biology letters

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Biol. Lett. 2005 **1**, 400-403
doi: 10.1098/rsbl.2005.0343

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doi:10.1098/rsbl.2005.0343
Published online 11 July 2005

MHC-assortative facial preferences in humans

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Individuals tend to choose mates who are sufficiently genetically dissimilar to avoid inbreeding. As facial attractiveness is a key factor in human mate preference, we investigated whether facial preferences were related to genetic dissimilarity. We asked female volunteers to rate the attractiveness of men from photographs and compared these results with individual genotypes at the major histocompatibility complex (MHC). In contrast to previously reported preferences based on odour, we found a non-significant tendency for women to rate MHC-similar faces as more attractive, suggesting a preference for cues to a self-similar MHC in faces. Further analysis revealed that male faces received higher attractiveness scores when rated by women who were MHC-similar than by MHC-dissimilar women. Although unexpected, this MHC-similar facial preference is consistent with other studies documenting assortative preferences in humans, including for facial phenotype.

Keywords: mate choice; beauty; HLA; good genes; heterozygosity; imprinting

1. INTRODUCTION

There is growing evidence that polymorphic major histocompatibility complex (MHC) genes influence human mate choice. In common with preferences observed in mice (Yamazaki *et al.* 1988; Potts *et al.* 1991; Roberts & Gosling 2003), three laboratory studies report disassortative odour preferences in humans (Wedekind *et al.* 1995; Wedekind & Furi 1997; Thornhill *et al.* 2003). A fourth study found preferences for an intermediate level of MHC-dissimilarity (Jacob *et al.* 2002). Evidence also exists for MHC-disassortative mating patterns among actual partners (Ober *et al.* 1997). Disassortative preferences may be adaptive as they increase offspring heterozygosity (Potts *et al.* 1991). MHC-related odours are thought to be soluble MHC molecules, bound peptides or metabolites made volatile by commensal microflora, detection of which may be influenced by close linkage between MHC loci and olfactory receptor genes (Penn & Potts 1998*a*,*b*).

To date, studies of MHC-correlated preferences have focused on perceived odour pleasantness as the mechanism for mate discrimination. Ober *et al.*'s (1997) speculation that other sensory modalities may be involved has not been pursued. This is perhaps unsurprising since a mechanism by which MHC-dissimilarity could be perceived is less obvious for visual or auditory traits. Nonetheless, as murine MHC-odour preferences are determined through familial imprinting (Yamazaki *et al.* 1988; Penn & Potts 1998*a*,*b*), a visually mediated preference may be plausible since facial preferences appear to develop in a similar way. Cross-fostering alters preferences of sheep and goats towards faces of their foster-species (Kendrick *et al.* 1998) and similar imprinting-like effects are known in humans: facial features of partners and opposite-sex parents are correlated (Bereczkei *et al.* 2002; Little *et al.* 2003), women born to older fathers prefer older faces in potential mates (Perrett *et al.* 2002) and adopted daughters choose mates whose faces resemble their adoptive father (Bereczkei *et al.* 2004).

Here we tested whether perceived facial attractiveness was associated with allele sharing at key MHC loci. We designed the experiment as a visual analogue of Wedekind's odour experiment (Wedekind *et al.* 1995) so that women were asked to rate photographs of three men who were MHC-similar to themselves and three men who were MHC-dissimilar.

2. MATERIAL AND METHODS

(a) *Experimental design*

Seventy-five beardless men and 92 women, aged 18–35, took part. All were students or staff at Newcastle University. To avoid confounding variables and minimize the potential effects of population stratification in allelic frequencies (Cao *et al.* 2001) we only included participants who were white and of British origin. It remains possible that preferences reported here are consistent with population substructure across different regions of the UK and, indeed, small scale individual differences in MHC frequency and facial appearance could potentially drive larger scale regional effects, but this is beyond the scope of this study and merits further attention.

Participants were genotyped by polymerase-chain reaction using sequence-specific primers at *HLA-A*, *-B* and *-DRB1* loci. We then pre-selected three MHC-similar (on average 3.21 shared alleles; range 1.67–4.67, s.d. = 0.68) and three MHC-dissimilar men (0.01, 0–0.67, 0.08) per woman. These means compare favourably with the number of common antigens in Wedekind's experiment (similar 3.3, dissimilar 0.1; Wedekind *et al.* 1995) and are based on matching at the same loci.

Digital photographs of men assuming a neutral expression were taken under standard lighting conditions. Images were masked to remove potentially confounding information about clothing, hair style and colour (Roberts *et al.* 2004). Having first been shown all the images, participants rated faces using a 7 point scale (1 = unattractive, 7 = attractive) in two contexts: seeking a short-term or a long-term relationship (definitions described in Perrett *et al.* 2002). Since menstrual cycle phase alters facial preferences (Penton-Voak *et al.* 1999*a*,*b*), we tested women in the late follicular phase (between days 10–14; Wedekind *et al.* 1995).

(b) *Analysis*

Following Wedekind *et al.* (1995), we analyse preferences using both women and men as the units of analyses. The second is potentially more powerful (Wedekind *et al.* 1995), despite a potentially reduced sample size (as here), because it controls for all other facial cues, including aspects unrelated to MHC, leaving the

Received 20 April 2005
Accepted 5 May 2005

relative similarity of raters as the only variable. Since women rated faces in two contexts, we analysed results using within-subjects ANOVA to investigate both main effects and potential interactions between preferences and rating context. As the comparison using men as the unit of analysis could be influenced by differential use of the rating scale among raters, we repeated this analysis using *z*-scores based on standardization within each woman's set of ratings (see also Roberts *et al.* 2005). Before standardization, we excluded the 20 men who were seen in only one condition (either similar or dissimilar). On average, the men remaining were seen 3.18 times (range 1–8) in the MHC-dissimilar condition and 3.54 times in the MHC-similar condition (range 1–10). As calculation of the average score for each male's face is based on different numbers of ratings, any resulting difference between the two groups is likely to be conservative. Mean short-term and long-term scores for the 92 women were normally distributed (Kolmogorov–Smirnov tests, both $p > 0.2$), as were long-term scores when separately analysed for judgments of similar and dissimilar faces. Mean scores given to each face (i.e. men as the unit of analysis) were always normally distributed. However, raters' short-term scores were not normally distributed ($p < 0.05$) when analysed separately among similar and dissimilar men. We proceeded with the within-subjects ANOVA because data for the more powerful comparison with men as the unit of analysis were always normally distributed, and because ANOVA is robust to deviations from normality, especially in samples over 30 and those (as here) which are not heavily skewed (Wilcox 2001). However, we also ran two-sample permutation tests (10 000 iterations) to compare against the main ANOVA results. We found that the results of ANOVA and permutation tests were consistent.

3. RESULTS

Within-subjects ANOVA (table 1) revealed a non-significant tendency ($p = 0.08$) for women to give higher attractiveness scores to faces of men who were MHC-similar to themselves (figure 1*a*). Women gave absolutely higher scores in the short-term than the long-term context ($p < 0.001$), but there was no significant context×MHC interaction. Permutation tests showed a similar effect of similarity on ratings, at least in the long-term context ($p = 0.07$; short-term, $p > 0.1$).

Using men as the unit of analysis, and thus controlling for any non-MHC correlated effects, ANOVA revealed significant effects of both similarity ($p = 0.031$) and context ($p = 0.002$), such that men received higher scores in the short-term than long-term context and when they were MHC-similar to the women raters (figure 1*b*). Again, permutation tests showed significant effects in the long-term context ($p = 0.027$; short-term, $p > 0.1$). Within-subjects ANOVA, using *z*-scores to control for differential use of the rating scale, revealed a significant interaction between MHC-similarity and context: the discrepancy in scores between similar and dissimilar conditions was greater when ratings were made in the long-term context.

4. DISCUSSION

Our results suggest perceptual sensitivity to facial characteristics associated with allele-sharing at MHC loci. The exact cues by which these preferences are mediated are unknown, although variation in facial shape appears to be a likely candidate and further work is planned to investigate them. A relationship between MHC-similarity and facial appearance may occur through two possible routes. First, there could be a relationship between physiognomy and polymorphic genes either within or closely linked to the MHC region. Dysmorphic facial phenotypes are diagnostic symptoms of defects in several genes in or near the MHC region, including *NEU1* (Young *et al.* 1987) and *COL11A2* (Snead & Yates 1999). For example, mutations in *COL11A2*, which encodes the fibril-forming collagen XI, are associated with Stickler syndrome, characteristic features of which include a flat midface with depressed nasal bridge, short nose, anteverted nares and micrognathia (Snead & Yates 1999). However, there is no evidence yet that

Table 1. Effects of MHC-similarity and rating context (short- or long-term) on attractiveness scores of male faces. (Data were analysed using within-subjects ANOVA.)

analysis	effect	*F*	d.f.	*p*
mean ratings per woman	MHC	3.07	1,91	0.083
	context	15.28	1,91	<0.001
	MHC×context	0.40	1,91	0.528
mean ratings per man (raw scores)	MHC	4.90	1,54	0.031
	context	10.86	1,54	0.002
	MHC×context	0.134	1,54	0.716
mean ratings per man (*z*-scores)	MHC	4.02	1,54	0.050
	context	0.01	1,54	0.929
	MHC×context	4.53	1,54	0.038

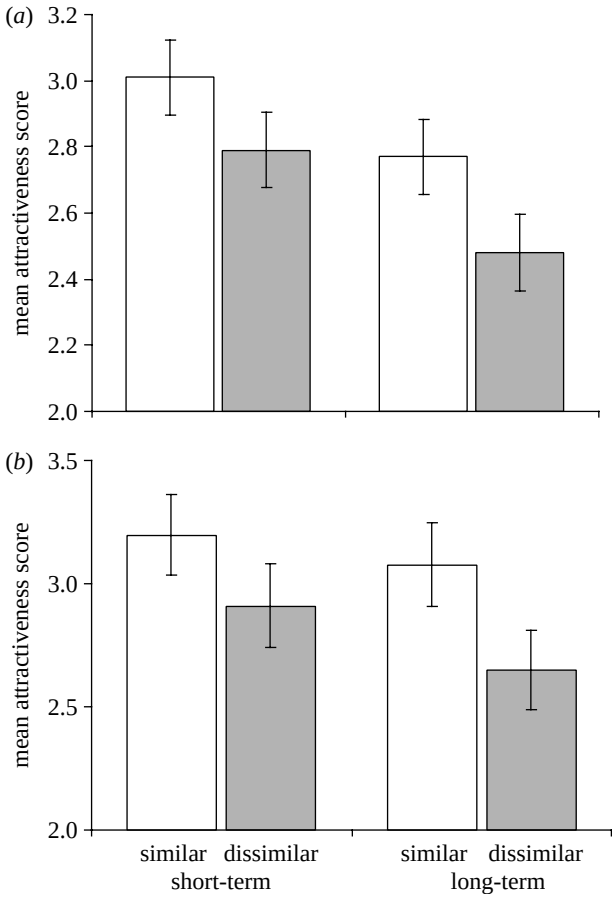

Figure 1. Attractiveness ratings of male images for short and long-term relationships. (*a*) Mean scores given to three men who are MHC-similar, and three who are MHC-dissimilar, to women raters. (*b*) Means scores given to each male face when rated by women who are MHC-similar or dissimilar to them. Error bars are 1 s.e.

COL11A2 is polymorphic, which would be a requirement of such a direct mechanism. We believe a more likely explanation is that MHC-similarity might be correlated with overall genomic similarity (Grob *et al.* 1998) or at least with similarity in a subset of genes that influence facial phenotype.

A preference for MHC-similar faces was surprising since the majority of MHC studies report disassortative preferences (e.g. Yamazaki *et al.* 1988; Potts *et al.* 1991; Wedekind *et al.* 1995; Wedekind & Furi 1997; Roberts & Gosling 2003), leading to departures from Hardy–Weinberg equilibrium (in terms of heterozygote excess) in human populations (Black & Salzano 1981). Given this, our study would undoubtedly benefit from replication by other interested researchers. However, our sample is large for a study of this kind (92 normally cycling women and 55 men compares favourably, for example, with 31 and 38 by Wedekind *et al.* 1995 and 49 and 6 by Jacob *et al.* 2002), suggesting that the unexpected effect is not determined by sample size. Furthermore, one previous result also finds evidence for greater within-couple MHC-similarity than expected under random mating (Rosenberg *et al.* 1983), while Thornhill *et al.* (2003) found a non-significant trend towards MHC-similarity in women's odour preferences (though male preferences were the opposite).

One explanation for the assortative preference found here may be a contextual issue: preferences for similarity were more evident when women rated faces for long-term partnerships. Although a context× MHC interaction was only found in this analysis, and so interpretation must be cautious, raters' concerns in long-term contexts could potentially shift from choosing attractive mates to choosing caring, agreeable companions. Selection could favour such preferences if this helps secure prolonged paternal investment. This idea is supported by results indicating individuals judge phenotypically self-similar faces as being more trustworthy, especially in the long-term context (DeBruine in press).

A second, more intriguing, explanation for the apparent discrepancy between odour and facial preferences is that the two modalities could combine to achieve an optimal level of genetic complimentary or outbreeding (Bateson 1978). Visible traits, such as faces, could be long-range cues of relative similarity, filtering out individuals of extremely different genotypes, while odour might secondarily filter out individuals with very similar genotypes. Although speculative, this idea is consistent with both bodies of evidence, as well as with studies finding no strong evidence for disassortative mating in human populations (Hedrick & Black 1997). Previous work has indeed suggested that an intermediate level of heterozygosity is favoured because high levels reduce the T-cell repertoire during thymic selection (Nowak *et al.* 1992).

Although the direction of preference was unexpected, our results are nonetheless consistent with very many studies that suggest that assortative mating is widespread in humans. In addition to social characteristics such as education (Jaffe & Chaconpuignau 1995), individuals prefer partners of similar physical attractiveness to themselves (Berscheid *et al.* 1973) and facial images digitally manipulated to appear self-similar (Penton-Voak *et al.* 1999*a*,*b*). Physical features are typically positively correlated within couples (Spuhler 1968), including height (Pawlowski 2003) and age (Jaffe & Chaconpuignau 1995). Moreover, married partners resemble each other to the extent that their faces can be correctly matched by strangers (Griffiths & Kunz 1973; Hinsz 1989; Bereczkei *et al.* 2002). The prevalence of studies showing assortative preferences in humans suggests there must be fitness benefits and our results add weight to this body of evidence. We hope that future studies will be carried out in this interesting area. These may need to address the intriguing problem of how apparently opposing facial and odour preferences are integrated during mate choice.

We are grateful to all our participants for taking part in this study, and to Lisa DeBruine, Candy Rowe and three anonymous referees for their valuable comments on the manuscript. The work was carried out with ethical permission from the Newcastle & North Tyneside NHS Trust Ethical Committee and was funded by the Wellcome Trust.

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