Letters to the Editor

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Injury and joint hypermobility syndrome in ballet dancers—a 5-year follow-up

SIR, We have previously reported on the prevalence of joint hypermobility and the joint hypermobility syndrome (JHS) in the Royal Ballet School and Company [1]. In this study, we observed, particularly among the female dancers, that skin hyperextensibility and joint dislocation were the principal clinical features that defined the presence of JHS, having removed joint pain and soft tissue injury from the analysis, given their relatively high prevalence throughout the study cohort. Generalized hypermobility was ubiquitous among the dancers.

A key finding, however, was a decrease in prevalence of JHS in ascending from junior school, through the senior school to Company, and within the Company from Corps de Ballet to principal dancer. We suggested that JHS may be associated with a greater risk of injury and/or prolonged periods of recovery post-injury, which may have an adverse affect on career development.

In this study, we undertook a 5-year follow-up of previous students in the schools and of the company. Using a self-reporting questionnaire, we identified the frequency and type of injuries and the periods of recovery requiring >6 weeks of rest from dancing. The presence or absence of JHS was defined by the original criteria of skin hyperextensibility and joint dislocation having identified that none of the previously defined non-JHS dancers reported dislocations at present.

The response rate was 69% with 93 of the original 135 dancers replying to the questionnaire. Of these, 50 dancers were still within the Royal Ballet Companies; and 55 were females and 38 males. Eighteen (33%) of the females and 12 (32%) of the males had previously been identified as having JHS in the first study [1]. Given that there were no significant differences in the proportion of dancers with JHS compared with what was found in the original study, we concluded that there had been no selection bias for the presence of JHS in the current study.

Table 1 shows the data for reporting symptoms for multiple joint pain, cervical, dorsal or lumbar pain, dislocations, ankle sprain, ligament injuries, shoulder capsulitis or fractures. There was no significant difference in reporting between JHS and non-JHS dancers, except for the males, in whom multiple joint pains were significantly more frequent in the JHS dancers than non-JHS.

Significant differences were seen in the occurrence of tendon injuries and having had to take time off from dancing for >6 weeks in favour of the non-JHS dancers in females. In men, a similar result was found in both tendon injuries and time off from dancing (Table 2).

TABLE 1. Symptoms reported over a 5-year period

Condition	Female, %	Male, %
Multiple joint pains	78	76
Neck pain	43	51
Dorsal pain	45	37
Lower back pain	70	53
Dislocations	8	8
Ankle sprain	46	40
One or more ligament injury	34	30
Shoulder capsulitis	6	10
Fractures	18	38

Dancers suffer from a variety of overuse injuries [2, 3], which have implications for training and performance. The 'fit to dance' studies reported that overuse of soft tissue and muscle accounted for 64% [4] and 51% [5] of injuries reported by the UK dance population. The prevalence of soft tissue injuries in our study was similar to these percentages and also similar between males and females. However, we identified that the reporting of at least one or more types of tendon injury was more common in the JHS than the non-JHS dance population for both females and males. Furthermore, dancers with JHS appeared more vulnerable in the sense that JHS was associated with a significantly greater risk of having to take time off from dancing because of injury. The length of time the dancers are off work has not been consistently recorded in other studies.

It remains unclear as to whether an injury in dancers with JHS simply takes longer to heal, or whether there is greater tissue damage before the injury is reported, or both. Either way, this study affirms our previous impression that the dancer with JHS is both more vulnerable to the effects of injury and that healing is likely to be more prolonged and may be incomplete.

The nature of ballet means that these dancers need to be both strong (powerful) and have stability, stamina and endurance. Muscle and tendon gradually respond to the work load by means of hypertrophy, becoming stronger in response to loading. However, if the loading is excessive, damage will occur either as overuse, premature degeneration or mechanical failure [6]. JHS may be considered a form of collagen deficiency, and in a JHS dance population the tendons may be weaker structurally and slower to respond to training effects, thus leaving them more vulnerable to injury during training or performance. Other causes of stress in a tendon can be due to faulty technique, anatomical factors and muscle imbalance [6].

Dance companies, instructors and health professionals including therapists should recognize the presence of JHS when supporting the injured dancer through a period of recovery, and training should focus on early identification and intervention to prevent injury in these individuals.

Rheumatology key message

- Early recognition and intervention may prevent recurrent injury in JHS.

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TABLE 2. Comparison of significant differences between JHS and non-JHS dancers, by gender

Condition	JHS, %	Non-JHS, %	Odds ratio (95% CI)	*P*-value
Female				
At least one tendon injury	50	21	3.62 (1.08, 12.17)	0.037
Stopped dancing >6 weeks due to injury	61	32	3.27 (0.87, 10.29)	0.047
Stopped dancing >6 weeks on more than one occasion	36	25	3.49 (0.68, 17.79)	0.1
Male				
At least one tendon injury	42	8	8.57 (1.36, 54.14)	0.02
Stopped dancing >6 weeks due to injury	83	35	9.44 (1.69, 52.73)	0.01
Stopped dancing >6 weeks on more than one occasion	30	50	–	–

CI: confidence interval.

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No evidence for association of the systemic lupus erythematosus-associated *ITGAM* variant, R77H, with rheumatoid arthritis in the Caucasian population

Sir, A non-synonymous integrin-α-M (*ITGAM*) variant (R77H) confers a strong risk for SLE in Caucasian, African and Hispanic populations [odds ratio $(OR)_{meta} = 1.83$] [1, 2]. *ITGAM* encodes the α-chain subunit of integrin-$\alpha_M\beta_2$, a cell surface receptor expressed predominantly on monocytes and neutrophils, which mediates activation, adhesion and migration of leucocytes through the endothelium, as well as phagocytosis of complement-coated particles, and neutrophil apoptosis [3]. Interaction of integrin-$\alpha_M\beta_2$ with intercellular adhesion molecules (ICAMs) mobilizes leucocytes to sites of inflammation, and *in silico* modelling suggests that the R77H substitution may alter the α1 domain that binds ICAM-1 [1, 3]. Polymorphism of *ICAM-1* is implicated in susceptibility to RA: a K469E variant (*rs5498*) in *ICAM-1* is associated with RA in Korean [4] and UK sample sets [5], but not in an Italian sample set [6].

SLE and RA are systemic autoimmune diseases that are known to share common genetic susceptibility through the 620W variant of *PTPN22* [7], *rs75674865* within *STAT4* and several variants within *TNFAIP3* [8]. We therefore tested for association of *ITGAM* R77H (*rs1143679*) with susceptibility to RA in Caucasian sample sets drawn from New Zealand (NZ) and the UK, including the Wellcome Trust Case Control Consortium (WTCCC).

A total of 746 NZ European Caucasian RA patients and 564 healthy controls were genotyped for *rs1143679* using a Taqman single nucleotide polymorphism (SNP) genotyping assay (Applied Biosystems, Foster City, CA, USA) on the Lightcycler 480 real-time PCR system (Roche, Indianapolis, IN, USA). The NZ Caucasian population is primarily descended from British immigrants. Genetic similarity is supported by the similar allele frequency of the RA-associated PTPN22 620W variant (9.9% in our NZ control samples [9], and 9.6% in WTCCC controls [5]). This variant is known to differ in frequency within Europe, with frequency increasing from south to north. All cases satisfied the ACR criteria for RA, and 66% of the patients were females. Of those patients for whom serological data were available, 83% (543/654) were RF positive, and 67.6% (276/408) were anti-cyclic citrullinated peptide (anti-CCP) antibody positive. All participants gave their written informed consent, and the NZ Multi-region Ethics Committee and the Lower South Ethics Committee approved the study.

The UK WTCCC study genotyped two SNPs within *ITGAM*, not including *rs1143679* or any SNP in high linkage disequilibrium (LD). We could not impute *rs1143679* for the WTCCC data because the necessary haplotypic data were not available from HapMap. Therefore, we imputed genotypes for 1861 WTCCC RA cases and 2938 controls for all other SNPs within *ITGAM* using impute [10]. We also included 729 RA cases from Oxford in the UK sample set that were genotyped for *rs1143679* as described above. All Oxford patients satisfied the ACR criteria for RA, and gave written informed consent. The sample comprised 71% females and 79% (567/720) were RF positive. The Oxford Research Ethics Committee granted study approval. Using the minor allele frequency (MAF) of the European–American SLE control group (0.11), and the allelic OR (1.73) [1], the NZ sample set has 98.7% power and the UK has 100% power at $\alpha = 0.01$ to detect an equivalent association. Association analysis was performed using PLINK (pngu.mgh.harvard.edu/~purcell/plink/).

All NZ *rs1143679* genotypes were in Hardy–Weinberg equilibrium (Table 1). We did not observe a statistically significant difference in allele and genotype frequencies between the RA case and control samples (allelic $P = 0.72$; OR = 0.95; 95% CI 0.73, 1.24). Previously, six SNPs (*rs9936831*, *rs9888879*, *rs12928810*, *rs9888739*, *rs11860650* and *rs6565227*) within *ITGAM* that are in very high LD with *rs1143679* (r^2 values approaching 1) have been reported in a European–American sample set [2]. The WTCCC imputed data for these SNPs are presented in Table 1. None of the SNPs demonstrated a significant difference in allele or genotype frequency between RA patients and controls (smallest allelic $P = 0.20$ for *rs9888879* and *rs12928810*; OR = 1.09; 95% CI 0.95, 1.26). Using these SNPs as proxies for *rs1143679*, the WTCCC data indicate that this SNP also does not alter the risk for RA in this cohort.

Stratification on RF and CCP status did not indicate any significant differences in the *rs1143679* genotype distribution for NZ RA cases (RF: $P = 0.38$; CCP: $P = 0.78$). Nor was a significant difference observed between RF-positive and RF-negative Oxford cases ($P = 0.44$) (Table 1). Serological data on the WTCCC samples were unavailable.

We used STATA 8.0 (http://www.stata.com) to meta-analyse the NZ and UK data (using imputed SNP *rs9888879* as a proxy for *rs1143679* in the WTCCC) (Table 1). The combined analysis confirms that there is no significant difference in the MAFs of cases *vs* controls ($P_{meta} = 0.51$; $OR_{meta} = 1.05$; 95% CI 0.93, 1.17).

In conclusion, there is no evidence from a combined analysis of 3336 cases and 3502 controls to support association, at a similar strength as observed in SLE, of the *ITGAM* variant, R77H, with RA in the Caucasian population. However, we cannot eliminate the possibility of a weaker effect for this variant in RA. Genotyping this variant in additional RA case–control sample sets is justified.

Rheumatology key message

- The strongly SLE-associated R77H (*rs1143679*) *ITGAM* variant does not confer a similar risk to RA in the Caucasian population.

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