The impact of long-term androgen deprivation therapy on cognitive function and socioeconomic decision making in prostate cancer patients

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Abstract
Objective: Androgen deprivation therapy (ADT) enhances survival of advanced prostate cancer patients and is therefore used as a concomitant therapy. However, ADT has been reported to cause negative side effects on cognition and emotional processing. So far, research referred to the effects of short-term treatment. Since the brain may adapt to androgen deprivation, we were especially interested in the long-term effects of ADT on cognitive and socioeconomic decision making.

Methods: Participants underwent a battery of tests that have been associated with testosterone. We compared the results of three matched test groups: (1) prostate cancer patients with ADT up to 20 years, (2) prostate cancer controls without treatment and (3) healthy controls. We further measured the morning testosterone content in participants’ saliva.

Results: Testosterone concentration was positively associated with visuospatial performance across and within the test groups. Patients with long-term ADT showed an overall decline in cognitive performance. Compared with untreated patients, ADT was also associated with a reduced intergroup bias during socioeconomic decision making, which was in line with previous observations in young men suggesting that testosterone may promote ingroup favoritism. Finally, depression scores were increased in ADT, while quality of life was negatively associated with the treatment.

Conclusion: These findings conform to results made after short-term treatment. ADT promotes negative side effects on cognitive function. We also show for the first time that testosterone deprivation may affect socioeconomic decision making. Nevertheless, it should be emphasized that these effects cannot outweigh the previously described advantages of ADT in the treatment of prostate cancer.

Keywords
androgen deprivation, androgens, cancer, cognition, economic decision making, mosaic test, oncology, prostate cancer, testosterone, ultimatum game

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1 | BACKGROUND

Androgen deprivation therapy (ADT) is a common method to treat aggressive testosterone-dependent prostate cancer in older men. Pharmacological androgen deprivation can be induced by gonadotropin releasing hormone (GnRH) analogues that reduce the biosynthesis of testosterone through direct modulation of the hypothalamic-pituitary-gonadal axis, or, in contrast, nonsteroidal antiandrogens locally block the androgen receptor binding site and thus indirectly influence testosterone production by negative feedback. ADT has been demonstrated to improve survival of prostate cancer patients and is therefore used as a common concomitant therapy for advanced prostate cancer patients. However, several negative side effects on cognition, physical capability and socioemotional processing have been reported. For instance, testosterone deficiency in men was found to impair life quality, memory, and visuospatial performance, as well as physical abilities such as walking. The ADT-induced testosterone deficit promotes depression and emotional distress and decreased sex drive up to a loss of libido and erectile dysfunction.

Although natural aging in men also leads to a decline of endogenous testosterone levels, this decline does not occur as abruptly as the chemical castration induced by ADT. Instead, it rather incorporates a constant and slow reduction over several years until old age, when the so called andropause is reached. Andropause can also be accompanied by some of the negative side effects shown for ADT. These include mental impairments like cognitive decline, but also physical disabilities like erectile dysfunction, whereby the link to testosterone deficiency has been demonstrated (for an overview see Reference [11]).

Cancer diagnosis as well is linked to cognitive decline and increased risk for depression. Especially chemotherapy seems to provoke reversible cognitive deficits in cancer patients. These neuronal impairments were associated with a decline in estrogen and testosterone, supposedly further contributing to the decline in cognitive function (for review see Reference [14]).

Here, we measured the free testosterone concentrations of 46 prostate cancer patients, who had not been treated with chemotherapy, and 22 healthy controls. Twenty-four of the cancer patients received long-term ADT, whereas the remaining 22 patients did not receive any testosterone-effective treatment. In this sample, we wanted to evaluate the effects of long-term ADT on visuospatial cognition with reference to previous findings from studies assessing short-term ADT-treatment (3-9 months) that had demonstrated a consistent decline in visuospatial cognition in men. Apart from that, we were especially interested in the effects of long-term chemical castration on two aspects of socioeconomic decision making that have previously been demonstrated as being highly testosterone sensitive, that is, fairness perception and intergroup biases in socioeconomic decision making.

Based on a rising number of findings that not only aging-related processes but also the decreasing habitual testosterone concentration may cause cognitive deficits in men (eg, References [16,17], for meta-analysis see Reference [6]), we hypothesized to find differences in visuospatial performance between the groups, with a marked visuospatial deficit in ADT patients. Furthermore, cancer patients without androgen suppression were expected to have lower self-reported depression scores, (but see Reference [3]), a higher quality of life and a better performance in the Mini Mental State examination (MMSE) than patients who receive long-term ADT (for meta-analysis see Reference [6]). Apart from that, another aim of this study was also to investigate, for the first time, whether testosterone deficiency may impair one aspect of social behavior that has repeatedly been associated with normal testosterone function. Previous research from our group agreed that higher endogenous testosterone may be associated with an intergroup bias in socioeconomic decision making, which may promote outgroup hostility, ingroup favoritism, or a combination of both. Based on these findings, we hypothesized that untreated prostate cancer patients would show a stronger intergroup bias in a socioeconomic exchange task when being compared with long-term androgen-deprived patients. This hypothesis rests on the assumption that the brain might adapt to the long-term suppression of testosterone concentrations in patients with ADT, which may for instance result in a reduction of the androgen receptor density thus reducing overall androgen sensitivity in the brain (eg, in aging rats; but see Reference [23]). To our knowledge, this is the first study that assessed the influence of ADT on socioeconomic decision making in the UG and its influence on the intergroup bias.

Patient groups and the control group were matched for age, which may correlate with natural decline of testosterone and education level. The direct comparison of men that receive long-term ADT (patients with hormonal intervention: HI) with untreated patients (prostate cancer controls: PCC) and healthy men (healthy controls: HC) of comparable age provides an ideal model to investigate the influences of declining testosterone on daily life quality and cognitive capacity, while controlling for the effect of age and cancer-diagnosis as well.

2 | METHODS

2.1 | Participants

In total, 68 men between 50 and 79 years were included in the study (mean age ± SD = 67 ± 7 years). Each subject gave written informed consent and ethical approval was obtained from the ethics committee of the Ärztekammer Hamburg (approval number: PV3948). Forty-six patients had a prostate cancer diagnose and were recruited from the Martini-Klinik at the University Hospital Hamburg-Eppendorf in Hamburg (Germany). Twenty-four of these patients received an ADT (HI group). Of these, 15 men received GnRH analogues (GA) and nine men took nonsteroidal antiandrogens (AA). We only included patients in the GA group that were treated for at least 5 months. The minimal intake period of AAs was 15 months. Another 22 patients did not receive antihormone treatment and thus participated as controls in...
the prostate cancer group (PCC group). In addition, 22 healthy men were recruited through advertisements (healthy control group; HC group). Groups were matched for age and education level and median time from prostate cancer diagnosis (33 months, range = 3-262) did not differ between the HI and PCC patients. The “Beck Depression Inventory II” (BDI) was used to evaluate depression severity, if any, in patients and controls. Quality of life was examined with the “Nürnberger Life Quality” questionnaire (NLQ). Further empathy score, digit ratio and trait impulsiveness were used as matching parameters. For details see online supplemental materials.

2.2 | Free testosterone measuring procedure

The free, bioactive testosterone concentration was determined from saliva. The participants were instructed to collect three saliva samples in Eppendorf tubes (2 mL) at the morning of the test day. The samples were frozen at -20°C until being analyzed with a “testosterone free in saliva ELISA” from Demeditec Diagnostics GmbH (Kiel, Germany). For details see online supplemental materials.

2.3 | Visuospatial performance and cognition

The block-design test from the Wechsler Adult Intelligence Scale IV (WAIS IV) was used to measure visuospatial performance. The block-design test is a core test to measure cognitive abilities like logical thinking and eye-hand coordination. The test was carried out according to the instructions given in the manual. The MMSE was further used to screen participants for cognitive impairment. See online supplemental materials for details.

2.4 | Socioeconomic decision making

The ultimatum game (UG) is an established socioeconomic decision-making experiment. Two players represent the proposer and the responder in a socioeconomic exchange game. The proposer offers a selected amount of points out of 10 points. The responder has the choice to accept or reject the offer. If the responder accepts the offer, both players will get the respective amount of points. If the responder rejects the offer, both will get zero points. Here we used an approved computer-based intergroup version of the UG to compare the behavior between the two patient groups. In this game, men with high testosterone levels were previously found to show either higher ingroup cooperation or increased outgroup hostility or both, especially during an intergroup competition. The intergroup UG was thereby specifically adapted to enable the comparison of the two patient groups. As an intergroup factor, we presented a pseudorandomized sequence of offers from fictitious prostate cancer patients of two different hospitals, one foreign hospital and the same hospital in which patients were treated for prostate cancer.

Please see Figure 1 for a schematic description of an experimental trial. A more detailed description of the offers and the group rewards can be found in the online supplemental materials.

2.5 | Data analysis

IBM SPSS statistics 25 was used to analyze the data. We used F-tests to investigate the influence of the test group on the behavioral variables and the appropriate post hoc t-tests or correlations for further analysis. Statistical effects were considered significant at $P < .05$ (two-tailed), if not otherwise indicated. Post hoc t-tests were used to further examine the group differences. $P$-values for post hoc tests were Bonferroni corrected, if necessary (see online supplemental materials).

The effects of the test group on matching parameters, life quality and depression state were analyzed with univariate ANOVAs and post hoc t-tests.

For analysis of the block-design test and MMSE scores, we used univariate ANCOVAs to investigate the influence of the test group (HI, PCC and HC) on the visuospatial performance and cognition. Z-testosterone was included as covariate. Post hoc Pearson correlations were used to analyze the correlations between Z-testosterone and the visuospatial performance.

With a $2 \times 2 \times 2$ ANCOVA, we further examined how the treatment group (HI group or PCC group), the intergroup bias (ingroup or outgroup) and the experimental context (neutral or group competition) affected the overall rejection rates for unfair offers. $Z$-testosterone was included as covariate. An unpaired t-test was used to examine the interaction between the test group and the intergroup bias. For this purpose, the rejection rates for unfair proposals from outgroup vs ingroup members were calculated ($\Delta$ rejection rates = unfair offers of outgroup - rejection rates unfair offers of ingroup). A higher $\Delta$ rejection rate indicates a stronger intergroup bias.

3 | RESULTS

3.1 | Participant information

All participants, except one patient of the PCC group, noted a German nationality. Eight participants of the PCC group, six of the HI group and five HC were still occupied. Four patients of the PCC group and nine patients of the HI group (five of the GA group and four of the AA group) had received additional radiotherapy previously. Twenty of the 22 PCC patients and 18 of the 24 HI patients had a prostate surgery (12 of the GA and six of the AA group).

Thirteen PCC patients had a Gleason score of 3 + 4, five had a score of 4 + 3, one had a score of 3 + 3 and one had a score of 4 + 5 at the time of testing. For two PCC patients the Gleason score was not specified. In the HI group, four patients had a Gleason score of 3 + 4 (three of the GA group and one of the AA group), six had a score...
of 4 + 3 (four GA, two AA), three had a score of 4 + 5 (two GA, one AA), one had a score of 5 + 3 (GA), five had a score of 5 + 4 (two GA, three AA) and for five patients the Gleason score was not specified (three GA, two AA).

The staging (TNM-system) of prostate cancer was N0 in 13 patients of the PCC group, N1 in five patients of the PCC group and NX in two patients of the PCC group (the stage was not specified in two of the PCC patients). In the HI group four times N0 (one GA, three AA), 15 x N1 (11 GA, four AA) and five times "not specified" was documented.

Nine patients of the PCC group, 13 patients of the HI group and 13 healthy controls noted comorbidities/conditions (e.g., diabetes or hypertension). For additional demographic information see Table 1.

3.2 Matching parameters and descriptive values

We could not find any differences in empathy score, digit ratio and trait impulsiveness between the treatment and the two control groups. Depression severity and quality of life were affected by the treatment. Patients who received hormonal intervention showed higher depression scores than the PCC group and the HC group and a more compromised life quality than patients of the PCC group. For details, see online supplemental materials.

3.3 Testosterone concentrations

Treatment significantly influenced the testosterone concentration ($F_{2, 65} = 13.28; P \leq .001; \eta_p^2 = 0.29$). Post hoc $t$-tests showed that

![FIGURE 1] Schematic description of a trial from the Ultimatum Game. The trial begins with a fixation cross, followed by the statement “New Game!” After that, the proposer makes his offer. The responder must then decide whether to accept or reject the offer. The responder is informed that he plays against real people that made their offers in a first part of the study.

| TABLE 1 | Sociodemographic information and descriptive values of the participants of this study, separated by "test group" |
|----------|---------------------------------------------------------------------------------------------------------------|
| Data                                             | Hormonal intervention (n = 24) | Prostate cancer controls (n = 22) | Healthy controls (n = 22) | P-value ($\eta_p^2$) |
| Mean age in years ± SD                          | 68.67 ± 7.3                     | 67.05 ± 6.6                       | 65.73 ± 7.4               | Matched groups     |
| Mean time from prostate cancer diagnosis in months ± SD (range) | 52.17 ± 56.6* (8-262)          | 39.19 ± 44.9* (3-222)            | Not applicable           | Matched groups     |
| Mean period of hormonal intervention in months ± SD (range) | 39.92 ± 55.8*b,c (5-267)       | Not applicable                    | Not applicable           | Not applicable     |
| Mean free testosterone in pg/mL ± SD (range)    | 62.13 ± 41.28                   | 108.89 ± 26.5                     | 105.44 ± 33.4             | $P < .001**$       |
|                                                   | (19.9-188.3)                    | (72.7-169.5)                      | (56.5-195.3)              | (0.29)             |

Note: Differences were analyzed with univariate ANOVAs. $P$-values are considered significant at $P < .05$. Mean values are indicated with SD.

*One patient did not provide details.

Two patients did not provide details.

GnRH analogues group 33.77 ± 32.8 (5-127) months; nonsteroidal antiandrogens group 48.78 ± 80.1 (15-267) months; not significant.

**Significant $P$-value.
endogenous testosterone was significantly lower in HI patients (n = 24; M ± SD = 62.12 ± 41.28) in comparison with PCC (n = 22; M ± SD = 108.89 ± 26.5; t_{44} = 4.52, P < .001, d = 1.34) and HC (n = 22; M ± SD = 105.44 ± 33.42; t_{44} = −3.88, P < .001, d = 1.16; Bonferroni corrected *P < .025). The groups PCC and HC did not differ in testosterone level (t_{42} = 0.38, P = .706). When considering the two patient groups with different types of hormonal intervention separately, patients that received GA (n = 15; M ± SD = 46.25 ± 20.74) had significantly lower testosterone than those receiving AA (n = 9; M ± SD = 88.58 ± 53.73; t_{22} = −2.26, P < .048, d = 1.05), suggesting that the global suppression of testosterone was strongest in patients who received GnRH analogues.

### 3.4 Visuospatial performance and general cognition

We found a significant main effect of the Z-testosterone concentration on visual motor performance (F_{1,62} = 4.29, P = .042, η_p^2 = 0.07). We further found a significant interaction between test group and Z-testosterone concentration (F_{2,62} = 3.72, P = .03, η_p^2 = 0.11), while there was no significant main effect of test group (for the complete results of the ANCOVA see online supplemental materials).

Across all groups, Z-testosterone was found to be positively correlated with the visuospatial performance (r = 0.248; P = .041) (Figure 2A).

When calculating correlations separately for the test groups, HI patients exhibited a positive correlation between Z-testosterone and visuospatial performance (r = 0.474; P = .019). In PCC patients, no significant correlation emerged (r = −0.206; P = .359), while in the HC group, visuospatial performance again positively correlated with Z-testosterone (r = 0.424; P = .049). See Figure 2B for the group results.

The analysis of the MMSE further indicated that the "test group" was associated with differences in cognitive capacity of the participants (F_{2,62} = 5.74; P = .005; η_p^2 = 0.16). We could not find any significant effect of the Z-testosterone concentration on the MMSE. Post hoc tests showed that patients with HI scored lower than the participants of the two control groups (Bonferroni corrected *P < .025; HI vs PCC: t_{44} = −2.321; P = .025, d = 0.69; HI vs HC: t_{44} = −3.244; P = .002, d = 0.96).

### 3.5 Socioeconomic decision making

We found a main effect of the intergroup bias (F_{1,41} = 28.88; P < .001; η_p^2 = 0.41), as well as a significant interaction between the intergroup bias and the context (F_{1,41} = 15.52; P < .001; η_p^2 = 0.28). Most interestingly, we also noted an interaction between the test group and the intergroup bias (F_{1,41} = 5.04; P = .030; η_p^2 = 0.11). No other significant effects or interactions were detected (see online supplemental materials for detailed results of the ANCOVA).

Patients of the PCC group showed a significantly higher Δ rejection rate than HI patients (PCC (mean ± SEM) = 29.55 ± 4.77; HI (mean ± SEM) = 12.12 ± 6.02; t_{42} = 2.267, P = .029, d = 3.19). Figure 3 shows the mean Δ rejection rates of the two groups (HI and PCC).

### 4 DISCUSSION

The present study investigated the influence of artificially decreased testosterone concentrations in elderly men on different aspects of emotional behaviors, cognition and life quality. In line with our predictions, we found small behavioral effects associated with the testosterone decline in patients with a long-term ADT. Treatment decreased testosterone concentrations in long-term ADT, with a significant difference between GA and AA treated patients. Similar to short-term treatment, long-term patients exhibited a reduced visuospatial performance in the block design test (for review see Reference [6]). This result

![Figure 2](image-url)
is in accordance with our hypothesis that decreasing habitual testosterone concentrations in men may cause cognitive deficits. We also tested the influence of testosterone deprivation on behavior in a testosterone-associated socioeconomic decision-making task, the intergroup UG. We found a difference in rejection rates for unfair offers between the PCC and the HI group, in line with a higher intergroup bias in patients with nondeprived testosterone. Life quality and depression state were also negatively affected by ADT. These results are in concordance with the literature that reported impaired life quality and higher depression severity in patients receiving ADT.

### 4.1 The influence of hormonal intervention on the free testosterone levels

As expected, treatment significantly influenced free testosterone concentrations of the patients. Previous research corresponds with this finding, but in contrast to our study, most research measured serum testosterone, but see Reference [35]. Measuring salivary testosterone offers the opportunity to detect the level of the free and bioactive testosterone. Since previous research on the modulatory effects of testosterone on behavior primarily focused on normal endogenous or exogenous testosterone concentrations, it was mandatory to investigate how the massive deprivation of testosterone, as experienced under ADT, was associated with behavioral changes. Interestingly, the artificially depressed-free testosterone concentrations were still in the lower range of the expected norm values for men between 15 and 55 (Demeditec manual: n = 83; testosterone concentration 33.6-205.0 pg/mL). Separating the patients of this study corresponding to their treatment, revealed that the patients that received GA treatment had lower testosterone concentrations than patients that were treated with AA therapy (mean ± SD: GA = 46.32 ± 20.74 pg/mL; AA = 88.65 ± 53.73 pg/mL). These values are in correspondence with the results of Braga-Basaria et al., who recorded similar concentrations in patients with GA treatment (n = 20; free testosterone [mean ± SD] = 50 ± 50 pg/mL).

### 4.2 The influence of testosterone treatment on visuospatial performance and cognition

Classically, the block design test has been used to examine cognitive decline in aging populations and its link to testosterone has also been examined. In a large-scale meta-analysis from 14 original articles, patients with ADT showed significantly lower visuospatial performance ability (effect size, $g = -0.67; P = .008$), which led to the assumption, that testosterone deficiency may be responsible for this aspect of cognitive impairment. However, the meta-analysis did not consider the endogenous testosterone concentration. Therefore, a direct association between testosterone and visual spatial performance could only be assumed.

We found that the $Z$-testosterone and the interaction between test group and $Z$-testosterone were significantly associated with visuospatial performance. Across all groups, $Z$-testosterone was positively correlated with visuospatial performance, whereas, when considering the groups separately, the positive correlation was only found in HI patients and the HC group. We suppose that the small effects of treatment may be traced back to the range of testosterone within the groups (HI: 19.93-188.34 pg/mL free testosterone; PCC: 72.62-169.52 pg/mL free testosterone; HC: 56.5-195.29 pg/mL free testosterone). As a result, we assume that the testosterone concentration across the groups represents a more reliable variable to measure those effects. This result is further in line with the literature that decreasing habitual testosterone concentrations in men may cause cognitive deficits, and specifically so in the block design test (for review see Reference [38]).

Furthermore, the meta-analysis of McGinty et al. could demonstrate that visuospatial deficits were especially discovered in studies that examined patients with short-term treatment (65% up to 9 months), whereas these effects were assumed to disperse over time. Here, we were able to supplement the findings from the meta-analysis by patients with long-term treatment (5-262 months), who nevertheless showed a persistent cognitive impairment.
A loss of cognitive functioning had previously not only been associated with increasing age, but also with the age-related loss of bioactive testosterone in men. Nevertheless, the literature discussed the effects of free testosterone on cognitive capacity controversially. During a 12-month testing of patients newly diagnosed with prostate cancer, who received ADT, researchers did not find a statistical difference in the MMSE (patients: mean ± SD = 27.1 ± 2.0 and controls: mean ± SD = 28.0 ± 1.4). Compared with the study by Salminen et al., the MMSE score of the present study was identical in the healthy control group (HC: mean ± SD = 28.0 ± 1.4), but was lower in our HI patients (HI: mean ± SD = 26.5 ± 1.7). Since we tested a HI group of comparable size as Salminen et al. and of a comparable mean age (our study: mean ±SD = 68.67 ± 7.34, range = 50-78; Salminen et al. = 64.4 ± 6.5, range = 49-75), we suppose that the treatment period (our study: mean ± SD = 39.9 ± 55.8 months; Salminen et al. = 12 months) may have had an influence on cognitive ability. It may be assumed that the long-term treatment of the patients of this study might have accelerated cognitive aging.

4.3 The influence of testosterone treatment on socioeconomic decision making

Socioeconomic decision making in the UG and related tasks has been associated with endogenous testosterone of healthy young men. Especially in paradigms that highlighted the factor “group association,” habitual testosterone seemed to be positively associated with ingroup cooperation and/or outgroup hostility. To expand the research on testosterone-related socioeconomic decision making, we used an intergroup version of the UG similar to the one employed by Diekhof et al. or Reimers et al. Through this, we wanted to investigate the association between decreased testosterone in elderly men and socioeconomic choice behavior in interactions with the intergroup bias, by comparing prostate cancer patients without hormone treatment (PCC) and HI patients.

We found that the PCC group showed a higher intergroup bias than the HI group. This result suggests that patients with higher testosterone, the PCC group, may also show higher ingroup favoritism and outgroup hostility than the androgen deprived HI patients.

This finding is in line with previous research that higher testosterone concentrations were associated with increased ingroup cooperation, yet also increased outgroup hostility. Nevertheless, Z-testosterone concentration within each group was not significantly correlated with the intergroup bias. The interindividual differences of the patient cohort (eg, large range in cancer treatment and testosterone concentration) may outweigh the supposedly small effects of testosterone concentration. Furthermore, the limited number of six unfair proposals from each group in two contexts limits interindividual differences in behavioral choice, which is different from score that reflects test performance in the block design test that shows a much higher variability between participants. The groupwise effect may therefore constitute a more reliable factor for the comparison between groups.

4.4 Study limitations

Since differences in the severity of prostate cancer between HI and PCC patients might contribute to differences in overall well-being and may thus indirectly influence cognitive capacity and even economic choice, all of these findings in relation to testosterone must be cautiously considered as preliminary. Although we only considered patients that were not treated with chemotherapy, several other side effects of prostate cancer diagnosis and supplementary treatments could have resulted in depression and impaired life quality. Furthermore, the wide range of individual testosterone concentrations within the HI group may have made the findings less clear. In order to verify our hypotheses, an extension of the sample size, with even more detailed patient information and a larger scattering of the treatment duration would benefit the quality of future studies. Since the sample size of patients with AA treatments was small, we summarized the treatments with Bicalutamid and Enzalutamid solely according to their effect mechanisms, but did not consider medical indications or binding forces here. This may have influenced the results and should be considered in future studies with larger samples.

4.5 Clinical implications

The findings of the present study reflect the expected, yet rather small effects of androgen deprivation on cognition and well-being in elderly men, even when considering the potential neuronal adaptation on testosterone decline after long-term treatment. It therefore needs to be emphasized that the negative side effects of ADT cannot outweigh the benefits of ADT on the course of advanced prostate cancer. Nevertheless, the findings may support the recommendations of recent literature that showed that clinicians should be aware that some androgen-deprived prostate cancer patients develop neurocognitive impairments, yet fail to seek psychological help, although it may be necessary in some cases.

4.6 Conclusion

As expected, ADT significantly reduced free testosterone concentrations in prostate cancer patients. The analysis of the test battery further showed that androgen deprivation influenced different aspects of cognition. In accordance with the literature, testosterone concentrations were negatively associated with visuospatial performance and a reduced intergroup bias in socioeconomic choice was found in the patient group with lower testosterone concentrations. Furthermore, depression severity, cognitive capacity and quality of life were negatively affected by antihormone treatment.

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CONFLICT OF INTEREST
The authors declare no conflict of interest. The manuscript contains original and unpublished work and is not being submitted for publication elsewhere.

DATA AVAILABILITY STATEMENT
The data that supports the findings of this study are available in the supplementary material of this article.

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**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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