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ORIGINAL ARTICLE

# The phenotypic correlates and quantitative genetics of masculinization in the rodent, *Octodon degus*

**This article has been corrected since Advance Online Publication and a corrigendum is also printed in this issue**

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In some mammals, female characteristics have been shown to depend, in part, on the intrauterine position during development of female fetuses relative to male fetuses. Females developing in close proximity to males show behavioral, physiological and life history characteristics that are masculinized. With the exception of one inconclusive study, nothing is known of the genetic basis of this phenomenon. In this paper, we reported an analysis of the quantitative genetic basis of masculinization, as indicated by the anogenital distance (AGD) at birth and weaning, in the rodent *Octodon degus*. Because AGD is related to weight, we included a genetic analysis of pup weight at birth and weaning. Pairwise correlations showed that AGD at birth varied negatively with litter size and parturition number but positively with weaning AGD, birth weight, dam AGD and percentage of males in the litter. AGD at weaning varied similarly except that it tended to vary positively with litter size. Genetic (co)variances of AGD at birth and weight at birth differed in females and males. In females, the best genetic model included substantial effects of direct additive, additive maternal and a negative additive genetic covariance between these two. In males, variances were small and there was difficulty in discriminating between additive maternal and common environmental variances. By weaning, genetic (co) variances had somewhat declined in weight and were not statistically significant in AGD in either sex. This paper showed the occurrence of both phenotypic and genetic components in masculinization with effects being greater in females.
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## INTRODUCTION

Sex in mammals is chromosomally determined with females being the homogametic sex (Gilbert, 2000). Nevertheless, in some species, individuals of each sex may fall along a continuum of being more or less masculinized (or feminized) with respect to physiology, behavior or life history characteristics. Such differences have been shown to derive from the intrauterine position, with female fetuses developing next to males tending to be more masculine in their features than females developing next to other females (Gandelman *et al.*, 1977; Meisel and Ward, 1981; Clark and Galef, 1988; Ryan and Vandenbergh, 2002; Bautista *et al.*, 2015). Generally, males have larger anogenital distance (AGD) than females; and within females, those with larger AGD show more masculinized behavior (Kerin *et al.*, 2003; Bánszegi *et al.*, 2009; Correa *et al.*, 2013), correlation with blood chemistry (Kerin *et al.*, 2003) and changes in reproductive patterns (Drickamer *et al.*, 1997; Zehr *et al.*, 2001; Ophir and DelBarco-Trillo, 2007; Bánszegi *et al.*, 2012; Szenczi *et al.*, 2013; Monclus *et al.*, 2014; Bautista *et al.*, 2015).

Although considerable attention has been paid to the importance of uterine position and the hypothesized hormonal contribution to morphology and behavior, relatively little attention has been given to the genetic basis of masculinization observed in female fetuses developing in the uterus next to males.

Crucially, we have no empirical evidence to suggest how additive genetic effects on masculinization of individuals (direct) are associated with additive genetic effects for maternal traits influencing offspring masculinization, since no previous study has estimated the covariance between direct and maternal additive genetic effects. Such a covariance has a fundamental role in the response to selection, often greatly increasing, decreasing or even changing the direction of the response expected when considering direct and maternal additive genetic variance independently (Griffing, 1967; Qvarnstrom and Price, 2001; Bijma *et al.*, 2007). However, the detection of direct and maternal additive genetic (co)variances is potentially difficult using pedigrees from wild populations (Kruuk and Hadfield, 2007) or even in traditional mating designs such as offspring on parent and special designs have been proposed to separate these components (Bondari *et al.*, 1978).

The only attempt to partition inter-individual variation in masculinization into variance components of genetic and non-genetic factors of which we are aware is the study by Fouqueray *et al.* (2014) on a wild population of yellow-bellied marmots. Fouqueray *et al.* (2014) measured anogenital distance (AGD), which is used across taxa as a reliable indicator of the degree of masculinization (Gandelman *et al.*, 1977; McDermott *et al.*, 1978; Clark and Galef, 1998; Cantoni *et al.*, 1999; Ryan and Vandenbergh, 2002). Fouqueray *et al.* (2014) showed

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that the fixed effect of litter sex-ratio significantly affected the AGD, whereas litter size was not significant. Importantly, Fouqueray *et al.* (2014) did not consider any genetic model that included a genetic covariance between direct additive genetic variance and additive maternal genetic variance. There was a significant contribution of maternal additive genetic variance but a model with both direct and maternal additive genetic variance components was not supported. However, either genetic component by itself was significantly greater than zero, the direct additive genetic variance being 14% (s.e. = 0.082) of the total variance and the maternal genetic variance being 8% (s.e. = 0.042) of the total variance.

In the present paper, we report a phenotypic and genetic analysis of pup weight and AGD in the South American rodent *Octodon degus* based on the pedigree from a laboratory breeding experiment. Degus, *Octodon degus,* is a small–medium (170–300 g) caviomorph diurnal rodent endemic to central Chile. In a previous study, it was shown that AGD varied among degus pups and that females with longer AGD were more dominant than other females (Correa *et al.*, 2013).

Maternal effects are common among mammals but typically decline with age (Meyer, 1992; Wilson *et al.*, 2005a; Wilson and Reale, 2006; Pettay *et al.*, 2008; Aksoy *et al.*, 2016) and thus it is generally important to measure such effects at several ages to assess the potential effect on response to selection. Therefore, in the present analysis, we assessed factors that could affect pup weight and AGD and estimated the genetic basis of these traits at birth and weaning.

## MATERIALS AND METHODS

### Experimental design

The experiment started with 12 sires and 28 dams obtained from a first generation of rodents born in Pontificia Universidad Católica de Chile (Ebensperger Lab) that came from a wild population in Rinconada de Maipú, 60 km west of Santiago City, Chile. At 3 months of age, the animals were transported to Valdivia (840 km south of Santiago), to begin the experiment. The animals were raised in polycarbonate transparent rat boxes ($45 \times 23 \times 21$ cm), with a bedding of hardwood chips, and water and food (Cisternas rabbit commercial pellets) provided *ad libitum*. The ambient temperature was maintained at $18 \pm 2$ °C with a 12:12 h light–dark cycle.

In the first generation, dams produced from one to six litters and were generally mated with a different sire for each litter. Offspring from these matings were used to produce a second generation in which females produced one to three litters with matings between unrelated animals. Although the pedigree structure did not explicitly follow one of the proposed designs for the separation of direct and maternal additive genetic variances, the multiplicity of relationships suggested that the separation of these components would be possible. Data on relatedness were obtained using the pedantics package in R: the results, where the coefficient of relatedness follows the number of connections in parentheses, were 263 (0.05), 1726 (0.125), 2826 (0.25), 25 (0.30) and 1390 (0.5).

AGD was defined as the distance from the ventral anus commeasure to base of genital papilla (Vandenbergh and Huggett, 1994) and measured at birth and at weaning (day 63). As AGD is expected to be correlated with overall size, we also measured body weight at birth and at weaning (63 days of age).

### Statistical approaches

We took two approaches to the analysis. First, we did pairwise correlation analysis using the mean family values, separated according to offspring sex and generation: variables included in the analyses were weight at birth and weaning, AGD at birth and weaning, generation (1 or 2), parturition number, litter size percent male in a litter ($57.3 \times$ arcsine-square-root transformed: results using the raw data did not change the results). Second, we estimated genetic parameters using the animal model (Asreml, Gilmour *et al.*, 2009) with parameters estimated using the Willham model (Willham, 1972). Males and females were analyzed separately.

The animal model analysis was done using the raw data and also data normalized by subtracting the mean and dividing by the standard deviation: the results did not differ and we present variance/covariance components estimated using the normalized data. Based on an initial multiple regression analysis, candidate fixed effects were generation, parturition number, parturition number squared, litter size, percent male in a litter ($57.3 \times$ arcsine-square-root transformed: results using the raw data did not change the results) and the interaction between generation and parturition number. As noted above, for the AGD measures weight at the age of AGD measurement was also entered as a fixed effect. For each model, only significant effects were included.

The most complex genetic model included, in addition to fixed effects, direct additive genetic variance ($V_a$), maternal additive genetic variance ($V_m$), the covariance between these two ($Cov_{am}$) and a common environmental variance, $V_c$. The common environmental variance includes the intrauterine environment as well as effects resulting from sharing the same nest. Some of these effects will be included in the fixed-effects components (for example, litter size). For clarity, we shall refer to the individual models by the combination of variance components (for example, the full model will be referred to as $V_a+V_m+Cov_{am}+V_c$). In total, we examined 10 models with the simplest being the constants-only model, in which there were no (co)variance components: $V_a+V_m+Cov_{am}+V_c$; $V_a+V_m+Cov_{am}$; $V_a+V_m+V_c$; $V_a+V_m$; $V_a+V_c$; $V_m+V_c$; $V_a$; $V_m$; $V_c$; Constants only.

Models were ranked using Akaike information criterion (AIC) and the Akaike weight, $w_i = \exp(-0.5\Delta_i)/\sum_{r=1}^{10}\exp(-0.5\Delta_r)$, where $\Delta_i$ is the difference between the $i$-th model and the model with the lowest AIC (Symonds and Moussalli, 2011). The Akaike weight varies between 0 and 1 with the sum of all weights being 1. One interpretation of this weight is that it is equivalent to the probability that a given model is the best approximating model (Symonds and Moussalli, 2011). Link and Barker (2006) confine this statement to only the models in the set under consideration (that is, better models may still exist), which is the sense in which we prefer to interpret the statement. The importance of each model component was further evaluated by summing the Akaike weights for each model in which the variance component appeared. The summed Akaike weight for a particular predictor variable (variance/covariance component) is interpreted as the probability that this variable is a component of the best model (Symonds and Moussalli, 2011).

We present the estimates for the models with the lowest AIC and also using full model averaging, for which the estimate of the (co)variance $\beta$ is $\beta = \sum_{i=1}^{R} w_i\beta_i$, where $R$ is the number of models that contain the relevant parameter (Lukacs *et al.*, 2009). Models that do not contain $\beta$ contribute zero to the estimate. There is no exact formula to the standard error but an approximation suggested by Lukacs *et al.* (2009) is $\mathrm{var}(\beta) = \sum_{i=1}^{R} w_i\left[\mathrm{var}(\beta_i) + (\beta_i - \beta)^2\right]$.

In models with the maternal covariance, the heritabilities of the additive genetic variance and the maternal heritability are not informative and so for these models we present the total heritability $h_T^2 = (V_a + 0.5V_m + 1.5Cov_{am})/V_P$, where $V_p$ is the total phenotypic variance (Willham, 1972).

## RESULTS

### Pairwise correlations using mean values separated according to offspring sex and generation

To better discern the overall correlations, we extracted all trait combinations in which at least one correlation had a probability value of 0.1 or less (for example, weight at birth was significantly correlated in at least one sex or generation with litter size, parturition number and weight at weaning: Table 1).

Pup weights at birth were consistently negatively correlated with litter size, parturition number and weight at weaning, which point to possible common environment effects. At weaning, pup weight was also negatively correlated with litter size but correlations with parturition number and percentage males in the litter were inconsistent. AGD at birth varied negatively with litter size, parturition number and weight at weaning but positively with birth weight, weaning AGD and dam AGD. A similar pattern was observed for

**Table 1 Pairwise correlations between traits separated by generation and pup sex**

| *Trait 1* | *Trait 2* | *Generation 1* | | *Generation 2* | |
|---|---|---|---|---|---|
| | | *Male* | *Female* | *Male* | *Female* |
| Birth wt | Litter size | **−0.468** | **−0.455** | **−0.649** | **−0.626** |
| | Parturition N | **−0.388** | *−0.202* | **−0.365** | **−0.363** |
| | Wt at weaning | **0.339** | **0.283** | **0.471** | ***0.322*** |
| Wt at weaning | Litter size | **−0.565** | **−0.592** | −0.201 | −0.191 |
| | Parturition N | 0.137 | **0.279** | −0.185 | **−0.442** |
| | Percent male | −0.172 | **−0.386** | −0.109 | 0.073 |
| AGD at birth | Litter size | −0.156 | *0.219* | **−0.447** | −0.173 |
| | Parturition N | ***−0.224*** | **−0.354** | ***−0.286*** | −0.269 |
| | Percent male | **0.604** | **0.586** | **0.464** | **0.464** |
| | Birth wt | **0.278** | ***0.201*** | 0.262 | 0.254 |
| | Wt at weaning | 0.053 | **−0.419** | −0.061 | −0.012 |
| | AGD at weaning | **0.641** | **0.769** | **0.564** | **0.702** |
| | Dam AGD | 0.036 | **0.347** | −0.155 | 0.196 |
| AGD at weaning | Litter size | −0.062 | **0.303** | 0.034 | −0.168 |
| | Parturition N | −0.087 | **−0.241** | −0.095 | −0.257 |
| | Percent male | **0.605** | **0.719** | **0.539** | **0.761** |
| | Wt at weaning | 0.064 | **−0.359** | **0.211** | 0.127 |
| | Dam AGD | 0.186 | **0.325** | −0.173 | **0.502** |

Abbreviations: AGD, anogenital distance; parturition N, parturition number; wt, weight.
Only combinations in which at least one of the correlations is significant are shown. Bold font ($P<0.05$), bold and italic font ($P<0.1$).

**Table 2 Coefficients of fixed effects**

| | *Female* | | *Male* | |
|---|---|---|---|---|
| | *Birth wt* | *Weaning Wt* | *Birth Wt* | *Weaning Wt* |
| G×N | | −2.09 (0.29) | | −0.75 (0.29) |
| Percent male[a] | | −0.01 (0.004) | | |
| Litter size | −0.28 (0.04) | −0.19 (0.04) | −0.30 (0.04) | −0.34 (0.04) |
| $N^2$ | | −0.10 (0.03) | | |
| N | | 2.73(0.37) | | 0.88 (0.31) |
| G | | 2.38 (0.41) | −0.56 (0.16) | 0.86 (0.39) |
| Intercept | 1.74 (0.26) | −1.40 (0.60) | 2.66 (0.35) | 1.03 (0.57) |
| | *AGD at birth* | *AGD at weaning* | *AGD at birth* | *AGD at weaning* |
| Wt at given age | 0.10(0.02) | | 0.09 (0.02) | 0.01 (0.003) |
| Percent male | 0.03(0.004) | 0.04 (0.004) | 0.03 (0.004) | 0.04 (0.005) |
| G | 0.92 (0.18) | | | |
| Intercept | −3.61 (0.49) | −1.66 (0.17) | −2.92 (0.38) | −3.45 (0.52) |

Abbreviations: AGD, anogenital distance; G, generation; N, parturition number.
[a]57.3 × arcsine-square-root transformation.
Effects are shown for the best-fitting model but results were qualitatively the same for all models.

weaning AGD except that it tended to vary positively with litter size. Taken together, these correlations suggest an environmental and/or genetic maternal effect on the AGD at birth and weaning.

### Animal model analysis: fixed effects

We present the results for the analysis of the fixed effects using the results from the most likely model (see below) but qualitatively, the probabilities for fixed effects did not differ among models (Table 2). The overall effects are consistent with those found with the pairwise correlations described above. Weights at birth and weaning decreased with litter size and at weaning with the interaction between parturition number and generation. Birth AGD and weaning AGD increased with percent males in the litter. Neither litter size nor parturition number had a significant effect on AGD at either age.

### Animal model analysis

The model with the lowest AIC for weight and AGD at birth in females was $V_a+V_m+Cov_{am}$ with all other models differing by more than 2 AIC units (Table 3). This model was highly supported by the Akaike weight (0.69) and all other models had little support (Akaike weight $\leqslant 0.10$, Table 3). However, by weaning models with a covariance component had little support (Akaike weight $\leqslant 0.09$). For birth weight, there was relatively strong support for the model $V_a+V_c$ (lowest AIC and Akaike weight = 0.61), with the next closest model being $V_a+V_m+V_c$ with an Akaike weight of 0.22 (Table 3). Model discrimination for AGD at weaning in females was very poor, the model with the lowest AIC being $V_a$ and an Akaike weight of only 0.20.

Males showed a somewhat different picture. The models $V_a+V_m$ and $V_a+V_c$ were equally supported for weight at birth and weaning but other models received very little support (Table 3). These two models provide evidence of additive genetic variance but cannot discriminate between additive genetic maternal variance and common environment variance. In contrast to females, AGD at birth in males showed little evidence of additive genetic variance. Three models, $V_m$, $V_c$ and Constants only, had the same low support (Akaike weight = 0.19). At weaning, the model with the highest support for AGD in males was $V_a+V_m+Cov_{am}$, though the small Akaike weight (0.27) does not provide convincing support for the model, especially as six other models, including the Constants-only model, differed by less than 2 AIC units (Table 3).

The summed Akaike weights showed very strong evidence for additive genetic variance, additive maternal genetic variance and the covariance between these in both birth weight and AGD at birth in females (Table 4). There is weak support for the presence of common environmental variance. Additive genetic variance in birth weight is evident at weaning but support for additive maternal genetic variance and the covariance between them declined significantly, whereas support for a common environmental variance increased very substantially. In contrast, support for any (co)variance component was relatively low for AGD at weaning.

In males, there is very strong evidence of additive genetic variance in weight at birth and weaning, but much less support for this variance in AGD at birth. There is reasonable support for additive genetic variance in AGD at weaning (Table 4). For both weight and AGD there is similar and modest support for additive maternal genetic variance. This support is slightly greater than that for a common maternal variance. There is no support for a genetic covariance components in males.

Heritability estimates were generally low but relatively large standard errors make assessment difficult (Table 5). (Co)variance components were generally better estimated. At birth, the additive genetic variance and additive genetic maternal variance of weight and AGD were significant in females with a large negative covariance between them (Table 5). By weaning, however, there was a substantial reduction in additive genetic variance in weight and no significant genetic variance component in AGD. The two models with the lowest AIC in male birth weight were identical except that the $V_m$ and $V_c$ components switched places (Table 5). This switching occurred in all

**Table 3 ΔAIC values for each model**

| Model | Female | | | | Male | | | |
|---|---|---|---|---|---|---|---|---|
| | *Birth wt* | *AGD at birth* | *Weaning wt* | *AGD at weaning* | *Birth wt* | *AGD at birth* | *Weaning wt* | *AGD at weaning* |
| $V_a+V_m+Cov_{am}+V_c$ | 2.50 (0.21) | 5.00 (0.06) | 3.81 (0.09) | 5.70 (0.01) | 5.26 (0.02) | 8.25 (0.00) | 24.37 (0.00) | 5.66 (0.02) |
| $V_a+V_m+Cov_{am}$ | **0.00 (0.75)** | **0.00 (0.69)** | 8.17 (0.01) | 3.70 (0.03) | 1.90 (0.13) | 3.62 (0.03) | 2.00 (0.15) | **0.00 (0.27)** |
| $V_a+V_m+V_c$ | 9.52 (0.01) | 6.98 (0.02) | 2.01 (0.22) | 4.00 (0.03) | 8.22 (0.01) | 2.65 (0.05) | 35.16 (0.00) | 5.37 (0.02) |
| $V_a+V_m$ | 9.49 (0.01) | 5.80 (0.04) | 8.97 (0.01) | 2.00 (0.07) | **0.00 (0.33)** | 1.90 (0.07) | **0.00 (0.41)** | 1.93 (0.10) |
| $V_a+V_c$ | 7.52 (0.02) | 4.98 (0.06) | **0.00 (0.61)** | 2.00 (0.07) | **0.00 (0.33)** | 1.90 (0.07) | **0.00 (0.41)** | 1.93 (0.10) |
| $V_m+V_c$ | 13.80 (0.00) | 10.06 (0.00) | 7.17 (0.02) | 2.31 (0.06) | 10.88 (0.00) | 0.41 (0.16) | 37.31 (0.00) | 5.25 (0.02) |
| $V_a$ | 10.22 (0.00) | 3.80 (0.10) | 35.89 (0.00) | **0.00 (0.20)** | 2.03 (0.12) | 3.56 (0.03) | 25.06 (0.00) | 1.07 (0.16) |
| $V_m$ | 15.29 (0.00) | 9.04 (0.01) | 13.95 (0.00) | 0.31 (0.17) | 5.12 (0.03) | **0.00 (0.19)** | 8.10 (0.01) | 1.99 (0.10) |
| $V_c$ | 11.80 (0.00) | 8.07 (0.01) | 5.17 (0.05) | 0.31 (0.17) | 5.12 (0.03) | **0.00 (0.19)** | 8.10 (0.01) | 1.99 (0.10) |
| Constants only | 15.29 (0.00) | 9.04 (0.01) | 13.95 (0.00) | 0.31 (0.17) | 5.12 (0.03) | **0.00 (0.19)** | 8.10 (0.01) | 1.99 (0.10) |

Abbreviations: AGD, anogenital distance; AIC, Akaike information criterion; $Cov_{am}$, covariance between $V_a$ and $V_m$; $V_a$, additive genetic variance; $V_c$, common environmental variance; $V_m$, additive maternal genetic variance; wt, weight.
Model(s) with the lowest AIC (shown in bold font) are given a value of zero. The Akaike weight is shown in parentheses to an accuracy of two decimal places.

**Table 4 Summed Akaike weights for the (co)variance components**

| | Female | | | | Male | | | |
|---|---|---|---|---|---|---|---|---|
| | *Birth* | | *Weaning* | | *Birth* | | *Weaning* | |
| | *Wt* | *AGD* | *Wt* | *AGD* | *Birth* | *AGD* | *Weaning* | *AGD* |
| $V_a$ | 0.996 | 0.968 | 0.936 | 0.422 | 0.923 | 0.423 | 0.978 | 0.677 |
| $V_m$ | 0.976 | 0.820 | 0.348 | 0.382 | 0.507 | 0.509 | 0.572 | 0.533 |
| $Cov_{am}$ | 0.962 | 0.748 | 0.100 | 0.044 | 0.149 | 0.035 | 0.152 | 0.290 |
| $V_c$ | 0.240 | 0.152 | 0.982 | 0.345 | 0.381 | 0.477 | 0.420 | 0.260 |

Abbreviations: AGD, anogenital distance; $Cov_{am}$, covariance between $V_a$ and $V_m$; $V_a$, additive genetic variance; $V_c$, common environmental variance; $V_m$, additive maternal genetic variance; Wt, weight.

male variance components models (italicized entries in Table 5) and indicates that in males additive maternal genetic variance ($V_m$) and common environmental variance ($V_c$, which may reflect common environment and/or maternal effects) cannot be distinguished.

## DISCUSSION

Previous work on various mammalian species has shown that masculinization of females is associated with intrauterine position of female fetuses; more specifically, females that develop next to males are masculinized (McDermott *et al.*, 1978; Clark and Galef, 1998; Ryan and Vandenbergh, 2002). Therefore, we predict that as the percentage of males in a litter increases, so will the AGD of females at birth. Not only was this observed but we also found that the AGD of male pups at birth increased with the percentage of males in the litter, which suggests a more complex interaction than that of simply a male effect on females.

As is generally found in mammals (Roff, 1992,2002), offspring weight decreased with an increasing litter size, which may be a consequence of reduced milk per individual and hence a maternal effect. This negative phenotypic correlation (for both weight and AGD) was not, however, evident as a fixed effect in the genetic analysis. AGD at birth was correlated with birth weight, whereas AGD at weaning in females was not correlated with weaning weight in the genetic models: in fact, in the first generation, there was a significant negative phenotypic correlation between these. This lack of a consistent relationship between AGD and body weight is important as it means that the body weight cannot be used as a surrogate for AGD, as done by David *et al.* (2015).

Maternal effects, reflected in part as common environmental effects, are common across all taxa (Mousseau and Fox, 1998), particularly so in mammals (Wolf *et al.*, 2011), and thus it is not surprising that models with common environmental variance components ($V_c$) or maternal genetic effects ($V_m$) were consistently found to give good fits. In males, there was a general pattern of the fitting algorithm failing to distinguish between $V_m$ and $V_c$. Maternal genetic variance was significant in females for both birth weight and AGD at birth, but these had largely dissipated by the age of weaning.

Both empirical (Wilson *et al*, 2005b; Koivula *et al.*, 2009) and theoretical (Holand and Steinsland, 2016) studies have shown that the exclusion maternal additive genetic effects when present can give highly misleading results on the course of evolutionary change. The reason for this is that a positive maternal genetic variance can increase the response to selection, whereas a negative genetic covariance between direct additive genetic variance and maternal additive genetic variance can substantially reduce the response to selection. Thus, for AGD at birth, the total additive genetic variance in females is $0.50 + 0.5 \times 0.36 - 1.5 \times 0.31 = 0.215$, which is considerably less than either $V_a$ or $V_m$ alone.

There was generally significant additive genetic variance for pup weight at both ages but there was some indication of a reduction in this variance by the time of weaning, at least in females. Maternal effects in mammals are often one of the largest components of variation for traits expressed early in life, with effects generally eroding after weaning (Wolf *et al.*, 2011).

At birth, maternal genetic (co)variances were significant but these clearly disappeared by weaning. The genetic maternal covariance for weight at birth was negative. Negative correlations between additive and genetic maternal variances in growth parameters have been found in mice, swine, sheep, cattle, mink and red deer (Ferraz and Johnson, 1993; Roff, 1997; Lee, 2002; Wilson and Reale, 2006; Calvillo *et al.*, 2008; Koivula *et al.*, 2009). As noted above, such correlations can substantially decrease the response to selection (Griffing, 1967; Roff, 1997; Bijma *et al.*, 2007; Rasanen and Kruuk, 2007; Kruuk *et al.*, 2008). There appears to be no satisfactory biological explanation for the negative genetic correlation (Lee, 2002).

The only other attempt to estimate genetic and maternal effects on AGD is that by Fouqueray *et al.* (2014) on the yellow-bellied marmot.

**Table 5 (Co)variance and heritability estimates (s.e. in parentheses) for the model(s) with the lowest AIC (shown in bold font)**

| *Model* | *Female* | | | | *Male* | | | |
|---|---|---|---|---|---|---|---|---|
| | *Birth wt* | *AGD at birth* | *Weaning wt* | *AGD at weaning* | *Birth wt* | *AGD at birth* | *Weaning wt* | *AGD at weaning* |
| *(Co)variances* | | | | | | | | |
| $V_a$ | **0.77 (0.35)** | **0.50 (0.23)** | **0.28 (0.17)** | **0.04 (0.06)** | **0.29 (0.17)** | *0.02 (0.07)* | **0.52 (0.24)** | **0.43 (0.30)** |
| | *0.75 (0.35)* | *0.41 (0.24)* | *0.27 (0.18)* | *0.02 (0.05)* | *0.28 (0.19)* | | *0.51 (0.25)* | *0.32 (0.28)* |
| $V_m$ | **0.46 (0.18)** | **0.36 (0.13)** | *0.01 (0.15)* | *<0.01 (0.03)* | **0.16 (0.08)** | **0.10 (0.05)** | **0.47 (0.15)** | **0.55 (0.35)** |
| | *0.38 (0.23)* | *0.14 (0.12)* | | | *0.07 (0.16)* | *0.04 (0.10)* | *0.26 (0.27)* | *0.20 (0.32)* |
| $Cov_{am}$ | **−0.53 (0.22)** | **−0.31 (0.15)** | *−0.01 (0.08)* | *<0.01 (0.02)* | *0.01 (0.13)* | *<0.01 (0.05)* | *<0.01 (0.21)* | **−0.48 (0.37)** |
| | *−0.47 (0.22)* | *−0.22 (0.15)* | | | | | | *−0.13 (0.27)* |
| $V_c$ | *0.03 (0.09)* | *0.01 (0.03)* | **0.46 (0.14)** | <0.01 (0.01) | **0.16 (0.08)** | **0.10 (0.05)** | **0.47 (0.15)** | *0.04 (0.09)* |
| | | | *0.46 (0.16)* | | *0.06 (0.08)* | *0.04 (0.05)* | *0.20 (0.20)* | |
| *Heritabilities*[a] | | | | | | | | |
| $h^2_T$ | 0.22 (0.20) | 0.17 (0.16) | | | | | | –0.004 (0.39) |
| $h^2_a$ | | | 0.29 (0.16) | 0.05 (0.08) | 0.38 (0.20) | | 0.48 (0.20) | |
| $h^2_m$ | | | | | 0.20 (0.10) | 0.13 (0.05) | 0.43 (0.11) | |

Abbreviations: AGD, anogenital distance; AIC, Akaike information criterion; $Cov_{am}$, covariance between $V_a$ and $V_m$; $V_a$, additive genetic variance; $V_c$, common environmental variance; $V_m$, additive maternal genetic variance; wt, weight.
[a]$h^2_T$, total additive heritability; $h^2_a$, direct additive heritability; $h^2_m$, direct additive maternal heritability.
In males, two models ($V_a$+$V_m$, $V_a$+$V_c$) have the same lowest AIC for birth weight and weaning weight: in these models, $V_a$ did not differ between the two and $V_m = V_c$. Estimates of (co)variances based on full model averaging are shown in italics.

Their analysis did not include $Cov_{am}$, and a model that included both $V_a$ and $V_m$ gave a marginally better fit than a model that excluded both ($P = 0.053$). A model that included only one of the variances was statistically significant but the two models were indistinguishable from each other. The present analysis suggests that differences may exist between the sexes, with genetic variances in females being determined at birth by direct and maternal additive genetic (co)variances that disappear at weaning. In males, direct additive genetic variances contribute but discrimination between direct additive maternal additive genetic variance and common environmental variance is unsatisfactory. As with females, genetic variances are not evident at weaning. The data on the yellow-bellied marmot were collected at weaning and pup sex was entered into the analysis as a fixed effect: it is thus possible that genetic estimates may have been confounded by the lack of separation of the sexes in the random component of the model (that is, genetic effects in female pups may have been masked by the lack of such effects in males).

As noted in the introduction, many aspects of physiology, life history and behavior are correlated with the AGD of females. Relatively little analysis has been given to the effect of AGD in males. AGD in male prairie voles (*Microtus ochrogaster*) was correlated with testes size, seminal vesical size, the number of sperm stored and female preference (Ophir and delBarco-Trillo, 2007). Aggression, home range size and the probability of dispersal are positively correlated with AGD in male wild house mice (*Mus domesticus*, Drickamer, 1996). Thus it seems reasonable to suppose that in Degus both female and male characteristics will vary with AGD. It has previously been shown that female aggression and social position in Degus is correlated with AGD (Correa *et al.*, 2013), and so it is likely that male aggression is likewise affected. How such effects modulate changes in life history, behavior and population dynamics in wild populations of Degus has yet to be determined but the present analysis strongly indicates that it will be important to take into account both the phenotypic and genetic basis of masculinization in males and females.

## DATA ARCHIVING

The data are available from the Dryad Digital Repository: http://dx.doi.org/10.5061/dryad.1fk40.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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