitudinal study at high risk for mental disorder? Comprehensive Psychiatry 49(4):393-8, 2008

Hara E, Matsuoka Y, Hakamata Y, Nagamine M, Inagaki M, Imoto S, Murakami K, Kim Y, Uchitomi Y: Hippocampal and amygdalar volumes in breast cancer survivors with posttraumatic stress disorder. J Neuropsychiatry Clin Neurosci 20(3):302-308, 2008

Matsuoka Y, Nishi D, Nakajima S, Yonemoto N, Hashimoto K, Noguchi H, Homma M, Otomo Y, Kim Y: The Tachikawa Cohort of Motor Vehicle Accident Study investigating psychological distress: Design, methods and cohort profile. Social Psychiatry and Psychiatric Epidemiology 2008 Sep 25 (Epub)

Nishi D, Matsuoka Y, Noguchi H, Sakuma K, Yonemoto N, Yanagita T, Homma M, Kanba S, Kim Y: Reliability and validity of Japanese version of the Peritraumatic Distress Inventory. Gen Hosp Psychiatry 31(1):75-79, 2009

Matsuoka Y, Nishi D, Nakajima S, Yonemoto N, Noguchi H, Otomo Y, Kim Y: Impact of psychiatric morbidity on quality of life after motor vehicle accident at 1-month follow-up. Psychiatry Clin Neurosci (2009, in press)

小西聖子: 性犯罪被害によってトラウマを受けた少年への対応. 犯罪学雑誌 74(3): 91-93, 2008

松本俊彦, 今村扶美, 勝又陽太郎, 木谷雅彦, 竹島正: 非行少年における自殺念慮のリスク要因. 精神医学 50: 351-359, 2008

松本俊彦, 堤敦朗, 井筒節, 千葉泰彦, 今村扶美, 竹島正: 矯正施設被収容少年における性被害体験の経験率と臨床的特徴. 精神医学 51: 23-31, 2009

松岡豊, 内富庸介: 海馬・扁桃体の体積計測法とサイコオンコロジー. Clinical Neuroscience 26(4): 427-430, 2008

西大輔, 松岡豊: 救命救急センターにおける自殺未遂者への対応. メディカル朝日 37(6):33-35, 2008

野口普子, 松岡豊, 西大輔, 中島聡美, 佐野恵子, 小西聖子, 金吉晴: 交通事故に関する認知と精神的苦痛との関連についての横断研究. 総合病院精神医学 20(3): 279-285, 2008

鈴木友理子：災害精神保健活動における役割分担と連携，保健医療科学 57 (3)
234-239, 2008

鈴木友理子：能登半島地震への派遣活動を通じて，日本トラウマティックストレス学会
誌:100-102, 2008. 6

鈴木友理子，本間寛子，堤敦朗，金吉晴：新潟中越地震 3 年後の地域高齢者における精神
障害の有病率調査．日本精神神経雑誌（印刷中）

IV. 研究成果の刊行物

ORIGINAL PAPER

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The Tachikawa cohort of motor vehicle accident study investigating psychological distress: design, methods and cohort profiles

Received: 24 July 2008 / Accepted: 11 September 2008 / Published online: 25 September 2008

Abstract *Background* The Tachikawa cohort of motor vehicle accident (TCOM) Study has been carried out in Tokyo since 2004. This study examined the association of medical and psychosocial variables

evaluated shortly after admission to the acute critical care center with long-term psychiatric morbidity risk in patients with accidental injuries. *Methods* Between May 2004 and January 2008, patients with accidental injury consecutively admitted were recruited to the TCOM Study. Psychiatric morbidity as a primary endpoint was measured using a structured clinical interview at 1, 6, 18 and 36 months after involvement in a motor vehicle accident (MVA). The baseline investigation consisted of self-administered questionnaires concerning acute psychological responses and personality. Medical information was obtained from patients' medical charts. Various socio-demographic data, health-related habits and psychosocial factors were assessed by interview. To examine potential biomarkers of psychological distress, blood samples were collected. *Results* Out of 344 patients who were asked to participate in this study, 300 (87%) patients with MVA-related injury were enrolled. Corresponding rates for the questionnaires on psychological responses and blood sampling were 98–99 and 79%, respectively. The cohort sample was composed of 78% men; the median age was 34 years; and 45% of the participants were motorcycle drivers. *Conclusions* The TCOM Study should prove useful for researchers examining the association between biopsychosocial variables and psychological distress and may contribute to the formation of a framework for providing care for patients with MVA-related injury.

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Key words motor vehicle accident – severe injury – cohort study – post-traumatic stress disorder – psychiatric morbidity

Introduction

Over the past decade, increasing attention has been devoted to psychiatric morbidity following physical injuries [7, 24, 30, 34, 38, 44]. This kind of research is

essential, because advances in injury care systems have increased the number of seriously injured people who are able to survive their injuries and can be assisted to recover through rehabilitation [21]. For instance, nearly one-third of injured patients appear to develop trauma-related psychiatric illness and the major diagnoses are post-traumatic stress disorder (PTSD) and major depressive disorder (MDD) [15, 30, 34, 38]. MDD and PTSD are independent sequelae of traumatic events, have similar prognoses, and interact to increase distress and dysfunction [38]. Both should be targeted by early treatment interventions and by neurobiological research [38]. Injuries affect all populations, regardless of age, sex, income and geographic region. From a global perspective, it was estimated that approximately 16% of the world's burden of disease was attributable to injury in 1998 [19]. In particular, injuries attributable to motor vehicle accidents (MVAs) are expected to be the third contributor to worldwide burden of disease by the year 2020 [27], and already the leading injury-related cause of death among youth is MVA [19]. However, there is as yet no valid epidemiological study examining psychiatric morbidity after a MVA in Japan. Furthermore, this important issue has been neglected because of lack of investigator and mental health resources.

We therefore deployed several trained research nurses, a resident psychiatrist and a research psychiatrist in an acute critical care center to overcome the barrier to study implementation. Then we designed and implemented a cohort study which is called the Tachikawa cohort of motor vehicle accident (TCOM) Study. The aims of the TCOM Study were to (1) identify the prevalence of PTSD, MDD and other common psychiatric diagnoses at 1, 6, 18 and 36 months following

MVA, (2) identify factors that increase risk of poor psychiatric outcomes, and (3) examine other post-injury outcomes including quality of life and posttraumatic growth. We assumed that the factors associated with psychiatric outcome would be heart rate, brain-derived neurotrophic factor (BDNF), omega-3 fatty acids, sense of life-threat, intrusive memory, negative cognitive appraisal, harm avoidance temperament, resilience to stress, litigation, and physical impairment. The unique point of this cohort is the collection of serum samples from baseline to follow-up. In an earlier interim publication, we presented psychiatric morbidity at 1 month post-injury in one part of the entire sample [23]. We believe that even observational research should be reported transparently so that readers can be updated on what was planned, performed and found, and what conclusions were drawn. In 2007, the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement was released [47] and in accordance with this statement, we disclose here the study design prior to publishing follow-up data. This transparency is important, because the primary endpoint should not be changed conveniently according to the follow-up data. Concealing the design or changing the endpoint renders comparability difficult.

This paper describes the design and implementation of the TCOM Study and presents baseline observations. We also describe the study methods in detail, including recruitment of the cohort, data collection methods, and our active follow-up system. We believe that the information described here can provide a background for future reports from the TCOM study and may give practical information for comparison with existing large studies [15, 30, 34–38, 44–46] (see review in Table 1).

Table 1 Existing large cohort studies evaluating the prevalence of psychiatric morbidity after injury

Study	City	Study sample and setting	No.	Follow-up	ISS	Primary endpoint	Instrument
Shalev et al. [38]	Jerusalem Israel	Traumatized patients Arriving at emergency room; MVA was most frequent (85.8%)	211	4 months	NA	PTSD and depression	CAPS SCID
Ursano et al. [44]	Unknown USA	Recruited through local police reports (28%), Hospitals (47%) & from police records (25%); all cases were MVA	122	1 year	NA	PTSD	SCID
Schnyder et al. [34, 35]	Zurich Switzerland	Injured accident patients Consecutively admitted to the ICU; MVA was most frequent (62%)	121	1 year	Range, 10–51 Mean, 21.8 SD = 9.9	PTSD and depression	CAPS HADS
O'Donnell et al. [30]	Victoria Australia	Injured patients consecutively Admitted to a level 1 trauma service; MVA was most frequent (74%)	363	1 year	≥15, 33% 10–14, 31% 0–9, 36%	Major psychiatric Diagnoses	CAPS SCID
Vaiva et al. [45, 46]	Lille France	Admitted to the Traumatology Dept.; All cases were MVA	108	1 year		PTSD	CAPS MINI
Gil et al. [15]	Haifa Israel	Injured accident patients Admitted to 2 surgical wards; MVA was most frequent (90%)	120	6 months	Mean, 5.8 SD = 3.6	PTSD and major Psychiatric diagnoses	CAPS SCID
Schnyder et al. [36]	Zurich Switzerland	Hospitalized for the treatment of physical Injuries at the Traumatology Dept.; MVA was third most frequent (31.4%)	255	6 month	Median, 9 Range, 1–66 Mean, 11.7	PTSD and depression	CAPS HADS

No. number of patients from whom written informed consent was obtained, ISS injury severity scale, NA not assessed, PTSD post-traumatic stress disorder
CAPS clinician administered PTSD scale, SCID structured clinical interview for DSM, HADS hospital anxiety and depression scale
MINI mini-international neuropsychiatric interview

Methods

■ Study setting and requirement procedure

The TCOM Study was approved by the Institutional Review Board and Ethics Committee of the National Disaster Medical Center (NDMC), Tokyo. The geographic area of the NDMC has a population of 1,700,000, and its acute critical care center is responsible for level 1 trauma service. Admission to an acute critical care center as defined by the NDMC refers to an admission to an intensive care unit on an emergency basis.

Participants admitted to the acute critical care center of the NDMC between 30 May 2004 and 8 January 2008 (about 44 months) were recruited consecutively. First, we took part in a daily conference held at the acute critical care center and reviewed the medical and nursing records of newly admitted patients; second, with the permission of the physicians, we screened eligible patients. Baseline investigations (T_1) were conducted after the cessation of intravenous narcotic administration; repeated assessments of cognitive function using the mini-mental state examination (MMSE) [12] were performed by trained research nurses or trained psychiatrists. After enrollment, patients underwent a short physical examination, and then completed questionnaires and interviews. All participants were given a gift voucher (1,000 JPY [9 USD]) for their participation after each assessment. The median number of days between the accidents and the baseline assessments was 2.3 days (range = 0–23). After providing a complete description of the study, written informed consent was obtained from every patient.

■ Eligibility criteria

The inclusion criteria were as follows: (1) MVA-related severe physical injury causing a life-threatening or critical condition; (2) consecutive admittance to the acute critical care center; (3) age between 18 and 69 years; and (4) native Japanese speaking ability. The exclusion criteria were as follows: (1) diffuse axonal injuries, brain contusion, and subdural and subarachnoid bleeding detected by computed tomography and/or magnetic resonance imaging (with the exception of concussion), because the presence of traumatic brain injury creates considerable difficulties when assessing psychological responses to injury; (2) cognitive impairment, defined as a score of <24 on the MMSE; (3) currently suffering from schizophrenia, bipolar disorder, drug (non-alcohol) dependence or abuse, or epilepsy prior to MVA; (4) marked serious symptoms such as suicidal ideation, self-harm behavior, dissociation, or a severe physical condition preventing the patient from tolerating the interview; and (5) living or working at a location more than 40 km from NDMC.

■ Baseline data and specimen collection

The assessments included general socio-demographics, detailed information about the MVA, injury severity score (ISS) [5], Glasgow coma scale (GCS) score [42], status during the MVA (e.g., vehicle driver), vital signs first recorded on admission to the emergency room, lifestyle, family history of psychopathology as determined in a structured interview, a sense of life-threat during the MVA as determined in the structured interview, feeling of self-reproach, loss of memory regarding the MVA (defined as having a score of <2.1 on the Gil's Memory of Traumatic Event Questionnaire) [15], pain as measured subjectively on a Likert scale, performance status as defined by the Eastern Cooperative Oncology Group [31], consumption of alcohol prior to the MVA as determined in the structured interview, and involvement in previous MVAs. The psychometric instruments used were the impact of event scale revised (IES-R) [4, 49], the hospital anxiety and depression scale (HADS) [20, 51], the peritraumatic dissociative experience ques-

tionnaire (PDEQ) [22], the peritraumatic distress inventory (PDI) [8], the temperament and character inventory [9, 18], the stress coping inventory [11] and the social support questionnaire [14, 33]. At the beginning of study, the PDEQ and PDI were not in fact included among the assessment tools, but were added in the middle of the study.

Serum collection

To examine the potential biomarkers of psychobiological distress and resilience (brain-derived neurotrophic factor, omega-3 fatty acids, neuropeptide Y, dehydroepiandrosterone, dehydroepiandrosterone sulfate, and cortisol) and its predictive value with regard to successful adaptation to extreme stress, 10-mL blood samples were drawn at baseline (T_1) and follow-up investigations. Serum samples from the subjects were collected between 10:00–12:00 or 14:00–17:00 before meals, and then stored in separate -80°C freezers.

■ Primary, surrogate and secondary endpoints at follow-up investigations

Table 2 shows the measures utilized, their content area, and the occasions on which they were used. Briefly, follow-up investigations were planned at 1 month (T_2), 3 months (T_3), 6 months (T_4), 9 months (T_5), 18 months (T_6), and 36 months (T_7) after MVA. The measures of the primary and surrogate endpoints are reviewed briefly below. We used telephone, e-mail and letter to correspond with the participants, and made an appointment or asked them to answer the questionnaire 2 weeks before the next investigation. As a general rule we allowed 4 weeks as the range of the investigation period. To maintain the response rate, we planned to distribute a seasonal newsletter to the participants at 2, 4 and 13 months after MVA. It contained a flow chart of the study, greeting and a short feature about seasonal news written by investigators.

Psychiatric diagnoses

Trained psychiatrists conducted the follow-up face-to-face assessments at 1, 6, 18, and 36 months after MVA. PTSD was diagnosed using the Clinician Administered PTSD Scale [6]. PTSD was diagnosed using the "1–2" rule (i.e., diagnostic criteria were met for each symptom if frequency ≥ 1 and intensity ≥ 2) [50]. Participants were deemed to have partial PTSD if they fulfilled only two out of the three symptom criteria [B (re-experiencing), C (avoidance), D (hyper-arousal)], and criteria A-1 (stressor), E (duration), and F (impairment) according to the diagnostic and statistical manual of mental disorders, 4th edition, text revision (DSM-IV-TR) [3]. Other common psychiatric illnesses were diagnosed using the Mini International Neuropsychiatric Interview (MINI) with the exception of the 2 modules pertaining to PTSD and antisocial personality disorder [32, 39]. Minor depressive disorder was defined according to the criteria of DSM-IV-TR for the presence of either a depressed mood or a loss of interest and a total of 2–4 depressive symptoms [3]. Psychiatric morbidity (at least one diagnosis of psychiatric illness, including minor depression or partial PTSD) and PTSD syndrome (full PTSD and partial PTSD) at 6 months post-accident were considered as the primary endpoint. Psychiatric morbidity and PTSD syndrome at 1 and 18 months post-accident were also of interest. Pre-accident common psychiatric illness was retrospectively assessed using the MINI. Regarding to the incidence of MVA-related psychiatric illness that is identified as occurring post-trauma, the retrospective structured interview provides the opportunity to exclude those who had a psychiatric illness at the time of injury. A random sample of 30 cases assessed by two raters (one conducting the interview and one observing) was used to assess

Table 2 Content areas and Instruments

Construct	Instrument	Occasion
Primary endpoint		
Psychiatric diagnoses	Clinician administered PTSD Scale Mini-international neuropsychiatric interview	T ₂ , T ₄ , T ₆ , T ₇
Surrogate endpoint		
Psychological distress	Impact of event scale revised Hospital anxiety and depression scale	T ₁ , T ₂ , T ₃ , T ₄ T ₅ , T ₆ , T ₇
Quality of life	Medical outcomes study 36-item short form Health survey	T ₂ , T ₄ , T ₆ , T ₇
Secondary endpoint		
Sense of Coherence	Sense of coherence	T ₃ , T ₆ , T ₇
Growth	Posttraumatic growth inventory	T ₅ , T ₆ , T ₇
Cognition	Posttraumatic cognitions inventory	T ₃ , T ₄
Service use	Ad hoc questionnaire	T ₂ , T ₄ , T ₆ , T ₇
Litigation	Ad hoc questionnaire	T ₂ , T ₄ , T ₆ , T ₇
Perceived loss	Ad hoc questionnaire	T ₂ , T ₄ , T ₆ , T ₇
Biological marker	Serum	T ₁ , T ₂ , T ₄ , T ₆ , T ₇
Other data		
Injury severity	Injury severity score	T ₁
Wakefulness	Glasgow coma scale	T ₁
MVA-related memory	The Gil's memory of traumatic event questionnaire	T ₁
Performance status	The eastern cooperative oncology group performance status	T ₁
Cognitive screening	The mini-mental state examination	T ₁
Dissociation	Peritraumatic dissociative experience questionnaire ^a	T ₁
Distress	Peritraumatic distress inventory ^a	T ₁ , T ₃
Personality	Temperament and character inventory	T ₁
Coping	Stress coping inventory	T ₂
Support	Social support questionnaire	T ₂

T₁ baseline, T₂ 1 month after MVA, T₃ 3 months after MVA, T₄ 6 months after MVA

T₅ 9 months after MVA, T₆ 1.5 years after MVA, T₇ 3 years after MVA

^aTaken among patients who had certain MVA-related memory from the middle of the study

inter-rater reliability. The ratings for three major diagnoses of PTSD syndrome, depression, and alcohol-related disorder were reliable, with kappa values of 1.0, 0.9, and 1.0, respectively. In addition, in case that the participant met the criteria of psychiatric morbidity, we did not treat him or her by ourselves during the follow-up period but rather referred him or her to an independent physician.

Psychological distress

To assess psychological distress, the IES-R [4, 49] and HADS [20, 51] were administered. HADS [20, 51] includes a 7-item anxiety subscale and a 7-item depression subscale for assessing general psychological distress for the preceding week. Each item is rated on a scale of 0-3, with high scores denoting greater psychological distress. On the other hand, the IES-R [4, 49] assesses the level of symptomatic responses to a specific traumatic stressor (MVA in our study) in the past week. The degree of distress for each item is rated on a 5-point scale, ranging from 0 = not at all to 4 = extremely. There are three subscales (i.e., intrusion, avoidance, and arousal).

Quality of life

To assess the level of functioning of the subjects, the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) [13, 25] was administered. The SF-36 is based on a conceptual model consisting of physical and mental health constructs, and is designed to measure perceived health status and daily functioning. It consists of 36 items scored in the following 8 domains; physical functioning, role-physical functioning, bodily pain, general health perception, vitality, social functioning, role-emotional functioning, and mental health [48].

The scores of the IES-R, HADS, and SF-36 were considered as the surrogate endpoint. Other measures considered as the secondary endpoint are shown in Table 2. Briefly, to assess a resilience to stress and the capacity to cope with it, the Sense of Coherence Scale [1, 2, 40] was administered. To assess positive psychological change against the traumatic event and examine the relationship between posttraumatic psychopathology and growth, the posttraumatic growth inventory [41, 43] was administered. To examine the value of cognitive appraisal on posttraumatic psychopathology, the posttraumatic cognitions inventory [10, 28] was administered. Furthermore, ad hoc questionnaires were used to assess service use, litigation and perceived loss.

Tracking those lost to follow-up

Participants considered "lost to follow-up" were determined primarily from (1) returned mailed invitations for follow-up investigations by the Japan Post Service as "undeliverable" or "moved, no forwarding address", (2) those who refused our offer to keep participating in the study on three consecutive occasions, and (3) inability to get hold of the participants by phone or e-mail. Establishing communication by telephone and e-mail was abandoned if unsuccessful after three attempts on three different days and at two different times (midday or evening).

Potential sources of bias

First, data were obtained from only one teaching hospital in the suburbs of Tokyo. From our clinical impression, the proportion of MVA occurring during motor sports or leisure time was higher in our sample than that actually observed in central Tokyo. In relation to sample characteristics, there are not a little cases of one-car accidents involving a motorcyclist, which allows us to examine the difference in incidence of PTSD between one-car accidents and

others types of accident. Second, many patients had to be excluded due to age (under 18 or over 70) and traumatic brain injury, which may limit the generalizability and clinical relevance of the study.

Sample size

In previous epidemiological studies, the incidence of overall psychiatric morbidity at 12 months post-injury varied from 21 to 26% [30, 34]. On the basis of our pilot investigation, we estimated that the incidence of overall psychiatric morbidity at 6 months post-injury would be 25% and the width of the 95% confidence interval would be 15%. According to the formula [16], 128 subjects were needed. However, the dropout rate in our pilot investigation using a mail questionnaire was 54% at 6 months post-injury. Therefore, we needed to recruit at least 280 subjects at the initial investigation.

Results

Nine thousand five hundred and eleven patients were admitted to the ICU of NDMC during the study period. Figure 1 shows a flow chart of the patients included and excluded from the study. Although dissociation is a frequent psychopathological symptom in the early aftermath of trauma, exclusion due to massive dissociation occurred only rarely ($n = 1$). After giving a complete description of the study, written informed consent was obtained from 300

patients (87.2%). The patients who refused to participate in the study ($n = 44$) did not significantly differ from those who participated ($n = 300$) in terms of sex, age, ISS score [5], GCS score [42], or status during the MVA. The median number of days between the accident and T_1 was 2.0 (range = 0–23, mean = 3.8, SD = 4.2). Demographic, behavioral and medical characteristics, and acute psychological distress at T_1 are shown in Tables 3, 4, and 5. The corresponding rates for the HADS and the IES-R were 98 and 99%, respectively. Of 300 participants, serum sample was obtained from 237 (79%) patients at T_1 .

Discussion

The most important contribution of this study that can be drawn from the data presented is that this is the first and largest Japanese cohort of patients with MVA-related injuries recruited and investigated. Cross-country differences including societal attitude toward trauma, levels of basic health care, accessibility to medical services, and inequality of income distribution or wealth distribution might play important roles in the development of PTSD. Second, we collected not only psychosocial variables but also

Fig. 1 Enrollment of study participants

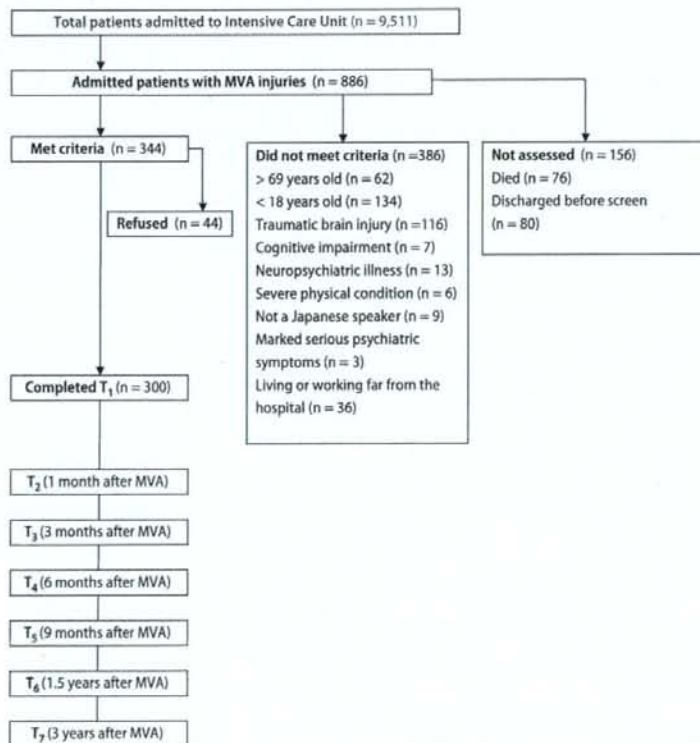


Table 3 Baseline demographics of 300 cohort members

Characteristic	No	%
Age, mean years \pm SD, range	36.5 \pm 15.0 (18–69)	
Gender		
Men	233	77.7
Women	67	22.3
Status during MVA		
Vehicle driver	70	23.3
Motorcycle driver	136	45.3
Passenger	17	5.7
Bicyclist	42	14.0
Pedestrian	29	9.7
Highest level of education		
Junior high school	66	22.0
High school	110	36.7
Junior or technical college	76	25.3
University or higher	48	16.0
Marital status		
Married or having a partner	131	43.7
Never married	142	47.3
Divorced or widowed	27	8.0
Living alone	71	23.7
Employment status		
Paid worker (full- or part-time)	228	76.0
Student	43	14.3
Unpaid work (homemaker, retired)	27	9.0
Unknown	2	0.7
Annual income (JPY)		
Less than five million	150	50.0
Five to ten million	88	29.3
More than ten million	15	5
Unknown	47	15.7

SD standard deviation, MVA motor vehicle accident

serum samples. Except for our study, only Vaiva et al. have collected blood samples and investigated plasma gamma amino-butyric acid levels in 108 patients with MVA-related injuries as a predictive factor for subsequent PTSD [45, 46]. Longitudinal cohort studies of posttraumatic stress provide an optimal method for exploring the course of PTSD and for examining its potential predictors; thus, we will be able to report the long-term consequence of MVA-related injuries and find new valid biomarkers for estimating the development of post-trauma psychiatric morbidity.

It has also been reported in the US that a large proportion of the population are involved at some time in a life-threatening accident (men 25%, women 14%) [17]. In Japan, as an example, about 10% of new patients requiring admission to an acute critical care center have severe physical injuries resulting from MVAs [29]. Furthermore, according to the National Comorbidity Survey Replication [26], an estimated 53.4% of adults in the US have 1 or more of the psychiatric or physical problems assessed in the survey. People with psychiatric or physical problems reported an average 32.1 more role-disability days in the past year than those without psychiatric or physical problems, which is equivalent to nearly 3.6 billion days of role disability in the population. Musculoskeletal disorders and major depression had the greatest effects on disability days. Therefore, this

Table 4 Baseline behavioral characteristics of 300 cohort members

Characteristic	No	%
Alcohol drinking		
Never drinker	51	17.0
Chance drinker	31	10.3
Drink 1–3 days a month	61	20.3
Drink 1–2 days a week	59	19.7
Drink 3–4 days a week	29	9.7
Drink almost every day	65	21.7
Past drinker	4	1.3
Smoking		
Never smoker	109	36.3
Past smoker	32	10.7
Current smoker	159	53.0
Habit of exercise		
Less than some days in a year	189	63.0
Once a month to twice a week	76	25.3
Three times a week or more	35	11.7
Having physical problem before MVA	91	30.3
Drinking alcohol before MVA within 2 hours	29	9.7
Taking medicine before MVA within 6 hours	32	10.7
Performance status		
0	7	2.3
1 (Symptomatic but completely ambulant)	77	25.7
2 (Symptomatic, < 50% in bed during the day)	53	17.7
3 (Symptomatic, > 50% in bed, but not bed bound)	100	33.3
4 (Bed bound)	63	21.0
Having pain	278	92.7
Involvement in previous MVAs	186	62.0
Sense of life threat during MVA	97	32.3
Loss of MVA-related memory	93	31.0
Feelings of self-reproach	162	54.0
Self-reported history of psychiatric illness	30	10.0
Family history of psychopathology ^a	34	11.3

SD standard deviation, MVA motor vehicle accident

^aIncluded first- and second-degree relatives

study will undoubtedly provide valuable public health data for future policy making for human health.

Swiss and Australian samples in previous similar and valid studies are useful for comparative purposes [30, 36] (see review in Table 1). All three sample populations were comparable with the present study in terms of sample size ($n = 300$), follow-up duration (3 years), the ISS score (median = 8, range, 1–48), and the primary endpoint and instruments (CAPS). More specifically, the present cohort study showed no difference in gender ratio (men 78%, women 22%) or mean age (36.5 years, SD = 15.0) from the three previous studies [30, 36]. Furthermore, our study showed no difference in other demographic characteristics such as marital status, living arrangement, employment status, and educational level from the Swiss studies [36]. Three samples differed in terms of the timing of baseline assessment; 2.0 days in the present study, 5.0 days in the Swiss studies [36] and 7.7 days in the Australian study [30]. Furthermore, the questionnaire assessing initial psychological distress was not identical to those in the previous studies [30, 36] and is likely to be non-comparable; however, IES-R and HADS data showed low levels of psychological distress at baseline. Finally, the unique point of our cohort is that we use serum samples.

Table 5 Baseline medical characteristics and acute psychological distress of 300 cohort members

Characteristic	No.	Mean	SD	Median (range)
Glasgow coma scale on admission	300			15.0 (3-15)
Heart rate on admission, bpm	300	84.9	16.5	
Systolic BP on admission, mmHg	300	137.4	26.4	
Diastolic BP on admission, mmHg	300	77.3	20.5	
RR on admission, times per min	300	20.0	6.9	
Laboratory data				
Leukocyte count/ μ l	295	8597	3564.1	
Erythrocyte count, $\times 10^9/\mu$ l	295	414.6	226.0	
Hemoglobin, g/dl	295	12.8	6.3	
Platelet, $\times 10^9/\mu$ l	295	23.0	11.1	
C-reactive protein, mg/dl	289			1.1 (0-19.1)
Creatine phosphokinase, IU/l	289			286 (15-11270)
Injury severity score IES-R	300			8.0 (1-48)
IES-R				
Total score	299	17.9	14.7	15.0 (0-62)
Intrusion	300			5.0 (0-26)
Avoidance	299			4.0 (0-30)
Hyper-arousal	300			5.0 (0-24)
HADS				
Total score	294	9.6	7.1	8.0 (0-35)
Anxiety	295			4.0 (0-21)
Depression	294			3.0 (0-19)

No. varied according to the number of patients who completed the assessment, SD standard deviation
BP blood pressure, RR respiratory rate, IES-R impact of event scale-revised, HADS hospital anxiety and depression scale

The present study has a strong methodology. First, a significant point to be emphasized is that, in addition to the assessment of PTSD, a broader area of outcomes were evaluated, including the number of psychiatric diagnoses, quality of life and posttraumatic growth. Second, we used both a standardized structured interview and self report scales in a face-to-face interview. The limitation of the present study is that the range of interval between admission and the time of initial assessment might have been wide. Further studies are needed to address such an issue. On the other hand, another advantage of the present study is that we could estimate the response rate at baseline investigation (i.e., 87%). This sufficient response rate was probably due to the close collaboration with the emergency department and the diligent recruitment by trained research nurses.

In conclusion, the results of future investigations on the bio-psychosocial variables associated with the psychiatric morbidity may have scientific and public mental health implications. It has been suggested that cohort studies may be the most rational way of choosing specific interventions to be tested in future

clinical trials. The results of the present study may also help guide healthcare providers in providing care for injured patients with post-trauma psychiatric morbidity.

Acknowledgments This study was supported by grants (16190501, 19230701 and 20300701) from the Japanese Ministry of Health, Labor, and Welfare (Research on Psychiatric and Neurological Disease and Mental Health). We thank Prof. Henmi, and Dr. Inoue for their generous support to this study, Mss. Sakuma, Sano, Hasegawa, Takahashi, and Kawase for careful recruitment and communication with the participants, and Mss. Akutsu, Kamoshida and Suzuki for data management and research assistance.

References

- Antonovsky A (1987) *Unraveling the Mystery of Health. How people Manage Stress and Stay Well*. Jossey-Bass, San Francisco
- Antonovsky A (1993) The structure and properties of the sense of coherence scale. *Soc Sci Med* 36:725-733
- American Psychiatric Association (2000) *Diagnostic and statistical manual of mental disorders, 4th edn, text revision; DSM-IV-TR*. American Psychiatric Association, Washington D.C. and London
- Asukai N, Kato H et al (2002) Reliability and validity of the Japanese-language version of the impact of event scale-revised (IES-R-J): four studies of different traumatic events. *J Nerv Ment Dis* 190:175-182
- Baker SP, O'Neill B (1976) The injury severity score: an update. *J Trauma* 16:882-885
- Blake DD, Weathers FW et al (1995) The development of a clinician-administered PTSD Scale. *J Trauma Stress* 8:75-90
- Blanchard EB, Hickling EJ et al (1996) Who develops PTSD from motor vehicle accidents? *Behav Res Ther* 34:1-10
- Brunet A, Weiss DS et al (2001) The peritraumatic distress inventory: a proposed measure of PTSD criterion A2. *Am J Psychiatry* 158:1480-1485
- Cloninger CR, Svrakic DM et al (1993) A psychobiological model of temperament and character. *Arch Gen Psychiatry* 50:975-990
- Foa EB, Ehlers A et al (1999) The posttraumatic cognitions inventory (PTCI): Development and validation. *Psychol Assess* 11:303-314
- Folkman S, Lazarus RS et al (1986) Dynamics of a stressful encounter: cognitive appraisal, coping, and encounter outcomes. *J Pers Soc Psychol* 50:992-1003
- Folstein MF, Folstein SE et al (1975) Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 12:189-198
- Fukuhara S, Bito S et al (1998) Translation, adaptation, and validation of the SF-36 Health Survey for use in Japan. *J Clin Epidemiol* 51:1037-1044
- Furukawa T, Sarason IG et al (1998) Social support and adjustment to a novel social environment. *Int J Soc Psychiatry* 44:56-70
- Gil S, Caspi Y et al (2005) Does memory of a traumatic event increase the risk for posttraumatic stress disorder in patients with traumatic brain injury? A prospective study. *Am J Psychiatry* 162:963-969
- Hulley SB, Cummings SR et al (2001) *Designing Clinical Research: An Epidemiological Approach, 2nd edn*. Williams & Wilkins, Inc., Philadelphia
- Kessler RC, Sonnega A et al (1995) Posttraumatic stress disorder in the National Comorbidity Survey. *Arch Gen Psychiatry* 52:1048-1060

18. Kijima N, Tanaka E et al (2000) Reliability and validity of the Japanese version of the temperament and character inventory. *Psychol Rep* 86:1050-1058
19. Krug EG, Sharma GK et al (2000) The global burden of injuries. *Am J Public Health* 90:523-526
20. Kugaya A, Akechi T et al (1998) Screening for psychological distress in Japanese cancer patients. *Jpn J Clin Oncol* 28:333-338
21. MacKenzie EJ, Rivara FP et al (2006) A national evaluation of the effect of trauma-center care on mortality. *N Engl J Med* 354:366-378
22. Marmar CR, Weiss DS et al (1994) Peritraumatic dissociation and posttraumatic stress in male Vietnam theater veterans. *Am J Psychiatry* 151:902-907
23. Matsuoka Y, Nishi D et al (2008) Incidence and prediction of psychiatric morbidity after a motor vehicle accident in Japan: The Tachikawa cohort of motor vehicle accident study. *Crit Care Med* 36:74-80
24. Mayou R, Bryant B (2001) Outcome in consecutive emergency department attenders following a road traffic accident. *Br J Psychiatry* 179:528-534
25. McHorney CA, Ware JE Jr et al (1993) The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Med Care* 31:247-263
26. Merikangas KR, Ames M et al (2007) The Impact of Comorbidity of Mental and Physical Conditions on Role Disability in the US Adult Household Population. *Arch Gen Psychiatry* 64:1180-1188
27. Murray CJ, Lopez AD (1997) Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. *Lancet* 349:1498-1504
28. Nagae N, Masuda T et al (2004) Prevalence Study of Negative Life Events among University Students and Development of Japanese Version of the Posttraumatic Cognition Inventory (in Japanese). *Jpn J Behav Ther* 30:113-124
29. Nishi D, Matsuoka Y et al (2006) Mental health service requirements in a Japanese medical centre emergency department. *Emerg Med J* 23:468-469
30. O'Donnell ML, Creamer M et al (2004) Psychiatric Morbidity Following Injury. *Am J Psychiatry* 161:507-514
31. Oken MM, Creech RH et al (1982) Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol* 5:649-655
32. Otsubo T, Tanaka K et al (2005) Reliability and validity of Japanese version of the Mini-International Neuropsychiatric Interview. *Psychiatry Clin Neurosci* 59:517-526
33. Sarason IG, Sarason BR et al (1987) A brief measure of social support: practical and theoretical implications. *J Soc Pers Relat* 4:497-510
34. Schnyder U, Moergeli H et al (2001) Prediction of psychiatric morbidity in severely injured accident victims at one-year follow-up. *Am J Respir Crit Care Med* 164:653-656
35. Schnyder U, Morgeli H et al (2000) Early psychological reactions to life-threatening injuries. *Crit Care Med* 28:86-92
36. Schnyder U, Wittmann L et al (2008) Posttraumatic stress disorder following accidental injury: rule or exception in Switzerland? *Psychother Psychosom* 77:111-118
37. Shalev AY, Freedman S et al (1997) Predicting PTSD in trauma survivors: prospective evaluation of self-report and clinician-administered instruments. *Br J Psychiatry* 170:558-564
38. Shalev AY, Freedman S et al (1998) Prospective study of posttraumatic stress disorder and depression following trauma. *Am J Psychiatry* 155:630-637
39. Sheehan DV, Lecrubier Y et al (1998) The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 59(Suppl 20):22-33 quiz 34-57
40. Takayama T, Asano Y et al (1999) Sense of coherence, stressful life events and psychological health (in Japanese). *Jpn J Public Health* 46:965-976
41. Taku K, Calhoun LG et al (2007) Examining posttraumatic growth among Japanese university students. *Anxiety Stress Coping* 20:353-367
42. Teasdale G, Jennett B (1974) Assessment of coma and impaired consciousness. A practical scale. *Lancet* 2:81-84
43. Tedeschi RG, Calhoun LG (1996) The posttraumatic growth inventory: measuring the positive legacy of trauma. *J Trauma Stress* 9:455-471
44. Ursano RJ, Fullerton CS et al (1999) Acute and chronic post-traumatic stress disorder in motor vehicle accident victims. *Am J Psychiatry* 156:589-595
45. Vaiva G, Boss V et al (2006) Relationship between posttrauma GABA plasma levels and PTSD at 1-year follow-up. *Am J Psychiatry* 163:1446-1448
46. Vaiva G, Thomas P et al (2004) Low posttrauma GABA plasma levels as a predictive factor in the development of acute posttraumatic stress disorder. *Biol Psychiatry* 55:250-254
47. von Elm E, Altman DG et al (2007) The strengthening of reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 370:1453-1457
48. Ware JE, Snow KK et al (1993) SF-36 health survey manual and interpretation guide. New England Medical Center, Boston
49. Weiss DS (2004) The impact of event scale-revised. In: Wilson JP, Keane TM (eds) *Assessing psychological trauma and PTSD*, 2nd edn. The Guilford Press, New York, pp 168-189
50. Weiss DS (ed) (2004) Structured clinical interview techniques for PTSD. In: Wilson JP, Keane TM eds. *Assessing psychological trauma and PTSD*, 2nd edn. The Guilford Press, New York
51. Zigmond AS, Snaith RP (1983) The hospital anxiety and depression scale. *Acta Psychiatr Scand* 67:361-370

When we published the article

"Matsuoka Y et al. (2008) The Tachikawa cohort of motor vehicle accident study investigating psychological distress: design, methods and cohort profiles. Soc Psychiatry Psychiatr Epidemiol (published online first 25.9.2008)" [The online version of the article can be found at <http://dx.doi.org/10.1007/s00127-008-0438-6>]

the author asked us to correct some of the values in his table 3. You may find the corrected table below:

Table 3 Baseline demographics of 300 cohort members

Characteristic	No	%
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Women	67	22.3
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Motorcycle driver	136	45.3
Passenger	17	5.7
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Pedestrian	29	9.7
Highest level of education		
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High school	111	37.0
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Employment status		
Paid worker (full- or part-time)	230	76.7
Student	43	14.3
Unpaid work (homemaker, retired)	26	8.7
Unknown	1	0.3
Annual income (JPY)		
Less than five million	150	50.0
Five to ten million	88	29.3
More than ten million	15	5
Unknown	47	15.7

SD standard deviation, MVA motor vehicle accident

The publisher apologises for any inconvenience caused by this mistake.

厚生労働科学研究費補助金（こころの健康科学研究事業）
大規模災害や犯罪被害者等による精神科疾患の実態把握と介入手法の開発に関する研究

平成 20 年度 総括・分担研究報告書

発行日 平成 21 (2009) 年 4 月
発行者 研究代表者 金 吉晴
発行所 国立精神・神経センター精神保健研究所 成人精神保健部
〒187-8553 東京都小平市小川東町 4-1-1
