Received: 30 May 2023 | Revised: 16 August 2023 | Accepted: 21 August 2023

DOI: 10.1002/pcn5.140

ORIGINAL ARTICLE

PCN Reports Psychiatry and Clinical Neurosciences Open Access

Hyperthymic temperament predicts neural responsiveness for nonmonetary reward

Yukiko Ogura PhD[1] | Yumi Wakatsuki MD, PhD[2] | Naoki Hashimoto MD, PhD[3] | Tamaki Miyamoto MD, PhD[3] | Yukiei Nakai PhD[4] | Atsuhito Toyomaki PhD[3] | Yukio Tsuchida PhD[5] | Shin Nakagawa MD, PhD[6] | Takeshi Inoue MD, PhD[7] | Ichiro Kusumi MD, PhD[3]

[1]Center for Experimental Research in Social Sciences, Hokkaido University, Sapporo, Japan

[2]Department of Psychiatry, The Hokkaido Medical Center, Sapporo, Japan

[3]Department of Psychiatry, Hokkaido University Graduate School of Medicine, Sapporo, Japan

[4]New Drug Research Center Inc., Hokkaido, Japan

[5]School of Education, Osaka University of Health and Sport Sciences, Osaka, Japan

[6]Division of Neuropsychiatry, Department of Neuroscience, Yamaguchi University Graduate School of Medicine, Yamaguchi, Japan

[7]Department of Psychiatry, Tokyo Medical University, Tokyo, Japan

Correspondence

Naoki Hashimoto, MD, PhD, Department of Psychiatry, Hokkaido University Graduate School of Medicine, Kita 15, Nishi 7, Kita-ku, Sapporo 060-8638, Japan.
Email: hashinao@med.hokudai.ac.jp

Funding information

Japan Society for the Promotion of Science, Grant/Award Numbers: JP14J08054, JP25860981

Abstract

Aim: Hyperthymic temperament is a cheerful action orientation that is suggested to have a protective effect on depressive symptoms. We recently reported that hyperthymic temperament can positively predict activation of reward-related brain areas in anticipation of monetary rewards, which could serve as a biomarker of hyperthymic temperament. However, the relationship between hyperthymic temperament and neural responsiveness to nonmonetary rewards (i.e., feedback indicating success in a task) remains unclear.

Methods: Healthy participants performed a modified monetary incentive delay task inside a functional magnetic resonance imaging scanner. To examine the effect of nonmonetary positive feedback, the participants performed feedback and no-feedback trials. We explored brain regions whose neural responsiveness to nonmonetary rewards was predicted by hyperthymic temperament.

Results: There was premotor area activation in anticipation of a nonmonetary reward, which was negatively predicted by hyperthymic temperament. Moreover, brain areas located mainly in the primary somatosensory area and somatosensory association area were activated by performance feedback, which was positively predicted by hyperthymic temperament.

Conclusion: We found that hyperthymic temperament is related to neural responsiveness to both monetary and nonmonetary rewards. This may be related to the process of affective regulation in the somatosensory area.

KEYWORDS

fMRI, hyperthymic temperament, major depressive disorder, monetary incentive delay, somatosensory area

INTRODUCTION

To identify risk factors for and predict the prognosis of psychiatric disorders, affective temperaments, which represent the temporally stable biological "core" of personality,[1] have been described by Akiskal et al.[2–4] Among them, hyperthymic temperament represents a cheerful, upbeat, and action-oriented disposition.[2,3] The other temperaments (i.e., depressive, cyclothymic, irritative, and anxious) described by Akiskal et al.[4,5] have depressive components to some extent.[6] Contrastingly, hyperthymic temperament is suggested to have a protective effect on depression,[7] with its biological uniqueness being further demonstrated by studies on the genetic background of affective temperaments.[8,9]

Recently, we reported that hyperthymic temperament is positively correlated with neural responsiveness to monetary rewards in the dorsal striatum and thalamus.[10] This finding could serve as a biomarker for hyperthymic temperament, and in the context of previous reports that neural responsiveness to rewards is reduced in depression,[11,12] we have elucidated part of the neurobiological foundation for the protective nature of hyperthymic temperament against depression. This is also consistent with a previous report that hyperthymic temperament is positively correlated with reward dependence.[5] However, research on the neurobiological substrates underlying protective characteristics against depression in individuals with higher hyperthymic temperament has only just begun, leaving much to be further investigated.

Monetary rewards are not the only type of reward. Generally, the term "rewards" refers to stimuli that induce subjective pleasure feelings and contribute to positive emotions, and to what act as positive reinforcers by increasing the frequency and intensity of behavior that leads to the acquisition of goal objects.[13] Therefore, cognitive constructs, such as novelty, challenge, beauty, acclaim, power, territory, and security, constitute cognitive rewards.[13] It is important to determine whether positive nonmonetary feedback after performing a motor task can be considered a reward.

Schneider et al.[14] modified the monetary incentive delay (mMID) task,[15] which is commonly used to examine neural activation following monetary and other types of rewards. Specifically, they set monetary and nonmonetary reward trials. In monetary reward trials, a monetary reward is acquired through a motor response during the onset of a visual stimulus, which is similar to the original monetary incentive task. In nonmonetary reward trials, visual feedback indicating success is provided after an appropriate motor response; however, no monetary reward is delivered. Schneider et al.[14] reported pupillary dilation in response to cue stimuli in nonmonetary reward trials even though it was not as much as in monetary reward trials; moreover, it was accompanied by activation in the salience network and attention-related brain regions. This physiological response was not observed in control trials that only involved a motor response without performance feedback.

Martin-Soelch et al.[16,17] also conducted an mMID task and compared regional cerebral blood flow using positron emission tomography between monetary and nonmonetary reinforcement trials. In the nonmonetary reinforcement trials, visual feedback was given to indicate success after a correct response, similar to the nonmonetary reward trials in Schneider et al.[14] Healthy participants showed increased regional cerebral blood flow in numerous reward-related areas, including the caudate and putamen, in the monetary reward condition. In the nonmonetary reinforcement trials, regional cerebral blood flow also increased in reward-related areas, including the midbrain and orbitofrontal cortex. Contrastingly, individuals with addiction, who are considered to have deficits in the dopaminergic transmission system, showed increased regional cerebral blood flow only in monetary reward trials. This indicates that neural responsiveness to nonmonetary rewards may be selectively impaired in individuals with deficits in the dopaminergic transmission system. Moreover, individuals with major depressive disorder (MDD), who have a lower hyperthymic temperament than healthy controls,[18] exhibit dopaminergic dysfunction.[19,20]

In summary, these previous studies suggest that nonmonetary rewards also elicit physiological and neural responses that may be similar to, but neurobiologically different from, those of monetary rewards. Therefore, in order to elucidate the neurobiological substrate of hyperthymic temperament, it is important to examine its relationship with neural responses to both monetary and nonmonetary rewards.

Accordingly, we aimed to conduct functional magnetic resonance imaging (fMRI) measurements during an mMID task in order to explore the relationship between hyperthymic temperament and neural responsiveness to nonmonetary rewards. In the mMID task, we conducted nonmonetary reward trials with and without positive feedback, with the contrast between these trials being considered as the neural responsiveness to nonmonetary reward. We hypothesized that neural responsiveness to nonmonetary rewards is positively predicted by hyperthymic temperament.

METHODS

Participants

We included the same participants enrolled in our previous study.[10] All participants included in the analysis satisfied the following criteria: (1) completed the study questionnaires (details provided below); (2) aged 20–35 years (to avoid the effect of aging[21,22]); (3) right-handed (i.e., with a positive Edinburgh Handedness Inventory score[23]); (4) no metabolic syndromes; (5) no structural deficits (e.g., calcification); (6) no serious distortion in functional images; and (7) no symptoms or history of any psychiatric disorders. Current psychiatric disorders were screened according to ICD-10 by psychiatrists with at least 5 years of clinical experience. Depressive and manic episodes were screened using the Japanese version of the Patient Health Questionnaire (PHQ)-9[24,25] and the Manic Episode Screening Questionnaire (MES),[26] respectively. Accordingly, all the analyzed participants were classified as psychiatrically healthy. The experiments were conducted following the Declaration of Helsinki[27] and

were approved by the Institutional Review Board of Hokkaido University Hospital (#010-0031).

Behavioral tasks

For the main task, we used an mMID task[28] identical to that in our previous report.[10,29] At the onset of the trial, a numeric cue ("500," "100," "−100," "0," or "[0]") was presented for 2000 ms. The cue indicated the monetary reward (in Japanese yen) that participants would receive if they succeeded in following the button press. The "0" represents the absence of monetary reward, while a "hit" or "miss" feedback is provided (Figure 1a). The "[0]" represents the absence of monetary reward, consistently associated with the presentation of a "miss" outcome, thereby no "hit" or "miss" feedback was given (Figure 1b). Following the presentation of a fixation cross (for 1500–2500 ms), a target indicated by a white square was presented. Subsequently, an outcome was presented for 2000 ms. When participants successfully pressed the button during the target presentation ("hit"), the acquired reward was presented in the upper line in white color. When participants failed to press the button during the target presentation ("miss"), the number zero was presented in the upper line in blue. The cumulative sum of obtained reward within each session was presented in the bottom line in white. Following a rest interval (500–2100 ms), the next trial was initiated, with each trial lasting 8 s. Participants were instructed about the numeric cues and understood the association between numeric cues and outcomes through the practice trials. Note that participants were instructed to try to "hit" the target regardless of the trial type and we still recorded whether participants pressed the button during the target presentation even in the "[0]" trials, as in the other trial types.

The present study focused on differences in responsiveness between the 0 and [0] trials. The effect of monetary reward has been described in a separate paper.[10]

To modulate and maintain hit rates of ≈ 60%–70%, the duration of the target presentation was initially set and adjusted through trials in a predetermined manner. For further details, please see Ogura et al.[10]

The main task comprised two runs, which each comprised 50 trials. Each cue type was pseudorandomly presented 10 times in each run. Thus, the participants completed 20 trials per trial type.

Functional MRI data acquisition

Structural and functional MRI data were acquired using a Siemens 3T Prisma scanner equipped with a 64-channel head coil. Prior to the main task, T1-weighted images were acquired using a magnetization-prepared rapid gradient-echo sequence. Second, to address geometric and intensity distortion of functional images, phase and magnitude maps were acquired using a gradient echo (GRE) field map sequence. Functional imaging was performed as the main task. Echo-planar images (EPIs) were obtained using a GRE sequence. Based on the anatomical information derived from the T1 image, the EPI field of view was tilted 30° to the forehead from the anterior commissure–posterior commissure plane to encompass the whole brain and minimize susceptibility artifacts in the orbitofrontal cortex.[30] Details of the scanning parameters can be found in Ogura et al.[10] Two hundred and eight volumes were acquired for the mMID task, while 60 volumes were acquired for the finger-tapping task.

The responses to a target were detected using response pads manufactured by Current Designs Inc. (HHSC-1×4-D or HHSC-2×4-C).

Functional MRI data preprocessing

The data were preprocessed in the following sequential steps: (1) field mapping, (2) spatial realignment and unwarping, (3)

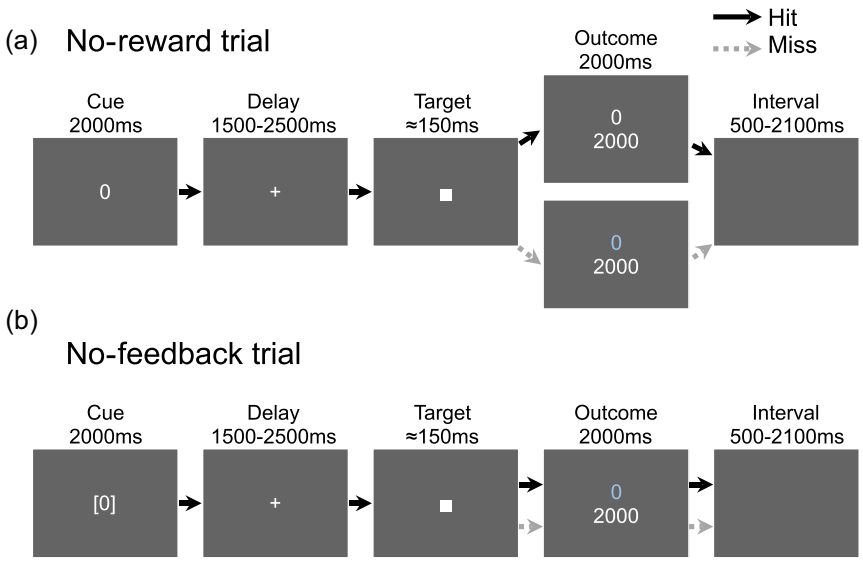


FIGURE 1 The modified version of the Monetary Incentive Delay task. (a) In the beginning of the No-reward trial, a numeric number "0" was presented, with the participant not getting any monetary reward. However, in the Outcome phase, they received feedback regarding whether they "hit" or "missed" the target based on the color of the "0" in the upper line (white for "hit" and blue for "miss"). (b) In the beginning of a No-feedback trial, a numeric number 0 in square brackets ("[0]") was presented, with the participant not receiving any monetary reward or feedback (a blue "0" was always displayed regardless of whether they "hit" or "missed" the target). However, we still recorded whether the participants "hit" or "missed" the target.

slice-timing correction, (4) spatial smoothing for individual images using a Gaussian filter (full width at half maximum [FWHM] = 4 mm), (5) motion correction, (6) removal and interpolation of global outlier volumes using adjacent nonoutlier volumes (outlier volumes were defined as rapid scan-to-scan motion >0.5 mm/TR or global signal intensity fluctuations >1.5%), (7) co-registering EPIs to the T1 image, (8) normalization to the EPI template (voxel-size resampled to $2 \times 2 \times 2$ mm^3), and (9) smoothing (FWHM = 8 mm). The preprocessing and analysis of the imaging data were performed using SPM12 (Version 6685; Wellcome Trust Centre for Neuroimaging, University College London, UK) and MATLAB (R2015b). For distortion and motion correction (steps [4] to [6]), the ArtRepair toolbox[31,32] and Alphascript (Version 2.0[33]; provided by F. Hoeft, personal communication, July 2014) were employed. Finally, a visual quality check of all the preprocessed images was performed using the FSLview software and Lin4Neuro Linux distribution.[34] Functional images displaying significant distortion even after the aforementioned motion correction and image repair were discarded.

Questionnaires

We employed the standardized Japanese version of the Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego Autoquestionnaire (TEMPS-A[4,35]) to evaluate temperament. Although it is capable of assessing five temperaments (depressive, cyclothymic, hyperthymic, irritable, and anxious), our focus was on hyperthymic temperament based on our previous study.[10] The questionnaire used to examine hyperthymic temperament consisted of 21 items, with responses of "Yes" and "No" assigned scores of 2 and 1, respectively, and the average score representing the temperament score.

Following the fMRI scan, the participants answered a post-experimental questionnaire, which assessed subjective pleasantness and tenseness associated with each monetary cue ("500," "100," "0," "[0]," and "−100") using a 7-point Likert scale ("extremely unpleasant" to "extremely pleasant" and "extremely calm" to "extremely tensed," respectively).

Statistics

Behavioral data

We obtained behavioral measures and questionnaire responses for two cue types ("0" and "[0]"). Regarding the behavioral measures, we computed the count of successful trials (hits) and the average response latency in those hit trials. The questionnaire responses were used to evaluate subjective levels of pleasantness and nervousness.

General linear model for fMRI data

In the first-level (individual) analysis, 15 task-related regressors were included: (1–5) cue presentation of "500," "100," "−100," "0," and "[0]"; (6–9) "hit" outcome presentation of "500," "100," "−100," and "0"; (10–13) "miss" outcome presentation of "500," "100," "−100," and "0"; (14) "no feedback" outcome (i.e., the outcome for cue "[0]"); and (15) button press. Furthermore, six regressors were included to account for head motion: x, y, z, pitch, roll, and yaw.

In the second-level (group) analysis, we performed one-sample *t* tests for whole-brain analysis ($p < 0.05$, family-wise error [FWE]-corrected) for three contrasts as follows: (1) cue phase comparison between "0" and "[0]," (2) outcome phase comparison of "hit" between "0" and "[0]," and (3) outcome phase comparison of "miss" between "0" and "[0]." Brain subregions demonstrating peak activations were identified using an atlas provided by Neuromorphometrics Inc.

Multiple regression for the beta value in extracted voxels by temperament scores

To examine the association between the activation levels for the aforementioned contrasts and temperaments, we performed multiple linear regressions using R (Version 4.2.0; https://www.r-project.org). The beta values from a 5-mm radius sphere centered on the peak of each contrast were extracted as responsive variables. Hyperthymic temperament scores, age, and sex ($M = 0$, $F = 1$) were used as explanatory variables. First, a linear model without interactions that comprised all explanatory values (full model) was assumed, and the Akaike information criterion (AIC) was calculated. Subsequently, we sequentially dropped one explanatory variable in a stepwise manner until the model with the lowest AIC was obtained.

RESULTS

The present study included 32 eligible participants (19 men and 13 women; mean age, 31.25 ± 2.76 years). This population was identical to the participants analyzed in our separate report.[10]

Behavior

Participants were significantly less successful in hitting a target in "0" trials compared with "[0]" trials (Supporting Information: Figure S1A; $Z = -4.33$, $p < 0.001$). There were no significant between-trial ("0" vs. "[0]") differences in the mean response latency (Supporting Information: Figure S1B; $t = -1.15$, $p = 0.258$). Further, the number of hit trials was not significantly correlated in the "0" or "[0]" trials with hyperthymic temperament ("0": $r = -0.24$, $p = 0.179$, "[0]": $r = -0.28$, $p = 0.117$). As previously reported,[10] the mean response latency in "0"

trials was not correlated with hyperthymic temperament (Supporting Information: Figure S2, upper: $r = -0.22$, $p = 0.226$). Contrastingly, the mean response latency in "[0]" trials showed a marginally significant correlation with hyperthymic temperament (Supporting Information: Figure S2, lower; $r = -0.34$, $p = 0.063$). Specifically, participants with higher hyperthymic temperament scores tended to have a shorter response latency in [0] trials. There were no significant between-trial differences in subjective pleasantness (Supporting Information: Figure S1C; $Z = 1.73$, $p = 0.250$) or subjective nervousness (Supporting Information: Figure S1D; $Z = -1.41$, $p = 0.500$). Hyperthymic temperament was not correlated with subjective pleasantness in the task ($r = 0.04$, $p = 0.832$) or indices for the overall task performance (mean presentation duration of the target: $r = -0.16$, $p = 0.387$; total reward amount: $r = 0.02$, $p = 0.922$).

Functional MRI and questionnaires

First, we set a threshold at $p < 0.05$ (FWE) and searched for significant peaks in each contrast. In the case of excessively large significant clusters ($k > 1000$), it was virtually impossible to extract peaks. Accordingly, we adopted progressively higher thresholds ($p < 0.01$, $p < 0.005$, $p < 0.001$, etc.) and adopted the threshold at which clusters with $k > 1000$ were not observed. Therefore, we adopted thresholds of $p < 0.05$, $p < 0.001$, and $p < 0.005$ (FWE corrected for each) for the "0" minus "[0]" in the cue phase, hit for "0" minus "[0]" in the outcome phase, and miss for "0" minus "[0]" in the outcome phase, respectively. Among the remaining peaks, we excluded peaks from the following regions since they were not of interest: the visual cortex, brainstem, diencephalon, cerebellum, and ventricle.

Anticipation phase 0 versus [0] contrast

Two peaks at the left superior frontal gyrus (SFG) and left precentral gyrus (preCG) remained in the contrast "0" minus "[0]" (Table 1). We examined whether the beta values of these two peaks could be predicted by the TEMPS hyperthymic score, age, and sex (Figure 2). Both selected models for the beta values at the right SFG and preCG comprised hyperthymic scores and sex variables. Beta values of both peaks were negatively predicted by the hyperthymic scores (left SFG: estimated coefficient = -1.00 ± 0.37, $p = 0.011$; left preCG: estimated coefficient = -0.95 ± 0.45, $p = 0.043$). Additionally, beta values of both peaks were smaller in men than in women (left SFG: estimated coefficient for men = -0.38 ± 0.14, $p = 0.010$; left preCG: estimated coefficient for men = -0.45 ± 0.17, $p = 0.011$).

TABLE 1 Brain areas activated by 0 (¥0 with feedback) − [0] (¥0 without feedback) contrast in the cue and outcome phases.

			MNI coordinates			Peak-level	Peak-level
	BA	*k*	*x*	*y*	*z*	T value	*p* value
Cue0-[0]							
Left precentral gyrus	6	21	−24	−10	62	6.17	0.014
Left superior frontal gyrus	6	2	−18	−8	62	5.71	0.042
Hit0-[0]							
Left postcentral gyrus	3	90	−28	−34	68	8.47	<0.0005
Left superior parietal lobule	5	9	−14	−54	62	7.67	<0.0005
Right supramarginal gyrus	1	41	52	−28	56	7.66	<0.0005
Right superior parietal lobule	40	1	38	−54	54	7.23	0.001
Miss0-[0]							
Left postcentral gyrus	3	145	−28	−34	68	8.39	<0.0005
Right superior parietal lobule	40	92	36	−54	56	8.09	<0.0005
Right supramarginal gyrus	1	122	52	−28	56	7.99	<0.0005
Left superior parietal lobule (medial)	5	65	−12	−54	62	7.90	<0.0005
Left superior parietal lobule (lateral)	40	81	−38	−50	54	7.07	<0.0005
Left precentral gyrus	6	4	−20	−20	74	6.51	<0.0005

Note: For outcome phases, hit trials and miss trials are separately described.

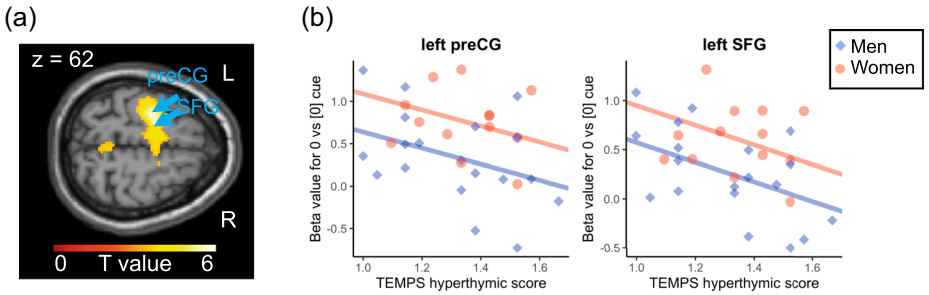


FIGURE 2 (a) Brain activations in response to 0-[0] contrast in the cue phase. The upper and lower arrows indicate the left precentral gyrus (preCG) and left superior frontal gyrus (SFG), respectively. For display purposes, the threshold is set at $p < 0.001$, uncorrected. (b) Plots and regression lines from the selected multivariate regression model. The *x*-axis denotes the TEMPS hyperthymic score, while the *y*-axis denotes parameter estimates of left preCG and left SFG activation for 0-[0] contrast in the cue phase. The regression lines are shown according to sex.

Outcome phase 0 versus [0] contrast

Hit for 0 versus feedback for [0] contrast

Four peaks in the right supramarginal gyrus (SMG), right superior parietal lobule (SPL), left postcentral gyrus (postCG), and left SPL remained (Table 1). We examined whether the beta values of the four peaks could be predicted by the TEMPS hyperthymic score, sex, and age. The selected model for the beta values at the right SMG, right SPL, and left postCG comprised hyperthymic scores (Figure 3; right SMG: estimated coefficient = 10.62 ± 4.93, $p = 0.039$; right SPL: estimated coefficient = 8.96 ± 4.17, $p = 0.040$; left postCG: estimated coefficient = 8.09 ± 3.50, $p = 0.028$). In contrast to the other peaks, beta values in the left SPL could not be predicted by hyperthymic temperament; the null model was selected for beta values at the left SPL.

Miss for 0 versus feedback for [0] contrast

Six peaks in the right SMG, right SPL, left postCG, left SPL (two peaks; lateral = lSPL and medial = mSPL), and left preCG remained (Table 1). We tested whether the beta values at the six peaks could be predicted by the TEMPS hyperthymic score, sex, and age. The beta value in the right SMG was positively predicted by hyperthymic temperament. The selected model for the beta values in the right SMG comprised hyperthymic scores (Figure 4; estimated coefficient = 11.02 ± 4.39, $p = 0.018$). Although the selected model for the beta values in the right SPL and left postCG comprised hyperthymic temperament, the *p* values for the coefficient were only marginally significant (Supporting Information: Figure S3; right SPL: estimated coefficient = 6.68 ± 3.77, $p = 0.087$; left postCG: estimated coefficient = 6.71 ± 3.60, $p = 0.073$). Contrastingly, the null model was supported for the beta values in the left mSPL and lSPL. The selected model for the beta values in the left preCG comprised hyperthymic scores and age (Supporting Information: Figure S3). However, the *p* value for the coefficient for hyperthymic scores was only marginally significant (estimated coefficient = 11.40 ± 6.28, $p = 0.080$), while that for age was not significant (estimated coefficient = −0.68 ± 0.42, $p = 0.115$).

DISCUSSION

To further examine the neural mechanisms underlying the protective effects of hyperthymic temperament on depression, this fMRI study examined brain regions related to nonmonetary rewards (i.e., positive feedback for motor performance) and modulated by hyperthymic temperament. Interestingly, in the anticipation phase, participants with low hyperthymic temperament had higher activity in the left SFG and left preCG, which are included in the premotor area. As expected, in the hit 0 versus feedback for [0] contrast of the outcome phase, hyperthymic temperament scores were positively correlated with the left postCG, right SMG, and right SPL. The left postCG and right SMG were included in the primary somatosensory cortex. The right SPL is located in the somatosensory association cortex. In the miss 0 versus feedback for [0] contrast of the outcome phase, hyperthymic temperament scores were positively correlated with the right SMG.

Implications for the neurobiological substrate underlying hyperthymic temperament

Areas activated by the contrast for anticipation of nonmonetary rewards were located in the premotor area, which partly form the dorsal attention network. Individuals with MDD have shown altered functional connectivity of the dorsal attention network.[36,37] Moreover, the dorsal attention network is involved in mental effort.[38] The observed negative correlation between premotor area activation by nonmonetary reward and hyperthymic temperament in the premotor area is apparently paradoxical. Participants with low hyperthymic temperament scores might require mental effort to work on tasks without monetary reward. Accordingly, the premotor area might be activated more in individuals with low hyperthymic temperament scores due to the compensatory reallocation of resources.[39]

Areas in the primary somatosensory cortex were activated by the contrast for feedback of nonmonetary rewards. Although the

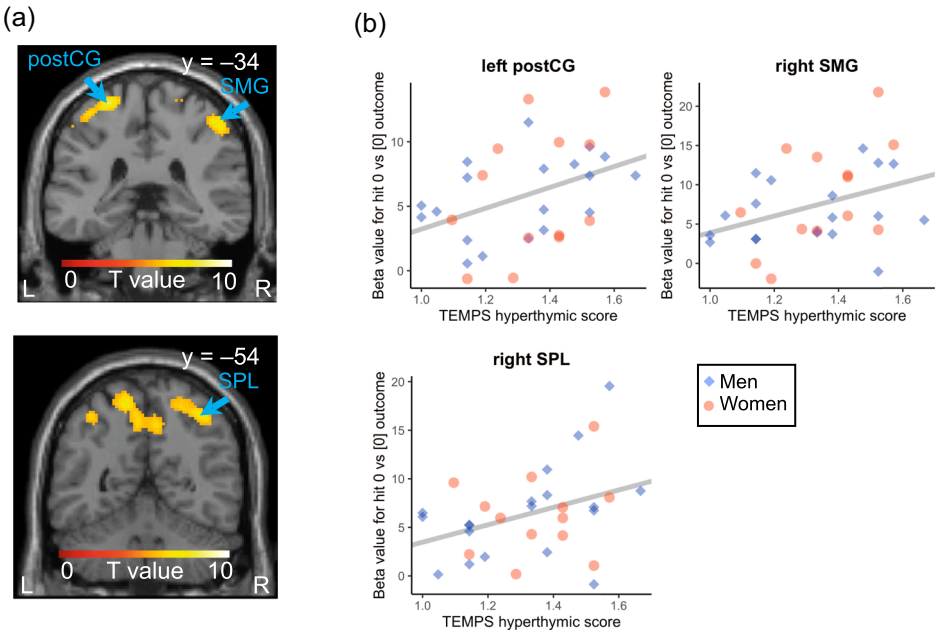
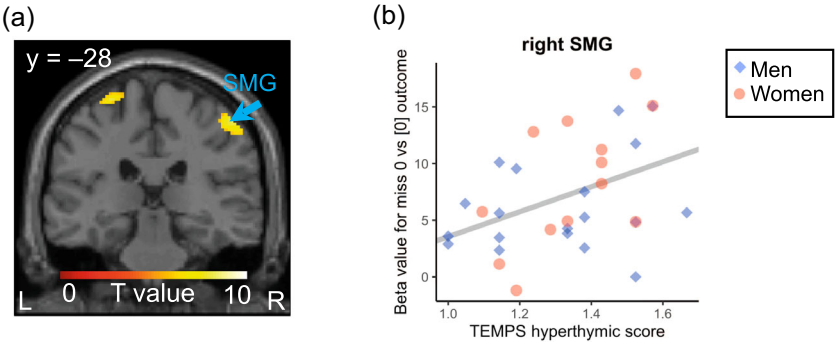


FIGURE 3 (a) Brain activations in response to "hit" outcome for 0 versus no feedback outcome for [0] contrast. The left postcentral gyrus (postCG; left arrow) and right supramarginal gyrus (SMG; right arrow) are indicated in the upper panel; furthermore, the right superior parietal lobule (SPL) is indicated in the lower panel. For display purposes, the threshold was set at $p < 0.05$, FWE. (b) Plots and regression lines from the selected multivariate regression model. The *x*-axis denotes the TEMPS hyperthymic score while the *y*-axis denotes parameter estimates of left postCG, right SMG, and right SPL activation for 0-[0] contrast in the outcome phase.

FIGURE 4 (a) Brain activations in response to the "miss" outcome for 0 versus no-feedback outcome for [0] contrast. The right supramarginal gyrus (SMG) is indicated. For display purposes, the threshold is set at $p < 0.05$, FWE. (b) Plots and regression lines from the selected multivariate regression model. The *x*-axis denotes the TEMPS hyperthymic score while the *y*-axis denotes parameter estimates of the right SMG.



primary somatosensory cortex is considered an acquisition and transformation sensory signal structure rather than a reward-related area, it has projections to the thalamus and striatum; further, it could be involved in associative learning.[40] Moreover, the somatosensory cortex is involved in emotion regulation.[41] The somatosensory cortex is activated upon recognition of a visual-emotional stimulus[42]; therefore, it may be recruited to process positive or negative affective states triggered by feedback regarding task performance. Additionally, we observed areas in the somatosensory association cortex that were activated by the contrast for feedback of nonmonetary rewards. Similar to the primary somatosensory area, the somatosensory association area represents affective states that govern emotional feelings.[43,44] Taken together, the greater activation of the primary somatosensory cortex and somatosensory association cortex by nonmonetary rewards among individuals with higher hyperthymic temperament scores might be related to a more intense affective state elicited by the performance feedback.

Individuals with MDD present dysfunction of the primary somatosensory cortex and somatosensory association cortex. For example, a resting-state fMRI study revealed hyperconnection between the medial thalamus and the primary somatosensory cortex,[45] which is associated with pleasure loss.[46] Additionally, adolescents with MDD have a relatively low total surface area and regional reduction in the somatosensory area.[47] Compared with healthy controls, individuals with untreated MDD have decreased regional neuronal synchrony in the somatosensory association area.[48] Furthermore, individuals with MDD have shown changes in the baseline low-frequency oscillations, which is an index of resting-state intrinsic brain activity in these region.[49] These findings are consistent with our findings and other reports regarding the protective effect of hyperthymic temperament on depression.

Limitations

This study had several limitations. First, the difference in reward valence between "0" and "[0]" might be insufficiently manipulated. Although the participants behaviorally differentiated between "0" and "[0]" (Supporting Information: Figure S1A), no difference was observed in terms of subjective ratings. Consequently, the "0" cue did not elicit activation in the typical "reward system" area. This result is inconsistent with a previous study.[17] While the previous study employed separate conditions for monetary reward trials, nonmonetary reward trials, and no-feedback (baseline) trials, the present study conducted these trials concurrently within the same session. Thus, the difference in reward valence between "0" and "[0]" may be relatively small compared to the previous study. Second, although we found that hyperthymic temperament can predict activation in the primary somatosensory areas and somatosensory association areas following nonmonetary reward feedback, the underlying mechanism through which this association modulates reward-oriented behavior remains unclear. Furthermore, although the regions of interest were selected based on the FWE correction, we did not apply multiple comparison corrections for subsequent multiple regression analysis. Because this is the first study to our knowledge that investigates the relationship between neural responsiveness to nonmonetary rewards and hyperthymic temperament, accordingly, we performed an exploratory investigation of related brain areas. Finally, as discussed in our separate paper,[10] the relationship of hyperthymic temperament with the default mode network remains unclear even though temperament generally refers to the temporally stable biological "core" of personality.

CONCLUSION

Our findings showed that hyperthymic temperament can predict neural responsiveness to nonmonetary rewards. These findings provide further perspectives on the neurobiological basis underlying hyperthymic temperament and its protective effects against depression.

AUTHOR CONTRIBUTIONS

Yukiko Ogura: Conceptualization; methodology; investigation; data curation; formal analysis; writing – original draft; writing – review & editing. **Yumi Wakatsuki**: Investigation; data curation; formal analysis. **Naoki Hashimoto**: Conceptualization; methodology; investigation; data curation; formal analysis; writing – review & editing. **Tamaki Miyamoto**: Investigation; data curation. **Yukiei Nakai**: Investigation; data curation. **Atsuhito Toyomaki**: Conceptualization; methodology; investigation; data curation. **Yukio Tsuchida**: Investigation; data curation. **Shin Nakagawa**: Conceptualization; supervision. **Takeshi Inoue**: Conceptualization; methodology; supervision. **Ichiro Kusumi**: Conceptualization; methodology; supervision.

All authors contributed to manuscript revision, read, and approved the submitted version.

ACKNOWLEDGMENTS

We deeply thank Dr. Akitoshi Ogawa for technical assistance with fMRI setup, and Dr. Akane Miyazaki for assistance with the experiment. We would also like to thank Editage (www.editage.com) for English-language editing. This study was supported by Japan Society for the Promotion of Science (JSPS) Grant-in-Aid for Scientific Research to Yukiko Ogura (JP14J08054) and Naoki Hashimoto (JP25860981).

CONFLICT OF INTEREST STATEMENT

Associate Professor Naoki Hashimoto has received personal fees from Janssen Pharmaceutical, Meiji Seika Pharma, Otsuka Pharmaceutical, Sumitomo Pharma, Takeda Pharmaceutical, Yoshitomiyakuhin, Nippon Boehringer Ingelheim and Lundbeck. Assistant Professor Atsuhito Toyomaki has received payment or honoraria for lectures, presentations, speeches from Sumitomo Pharma, Ohtsuka Pharma, Mochida Pharma, and Nippon Boehringer Ingelheim. Professor Shin Nakagawa has received grants from Astellas, Eli Lilly, Nihon Medi-physics and Tanabe Mitsubishi Pharma; grants and personal fees from Eisai and Otsuka Pharmaceutical; and personal fees from Daiichi Sankyo, FUJIFILM, Janssen Pharmaceutical, Kyowa Pharmaceutical Industry, Lundbeck, Meiji Seika Pharma, Mochida Pharmaceutical, MSD, Mylan, Pfizer, Shionogi, Sumitomo Pharma, Takeda Pharmaceutical, Tsumura, Viatris and Yoshitomiyakuhin. Professor Takeshi Inoue has received personal compensation from Mochida Pharmaceutical, Takeda Pharmaceutical, Eli Lilly, Janssen Pharmaceutical, MSD, Taisho Toyama Pharmaceutical, Yoshitomiyakuhin, and Daiichi Sankyo; grants from Shionogi, Astellas, Tsumura, and Eisai; and grants and personal compensation from Otsuka Pharmaceutical, Dainippon Sumitomo Pharma, Mitsubishi Tanabe Pharma, Kyowa Pharmaceutical Industry, Pfizer, Novartis Pharma, and Meiji Seika Pharma; and is a member of the advisory boards of Pfizer, Novartis Pharma, and Mitsubishi Tanabe Pharma. Professor Ichiro Kusumi has received honoraria from Eisai, Eli Lilly, Janssen Pharmaceutical, Meiji Seika Pharma, Mochida Pharmaceutical, Novartis Pharma, Otsuka Pharmaceutical, Shionogi, Sumitomo Pharma, Takeda Pharmaceutical, Viatris, and Yoshitomiyakuhin; and has received research/grant support from Asahi Kasei Pharma, Astellas, Daiichi Sankyo, Eisai, Eli Lilly, Mochida Pharmaceutical, Nihon Medi-Physics, Otsuka Pharmaceutical, Pfizer, Shionogi, Sumitomo Pharma, Takeda Pharmaceutical and Tanabe Mitsubishi Pharma.

DATA AVAILABILITY STATEMENT

Data are available from the corresponding author upon request.

ETHICS APPROVAL STATEMENT

This study was conducted in accordance with the Declaration of Helsinki (World Medical Association, 2013). The study design was approved by the institutional review board of Hokkaido University Hospital (#010-0031).

PATIENT CONSENT STATEMENT

All study participants provided written informed consent according to the approved study design.

CLINICAL TRIAL REGISTRATION

This study was not conducted as a clinical trial, therefore this section is not applicable.

ORCID

Yukiko Ogura http://orcid.org/0000-0002-2702-2221
Yumi Wakatsuki https://orcid.org/0000-0003-4563-2848
Naoki Hashimoto https://orcid.org/0000-0001-8311-7148
Atsuhito Toyomaki https://orcid.org/0000-0001-9333-8833
Takeshi Inoue https://orcid.org/0000-0001-5248-1289
Ichiro Kusumi https://orcid.org/0000-0002-8747-5070

REFERENCES

1. Rihmer Z, Akiskal KK, Rihmer A, Akiskal HS. Current research on affective temperaments. Curr Opin Psychiatry. 2010;23(1):12–8.
2. Akiskal HS. Delineating irritable and hyperthymic variants of the cyclothymic temperament. J Pers Disord. 1992;6(4):326–42.
3. Akiskal HS. Towards a temperament-based approach to depression: implications for neurobiologic research. Adv Biochem Psychopharmacol. 1995;49(7):99–112.
4. Akiskal HS, Akiskal KK, Haykal RF, Manning JS, Connor PD. TEMPS-A: progress towards validation of a self-rated clinical version of the Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego Autoquestionnaire. J Affect Disord. 2005;85(1–2):3–16.
5. Akiskal HS, Mendlowicz MV, Jean-Louis G, Rapaport MH, Kelsoe JR, Gillin JC, et al. TEMPS-A: validation of a short version of a self-rated instrument designed to measure variations in temperament. J Affect Disord. 2005;85(1–2):45–52.
6. Rihmer Z, Erdos P, Ormos M, Fountoulakis KN, Vazquez G, Pompili M, et al. Association between affective temperaments and season of birth in a general student population. J Affect Disord. 2011;132(1–2):64–70.
7. Karam EG, Salamoun MM, Yeretzian JS, Mneimneh ZN, Karam AN, Fayyad J, et al. The role of anxious and hyperthymic temperaments in mental disorders: a national epidemiologic study. World Psychiatry. 2010;9(2):103–10.
8. Gonda X, Rihmer Z, Zsombok T, Bagdy G, Akiskal KK, Akiskal HS. The 5HTTLPR polymorphism of the serotonin transporter gene is associated with affective temperaments as measured by TEMPS-A. J Affect Disord. 2006;91(2–3):125–31.
9. Gonda X, Fountoulakis KN, Rihmer Z, Lazary J, Laszik A, Akiskal KK, et al. Towards a genetically validated new affective temperament scale: a delineation of the temperament 'phenotype' of 5-HTTLPR using the TEMPS-A. J Affect Disord. 2009;112(1–1):19–29.
10. Ogura Y, Wakatsuki Y, Hashimoto N, Miyamoto T, Nakai Y, Toyomaki A, et al. Hyperthymic temperament predicts neural responsiveness for monetary reward. J Affect Disord. 2023;320:674–81.
11. Pizzagalli DA, Holmes AJ, Dillon DG, Goetz EL, Birk JL, Bogdan R, et al. Reduced caudate and nucleus accumbens response to rewards in unmedicated individuals with major depressive disorder. Am J Psychiatry. 2009;166(6):702–10.
12. Stoy M, Schlagenhauf F, Sterzer P, Bermpohl F, Hägele C, Suchotzki K, et al. Hyporeactivity of ventral striatum towards incentive stimuli in unmedicated depressed patients normalizes after treatment with escitalopram. J Psychopharmacol. 2012;26(5):677–88.
13. Schultz W. Multiple reward signals in the brain. Nat Rev Neurosci. 2000;1(3):199–207.
14. Schneider M, Leuchs L, Czisch M, Sämann PG, Spoormaker VI. Disentangling reward anticipation with simultaneous pupillometry/fMRI. Neuroimage. 2018;178:11–22.
15. Knutson B, Fong GW, Adams CM, Varner JL, Hommer D. Dissociation of reward anticipation and outcome with event-related fMRI. Neuroreport. 2001;12(17):3683–7.
16. Martin-Soelch C, Leenders KL, Chevalley AF, Missimer J, Künig G, Magyar S, et al. Reward mechanisms in the brain and their role in dependence: evidence from neurophysiological and neuroimaging studies. Brain Res Rev. 2001;36(2–3):139–49.
17. Martin-Sölch C, Magyar S, Künig G, Missimer J, Schultz W, Leenders K. Changes in brain activation associated with reward processing in smokers and nonsmokers. Exp Brain Res. 2001;139(3):278–86.
18. Solmi M, Zaninotto L, Toffanin T, Veronese N, Lin K, Stubbs B, et al. A comparative meta-analysis of TEMPS scores across mood disorder patients, their first-degree relatives, healthy controls, and other psychiatric disorders. J Affect Disord. 2016;196:32–46.
19. Dunlop BW, Nemeroff CB. The role of dopamine in the patho-physiology of depression. Arch Gen Psychiatry. 2007;64(3):327–37.
20. Belujon P, Grace AA. Dopamine system dysregulation in major depressive disorders. Int J Neuropsychopharmacol. 2017;20(12):1036–46.
21. D'Esposito M, Zarahn E, Aguirre GK, Rypma B. The effect of normal aging on the coupling of neural activity to the bold hemodynamic response. Neuroimage. 1999;10(1):6–14.
22. Dhingra I, Zhang S, Zhornitsky S, Le TM, Wang W, Chao HH, et al. The effects of age on reward magnitude processing in the monetary incentive delay task. Neuroimage. 2020;207:116368.
23. Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia. 1971;9(1):97–113.
24. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9. J Gen Intern Med. 2001;16(9):606–13.
25. Muramatsu K, Kamijima K, Yoshida M, Otsubo T, Miyaoka H, Muramatsu Y, et al. The patient health questionnaire, Japanese version: validity according to the mini-international neuropsychiatric interview-plus. Psychol Rep. 2007;101(3 Pt 1):952–60.
26. Kameyama R, Inoue T, Uchida M, Tanaka T, Kitaichi Y, Nakato Y, et al. Development and validation of a screening questionnaire for present or past (hypo)manic episodes based on DSM-IV-TR criteria. J Affect Disord. 2013;150(2):546–50.
27. World Medical Association. World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191–4.
28. Knutson B, Westdorp A, Kaiser E, Hommer D. FMRI visualization of brain activity during a monetary incentive delay task. Neuroimage. 2000;12:20–7.
29. Wakatsuki Y, Ogura Y, Hashimoto N, Toyomaki A, Miyamoto T, Nakagawa S, et al. Subjects with bipolar disorder showed different reward system activation than subjects with major depressive disorder in the monetary incentive delay task. Psychiatry Clin Neurosci. 2022;76(8):393–400.
30. Deichmann R, Gottfried JA, Hutton C, Turner R. Optimized EPI for fMRI studies of the orbitofrontal cortex. Neuroimage. 2003;19(2):430–41.
31. Mazaika P, Whitfield-Gabrieli S, Reiss AL Artifact repair for fMRI data from high motion clinical subjects. In: 13rd Annual Meeting of the Organization for Human Brain Mapping. Chicago, IL; 2007.
32. Mazaika P, Hoeft F, Glover GH, Reiss AL Methods and software for fMRI analysis for clinical subjects. In: 15th Annual Meeting of the Organization for Human Brain Mapping. San Francisco, CA; 2009.
33. Marzelli M, Hoeft F, Mazaika P, Sheau K Alphascript for fMRI Preprocessing at CIBSR. 2010.
34. Nemoto K, Dan I, Rorden C, Ohnishi T, Tsuzuki D, Okamoto M, et al. Lin4Neuro: a customized Linux distribution ready for neuroimaging analysis. BMC Med Imaging. 2011;11(1):3.
35. Matsumoto S, Akiyama T, Tsuda H, Miyake Y, Kawamura Y, Noda T, et al. Reliability and validity of TEMPS-A in a Japanese non-clinical population: application to unipolar and bipolar depressives. J Affect Disord. 2005;85(1–2):85–92.

36. Sambataro F, Visintin E, Doerig N, Brakowski J, Holtforth MG, Seifritz E, et al. Altered dynamics of brain connectivity in major depressive disorder at-rest and during task performance. Psychiatry Res Neuroimaging. 2017;259:1–9.
37. Geng X, Xu J, Liu B, Shi Y. Multivariate classification of major depressive disorder using the effective connectivity and functional connectivity. Front Neurosci. 2018;12:1–16.
38. Alnaes D, Sneve MH, Espeseth T, Endestad T, van de Pavert SHP, Laeng B. Pupil size signals mental effort deployed during multiple object tracking and predicts brain activity in the dorsal attention network and the locus coeruleus. J Vis. 2014;14(4):1.
39. Cabeza R, Anderson ND, Locantore JK, McIntosh AR. Aging gracefully: compensatory brain activity in high-performing older adults. Neuroimage. 2002;17(3):1394–402.
40. Aronoff R, Matyas F, Mateo C, Ciron C, Schneider B, Petersen CCH. Long-range connectivity of mouse primary somatosensory barrel cortex. Eur J Neurosci. 2010;31(12):2221–33.
41. Kropf E, Syan SK, Minuzzi L, Frey BN. From anatomy to function: the role of the somatosensory cortex in emotional regulation. Braz J Psychiat. 2019;41(3):261–9.
42. Adolphs R, Damasio H, Tranel D, Cooper G, Damasio AR. A role for somatosensory cortices in the visual recognition of emotion as revealed by three-dimensional lesion mapping. J Neurosci. 2000;20(7):2683–90.
43. Anders S, Birbaumer N, Sadowski B, Erb M, Mader I, Grodd W, et al. Parietal somatosensory association cortex mediates affective blindsight. Nature Neurosci. 2004;7(4):339–40.
44. Anders S, Lotze M, Erb M, Grodd W, Birbaumer N. Brain activity underlying emotional valence and arousal: a response-related fMRI study. Hum Brain Mapp. 2004;23(4):200–9.
45. Brown EC, Clark DL, Hassel S, MacQueen G, Ramasubbu R. Thalamocortical connectivity in major depressive disorder. J Affect Disord. 2017;217:125–31.
46. Kang L, Zhang A, Sun N, Liu P, Yang C, Li G, et al. Functional connectivity between the thalamus and the primary somatosensory cortex in major depressive disorder: a resting-state fMRI study. BMC Psychiatry. 2018;18(1):339.
47. Schmaal L, Hibar DP, Sämann PG, Hall GB, Baune BT, Jahanshad N, et al. Cortical abnormalities in adults and adolescents with major depression based on brain scans from 20 cohorts worldwide in the ENIGMA Major Depressive Disorder Working Group. Mol Psychiatry. 2017;22(6):900–9.
48. Huang X, Huang P, Li D, Zhang Y, Wang T, Mu J, et al. Early brain changes associated with psychotherapy in major depressive disorder revealed by resting-state fMRI: evidence for the top-down regulation theory. Int J Psychophysiol. 2014;94(3):437–44.
49. Tadayonnejad R, Yang S, Kumar A, Ajilore O. Clinical, cognitive, and functional connectivity correlations of resting-state intrinsic brain activity alterations in unmedicated depression. J Affect Disord. 2015;172:241–50.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Ogura Y, Wakatsuki Y, Hashimoto N, Miyamoto T, Nakai Y, Toyomaki A, et al. Hyperthymic temperament predicts neural responsiveness for nonmonetary reward. Psychiatry Clin Neurosci Rep. 2023;2:e140. https://doi.org/10.1002/pcn5.140