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HAL Id: hal-01953572

https://hal-univ-bourgogne.archives-ouvertes.fr/hal-01953572

Submitted on 21 Jul 2022

Type A competitiveness traits correlate with downregulation of c-Fos expression in patients with type 1 diabetes

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Abstract

Aim. – Type A personality has been associated with increased survival in people with type 1 diabetes (T1D). Systemic low-grade inflammation may play a critical role, as suggested in recent reports, although the links between the inflammatory circulating transcriptome and Type A remain unknown. This prompted our exploration of the potential associations between Type A personality and c-Fos gene expression, a candidate gene closely linked to inflammatory processes, in T1D.

Methods. – Type A personality was assessed by Bortner questionnaire in patients with T1D, and two subscales—'speed' and 'competitiveness'—were used to measure these specific dimensions of Type A. Expression of the c-Fos gene was assessed by a quantitative real-time polymerase chain reaction technique.

Results. – This pilot study included 20 men with T1D. Multivariable analyses showed an independent inverse association between Type A competitiveness score and c-Fos expression, while a regression model adjusted for age, body mass index and HbA1c levels revealed a significant inverse relationship between c-Fos transcripts and Type A competitiveness ($P = 0.003$).

Conclusion. – This strong association between Type A competitiveness and reduced c-Fos expression is in line with recent data suggesting a psychobiological influence of the Type A profile in T1D *via* inflammatory pathways.

Keywords: c-Fos; Competitiveness; Diabetes; Inflammation; Personality; Type A

INTRODUCTION

The Type A personality, which is characterized by time urgency, strong drive, and need for achievement and competitiveness, has been suggested to influence health outcomes [1,2]. Although earlier reports mentioned that Type A was associated with a greater risk of developing coronary heart disease, subsequent studies dismissed the link and instead focused attention on hostility as the 'toxic' component, as other Type A personality components, such as competitiveness, could have a positive impact [1,2]. In fact, in type 1 diabetes (T1D), the Type A personality has been associated with lower cardiovascular and all-cause mortality [3].

Among the biological mechanisms potentially mediating the association between Type A personality and clinical outcomes, systemic low-grade inflammation may play a critical role, as suggested in recent reports wherein Type A was associated with reduced plasma C-reactive protein (CRP) in patients with T1D [1]. To date, however, the links between the inflammatory circulating transcriptome and Type A personality have remained unknown in diabetes. More specifically, the Finkel–Biskis–Jinkins osteosarcoma virus (c-Fos) gene has been even more closely linked to inflammatory processes in circulating blood cells [4] than is the CRP marker, although its links to psychobiological phenomena have remained unexplored in diabetes. Indeed, this prompted the present pilot study of 20 patients with T1D to look for a potential association between Type A personality and c-Fos gene expression.

METHODS

Participants

The study population consisted of men aged 35–45 years with T1D, all of whom had been seen as outpatients in the Endocrinology and Metabolic Diseases Department of Dijon University Hospital.

Ethics

The study (NCT02080741) received approval from the local ethics committee. Prior to the patients' interviews and measurements, the interviewer described the aim of the study to each participant and obtained their full written consent.

Clinical and biological measurements

Male participants with T1D were recruited at the Endocrinology and Metabolic Diseases Department of Dijon University Hospital. All underwent standardized clinical examinations, and their clinical data were recorded by direct interview and by a review of their medical records. Patients participating in intense physical activity were not included in the study.

For each recruited participant, blood was drawn at 0800 h in the morning in a fasting state to assess levels of glycated haemoglobin (HbA1c) and c-Fos gene expression. All biological parameters were determined at the Dijon University Hospital laboratory. HbA1c was measured by ion-exchange high-performance liquid chromatography (HPLC; Bio-Rad Laboratories, Hercules, CA, USA) as previously described [1]. Leucocyte ribonucleic acid (RNA) was extracted from peripheral blood samples.

Levels of transcripts in blood leucocytes were measured by the quantitative real-time polymerase chain reaction (qRT-PCR) method, as described previously in detail [5]. Purity and quality were assessed by absorbance at ultraviolet (UV) wavelengths of 260

nm and 280 nm, and a 260/280 ratio > 1.8 was required for further analysis. The quality of RNA, computed as the RNA integrity number (RIN), was assessed with a 2100 Bioanalyzer (Agilent Technologies, Santa Clara, CA, USA) using RNA 6000 Nano Chips (Agilent Technologies). For quantification of transcripts, mean cycle threshold (Ct) values of target and reference genes in the different groups were analyzed and compared using the relative expression software tool (REST; 2008 V2.0.7), which provides a normalized expression ratio for each gene and calculates the significance of differences in gene expression using a randomization algorithm.

Psychological measurements

Type A personality: speed and competitiveness dimensions

To measure Type A, the Bortner Type A Rating Scale (BTRS) was used [6]. This scale was translated and validated for the French population against the Friedman and Rosenman structured interview for assessing Type A [7], and found to have an observed agreement of 71.5% [8]. The BTRS is recognized for its ability to assess time urgency and impatience, competitiveness and job involvement without measuring hostility [9]. It is worth noting that an association between Type A and lower rates of mortality in patients with diabetes [3] was found with the BTRS. According to Edwards et al. [10], two subscales—nine items for 'speed' (never late, rushed, impatient, goes all out, does lots at once, forceful, wants job recognition, fast, hides feelings) and three items for 'competitiveness' (competitive, hard-driving, ambitious)—were used to assess these specific dimensions of the Type A personality.

Statistical analysis

Descriptive data for continuous variables have been reported as means ± SD (standard deviation). As reliance on a binary cut-off point could produce spurious results, the BTRS score was considered a continuous variable. Univariate correlation analysis was performed by calculation of Pearson's coefficient. The gene expression variable was the mean Ct ratio of c-Fos/glyceraldehyde-3-phosphate dehydrogenase (GAPDH). Multivariable analyses were performed by multiple linear regression to determine the independent association between personality traits and c-Fos gene expression, the dependent variable, while taking into account the potentially confounding factors of age, body mass index (BMI), diabetes duration and HbA1c levels.

A two-tailed probability (P) level of 0.05 was accepted as statistically significant. All statistical analyses were performed using SPSS software (IBM Corp., Armonk, NY, USA).

RESULTS

General characteristics

This pilot study included 20 European men ages 35 to 45 (40.86 ± 3.62) years, and followed them between 2015 and 2017. All had been diagnosed with T1D (mean duration of disease: 22.91 ± 9.11 years; mean HbA1c levels: 7.31 ± 1.29%; mean BMI: 28.87 ± 5.62 kg/m^2). As for diabetes complications, only six men (30%) had retinopathy; none had coronaropathy, nephropathy or neuropathy; all were non-smokers; and no alcohol misuse was observed. In addition, their mean total BTRS score was 200.00 ± 43.57, their mean speed dimension score was 139.27 ± 35.22 and their mean competitiveness dimension score was 37.36 ± 14.05. The mean c-Fos transcript Ct was 0.91 ± 0.04.

Association between c-Fos gene expression and Type A personality

Bivariate analyses indicated that Type A competitiveness traits correlated with c-Fos expression (r = -0.708, P = 0.001; Fig. 1) and HbA1c levels (r = -0.544, P = 0.011), but not with either age or BMI. On the other hand, Type A speed traits correlated with BMI (r = 0.465, P = 0.019), but not with age, c-Fos or HbA1c levels. In multiple regression analyses, c-Fos was significantly associated with competitiveness independently of age, BMI and HbA1c (P = 0.003).

DISCUSSION

The present study, the first to examine the relationship between Type A personality and c-Fos gene expression in patients with T1D, has identified an inverse association between the Type A competitiveness dimension and c-Fos expression. Fickley et al. [3] revealed that cardiac and all-cause mortality were lower in individuals with Type A personality and T1D. While the reasons for this reduced mortality are still unknown, our present data suggest that it might be mediated by inflammatory processes, which is in line with recent data showing an inverse relationship between Type A and plasma CRP levels [1]. As Type A competitiveness encompasses both the 'proactive' and 'goal-striving' components of the Type A profile that are similar to the higher-order conscientiousness personality dimension [11], our results are also consistent with an association of conscientiousness with reduced inflammation [12]. In addition, several reports have suggested that being highly reactive (as are people scoring high on Type A competitiveness) in a challenging environment (such as T1D) could be beneficial in terms of producing more effective behavioural coping strategies [13]. Indeed, people with high levels of Type A competitiveness, who are mainly 'goal-oriented' and conscientious, may be more likely to display protective health behaviours, such as engaging in physical activity [3].

Consistent with this view, Type A has been shown to be associated with more problem-focused coping strategies [14], including searching for appropriate medical treatments [7], adherence to screening [15] and a greater sense of self-efficacy [16], which is associated with better adherence to diabetes regimens [17]. Overall, it could be suggested that individuals with high levels of competitiveness may display more adaptive health behaviours in the face of diabetes, thus eventually resulting in better clinical outcomes. Competitiveness has also been associated with longer telomere lengths [13], lower plasma CRP levels [1] and, in our present study, reduced c-Fos gene expression. All these data suggest a potentially direct link between Type A competitiveness and biology and, more precisely, inflammatory markers.

In addition, bivariate analysis has revealed a significant inverse correlation between Type A competitiveness and glycaemic control, as measured by HbA1c levels. As previously discussed, it is possible that those with strong competitiveness traits may have better adaptive behaviours and good medication adherence. However, controversial literature also suggests that the relationship between Type A and better clinical outcomes may not be supported by an independent link between Type A personality and HbA1c levels [3,18,19].

The Type A speed dimension was positively associated with BMI, which appears to be in agreement with previous studies showing an association between impatience or motor impulsiveness and increased BMI [20,21]. Nevertheless, it is noteworthy that these results were obtained in people without diabetes. Moreover, the present study, performed in patients with T1D, revealed no influence of BMI on the significant association between Type A competitiveness and c-Fos expression. Thus, it may be speculated that a negative effect of the Type A speed dimension on food intake might be counterbalanced by Type A competitiveness traits in patients with T1D.

In this pilot study of 20 patients with T1D, there are some limitations mostly due to its cross-sectional and observational design whereby associations, but never causal relationships, between the competitiveness personality traits and c-Fos expression have been demonstrated. Indeed, despite the fact that the literature exhaustively supports top-down effects of psychological features on the inflammatory process, some reports have consistently highlighted the bottom-up impact of inflammation on the brain and behaviour [22]. Therefore, in T1D, inflammation could be altering personality traits by reducing both the physical and cognitive capacity to deal with adversity, thereby altering Type A competitiveness. In this regard, our study design was not able to tease out the possible reciprocal relationships between Type A competitiveness and inflammatory pathways. Moreover, certain clinical and biological data, such as depression, physical activity and CRP plasma levels, were not assessed in this pilot study, whereas it cannot be excluded that those unmeasured factors, commonly associated with systemic inflammation, may have confounded the link between competitiveness and c-Fos expression [23–25].

Nevertheless, it seems important to note that all patients enrolled in our study were non-smokers, thereby eliminating a major confounding factor shown to be the strongest predictor of c-Fos transcript levels [26]. In addition, T1D patients participating in intense physical activity were excluded from our study. Finally, despite some limitations, our findings have demonstrated a strong association between Type A competitiveness and reduced c-Fos expression, which is in line with recent data linking Type A and low-grade inflammation in T1D [1].

CONCLUSION

Although the mechanism(s) underlying the relationship between Type A personality and inflammatory processes remain unclear, the present study has identified some potential

genomic links between Type A personality and c-Fos expression in T1D. Further longitudinal studies are now needed to examine the potential role of low-grade inflammation in mediating the association of Type A with clinical outcomes in diabetes, and to clarify the mechanisms that may link personality and inflammation.

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Figure legend

Fig. 1. Correlation between levels of c-Fos gene expression (r = -0.708, P = 0.001) and

Type A competitiveness score (Bortner questionnaire).