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Attenuating posttraumatic distress with omega-3 polyunsaturated fatty acids among disaster medical assistance team members after the Great East Japan Earthquake: The APOP randomized controlled trial

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Abstract

Background: On March 11, 2011, a magnitude 9.0 earthquake, the most powerful ever recorded in Japan, and a massive tsunami struck off the coast of the Sanriku region. A Disaster Medical Assistance Team, a mobile medical team with specialized training that is deployed during the acute phase of a disaster, was dispatched to areas with large-scale destruction and multiple injured and sick casualties. Previous studies have reported critical incident stress (i.e. posttraumatic stress disorder symptoms and depressive symptoms) among rescue workers as well as the need for screening and prevention for posttraumatic stress disorder. So far we have shown in an open trial that posttraumatic stress disorder symptoms in critically injured patients can be reduced by taking omega-3 fatty acids intended to stimulate hippocampal neurogenesis.

Method/Design: This study is designed to determine the effectiveness of attenuating posttraumatic distress with omega-3 polyunsaturated fatty acids among Disaster Medical Assistance Team members after the Great East Japan Earthquake, and is named the APOP randomized controlled trial which is currently ongoing. First, we will provide psycho-education on posttraumatic distress, which is common in responders to the Disaster Medical Assistance Team members deployed to the disaster area. Second, observational research will be conducted to evaluate critical incident stress following the completion of medical activities. Third, team members who provide consent to participate in the intervention research will be randomly divided into a group given an omega-3 fatty acid supplement and a group not given the supplements. Outcome will be evaluated at 12 weeks after the supplements are shipped to the team members.

Discussion: Measures that address critical incident stress in disaster responders are important, but there is no substantial evidence that links such measures with prevention of posttraumatic stress disorder. Thus, any confirmation through this study that the intake of omega-3 fatty acid supplements serves as a simple preventative measure for critical incident stress will be of great significance.

Trial registration: UMIN Clinical Trials Registry, UMIN000005367

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Background

On March 11, 2011 at 14:46, a magnitude 9.0 earthquake, the most powerful ever recorded in Japan, and a massive tsunami struck off the coast of the Sanriku region, leaving over 20,000 dead or missing. The earthquake and subsequent tsunami, now known as the Great East Japan Earthquake, was the worst disaster Japan has experienced since World War II, causing psychological trauma among the survivors as well as critical incident stress among the rescue workers.

Even veteran responders with medical expertise deployed to disaster areas may experience significant psychological effects from exposure to the tragic circumstances they witness. More specifically, they may experience a variety of psychological reactions, including irritability, difficulty sleeping, feeling that the situation and work at the disaster site are unreal, recounting disaster efforts, nightmares, avoidance or reluctance to talk about people and objects that trigger memories of disaster areas, feelings of powerlessness in being unable to do anything, strong feelings of self-reproach, and anger. In fact, a study on the effects of critical incident stress in firefighters found an association between work-related psychological trauma and the onset of posttraumatic stress disorder (PTSD) [1]. Moreover, in a study of 355 medical care personnel sent to aid trauma victims of an airline crash, 13.5% developed PTSD within 18 months of the crash [2]. Similarly, in a study of 207 aid workers deployed to the site of the September 11 terrorist attack in New York in 2001, 16.7% developed PTSD and 21.7% developed depression at 13 months after the attack [3]. Appropriate evaluation of critical incident stress and screening and prevention of secondary psychiatric illness are thus crucial tasks.

In the pathogenesis of PTSD, fear memories become excessively consolidated and extinction learning does not progress [4]. Kitamura recently found that the period of hippocampus-dependent fear memory is longer in mice with decreased hippocampal neurogenesis and shorter in mice with active hippocampal neurogenesis [5], indicating that the level of hippocampal neurogenesis is a crucial factor in determining the period of hippocampal-dependent fear memory. This finding suggests that the fear memories characteristic to PTSD may be controlled by aptly regulating hippocampal neurogenesis [6]. We are currently conducting a randomized controlled trial different from the one described herein to investigate the preventive effectiveness of omega-3 fatty acids for preventing PTSD in physically injured patients (ClinicalTrials.gov Identifier: NCT00671099) since these fatty acids have been confirmed to enhance hippocampal neurogenesis in animal studies [7,8]. The open preliminary trial found that post-trial PTSD symptoms were significantly alleviated in injured patients who took the omega-3 fatty acids [9].

The present study aims to determine the effectiveness of attenuating posttraumatic distress with omega-3 polyunsaturated fatty acids among Disaster Medical Assistance Team (DMAT) members who are deployed during the acute disaster phase following the Great East Japan Earthquake. This study named the APOP randomized controlled trial aims to (1) provide psychoeducation on posttraumatic distress common among rescue workers to DMAT members dispatched to disaster areas, (2) assess critical incident stress among the DMAT members following completion of their medical duties, and (3) recruit these DMAT members to a 12-week study investigating the effects of omega-3 fatty acids in reducing stress, with consenting participants randomly allocated to either an omega-3 acid fatty acid supplementation group or a non-supplementation group. The efficacy of omega-3 fatty acids in reducing critical incident stress (PTSD symptoms or depressive symptoms) at 12 weeks will be examined.

Methods/Design

Study Design

The present study is a randomized clinical trial that will compare an intervention group that receives psychoeducation and omega-3 fatty acid supplementation with a parallel control group that receives psychoeducation only.

Participants

The DMAT service was established by the Ministry of Health, Labour and Welfare of Japan in April 2005 and operates from the Disaster Medical Center of the National Hospital Organization. DMAT members are physicians, nurses, and operational coordination staff (medical or clerical staff who are neither physicians nor nurses) who are dispatched as a mobile medical team with specialized training that is capable of acting during the acute phase (roughly within 48 hours) of a large-scale disaster and in the event there are multiple injured or sick casualties. Following the Great East Japan Earthquake, DMAT activities commenced on the same day, namely March 11, and concluded on March 22. Recruited DMAT members deployed to the disaster area met the following inclusion criteria: 1) aged 18 years or older; 2) a native Japanese speaker or non-native speaker with Japanese conversational abilities; and 3) physically and psychologically capable of understanding and providing consent for study participation. The exclusion criterion was regular intake of warfarin for at least 3 months before deployment.

Estimation of Sample Size

The required sample size for intervention research was estimated at 48 cases per group. Based on our previous research [9,10], we estimated that the mean of improvement in the Impact of Event Scale-Revised (IES-R) score as

a primary outcome measure would be 10 (SD = 15) for the intervention group and 0 (SD = 15) for the non-intervention group. We set α level at .05 and β at .10. This brought us to our required sample size estimation of 48 cases per group. This study set case numbers above that required, with consideration given in its design for the following: the sample would be recruited from a population different from that of previous studies (i.e. medical assistance members); the control group would receive psychoeducation; and the actual participant number was estimated. Thus, we allowed up to 150 cases for the intervention group and 300 cases for the control group.

Enrolment procedure

The procedure for participant enrollment is shown in Figure 1. A written guide to the study was posted to the Emergency Medical Information System (EMIS) by the DMAT office and affiliated hospitals with DMAT members were notified of the posting by their local municipalities. The written guide contained a written explanation of the research, a consent form, a questionnaire for assessing critical incident stress, a leaflet on psychoeducation, and reference materials on the intervention research (a copy of a general medical journal article summarizing the preliminary trial and the original manuscript of the

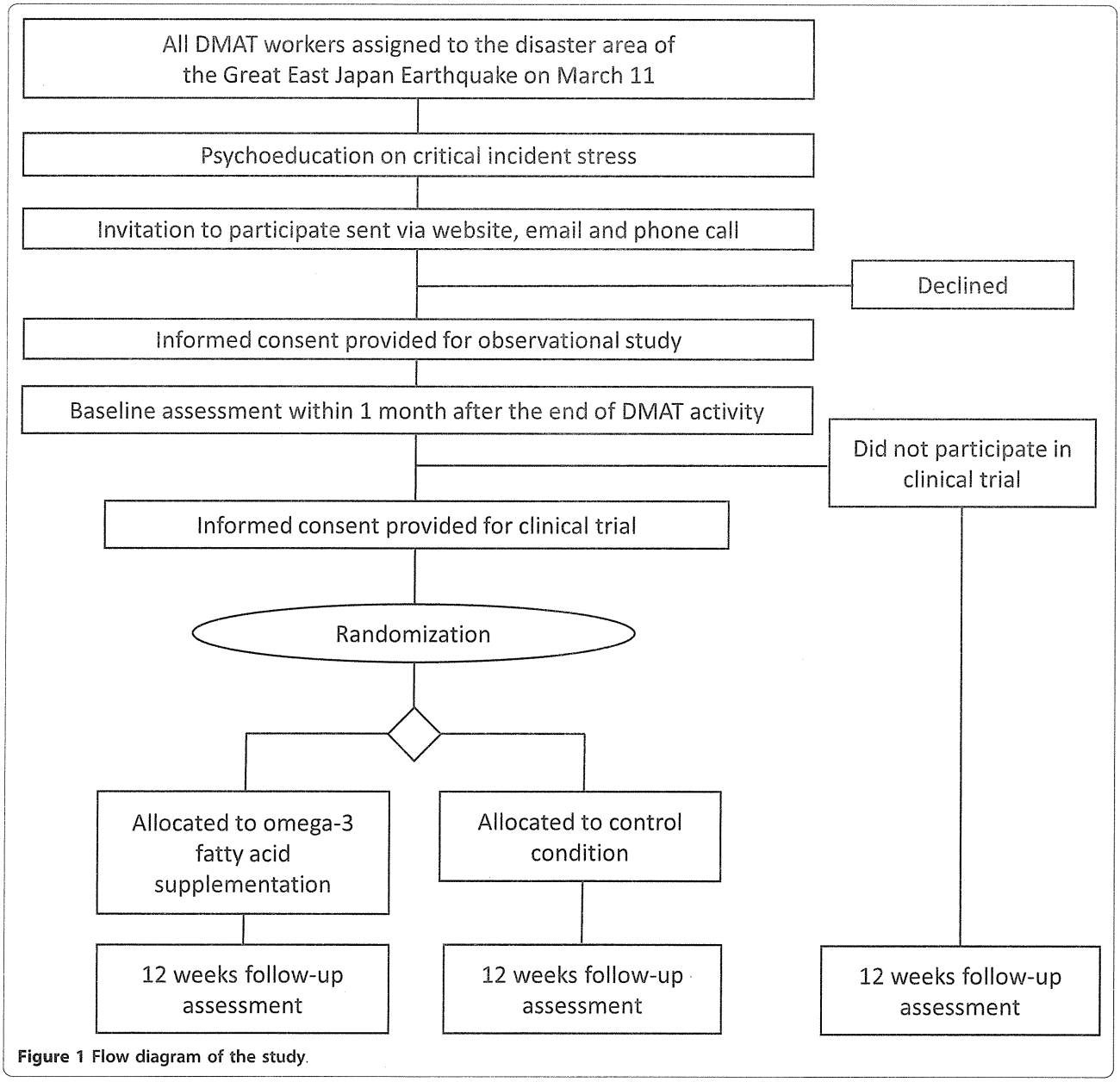

Figure 1 Flow diagram of the study.

researchers [9]) uploaded to the EMIS website. All documents were then mailed to DMAT members and a mass email was sent to all DMAT members who had been deployed to the disaster area. In addition, the DMAT Office at each of the DMAT members' affiliated hospitals was called to request that members be encouraged to participate in the study. Because individual explanation to eligible members was difficult to provide, eligible members could take time to read the written documents on their own and provide consent by returning the informed consent form (by fax or mail). Consent for participation was confirmed for each of two stages of the study: the first stage was participation in only observational research to assess critical incident stress following deployment to the disaster areas; the second stage was participation in intervention research involving omega-3 fatty acid supplementation after the assessment of critical incident stress.

Interventions

Omega-3 fatty acid supplementation in the intervention group

In line with previous research [11], participants are taking 7 capsules per day, each containing 320 mg of oil following return from their duties in the disaster area. The omega-3 fatty acid composition of each capsule is 70% docosahexaenoic acid and 7% eicosapentaenoic acid. Each capsule is placed in a brown 500-ml polyethylene container with a wide opening. Participants were instructed to take the capsules after eating and additionally told that they may take a full day's dosage at one time. Participants will be contacted to ensure regular capsule intake and safety monitoring at 2, 4, 8, and 12 weeks from the start of the intervention. Whenever inquiries are received from participants, necessary information will be provided to them.

Control condition

A placebo capsule was not prepared. A leaflet on psychoeducation about posttraumatic distress focusing on critical incident stress was provided to participants and they will be contacted about their situation at 2, 4, 8, and 12 weeks. Whenever inquiries are received from participants, necessary information will be provided to them.

Randomization

In regard to participant enrollment and group assignment, DMAT members who returned the informed consent form for the omega-3 fatty acid intervention research have been enrolled as participants. Central registration involved assigning participants to groups according to an assignment diagram developed by trial statisticians. Core investigators were single-blinded, and participants were randomly allocated to either the omega-3 acid group or the control group using block randomization. The participants were stratified by sex, and randomization was conducted by permuted block method using a four-person block. Sex was an adjustment factor, as previous studies show that the prevalence of PTSD and major depressive disorder are higher in women than in men [12]. Omega-3 fatty acid capsules were individually shipped to the address designated by each participant following random assignment. All information on case assignments will be disclosed after the final follow-up on participants has been completed and all data secured.

Informed Consent

The following describes the explanation and information used in obtaining consent from eligible participants. Participation in the study is voluntary. There is no penalty for declining to participate. Participants may withdraw from the study at anytime without penalty. Information provided covered the following areas: reasons for selection, the names and occupational titles of the researchers, the meaning, purpose, method, research period, expected benefits of participation, protection of privacy, possibility of patents from the study, possible risks or unpleasant physical adverse effects, disclosure of results related to the study, the publication of results without participant identifiers, possible risks, affiliated organizations of researchers and their relationships with the organizations, methods of data use, and period of data preservation.

Baseline Assessment

Basic information on the participants

Basic information obtained from the participants comprised name, sex, age, hospital affiliation, contact information, e-mail address, height, weight, occupation, marital status, number of children, highest education completed, smoking and drinking habits, years of experience, experience of deployment to disaster areas, use of omega-3 supplements, dietary habits, physical illness, and previous history of physical and psychiatric illnesses.

Information about traumatic events

Participants were surveyed about the following items, in addition to those variables identified as risk factors for PTSD in previous research [2,13]: period of deployment, stress prior to deployment, injury during deployment, experience of saving a child during deployment, experience of contact with corpses, fears of radiation, duration of time spent watching earthquake news reports, and current subjective physical symptoms.

Peritraumatic Distress Inventory

The Peritraumatic Distress Inventory (PDI) is a 13-item questionnaire, developed by Brunet et al [14], for quantification of fear and sense of helplessness in the trauma

cycle (the period during and directly after a traumatic experience). Previous studies have shown that one set of the PDI items predict PTSD symptoms [15]. With permission from creators Brunet and Marmar, we previously created the Japanese version and confirmed its validity and reliability [16,17].

Impact of Event Scale- Revised

The Impact of Event Scale-Revised (IES-R) is a self-reporting questionnaire about PTSD symptoms that was developed in the U.S. It is the most widely used measure internationally in all forms of disaster-area research [18]. The IES-R is composed of 22 items on the three largest symptoms in the diagnostic criteria of PTSD, namely re-experiencing, avoidance, and increased physiological arousal. Respondents rate symptoms experienced in the previous week. The validity and reliability of the Japanese version of the IES-R has been confirmed [19].

The Center for Epidemiologic Studies Depression Scale

The Center for Epidemiologic Studies Depression Scale (CES-D) is a self-reporting questionnaire on depression that was developed by Radloff et al [20]. The higher the total score is to the maximum score of 60, the more severe the depressive state. The cut-off score for a mood disorder is considered to be 16 points. Validity and reliability of the Japanese version have been confirmed [21].

Kessler K6 Scale

The Kessler 6 Scale (K6) is a self-reporting questionnaire designed to effectively screen for psychiatric disorders and mood and anxiety disorders, where respondents rate their condition for the last month [22]. Validity and reliability of the Japanese version has been confirmed [23]. An adequate cut-off score on the K6 for serious mental illness is 0-12 vs. 13 or more [24].

Resilience Scale and Resilience Scale-Short Version

The 25-item Resilience Scale (RS) and its shortened 14-item version (RS-14) are self-reporting questionnaires developed by Wagnild and Young for quantitative evaluation of resilience [25]. Among European and U.S. scales for resilience, its reliability and validity are considered the most established. We created Japanese versions of the RS and RS-14 with the permission of Wagnild and confirmed their reliability and validity [26]. The present study used the short RS-14 version.

Follow-up Assessment Schedule

The overall procedure of the trial is shown in Figure 1. Follow-up assessment schedule from baseline to 12 weeks is shown in Table 1.

Outcomes

Primary outcome

The total score on the IES-R at 12 weeks after shipment of the supplements is the primary outcome measure.

Secondary outcomes

Total scores on each of the CES-D, the RS-14, and the K6 at 12 weeks after shipment of the supplements constitute the secondary outcome measure.

Safety Management and Study Monitoring

Safety of the intervention is evaluated by the presence of an adverse event during the observation period. The investigators will contact the participants regarding the presence of any adverse events at 2, 4, 8, and 12 weeks after the start of the omega-3 fatty acid supplementation intervention. When an adverse event occurs, the investigators will rate the degree of the event as either "mild", "moderate", or "severe".

The principal investigator will assess the circumstances surrounding the occurrence of a serious adverse event and/or an event that may affect the future of the investigation. Cases will be reported to an independent data safety monitoring board and the company providing the trial capsules, and related information will be shared with them. The blinding of cases may be discontinued as

Table 1 Summary of outcome measures of the APOP clinical trial

Primary Outcome	Baseline	2 weeks	4 weeks	8 weeks	12 weeks
IES-R	X				X
Secondary Outcomes					
CES-D	X				X
K6	X				X
RS-14	X				X
Safety monitoring		X	X	X	X
Determinants					
Demographic	X				
Life style	X				
Past medical history	X				
Detailed information about disaster-related event	X				
PDI	X				

deemed necessary and information gathered so that the causes behind the occurrence may be investigated. The ethics committee of the facility may also be notified.

The investigation will cease when (1) discontinuation of the study is recommended by the data safety monitoring board due to an adverse event or side effect that makes continuation of the investigation difficult or (2) the principal investigator decides not to continue implementation.

Statistical analysis

All analyses were conducted according to the intention-to-treat principle. Analysis of covariance (ANCOVA) will be used to obtain differences between the means, 95% confidence interval values, and P values. Covariates for ANCOVA are sex, age, and IES-R scores at baseline. A two-tailed test will be used, with the α level set at .05%. Evaluation by regression models will be conducted as necessary. Validity of the results will be evaluated through sensitivity analysis and filling missing data.

Analysis of the secondary outcome measure will be conducted to add to discussion of the results of the primary outcome measure. Adjustment will not be conducted for data duplication because secondary statistical analyses are exploratory. A two-tailed test will be used, with the α level set at .05%. Evaluation by regression models will be conducted as necessary. Validity of the results will be evaluated through sensitivity analysis and filling missing data.

Time periods during the study

Research will be conducted from April 1 to September 30, 2011. Participant registration for observational research was from April 2 to 22, and participant registration for intervention research was from April 2 to 12. Follow ups are to be conducted after the omega-3 supplement shipments until August 31.

Ethical Considerations

The present study protects the rights and welfare of participants in the spirit of ethical guidelines outlined under the Declaration of Helsinki. The study further respects the ethical principles of the Ministry of Health, Labour, and Welfare of Japan. Confidence can be assured in the ethics, safety, scientific rigor, and reliability of the research. Personal information obtained in the course of the research will be strictly secured to avoid external leaks. Because the study is a dietary intervention, no special compensation will be paid in the event of health damage directly related to the research. The research plan (2010-32) was deliberated upon and approved by the Ethics Committee of the National Disaster Medical Center on April 1, 2011.

Discussion

Declines in physical and mental health due to critical incident stress in disaster aid workers or rescue workers has been demonstrated in previous research, but specific, adequate measures to counter critical incident stress have not been developed. The development of measures that can realistically be practiced by large numbers of aid workers is extremely important. Six years have passed since the DMAT service was established and little examination of critical incident stress among DMAT members has been conducted thus far. This study is designed to understand the phenomenon of critical incident stress among DMAT members and conduct the APOP clinical trial. The trial will provide omega-3 acid supplements to DMAT members stationed in all regions of Japan as a method to promote mental health without requiring individualized care from a mental health professional.

The use of self-reporting questionnaires while inferior to that of a clinical interview as an assessment of the APOP study research outcomes for PTSD and depressive symptoms, it is a reasonable assessment method given this type of emergency situation. We are currently implementing separate random comparative trials to prevent PTSD in physically injured patients (ClinicalTrials.gov Identifier: NCT00671099) and are evaluating PTSD through structured clinical interviews. The APOP study was designed at a time of crisis, 1 week after the earthquake occurred, and recruiting sufficient participants was considered difficult if a placebo group were to be used. Another limitation of the study is that fatty acid composition of red blood cell membranes could not be measured to confirm intake compliance of the omega-3 fatty acid supplements. With these limitations in mind, we do believe the results of the APOP clinical trial will be of importance: natural and man-made disasters occur across the globe and omega-3 fatty acid supplementation, if found to be efficacious for preventing critical incident stress, could contribute to maintaining the mental health of disaster relief workers in the future.

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Authors' contributions

YM and DN conceived the study and drafted the original protocol. YM, DN, NN, TS, KH, TH, and YK participated in the refinements of the protocol. YM, DN, KH, and TH decided the content of the omega-3 fatty acid supplementation, YK managed the enrolment procedure and overall regulation of the trial, all authors contributed to the design of the study, and TS and NN calculated sample size and decided the analytic strategy. All authors read and approved the final manuscript.

Competing interests

Dr. Matsuoka has received research support from the Japan Science and Technology Agency, CREST, and the Ministry of Health, Labor, and Welfare of Japan and lecture fee from Eli Lilly Japan. Dr. Nishi has received research support from Toray Industries, Inc., and the Foundation for Total Health Promotion and lecture fee from Qol Co., Ltd. Dr. K. Hamazaki has received research support from the Japan Society for the Promotion of Science, the Tamura Foundation for Promotion of Science and Technology, and the Ichiro Kanehara Foundation for Promotion of Medical Sciences and Medical Care, and consultant fees from Polyene Project, Inc. and Otsuka Pharmaceutical Co., Ltd., and lecture fee from Nippon Suisan Kaisha, Ltd. Dr T. Hamazaki has received research support from the Japan Society for the Promotion of Science, Open Research Center for Lipid Nutrition (Kinjo Gakuin University), and Nippon Suisan Kaisha, Ltd., and consultant fees from Polyene Project, Inc. and Otsuka Pharmaceutical Co., Ltd., and lecture fees from Mochida Pharmaceutical Co., Ltd. Dr. Koido has received research support from the Ministry of Health, Labor, and Welfare of Japan, Ono Pharmaceutical Co., Ltd., Astrazeneca K.K., Bristol-Myers Squibb Company, and National Center of Global Health and Medicine. All other authors declare that they have no competing interests with this work.

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Potential Role of Brain-Derived Neurotrophic Factor in Omega-3 Fatty Acid Supplementation to Prevent Posttraumatic Distress after Accidental Injury: An Open-Label Pilot Study

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It is known that severity of depression is associated with low levels of erythrocyte omega-3 polyunsaturated fatty acids (n-3 PUFA) [1] and serum brain-derived neurotrophic factor (BDNF) [2]. Dietary n-3 PUFA promote the maturation of neurons and hippocampal neurogenesis in adult rats [3] and have been found to increase the levels of BDNF in rat hippocampus [4, 5]. BDNF exerts various effects on the nervous system, including neuronal outgrowth, differentiation, synaptic connectivity as well as neuronal repair and survival during development and in adulthood [6–8]. These findings indicate that supplementation with n-3 PUFA enhances the effect of BDNF-related synaptic plasticity and neurogenesis.

Recently, Kitamura et al. [9] have shown that hippocampal neurogenesis contributes to the clearance of artificially induced fear memory in mice. It is suggested that adult neurogenesis may play a role in the periodic clearance of hippocampal memory traces in contextual fear conditioning. Therefore, we hypothesized that n-3 PUFA-induced neurogenesis occurring early in the transition period might, by increasing BDNF, facilitate the clearance of fear memory and attenuate posttraumatic distress as a consequence. The aims of the present study were to answer the following questions: whether supplementation with n-3 PUFA increases serum levels of BDNF, and whether change in serum BDNF is associated with the alleviation of posttraumatic distress at follow-up in our pilot trial [10].

From among 122 consecutive patients who were recruited from the intensive care unit of the National Disaster Medical Center within 240 h of accidental injury during a 23-week period, 27 met the inclusion criteria. Of these 27 eligible patients, 15 agreed to and provided prior written informed consent to participate in the study. The study protocol was reviewed and approved by the institutional review boards and registered at http://clinicaltrials.gov/ as NCT00671489. Of the 15 patients enrolled, 11 completed the 12-week follow-up. Three patients cancelled a visit at the last minute and 1 lost contact after the 4-week follow-up visit. Patients who completed the trial did not significantly differ from those who did not complete the trial in terms of sex, age, vital signs, and injury severity score [11], Glasgow Coma Scale [12] and peritraumatic distress inventory scores [13].

A total of 7 n-3 PUFA capsules (Kentech Co. Ltd., Japan) containing 1,470 mg docosahexaenoic acid (22:6 n-3) and 147 mg eicosapentaenoic acid (20:5 n-3) were administered daily for 12 weeks in an open-label fashion. Trained psychiatrists assessed posttraumatic stress disorder (PTSD) and major depressive disorder (MDD) by structured clinical interviews [14, 15] at weeks 4 and 12. The interrater reliability for diagnosis of PTSD and MDD was reliable, with κ values of 1.0 and 0.9, respectively [16]. To assess the serum BDNF levels, 7–10 ml of whole blood were obtained in ethylenediaminetetraacetic acid tubes in the emergency room (week 0), and in week 4 and week 12. Serum BDNF levels were measured using the BDNF Emax Immunoassay System Kit (Promega, Madison, Wisc., USA).

The difference between serum BDNF levels at weeks 0 and 12 was compared by paired t test. Scatter plots show the association between the changes in serum BDNF levels and posttraumatic distress as determined by the structured interview at weeks 4 and 12. The distress group consisted of those patients who met the criteria for MDD or PTSD during the trial. We then examined the intergroup differences in changes in serum BDNF levels from week 0 to the endpoint at week 12 using the Wilcoxon rank-sum test. All tests were two-sided, and $p < 0.05$ was considered statistically significant.

During the first 4 weeks after accident, 1 patient met the criteria for PTSD and remained essentially the same at week 12. Another patient met the criteria for MDD at the 4-week follow-up, but symptoms had disappeared at the 12-week follow-up. Overall, serum BDNF levels were significantly elevated from week 0 to week 12 [n = 11; 52.36 ng/ml (SD = 16.69) vs. 79.83 ng/ml (SD = 13.79); p = 0.001), although they were largely unchanged in the distress group (fig. 1). Changes in BDNF levels between weeks 0 and 12 were significantly greater in the nondistressed group than in the distress group (median 33.5 ng/ml, range 8.5–56.0 vs. median 5.4 ng/ml, range 4.4–6.4; p = 0.037). There was no significant association between changes in serum BDNF level and age, sex, injury severity score, vital signs or peritraumatic distress inventory score (data not shown).

We confirmed that supplementation with n-3 fatty acids increased serum BDNF levels. As shown in the figure, the changes seen in serum BDNF levels might be associated with reduced posttraumatic distress on follow-up. Although the present study

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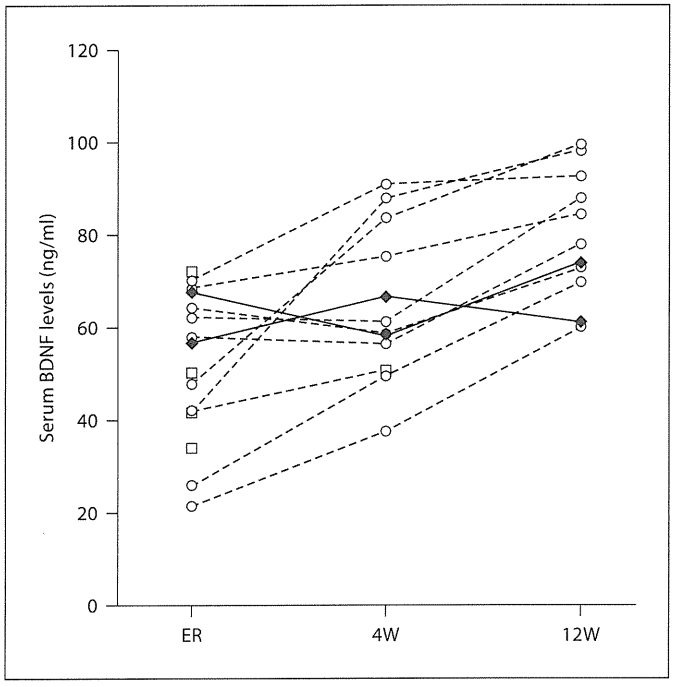

Fig. 1. Supplementation with n–3 PUFA increased serum BDNF levels in accident-injured patients. Solid lines (n = 2): patients who developed PTSD or MDD during the trial. Dotted lines (n = 9): patients who did not develop a psychiatric illness during the trial. Squares: patients who dropped out (n = 4). ER = Emergency room; 4W and 12W = 4- and 12-week follow-up assessments.

was not a placebo-controlled trial, the results suggest a potential role for BDNF in the prevention of posttraumatic distress by n–3 fatty acid supplementation.

As to previous research, an animal study indicated that a docosahexaenoic acid-enriched diet increased levels of pro-BDNF and mature BDNF in the hippocampus [4]. In a postmortem brain study, increased hippocampal BDNF expression was found in subjects treated with antidepressant medications compared with untreated subjects [17]. Serum BDNF levels in antidepressant-treated patients with MDD were higher than in untreated MDD patients [2]. In addition, Venna et al. [18] showed that dietary supplementation with n–3 PUFA containing 70% α-linolenic acids for more than 5 weeks exerted antidepressant-like effects, and was associated with an increase in hippocampal volume, an overexpression of synaptophysin and BDNF, and an increase in the number of newborn cells in mice. A significant correlation was found between n–3 PUFA consumption and gray matter volume in the amygdala, hippocampus and anterior cingulate cortex in healthy adults [19]. Against such a background, the preventive effect on posttraumatic distress of n–3 PUFA supplementation seen in the present study may well be due to an antidepressant effect, alongside structural and molecular changes occurring in the hippocampus. To overcome the limitations of our study such as the small sample size and the lack of a parallel control group, we have started a randomized controlled trial (NCT00671099).

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5

Peritraumatic Distress in Accident Survivors: An Indicator for Posttraumatic Stress, Depressive and Anxiety Symptoms, and Posttraumatic Growth

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1. Introduction

In 1997, the Global Burden of Disease Study (Murray, 1997) predicted that by 2020 motor vehicle accident would be the third biggest contributor to worldwide burden of disease. With more than 50 million people reported in 2007 to be injured each year in road traffic accidents worldwide (Derriks & Mark, 2007), motor vehicle accidents are indeed contributing highly to burden of disease. Moreover, such accidents are regarded as one of the leading causes of posttraumatic stress disorder in today's world. As advances in injury care systems have increased the number of seriously injured people who are able to survive their injuries (MacKenzie et al., 2006), this has drawn increasing attention to psychiatric morbidity after injury among such survivors.

Recent studies have shown that accident-related posttraumatic stress disorder is fairly common. The prevalence of posttraumatic stress disorder determined by structured clinical interviews with injured patients consecutively admitted to the intensive care unit or emergency department ranges from 5–30% at 0–3 months after injury to 2–23% at 4–12 months after it (Bryant et al., 2010; Hamanaka et al., 2006; Hepp et al., 2008; Matsuoka et al., 2008; Matsuoka, Nishi, Yonemoto, Nakajima et al., 2010; O'Donnell et al., 2004; Schnyder, Moergeli, Klaghofer et al., 2001; Schnyder et al., 2008; Shalev et al., 1998). Recent large epidemiological studies using questionnaires have reported a 17–23% point prevalence of clinically significant posttraumatic stress disorder symptoms at 4–12 months after injury (Zatzick et al., 2007; Mayou et al., 2001). It is well known that this disorder can be associated with higher psychiatric comorbidity, attempted suicide, and physical illnesses such as asthma, hypertension, and peptic ulcer (Davidson et al., 1991), as well as carry high healthcare costs (O'Donnell et al., 2005; Walker et al., 2003). It remains, therefore, a serious public health problem that needs to be addressed (Kessler et al., 1995; Kessler et al., 2005.)

1.1 Depression and other anxiety disorders after motor vehicle accidents

Major depression is also highly prevalent in individuals injured in a motor vehicle accident. The prevalence of major depression as determined by structured clinical interviews ranges from 10–19% at 0–3 months after the accident (O'Donnell et al., 2004; Matsuoka et al., 2008; Shalev et al., 1998) to 10–14% at 4–12 months after it (O'Donnell et al., 2004; Shalev et al., 1998). Although many symptoms overlap between posttraumatic stress disorder and major depression, the high comorbidity cannot be explained solely by this (Franklin & Zimmerman, 2001). Exposure to traumatic events has been shown to be linked not only to posttraumatic stress disorder, but also to depression (Duncan et al., 1996; Kilpatrick et al., 1987), and a recent study suggested that traumatic experiences during young adulthood and middle age are strong predictors of anxiety and depression among older adults (Dulin & Passmore, 2010). The treatment of psychiatric morbidity after injury is thus a matter of some urgency, especially for high-risk individuals. However, as it is difficult for emergency department staff to screen patients early after the event using a conventional questionnaire-based tool, given the large number of motor vehicle accident survivors they handle (Nishi et al., 2006), it is desirable to find indicators for posttraumatic stress disorder which can be easily assessed in order to provide preventive strategies as early as possible.

1.2 The importance of assessing peritraumatic distress

Among the indicators for posttraumatic stress disorder, peritraumatic distress is a good candidate for screening individuals at high risk of developing the disorder. Peritraumatic stress can enhance trauma-related memory and sensitize the neurobiological systems (Charney et al., 1993), which links to the development of posttraumatic stress disorder. Many clinical studies and a meta-analysis have shown that perceived threat to life is a predictor of posttraumatic stress disorder (Holbrook et al., 2001; Matsuoka et al., 2008; Ozer et al., 2003; Schnyder, Moergeli, Trentz et al., 2001) and psychiatric morbidity (Matsuoka et al., 2008; Schnyder, Moergeli, Trentz et al., 2001). Peritraumatic distress is also linked with posttraumatic growth, which Tedeschi & Calhoun (2004) define as the positive psychological change experienced as a result of the struggle with highly challenging life circumstances. They state that only psychologically 'seismic' events shake the assumptive world, which leads to posttraumatic growth. Accordingly, peritraumatic distress can be an indicator for posttraumatic growth. A better understanding of peritraumatic distress would be significant for both prevention, especially in emergency settings, and treatment of posttraumatic stress disorder.

The aim of this chapter is to elucidate the predictive usefulness of peritraumatic distress and to examine the future directions for prevention with a focus on the use of the Peritraumatic Distress Inventory, an assessment tool for peritraumatic distress.

2. Method

2.1 Participants

Participants were selected from the Tachikawa Cohort of Motor Vehicle Accidents study conducted at the National Disaster Medical Center in Tokyo, Japan (Matsuoka et al., 2009). The inclusion criteria in the present study were as follows: 1) motor vehicle accident-related severe physical injury causing a life-threatening or critical condition; 2) age between 18 and 69 years; and 3) native Japanese speaking ability. The exclusion criteria were the following:

1) diffuse axonal injury, brain contusion, and subdural and subarachnoidal bleeding detected by either computed tomography or magnetic resonance imaging or both (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 Mini Mental State Examination; 3) currently suffering from schizophrenia, bipolar disorder, drug dependence or abuse, or epilepsy before the accident; 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 the National Disaster Medical Center.
The above-mentioned study was conducted between 30 May 2004 to 8 January 2008, and the present study is part of that larger study. Patients with motor vehicle accident-related physical injury were consecutively admitted to the intensive care unit of the National Disaster Medical Center between 18 August 2005 and 8 January 2008. Of the 221 patients who met the inclusion criteria, 189 agreed to participate in the study. Fifty-nine patients were excluded because their peritraumatic distress could not be assessed due to memory loss. Ultimately, 130 patients participated in this study.

2.2 Procedures

The study protocol was approved by the Institutional Review Board and Ethics Committee of the National Disaster Medical Center. After providing a complete description of the study to the subjects, written informed consent was obtained from them. The median number of days between the motor vehicle accident and the initial assessment was 2 days (range, 0–23 days). The initial assessment was conducted after cognitive function was assessed by a trained research nurse or psychiatrist using the Mini Mental State Examination.
In a structured interview, data was collected on general socio-demographics, the motor vehicle accident in detail, injury severity score (Baker & O'Neill, 1976), Glasgow Coma Scale score (Teasdale & Jennett, 1974), status during the accident (e.g., vehicle driver), vital signs first recorded on admission to the emergency room, lifestyle, and family history of psychopathology. Also, the Peritraumatic Distress Inventory was conducted at initial assessment. Follow-up assessments were performed at 1 month (median, 37 days, range, 24-76 days) and 18 months (median, 561.5 days, range, 442-700 days) after the accident. The Impact of Event Scale-Revised and the Hospital Anxiety and Depression Scale were conducted at 1 month post accident, and the Posttraumatic Growth Inventory was conducted at 18 month post accident. The participants were asked to visit the National Disaster Medical Center or to return the completed self-report questionnaires in a stamp-addressed envelope. After each assessment, participants were given a gift voucher for their participation (1,000 JPY [12 USD]).

2.3 Measures

2.3.1 The Peritraumatic Distress Inventory

The Peritraumatic Distress Inventory is a 13-item self-report questionnaire which assesses not only any threat to life experienced but various emotional responses experienced during and immediately after a critical incident (Brunet et al., 2001). Responses are provided on a 5-point Likert scale ranging from 0 to 4 (0, not at all to 4, extremely true). It typically takes only several minutes to complete all of the items, meaning the Inventory can be used immediately after a motor vehicle accident.

The original Peritraumatic Distress Inventory has been demonstrated to be internally consistent, stable over time, and with good to excellent correlations between item and total scores (Brunet et al., 2001). Moreover, it was found to be valid against posttraumatic symptoms and peritraumatic dissociation as assessed by the Impact of Event Scale-Revised and the civilian version of the Mississippi Scale for Combat-Related Posttraumatic Stress Disorder.

With the original authors' permission, we translated the original English Peritraumatic Distress Inventory into Japanese. We followed the standard procedure of back-translation. Namely, the first author (DN) translated the English version into Japanese. This preliminary Japanese version was then backtranslated into English by an independent translator. The backtranslated version was examined by the original authors. Then we corrected the Japanese translation accordingly. This process was repeated until both sets of authors agreed that the original and backtranslated versions matched closely. Subsequently, we verified the internal consistency, test-retest reliability, concurrent validity with measures of peritraumatic dissociation and posttraumatic symptoms, and divergent validity of the Japanese version of the Peritraumatic Distress Inventory (Nishi et al., 2009).

2.3.2 The Impact of Event Scale-Revised

The posttraumatic stress symptoms as assessed using the Impact of Event Scale- Revised at follow-up were considered to be the outcome. The Impact of Event Scale-Revised is a 22-item self-report questionnaire used to determine the level of symptomatic responses to a specific traumatic stressor (motor vehicle accident in the present study) in the past week (Asukai et al., 2002; Wolfe & Kimerling, 1997). The degree of distress for each item is rated on a 5-point scale (0, not at all to 4, extremely; range, 0-88).

2.3.3 The Hospital Anxiety and Depression Scale

Depressive and anxiety symptoms as assessed using the Hospital Anxiety and Depression Scale were also considered as the outcome. The Scale is comprised of a 7-item anxiety subscale and a 7-item depression subscale that assess general psychological distress for the preceding week (Kugaya et al., 1998; Zigmond & Snaith, 1983). Each item is rated on a scale of 0–3, with high scores denoting greater psychological distress (range, 0-42).

2.3.4 The Posttraumatic Growth Inventory

The Posttraumatic Growth Inventory, which assesses posttraumatic growth, measures the degree of change experienced in the aftermath of a traumatic event. The 21-item Inventory evaluates five factors: relating to others, new possibilities, personal strength, spiritual change, and appreciation of life. The degree of posttraumatic growth for each item is rated on a 6-point scale (range, 0-105) (Taku et al., 2007; Tedeschi & Calhoun, 1996).

2.4 Statistical analysis

Univariate regression analysis was used to examine the relationships of total score and individual item scores on the Peritraumatic Distress Inventory with posttraumatic symptoms and depressive and anxiety symptoms. In a model for determining the predictive value of the Peritraumatic Distress Inventory, multivariate regression analysis was used to examine the relationships of the Peritraumatic Distress Inventory with posttraumatic stress symptoms and depressive and anxiety symptoms adjusted for 7 other covariates based on the following theoretical considerations.

For the covariates, age at motor vehicle accident, being female, history of psychiatric illness, family history of psychopathology, and lower education level are well-established pretraumatic risk factors across trauma type (Brewin et al., 2000; Ozer et al., 2003). As for educational level, we used graduation from junior high school as a reference (0), and assigned 1 to graduation from high school, 2 to graduation from junior or technical college, and 3 to graduation from university or higher educational institutions according to the Japanese educational system. Heart rate on admission was selected because some reports in the literature on motor vehicle accident showed its association with posttraumatic stress disorder (Bryant et al., 2000; Shalev et al., 1998; Zatzick et al., 2005). Injury Severity Score divided into 10-point increments was assigned as the objective accident-related variable. Injury Severity Score is a scoring system that provides a total score for patients with multiple injuries, and it correlates with measures of severity such as mortality and hospital stay (Baker & O'Neill, 1976).

Univariate regression analysis was also conducted to examine the relationships of total score on the Peritraumatic Distress Inventory with total score and individual subscale scores on the Posttraumatic Growth Inventory. Any association between the dependent variable and the independent variable was expressed as a regression coefficient (beta weight) and quantified by the 95% confidence interval (95% CI).

All statistical analyses used two-tailed tests. Statistical significance was established at a P value < 0.05. All data analyses were performed using SPSS statistical software version 19.0J for Windows (SPSS, Tokyo, Japan).

3. Results

Of the 130 patients participating, 79 (60.8%) attended the 1-month follow-up assessment and 51 (39.2%) attended the 18-month one. The patients who dropped out of the study did not differ significantly from those who participated in terms of the variables selected for investigation in this study, including total Peritraumatic Distress Inventory score.

Of the 79 participants at first follow-up, 16 (20.3%) were women and median age was 37.0 years (mean, 39.7; range 18-69), and 7 (8.9%) reported a past history of psychiatric illness. Median ISS was 6.0 (range 1-41) and median Peritraumatic Distress Inventory score was 15.0 (range 0-40).

The relationships of total score and individual item scores on the Peritraumatic Distress Inventory with posttraumatic stress symptoms and depressive and anxiety symptoms are shown in Table 1. The Peritraumatic Distress Inventory was an independent predictor for posttraumatic stress symptoms and depressive and anxiety symptoms after adjusting for potential confounders.

PDI item	IES-R		HADS	
	Beta (95% CI)	P	Beta (95% CI)	P
Univariate regression analysis				
1. I felt helpless to do more	4.00 (2.05, 5.94)	<0.01	1.80 (0.86, 2.74)	<0.01
2. I felt sadness and grief	3.05 (1.03, 5.06)	<0.01	0.94 (-0.06, 1.93)	0.06
3. I felt frustrated or angry I could not do more	2.99 (1.11, 4.87)	<0.01	0.74(-0.20, 1.68)	0.12

PDI item	IES-R		HADS	
4. I felt afraid for my safety	3.02 (1.04, 5.00)	<0.01	1.21 (0.24, 2.17)	0.02
5. I felt guilt that more was not done	1.43 (-0.97, 3.83)	0.24	0.23 (-0.92, 1.38)	0.69
6. I felt ashamed of my reactions	0.76 (-2.47, 3.99)	0.81	0.53 (-1.01, 2.07)	0.50
7. I felt worried about others	1.40 (-0.66, 3.46)	0.18	0.20 (-0.80, 1.19)	0.70
8. I was about to lose control	2.31 (-0.82, 5.45)	0.15	0.07 (-1.45, 1.59)	0.93
9. I had difficulty controlling my bowel and bladder	1.39 (-3.89, 6.67)	0.60	0.84 (-1.68, 3.36)	0.51
10. I was horrified	3.41 (1.46, 5.37)	<0.01	0.99 (0.01, 1.97)	0.047
11. I had physical reactions like pounding heart	4.04 (2.14, 5.93)	<0.01	1.64 (0.71, 2.58)	<0.01
12. I felt I might pass out	0.90 (-1.12, 2.92)	0.38	0.51 (-0.45, 1.48)	0.29
13. I felt I might die	2.63 (0.74, 4.52)	<0.01	1.00 (0.08, 1.92)	0.03
PDI total score	0.61 (0.34, 0.89)	<0.01	0.21 (0.07, 0.35)	<0.01
Multivariate regression analysis*				
PDI total score	0.49 (0.18, 0.80)	<0.01	0.15 (0.00, 0.30)	0.046

*In the multivariate analysis, the predictive value of the PDI was adjusted for 7 covariates; age at MVA, being a female, history of psychiatric illness, family history of psychopathology, education level, heart rate at admission and Injury Severity Score.
P, p value; CI, confidential interval; HADS, Hospital Anxiety and Depression Scale; IES-R, the Impact of Event Scale-Revised; PDI, the Peritraumatic Distress Inventory

Table 1. The predictive value of the Peritraumatic Distress Inventory for Impact of Event Scale-Revised and Hospital Anxiety and Depression Scale at follow-up (N=79)

The relationships between total score on the Peritraumatic Distress Inventory and total score and individual subscale scores on the Posttraumatic Growth Inventory are shown in Table 2.

	PDI total score (independent variable)			
	Beta	95%CI	P value	R^2
PTGI subscales (dependent variables)				
Relating to others	0.25	0.02 - 0.48	0.03	0.09
New possibilities	0.14	-0.02 - 0.30	0.08	0.06
Personal strength	0.06	-0.07 - 0.18	0.36	0.02
Spiritual change	0.07	0.01 - 0.11	0.03	0.10
Appreciation of life	0.20	0.10 - 0.30	<0.01	0.26
PTGI total score	0.72	0.12 - 1.31	0.02	0.11

CI, confidential interval; PDI, Peritraumatic Distress Inventory; PTGI, Posttraumatic Growth Inventory; R^2, multiple correlation coefficient, the index of goodness fitness in the model

Table 2. The predictive value of the PDI for PTGI at follow-up (N=51)

4. Discussion

4.1 Summary in the present study

This study showed that the Peritraumatic Distress Inventory could predict posttraumatic stress and depressive and anxiety symptoms at 1 month after motor vehicle accident and posttraumatic growth at 18 months after the accident. The predictive value of the Peritraumatic Distress Inventory for the Impact of Event Scale-Revised and the Hospital Anxiety and Depression Scale remained after adjusting for covariates in a multivariate regression analysis.

4.2 An indicator for posttraumatic stress symptoms

As mentioned in the Introduction, it is no surprise that the Peritraumatic Distress Inventory predicted posttraumatic symptoms in the present study. Although some previous prospective studies have failed to show that this Inventory is an independent predictor of posttraumatic stress disorder, these studies used the Inventory from 2 weeks (Kuhn et al., 2006) to several months (Birmes et al., 2005; Simeon et al., 2005) following a traumatic event. The time of assessment in the present study was within several days following the traumatic event in most participants, in order to minimize the effects of inaccurate memory over time. It is likely that the Peritraumatic Distress Inventory has a better predictive value when used early after a traumatic event, making it well suited for use in emergency departments.

4.3 An indicator for depressive and anxiety symptoms

The Peritraumatic Distress Inventory also predicted depressive and anxiety symptoms in the present study, although the predictive value for these symptoms was lower than that for posttraumatic symptoms. A previous study reported that posttraumatic stress disorder symptoms were a reliable predictor for depressive symptoms (Erickson et al., 2001). The Impact of Event Scale-Revised is one of the tools used most frequently for measuring posttraumatic stress symptoms; however, the it was intended to assess posttraumatic stress disorder symptoms over the previous 7 days, whereas the Peritraumatic Distress Inventory can be used immediately after motor vehicle accident. Given our findings, the Peritraumatic Distress Inventory seems to be a useful indicator not only for posttraumatic stress disorder but also major depression or other anxiety disorders.

4.4 Two Peritraumatic Distress Inventory items showed high predictive values

Items 1 and 11 of the Peritraumatic Distress Inventory showed higher predictive values for both posttraumatic stress and depressive and anxiety symptoms than other items. Item 1 inquires about helplessness. The author and colleagues previously discussed that non-drivers (passengers, bicyclists, or pedestrians) might be susceptible to subsequent posttraumatic stress disorder and other psychiatric morbidity (Matsuoka et al., 2008). Loss of control in a motor vehicle accident is suggested to be an important risk factor. Regarding item 11, some studies showed that high heart rate shortly after a motor vehicle accident is a predictor for later posttraumatic stress disorder (Bryant et al., 2000; Shalev et al., 1998; Zatzick et al., 2005), although other studies reported that heart rate was not an independent predictor (Buckley et al., 2004; Kraemer et al., 2008) and a review indicated that it cannot be accurately used to identify individuals who are at high risk for later posttraumatic stress

disorder (Bryant, 2006). To ask if survivors felt any physical reactions might be a better alternative to predict subsequent psychiatric morbidity.

4.5 An indicator for posttraumatic growth

The present results also suggested that the Peritraumatic Distress Inventory could predict posttraumatic growth, especially the 3 aspects of appreciation of life, spiritual change, and relating to others at 18 months after the accident. Multivariate regression analysis was not used to examine the predictive value of the Peritraumatic Distress Inventory for the Posttraumatic Growth Inventory because predictors for posttraumatic growth are not well established and our sample size was modest; however, the result was consistent with that of previous studies. According to Janoff-Balman, these 3 subscales can best be understood as existential reevaluation (Janoff-Bulman, 2004), and a previous study showed that they had a positive association with posttraumatic stress disorder (Taku et al., 2007). The author and colleagues also showed that appreciation of life and spiritual change were positively correlated with posttraumatic stress disorder symptoms, which can be regarded as signifying coping effort in the face of enduring distress, rather than an outcome of coping success (Nishi, Matsuoka and Kim, 2010). The predictive value of the Peritraumatic Distress Inventory for appreciation of life was quite high in the present study, so managing peritraumatic distress may need specific coping efforts. This would point to the importance of clinicians and researchers identifying and being attentive to the survivor's own meanings and interpretations.

4.6 The potential use of the Peritraumatic Distress Inventory in emergency departments

The author and colleagues previously showed that a cut-off score of 23 on the Peritraumatic Distress Inventory maximized the balance between sensitivity (77%) and specificity (82%) (Nishi, Matsuoka, Yonemoto et al., 2010). Further investigation is required to determine its adequate usage bearing in mind its low positive predictive value (53%). However, the early identification of motor vehicle accident survivors who appear not to be at risk of developing posttraumatic stress disorder is one potential use of the Peritraumatic Distress Inventory because of its high negative predictive value (93%). Given the typical limits on the psychiatric resources available, the Peritraumatic Distress Inventory would likely be a useful indicator for posttraumatic stress disorder and psychiatric morbidity in emergency departments.

4.7 Limitations

This study has some limitations. Firstly, the sample size was modest. Secondly, the attrition rate was relatively high, although the patients who dropped out were not significantly different from those who participated in the follow-up assessments in terms of the Peritraumatic Distress Inventory and other covariates. In an earlier publication, we revealed that the factors of being male, unconscious during MVA, low cooperativeness, and less severe injuries were significant predictors of dropout (Nishi et al., 2008). Participants with less severe injuries did not need to come to the National Disaster Medical Center for treatment after discharge which might have affected the attrition rate. Also, those with low cooperativeness might have been reluctant to continue participating in the study.

5. Future directions

5.1 Consolidation of fear memory

Fear memory, which is the important component of peritraumatic distress, has attracted considerable attention especially preclinically. An excellent review by Ressler & Mayberg (2007) has demonstrated that memories do not immediately become permanent at the time of initial experience but exist in a labile state for at least a period of hours and possibly days, during which time they become consolidated into more permanent memory. During this consolidation, molecular, synaptic, neurotransmitter, and system-level changes occur consecutively (McGaugh, 2000). The neural circuitry implicated in fear memory likely involves complex interactions between the hippocampus, the amygdala, and the medial prefrontal cortex (Nemeroff et al., 2006). Because the hippocampus processes and temporarily stores new memory before transferring labile memory to the cortex for permanent storage (Feng et al., 2001), it may be possible to modulate the consolidation of new fear memories while they are being formed (Pitman & Delahanty, 2005) .

5.2 Role of hippocampal neurogenesis in memory consolidation

A previous study showed that exercise on a running wheel, which promotes neurogenesis, increased the rate of loss of hippocampus-dependent contextual fear memory (Kitamura et al., 2009). The study suggested that the level of hippocampal neurogenesis could be modulated and was associated with a causal relationship between adult neurogenesis and the hippocampus-dependent period of fear memory. It is theoretically possible, therefore, that promoting adult neurogenesis early in the transition period might facilitate the clearance of fear memory from the hippocampus. Modulating memory consolidation would mean that posttraumatic stress disorder could be prevented in the aftermath of a traumatic event.

5.3 Omega-3 fatty acids and hippocampal neurogenesis

Fear consolidation can be blocked by an antagonist of noradrenergic activation, and the effectiveness of beta blockers for secondary prevention of posttraumatic stress disorder has been studied in clinical trials (Pitman et al., 2002; Vaiva et al., 2003). However, as traumatized individuals are not psychiatric patients, daily life-based intervention for the prevention of posttraumatic stress disorder is preferable.

Based on the animal research conducted to date, omega-3 fatty acids are the most promising candidate for dietary intervention in the aftermath of a traumatic event to facilitate adult hippocampal neurogenesis (Beltz, 2007; Calderon & Kim, 2004; Kawakita et al., 2006; Wu et al., 2004, 2008). The possible effects of omega-3 fatty acids on brain structures have also been observed clinically: a significant correlation was found between omega-3 fatty acid consumption and gray matter volume of the amygdala, hippocampus, and anterior cingulated gyrus in healthy adults (Conklin et al., 2007). Conversely, a selective deficit of docosahexaenoic acid was reported in the postmortem frontal cortex of patients with depressive disorder (McNamara et al., 2007). Following discussion of these results in the literature, Matsuoka proposed that promoting hippocampal neurogenesis by omega-3 fatty acid supplementation after trauma could reduce subsequent posttraumatic stress disorder symptoms (Matsuoka, 2011).

Support for the ability of omega-3 fatty acids to minimize subsequent posttraumatic stress disorder symptoms comes from one published but preliminary open trial (Matsuoka, Nishi, Yonemoto, Hamazaki et al., 2010). The author and colleagues recruited 15 consecutive patients admitted to the intensive care unit oft a Japanese general hospital immediately following accidental injury (mostly motor vehicle accidents). Patients received omega-3 fatty acid capsules containing 1,470 mg docosahexaenoic acid and 147 mg eicosapentaenoic acid daily for 12 weeks. The primary efficacy variable was score on the Clinician-Administered Posttraumatic Stress Disorder Scale (CAPS). Omega-3 fatty acid supplementation was well tolerated and resulted in a significantly increased docosahexaenoic acid concentration in erythrocytes. Compared with the hypothetical mean calculated in our previous cohort study (Matsuoka et al., 2009), omega-3 fatty acid supplementation resulted in a significantly reduced mean total score on the Clinician-Administered PTSD Scale (11 vs. 25, $p = 0.03$). This pilot study provided promising support for our hypothesis that omega-3 fatty acid supplementation started shortly after accidental injury may be efficacious in attenuating the symptoms of posttraumatic stress disorder. However, because of the open-label design and the lack of controls, no definitive conclusion could be drawn from the trial and we must wait for the results of an adequately powered randomized controlled trial (ClinicalTrials.gov Identifier: NCT00671099).

6. Conclusion

Peritraumatic distress can be assessed quickly and efficiently by using the Peritraumatic Distress Inventory and is an indicator for posttraumatic stress, depressive and anxiety symptoms, and posttraumatic growth in motor vehicle accident survivors. The Peritraumatic Distress Inventory can be used in the emergency department for early identification of motor vehicle accident survivors who are unlikely to develop posttraumatic stress disorder, and the combination of screening with the Peritraumatic Distress Inventory and supplementation with omega-3 fatty acids might be an effective preventive strategy for posttraumatic stress disorder in motor vehicle accident survivors.

7. References

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