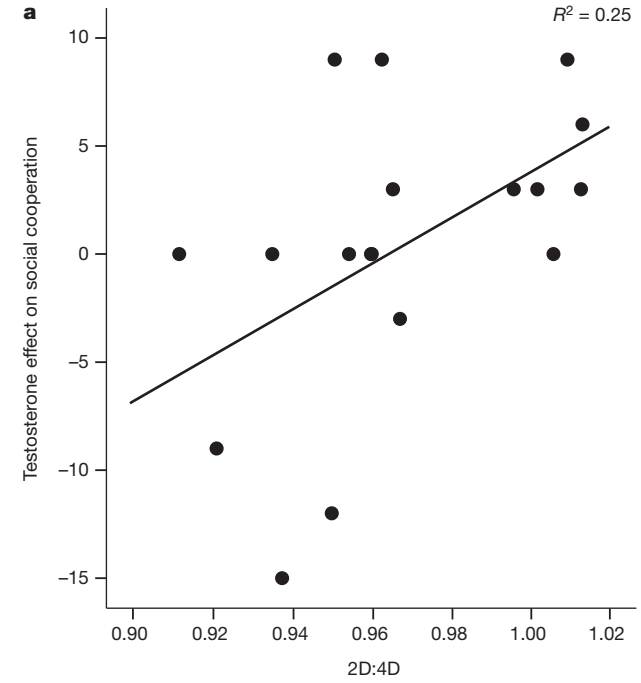
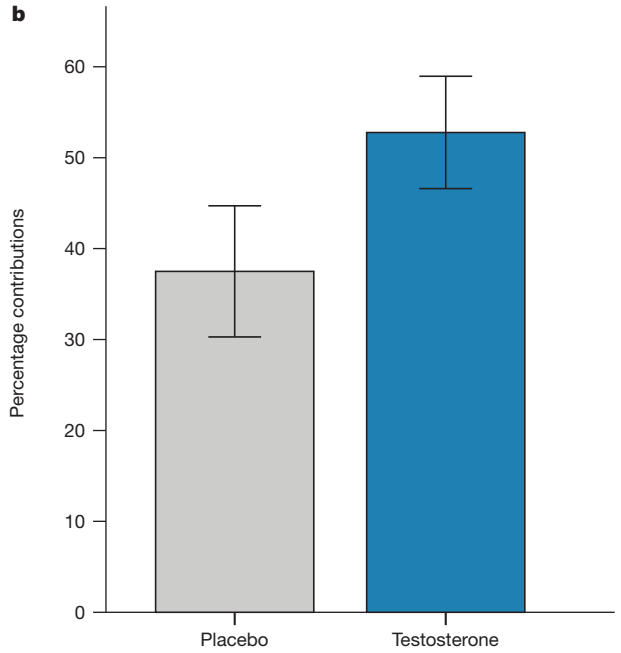
New evidence on testosterone and cooperation

ARISING FROM C. Eisenegger, M. Naef, R. Snozzi, M. Heinrichs & E. Fehr *Nature* **463,** 356–359 (2010)

In February 2010, Eisenegger *et al.* reported increased fair bargaining behaviour after administration of testosterone in an ultimatum game[1]. However, unfair offers in the ultimatum game typically are rejected; thus, not only the motives for social cooperation but also the threat of financial punishment may have accounted for these effects. Here, using the public goods game (PGG), we unambiguously show increased social cooperation after testosterone administration, but only among subjects with low levels of prenatal testosterone (measured by the right hand's second-to-fourth-digit ratio (2D:4D)). This finding establishes positive effects of testosterone on social cooperation, with prenatal hormonal priming providing for important individual variability.





Eisenegger *et al.* show increased fairness in bargaining behaviour after testosterone administration in young females, and the authors suggest that this prosocial behaviour is strategically driven by concerns for social status[1]. Indeed, in the ultimatum game such strategic concerns have a role, and the hormone testosterone repeatedly has been associated with status concerns in humans and other animals[2,3]. However, unfair ultimatum game offers are typically rejected with all money being lost. Hence, the threat of financial punishment may have played a part in fair bargaining behaviour after testosterone administration[1]. We therefore tested the effects of testosterone on social-cooperative behaviours with the PGG, a game without such threat of financial punishment, wherein non-cooperation can actually lead to greater profits[4]. In an experiment (approved by our ethics committee) we administered testosterone and placebo on separate days to 24 female students in a double-blind within-subject design[5], and tested them in a three-player PGG lasting eight rounds. Each round the players received an endowment of 3 monetary units (MU), which they could either keep for themselves or contribute to the public good[4] (see Methods).

Using a repeated-measures generalized estimating equations (GEE) analysis over all eight trials (PGG placebo versus testosterone) we found no main effect of testosterone (Wald $\chi^2 = 0.048$, $P = 0.826$). However, we also measured a proxy of prenatal testosterone, the 2D:4D ratio[6,7], which has recently been shown to be a powerful predictor for effects of testosterone administration on social function[8] (Methods). With 2D:4D ratio as covariate in the analyses the effect of testosterone on social cooperation was significant (Wald $\chi^2 = 9.630$, $P = 0.002$) as, importantly, was the 2D:4D × testosterone interaction (Wald $\chi^2 = 10.140$, $P = 0.001$) (Fig. 1a). Next, we applied a median split on the 2D:4D measurements to compare individuals with relatively low versus high prenatal testosterone exposure. GEE analyses computed in both groups separately showed that subjects with low prenatal testosterone exposure (high 2D:4D) contributed more to the group after testosterone administration (Wald $\chi^2 = 7.894$, $P = 0.005$), whereas subjects with high prenatal testosterone exposure (low 2D:4D) showed no change (Wald $\chi^2 = 1.791$, $P = 0.181$) (Fig. 1b). A forced-choice test establishing that subjects were unaware of treatment condition also revealed no belief effects on public good contributions (all P values > 0.10). Thus, unlike in the Eisenegger *et al.* study, folk beliefs about testosterone did not mediate behaviour in the PGG[1], which is not unexpected because unfair ultimatum game offers (and not PGG non-contributions) are antisocial and risky, and fit with mainstream ideas on how testosterone affects behaviour[9,10].

Figure 1 | Prenatal sex hormone priming (2D:4D) moderates effects of testosterone on social cooperation. **a**, Individual 2D:4D measurements plotted against testosterone effect on social cooperation (mean amount of MU contributed in the placebo condition subtracted from mean amount of MU contributed after testosterone administration). Line depicts regression wherein 2D:4D ratio explains 25% of the variance in the overall effect of testosterone on cooperation. **b**, Mean and standard error of the mean of the percentage of overall PGG contribution after testosterone and placebo administration in subjects with relatively low prenatal testosterone (high 2D:4D) on the basis of median split. The data show significantly more overall contribution to the public good after administration of testosterone compared to placebo in high 2D:4D subjects. We thank D. Tromp for her help in collecting these data.

The present result supports past research in which we also show effects of testosterone that vary strongly with prenatal testosterone exposure. In that case, high prenatal testosterone exposure (low 2D:4D) boosted the negative effect of testosterone administration on cognitive empathy[8]. Crucially, the 2D:4D ratio apparently is interactively shaped by testosterone and oestradiol *in utero*, and a high 2D:4D ratio points to relatively low prenatal testosterone versus high prenatal oestradiol[11–13]. Furthermore, many effects of testosterone on social behaviour are thought to arise after metabolism to oestradiol[2,3], but this metabolism differs between individuals[14]. Hypothetically, the balance between the sex steroids prenatally, marked by the 2D:4D ratio[11–13], would be predictive for the rate of metabolism of testosterone into oestradiol. That is, subjects who are prenatally more strongly primed by oestradiol may also metabolize more testosterone into oestradiol[13], and this could have caused the selective effect in our high 2D:4D group. Further research is necessary to test this hypothesis.

Here we challenge Eisenegger *et al.* by establishing the positive effects of testosterone on social cooperation in which prenatal sex hormone priming, approximated by determining 2D:4D ratios, conveys important individual variability. These data have strong implications for past and future hormone research.

METHODS SUMMARY

For the PGG, all three players receive 3 MU per round and can contribute all or nothing to the public good. Only when at least two players contribute does each player receive an extra 6 MU irrespective of whether they made a contribution; thus non-contributors can profit most (9 MU). To create three-person groups, confederates were used to ensure there were three players involved each time, and their decisions were randomized. After the experiment we checked that no suspicions were raised about this procedure (six non-believers were excluded from analyses). For 2D:4D measurements, subjects' right hands were scanned, and 2D:4D ratios were computed twice by an experienced rater[15] (correlation between measurements, $P < 0.0001$).

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Eisenegger *et al.* reply

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van Honk and colleagues have taken our findings on the role of testosterone in ultimatum game bargaining[1] a step forward by showing that the hormone has important prosocial effects beyond the ultimatum game by increasing cooperation in the public goods game (PGG)[2]. In contrast to the ultimatum game, participants in the PGG decide simultaneously about their cooperation levels and are not confronted with a rejection threat from other participants, suggesting a much more universal effect of testosterone on prosociality than revealed by our study[1]. As the PGG captures a large class of evolutionarily and contemporaneously important situations, their findings are of great interest, and considerably extend our knowledge about the causal effect of testosterone on social behaviour. In addition, their results raise intriguing questions regarding the motivational and biological mechanisms through which testosterone increased cooperation levels, suggesting that the study will trigger further important experiments.

One possibility is that testosterone directly affects people's social preferences, that is, it directly renders their motives more prosocial—an explanation that seems to be favoured by van Honk and colleagues[2]. A second possibility is that the hormone influences subjects' beliefs about the other players' cooperation levels. For example, a subject who received testosterone may believe that others are more cooperative while their own motives remain unchanged. The rules of the PGG used in van Honk *et al.* are such that it is in the third player's financial interest to contribute to the public good if that subject believes that precisely one of the two other players contributes her endowment as well. Thus it is possible that the positive effect of testosterone on cooperativeness is due to the hormone's effect on beliefs about other participants' cooperation level. Of course, the two mechanisms described above are not mutually exclusive; testosterone may have causally affected subjects' motives and beliefs about others' cooperation. So far, no study has examined testosterone's causal effects

on beliefs about others' social preferences or others' prosocial behaviour—suggesting this as a topic for future studies.

Interestingly, the results of van Honk *et al.* are also compatible with the hypothesis that testosterone increases concerns for one's status[3,4]. One study[5] has shown that participants in a PGG confer higher status to cooperative group members than to non-cooperative ones. Another study[6] reported that third-party observers who did not benefit in any way from high contributions also rated cooperative individuals higher on status. Thus, if subjects have internalized the link between cooperation in the PGG and their status in the group, the increased cooperation levels observed by van Honk *et al.* could have been caused by an increased concern about one's status.

The study by van Honk and colleagues also raises intriguing questions regarding the biological mechanisms underlying the hormone's effect on social behaviour. As testosterone is partially converted to oestradiol by the enzyme aromatase, the results obtained by van Honk *et al.* suggest that testosterone's effect on cooperation in the PGG in subjects with a high digit ratio might be mediated by oestradiol. This idea is based on a recent study which shows that the digit ratio is related to an individual's relative amount of androgen to oestrogen activity during early fetal development, and that oestradiol heightens the digit ratio[7]. This suggests that effects of testosterone on social behaviour may be mediated by an individual's relative androgen versus oestrogen system activity or sensitivity, for which the digit ratio might serve as an important biomarker[7,8]. Thus, future studies should test whether a high digit ratio directly predicts social cooperation after oestradiol administration, as this might provide further insights into the biological mechanism behind the behavioural impact of sex hormones.

The study by van Honk *et al.* considerably broadens the causal role of testosterone on important prosocial behaviours while simultaneously suggesting a more specific biological underpinning based on the idea that the digit ratio is a biomarker for individuals' androgen versus oestrogen system activity or sensitivity. In addition, the study raises important questions regarding the mechanisms underlying the relationship between testosterone administration and prosocial behaviour. In particular, studies that are able to distinguish between the three hypotheses—that testosterone affects social preferences, beliefs, or status seeking—are likely to move the field forward further.

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