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More than just a pretty face? The relationship between immune function and perceived facial attractiveness

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It has long been hypothesized that attractiveness provides a cue to a target's health and immunocompetence. However, much of the research testing this hypothesis has relied on a small number of indirect proxies of immune function, and the results of this research have been mixed. Here, we build on this past research, examining the relationship between target attractiveness and (i) self-reported health, (ii) *in vivo* measures of inflammation and white blood cell count/composition, and (iii) *in vitro* tests of targets' immune function, including (c_1) leucocyte proliferation in response to immunological stimulants, (c_2) phagocytosis of *Escherichia coli* bioparticles, (c_3) NK cell-mediated lysis of target tumour cells, and (c_4) *Staphylococcus aureus* growth in isolated plasma. Results revealed multiple, sometimes sex-differentiated, relationships between targets' immune function and others' perceptions of their attractiveness. Together, this work suggests complex, often sex-differentiated relationships between immune function, health, and attractiveness.

1. Introduction

Why does the human perceptual system evaluate some targets as being more attractive than others? Although the answer to this question is undoubtedly complex, involving features that are age- [1], sex- [2], culture- [3], and person-specific [4,5], sexual selection theory suggests that perceptions of attractiveness should reflect a preference for traits that have historically been linked to their possessor's quality as a mate, including health and immune function (e.g. [6,7]). Although intuitively and theoretically appealing, this hypothesis has not been subject to rigorous empirical scrutiny. Here, we seek to address this empirical gap by conducting what is, to our knowledge, the most extensive study to date examining the links between physical appearance and immune function to better understand the benefits of beauty to the genes of the beholder.

Facial attractiveness has been of interest to researchers in the social and biological sciences for many years (for review, see [8]). An examination of this literature reveals that standards of beauty, although sometimes punctuated by idiosyncrasies (e.g. [9]), are most-often consistent across time and space. Research finds that features such as clear skin, prominent cheekbones, bright eyes, and full, red lips have been deemed attractive throughout recorded human history [10–12]. Research also finds a consistent preference for symmetrical and average faces [13–22]. Although some argue that standards of beauty are primarily the product of Western media exposure (e.g. [23]), research suggests these standards transcend age and cultural boundaries, being demonstrated in infants [24,25], as well as in those living in societies with little exposure to Western media [19,26,27].

Given that so many attractiveness standards are shared by humans, regardless of age, race or cultural background, evolutionary scientists have proposed that they may emerge from perceptual adaptations that function to promote successful mate choice [18,28]. Accordingly, the features that humans

universally perceive as attractive may provide cues to unobservable qualities possessed by a target that impact fitness, including health and immune function (e.g. [6,7]). Given the substantial threat that infection and disease have posed to human survival [29], it is reasoned that individuals who exhibited a preference for faces possessing cues linked to immunocompetence would have passed down this preference to a greater number of surviving offspring than individuals lacking this preference, making it a universal feature of the human perceptual system.

The idea that attractiveness may provide cues to health and the functioning of the immune system is an idea that is intuitively appealing because of the profound selection pressures that pathogens and parasites have reliably imposed on humans. For example, infectious disease has been the leading cause of death through human history, accounting for about 60% of all deaths in mid-ninteenth century England [30] and still accounting for upwards of 8.5 million deaths in 2016 [31]. However, the hypothesis that attractiveness provides cues to health and immune function has received only mixed empirical support. For example, research finds that attractiveness is positively related to longevity [32] and negatively related to the reported number of colds in the past year [33] in women, whereas in men, it is positively linked to cardiovascular health [34]. Others find that attractiveness, while associated with perceived health in both sexes, is not associated with actual health in either [35].

The literature examining the links between attractiveness and immune function is equally mixed. For example, research finds that attractiveness predicts the strength of men's antibody response to vaccines [36]; however, others have failed to find this pattern [37], and it has not been found in women [38]. Others find no relationship between attractiveness and salivary immune measures in either sex ([39]; only women, [40]). In short, the current literature fails to provide conclusive support for a consistent relationship between attractiveness and immune function, although it does indicate that these relationships may exist and—when they do—they may be sex differentiated.

In the current research, we examine the links between physical appearance, health, and immune function. Specifically, we examine the relationship between target attractiveness and (i) self-reported health, (ii) *in vivo* measures of inflammation and blood cell count/composition, and (iii) multiple *in vitro* tests of targets' immune function. The overall research hypothesis is that perceptions of facial attractiveness will be positively related to immunological functioning. We are treating the investigation into (i) whether the links between facial attractiveness and immune function occur equally across each of our chosen measures, and (ii) whether the links are sex differentiated as exploratory.

Although we did not have any *a priori* predictions about the nature of the sex-differentiation in the links between immune function and facial attractiveness, the extant research suggests that such differences probably exist (e.g. [32–34,36–38,40]). Indeed, much research demonstrates that males' and females' immune systems differ in several functionally meaningful ways [41]. For example, research finds that women's immune systems tend to be biased towards TH2 responses [42], which prioritize immunity mediated though interleukin 4 (IL-4), IL-5, IL-6, and IL-10 production. Conversely, men tend to exhibit a bias towards TH1 responses, relying on elevated interferon gamma, IL-2, and immunogobulin G2a (IgG2a) [42]. These differences are believed to have emerged in response to the adaptive problems confronting women in the context of pregnancy and childbirth [43,44].

There are also important differences in the variability of men's and women's immune function stemming from greater reproductive variance in males [45,46] and greater importance of physical condition for reproduction in females [47]. These sex-differentiated selective forces have led to greater variability in men's health and immunological outcomes than is observed in women (the susceptible male hypothesis: [42,48,49]). For example, research finds that women's immune function is less vulnerable to the effects of environmental adversity (e.g. [50]) and that women outperform men on most measures of immune function [51]. Additionally, while facial femininity in women is considered attractive cross-culturally, this effect is not reliably found for facial masculinity in men [52,53]. Given the heterogeneity of men's and women's immunological responses, and sex-specific features of attractiveness, it stands to reason that the links between immune function and attractiveness may themselves be sex-differentiated, although we do not have specific predictions regarding this sex-differentiation.

2. The present research

The current research was designed to examine links between targets' attractiveness and immune function using multiple, functional immunoassays (assays that measure immune function in response to challenge). Common immunoassays employed include those that measure the response of one's peripheral blood mononuclear cells (PBMCs) to varied immunological stimulants (e.g. [54,55]). They are the gold standard for measuring key aspects of immune function in peripheral blood (e.g. phagocytosis, cell lysis, proliferation, etc.). Accordingly, in phase I of the study, we collected photographs, self-reports of health and mate value, and blood samples from participants (henceforth, *targets*). Targets' PBMCs were isolated and tested for (i) phagocytic capacity using fluorescent dye-labelled *Escherichia coli* bioparticles, (ii) proliferation in response to, and in the absence of, stimulation with each lipopolysaccharide (LPS), phytohaemagglutinin (PHA), and polyinosinic:polycytidylic acid (poly [I : C]), (iii) ability of natural killer (NK) cells to lyse target tumour cells, and (iv) cytokine release in response to stimulation with a bacterial endotoxin (i.e. LPS). Additionally, targets' plasma was assayed for levels of IL-6 and tumour necrosis factor α (TNF-α) and also used in a live *Staphylococcus aureus* growth assay. Finally, a separate tube of whole blood was drawn for haematology analysis. See table 1 for more information about relevant immune measures.

In phase II of the study, phase I targets' photographs were rated for attractiveness by opposite sex participants. Based on research that finds men prioritize attractiveness in potential romantic partners, while women prioritize social status and wealth (e.g. [2]), we asked participants to rate targets on these traits as well. We hypothesized that targets' immunological competence would be positively related to others' perceptions of their attractiveness. Exploratory analyses were also conducted to examine whether these patterns were sex-differentiated and to explore the links between perceptions of health and immune function, along with self-reported health and immune function. These latter analyses

Table 1. Summary of immune measures assessed.

immunological assay type	what the assay measures	what is 'better' immune function?	branch of immune system	heritability[a]
phagocytosis (of *E. coli* bioparticles)	the process by which white blood cells engulf and destroy microbes and damaged host cells	those with higher levels of phagocytosis hypothesized to be less likely to experience microbial infection	primarily innate (based upon how our assay was conducted)	heritability found for numbers of phagocytes
haematology counts	the relative numbers and composition of white blood cells a person possesses can impact their immune function	different numbers/ratios of these cells correspond to different facets of immune function. There is no ideal composition; extreme deficiencies/excesses in cell types/platelet counts may be harmful	lymphocytes primarily adaptive; monocytes and neutrophils innate; eosinophils and basophils involved in allergy/macroparasite defence	moderate to high heritability found for peripheral blood cell counts
plasma proinflammatory cytokines (IL-6 and TNF-α)	heightened levels of these cytokines in plasma indicate the illness or systemic inflammation	inflammation protects against acute threats but is damaging to the body in the long term. Lower plasma levels of inflammation predict better long-term health	primarily innate	degree of heritability found for plasma levels of IL-6 and TNF-α varies by study
PBMC proliferation	measures mitosis and clonal expansion of new PBMCs in response to immunological stimulation	greater proliferation in response to immunological stimulation hypothesized to be linked to a more robust immune response	both innate and adaptive	no data available, but see stimulated cytokine release
NK cell cytotoxicity	NK cells destroy virus-infected cells and neoplastic growth	greater cytotoxicity (i.e. higher rates of killing) indicates more robust NK cell function; although confers risk of collateral damage to host cells	primarily innate	moderate to high heritability for NK cell counts and function
stimulated cytokine release	when PBMCs are exposed to an immunological stimulant in culture, proinflammatory cytokines are released	in the context of an immunological stimulant, higher levels of cytokine release indicate more robust immune function (although excessive/protracted inflammation can indicate dysfunction)	primarily innate	moderate (IL-6, TNF-α) to high (IL-1β) estimates of heritability
S. aureus growth in plasma	prevention of bacterial growth by participant serum *in vitro*	less bacterial growth over time may indicate more robust anti-bacterial defences	may relate to higher complement system activity, circulating antibodies or antimicrobial peptides	no data available

Note: *E. coli*, *Escherichia coli*; IL-6, interleukin six; TNF-α, tumour necrosis factor α; PBMC, peripheral blood mononuclear cells; NK, natural killer; IL-1β, interleukin one beta; *S. aureus*, *Staphylococcus aureus*.

[a]Heritability of immune measures varies by study and are influenced by many factors. See the electronic supplementary material for references (S33–S39).

were performed to better elucidate the degree to which individuals' perceptions of health (which are often used as a critical measure in health research) map onto the various immunological parameters assessed in the current study.

3. Method

(a) Phase I

(i) Targets

The sample included 159 participants (79 women; $M_{age} = 20.17$ years, s.d. = 2.75) who were students at Texas Christian University or members of the nearby community. Participants were screened in advance to ensure that they were: (i) without a history of chronic medical problems, including depression/other mental illnesses, (ii) non-obese (body mass index (BMI) < 30), (iii) free from acute illnesses for the two weeks leading up to the study, (iv) not using hormonal contraceptives, (v) willing to abstain from steroidal and anti-inflammatory medications, exercise, and alcohol consumption for 2 days prior to participation, and (vi) willing to fast the morning of participation. All women participated during the early follicular phase of their ovulatory cycle (days 4–7), when sex steroid levels are low, to control for the impact of sex steroid hormones, which fluctuate across women's ovulatory cycles, on immune function and inflammatory processes [44]. We used a forward counting method [56] to schedule women based on the start date of their most recent menstrual cycle. Participants were compensated for their participation with partial course credit or a $50 gift card.

(ii) Procedure

Participants provided informed consent prior to participation, and the research was approved by the Texas Christian University Institutional Review Board (approval no: 1411-117-1606). Prior to their laboratory visit, participants completed online demographic and lifestyle questionnaires using Qualtrics experimental survey software (Qualtrics, Provo, UT). On the day of the testing session, participants reported to the laboratory at 07.30 after fasting for a minimum of 8 h, provided informed consent, responded to compliance questions (e.g. fasting, abstaining from alcohol) and then completed behavioural tasks and additional questionnaires as a part of a larger study.

Next, participants were taken to a private room to be photographed. Participants removed any make-up using provided facial wipes prior to being photographed. All photographs were taken with a Sony Cybershot DSCW150 8.1MP Digital Camera (Sony, Tokyo, Japan) from 0.72 m away with the same lighting. Participants were told to look straight ahead and maintain a neutral facial expression and were photographed from the neck up.

Participants were then led into an adjoining study room where their height and weight were measured and 85 ml of blood was collected via venipuncture into heparinized and EDTA-containing Vacutainer tubes (Becton-Dickinson, Franklin Lakes, NJ). After the blood draw, participants were thanked, debriefed, and compensated.

Following blood collection, PBMCs were isolated for use in functional assays (see the electronic supplementary material). Additionally, plasma was collected and frozen at −80°C until thawed and assayed for IL-6 and TNF-α and for use in a live *S. aureus* growth assay. Finally, a separate tube of whole blood was taken for haematology analysis.

(iii) Measures

Details of all measures can be found in the electronic supplementary material. Biological measures included the following: PBMC proliferation assays, NK cell cytotoxicity assays, *S. aureus* plasma growth assays, stimulated cytokine release assays, phagocytosis of *E. coli* bioparticles assays, proinflammatory cytokine assays, and haematology cell counts. Participants also responded to a variety of questionnaires as a part of a larger study. The measures relevant to the current investigation include self-perceived mate value, general health, family health, and present health. Additional measures were included to use as covariates in subsequent analyses. These include target race, age, BMI, adult socioeconomic status (SES), exercise, day length, smoking behaviour, and recent stress.

(b) Phase II

(i) Participants

Facial attractiveness ratings were collected from 492 participants (259 women; $Range_{age}$ 18–29, $M_{age} = 25.47$ years, s.d. = 2.57). Raters were recruited on Amazon's Mechanical Turk survey hosting platform and received $2 as compensation for their participation.

(ii) Materials

Target photographs collected during phase I were prepared for rating using Adobe Photoshop. Of the 159 target photographs obtained from phase I, 152 photographs were included in phase II. Seven photographs were excluded owing to technical errors (e.g. the participant smiled) or lack of consent for including the photograph in research. All photographs were cropped to remove shoulders and were 1080 × 1080 pixels.

(iii) Procedure

Research was approved by the Texas Christian University Institutional Review Board (approval no: 1711-03). The survey was completed using Qualtrics software. Upon consent, participants were shown an image containing all photos they could be asked to rate, which remained on the screen for at least 45 s. This was done to ensure that raters were aware of the range of attractiveness in our sample, thereby minimizing ceiling and floor effects. Raters then rated 25 randomly selected opposite sex target photographs (obtained from phase I) on an assortment of characteristics which included attractiveness (i.e. 'This person is physically attractive'), status, wealth, desirability, health, longevity, genetic quality, and immune function (see the electronic supplementary material for more information). All photographs were presented in a random order. After rating target photographs, participants responded to demographic questions and were thanked, debriefed, and compensated.

(c) Data analytic plan

See the electronic supplementary materials for full Data Analytic Plan.[1] Briefly, all models were estimated using Mplus statistical software (Mplus 7.4; [56]). Latent variables of attractiveness (comprised of ratings of attractiveness, desirability, status, and genes) and health (comprised of rating of healthiness, longevity, immune function, and genes) were used as dependent variables in the subsequent models.

First, both of the latent factors (attractiveness' and 'health) were regressed on potential covariates (including race, age, BMI, adult SES, exercise, day length, smoking behaviour, and recent stress levels). Non-significant covariates ($p > 0.100$) were then dropped from subsequent models to preserve power and prevent overfitting (see [57]). In our first target model, perceived attractiveness and health were regressed on targets' self-reported measures of health (present health, general health, and family health). Next, each latent construct was regressed on each of the target's immunological measures. Measures of phagocytosis,

plasma levels of proinflammatory cytokines, and haematology count data lacked nested structures. Accordingly, attractiveness and health ratings were simultaneously regressed on these predictors in a single-level model. The remaining data contained nested structures (see the electronic supplementary material for details).

In each of these models, we also tested for a moderating impact of sex. When significant interactions ($p < 0.100$) were found between sex and a predictor, these interactions were probed by examining sex differences at high and low levels (i.e. one standard deviation above and below the mean) of each predictor, as well as simple slopes analyses within each sex. Owing to the complexity of the *S. aureus* growth model, sex differences were investigated by splitting the data by sex and reporting results for each sex separately.

4. Results

See the electronic supplementary material, table S2 for detailed statistics and model fit information, and for results of a harmonic mean *p*-value analysis, conducted to correct for the potential of increased familywise error rates when investigating multiple comparisons. See table 2 for a summary of attractiveness results.

(a) Summary of perceived attractiveness results

Results revealed that attractive targets (compared to less attractive targets) had higher rates of phagocytosis of *E. coli* bioparticles ($p = 0.042$), higher basophil counts ($p = 0.004$), lower neutrophil counts ($p = 0.043$), greater NK cell cytotoxicity ($p = 0.033$; although see figure 1 for interaction effect), and slower rates of *S. aureus* growth in plasma ($p = 0.028$; although this effect was stronger in women, $p \leq 0.001$, than in men, $p = 0.224$). There were no significant relationships between attractiveness and cellular proliferation or cytokine production in response to any mitogen or current levels of inflammation (*in vivo*).

Phagocytosis is the process by which specific white blood cells—such as neutrophils and monocytes—ingest foreign particles like bacteria. That attractive targets had higher rates of phagocytosis, and lower plasma bacterial growth indicates that attractiveness may be related to anti-bacterial immunity. That attractive targets had high rates of phagocytosis, and low neutrophil counts—together—is also consistent with this possibility, demonstrating that attractiveness may also be related to one's immunological efficiency in the face of bacterial threats.

Relationships between perceived target attractiveness and NK cell function (interaction $p \leq 0.001$; figure 1 for interaction effect), and between perceived target attractiveness and plasma levels of TNF-α (interaction $p = 0.032$) were found to be sex-differentiated. In particular, the results of our study found that women perceived male targets with high-functioning NK cells as being more attractive than those with low-functioning NK cells ($p = 0.033$). Further, women perceived men with low levels of plasma TNF-α to be somewhat more attractive than those with higher levels of this cytokine (although this latter simple effect was non-significant, $p = 0.175$). By contrast to the results for male targets, female targets with low levels of NK cell cytotoxicity were rated as more attractive than those with high levels of NK cell cytotoxicity ($p = 0.008$).

5. Discussion

It has long been hypothesized that facial attractiveness is linked to immune function [7,13]. However, this hypothesis has not been subject to rigorous empirical scrutiny. The current research was designed to address this gap, examining links between immunological function, including functional *in vitro* leucocyte assays, and facial attractiveness.

Results revealed associations between attractiveness and immune function, particularly aspects of immune function related to efficiently managing bacterial threats. Additionally, they revealed a sex-differentiated association between target attractiveness and NK cell function, with this parameter being positively associated with men's attractiveness and negatively related to women's attractiveness. Although others have found no relationship between target attractiveness and salivary immune measures of anti-bacterial capacity and lysozyme activity against bacteria [40], the consistency of the pattern observed across measures used in the current study suggests that attractiveness may be linked to blood-based measures of anti-bacterial immunity and NK cell function.

While the current results found evidence of a link between target attractiveness and various facets of immune function, little evidence was found linking target attractiveness to measures of acute health (e.g. *in vivo* inflammation, self-reported current health). These results indicate that inflammatory activity, at least in relatively healthy, college-aged participants, may not present visual cues associated with facial attractiveness. Given extant work that finds links between acute inflammatory activity and attractiveness via scent-based cues [58], these results suggest that immune function and acute health may be assessed via different sensory modalities, with cues to acute inflammation being assessed via scent- rather than visually mediated cues.

The lack of relationship between measures of acute inflammation and perceived attractiveness is also noteworthy because it suggests that perceptions of attractiveness may play a more important role in guiding the choice of partners with high-functioning immune systems than merely preventing contact with those with acute infection (e.g. [59]). This is an important distinction, as many researchers examining links between facial attractiveness and health have assumed that the primary function of these links is one of pathogen avoidance (offering the perceiver health maintenance benefits), rather than immune system assessment (presumably offering the perceiver greater access to indirect (and direct) fitness benefits) (e.g. [8,60–64]). The current results suggest that perceptions of attractiveness—at least in a relatively healthy population—may be more informative of the latter than the former. Indeed, many of the aspects of innate immunity measured here are strongly influenced by genetic factors (e.g. [65]) and undoubtedly grant their bearers improved ability to provide direct benefits as well, such as being a good provider or an investing parent (for a discussion of direct benefits cued by attractiveness see [62–64]). It is further possible that these potential direct benefits are sex-differentiated (e.g. [62]), an idea which also warrants additional research.

Further, the current results suggest that links between attractiveness and immune function may be more closely tied to a target's ability to avoid bacterial rather than viral threats (with the exception of NK cell function in men,

Table 2. Summary of model results; relationships between immune measures and perceptions of attractiveness.

within-target measures	perceived attractiveness *B* (s.d.)
self-reported health	n.s.
phagocytosis of *E. coli* bioparticles	0.20(0.10)* ↑
haematology counts	basophils: 0.52(0.18)* ↑ neutrophils: −0.30(0.15)* ↓
inflammation (plasma)	n.s.
sex*TNF-α interaction	0.15(0.07)* (electronic supplementary material, figure S1)
PBMC proliferation	n.s.
NK cell cytotoxicity	0.18(0.09)*
sex*NK interaction	−0.28(0.08)* (figure 1)
stimulated cytokine release	n.s.
S. aureus growth, men	n.s.
S. aureus growth, women	slope of growth *↓

Note: *E. coli*, *Escherichia coli*; TNF-α, tumour necrosis factor α; PBMC, peripheral blood mononuclear cells; NK, natural killer; *S. aureus*, *Staphylococcus aureus*; ↑immune measure positively related to outcome; ↓immune measure negatively related to outcome; *significant effects ($p \leq 0.050$); †marginal effects ($p \leq 0.100$); n.s., non-significant effect ($p > 0.100$). Measures in bold represent those predicted to be associated with attractiveness at pre-registration. Sex differences in all relationships and relationships between *S. aureus* growth and attractiveness were exploratory.

which was positively related to facial attractiveness). It is important to note, however, that absence of evidence demonstrating strong links between anti-viral activities and attractiveness should not be interpreted as evidence of absence. Future research would benefit from examining the links between each anti-viral and anti-bacterial immunity in a more systematic way, as these two types of immunity often overlap, and the current research used a limited number of anti-viral measures. Nonetheless, the reported associations between facets of anti-bacterial immunity and facial perception are consistent with the types of threats that are likely to have been confronted among those living in small hunter–gatherer groups, long before the advent of agricultural societies and large cities. Researchers have suggested that the transition to urban living and modern medicine has promoted an increase in viral richness, relative to the richness of bacteria and macroparasites, which were believed to have been the primary pathogenic concerns in ancestral populations [66]. This explanation is speculative, however, and warrants additional theoretical scrutiny.

Lastly, the current research also found that—consistent with past research (e.g. [33])—targets perceived as being attractive were also perceived as being healthier. However, neither perceived attractiveness nor perceived health was related to any of our target's self-reported health measures. These results suggest that self-reported health may not be linked to perceivable cues that impact perceptions of physical attractiveness or health; however, these data were collected from a relatively healthy sample of young adults, which may have limited our ability to capture this relationship. It is also possible that links between attractiveness and health may be obscured in in modern humans, given that human mate preferences were forged before the advent of modern medicine [67]. That is, although attractiveness may have cued both health and immune function in ancestral populations, the links with health may no longer occur as modern medicine allows those with low immunocompetence to stay in relatively good health. Future research, perhaps conducted within populations in developing countries, is needed to better understand these relationships.

(a) Sex differences

Relationships between perceived target attractiveness and NK cell function (and between perceived target attractiveness and plasma levels of TNF-α) were found to be sex-differentiated. Specifically, women perceived male targets with high-functioning NK cells as being more attractive than targets with low-functioning NK cells. NK cells primarily function to protect the body from viral infection, and poor NK cell cytotoxicity may put one at increased risk of neoplastic growth [68] or viral infection. Further, women perceived men with relatively low levels of plasma TNF-α to be attractive.[2] While it is possible that these results reflect unrelated preferences, TNF-α is instrumental in the coordination of NK cell function [69], again suggesting the possibility that perceived attractiveness is related to immunological efficiency. Because TNF-α is key to an effective NK cell response, the preference for men possessing high-functioning NK cells despite being able to keep levels of TNF-α low raises the possibility that women prefer men who are well equipped to efficiently combat viral threats and neoplastic growth.

That men find women with high-functioning NK cells to be less attractive than women with low-functioning NK cells is surprising. One potential explanation for this result involves the influence of oestrogen. Some literature reports that NK cell function is lower in the context of high oestrogen during pregnancy [70] and in postmenopausal women receiving oestrogen replacement therapy [71]. As such, it is possible that women rated as attractive in our sample had higher levels of oestrogen, which is a factor related to attractiveness ratings in previous research (e.g. [72]). While this is a speculative explanation, future research should investigate the relationships between facial attractiveness, NK cell cytotoxicity, facial femininity, and oestrogen levels across women's ovulatory cycles.

Overall, attractive targets exhibited slower plasma growth rates of *S. aureus*. However, this result, too, was sex-differentiated. Specifically, women with slower rates of *S. aureus* growth in their plasma were perceived as more attractive than women with faster rates of *S. aureus* growth in their plasma, while this effect was absent in men. These results indicate that attractiveness is related, in a sex-differentiated fashion, to some factor that modulates the growth rates of *S. aureus* in plasma. Plasma contains micronutrients, complement proteins, antibodies, antimicrobial peptides,

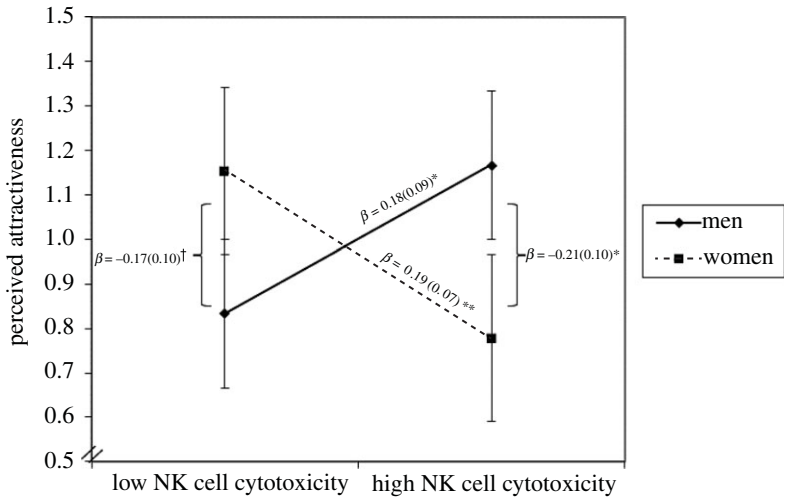

Figure 1. Interaction between natural killer cell cytotoxicity and target sex on attractiveness ratings. Note: NK, natural killer; β, standardized beta coefficient (standard error). $^{**}p \leq 0.01$; $^{*}p \leq 0.05$; $^{\dagger}p \leq 0.10$.

hormones, and other substances, but no blood cells. As such, growth rates of *S. aureus* in target's plasma could be driven by mineral levels [73], glucose levels, neutralizing antibodies, and/or the presence of complement proteins [75]. For example, because iron is essential to bacterial growth [75], one potential explanation for this pattern of results is that having lower levels of iron in one's plasma (which inhibits bacterial growth) is perceived as attractive in women, despite not being perceived as attractive in men. Overall, these results suggest that people may be sensitive to multiple cues bearing on one's ability to withstand bacterial threats, beyond those that are present in blood cells. Further research is needed to understand which components of plasma impact bacterial growth, and potential sex differences in these relationships, to clarify this result.

(b) Strengths, limitations, and future directions

The current research has three strengths that should be noted when comparing the current results with results of other work examining the relationship between attractiveness and immune function. First, rather than relying on very limited, often secondary biological markers of immunological function (frequently measured using saliva), we assessed a relatively broad range of immunological measures, including multiple live immune challenge assays using participants' cultured leucocytes (e.g. functional assays). While salivary measures do provide useful insights into specific aspects of immune function, relying upon a limited number of markers of immune function to assess relationships between attractiveness and immune function limits understanding of these relationships. A strength of the current work is that we used a more extensive set of measures than what has been used in previous research; however, the use of venipuncture may have induced stress in some participants, which could have influenced measures of their immune function. Although our measures still provide an incomplete picture of immune function, the breadth of our included measures presents a more comprehensive picture of the links between attractiveness and immune function than what has been previously investigated. Additionally, phase I was conducted using very stringent participation criteria (e.g. all participants abstained from exercise for 48 h, all women were naturally cycling) to help detract from the number of third variables that could provide an alternative account for our results. Despite these strict controls, we were still able to collect a large sample size relative to extant research conducted on this topic. We also employed a large sample of raters to ensure that faces were rated accurately.

Along with the strengths of the current research, there are also important limitations that should be considered when interpreting the present results. Foremost, although the current research found evidence of a relationship between key facets of immune function and perceptions of attractiveness (particularly in men), it is not clear which facial features were driving this association. What are the specific facial features—such as contour, skin texture and coloration, and masculinity/femininity—that covary with immunological function? Or is it the gestalt created by multiple features that covary with differences in immunological function? Some recent research has failed to find associations between facial attractiveness and carotenoid-based skin colour [40]; however, there is still much to be explored here. Although addressing these mechanistic questions is beyond the scope of the current work, this is an important area for future research. Such research would likewise benefit from having participant raters evaluate the attractiveness of both opposite- and same-sex faces to determine whether these same patterns are evident in humans' evaluations of same-sex peers. Further, other aspects of one's appearance, such as body attractiveness, may also influence these associations.

Additionally, we collected data cross-sectionally, preventing causal inquiry into how changes in immunological parameters affect attractiveness. Further, we collected data from relatively healthy, college-aged participants and did not expose participants in the current work to live, *in vivo* pathogenic challenges, which would have offered insight into targets' immune system function in a more naturalistic, ecologically valid context. Although a strength of the *in vitro* functional assays we performed is that we are able to isolate specific features of immune function outside the context of acute illness, and tease apart their relationships with attractiveness, increasing internal validity in this way comes at the expense of some external validity. Given that the immune system is comprised of myriad cells and functional

capabilities that work together to combat infectious disease, it is possible that the results might look different if immune function was measured using *in vivo* challenges. Such an approach might involve collecting target photographs and measuring their immune function both within and outside the context of a naturally occurring infection. Along the same lines, investigating relationships between immune function and attractiveness in a larger, more diverse population, which includes both healthy and sick individuals, is a vital next step before the current results can be generalized to a broader population.

Lastly, it is noteworthy that links between immune function and perceptions of attractiveness appear to be sex-differentiated. This was especially true for NK cell cytotoxicity, which was positively and negatively associated with male and female attractiveness, respectively. This result—particularly when interpreted in light of recent evidence indicating that there may be important differences in men's and women's immunological vulnerabilities (e.g. [51])—suggests that the relationship between attractiveness and immune function may be sex-differentiated in ways that require this question to be explored separately between the sexes. There are probably also additional factors influencing relationships between immune function and attractiveness—such as race, cultural background, age, sexual orientation, and health status—that we were unable to adequately investigate given the homogeneity of the current sample. Although we controlled for many of these factors in our analyses, future research is needed to address the impact of these and other individual differences on the relationship between attractiveness and immune function.

6. Conclusion

Researchers have long speculated that perceptions of attractiveness reflect preferences for traits historically linked to health and, ultimately, immune function (e.g. [6]). The results of the current research suggest that facial attractiveness may provide insights into one's immune function, particularly as it relates to one's ability to efficiently combat (primarily) bacterial threats. Additionally, for men, facial attractiveness may also provide cues to their ability to efficiently manage viral threats and neoplastic growth. Although future research is needed replicate these results, the current research suggests that a relationship between facial attractiveness and immune function is likely to exist.

Ethics. Our research was approved as compliant with ethical standards by the Texas Christian University Institutional Review Board (approval nos: 1411-117-1606 and 1711-03), and informed consent was obtained from all subjects prior to participation.

Data accessibility. This study package was pre-registered, and the processed data analysed for this study are publicly available on the Open Science Framework: https://osf.io/8atkj.

Authors' contributions. S.M.: conceptualization, data curation, formal analysis, investigation, methodology, project administration, writing—original draft, writing—review and editing; J.G.: conceptualization, data curation, formal analysis, investigation, methodology, project administration, writing—review and editing; M.L.P.: conceptualization, data curation, funding acquisition, investigation, methodology, project administration, writing—review and editing; G.W.B.: conceptualization, data curation, funding acquisition, investigation, methodology, project administration, resources, supervision, writing—review and editing; S.E.H.: conceptualization, funding acquisition, investigation, methodology, project administration, supervision, writing—original draft, writing—review and editing. All authors gave final approval for publication and agreed to be held accountable for the work performed therein.

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Endnotes

[1]The electronic supplementary material also contains factor analysis results, results of models in which rated attractiveness was used as a single-item dependent variable (results remain unchanged), results of analyses investigating relationships between perceived health and immune function and results of analyses investigating relationships between target's self-reported health and immune function. Results for these analyses are reported while controlling for significant covariates and the latter without testing for sex differences.

[2]Although an interaction emerged between sex and TNF-α on attractiveness, the simple effect for men was non-significant. Interpret these results with caution.

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