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Original article

Relationship between leukocyte telomere length and personality traits in healthy subjects

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ABSTRACT

Background: It has been shown that certain personality traits are related to mortality and disease morbidity, but the biological mechanism linking them remains unclear. Telomeres are tandem repeat DNA sequences located at the ends of chromosomes, and shorter telomere length is a predictor of mortality and late-life disease morbidity. Thus, it is possible that personality traits influence telomere length. In the present study, we examined the relationship of leukocyte telomere length with personality traits in healthy subjects.

Subjects and methods: The subjects were 209 unrelated healthy Japanese who were recruited from medical students at 4th–5th grade. Assessment of personality traits was performed by the Revised NEO Personality Inventory (NEO-PI-R) and the Temperament and Character Inventory (TCI). Leukocyte relative telomere length was determined by a quantitative real-time PCR method for a ratio of telomere/single copy gene.

Results: In the stepwise multiple regression analysis, shorter telomere length was related to lower scores of neuroticism ($P < 0.01$) and conscientiousness ($P < 0.05$) of the NEO-PI-R, and lower scores of harm avoidance ($P < 0.05$) and reward dependence ($P < 0.05$) of the TCI.

Conclusions: The present study suggests that leukocyte telomere length is associated with some personality traits, and this association may be implicated in the relationship between personality traits and mortality.

1. Introduction

There is increasing evidence suggesting that certain personality traits are associated with mortality [14,35] and disease morbidity such as coronary heart disease [33]. Specifically, individuals low in conscientiousness, as measured by the NEO Personality Inventory [11], were reported to display early mortality [14,35,37] and this finding was confirmed by meta-analyses [3,19,30]. Meanwhile, there have been several studies suggesting the associations of early mortality with high neuroticism and low agreeableness [37], but two meta-analyses produced inconsistent results [19,30]. Although involvement of health-harming behaviors such as smoking, alcohol use and overeating has been suggested [3], the biological mechanism linking personality traits and mortality remains unclear.

Telomeres are tandem repeat DNA sequences $(TTAGGG)_n$ located at the ends of chromosomes and play a crucial role in preventing chromosome fusion and in maintaining genome stability [2]. Prospective studies have shown that shorter telomere length is a predictor of coronary heart disease [4], cancer [22,36], progression of diabetic nephropathy in patients with type 1 diabetes [16], dementia in post-stroke patients [23], and mortality [6,13]. It has been reported that telomere length is influenced by a wide range of factors such as age, gender, race, smoking, physical activity, socioeconomic status, obesity, multivitamin intake, alcohol consumption and hormone replacement therapy [24].

Recent studies focusing on the relationships between telomere length and psychological factors suggested that shorter telomere length was associated with current life stress [12,28] and maltreatment [34] and adversity [20,26] during childhood. In relation to personality, shorter leukocyte telomere length was associated with high pessimism, as assessed by the Revised Life Orientation Test [31] in one study [27], and with high hostility, as evaluated by using the Cook Medley Hostility Scale [10] in other study [5]. However, these

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studies focused on specific personality traits only and thus, the association of telomere length with broad dimensions of personality remains to be elucidated. Therefore, in the present study, we examined the relationship of telomere length with broad dimensions of personality assessed by the most widely used scales, i.e., the revised NEO Personality Inventory (NEO-PI-R) [11] and the Temperament and Character Inventory (TCI) [9]. The hypothesis of the present study is that shorter telomere length is associated with low conscientiousness and possibly with high neuroticism and low agreeableness. Because of the involvement of various factors such as age and race in telomere length as mentioned above, the subjects were limited to Japanese medical students with a relatively narrow age range (20–30 years old).

2. Subjects and methods

2.1. Participants

Originally, 249 physically healthy Japanese were recruited from medical students at 4th–5th grade of Yamagata University School of Medicine. Psychiatric screening was conducted by interviews by well-trained psychiatrists and a questionnaire on psychiatric treatment and diagnosis. Out of the 249 cases, 11 had psychiatric disorders and three had missing data. Data of 26 subjects were excluded due to failure of DNA extraction or PCR amplification. The remaining 209 subjects were used for analyses. One hundred twenty-eight were males and 81 were females. The mean ± SD (range) of age was 23.3 ± 1.7 (20–30) years. The subject's characteristics are shown in Table 1. The study protocol was approved by the ethics committee of the Yamagata University School of Medicine. After complete description of the study to the subjects, written informed consent was obtained from all subjects. Data collection was performed from January 2009 to October 2011.

2.2. Assessment for personality traits

Both the NEO-PI-R [11] and the TCI [9] are self-report scales with 240 items that evaluate broad dimensions of personality. The NEO-PI-R consists of five domains, i.e., neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness [11]. The TCI has seven dimensions, i.e., novelty seeking, harm avoidance, reward dependence, persistence, self-directedness, cooperativeness, and self-transcendence [9]. In the present study, assessment of personality traits was performed using the Japanese version of the NEO-PI-R [32] and the TCI [21], which have been verified to have high reliability and validity.

Table 1
Characteristics of subjects, relative telomere length, NEO-PI-R scores, and TCI scores.

	Total subjects (n = 209)	Males (n = 128)	Females (n = 81)
	Mean (SD)	Mean (SD)	Mean (SD)
Age, y.o.	23.3 (1.7)	23.5 (1.8)	23.1 (1.5)
Telomere length, z-score	0.0 (1.0)	−0.1 (0.9)	0.1 (1.1)
NEO-PI-R, score			
Neuroticism	99.4 (21.8)	95.9 (21.4)	105.0 (21.3)**
Extraversion	104.6 (17.5)	105.5 (16.5)	103.3 (19.0)
Openness to experience	116.4 (15.9)	113.8 (15.8)	120.6 (15.3)**
Agreeableness	107.3 (14.6)	105.5 (14.9)	110.1 (13.8)*
Conscientiousness	100.3 (18.1)	100.1 (17.2)	100.8 (19.5)
TCI, score			
Novelty seeking	22.3 (5.3)	22.8 (5.3)	21.6 (5.2)
Harm avoidance	18.4 (5.8)	17.9 (5.7)	19.1 (5.8)
Reward dependence	15.7 (3.6)	15.2 (3.6)	16.4 (3.6)*
Persistence	4.4 (1.8)	4.5 (1.8)	4.2 (1.8)
Self-directedness	29.1 (6.6)	29.1 (6.3)	29.2 (7.1)
Cooperativeness	27.9 (5.3)	27.3 (5.5)	28.9 (4.8)*
Self-transcendence	9.0 (4.7)	8.9 (5.1)	9.2 (4.1)

NEO-PI-R: Revised NEO Personality Inventory; TCI: Temperament and Character Inventory.
*$P < 0.05$, **$P < 0.01$ compared to males in the Student t-test.

2.3. Leukocyte telomere length

Genomic DNA was extracted from peripheral leucocytes using a QIAamp DNA Blood Kit (Qiagen, Tokyo, Japan), and was stored at −80 °C. Leukocyte relative telomere length, assessed by a ratio of telomere/single copy gene with the mean data from the triplicate runs, was determined by a quantitative real-time PCR method of Cawthon [7] with the following modifications. The *36B4* gene was used as a single copy reference gene. PCR reactions were performed separately for the telomere and *36B4* in 96-well plates in which well positions were matched between the telomere and 36B4. Genomic DNA dilution series (2.5, 5.0, 10.0, 20.0, 40.0, and 80.0 ng) were included in every plate to create a standard curve, which was used to perform absolute quantification of each DNA sample. Twenty ng of DNA was used for each individual reaction. The primers were as follows; Tel-1b (5′-CGG TTT GTT TGG GTT TGG GTT TGG GTT TGG GTT TGG GTT-3′) and Tel-2b (5′-GGC TTG CCT TAC CCT TAC CCT TAC CCT TAC CCT TAC CCT-3′) for the telomere and 36B4-F (5′-AGC ACA TAA TAG CAA TTC ACA-3′) and 36B4-R (5′-TGG CTT TAG TCA CAT TAA ATA G-3′) for the *36B4*. The amplification was carried out in a 25 μL volume containing genomic DNA, each primer set (0.1 μM of Tel-1b and 0.8 μM of Tel-2b for the telomere and 0.3 μM of 36B4-F and 36B4-R for the *36B4*), and 12.5 μL of SYBR Premix DimerEraser (Takara Bio Inc, Otsu, Japan). The PCR amplification and the fluorescence detection were performed using the Thermal Cycler Dice® TP800 Real Time System (Takara Bio Inc, Otsu, Japan). Cycle conditions were as follows; 30 s at 95 °C followed by 25 cycles at 95 °C for five seconds and 52 °C for 60 s for the telomere reaction, and 30 s at 95 °C followed by 35 cycles at 95 °C for five seconds, 55 °C for 30 s, and 72 °C for 60 s for the *36B4* reaction. All plates included a genomic DNA control sample for the calibration of plate and well effects. Specificity of primer binding was monitored by melting curve analysis. The mean correlation coefficients of the standard curves in the telomere and *36B4* assay were 0.997 and 0.999, respectively, and the corresponding mean PCR efficacies were 98.6% and 90.5%, respectively. The mean coefficient of variation was 4.4% for the telomere reaction, 4.3% for the *36B4* reaction, and 13.5% for the telomere/single copy gene. Relative telomere length was expressed as a standardized z-score.

2.4. Statistical analyses

Gender differences and inter-correlations in relative telomere length, NEO-PI-R scores, TCI scores, and age were tested by the Student's t-test and the Pearson's linear regression test, respectively. Relationships of relative telomere length with the NEO-PI-R scores or the TCI scores were analyzed by the stepwise multiple regression analyses with telomere length as a dependent variable and with the NEO-PI-R scores or the TCI scores, age, and gender as independent variables. A dummy variable was used for gender (female = 0, male = 1). In the multiple regression analyses, age, gender, and 5 domain scores of the NEO-PI-R or 7 dimension scores of the TCI were entered all in once. All statistical analyses were performed by SPSS 14.0 J for Windows (SPSS Japan Inc, Tokyo, Japan), and a P value of less than 0.05 (two-tailed) was regarded as significant.

3. Results

The relative telomere length, NEO-PI-R scores, and TCI scores in total subjects, males, and females are shown in Table 1. Females