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Psychogenic fever: how psychological stress affects body temperature in the clinical population

Takakazu Oka*

Department of Psychosomatic Medicine; Graduate School of Medical Sciences; Kyushu University; Fukuoka, Japan

Keywords: emotional fever, fever of unknown origin, psychogenic fever, stress-induced hyperthermia, stress, human

Abbreviations: A, adrenaline; BAT, brown adipose tissue; CFS, chronic fatigue syndrome; CRP, C-reactive protein; DBP, diastolic blood pressure; DMH, dorsomedial hypothalamus; FMS, fibromyalgia syndrome; HMS, hypothalamic-medullary-sympathetic; HR, heart rate; 5-HT, 5-hydroxytryptamine; IL, interleukin; NA, noradrenaline; NSAIDs, nonsteroidal antiinflammatory drugs; PG, Prostaglandin; PSH, psychological stress-induced hyperthermia; POA, preoptic area of the hypothalamus; SBP, systolic blood pressure; SSRI, selective serotonin reuptake inhibitor; Tc, core body temperature; UCP1, uncoupling protein1.

Psychogenic fever is a stress-related, psychosomatic disease especially seen in young women. Some patients develop extremely high core body temperature (Tc) (up to 41°C) when they are exposed to emotional events, whereas others show persistent low-grade high Tc (37–38°C) during situations of chronic stress. The mechanism for psychogenic fever is not yet fully understood. However, clinical case reports demonstrate that psychogenic fever is not attenuated by antipyretic drugs, but by psychotropic drugs that display anxiolytic and sedative properties, or by resolving patients' difficulties via natural means or psychotherapy. Animal studies have demonstrated that psychological stress increases Tc via mechanisms distinct from infectious fever (which requires proinflammatory mediators) and that the sympathetic nervous system, particularly β3-adrenoceptor-mediated non-shivering thermogenesis in brown adipose tissue, plays an important role in the development of psychological stress-induced hyperthermia. Acute psychological stress induces a transient, monophasic increase in Tc. In contrast, repeated stress induces anticipatory hyperthermia, reduces diurnal changes in Tc, or slightly increases Tc throughout the day. Chronically stressed animals also display an enhanced hyperthermic response to a novel stress, while past fearful experiences induce conditioned hyperthermia to the fear context. The high Tc that psychogenic fever patients develop may be a complex of these diverse kinds of hyperthermic responses.

What is Psychogenic Fever?

Among those who develop episodic or persistent high core body temperature (Tc) without any inflammatory causes, there are patients whose high Tc is associated with psychological stress.[1-14] Some patients develop a high fever (up to 41°C) when they are exposed to emotional events (**Fig. 1**), whereas others show a persistent low-grade fever (37–38°C) lasting months and even years, either during or after situations of chronic stress (**Fig. 2**) (for review, see).[15,16] The existence of such patients has been recognized since the early twentieth century[17] and their high Tc has been called "psychogenic fever"[2,18,19] or "neurogenic fever."[20,21] Psychogenic fever is bothersome for both patients and physicians because, although many patients consider the fever to be disabling, there is no abnormal finding to account for their high Tc and antipyretic drugs do not reduce their fever. Moreover, there are still physicians who do not recognize the fact that psychological stress can cause high Tc.

Therefore, to obtain a better understanding of patients with psychogenic fever, this article reviews how psychological stress affects Tc in laboratory animals, healthy human subjects, and clinical populations.

Acute Psychological Stress-Induced Hyperthermia in Laboratory Animals

Animal studies have demonstrated that many, but not all, types of acute psychological stress increase Tc. For example,

*Correspondence to: Takakazu Oka; Email: oka-t@cephal.med.kyushu-u.ac.jp
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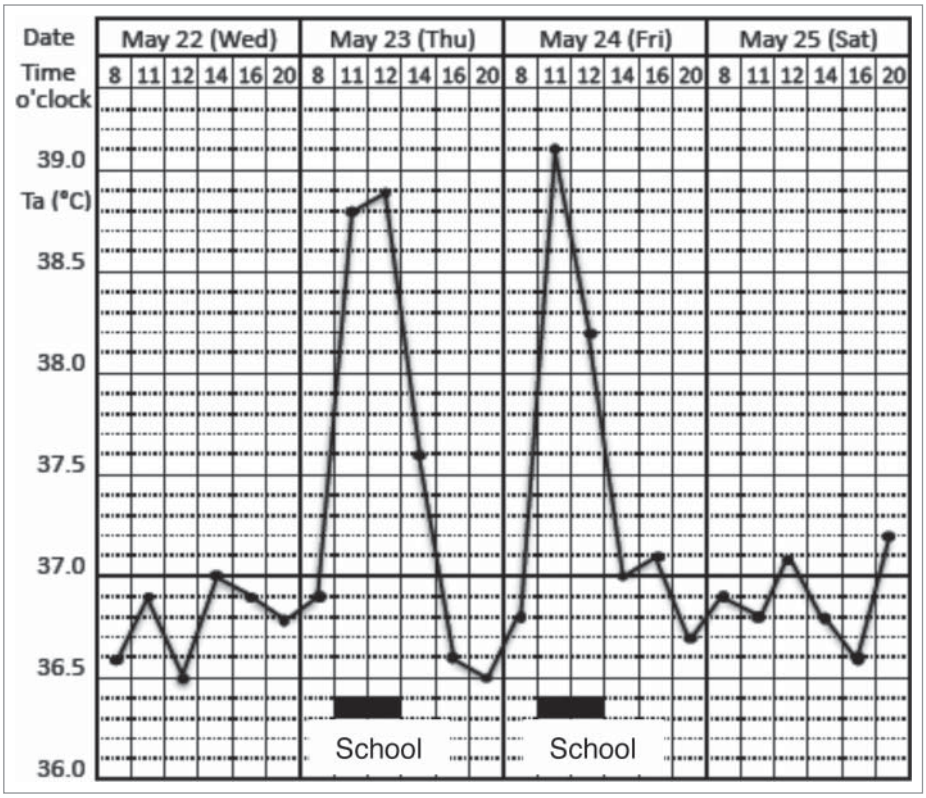

Figure 1. Prominent psychogenic fever observed in a 15-year-old schoolgirl. She was referred from a pediatrician to my outpatient clinic because she repeatedly developed antipyretic drug-resistant fever of unknown causes. I asked the patient to record her axillary temperature (Ta) using an electrothermometer 4 times a day (8 a.m., 12 a.m., 4 p.m., and 8 p.m.) and the events of the day in a "fever diary" to better understand mind (stressor)-body (temperature) relationships. I also asked her mother and school nurse to make sure the temperature she recorded was accurate. The fever diary demonstrated that she developed a high Ta up to 39°C only on the days when she went to school (underlined black bar). (Unpublished observation.)

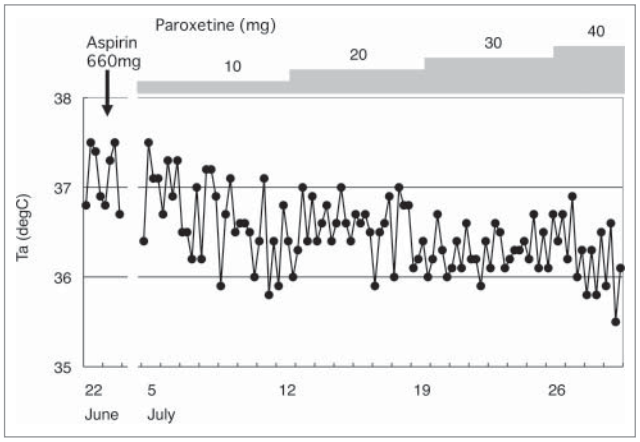

Figure 2. Chronic psychological stress-associated, persistent low-grade high axillary temperature (Ta) observed in a 56-year-old head nurse. She had antipyretic drug-resistant, low-grade (37–38°C) high Ta for more than 3 months. © Japanese Society of Psychosomatic Internal Medicine. Reproduced by permission of Japanese Society of Psychosomatic Internal Medicine. Permission to reuse must be obtained from the rightsholder.

exposing rats or mice to stressors such as being placed into an unfamiliar space or an open field (novelty stress),[22-24] changing home cages (cage-change stress or cage switch stress),[25-27] restraint/immobilization,[28-31] removing cage-mates (cage-mate removal stress),[27,32-34] and exposure to dominant animals (social defeat stress)[35-38] or an intruder[39] increases Tc. **Fig. 3** shows that social defeat stress, i.e., exposing rats to a dominant conspecific, increases Tc by up to 2°C within 30 min.[37] As represented by this model, a single exposure to psychological stress induces a transient, monophasic increase in Tc, known as psychological stress-induced hyperthermia (PSH). Existence of PSH has been observed not only in rats and mice but also in rabbits,[40,41] tree shrews,[42,43] sheep,[44] squirrels,[45,46] chimpanzees,[47] impalas,[48] Pekin ducks,[49] and pigeons.[50]

Psychological or emotional stress increases Tc via mechanisms that are distinct from fever that animals develop when they suffer from infectious and inflammatory diseases (for review, see).[51,52] Infection- and inflammation-induced fever is induced when PGE_2 acts on neurons in the preoptic area of the hypothalamus (POA).[53,54] When animals suffer from infectious diseases, fever is initiated by the release of brain-permeable PGE_2 from hepatic and pulmonary macrophages.[55,56] Macrophages also release proinflammatory cytokines such as interleukin-1β and interleukin-6 and these cytokines stimulate synthesis and release of acute phase proteins such as C-reactive protein (CRP) from hepatocytes. Furthermore, macrophage-derived proinflammatory cytokines stimulate synthesis of PGE_2 from endothelial cells of the brain vessels[57,58] or perivascular cells[59] and cause prolonged fever.[60,61] Activation of the dorsomedial hypothalamus (DMH)–medullary raphe region (including the rostral raphe pallidus and adjacent raphe magnus nuclei)–sympathetic (hypothalamic-medullary-sympathetic, HMS) axis increases Tc by activating β3-adrenoceptor-mediated non-shivering thermogenesis in brown adipose tissue (BAT) and α-adrenoceptor-mediated peripheral vasoconstriction to inhibit heat loss.[62,63] Stimulation of the DMH and the medullary raphe region also induces shivering thermogenesis in skeletal muscles.[64-66] Usually, the POA sends tonic inhibitory input to the HMS axis. PGE_2 causes fever by inhibiting the POA neurons, i.e., by disinhibiting the HMS axis.[67-69] Consequently, fever is attenuated by nonsteroidal antiinflammatory drugs (NSAIDs), which block PGE_2 synthesis (**Fig. 4**).

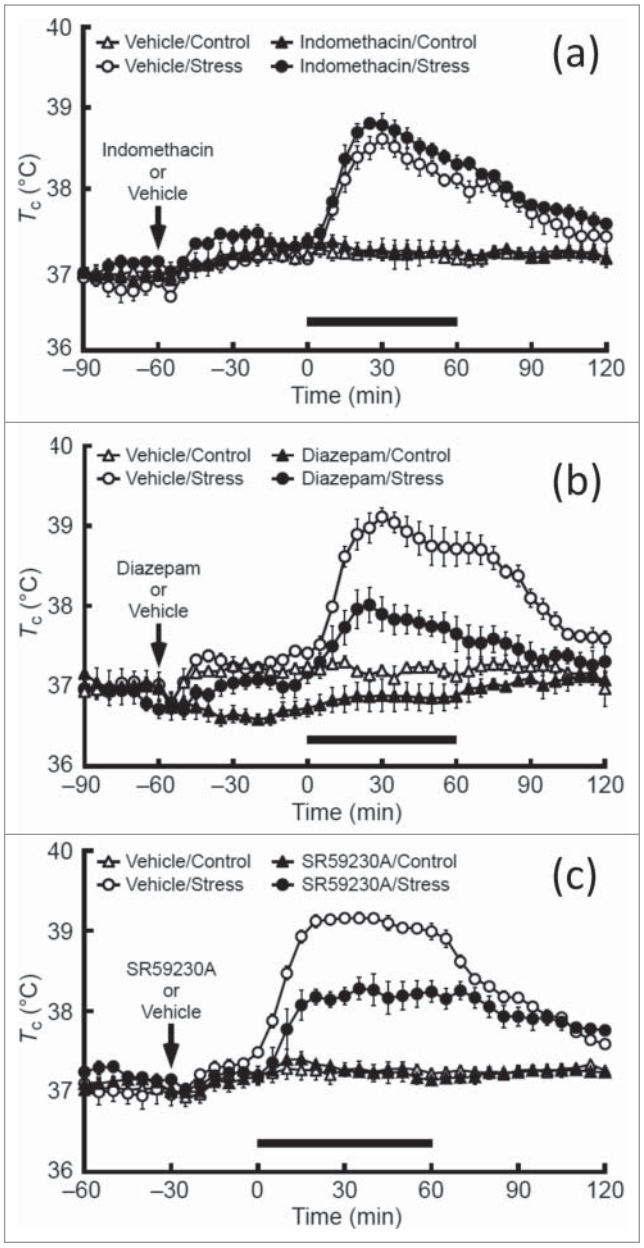

Figure 3. Effects of indomethacin (**A**), diazepam (**B**), and SR59230A (**C**), on social defeat stress-induced hyperthermia in rats. Rats received an intraperitoneal injection of indomethacin, a cyclooxygenase inhibitor (5 mg/kg), diazepam, an anxiolytic drug (4 mg/kg), SR59230A, a β3-adrenoceptor antagonist (5 mg/kg), or their respective vehicles at the time point indicated by arrows and were subsequently exposed to social defeat stress (Stress) or left undisturbed (Control) during the period indicated by the horizontal bars.

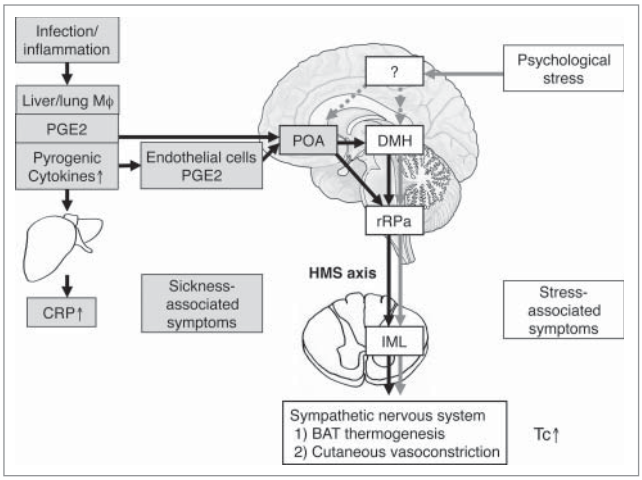

Figure 4. Possible mechanisms of psychological stress-induced hyperthermia in comparison with infectious fever. Infectious fever is induced by warmth-seeking behavior and shivering thermogenesis of the skeletal muscles, as well as sympathetic nerve-mediated non-shivering thermogenesis in brown adipose tissue and peripheral vasoconstriction. The HMS axis is known to mediate both sympathetic activation and shivering. In contrast, the brain region responsible for warmth-seeking behavior is currently unknown. Evidence suggests that neither the POA nor the DMH mediate warmth-seeking behavior.[129] Infectious/inflammatory fever is accompanied with elevated acute-phase proteins such as CRP and sickness behavior. By contrast, psychological stress increased Tc without accompanying sickness-related symptoms because it increases Tc via cytokines and PGE_2-independant manner. So far, it is not known how psychological stress activates the DMH neurons to increase Tc or how the POA and other brain regions are involved in the psychological stress-induced hyperthermia. BAT, brown adipose tissue; CRP, C-reactive protein; DMH, dorsomedial hypothalamic nucleus; HMS, hypothalamic-medullary-sympathetic; IML, intermediolateral cell column; IL, interleukin; Mϕ, macrophage; PG, prostaglandin; POA, preoptic area; rRPa, rostral raphe pallidus nucleus; Tc, core body temperature.

By contrast, recent studies have demonstrated that acute psychological stress also activates the HMS axis and increases Tc,[37-39,70-72] albeit via proinflammatory cytokine- and PGE_2-independent mechanisms.[27,37,38,72,73] Therefore, systemic administration of cyclooxygenase inhibitors, such as indomethacin, do not inhibit PSH,[33,52] while anxiolytic drugs such as diazepam or 5-HT_{1A} agonists[74-76] and β3-adrenoceptor antagonists, such as SR59230A, do attenuate PSH (**Fig. 3**).[37] Other brain regions, such as the prefrontal cortex,[77] the POA,[78,79] the medial amygdala,[80] or the lateral habenula,[81] in addition to orexin neurons[82] are also suggested to be involved in the development of PSH. However, so far, it is not fully understood how psychological stress activates DMH neurons or how other brain regions affect the HMS axis during psychological stress.

Effects of Repeated and Chronic Stress on Tc

Regardless of the source of stress, acute PSH is represented by a transient, monophasic increase in Tc, and the high Tc returns to baseline levels within several hours if the stressor is terminated. In contrast, repeated or chronic exposure to psychological stress has complex effects on Tc. First, repeated exposure to uncontrollable stressors such as daily confrontation with a dominant rat at fixed time intervals induces anticipatory or learned hyperthermia,

i.e., Tc becomes higher during the hour preceding the scheduled time of stress application or during the hour when animals have been exposed to dominant rats even if they are kept in their home cages without stress exposure.[36,83,84] Second, repeated application of stressors (for more than several weeks) either reduces diurnal changes in Tc, mostly by increasing Tc in the light (inactive) period,[85] or slightly increases Tc (around 0.2–0.3°C) throughout the day.[36,86] Third, repeated or chronic stress enhances the magnitude of the hyperthermic effect induced by a novel stressor[87] or intravenous administration of noradrenaline (NA).[88] Fourth, these rats display depressive-like behavior rather than increased anxiety-like behavior.[36,89] Fifth, these changes can be observed even several days after cessation of the final stress exposure.[36,85,86]

Hyperthermic responses in rats exposed to repeated or chronic stress do not seem to be induced by exactly the same mechanisms as acute PSH. First, the hyperthermic response during conditioned fear does not appear to involve activation of BAT.[90] Contextual conditioned fear does not induce the expression of Fos, a marker of neuronal activation, in the DMH, but does increase Fos in spinally projecting neurons in the perifornical area of the hypothalamus.[91] Second, after repeated immobilization, the magnitude of the NA-induced increase in Tc, interscapular BAT temperature, and oxygen consumption become greater in stressed rats versus controls.[88] As repeated immobilization stress induces interscapular BAT hyperplasia[92] and increases uncoupling protein 1 (UCP1), a protein that generates heat according to its expression and function[30] in BAT, these changes may lead to prominent PSH (**Fig. 5**).[92,93] Thirdly, psychological stress induces microglial activation[94-96] and subsequent proinflammatory cytokine production[97] in the central nervous system. As brain-derived cytokines also increase Tc[98,99] and induce depressive-like behavior,[100-102] there is a possibility that hyperthermia and depressive-like behaviors in rats exposed to chronic stress are mediated, at least in part, by activated microglia and subsequent proinflammatory cytokines within the brain. However, additional studies are necessary to make sure if this is the case.

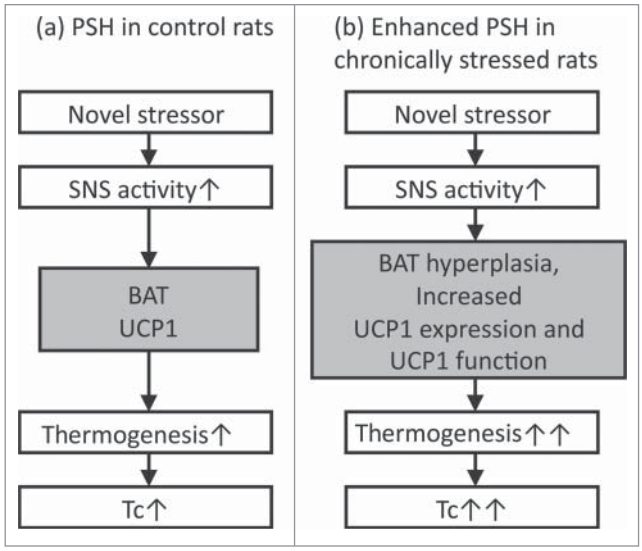

Figure 5. Possible mechanisms for enhanced psychological stress-induced hyperthermic response in chronically stressed rats. BAT, brown adipose tissue; SNS, sympathetic nervous system; Tc, core body temperature, UCP1, Uncoupling protein 1.

Stress-Induced Hyperthermia in Healthy Subjects

As in laboratory animals, psychological stress increases the Tc in healthy humans. Previous studies have demonstrated that Tc just before emotional events is higher than Tc after these events or at the same hour of the day under non-stressful conditions.[103-110] For example, the mean oral temperature before boxing contests (37.55°C) in 12 school boys (12–14 years old) was 0.8°C higher than that taken at home at the same hour of the day (36.75°C).[107] The mean oral temperature on movie-watching days in separate groups of females in their teens and twenties (37.55°C and 37.46°C) was 0.53°C and 0.27°C higher than that of the same hour on preceding or following days (37.03°C and 37.19°C), respectively.[104] The hyperthermic effect of examination stress is reported to be weaker than the effects of the emotional events described above. For example, the mean oral temperature of 40 subjects immediately before taking a nurses' registration examination (37.17°C) was 0.34°C higher than observed after the examination (36.83°C).[103] The mean axillary temperature of 22 residents (26 – 33 years old), 10 to 15 min before a yearly university examination (37.00°C), was 0.6°C higher than the temperature taken 2 to 3 weeks later after having sat and relaxed for at least 30 min (36.40°C).[108] The mean oral temperature of 108 medical students (18 – 27 years old) immediately before examination (37.4°C) was 0.18°C higher than what was taken at the same hour of the day 3 days after the exam (37.22°C).[109] The mean oral temperature of medical students (17 – 19 years old) 5 – 7 days before examination (36.91°C) was 0.17°C higher than that at the same time 5 – 7 days after the examination (36.74°C).[110] In contrast, one study demonstrated that exposing healthy subjects to a standardized laboratory stress task (the Trier Social Stress Test) did not change temporal artery temperature and also decreased intestinal temperature, both of which are assumed to reflect Tc.[111]

Psychogenic Fever

In 1930, Falcon-Lesses[18] made precise descriptions of a 20-year-old woman who exhibited a high oral temperature around 37.8°C when she visited the clinic but a normal temperature at home. Her temperature increased following venipuncture, a visit by physicians, or vaginal examination in the hospital as well as during arguments with her sister at home. For example, venipuncture increased her Tc from 36.61°C to 37.39°C (a 0.78°C increase), occurring within 5 min. Falcon-Lesses termed these stress-induced hyperthermic responses of this patient "psychogenic fever."

Psychogenic fever is comprised of several subtypes in terms of magnitude and duration. I would like to describe some

patients I have treated. **Fig. 1** indicates an acute onset, short-lasting, prominent psychogenic fever in a 15-year-old schoolgirl. Like this case, some patients develop a high Tc abruptly (up to 41°C) when they are exposed to emotional events. She repeatedly developed an antipyretic drug-resistant high axillary temperature around 39°C only on the days when she went to school (underlined black bar) that returned to around 36.5°C after coming back home and remained normal on days when she stayed at home. There were no inflammatory signs even when she exhibited a high temperature. The fever was not factitious, either. She was a courteous, obedient, and good girl. Via diagnostic interview, she said she wanted to go to school but felt very tense and sad at school because some classmates teased and bullied a friend who had a physical handicap. She hated to see it, but could not do anything. While she wanted to stay at school even when she had a high temperature, she gradually felt hotter and fatigued as her temperature increased. Consequently, her school nurse regularly asked her to go home or to the hospital. Eventually, she changed to another school. Thereafter, her "school fever" disappeared. In addition to the emotional events that provoke negative affect such as anxiety, anger, or fear, other psychological stressors that induce remarkable hyperthermia include separation from nurturing persons (emotional deprivation)[1,19] and suppression of negative emotion.[3] Stress interviews, i.e., recalling and talking about stressful life events, also increases Tc (**Fig. 6**).[13,14]

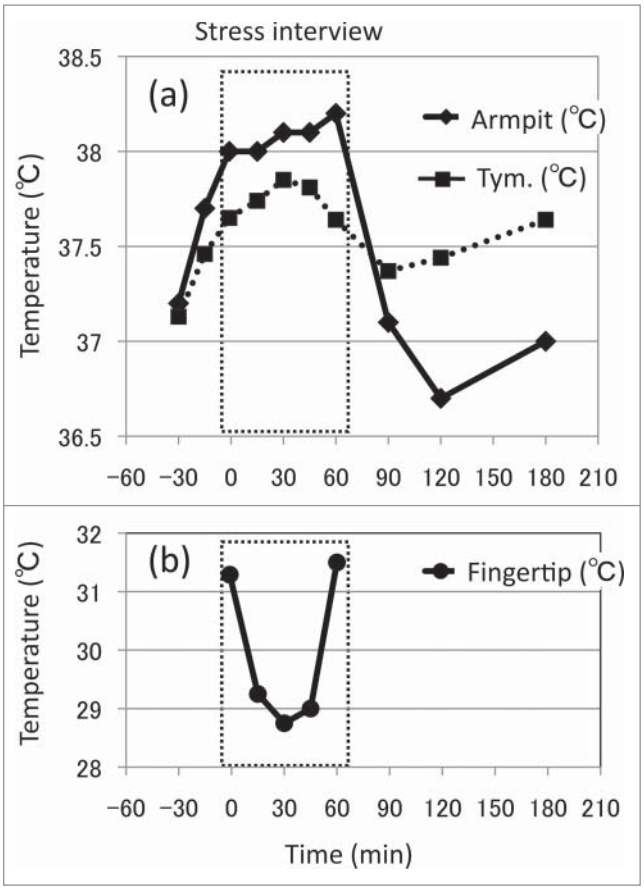

Figure 6. Effects of stress interview on core and peripheral temperatures in a 26-year-old CFS patient. Changes in axillary (armpit) and tympanic membrane (tym.) temperatures (**A**) and fingertip temperature (**B**) during and after a 60-minute stress interview. Stress interview was conducted for one hour (0 min – 60 min). © BioMed Central. Reproduced by permission of BioMed Central. Permission to reuse must be obtained from the rightsholder.

In contrast, other patients show a persistent low-grade fever (37–38°C) lasting months and even years, either during or after situations of chronic stress. **Figure 2** shows the chronic psychological stress-associated, persistent low-grade high Tc observed in a 56-year-old head rheumatology nurse. She suffered from NSAIDs- and adrenocorticosteroid-resistant, low-grade (37–38°C) high Tc for more than 3 months. Her doctor, a rheumatologist, conducted thorough medical tests but could not discern any findings to account for her fever. For diagnostic purposes, the doctor asked her to take NSAIDs and corticosteroids, but they were ineffective in reducing her fever. Subsequently, she was referred to my outpatient clinic. Through a diagnostic interview, I realized that she was in a physically and psychologically demanding situation because of cumulative stressful life events at the time she noticed the low-grade high Tc in April. She had been working as a nurse for more than 30 years while at home taking care of her father with dementia in recent years. In January, she was shocked to hear that her younger sister was diagnosed with breast cancer. In March, one hospital nurse suddenly quit and the patient had to substitute for her and had to work an overnight duty as well. Her Tc showed diurnal changes but was 37.4–37.8°C in the afternoon. There were no inflammatory signs accounting for her high Tc. Although it was just a slightly elevated Tc, she felt strong discomfort and increased fatigue when the Tc increased above 37.0°C. Therefore, she was suspended from her job. However, even after taking sufficient time off for recuperation for more than 3 months, her high Tc did not decrease until she began to take paroxetine, a selective serotonin reuptake inhibitor (SSRI).[112]

Certain forms of psychogenic fever have been given additional labels, e.g., prolonged low-grade high Tc in nervous patients has been termed "habitual hyperthermia"[113] and abrupt increases in Tc in hysterical patients was previously called "hysterical fever."[114,115]

Differences Between PSH in Healthy Subjects and Psychogenic Fever

The clinical significance of high Tc in patients with psychogenic fever is different from PSH in healthy subjects in several ways.[116] Remarkable differences include the magnitude of increase in Tc and the associated symptoms. First, in healthy subjects, although emotional events increase Tc, its magnitude is <1°C and the maximal Tc they show is <37.5°C in most cases.[103-110] By contrast, in some patients with psychogenic fever, emotional events increase Tc to 39–41°C (**Fig. 1**).[4,6,8] Such differences may arise according to the severity of stressors. However, as was shown in animal studies, it is also possible that chronic

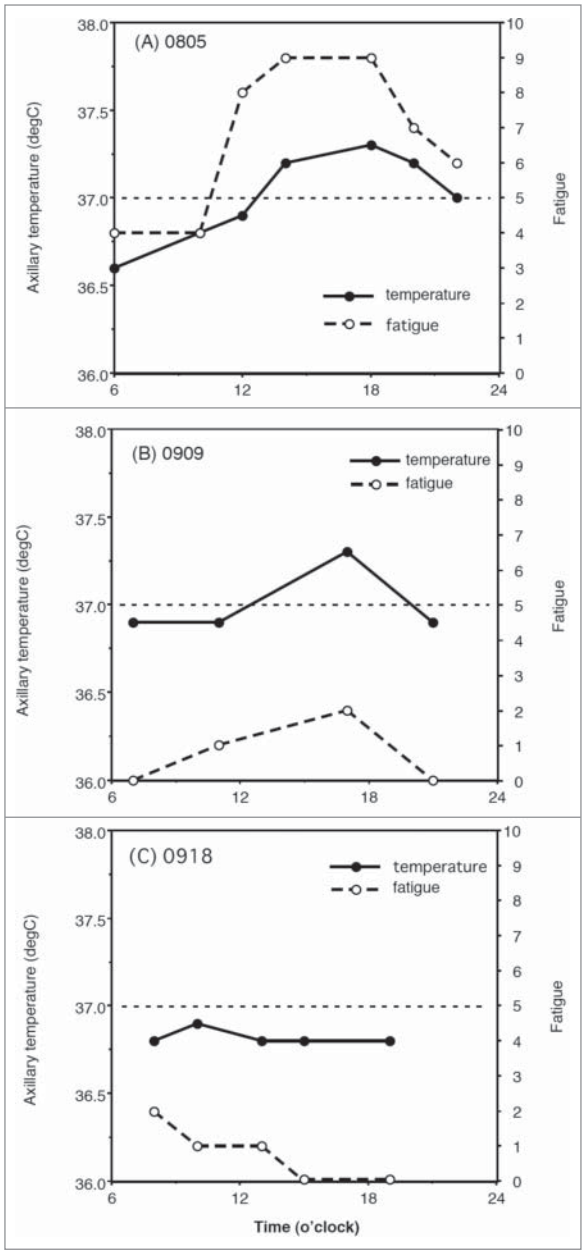

Figure 7. Inhibitory effects of tandospirone, a 5-HT1A receptor agonist, on the axillary temperature (Ta) and severity of fatigue in a 30-year-old woman with psychogenic fever. Vertical lines show axillary temperature (black line) and fatigue level (dotted line, with numerical rating scale in which 10 represents the most severe fatigue imaginable and 0 represents none). (**A**) Before the treatment (August 5th), (**B**) After tandospirone treatment Sep. 9th, and (**C**) After tandospirone treatment Sep. 18th. The patient started to take tandospirone, a 5-HT1A agonist, 30 mg from Sep. 2nd and 60 mg from Sep. 9th. © Japanese Society of Psychosomatic Internal Medicine. Permission to reuse must be obtained from the rightsholder. Before the treatment, as her Ta induced 0.5°C increased from 36.8°C to 37.3°C, her fatigue level increased remarkably from 4 to 9. She asked for the treatment of her low-grade fever hypochondriacally (**A**). However, after the treatment with tandospirone, she became less concerned about her low-grade fever, when although her Ta increased from 36.8°C to 37.3°C, her fatigue level increased from just 1 to 2 (**B**). Her Ta did not exceed 37°C (**C**).

stressors that the patient has experienced cause the induction of a prominent hyperthermic response when the patient is exposed to emotional events. Second, healthy subjects do not complain of symptoms even when they exhibit high Tc. By contrast, although some patients have no complaints except for the high Tc, others complain of numerous symptoms in addition to high Tc. These symptoms include insomnia, fatigue, headache, nausea, and/or abdominal pain. As increases in Tc are frequently associated with these symptoms (**Fig. 7**), patients consider the high Tc disabling. Some patients are neurotic and have high anxiety.[20] Psychogenic fever is also observed in patients who have traumatic experiences in their early lives[115] and with psychiatric disorders such as anxiety (panic and post-traumatic stress) disorders,[8] mood (depressive and bipolar) disorders,[7,11] somatoform (conversion) disorders,[115] catatonia,[5,117] and borderline personality disorders.[6] For these reasons, they worry about their high Tc and may consult their physicians asking for treatment.

Low-Grade Fever in Patients with Chronic Fatigue Syndrome and Fibromyalgia Syndrome

Patients with chronic fatigue syndrome (CFS) and fibromyalgia syndrome (FMS) also exhibit low-grade fever of unknown causes.[14,118] It is well known that psychological stress exacerbates their symptoms, and this may be the case with their low-grade fever. For example, some patients show "workday hyperthermia," i.e., higher Tc on working days compared with holidays.[14] **Figure 8** shows the record of Tc and severity of fatigue of a 24-year-old woman having both CFS and FMS. It demonstrates that her Tc and fatigue scores were higher during working days compared to days off. As she was a telephone operator, she remained sitting almost all day but kept concentrating on numerous phone conversations. Therefore, the higher Tc may not be due to increased activity during the working day, but due to psychological strain.

Another example is the remarkable psychological stress-induced hyperthermic response in these patients. A 26-year-old female nurse with CFS noticed that her Tc became higher (up to 38.5°C) when she felt stressed at work. To investigate the mechanisms for her PSH, we conducted a 60-minute stress interview, in which we asked her to recall and talk about her difficult life.[14] Her Tc at baseline was 37.2°C, and increased to 38.2°C (a 1.0°C increase) by the end of the interview. In contrast, her fingertip temperature decreased during the interview (**Fig. 6**). During the stress interview, blood levels of pyretic cytokines, such as IL-1β and IL-6, or antipyretic cytokines, such as TNF-α and IL-10, did not change but heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and plasma levels of NA and adrenaline (A) increased. These results suggest that stress interview-induced hyperthermia is not mediated by pyretic cytokine production but by emotional expression-associated sympathetic activation. Considering these findings on the effects of chronic stress on acute PSH in animals, it is possible that the patient's difficult daily life acts as a chronic stressor, leading the patient to exhibit robust increases in Tc when she/he is exposed to emotional events.

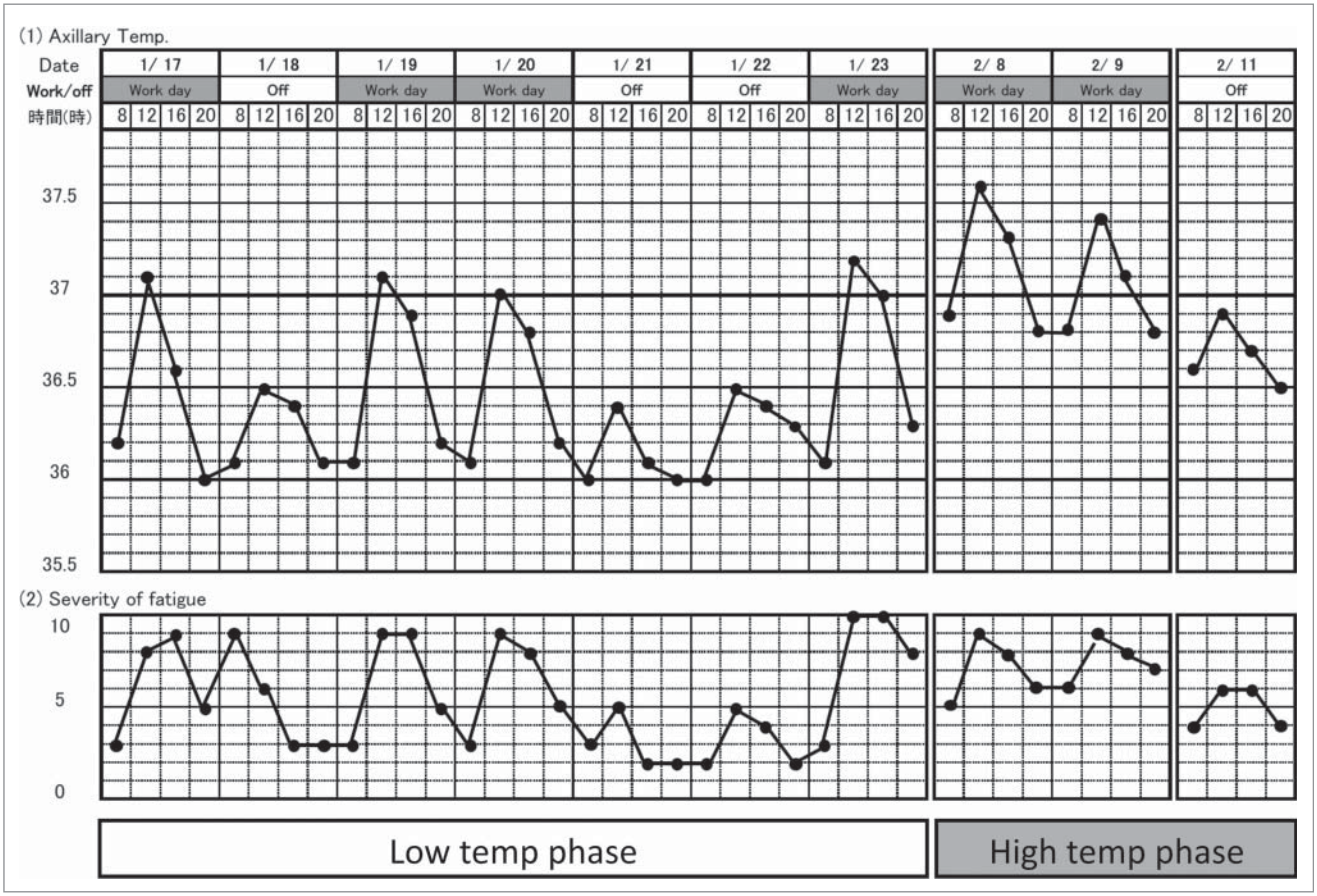

Figure 8. Fever and fatigue chart recorded by a 24-year-old patient with chronic fatigue syndrome and fibromyalgia syndrome. She worked as a telephone operator, a sedentary job. This chart tells that her axillary temperature is higher on the workday than on a day-off, showing that "workday hyperthermia" and the increase in axillary temperature is associated with increased fatigue. Reprinted from Advances in Neuroimmune Biology, Vol 4, Oka T, Influence of psychological stress on chronic fatigue syndrome, Pages 301-9. © IOS Press. Reproduced by permission of IOS Press. Permission to reuse must be obtained from the rightsholder.

How Does Psychological Stress Increase Tc in Humans?

Animal studies have demonstrated that psychological stress increases Tc via PGE_2- and proinflammatory cytokine-independent mechanisms. This seems to be the case in patients with psychogenic fever. First, NSAIDs do not attenuate the high Tc in these patients. Second, stress interview-induced hyperthermia is not associated with changes in blood levels of PGE_2 or proinflammatory cytokines.[13,14]

In rodents, BAT thermogenesis plays a crucial role in the development of PSH. In humans, BAT is distributed exclusively in an interscapular region in infants[119] and in thyroid/tracheal, mediastinal, paracervical/supraclavicular, parathoracical, supra- and peri-renal regions in adults.[120-123] As in rodents, BAT induces non-shivering thermogenesis when humans are exposed to a cold environment. Therefore, it is possible that psychological stress increases Tc via sympathetic nerve-mediated non-shivering thermogenesis in BAT in humans as well. Recently, the author found that patients with psychogenic fever exhibit greater HR response to orthostatic stress and increased prevalence of postural orthostatic tachycardia syndrome, one form of orthostatic intolerance, compared with healthy subjects,[124,125] suggesting a heightened sympathetic response to stress in patients with psychogenic fever. This might account for prominent hyperthermic responses to stressful events in patients with psychogenic fever. However, a role of BAT in PSH in healthy subjects or high Tc in patients with psychogenic fever has not yet been elucidated.

Previous clinical case reports have demonstrated that patients who exhibit persistent low-grade high Tc were treated successfully with drugs that produce sedative effects such as opium[113] or phenobarbital,[6,7] serotonergic tricyclic antidepressants such as amitriptyline and clomipramine,[8,126] SSRIs such as paroxetine (**Fig. 2**),[112] or serotonin 1A receptor agonists such as tandospirone (**Fig. 7**).[127] Furthermore, relaxation training,[8,12] solving their difficulties, and psychotherapy to ventilate suppressed negative emotion and conflicts verbally[6,115] or non-verbally[10] are also helpful strategies.

About the Name "Psychogenic Fever." Why not "Functional Hyperthermia?"

I propose to call psychological stress-associated high Tc "functional hyperthermia" instead of psychogenic fever. This is

in part because psychological stress-associated high Tc is induced by mechanisms distinct from infection/inflammation-associated fever, where proinflammatory mediators play a pivotal role. Furthermore, "psychogenic" sounds stigmatic for some patients and their families. I do not want to call their high Tc emotional hyperthermia, either, because it sounds like a physiological response, which does not require treatment. I prefer to call it functional because in the clinical setting the naming of diseases including the term "functional," such as functional dyspepsia, functional gastrointestinal disorders, or functional somatic syndrome, connotes both stress-related pathology and impaired functioning of the autonomic nervous system.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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About the Author

Takakazu Oka *is a physician specializing in psychosomatic medicine. He exclusively treats patients with psychosomatic diseases, i.e., physical diseases and conditions affected by psychosocial factors. One such disease is psychogenic fever. When he was a resident in psychosomatic medicine and internal medicine, he met some patients with fever of unknown causes that developed during highly stressful situations. In spite of repeated and thorough medical tests, abnormal findings were not detected and antipyretic drugs failed to attenuate their high body temperature. However, their high temperature was normalized after psychotherapy sessions. Since then, he has been conducting basic research on the mechanisms of psychogenic fever as well as seeing patients as a clinician.*

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