Serum uric acid and the Five Factor Model of personality: Implications for psychopathological and medical conditions

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ABSTRACT

Elevated serum uric acid (SUA) is associated with a variety of medical and psychopathological conditions. This study investigated whether elevated SUA is associated with the Five Factor Model of personality. Participants underwent a health examination at two points of time, T1 (N = 3706) and T2 (N = 2104), about 18 months apart. Ordinary least squares (OLS) regressions were used to examine the concurrent and over-18-month associations between the FFM factors and SUA levels. Extraversion was associated with elevated SUA at T1 and T2. Conscientiousness was associated with decreased SUA at T1. The associations of Extraversion and Conscientiousness with SUA decreased to marginal significance when adjusted for body weight as a possible mediator. Agreeableness was associated with decreased SUA at T1 and T2 and persisted after adjustment of covariates. A secondary analysis conducted to examine whether the FFM could predict individuals having above normal SUA levels, showed a trend similar to that observed for the OLS regressions. The associations found have direct relevance to medical and psychopathological conditions associated with elevated SUA.

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1. Introduction

Serum uric acid (SUA), the end-product of purine metabolism, is one of the biochemical factors that has received considerable attention in the past few decades and has been associated with a variety of medical conditions, such as gouty arthritis, high blood pressure, cardiovascular disease, metabolic syndrome, kidney stones and chronic kidney disease (Feig, Kang, & Johnson, 2008). Additionally, recent evidence from genetic and clinical studies suggests that urinergic system dysfunction, as indicated by elevated SUA levels, might play an important role in psychopathology. Elevated SUA levels were found in individuals with Lesch–Nyhan syndrome, a neurodevelopmental disorder associated with severely self-injurious behavior (Nyhan, 1997), bipolar disorder (e.g., Zarate & Manji, 2008; Machado-Vieira, Soares, et al., 2008), pathological gambling disorder (Manowitz, Amorosa, Goldstein, & Carlton, 1993) and attention-deficit/hyperactivity disorder (Barrera, Ruiz, & Dunlap, 1988).

Substantial individual variations in SUA levels suggest that psychological factors might affect these levels. Thus, the aim of the present study was to address the links between personality, relatively stable psychological characteristics, and SUA.

In the present study, personality was conceptualized based on the Five Factor Model (FFM, also known as the Big Five) of personality (Costa & McCrae, 1992). It is the predominant dimensional model of general personality structure within psychology (e.g., Costa & McCrae,

1992), and a widely adopted framework in the study of associations between personality and medical and psychopathological conditions (e.g., Chapman, Roberts, & Duberstein, 2011; Malouff, Thorsteinsson, & Schutte, 2005). The FFM classifies most personality traits under five dimensions: Extraversion (bold, energetic, talkative), Agreeableness (cooperative, sympathetic, warm), Conscientiousness (organized, efficient, practical), Neuroticism (moody, touchy), and Openness (imaginative, intellectual) (Costa & McCrae, 1992; Saucier, 1994).

Although scarcely studied, few personality traits have been associated with SUA. For example, studies dating from the 1970s, related to Eysenck's trait Psychoticism (see Eysenck & Eysenck, 1976, for a review), indicated that the personality trait of Psychoticism is correlated with SUA. In terms of the FFM, Psychoticism correlates negatively with both Conscientiousness and Agreeableness, and is strongly associated with impulsiveness and disinhibition. Elevated SUA levels were found to be associated with Extraversion (Raina & Vats, 1982), including energy/drive, positive affect, leadership (characteristics of high Extraversion) (reviewed by Katz & Weiner, 1972; Lorenzi, Borba, Dutra, & Lara, 2010) and disinhibition (a sub-component of (low) Conscientiousness). Sutin et al. (2013) used the FFM inventory, but focused only on personality traits related to impulsivity. They also found that elevated SUA levels were associated with impulsiveness (a sub-component of (low) Conscientiousness) and excitement seeking (a sub-component of Extraversion), both concurrently and 3 to 5 years later.

The present study investigated the relationship between the full spectrum of the FFM personality factors and SUA in order to understand the nature of the relationships between them. To test the stability of the associations, SUA levels were measured twice, approximately

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18 months apart. The study was conducted on a large, heterogeneous sample of participants, adjusting for socio-demographic and health status. Because smoking status and body weight are associated with both personality (Armon, Melamed, Shirom, Shapira, & Berliner, 2013; Sutin, Ferrucci, Zonderman, & Terracciano, 2011) and SUA (Johnson, 2012; Haj Mouhamed et al., 2011), the potential mediating effects of these variables were tested.

2. Method

2.1. Participants

The study population (N = 3850) was employees attending the Center for Periodic Health Examinations of the Tel-Aviv Sourasky Medical Center for a routine health examination at Time 1 (T1) and Time 2 (T2), who voluntarily agreed to participate in the Tel Aviv Medical Center Inflammation Survey (TAMCIS) study (92% response rate). The average time between T1 and T2 was 18 (SD = 7.01) months. These periodic health examinations were provided as a subsidized fringe benefit. A total of 2279 (60%) employees returned for a second visit (T2). Compared with the study participants, the personality traits and SUA levels of those examined at T1 who did not return for a follow-up examination did not differ from those who returned at T2. However, they were more likely to be less educated; consistent with previous reports on attrition bias in health survey studies (e.g., Ployhart & Vandenberg, 2010).

Participants with one of the following criteria were excluded. (1) A physician diagnosis gout [N(T1 sample) = 10; N(T2 sample) = 10]. Gout is a rheumatic disease, often marked by abnormally high SUA levels (Sturrock, 2000). Individuals with gout were excluded to avoid reverse causation and the confounding effects of anti-gout medications. (2) A history of psychiatric morbidity (for example, bipolar disorder, anxiety, clinical depression, or schizophrenia) [N(T1 sample) = 134; N(T2 sample) = 165]. Those with psychiatric morbidity were excluded to examine whether the FFM-SUA associations were primarily driven by psychiatric illness. Thus, the final samples consisted of 3706 (62% men) participants at T1 and 2104 (63% men) at T2.

2.2. Procedure

The study protocol was approved by the Ethics Committee of the Tel Aviv Sourasky Medical Center. Confidentiality was assured and each participant signed an informed consent document. As a part of the periodic health examination, each participant answered the study questionnaire, provided a medical history, underwent blood sampling after an overnight fast, a physical examination by a physician, urinalysis, stress ECG, spirometry, and vision and hearing function tests.

2.3. Measures

The FFM was assessed by the Big Five Mini-Marker scale (Saucier, 1994), which consists of 40 adjectives that measure five personality factors (eight for each factor): Extraversion, Agreeableness, Conscientiousness, Neuroticism, and Openness to experience. Respondents were asked to indicate how well these adjectives described them, on a 9-point Likert scale ranging from 1 (extremely inaccurate) to 9 (extremely accurate). The back-translation procedure was used to test the reliability of the translation of this instrument from English to Hebrew. Three independent judges assessed the adequacy of the translation, with an inter-rater reliability of .83. The scores and the Cronbach internal consistency reliabilities of the FFM (α range = .70–.80) were largely on par with those reported in the original version (Saucier, 1994) and with those reported in and the Hebrew version of the Mini-Marker scale (e.g., Ein-Gar, Goldenberg, & Sagiv, 2008).

Serum uric acid was determined using the ADVIA 1650 analyzer (see Zhao et al., 20019 for a review). The test is based on the Fossati enzymatic reaction in the presence of uricase, which oxidizes uric acid to allantoin and hydrogen peroxide with 4-aminoantipyrine and TOOS [N-ethyl-N-(2-hydroxy-3-sulfopropyl)-3-methylaniline]. A color complex was formed and the absorption was measured at the reaction end-point at 545 nm and expressed in mg/dl.

The following variables were assessed at baseline for covariate adjustment purposes: gender, age, and education (years). The following covariates were assessed both at baseline and after 18 months: *Physical health status* was scored as 1 for participants who reported having diabetes or taking any of the following medications, including oral antidiabetics, insulin use, antihypertensive drugs, diuretics, and medication for angina pectoris, or as 0 otherwise. *Physical health* and *smoking status* (yes/no) were recorded based on an in-person medical interview conducted by a physician at the medical center (Bergmann, Jacobs, Hoffmann, & Boeing, 2004). *Body Mass Index* (BMI) was derived from weight and height assessed during the clinical examination.

2.4. Statistical analyses

Ordinary least squares (OLS) regressions were used (SPSS 19 software) to examine the concurrent and over-18-month associations between the FFM factors and SUA levels. Model 1 presents the associations between the FFM factors and baseline and over time levels of SUA (Tables 2) after adjusting for physical health status and socio-demographic covariates (age, gender, and education). Model 2 presents the extent to which the associations between the FFM factors and baseline and over time levels of SUA were attenuated by smoking status and BMI added to Model 1. These covariates were considered as potential mediators of personality associations with levels of SUA. Attenuation attributed to the possible mediators under consideration (as appeared in Model 2) was calculated using the formula "100 × (β Model 1 − β Model 2) / (β Model 1)". This approach is widely used in epidemiology (e.g., Hagger-Johnson et al., 2012) and is broadly equivalent to testing for mediation because the percentage of attenuation estimates the proportion of the association explained by the proposed mediator. The standardized indirect effects and their corresponding confidence intervals are reported using mediation analyses (PROCESS procedure; Hayes, 2012).

2.5. Secondary analyses

To supplement the above analyses, logistic regressions were used to test whether the FFM factors were associated with above normal SUA levels. Concentrations of SUA are considered elevated in an absolute sense when they exceed the upper limit of an arbitrary normal range (indicating solubility of monosodium urate in serum), which in most studies is 7.0 and 6.0 mg/dl for men and women, respectively (Kelly & Palella, 1987).

3. Results

All study variables were systematically examined to detect outliers or non-normal distributions (skewness > 2.0 and kurtosis > 5.0); none was detected. Descriptive statistics for the study variables are shown in Table 1. There was no change in levels of SUA from T1 to T2. The likelihood of smoking decreased (p < .01). A zero-order correlations matrix is available from the author upon request.

Results of the OLS regression analyses are as follows: Extraversion was positively associated with SAU levels at T1 and over 18 months (β = −.06, .06; p < .01, respectively) (Table 2, Model 1). The associations were attenuated by 17% and 33% dropped to marginal significance when BMI was included in the model (Table 2, Model 2). Mediation analyses (PROCESS procedure; Hayes, 2012) indicated that the association between Extraversion and SUA was mediated, in part, by higher BMI at both time points (point estimate = .023 [95% confidence interval = .018–.038] and point estimate = .019 [95% confidence interval = .007–.032], respectively for Time 1 and Time 2). Conscientiousness was