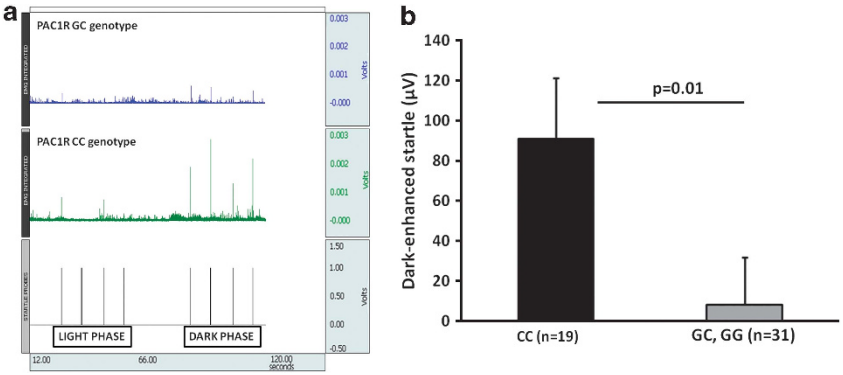

Figure 1. (**a**) Representative electromygraphic recordings of eyeblinks from children with GC and CC genotypes during the last light and dark blocks of the dark-enhanced startle (DES) session. Each black line represents a startle probe. (**b**) Mean + s.e. DES (eyeblink startle magnitude during the dark minus light phase) between CC genotype and G allele carriers. Statistical analyses presented are after co-varying for child age, in addition to maternal trauma levels, posttraumatic stress disorder symptoms and depressive symptoms.

interaction effects of block × dark × genotype on startle magnitude, $F(1,37) = 4.95$, $P = 0.03$, and an interaction of block × dark × maternal trauma, $F(1,37) = 7.33$, $P = 0.01$. The interaction of block × dark indicated that the effect of darkness was greater in the second block. Using a one-way analysis of variance, we compared DES (measured as the difference in startle during dark vs light phases) during the second block between CC and G-allele carriers and found a significant effect of genotype, $F(1,49) = 4.52$, $P = 0.04$; but no effect of sex, $F(1,49) = 0.03$, $P > 0.1$ (Figure 1b). After controlling for child's age and race, the mother's trauma and symptoms of PTSD and depression, the effect of genotype was strengthened, $F(1,37) = 7.39$, $P = 0.01$. Adding the child's trauma exposure to the model as a covariate did not change the significant effect of genotype, $F(1,31) = 6.62$, $P = 0.01$.

These results replicate our previous findings of PAC1R genotype effects on DES in a sample of male and female children. However, in adults we found the effects of CC genotype only in women.[2] A limitation of the study is a lack of estrogen assays in the children, especially as the older girls may have elevated estrogen levels with puberty onset. However, these data suggest that genetic vulnerability for anxiety is evident in both males and females during child development, but may only be present in females after adolescence due to changes in the estrogen system, given the effects of estrogen on PAC1R regulation.[2]

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1 Hammack S, Roman C, Lezak K, Kocho-Shellenberg M, Grimmig B, Falls W *et al. J Mol Neurosci* 2010; **42**: 327–340.
2 Ressler KJ, Mercer KB, Bradley B, Jovanovic T, Mahan A, Kerley K *et al. Nature* 24; 2011: **470**: 491–497.
3 Grillon C, Morgan III CA, Davis M, Southwick SM. *Am J Psychiatry* 1998; **155**: 812–817.
4 Grillon C, Dierker L, Merikangas KR. *J Am Acad Child Adolesc Psychiatry* 1997; **36**: 925–932.
5 Kamkwalala A, Norrholm SD, Poole JM, Brown A, Donely S, Duncan E *et al. Psychosom Med* 2012; **74**: 153–159.
6 Jovanovic T, Smith A, Kamkwalala A, Poole J, Samples T, Norrholm SD *et al. J Child Psychol Psychiatry* 2011; **52**: 844–852.
7 Bernstein DP, Stein JA, Newcomb MD, Walker E, Pogge D, Ahluvalia T *et al. Child Abuse Neglect* 2003; **27**: 169–190.
8 Foa EB, Riggs DS, Dancu CV, Rothbaum BO. *J Trauma Stress* 1993; **6**: 459–473.
9 Beck AT, Ward CH, Mendelsohn M, Mock J, Erbaugh J. *Arch Gen Psychiatry* 1961; **4**: 561–571.
10 Ribbe D, Stamm BH (eds). *Measurement of Stress, Trauma, and Adaptation*. Lutherville, MD: Sidran Press, 1996; 386–387.

Open

Peritraumatic distress after an earthquake: a bridge between neuroimaging and epidemiology

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Sekiguchi *et al.*[1] demonstrated in a neuroimaging study that survivors of the Great East Japan Earthquake who had a smaller anterior cingulate cortex (ACC) volume before the earthquake and survivors with a decreased orbitofrontal cortex (OFC) volume through the earthquake disaster were likely to have symptoms of posttraumatic stress disorder (PTSD).[1] As both the ACC and OFC are involved in the processing of anxiety and fear, such structural changes seem to show some similarity with the findings of epidemiological studies on peritraumatic distress (distress at the time of trauma and immediately thereafter).

Fear memory becomes excessively consolidated[2] in the development of PTSD and is thought to be enhanced by

peritraumatic distress. Indeed, peritraumatic distress is one of the strongest predictors for PTSD.[3] The presence of peritraumatic distress was shown to be a relatively weak indicator of the presence of PTSD, whereas its absence was found to be a strong indicator of the absence of PTSD.[4] Recently, we in our epidemiological study, examined the predictors of PTSD among rescue workers 1 month after the Great East Japan Earthquake as, alongside survivors in the disaster area, they were deemed to be at high risk for developing PTSD. Peritraumatic distress as assessed by the Peritraumatic Distress Inventory (PDI)[5,6] and watching television for extended period of time predicted PTSD symptoms at 4 months after the earthquake.[7] Moreover, in an online survey conducted by Bui *et al.*[8] in France, Canada and the United States, within 2 weeks of the earthquake, peritraumatic distress was found to be a predictor of disruptive nocturnal behavior and PTSD symptoms among respondents, and that it significantly mediated a relationship between internet coverage of the disaster and presence of PTSD symptoms.

Failure to regulate fear responses to traumatic events could be due to dysfunction in the ACC.[9] As Sekiguchi *et al.*[1] showed decreased volume of the ACC might reflect genetic and epigenetic vulnerability, and vulnerable individuals might be prone to peritraumatic distress. We suggested that the different types of peritraumatic distress occurring in response to various traumatic events might be important.[7] For example, loss of emotional control and feeling shame might be more important for predicting PTSD than other types of peritraumatic distress in rescue workers after disasters, although helplessness and experiencing physical reactions might be more important in traffic accident survivors. These differences could provide insights into not only effective prevention but also future neurobiological study of PTSD.

The current diagnostic criterion A2 for PTSD requires fear, helplessness or horror at the time of the event. Removal of this criterion from the fifth edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-5) has been proposed.[10] This change could be a reasonable one because the positive predictive value of this criterion for PTSD is relatively low, and as many patients with PTSD visit psychiatrists long after a traumatic event, recall bias would be considerable. However, assessment of peritraumatic distress, at least in settings where it could be assessed soon after a traumatic event, could screen out individuals unlikely to develop PTSD as well as contribute to elucidating the pathogenesis of PTSD.

A foremost function of the OFC is its involvement in the extinction of conditioned fear.[1] TV and Internet viewing for extended periods after a traumatic event might be harmful to the OFC structure and consequently impair its important functioning for the extinction of fear memory. Thus the results of Sekiguchi *et al.*'s[1] neuroimaging study coincide with the findings from epidemiological studies, although it remains unclear whether such viewing might constitute traumatic exposure or be a part of ineffective coping.

The use of longitudinal neuroimaging data to examine vulnerability factors and acquired sign of PTSD symptoms is of considerable interest for both understanding the pathogenesis of PTSD and developing preventive strategies for it. It is our mission to learn more from this latest tragic event for the future.

CONFLICT OF INTEREST

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REFERENCES

1 Sekiguchi A, Sugiura M, Taki Y, Kotozaki Y, Nouchi R, Takeuchi H *et al. Mol Psychiatry* 2012.
2 Ressler KJ, Mayberg HS. Ash. *Nat Neurosci* 2007; **10**: 1116–1124.
3 Ozer EJ, Best SR, Lipsey TL, Weiss DS. Ash. *Psychol Bull* 2003; **129**: 52–73.
4 Nishi D, Matsuoka Y, Yonemoto N, Noguchi H, Kim Y, Kanba S. Ash. *Psychiatry Clin Neurosci* 2010; **64**: 149–156.
5 Brunet A, Weiss DS, Metzler TJ, Best SR, Neylan TC, Rogers C *et al.* Ash. *Am J Psychiatry* 2001; **158**: 1480–1485.
6 Nishi D, Matsuoka Y, Noguchi H, Sakuma K, Yonemoto N, Yanagita T *et al.* Ash. *Gen Hosp Psychiatry* 2009; **31**: 75–79.
7 Nishi D, Koido Y, Nakaya N, Sone T, Noguchi H, Hamazaki K *et al.* Ash. *PLoS One* 2012; **7**: e35248.
8 Bui E, Rodgers RF, Herbert C, Franko DL, Simon NM, Birmes P *et al.* Ash. *Am J Psychiatry* 2012; **169**: 221–222.
9 Villarreal G, King CY. Ash. *Semin Clin Neuropsychiatry* 2001; **6**: 131–145.
10 American Psychiatric Association. Available from: http://www.dsm5.org/ProposedRevision/Pages/proposedrevision.aspx?rid = 165.

Therapygenetics: the *5HTTLPR* as a biomarker for response to psychological therapy?

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Psychiatric illnesses are under polygenic influence and are associated with interactions between genetic variants and environmental exposures.[1] Gene–environment interactions might not only predict onset of disease, but genetic biomarkers might also help the clinician to select the optimal treatment for patients.[2] However, there is a lack of studies on therapygenetics for psychological treatment of psychiatric diseases.

The serotonin transporter gene promoter region (*5HTTLPR*) in depression and anxiety is particularly of interest, because it is associated with response to stress,[3] and may represent susceptibility to environmental influences.[4,5] Recently, in this journal, Eley *et al.*[6] reported preliminary results showing that children with an anxiety disorder carrying the short–short (SS) genotype were significantly more likely to respond to cognitive behavioral therapy (CBT) than those carrying a long allele (SL/LL). The authors state that independent replication is necessary. Moreover, a control group not receiving CBT was lacking and the association did only emerge at follow-up. In an independent sample, using a randomized clinical trial design, we examined whether the short–short allele in recurrently depressed patients was associated with better response to CBT in preventing recurrence compared with a control group.