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LETTER TO THE EDITOR

# Correlation between psychological distress and C-reactive protein

## Comment on Puustinen et al., "Psychological distress and C-reactive protein: do health behaviours and pathophysiological factors modify the association?" (Eur Arch Psychiatry Clin Neurosci 2011;261:277–84)

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Puustinen et al. reported a significant relationship between the serum C-reactive protein (CRP) and the 12-item General Health Questionnaire (GHQ-12) in middle-aged Caucasian subjects [1]. A significant odds ratio for CRP >3 mg/l was observed in high category of GHQ-12 (≥4) judged by summing up of the original GHQ score (0-0-1-1) by multiple logistic regression analysis. They also used gender, age, body mass index (BMI), current smoking habit, alcohol drinking, and leisure time physical activity as independent variables. As a result, significant odds ratios were observed in BMI and high category of GHQ-12, presenting 1.18 (1.13–1.23) and 1.79 (1.05–3.04), respectively.

They concluded that CRP, a marker of cardiovascular disease, was associated with psychological distress measured by GHQ-12, although they mentioned the limitation of cross-sectional study design. Although they speculated the biological mechanism between inflammation and psychological distress, many confounders exist which should be adjusted for the analysis.

Puustinen et al. reported a cross-sectional study concluding that psychological distress was significantly associated with Framingham cardiovascular risk score in men [2] and also conducted 7-year follow-up study concluding that psychological distress could predict the development of the metabolic syndrome [3].

I conducted a cross-sectional study in male workers (Study-I) and also conducted a three-year cohort study to know the effect of psychological distress on CRP (Study-II). As a validation study, the main outcomes of those studies were presented according to the method adopted by Puustinen et al. [1].

### Study-I

A cross-sectional study in 2011 on 4,725 male workers of a car-manufacturing company was conducted. Serum CRP ≥10 mg/l was excluded from the database to rule out any occult inflammation. The means and standard deviations of age and BMI were 42.9 ± 8.9 and 24.0 ± 3.6, respectively.

Multiple logistic regression analysis identified that BMI, not current smoking and not everyday drinking were significantly associated with the presence of CRP >3 mg/l, with odds ratios (95% confidence intervals) of 1.15 (1.11–1.19; $P < 0.001$), 0.63 (0.48–0.83; $P < 0.01$) and 1.58 (1.13–2.20; $P < 0.01$), respectively. In contrast, odds ratios (95% confidence intervals) of medium (GHQ-12 scores: 1–3) and high (GHQ-12 scores: 4–12) psychological distress against low (GHQ-12 scores: 0) psychological distress for the presence of CRP >3 mg/l were 1.24 (0.83–1.84) and 1.09 (0.75–1.58), respectively.

### Study-II

Baseline study had conducted in 2008 on male workers of the same company ($n = 2{,}688$). Serum CRP was measured in 2011, and CRP ≥10 mg/l was excluded from the database. Mean and standard deviation of age and BMI were 44.0 ± 6.1 and 23.9 ± 3.6, respectively.

Multiple logistic regression analysis identified that age and BMI were significantly contributed to the presence of CRP >3 mg/l, with odds ratios (95% confidence intervals) of 0.96 (0.93–0.99; $P < 0.05$) and 1.15 (1.10–1.20;

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$P < 0.001$), respectively. In contrast, odds ratios (95% confidence intervals) of medium (GHQ-12 scores: 1–3) and high (GHQ-12 scores: 4–12) psychological distress against low (GHQ-12 scores: 0) psychological distress for the presence of CRP >3 mg/l were 1.34 (0.63–2.88) and 1.54 (0.76–3.13), respectively.

From these cross-sectional and three-year follow-up studies, the relationship between GHQ-12 and increased serum CRP could not be observed. There are ethnic differences in CRP [4], and information derived from Japanese local data cannot be extended to other ethnic group. I previously put into question on the relationships between biological and psychological indicators [5]. There are some other factors that may interact with GHQ-12 and CRP, and these factors cannot adequately be used in an epidemiological study because of a lack of sufficient knowledge on health and behaviour.

Cause-effect relationship becomes stronger when the relationship was also observed in other fields and in different times. I believe that the relationship between biological and psychological data should be repeated by presenting precise information on test situation of the study.

**Conflict of interest** There is no conflict of interest in this study.

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