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Rheumatoid arthritis and schizophrenia: a negative association at a dimensional level

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Abstract

There is wide evidence for a decreased risk of rheumatoid arthritis in patients with schizophrenia. Nevertheless, very few studies have looked at the risk of schizophrenia in a group of patients with rheumatoid arthritis.

We prospectively investigated, with the SCL-90R, 220 consecutive outpatients with rheumatoid arthritis and 196 consecutive outpatients with various medical conditions, half of them suffering from psoriatic arthritis (a medical condition close to rheumatoid arthritis).

The SCL-90R appears to be a valuable tool to distinguish patients with schizophrenia from the outpatients of our sample, the former having more “paranoid ideation” ($p=0.004$) and more “psychoticism” ($p<0.001$) than the latter. The “paranoid ideation” dimension was significantly lower (25% decrease) in the sample of patients with rheumatoid arthritis compared to the combined control group ($p=0.005$), ratings under the median value being more frequent in the former group ($p=0.025$). Confounding factors might not explain this difference according to the regression logistic analysis performed.

As patients with rheumatoid arthritis have a lower score of paranoid ideation than controls in our sample, even after controlling for age, gender and severity of the disease, these data represent further evidence for a decreased risk of schizophrenia in individuals with rheumatoid arthritis.

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Keywords: Rheumatoid arthritis; Schizophrenia; SCL-90R; Psychoticism; Inflammatory; Genetics

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1. Introduction

Fifteen epidemiological studies analyzing the prevalence of rheumatoid arthritis (RA) in psychiatric populations (with various diagnoses) reported a much smaller than expected frequency of RA. The meta-analysis of these studies (Oken and Schulzer, 1999) showed a reasonable homogeneity between samples ($p=0.3$), and the computed odds-ratio for the risk of RA in schizophrenic patients was significantly below 1 (OR=0.29; $p<0.0001$; 95%CI [0.22–0.38]) when compared to other psychiatric, but nonschizophrenic, patients. Nine studies focused more specifically on schizophrenia, and showed a median frequency of comorbid schizophrenia and RA of 0.05%, well below the expected 1% (Spector, 1990). A recent and large study including 29,000 patients with schizophrenia also found a low frequency (0.09%) of association between schizophrenia and RA (Oken and Schulzer, 1999).

Several potential confounding factors have been proposed to explain such low detected comorbidity in schizophrenic patients, including lack of access to care, patient inability to clearly appreciate or describe a medical problem, and patient reluctance to discuss such problems (Goldman, 1999). Nevertheless, a true decrease of RA frequency in schizophrenic patients may exist as similar results were obtained (1) in various countries, (2) in large samples of individuals with schizophrenia specifically assessed for RA (i.e. independently of any specific request for care) (Gregg, 1939; Rothermich and Philips, 1963; Baldwin, 1980; Allebeck et al., 1985), (3) with relevant control populations such as patients with other psychiatric diagnoses (Baldwin, 1980; Mohamed et al., 1982; Allebeck et al., 1985; Mors et al., 1999), and (4) despite various methods of assessment (for review, see Eaton et al., 1992). Furthermore, different interesting explanations have shed light on this “negative association”, mainly at the immune system level. These explanations involved, for example, prostaglandin synthesis (Horrobin, 1977), tryptophan metabolism (Taylor, 1978), T- and B-lymphocytes (Smith, 1992; McAllister et al., 1989), serum interleukin receptor concentration (Ganguli et al., 1993), IGF-II (Holden, 1995), microglia (Munn, 2000), or natural resistance genes (Rubinstein, 1997). The role of HLA polymorphisms was particularly analyzed in both disor-

ders, with some convergent data regarding DR4 antigen, positively associated with RA (van Jaarsveld et al., 1998) and negatively with schizophrenia (Knight et al., 1992).

On the other hand, in the single study which assessed the risk for schizophrenia in a large sample of patients with RA, no lower risk was observed (Lauerma et al., 1998). However, this study did not investigate a specific comparison group with close clinical characteristics such as other chronic arthritis. Furthermore, the analyses were exclusively qualitative (frequency of the disorder), without looking at the dimensional level (comparing mean scores).

We thus reassessed the link between RA and schizophrenia with a different method. After depicting the item that distinguished outpatients with schizophrenia from outpatients with other medical conditions, we compared this item (i.e. paranoid ideation) in 220 patients with RA with those of 196 medical outpatients, roughly half of them suffering from psoriatic arthritis, controlling for confounding factors.

2. Methods

We prospectively recruited four original samples of consecutive outpatients. Patients were enrolled by rheumatologists (for rheumatoid arthritis and psoriatic arthritis patients), or by a psychiatrist (for the schizophrenic patients). All patients included gave written informed consent.

- The study sample consisted of 220 consecutive outpatients with rheumatoid arthritis, fulfilling the American College of Rheumatology criteria (Arnett et al., 1988), who were followed as outpatients in 15 different centers in France, mainly university hospitals.
- The first control sample recruited in the same 15 centers during the same period of time, consisted of 88 consecutive outpatients with psoriatic arthritis, satisfying the criteria published by Glodman et al. (1987), a condition that was chosen in order to potentially match different characteristics of the first study sample (mainly regarding disability and severity).
- The second control sample consisted of 108 outpatients with nonspecific medical problems

who were recruited in a university hospital (Louis Mourier Hospital in Paris suburb). These patients represented the majority (92%) of a medical consultation in 11 consecutive days, and were enrolled during the same period of time the other samples were constituted.

- The last sample consisted of 44 schizophrenic outpatients (ICD-10 criteria) followed at Louis Mourier hospital, representing the majority of patients who could read and understand the questionnaire (94%) for the same 11 consecutive days.

In order to reinforce the statistical power of the analysis, the first and second control samples were combined in the first part of the analysis (under the title “combined control group”), reaching a size ($N=196$) close to that of the study sample ($N=220$).

All 460 included outpatients fulfilled the SCL-90R questionnaire (Derogatis, 1983). This is a 90-item self-report multidimensional symptom inventory, oriented towards the measurement of psychopathology in psychiatric and medical outpatients (Derogatis et al., 1976). This instrument assesses 10 different domains, namely, somatization, obsessive-compulsive traits, interpersonal sensitivity, depression, anxiety, hostility, phobia, paranoid ideation and psychoticism. Response modalities are 0 (not at all), 1 (a little), 2 (moderately), 3 (quite a lot) and 4 (extremely). The total score (psychoneuroticism) ranges from 0 to 360, each dimension has 0 as lowest value, and between 40 (for hostility) and 105 (for depression) for maximum value. Thirty is the maximum for the “paranoid ideation” dimension and 80 for the “psychoticism” dimension. There are no generally accepted cut-off scores (Wiznitzer et al., 1992) for classifying the individuals.

Two dimensions of the SCL-90R theoretically distinguish patients with schizophrenia from others, namely, “paranoid ideation” and “psychoticism” (Derogatis, 1983).

With a standard deviation of 3.7 for the “paranoid ideation” dimension (this was observed in our sample), and an α risk of 5% and a β risk of 10%, 400 subjects need to be analysed in order to reveal a significant difference of at least 0.8 in the “paranoid ideation” score between two subgroups. For qualitative analyses performed with these parameters

($N=400$, $\alpha=5\%$ and $\beta=10\%$), a 10% frequency difference is significant.

Gender and age were collected for each patient, as potential confounding factors (Oken and Schulzer, 1999). Disease severity of RA and psoriatic patients was assessed by the Steinbrocker’s functional criteria that range from 0 to 4 (Steinbrocker et al., 1949).

Qualitative data were compared with χ^2 tests, and quantitative variables were analyzed with parametric analysis of variance, univariate or multivariate ANOVA and ANCOVA when appropriate. Parametric correlation analyses were performed between quantitative variables and the “paranoid ideation” score.

Considering the number of potentially confounding variables, a forward stepwise logistic regression analysis was performed to reveal parameters that may be important to distinguish RA from other medical conditions. Default p -values for stepwise entry ($p=0.10$) and removal ($p=0.15$) of predictors into the logistic model were retained (Hosmer and Lemeshow, 1980).

Statistic analyses were performed using SPSS® (SPSS, Chicago, IL, USA).

3. Results

The main characteristics of the four groups of patients are given in Table 1. The mean age of the patients was 57.4 years (standard deviation = 17.1) in the RA group, 48.8 years (s.d. = 12.6) in the psoriatic arthritis group, 44.2 (s.d. = 16.8) in the nonspecific medical problems group, and 41.3 (s.d. = 14.5) in the schizophrenic patients. There was heterogeneity between patients’ group for age ($F_{3,446}=29.89$, $p<0.0001$), and for the three qualitative variables presented in Table 1 (i.e., gender, employment status and impact of the disorder).

The first analysis verified the ability of the “psychoticism” and “paranoid ideation” dimensions of the SCL-90R questionnaire to distinguish schizophrenic patients from others, thus comparing outpatients with schizophrenia ($N=44$) and the remaining included patients, i.e., outpatients with various types of somatic disorders ($N=416$). We found that patients with schizophrenia had less hostility (2.00 ± 2.45 versus 3.24 ± 3.32 ; $F_{1,451}=5.79$, $p=0.017$, ANOVA) and somatization (5.95 ± 5.97 versus 9.81 ± 8.19 ; $F_{1,451}=9.22$, $p=0.002$, ANOVA) but more paranoid ideations

Table 1
Description of the four groups of outpatients according to diagnostic criteria

| Characteristics | Selection criteria of the samples recruited | | | | Schizophrenia N = 44 |
|---|---|-----------------------|--------------------------|-----------------------------------|-------------------------|
| | Study group | Control group | | | |
| | RA N = 220 | Psoriatic A N = 88 | Miscellaneous N = 108 | Combined control group N = 196 | |
| <i>Gender^a</i> | | | | | |
| Female | 76.74% | 51.72% | 74.76% | 64.21% | 36.11% |
| Male | 23.26% | 48.28% | 25.24% | 35.79% | 63.89% |
| <i>Employment status^b</i> | | | | | |
| Working | 27.78% | 46.43% | 51.85% | 47.75% | 25.71% |
| Unemployed | 11.11% | 11.9% | 18.52% | 13.51% | 11.43% |
| Retired | 43.52% | 19.05% | 22.22% | 19.82% | 14.29% |
| Disabled | 17.59% | 22.62% | 7.41% | 18.92% | 48.57% |
| <i>Impact of the disorder^c</i> | | | | | |
| None | 3.29% | 2.35% | 21.21% | 12.5% | 28.57% |
| Minimal | 13.62% | 10.59% | 23.23% | 17.39% | 5.71% |
| Moderate | 34.27% | 36.47% | 32.32% | 34.24% | 28.57% |
| Important | 44.13% | 44.71% | 18.18% | 30.44% | 37.14% |
| Extreme | 4.69% | 5.88% | 5.05% | 5.43% | 0.00% |

RA = rheumatoid arthritis.

Pso A = Psoriatic arthritis.

^a $\chi^2 = 37.15$, $df = 3$, $p < 0.0001$.

^b $\chi^2 = 46.12$, $df = 9$, $p < 0.0001$.

^c $\chi^2 = 65.92$, $df = 12$, $p < 0.0001$.

(4.93 ± 4.29 versus 3.22 ± 3.63 ; $F_{1,451} = 8.48$, $p = 0.004$, ANOVA) and psychoticism (5.89 ± 6.42 versus 2.81 ± 3.92 ; $F_{1,451} = 21.15$, $p < 0.001$, ANOVA) than the other patients. The scores of the other dimensions were not significantly different ($F > 1.66$, $p > 0.20$, ANOVA).

When taking into account the differences in age between samples, only scores of paranoid ideation ($F_{1,439} = 4.71$, $p = 0.030$) and psychoticism ($F_{1,439} = 6.71$, $p = 0.010$) dimensions distinguished schizophrenic patients from the others. For both dimensions, the scores were also significantly different between schizophrenic patients and the others in subgroup analyses restricted to males ($F_{2,140} = 5.89$, $p = 0.004$; $F_{2,140} = 5.41$, $p = 0.005$, respectively) and females ($F_{2,295} = 3.93$, $p = 0.02$; $F_{2,295} = 3.31$, $p = 0.04$, respectively) after controlling for age.

We then explored the variables that could differentiate the patients with RA from the group of other medical outpatients. The scores of “paranoid ideation” and “hostility” dimensions were lower (less severe) in the group of RA patients than in the combined control

group of medical outpatients ($F_{1,401} = 7.90$; $p = 0.005$; $F_{1,401} = 5.33$, $p = 0.02$, respectively). The remaining eight dimensions, including “psychoticism”, did not significantly ($p > 0.32$) differentiate patients with RA from other medical outpatients (Table 2).

A qualitative approach to the “paranoid ideation” dimension showed that patients who rate under the value of 3 (the median value observed in our sample) were significantly more frequent in the group of RA than in the combined control group ($\chi^2 = 5.01$, $df = 1$, $p = 0.025$).

Compared to the combined control group, patients with RA were more likely to be female (76.7% versus 64.2%; $\chi^2 = 7.67$, $df = 1$, $p = 0.006$), were older (average = 57.5 versus 46.8; $F_{1,406} = 62.35$, $p < 0.0001$, ANOVA) and had a more severe disease impact (average = 3.3 versus 3.0; $F_{1,395} = 11.9$, $p = 0.0006$, ANOVA). Of these three potentially confounding variables, only disease severity ($r = 0.15$; $df = 395$, $p = 0.003$) was correlated with the “paranoid ideation” score for the whole sample excluding schizophrenic patients, and also for both limited groups of patients

Table 2
Description of the SCL-90R scores in four samples of outpatients according to ICD-10 diagnostic criteria

| SCL-90R dimensions | Selection criteria of the samples recruited | | | | | | | | | | Significant differences between groups (ANOVA) | |
|----------------------|---|------|-----------|-------|------------------|------|----------------|------|-------------------|------|--|---------------------|
| | RA (1) | | Pso A (2) | | Non-specific (3) | | Combined (2+3) | | Schizophrenia (4) | | <i>p</i> < 0.05 | <i>p</i> < 0.005 |
| | Mean | s.d. | Mean | s.d. | Mean | s.d. | Mean | s.d. | Mean | s.d. | | |
| Somatisation | 9.69 | 7.66 | 10.02 | 8.36 | 9.88 | 9.1 | 9.94 | 8.76 | 5.95 | 5.97 | (1,4) (1,2+3) (2,4) (3,4) | (2+3,4) |
| Obsessive-compulsive | 7.53 | 6.69 | 7.33 | 7.57 | 7.18 | 7.03 | 7.25 | 7.25 | 8.2 | 7.42 | | |
| Sensitivity | 4.91 | 5.45 | 5.95 | 6.53 | 5.41 | 5.52 | 5.65 | 5.98 | 5.89 | 5.37 | | |
| Depression | 10.49 | 8.91 | 11.07 | 11.07 | 9.09 | 8.86 | 9.97 | 9.93 | 9.98 | 9.75 | | |
| Anxiety | 5.24 | 5.36 | 6.38 | 6.93 | 5.69 | 5.92 | 0.06 | 6.38 | 5.54 | 6.21 | | |
| Hostility | 2.85 | 2.88 | 3.85 | 3.94 | 3.53 | 3.52 | 3.67 | 3.71 | 2.00 | 2.45 | (1,4) (1,2+3) (3,4) | (2,4) (2+3,4) |
| Phobia | 2.58 | 3.73 | 3.42 | 5.15 | 2.93 | 4.84 | 3.15 | 4.97 | 3.84 | 4.45 | | |
| Paranoid ideation | 2.71 | 3.2 | 3.35 | 3.82 | 4.15 | 4.06 | 3.79 | 3.97 | 4.93 | 4.29 | (1,3) (2,4) | (1,4) (1,2+3) (3,4) |
| Psychoticism | 2.61 | 2.83 | 3.14 | 4.49 | 2.94 | 5.11 | 3.03 | 4.83 | 5.89 | 6.42 | (2,4) | (1,4) (3,4) (2+3,4) |
| Miscellaneous | 5.23 | 0.04 | 5.88 | 5.37 | 5.72 | 4.88 | 5.23 | 0.04 | 5.14 | 3.75 | | |

RA = Rheumatoid arthritis.
Pso A = Psoriatic arthritis.
s.d. = Standard deviation.

with RA and patients with psoriatic arthritis (data not shown). We thus compared, in a covariance analysis controlling for the latter confusing factor, the group of patients with RA with the combined control group, and with the limited group of patients with psoriatic arthritis, showing that the “paranoid ideation” score was still decreased in the RA group ($F_{2,395} = 11.32$, $p < 0.001$ and $F_{2,296} = 7.79$, $p = 0.001$, respectively).

Numerous factors are potentially involved to explain the “paranoid ideation” score. Therefore, a forward stepwise logistic regression analysis was also performed (Table 3), introducing in the model all the variables that characterize the group of patients with RA versus the combined control group of outpatients. In this analysis, age was the first factor that significantly predicted RA ($\chi^2 = 45.9$, $df = 1$, $p < 0.0001$),

then gender ($\chi^2 = 8.88$, $df = 1$, $p = 0.003$), then paranoid ideation score ($\chi^2 = 7.34$, $df = 1$, $p = 0.008$), and finally, severity of illness ($\chi^2 = 8.159$, $df = 1$, $p = 0.005$).

RA patients were then specifically compared with those having psoriatic arthritis, these latter patients being more adequately matched for disability and access to care (such as consulting in the same rheumatology departments). As expected, the disease severity did not differ between the two chronic arthritis conditions (3.33 versus 3.41, $F_{1,290} = 1.32$, $p = 0.25$), but patients with psoriatic arthritis were significantly younger (44.2 versus 57.4; $F_{1,306} = 26.1$; $p < 0.001$) and more commonly males ($\chi^2 = 18.3$, $df = 1$, $p < 0.001$) (Table 1). There was no significant difference for the paranoid ideation dimension scores between RA and psoriatic arthritis patients (2.71 versus 3.35, $F_{1,293} = 1.08$; $p = 0.30$), even after taking into account the role of age, gender and severity in a multivariate analysis ($F_{1,291} = 2.27$; $p = 0.13$).

Table 3
Logistic regression analysis (step-by-step) distinguishing patients with rheumatoid arthritis from others (patients from the combined control group)

| Steps | Variable | OR | <i>p</i> | 95% CI |
|--------|-------------------|------|----------|-----------|
| First | Age | 0.95 | < 0.0001 | 0.93–0.97 |
| Second | Gender | 2.04 | 0.003 | 1.57–2.51 |
| Third | Paranoid ideation | 1.09 | 0.008 | 1.03–1.15 |
| Last | Severity | 0.72 | 0.005 | 0.49–0.95 |

4. Discussion

In our study we found that the “paranoid ideation” score of the SCL-90R questionnaire is significantly lower in a group of patients with RA (roughly a 25%

decrease) than in patients presenting other medical conditions, even after controlling for potentially confounding variables such as age, gender and severity of illness. This result may be regarded as further evidence in favor of the previously published negative association between schizophrenia and RA, but performed at the dimensional level.

Vulnerability factors in RA that may be protective in schizophrenia mainly concern the inflammatory response system. The role of cytokines, for example, has been suggested in schizophrenia, as cytokines can modify the metabolism of neurotransmitters or influence neural development (Dinarello, 1996; Rothwell and Hopkins, 1995). Aberrant proportions of immune-competent cells, indicating immunological dysfunctions, have often, but not always, been reported in schizophrenia (Kirch, 1993). The genes that code for interleukin-1 [IL-1], interleukin-6 [IL-6] and tumor necrosis factor [TNF- α] constitute different haplotypes (as these three genes are clustered on the 2q13–21 region) that were significantly different in 50 schizophrenic patients compared to 400 controls (Katila et al., 1999).

Numerous candidate factors have thus been suggested, but the HLA system has been the most studied. The modest but positive association between HLA DR4 antigen and RA (van Jaarsveld et al., 1998) could thus be related to the hypothesis that DR4 antigen is a protective factor against schizophrenia (Knight et al., 1992). The low frequency of DR4 antigen reported in various samples of schizophrenic patients (Sasaki et al., 1999; Wright et al., 1996; Arinami et al., 1998; Sasaki et al., 1999) favors the hypothesis that a risk factor of one disorder (rheumatoid arthritis) is less represented in another (schizophrenia). However, DR4 antigen has probably a weak and heterogeneous effect on RA (de Jongh et al., 1986), and a low frequency of DR4 antigen in schizophrenia has not been found in all studies (Gibson et al., 1999; Hawi et al., 1999). Presence of vulnerability genes involved in the immune response is compatible with the role of various infectious agents that have been proposed in both disorders (such as retroviruses, mycobacterium 65-kDa HSP, herpes viruses or toxoplasma gondii). These microorganisms could act as triggering an autoimmune reaction causing the disease process (for review, see Torrey and Yolken, 2001).

As the different factors potentially involved in the pathogenesis of schizophrenia are mainly nonspecific and have a moderate effect, it can be expected that their impact on the disorder is partial, moderately modifying the vulnerability to schizophrenia. Thus, it may be more relevant to investigate the analyses on the dimensional level of the disorder rather than the qualitative presence or absence of the syndrome. Such analyses may be more in accordance with the liability threshold model of schizophrenia. Also, the dimensional approach may be more relevant for this type of probable broad protective effect that has a low chance of being very specific to schizophrenia. The exact specificity of schizophrenia in the large psychotic spectrum (or phenotype) is in fact regularly doubted according to the biological markers that have been studied (for example, see Cloninger, 1987).

Several limitations of our study need to be discussed.

Firstly, chance findings cannot be ruled out, specifically due to the limited size of our study, and given the fact that the single study that looked for schizophrenia in a group of RA patients did not show a decreased frequency of schizophrenia compared to patients with appendicitis (Lauerma et al., 1998). Nevertheless, in the latter study, the ability to show variations of schizophrenia frequency in the two samples might have been limited by the way schizophrenia diagnosis was concluded, since it was only based on the analyses of hospital files during an 8-year period. In our study, the comparison with psoriatic arthritis, which was chosen as an arthritis control group close to RA, was not significant, although with more than 400 medical outpatients included in the study, the size of this sample should be large enough to detect relatively modest effect (see Methods). On the other hand, this absence of significant difference may be explained by the reduced power of the analysis, owing to a smaller comparative group in this analysis. The fact that the mean “paranoid ideation” dimension in the RA group (2.71) is reduced compared to the combined control group (3.79) or to the psoriatic arthritis group (3.34) favors this hypothesis (Table 2). Furthermore, when the most important confounding factor (i.e. severity) was the single parameter controlled in analyses of covariance (as it was the only variable correlated with the paranoid ideation score), the RA group was significantly differ-

ent from both the combined control group and the group of patients with psoriatic arthritis.

Secondly, the SCL-90R is one of the most frequently used instruments for screening medical outpatients but its ability to detect psychotic disorders may be limited (Wetzler and Marlowe, 1993). Initially, schizophrenic patients were considered to rate differently on two dimensions of the SCL-90R, namely, “psychoticism” and “paranoid ideation” (Derogatis, 1983). Hence the fact that only the latter dimension distinguished RA patients from the combined control group in this study may be a surprising finding. However, this could be explained by a higher reliability of the “paranoid ideation” dimension than that of the “psychoticism” dimension. When patients’ SCL-90R ratings were compared to therapist evaluations, only two dimensions were not concordant, including “psychoticism” (Kass et al., 1983). In another study, “paranoid ideation” dimension score was also the only variable that distinguished psychotic patients from others (Wilson et al., 1985). Furthermore, we were able to confirm that medical outpatients were mainly different from a small group of schizophrenic outpatients according to this “paranoid ideation” dimension, particularly when gender and age effects were taken into account. The ability of this dimension to distinguish schizophrenic patients from others has thus been assessed and replicated in our sample. The only dimension that was also significantly different between RA patients and the combined control group was hostility, but the significance of this variable did not achieve the Bonferroni correction used for multiple comparisons ($0.05/10=0.005$), and was not detected by the logistic regression approach.

Alternatively, the “paranoid ideation” and “psychoticism” dimensions could reflect different aspects of schizophrenia, rheumatoid arthritis being specifically protected from only some of them. In this view, the “paranoid ideation” dimension has been described by the authors (Derogatis et al., 1976) as being more specific of delusional symptoms of schizophrenia, mainly assessing projective thoughts, hostility, suspiciousness, grandiosity, centrality, fear of loss of autonomy and delusions. The “psychoticism” dimension is, on the other hand, partly devoted to detect hallucinatory symptoms (auditory hallucinations and thoughts broadcasting) but also to a larger set (6 items

out of 10) of symptoms related to schizoid life (being withdrawn and isolated). The lower “paranoid ideation” score observed in the RA group could thus be explained by the fact that patients with rheumatoid arthritis may have a lower risk for positive (delusional syndrome) rather than negative (schizoid isolation) schizophrenic symptoms.

Thirdly, as patients were not seen in a face-to-face interview by a psychiatrist but rather by a rheumatologist, it was not possible to identify cases of schizophrenia. It is thus difficult to extend the fact that we found differences specifically at a dimensional level (i.e., a lower “paranoid ideation” dimension score in the group of RA) to the differences in frequency of affected cases (i.e., lower number of cases of schizophrenia in the group of RA). However, the distribution of the “paranoid ideation” dimension score in the RA group differs mainly from the combined control group because of an excess of low level ratings (below the median value). Hence, the larger group of patients in the RA group having a low score in “paranoid ideation” dimension may decrease the mean score of the “paranoid ideation” dimension in the complete group. It would be useful to complete this study by a psychiatric interview of a large sample of RA and confront the dimensional data obtained by the SCL-90R to the syndromic level. It would also be interesting to compare RA patients according to their HLA DR4 antigen status.

Since studies of large population-based samples are difficult, the convergence of results derived from various methods is of importance. In this study, after controlling for potential confounding factors including gender, age and disease severity, we showed that the “paranoid ideation” dimension score of the SCL-90R is significantly lower in RA patients than in a broad group of outpatients with various medical conditions, including psoriatic arthritis. This result adds further evidence for a negative association between RA and schizophrenia.

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