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ORIGINAL PAPER

Microsatellite length polymorphisms associated with dispersal-related agonistic onset in male wild house mice (*Mus musculus domesticus*)

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Abstract Dispersal propensity, reflecting one of the most decisive mammalian life history traits, has been suggested to vary heritably and to locally adapt to prevailing dispersal conditions in wild house mouse populations. Because individual dispersal propensity highly significantly covaries with the developmental timing of the onset of agonistic interactions between littermate brothers, we used agonistic onset as an endophenotype to explore the potential genetic basis of dispersal-related behavioral variation in male house mice. We found significant covariation of microsatellite marker compositions with the probability of fraternal pairs to exhibit agonistic relationships before the age of 2 months. In particular, the presence of two alleles associated with a serotonin transporter protein gene (Slc6a4) and a testosterone dehydrogenase gene (Cyp3a11), respectively, strongly covaried with the probability of early agonistic onset. These results are congruent with recent findings of microsatellite length polymorphisms marking regulatory variation of gene expression that is relevant for social behavior, including dispersal propensity development, in other mammals. Genetic variability for ontogenetic timing of agonistic onset would be in agreement with genotypic differentiation of the dispersive behavioral syndrome in natural populations that could lead to local adaptation.

Keywords Dispersive behavioral syndrome · Serotonin transporter protein · Slc6a4 · Steroid inducible cytochrome P450 · Cyp3a11

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Introduction

Timing of emigration from the natal group represents one of the most decisive life history traits in mammals (Gaines and McClenaghan 1980; Stenseth and Lidicker 1992). However, little is known about the presumably complex genetic mechanisms governing the behavioral decisions involved, strongly hampering our understanding of the evolutionary biology of dispersal strategies (Bowler and Benton 2005). In wild house mice, *Mus musculus domesticus*, natal dispersal propensity has been suggested to vary between populations due to local adaptation to geographically variable dispersal regimes, involving changes in aggressivity as well as morphological traits (Corti and Rohlf 2001). In accordance with the supposition of local adaptation, male dispersal propensity exhibited heritable components in wild house mice (Krackow 2003).

In naked mole rats, *Heterocephalus glaber*, a presumed "dispersive morph" differs from other males both behaviorally and morphologically (O'Riain et al. 1996; Scantlebury et al. 2006). In Rhesus macaques, *Macaca mulatta*, age at natal dispersal strongly covaries with the presence of a deletion in the promotor region of the serotonin transporter protein gene that is marked by a microsatellite polymorphism (*SLC6A4*; Trefilov et al. 2000). Thus, there is evidence for dispersive behavioral syndrome differentiation in mammals that might be caused by gene expression variability.

Genetically polymorphic dispersal phenotypes are well known from a diverse range of taxa (Clobert et al. 2001), and fast evolving expression level mutations are proposed to particularly affect complex traits (Rifkin et al. 2005). However, molecular evidence of gene expression determining genotypic variation of complex behavioral phenotypes is only beginning to emerge in mammals (Hovatta et al. 2005). Moreover, dispersal in mammals is generally seen as a plastic behavioral response (Ims and Hjermann 2001; Pocock et al. 2005) not necessarily exhibiting genetic diversity. Hence, it appears highly warranted to elucidate the molecular genetic mechanisms governing wild house mouse dispersal-related behavioral variation.

To initiate such research, we took advantage of a standardized behavioral measure that is phenotypically strongly correlated with dispersal propensity in male wild house mice. Ontogenetic timing of agonistic onset between littermate brothers kept in pairs after weaning is characterized by an abrupt change from amicable to agonistic behavior around the second month of life (Krackow 2005). Such behavioral change mimics the abrupt outbreak of agonistic interactions around 2 months of age followed by dispersal in male wild house mice kept under seminatural conditions (Gerlach 1996). Indeed, males from fraternal pairs having passed that behavioral switch more often dispersed than stayed when exposed to a social group containing a superior territorial male. In contrast, males of the same age which behaved amicable until testing far more frequently integrated into the group (Rusu and Krackow 2005). Therefore, agonistic onset is seen here to represent an endophenotype (*sensu* Gottesman and Gould 2003) of a presumed behavioral dispersal syndrome, i.e., a suite of correlated behavioral characters that coevolve under natural conditions (Sih et al. 2004).

The highly significant within-individual correlation between agonistic onset and dispersal propensity (Rusu and Krackow 2005), and the indication of heritable variation for both traits (Krackow 2003, 2005), led us to assume genetic covariance between the traits not only under the experimental restrictions of the above experiment. In other words, the evidence supports the view that selection on dispersal propensity in male house mice would lead to a correlated response in agonistic onset timing. We, thus, attempted to identify covariation of marker polymorphisms with the timing of agonistic onset as an indicator of genetic dispersive behavioral syndrome variation. Because potent markers of genetic expression level variation are generally found near the respective structural genes (Cheung et al. 2005), we selected microsatellite markers near genes we suspected to potentially being involved in pathways related to ontogenetic agonistic development. The rationale was that regulation of gene products involved in physiological pathways affecting emotional state, stress (injury) response, steroid metabolism, social signalling, or neurological developmental processes might play a role for development of agonistic tendencies (see Table 1). Here, the most prominent candidate gene was Slc6a4, as variation in the aforementioned *SLC6A4* Rhesus macaque gene highly significantly covaried with ontogenetic timing of dispersal, although the causative promotor deletion itself is not present in house mice (Lesch et al. 1997).

Our aim was to identify microsatellite polymorphisms that covary with agonistic onset which we assert to represent a dispersal-related behavioral trait, to establish molecular tools for genetic variation of a behavioral syndrome in a mammal. Furthermore, although we cannot give any evidence on the causality of genetic effects, for heuristic purposes, we provide a short account of possible pathways that might have caused significant covariances with the plausible candidate genes used in our study.

Table 1 Microsatellite markers used, as well as acronyms and description of loci of colocalized genes of interest (cf. "Materials and methods")

Marker	Locus	Description	Rationale
D11Mit90	Slc6a4	Serotonin transporter	Emotional regulator
D8Mit15	Slc6a2	Noradrenalin transporter	Emotional regulator
D7Mit266	Abpa(g)	Androgen binding protein	Reactivity to testosterone level
D13Mit17	Akr1c6	Aldo-keto reductase *formerly*: hydroxysteroid dehydrogenase	Steroid metabolism
D13Mit231	Srd5a1	Steroid reductase	Steroid metabolism
D3Mit12	Hsd3b1(–4)	Hydroxysteroid dehydrogenases	Steroid metabolism
D5Mit122	Cyp3a11	Steroid inducible cytochrome P450 *formerly*: testosterone dehydrogenase	Steroid metabolism
D19Mit25	Adra2a	Adrenergic receptor	Stress response level
D5Mit24	Adrbk2	Adrenergic receptor kinase	Stress response modulation
D17Mit87	Ptprs	Protein tyrosine phosphatase receptor type S	Developmental regulator
D17Mit28	H2-K	Histocompatibility region K	MHC determination
D17Mit20	C3	Complement component 3	Injury response

The rationale for suspecting potential involvement of gene expression regulation in agonistic development determination is shortly indicated.

Materials and methods

Experimental animals were offspring from descendants of wild-caught house mice (*M. musculus domesticus*, 2n=24 chromosomes; for chromosomal variants in the house mouse, see Piálek et al. 2005). Animals were from four geographically separated Swiss lowland commensal populations in the Kanton of Zürich, northern Switzerland (villages Hinwil and Gähwil, town of Zürich: Irchel and Zürichberg). Mice were bred monogamously under standard laboratory conditions (perspex Macrolon cages of 26.5×42×15 cm; 12:12 h light/dark cycle with lights on at 0700 hours; 22±1°C; 50–60% relative humidity). Mating pairs were composed according to availability of potential mates in the breeding colony, where outbreeding was maximized and sib mating excluded. Pups were weaned at 21 days of age into fresh cages with same-sex littermates, except for experimental males that were transferred into fresh cages in fraternal pairs and left undisturbed until 61 days of age.

Males from 144 pairs of littermate brothers screened for agonism at 61 days of age in the course of another experiment (Rusu and Krackow 2005) were available for genetic typing. Fraternal pairs were categorized as either showing evidence of agonistic interactions at that age (agonistic pairs) or not (amicable pairs). Details of experimental determination of agonistic status are given in Rusu and Krackow (2005). In short, males were judged to have established agonistic relationships when exhibiting scarring of tail and/or back of body. Males not exhibiting clear signs of an established agonistic relationship were subjected to an aggression test. For that, brothers were separated into individual cages (22×36×15 cm) for at least half an hour, and subsequently, both cages were connected to a clean cage using Plexiglas tubes (4-cm diameter). Social behavior was recorded for 15 min after the first contact of individuals. Pairs qualified as agonistic when aggressive interactions occurred, and were otherwise considered amicable (non-agonistic).

Microsatellite markers

DNA was extracted postmortem from ear lobe cuts using the salt-chloroform method (Müllenbach et al. 1989). Fragments were amplified applying 7 min at 94°C, 31 cycles of 30 s at 94°C, 45 s at 58°C, 1 min at 72°C, 20 min at 72°C, with 20- to 100-ng DNA template, 1.5×GeneAmp polymerase chain reaction (PCR) Gold Buffer (Applied Biosystems), 2.5 mM MgCl (Applied Biosystems), 0.25 mM dNTPs, 2.0 U Amplitaq Gold polymerase (Applied Biosystems), and 0.4 mM of each primer. After amplification, we added 1.5 μl of PCR product to 9 μl of formamide and analyzed each probe on an ABI PRISM 310 genetic analyzer (ABI) with pop4™. Scores for alleles were compiled and analyzed with Genescan version 3.1 and Genotyper™ version 2.1 software (ABI) using the Southern method with standard ROX500. Altogether, 12 polymorphic microsatellite markers were typed, including D11Mit90 marking Slc6a4 (Table 1).

To possibly enhance the likelihood of markers to cosegregate with agonistic phenotype, markers were opportunistically selected for their proximity to genes that coded for a product suspected to be of potential significance for agonistic development (summarized in Table 1). Proximity was assumed when microsatellite markers were at the same genetic map position as candidate genes, using the Mouse Genome Informatics Database (http://www.informatics.jax.org) with a resolution of 1 cM. The assumption was that markers physically near to genes suspected to be potentially involved in relevant physiological effects for agonistic behavior would have elevated chances to cosegregate with such genes' expression regulators (cf. "Introduction"; Cheung et al. 2005).

Data analysis

To explore whether the presence of any allele per locus significantly coincided with agonistic phenotype shown by fraternal pairs, we first determined for each microsatellite marker the total number of alleles (alleles differ in length of PCR fragment in bp) found in all individuals. For each allele, we then created a variable containing the number of times that allele was present in each fraternal pair (values thus varied from 0 to 4). The effect of allele (or fragment) compositions of each marker on the occurrence of agonism within fraternal pairs was then determined using multiple logistic regressions, i.e., assuming binomial error distribution of the binary response (agonistic/amicable), and using a logit link function for maximum likelihood parameter estimation (proc logistic, SAS version 8). However, alleles that only occurred in maximally five, or were absent from five or fewer fraternal pairs, did prevent the algorithms from converging. Consequently, those fragments were not entered into the models. Loglikelihood-ratio test statistics are given for each marker when retaining all other alleles as independent variables (overall model), and for the final model from a stepwise logistic regression that eliminates statistically redundant independent variables (stepwise model, retention criterion $P<0.1$). Hence, based on our a priori hypotheses, this approach tests the effects of alleles at each of the 12 loci, and stepwise regression, using synchronous or type III modeling (Grafen and Hails 2002), identifies the statistically most likely effects in each model.

Alleles at separate loci might covary, e.g., due to epistasis. Hence, the set of retained independent variables

(i.e., alleles per microsatellite locus that significantly increased or decreased the occurrence of agonism) was entered into a multiple stepwise logistic regression model to identify significantly independently effective alleles. Our analysis, therefore, determines the statistically most likely microsatellite marker polymorphisms that covary with the phenotypic onset of agonistic behavior. It might be noted that statistical likelihood, in the face of obvious covariation, cannot ultimately rule out biological significance of nonsignificant allele effects. Hence, we also expose all significant allelic effects from the single locus analyses, in Table 2.

Taking into account the possibility that the effect of number of alleles present within fraternal pairs might not be linear, the whole analysis was repeated coding the occurrence per se (i.e., values were either 0 or 1 per fraternal pair, indicating that none of the two brothers had a copy of the specific allele, or any of them had at least one). Furthermore, to prevent spurious statistical correlations due to random between-population effects, we tested the final model using only data from the local population representing the largest proportion of fraternal pairs in our sample (56 pairs out of the 85 used in the complete analysis).

Results

Of the 144 fraternal pairs, 89 were classified as agonistic and 55 as amicable, at 61 days of age. For accidental reasons, genetic data were missing for one male each of four agonistic pairs that were, therefore, omitted from further statistical analysis. The distribution of alleles at 12 microsatellite markers in agonistic and amicable fraternal pairs is shown in Fig. 1.

Multiple logistic regression per microsatellite showed that allele frequency distributions of several microsatellites significantly covaried with agonistic phenotype (Table 2). Stepwise logistic regressions for each microsatellite's allele composition retained seven significant fragment length effects for six microsatellites (Table 2). Multiple stepwise logistic regressions using those seven alleles retained fragment 162 of microsatellite D11Mit90 ($\chi^2_1 = 5.81$, P=0.02) and, possibly, fragment 158 of microsatellite D5Mit122 ($\chi^2_1 = 3.28$, P=0.08). Hence, given these two covariates, no other allele significantly covaried with the probability of agonism in this final model (model likelihood ratio $\chi^2_2 = 11.66$, P=0.003). For both effects, the occurrence of agonism increased with an increasing number of copies being present in a fraternal pair (Fig. 2).

When using allele occurrences rather than frequencies per fraternal pair (see "Materials and methods"), our model revealed qualitatively identical results. Stepwise regression yielded significant covariation for five of the six loci identified in Table 2, with D19Mit25 being not significant, but with marker D3Mit12 showing up significant. The final model left the same two alleles significantly covarying with agonistic phenotype as in the model using allele frequencies per fraternal pair (model

Table 2 Exploration of marker polymorphism effects on agonistic phenotype

Marker	*N*	Overall model			Stepwise model			Alleles retained	
		χ^2	*df*	*P*<	χ^2	*df*	*P*<	Agonistic	Amicable
D3Mit12	8	5.42	6	0.49					
D5Mit24	8	3.93	5	0.56					
D5Mit122	7	9.53	6	0.15	5.84	1	0.02	158[a]	
D7Mit266	9	15.00	8	0.06	5.39	1	0.03	114	
D8Mit15	11	4.77	7	0.69					
D11Mit90	10	16.45	8	0.04	8.37	1	0.004	162[a]	
D13Mit17	6	5.43	5	0.37					
D13Mit231	8	12.34	7	0.09	6.58	1	0.02		112
D17Mit20	4	3.24	3	0.37					
D17Mit28	12	6.23	7	0.52					
D17Mit87	7	10.12	6	0.12	5.42	1	0.02	90	
D19Mit25	8	16.99	5	0.005	10.72	2	0.005		136, 152

Occurrence of agonism early in life (before 61 days of age) was logistically regressed for each microsatellite on the number of fragments of each length (alleles) per fraternal pair. The overall model contained variables for all alleles that occurred in at least five or were absent from maximally five fraternal pairs (*N* number of alleles in sample, *df*+ *1* number of alleles in model). The stepwise model retained only the highest scoring alleles with significant influence (see "Materials and methods"). Non-entries mean that there were no variables retained in the model. The direction of the effect of the frequency of occurrence of retained alleles is indicated in the rightmost columns, i.e., alleles appearing under "agonistic" imply that their frequency of occurrence increases the probability of fraternal pairs exhibiting agonism.

[a] Effects stayed significant after combining retained fragments per microsatellite into the final stepwise logistic regression model (cf. "Materials and methods"; exact *P* values in "Results").

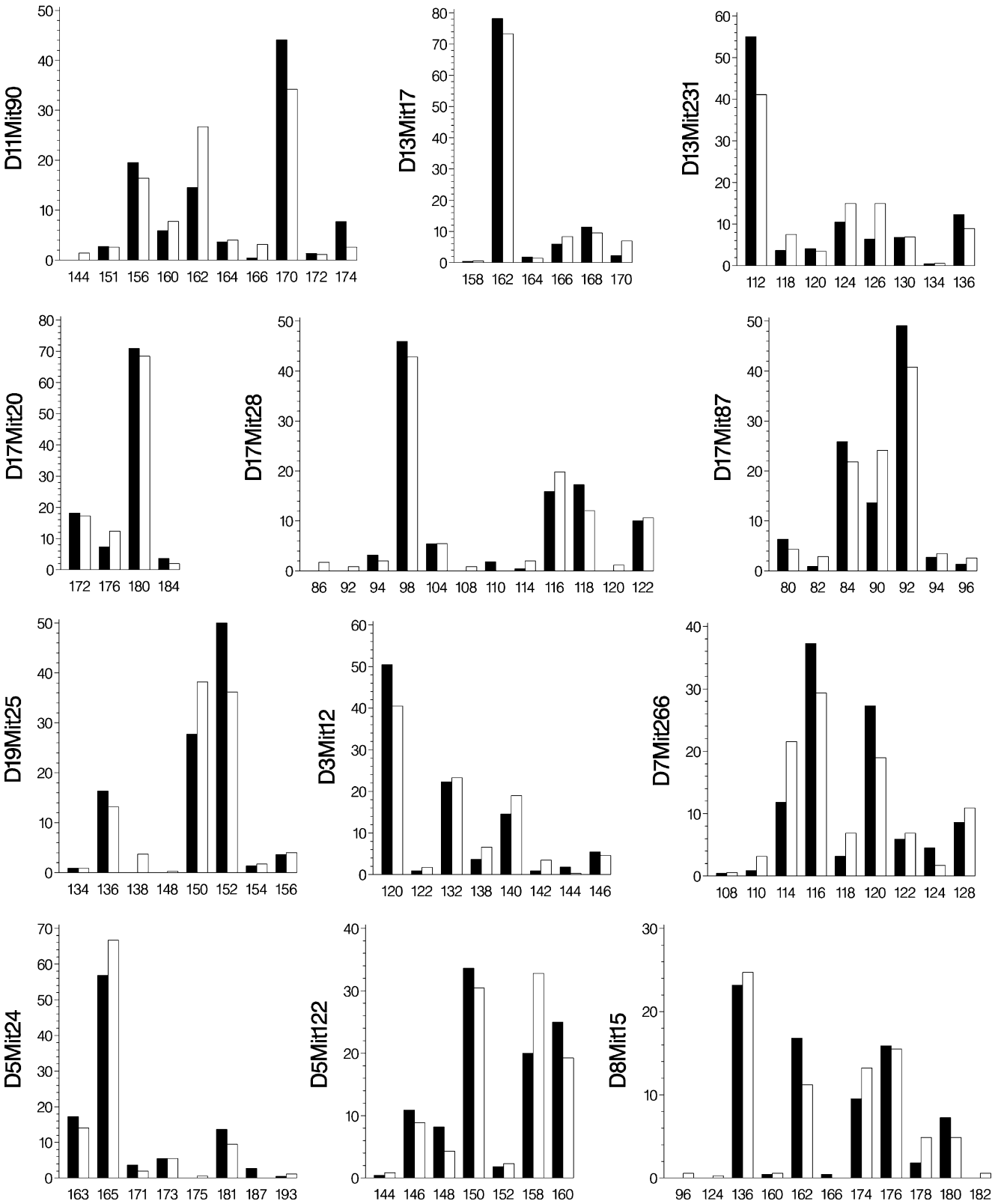

Fig. 1 Proportional distributions (group sums set to 100%) of microsatellite alleles (fragment lengths of PCR products) in agonistic (*open bars*) and amicable fraternal pairs (*solid bars*)

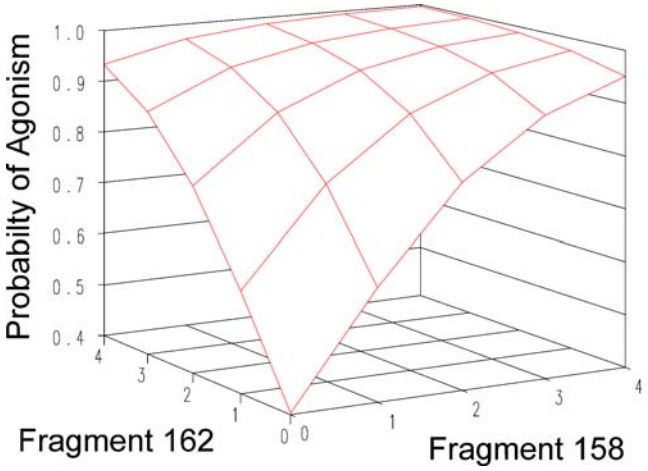

Fig. 2 Probability of agonistic relationships having been established in fraternal pairs before 61 days of age, as a function of the number of copies of allele 162 of marker D11Mit90 and allele 158 of marker D5Mit122, per fraternal pair

$\chi^2_2 = 11.46$, P=0.004; fragment 162: $\chi^2_1 = 4.35$, P=0.04; fragment 158: $\chi^2_1 = 5.42$, P=0.02).

In the 56 fraternal pairs representing the population contributing the highest proportion of fraternal pairs in our sample (Hinwil), the presence of alleles 162 and 158, respectively, equally significantly covaried with the occurrence of agonistic relationships as in the complete sample ($\chi^2_1 = 5.08$, P=0.025 and $\chi^2_1 = 5.92$, P=0.015, respectively).

As outlined in the "Materials and methods," alleles that were present in maximally five, or were absent from five or fewer fraternal pairs, were excluded from the above analyses. Hence, rare allele effects could not be determined. In addition, fragment 138 of microsatellite D19Mit25 had to be excluded from the group of regressor variables, as the analysis indicated "pseudoseparation of data." That was because all fragments of length 138 were found in ten agonistic pairs, this imbalance being of low probability itself (P<0.007; two-sided Fisher's exact probability).

Discussion

Our results indicate that the presence of at least two microsatellite alleles independently coincided with accelerated agonistic onset during ontogenetic development in wild house mouse males. Clearly, agonistic onset represents a complex social behavior that includes a strong phenotypic correlation with dispersal propensity under seminatural conditions (Rusu and Krackow 2005). Hence, the underlying genetic architecture might be complex as well, potentially involving any combination of pleiotropy, polygeny, and epistasis (Sinervo and Clobert 2003; Sih et al. 2004) and also epigenetic impacts (*sensu* Wolf et al. 2001). Nevertheless, other at first glance complex behavioral strategies have been found to exhibit straightforward additive genetic variance, as for example, migratory phenotype in the southern German blackcap (*Sylvia atricapilla*; Pulido et al. 2001), or reproductive strategies in side-blotched lizards (*Uta stansburiana*; Sinervo et al. 2001). In the ruff (*Phylomachus pugnax*), the differentiation into satellite or lekking males appears to depend on a single locus (Lank 1995). Thus, the microsatellite polymorphisms observed in our study might be indicative of a major gene effect of an allele segregating in natural populations.

Another possibility would be the involvement of regulatory genetic elements for which there is increasing molecular evidence. As outlined in the "Introduction," dispersal propensity in Rhesus macaques strongly covaries with a promotor polymorphism of a serotonin transporter protein gene *SLC6A4* (Trefilov et al. 2000). Given the strong phenotypic correlation between agonistic onset and dispersal propensity (Rusu and Krackow 2005), our finding of an increased probability of early agonism in the presence of fragment 162 of microsatellite D11Mit90, which marks the Slc6a4 locus, might imply that allelic variation at that locus leads to expression level differences that are effective in controlling the ontogenetic timing of agonism.

Fragment 158 of D5Mit122 also tended to be associated with increased male agonism. This microsatellite is located near a testosterone dehydrogenase gene (Cyp3a11; see Table 1). The effect exhibited by fragment 158 might therefore suggest potential involvement of the steroid regulatory pathways in control of the agonistic onset. This is of potential significance, as regulatory networks of the P450 subfamilies of genes, Cyp2b, Cyp2c, and Cyp3a, which are inducible by external stimuli, are known to be important for differential testosterone metabolism regulation in the rat brain (Rosenbrock et al. 1999). In house mice, testosterone levels determine the development of aggressivity phenotypes (Compaan et al. 1994).

Furthermore, in monogamous *Microtus ochrogaster*, as opposed to promiscuous vole species like *M. pennsylvanicus* and *M. montanus*, the vasopressin V1a receptor (V1aR) is expressed at higher levels in the ventral forebrain (Insel et al. 1994), which is causal for the difference in social behavior (Lim et al. 2004). Moreover, species expression level divergence appears to be caused by a microsatellite length difference (Hammock and Young 2004, 2005). This implies that expression differences result from conformational changes caused by the length of repetitive elements, as is well known from mini- and microsatellite effects in other contexts (Goldstein and Schlötterer 1999; Contente et al. 2002). Repeat length variation caused by slippage mutations cannot, therefore, be ruled out as a possible effect mediating the coincidence of microsatellite length polymorphism and agonistic onset variation in our study.

Our findings of microsatellite polymorphisms covarying with agonistic onset variation can obviously not differentiate between direct effects of fragment lengths, marking of genetic variation of regulatory elements, or major gene effects. In fact, recently accessible exact physical positions of house mouse genes (e.g., http://www.ensembl.org) locate D11Mit90 about 7 Mbp upstream of the Slc4a6 gene in a region without assigned functionality, and D5Mit122 about 5.35 Mbp upstream of the Cyp3a11 gene in a region assigned as an intron of a structural gene without currently known function. That renders direct involvement in a promotor sequence implausible, although not ruling out effects via some enhancer activity. However, the covariations found in our study open the potential for detailed characterization of the genetics of a complex social trait.

We consider agonistic onset as an endophenotype of a dispersive behavioral syndrome, as there is evidence that agonistic onset and dispersal propensity are heritable traits and exhibit strong within-individual correlation (see "Introduction"). Assuming that these covariations are not restricted to our populations of mice or our seminatural environmental condition, but apply to natural populations in general, our findings corroborate earlier hints at locally adapted dispersive syndrome phenotypes that are related to agonistic traits in male wild house mice (Corti and Rohlf 2001). Hence, the microsatellites analyzed might mark functional genetic variation of the dispersive behavioral syndrome in house mice.

Further investigation of this functional genetic variation could reveal how natural selection may shape genetic architectures to optimize the development of suites of correlated behavioral tendencies in respect to ecological variation (Wolf et al. 2001; Hovatta et al. 2005). Mammalian dispersal behavior variation is generally expected to represent plastic responses to environmental cues of relative costs and benefits of philopatry vs dispersal (Ims and Hjermann 2001; Pocock et al. 2005), rather than the consequence of heritable variation. Thus, the involvement of natural selection in locally adapting dispersal thresholds in response to spatial and temporal differences in dispersal risk in territorially structured house mouse meta-populations (*sensu* Corti and Rohlf 2001) is of particular behavioral ecological interest. Whether genetic variation of an average dispersal strategy with plastic variation will evolve in meta-populations depends, theoretically, on many population ecological details (Kisdi 2002; Parvinen et al. 2003). Such details are not yet known for any house mouse meta-population and are hard to get at (cf. Pocock et al. 2005) in the first place. The empirical decomposition of the genetic architecture involved would therefore be of utmost importance in resolving the issue of locally adapted dispersal phenotypes.

Our results, therefore, strongly encourage further investigation of the molecular genetics and ecology of the dispersive behavioral syndrome that is of fundamental relevance in mammalian life-history evolution.

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References

Bowler DE, Benton TG (2005) Causes and consequences of animal dispersal strategies: relating individual behaviour to spatial dynamics. Biol Rev 80:205–225

Cheung VG, Spielman RS, Ewen KG, Weber TM, Morley M, Burdick JT (2005) Mapping determinants of human gene expression by regional and genome-wide association. Nature 437:1365–1369

Clobert J, Danchin E, Dhondt AA, Nichols JD (2001) Dispersal. Oxford University Press, Oxford

Compaan JC, Hutchison JB, Wozniak A, Deruiter AJH, Koolhaas JM (1994) Brain aromatase activity and plasma testosterone levels are elevated in aggressive male mice during early ontogeny. Dev Brain Res 82:185–192

Contente A, Dittmer A, Koch MC, Roth J, Dobbelstein M (2002) A polymorphic microsatellite that mediates induction of PIG3 by p53. Nature Genet 30:315–320

Corti M, Rohlf FJ (2001) Chromosomal speciation and phenotypic evolution in the house mouse. Biol J Linn Soc 73:99–112

Gaines MS, McClenaghan LR (1980) Dispersal in mammals. Ann Rev Ecol Syst 11:163–169

Gerlach G (1996) Emigration mechanisms in feral house mice—a laboratory investigation of the influence of social structure, population density, and aggression. Behav Ecol Sociobiol 39:159–70

Goldstein DB, Schlötterer C (1999) Microsatellites. Evolution and applications. Oxford University Press, Oxford

Gottesman II, Gould TD (2003) The endophenotype concept in psychiatry: etymology and strategic intentions. Am J Psychiatry 160:636–645

Grafen A, Hails R (2002) Modern statistics for the life sciences. Oxford University Press, Oxford

Hammock EAD, Young LJ (2004) Functional microsatellite polymorphism associated with divergent social structure in vole species. Mol Biol Evol 21:1057–1063

Hammock EAD, Young LJ (2005) Microsatellite instability generates diversity in brain and sociobehavioral traits. Science 308:1630–1634

Hovatta I, Tennant RS, Helton R, Marr RA, Singer O, Redwine JM, Ellison JA, Schadt EE, Verma IM, Lockhart DJ, Barlow C (2005) Glyoxalase 1 and glutathione reductase 1 regulate anxiety in mice. Nature 438:662–666

Ims RA, Hjermann DØ (2001) Condition-dependent dispersal. Disperal. Oxford University Press, Oxford, pp 203–216

Insel TR, Wang ZX, Ferris CF (1994) Patterns of brain vasopressin receptor distribution associated with social organization in microtine rodents. J Neurosci 14:5381–5392

Kisdi É (2002) Dispersal: risk spreading versus local adaptation. Am Nat 159:579–596

Krackow S (2003) Motivational and heritable determinants of dispersal latency in wild male house mice (*Mus musculus musculus*). Ethology 109:671–689

Krackow S (2005) Agonistic onset during development differentiates wild house mouse males (Mus domesticus). Naturwissenschaften 92:78–81

Lank DB (1995) Genetic polymorphism for alternative mating behaviour in lekking male ruff, Phylomachus pugnax. Nature 378:59–62

Lesch KP, Meyer J, Glatz K, Flugge G, Hinney A, Hebebrand J, Klauck SM, Poustka A, Poustka F, Bengel D, Mossner R, Riederer P, Heils A (1997) The 5-HT transporter gene-linked polymorphic region (5-HTTLPR) in evolutionary perspective: alternative biallelic variation in rhesus monkeys. J Neural Transm 104:1259–1266

Lim MM, Wang Z, Olazábal DE, Ren X, Terwilliger EF, Young LJ (2004) Enhanced partner preference in a promiscuous species by manipulating the expression of a single gene. Nature 429:754–757

Müllenbach R, Lagoda PJL, Welter C (1989) An efficient salt-chlorophorm extraction of DNA from blood and tissues. Trends Genet 5:391

O'Riain MJ, Jarvis JUM, Faulkes CG (1996) A dispersive morph in the naked mole-rat. Nature 380:619–621

Parvinen K, Dieckmann U, Gyllenberg M, Metz JAJ (2003) Evolution of dispersal in metapopulations with local density dependence and demographic stochasticity. J Evol Biol 16:143–153

Piálek J, Hauffe HC, Searle JB (2005) Chromosomal variation in the house mouse. Biol J Linn Soc 84:535–563

Pocock MJO, Hauffe HC, Searle JB (2005) Dispersal in house mice. Biol J Linn Soc 84:565–583

Pulido F, Berthold P, Mohr G, Querner U (2001) Heritability of the timing of autumn migration in a natural bird population. Proc R Soc Lond B 268:953–959

Rifkin SA, Houle D, Kim J, White KP (2005) A mutation accumulation assay reveals a broad capacity for rapid evolution of gene expression. Nature 438:220–223

Rosenbrock H, Hagemeyer CE, Singec I, Knoth R, Volk B (1999) Testosterone metabolism in rat brain is differentially enhanced by phenytoin-inducible Cytochrome P450 isoforms. J Neurosci 11:597–604

Rusu AS, Krackow S (2005) Agonistic onset marks emotional changes and dispersal propensity in wild house mouse males (*Mus domesticus*). J Comp Psychol 119:58–66

Scantlebury M, Speakman JR, Oosthuizen MK, Roper TJ, Bennett NC (2006) Energetics reveals physiologically distinct castes in a eusocial mammal. Nature 440:795–797

Sih A, Bell AM, Johnson JC, Ziemba RE (2004) Behavioral syndromes: an integrative overview. Q Rev Biol 79:241–277

Sinervo B, Clobert J (2003) Morphs, dispersal behavior, genetic similarity, and the evolution of cooperation. Science 300: 1949–1951

Sinervo B, Bleay C, Adamopoulou C (2001) Social causes of correlational selection and the resolution of a heritable throat color polymorphism in a lizard. Evolution 55:2040–2052

Stenseth NC, Lidicker WZ (1992) Animal dispersal. Small mammals as a model. Chapman & Hall, London

Trefilov A, Berard J, Krawczak M, Schmidtke J (2000) Natal dispersal in rhesus macaques is related to serotonin transporter gene promoter variation. Behav Genet 30:295–301

Wolf JB, Frankino WA, Agrawal AF, Brodie ED, Moore AJ (2001) Developmental interactions and the constituents of quantitative variation. Evolution 55:232–245