Factor	loss group (N = 22)		non-loss group (N = 32)		
	Mean	SD	Mean	SD	p^a
Age (years)	42.7	8.8	43.8	8.9	0.646[a]
CAPS score	32.8	6.1	30.4	6.6	0.178[a]
Marital status (% married)	94.5		96.9		0.786[b]
Family composition after the earthquake (%)					
Alone	31.8		3.1		**0.004**[b]
With spouse or relatives	68.2		96.9		**0.004**[b]
Damage to housing (%)					
Completely destroyed house	59.1		12.5		**0.001**[b]
Semi-destroyed house	31.8		37.5		0.667[b]
No damage	9.1		50.0		**0.002**[b]
Lifestyle evaluation after the earthquake	1.4	1.3	3.5	1.7	**0.001**[a]

[a] Two sample t-test (two-tailed), [b] Pearson's chi-square test (two-tailed)
SD, standard deviation; CAPS, Clinician-Administered Post-Traumatic Stress Disorder Scale

TABLE 2. PSYCHOLOGICAL MEASURES FOR EACH GROUP

Factor	loss group		non-loss group		
	Mean	SD	Mean	SD	p^a
Physical health subscale (WHO-QOL26)	3.29	0.42	3.33	0.51	0.761
Psychological health subscale (WHO-QOL26)	2.95	0.45	3.26	0.41	**0.012**
Social relationship subscale (WHO-QOL26)	3.21	0.48	3.56	0.42	**0.006**
Environment subscale (WHO-QOL26)	2.71	0.49	3.12	0.50	**0.004**
GHQ score	8.59	6.67	5.78	3.97	0.058
CES-D score	15.95	7.49	12.66	6.33	0.087
Salivary cortisol level	9.80	8.23	6.64	5.97	0.107

[a] Two sample t-test (two-tailed)
SD, standard deviation; WHO-QOL26, World Health Organization Quality of Life 26; GHQ, General Health Questionnaire; CES-D, Center for Epidemiologic Studies Depression Scale

strated significantly lower scores on the psychological health, social relationship and environment subscales of the WHO-QOL26 than the non-loss group [psychological health score: $t = 2.593$, $df = 52$, $p < 0.05$; social relationship score: $t = 2.854$, $df = 52$, $p < 0.01$; environment score: $t = 3.008$, $df = 52$, $p < 0.01$]. The loss group had higher GHQ and CES-D scores than the non-loss group; however, these results were only marginally significant [GHQ score: $t = -1.939$, $df = 52$, $p = 0.058$; CES-D score: $t = -1.746$, $df = 52$, $p = 0.087$].

B. Salivary stress markers

The comparison results of the salivary cortisol levels are shown in Table 2 and Figure 1. The loss group had higher salivary cortisol levels than the non-loss group. However, this result was not significant [$t = -1.638$, $df = 52$, n.s.].

C. Correlation analyses

A Pearson correlation analysis for each group is shown in Tables 3 and 4. In the loss group, the salivary cortisol levels were negatively correlated with the physical and psychological health scores of the WHO-QOL26. Furthermore, the physical health scores of the WHO-QOL26 were positively correlated with the psychological health, social relationship and environment WHO-QOL26 scores and negatively correlated with the GHQ scores. The psychological health scores of the WHO-QOL26 were positively correlated with the social relationship and environment WHO-QOL26 subscales and negatively correlated with the GHQ and CES-D scores. The environment scores of the WHO-QOL26 were negatively correlated with the GHQ and CES-D scores. Finally, the GHQ scores were positively correlated with the CES-D scores. On the other hand, in the non-loss group, the salivary cortisol levels were not significantly correlated with any psychological measures. The physical health subscale of the WHO-QOL26 was positively correlated with the WHO-QOL26 psychological health and environment scores and negatively correlated with the CES-D scores. The psychological health subscale of the WHO-QOL26 was negatively correlated with the CES-D scores and positively correlated with the social relationship subscale of the WHO-QOL26. The CES-D scores were positively correlated with the GHQ scores.

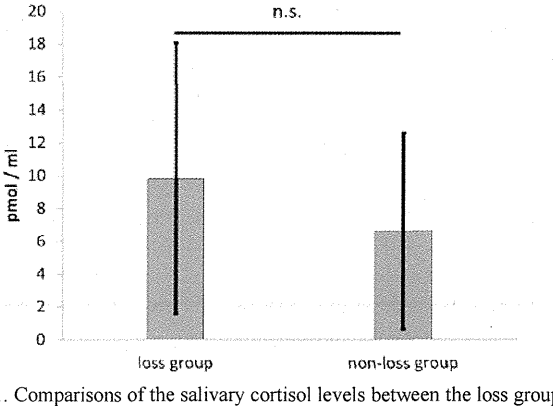

Fig. 1. Comparisons of the salivary cortisol levels between the loss group and the non-loss group
The salivary cortisol levels of the loss group were high compared with those of the non-loss group. However, there were no statistically significant differences.

TABLE 3. PEARSON CORRELATIONS AMONG STUDY VARIABLES—LOSS GROUP (N = 22)

	CAPS score	Physical health score (WHO-QOL26)	Psychological health score (WHO-QOL26)	Social relationship score (WHO-QOL26)	Environment score (WHO-QOL26)	GHQ score	CES-D score	Salivary cortisol level
1. CAPS score	1.00							
2. Physical health score (WHO-QOL26)	.15	1.00						
3. Psychological health score (WHO-QOL26)	−.03	.82***	1.00					
4. Social relationship score (WHO-QOL26)	−.06	.56**	.62**	1.00				
5. Environment score (WHO-QOL26)	−.03	.50*	.49*	.13	1.00			
6. GHQ score	.45	−.45*	−.43*	−.36	−.45*	1.00		
7. CES-D score	.12	−.38	−.52*	−.23	−.44*	.56**	1.00	
8. Salivary cortisol level	.04	−.54**	−.53*	−.38	.04	.04	−.02	1.00

* $p < .05$, ** $p < .01$, *** $p < .001$ (two-tailed)

CAPS, Clinician-Administered Post-Traumatic Stress Disorder Scale; WHO-QOL26, World Health Organization Quality of Life 26; GHQ, General Health Questionnaire; CES-D, Center for Epidemiologic Studies Depression Scale

TABLE 4. PEARSON CORRELATIONS AMONG STUDY VARIABLES—NON-LOSS GROUP (N = 32)

	CAPS score	Physical health score (WHO-QOL26)	Psychological health score (WHO-QOL26)	Social relationship score (WHO-QOL26)	Environment score (WHO-QOL26)	GHQ score	CES-D score	Salivary cortisol level
1. CAPS score	1.00							
2. Physical health score (WHO-QOL26)	.17	1.00						
3. Psychological health score (WHO-QOL26)	−.23	.59***	1.00					
4. Social relationship score (WHO-QOL26)	−.02	.29	.41*	1.00				
5. Environment score (WHO-QOL26)	−.19	.54***	.16	.06	1.00			
6. GHQ score	.06	−.38*	−.28	−.12	.05	1.00		
7. CES-D score	.21	−.61***	−.54***	−.24	.25	.58***	1.00	
8. Salivary cortisol level	.27	−.05	−.05	−.17	−.24	.03	−.03	1.00

* $p < .05$, ** $p < .01$, *** $p < .001$ (two-tailed)

CAPS, Clinician-Administered Post-Traumatic Stress Disorder Scale; WHO-QOL26, World Health Organization Quality of Life 26; GHQ, General Health Questionnaire; CES-D, Center for Epidemiologic Studies Depression Scale

IV. DISCUSSION

The novelty of this study is that there are identified the psychological effects on women with mild PTSD derived from natural disasters such as earthquakes. The objective of the present study was to investigate the psychological effects on women who live in the disaster area of the Great East Japan Earthquake using psychological data collected six months after the earthquake, particularly comparing women who lost a member of their household and/or a relative and women who did not. The present study revealed heavy psychological effects in women who live in the disaster area affected by the earthquake, especially those who lost a member of their household and/or a relative. These results are consistent with our hypothesis that women who lose a member of their household and/or a relative suffer worse psychological effects than women who do not. In addition, based on these results, the relationship between higher cortisol levels and psychological stress suggests that high-stress conditions

induce alterations in the HPA axis that stimulate the release of cortisol [61–63].

In terms of the results of the psychological measures, the loss group had significantly lower WHO-QOL26 subscale scores (psychological, social relationship, environment) compared to the corresponding scores of the non-loss group. It was estimated that the women in the loss group were strongly influenced with respect to their quality of life, health and psychology by negative experiences of the loss of a relative in the disaster. Previous studies have reported that women' mental health and quality of life were worse after the earthquake [61–63]. These studies suggest that a poor QOL is a consequence of the earthquake. Although previous studies have not reported much in detail regarding the background of women' mental health, the results of our study clarified the psychological effects in women under more concrete situations in which they lost a relative in the disaster. In this disaster, many areas along the Sanriku shoreline sustained damage from the tsunami rather than the earthquake. Many people who live in the disaster area had negative experiences such as being in buildings broken by tremendous shaking. Moreover, many people who live in the coastal area of the disaster experienced the tsunami; their family members and others were carried away by the tsunami in front of their eyes and they witnessed people dying in front of them after the tsunami. This experience led to a sense of loss of the family and significant others that were part of the mental bases the subjects had thus far built. These are called object losses [64] and losses [65]. This loss experience includes negative feelings such as anger, pain, a sense of powerlessness, despair and sadness. A previous study suggested that a series of psychological reactions triggered by loss leads to mourning [64]. Previous studies also suggest that such persons undergo several stages of mourning [66–68]. First, the loss and mourning results in shock about the experience and feelings of sadness and pain. Then, a condition of spiritless persists. After a while, people gradually respond to the fact of the loss and begin to develop positive feelings. A previous study suggested that psychological recovery can be delayed, so that the attachment to the loss remains strong [69]. Additionally, a previous study suggested that women tend to be in a depressive condition for a longer time after separation than men [70]. We considered that the women in this study responded to the fact that their loss caused by the disaster had occurred in the stage of six months after the disaster; however, the subjects had not yet relinquished their sense of loss.

Additionally, psychological responses in times of disaster can be categorized into three steps: 1) reactions, 2) factors, and 3) psychodynamics [71, 72]. The period of this study was six months after the earthquake. We believe that the residents of the disaster areas of six months after the disaster were in transition from factors to psychodynamics. Although there were cases of spontaneous psychological recovery, many survivors still had strong negative feelings such as depression, anger and discontentment regarding the earthquake during this period. Living conditions changed dramatically soon after the earthquake due to the need to live in temporary evacuation centers, the inconvenience of obtaining things, the lack of essential utilities and so on. Moreover, as the affected people were forced to live in complex and unfamiliar environments, it is believed that they felt more anxiety and fatigue than usual in their daily living and human relationships [73]. Although this study was conducted six months after the earthquake disaster, the subjects were still living with anxiety due to continuing aftershocks and unstable life security.

Social support is also disrupted after an earthquake disaster. Many of the survivors of this period were forced to move to a permanent or temporary house from a shelter. They broke off personal relationships they formed in the shelter and had to remake personal relationships in a new environment. When living in new environment such as a temporary residence, people often avoid telling others about having lost a family member because they think that there are many people who went through terrible experiences. Therefore, they cannot create relationships easily and make only necessary and minimum contact with others. Therefore, people are still isolated from people. A previous study suggested that the existence of social support has a positive effect on psychological recovery from loss [74]. However, it is assumed that social support in the aftermath of disaster may not be adequate. With these points in mind, we believe that the altered daily life environment and psychological stress caused by the disaster resulted in increases in the salivary cortisol levels in our study.

The salivary cortisol levels of both groups were higher than the standard values for women (3.46 ± 3.20 pmol/ml, 4:00 p.m.) reported in a previous study [75], and the average salivary cortisol level of the loss group was higher than that of the non-loss group. This finding is consistent with the results of previous studies, such as those of victims of the Hanshin-Awaji Earthquake and the Wenchuan Earthquake, which also reported higher cortisol levels [2, 76]. Cortisol is an indicator of psychological and physiological stress that can be used to examine PTSD pathophysiology [77]. Anxiety may have exacerbated the salivary cortisol levels due to disruption of access to daily information, damage to homes or businesses and safety-related concerns after the earthquake. Many people affected by the disaster still feel stress, fear, fatigue, helplessness and disappointment [78] due to the earthquake, and it appears that these factors continue to influence psychological responses six months after the disaster.

To summarize the above, although half a year has passed since the earthquake, psychological damage remains strong among women who live in the hardest-hit coastal areas, especially women who lost a relative in the disaster. We believe that enriching mental health, livelihood and social support for women in the disaster area such as preventing social isolation and hardship as quickly as possible is necessary. These kinds of activities will aid the early detection of women's PTSD symptoms and provide psychological care and livelihood support for women who have not recovered from negative experiences.

Finally, this study is associated with some limitations: 1) the sample size of this study was small because the number of subjects in the overarching interventional study was 54;

2) There was a clear difference between the loss group and the non-loss group. It was loss experience of family members by the Great East Japan Earthquake. The loss group consisted of women who lost a member of their household and/or a relative by the earthquake. On the other hands, the non-loss group consisted of women whose a member of their household and/or a relative was safe in the earthquake; and 3) we were unable to conduct follow-up with these women because they participated in a scheduled interventional study after this examination and were affected by that intervention. Therefore, in the future, we will review the number of respondents to surveys and will investigate the trends of the recovery process of psychological and physical health by studying women survivors' mental health continuously in the disaster area.

V. CONCLUSION

The purpose of this study was to investigate psychological effects in women who live in the disaster area using psychological data collected six months after the Great East Japan Earthquake. Our research demonstrated that women who live in the disaster area and lost a member of their household and/or a relative were strongly affected by the earthquake (i.e., they have a lower QOL and poorer mental health than those who did not suffer such a loss). In the future, we would like to examine further time-dependent changes in people living in the affected areas while simultaneously supporting the survivors.

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［短　報］

震災後精神症状の脆弱性・獲得因子の神経基盤の解明

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災害ストレスに起因する精神症状と脳形態変化について多数報告はあるが，災害ストレス暴露後の横断研究が主であり，災害後精神症状の脆弱性／獲得因子としての脳形態変化は未解明であった．本稿では，我々が発表した脳形態変化と震災後精神症状の脆弱性因子／獲得因子を解明した最新の研究を紹介し，複数の脳画像データが示唆する生物学的背景について文献的考察を加え，今後の災害ストレスに関わる脳画像研究の方向性を探る．

Key Words　東日本大震災，震災後精神症状，脳形態変化，脆弱性因子，獲得因子

背　景

東日本大震災による家屋の倒壊や津波の被害などは，仙台市中心部に位置する東北大学の周辺では沿岸部と比してはるかに少なかった．しかし，多くの被災者はライフラインの寸断，たび重なる余震，原発事故などの多大なストレスに晒され，心的外傷後ストレス障害（PTSD）に至らずとも，幅広い心理的ケアが必要であった[7, 13]．

ストレス暴露に関連する脳形態の変化は，海馬，扁桃体，前帯状皮質，眼窩前頭皮質などの灰白質の減少や，帯状束での白質統合性の低下が指摘されている．これら変化はPTSD患者[19]のみならず，ストレス暴露後の健常者[3, 18]にも認められる．しかし，前向き研究の困難さから[20]ストレス暴露後の脳画像評価が主であり，ストレス暴露と脳形態変化の因果関係は未解明であった．

我々の研究室では，主に東北大学の健常学生を対象とした脳画像研究を行っており，震災前の脳画像のデータを多数保有しており，これらデータベースを活用して，震災前後の縦断的な脳画像研究を行うことができた．本稿では，最近発表した脳灰白質／白質の形態変化と震災後精神症状の脆弱性因子／獲得因子に関する研究[22, 23]を紹介し，脳灰白質変化と脳白質変化の一致点・不一致点および，複数の脳画像データセットから得られる生理学的背景について文献的考察を加える．

方　法

我々の研究室では，主に健常大学生を対象とし，MRIを用いた脳画像研究を行っており，震災前の脳画像を多数保有している．今回，震災前の脳形態画像（T1強調画像）が存在する被験者に連絡をとり，42名（男／女：33／9人，年齢，21.7 ± 1.7歳）を再募集することができた．これら被験者に対して，震災後3～4カ月の時点でT1強調像を撮像した．また42名のうち，震災前の拡散強調画像が存在した30名（男／女：24／6人，年齢，21.0 ± 1.6歳）に対して，拡散強調

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画像を撮像した．MRI 撮像は Philips 社の 3.0 テスラ・インテラ・アチーバにて行った．MPRAGE (Magnetization-Prepared Rapid Acquisition with Gradient Echo) シーケンス (240 × 240 matrix, repetition time＝6.5 ms, echo time＝3 ms, field of view＝24 cm, 162 slices, 1.0 mm slice thickness) による T1 強調画像，およびスピン・エコー EPI シーケンス (TE＝55 ms, FOV＝22.4 cm, 2 × 2 × 2 mm^3 voxels, 60 slices) による拡散強調画像 (32 軸，b value=1,000s/mm^2) を用いて，脳白質統合性の指標となる拡散異方性 (fractional anisotropy；FA) を算出した．

心理尺度として PTSD 臨床診断面接尺度 (CAPS)[1] にて PTSD 症状を，State Ttrait Anxiety Inventory (STAI)[14] を用いて状態／特性不安を評価した．さらに，精神疾患の合併の有無を精神疾患簡易構造化面接法 (MINI)[17] で評価した．被験者の CAPS スコアは最大 39 点であり，MINI においても PTSD の診断基準を満たすものは認めなかった．

T1 強調画像の前処理には，VBM2[8] を使用し，脳画像統計解析には統計画像解析ソフト SPM5 を使用した．前処理では，脳灰白質，脳白質，脳脊髄液腔の各分画を作成し，脳灰白質量を算出した．さらに，空間的標準化，半値幅 8 mm で画像平滑化を行った．CAPS スコアを従属変数と，震災前の脳灰白質量および震災前後の脳灰白質変化量を独立変数とした重回帰分析解析を行った．共変量として，被験者の性別，全脳体積，震災前後の撮像間隔（日）を補正した．震災前の脳灰白質量と震災後の CAPS スコアが負相関を示す脳部位を震災後 PTSD 症状の脆弱性因子の神経基盤として，震災前後の脳灰白質量の変化量と震災後の CAPS スコアが正相関を示す脳部位を震災後 PTSD 症状の獲得因子として評価した．脳画像解析は各関心領域内（海馬，扁桃体，前帯状皮質，眼窩前頭皮質）での多重比較補正（スモール・ボリューム・コレクション；SVC)[25] を行い，統計閾値は p＝0.05 とした．

拡散強調画像により算出した FA に関しても，SPM5 を用いた脳画像統計解析を行った．空間的標準化，半値幅 10 mm で画像平滑化を行った．状態不安スコアを従属変数と，震災前の脳灰白質量および震災前後の脳灰白質変化量を独立変数とした重回帰分析解析を行った．共変量として，被験者の性別，震災前後の撮像間隔（日）を補正した．震災前の脳灰白質量と震災後の状態不安スコアが負相関を示す脳部位を震災後不安症状の脆弱性因子の神経基盤として，震災前後の脳灰白質量の変化量と震災後の状態不安スコアが正相関を示す脳部位を震災後不安症状の獲得因子として評価した．脳画像解析は，全脳での検定を行い，多重比較補正はクラスターサイズによる補正を行い[6]，統計閾値は p＝0.05 とした．

倫理的手続き

本研究は，東北大学大学院医学研究科倫理委員会の承認を得ている．また，ヘルシンキ宣言に則り，口頭および書面により実験の必要性，安全性について説明を行い，全被験者から書面による同意書を得た．また，震災前のデータの再利用に関しても，書面による同意を得ていた．

結　果

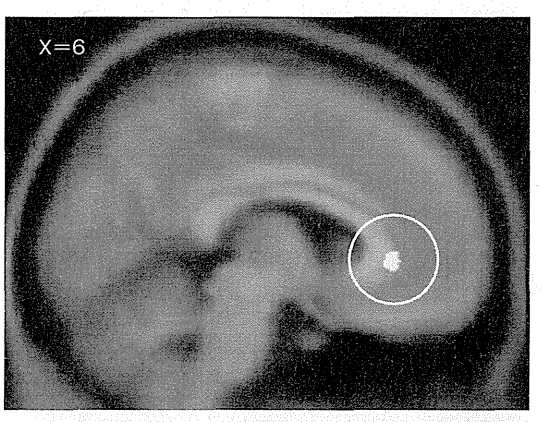
脳形態画像解析の結果，右腹側前帯状皮質において CAPS スコアと震災前の脳灰白質量が有意な負相関を（**図 1a**），左眼窩前頭皮質において震災前後の脳灰白質変化量と有意な負相関を示した（**図 1b**）．また，右前帯状束において状態不安スコアと震災前の FA が有意な負相関を（**図 2a**），左前帯状束および左鉤状束において震災前後の FA 変化量と有意な正相関を示した（**図 2b**）．

考　察

本研究により，震災後精神症状の脆弱性因子の神経基盤として，右前帯状皮質の脳灰白質体積減少および右前帯状束の脳白質統合性の低下が，震災後精神症状の獲得因子の神経基盤として左眼窩前頭皮質の減少および左帯状束・鉤状束の白質統合性の上昇が認められた．

前帯状束は前帯状皮質から延びる神経線維を含み，大脳辺縁系の一部の構成要因としても知られている[10]．その機能として，恐怖や不安の処理が知られており[5]，震災後の不安症状の病態にも

a）右前帯状皮質［6 32 0］



b）左眼窩前頭皮質［−20 52 −6］

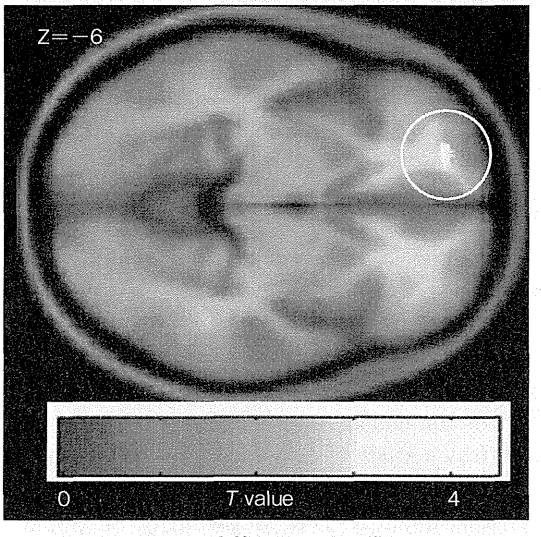
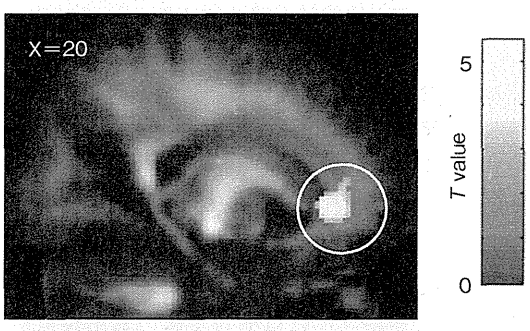


図1　震災後 PTSD 症状の脆弱性・獲得因子の神経基盤（文献[22]より改変）

a）PTSD 症状の脆弱性因子の神経基盤．震災前の右腹側前帯状皮質の局所灰白質量と震災後 CAPS スコアが有意な負相関を示した．b）PTSD 症状の獲得因子の神経基盤．震災前後の左眼窩前頭皮質の局所灰白質量の変化量と震災後 CAPS スコアが有意な負相関を示した．

深く関与している[12]．本研究により，これら恐怖や不安の処理の機能不全が，震災後精神症状の脆弱性因子として関与することが示唆された．また，眼窩前頭皮質は，隣接する鉤状束を介して情動処理に関与する扁桃体の活動と協調し[9]，情動制御に重要な役割を果たしている[16]．PTSD 患者においても恐怖記憶の消去[2]や情動制御[15]の際

a）右帯状束［20 36 0］



b）左帯状束［−22 34 18 ○］
左鉤状束［−16 26 −8 ◌］

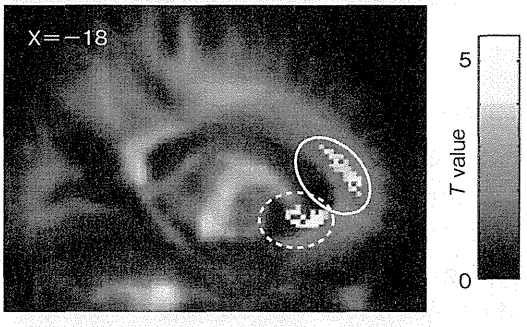


図2　震災後不安症状の脆弱性・獲得因子の神経基盤（文献[23]より改変）

a）震災後不安症状の脆弱性因子の神経基盤．震災前の右前帯状束の白質統合性と震災後の状態不安スコアが有意な負相関を示した．b）震災後不安症状の獲得因子の神経基盤．震災前後の左帯状束・鉤状束の白質統合性の変化量と震災後の状態不安スコアが有意な負相関を示した．

に眼窩前頭皮質の活動が低下しているとの報告もある．さらに，左前帯状束／鉤状束の白質統合性の増加は，震災後不安症状の脆弱性因子として不安や恐怖の処理機能不全が存在し，情動制御の必要性が高まったことが震災後早期の不安症状の獲得の背景に存在していたことが示唆された[23]．

上述の脳形態変化は各々が隣接する領域であることから，解剖学的な位置関係は概ね一致していた．右前帯状皮質の灰白質量と，隣接する右帯状束の白質統合性はともに精神症状と負相関を示しており，灰白質量の減少と白質統合性の低下はともに当該領域の機能不全を示唆する所見として，震災後精神症状の脆弱性因子として解釈されている[22]．一方で，左側眼窩前頭皮質の灰白質変化

量と精神症状は負相関を示したが，隣接する左鉤状束，帯状束の白質統合性の変化量は精神症状と正相関を示しており，右前帯状皮質／帯状束の結果とは一見して矛盾する結果のように見える．これら不一致は，心理的ストレスにより引き起こされる生物学的変化が脳部位によって異なることに起因すると考えられる．前帯状皮質の脳灰白質量の低下は，ストレスホルモンとして知られるコルチゾールの影響で引き起こされることが報告されており[24]，組織学的には樹状突起の縮小が主な要因であるとされている[4,11]．樹状突起の縮小は，白質統合性の低下にも直結する変化であり前帯状皮質の灰白質量低下と前帯状束の白質統合性の低下は同一の生物学的背景に起因すると考えられる．一方，眼窩前頭皮質では，慢性ストレスにより樹状突起が増加するとの報告があり[21]，鉤状束における白質統合性の増加を支持する知見である．一見して相反する結果であるが，心理的ストレスに対する脳部位ごとの神経細胞の組織学的な反応の違いが，脳形態画像変化にも反映されていたものと考えられる．複数の脳画像データの検証により，画像所見として現れる生物学的変化についてより深い考察ができた好例であり，複数の脳画像データセットによる検証の重要性が示唆されたものと考えられる．

結　語

今回紹介した脳画像研究は，大規模災害前後の脳灰白質量，白質統合性の形態変化を報告した世界で初めての研究である．災害ストレスへの適応過程に対する理解を深め，災害後精神症状の早期発見，予防に資する基礎研究として意義深いものと考える．一方で，これらは比較的軽度な被災をした健常レベルの大学生の結果であり，より強烈なトラウマ体験をした被災者への応用は慎重を期する必要がある．今後，より広い世代に渡る，さまざまなレベルのトラウマ体験をした被災者を対象とした検証が待たれるところである．

現在筆者は，震災後に東北大学に新設された東北メディカル・メガバンク機構において，宮城県沿岸部および内陸部の住民を対象とした大規模なゲノムコホート調査の立ち上げに参加しており，一部対象者から脳形態画像および認知機能データを収集する計画に従事している．本コホート調査を通して，近い将来には，脳形態，認知機能，遺伝要因，生活習慣との関連が明らかとなり，災害ストレス暴露後の精神症状の増悪に対する個別化予防，個別化医療が可能になると期待している．

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