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D2 antagonist during development decreases anxiety and infanticidal behavior in adult female prairie voles (*Microtus ochrogaster*)

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Abstract

On postnatal day eight, prairie vole pups were randomly assigned a treatment of 1 mg/kg SKF38393 (D1 agonist), quinpirole (D2 agonist), SCH23390 (D1 antagonist), eticlopride (D2 antagonist), or saline vehicle. As adults, females treated with eticlopride exhibited reduced anxiety-like behavior in an elevated plus maze and a reduction in infanticidal behavior. These behavioral effects were not seen in males. These data demonstrate that a single exposure to a D2 antagonist during development can have persistent, sex-specific effects on behavior into adulthood.

Keywords

prairie vole; anxiety; alloparenting; dopamine

Prairie voles (*Microtus ochrogaster*) are microtine rodents that are characterized by affiliative social behaviors including selective partner preferences, biparental care, and cooperative breeding [15]. The early endocrine and neuroendocrine environments play a critical role in the development of these species-specific behaviors. A number of hormones that play a key role in the expression of adult prairie vole social behavior have also been shown to play a developmental role as well (corticosterone: [30]; testosterone: [30]; oxytocin: [5–8,14,29] arginine vasopressin: [37]).

Recently dopamine has emerged as a key neurotransmitter in the regulation of prairie vole pair-bonding [3,4,17,23,39]. Prairie voles have been shown to be developmentally sensitive to early exposure to amphetamine, a dopamine reuptake inhibitor [28]. Daily administration of amphetamine over PND 13–15 changed social affiliation levels in adult prairie voles. Both male and female subjects given high doses of amphetamine spent more time alone than saline controls. However, low dose exposed animals showed sexually dimorphic responses to treatment when compared to controls: males spent more time alone, whereas females spent more time affiliating with the stranger. These data indicate that the developing

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dopaminergic system of the prairie vole is sensitive to neonatal manipulation in a potentially sexually dimorphic fashion, with persistent effects on social behavior into adulthood.

Acute (as opposed to chronic or repeated) neonatal treatments may also cause significant developmental changes in this species. For example, early treatments of oxytocin (OT), arginine vasopressin (AVP), and their antagonists have significant behavioral and physiological consequences in prairie voles. Treatment with OT at PND8 can at least partially ameliorate the effects of an OT antagonist (OTA) administered at PND1 and other forms of adverse early experience [9]Bales, unpublished data], suggesting that a single pharmacological manipulation on PND8 can have long-term effects in this species. The end of the first postnatal week is also a critical period for development of the dopamine system. The late neonatal period (in rats, PND5 to adult) is a period of rapid increase in both D1 and D2 receptor binding sites, in parallel with increasing dopaminergic innervation and maturation of dopaminergic neurons [20]. There is also a peak in striatal dopaminergic synaptic density around PND7 in rats [2].

We therefore hypothesized that alterations in dopamine receptor activity at PND8 may have potential long-term effects on behavior. Given that dopamine has been associated with anxiety-related behaviors and maternal behavior in a number of other previously studied species, we also hypothesized that behavior in an elevated plus maze and alloparental responsiveness in prairie voles are influenced by dopaminergic activity. This study was designed to examine the developmental consequences of a single pharmacological intervention on the later expression of behavior in an elevated plus maze and alloparental care test.

Subjects were male and female prairie voles bred in our laboratory at University of California, Davis, from an outbred stock originally captured in Illinois. Animals were maintained until a 14:10-hr light-dark cycle and controlled temperature. Purina high-fiber rabbit diet and water were available *ad libitum*. Breeding pairs were monitored daily, and within 24h of litter birth, all pups were sexed and toe-clipped for identification. At 8 days of age, each pup was randomly assigned one of the following treatments: saline (vehicle control), 1 mg/kg SKF38393 (D1 agonist), quinpirole (D2 agonist), SCH23390 (D1 antagonist), and eticlopride (D2 antagonist) in 25 μ l volume. Quinpirole, SKF38393, and SCH23390 have been previously used in rodent neonatal studies at this dosage (quinpirole: [12,13,21]; SKF38393: [25]; SCH23390: [35]). As eticlopride has not been used neonatally before in rodents, our initial dosage was chosen to match the other treatments. These compounds all cross the blood-brain barrier and have behavioral effects on adult prairie voles [4,39]. Treatment was administered i.p. with a gas-tight Hamilton syringe. At PND21, subjects were weaned and housed in same sex pairs in standard mouse cages (27cm $\times$ 16cm $\times$ 13 cm). All subjects were weaned before the birth of the next litter, and were therefore pup naïve. Sample sizes for each behavioral test varied by sex and treatment, and are presented in Figures 1 and 2.

At 60–75 days of age, subjects were tested on the elevated plus maze (EPM). The EPM is elevated 18 inches off the ground and consists of two high-walled enclosed arms and two clear, open Plexiglas arms (67cm long $\times$ 5.5 cm wide [18]). The animal was placed in the maze for five minutes and scored continuously for location and autogrooming using Behavior Tracker 1.5 software (<http://www.behaviortracker.com>). If subjects fell off the apparatus, then recording was paused, the animal retrieved, and placed in the middle of the maze and recording resumed. Testing was stopped if animals jumped or fell from the apparatus three times, and these subjects were excluded from analysis. Of 114 subjects tested, 8 were excluded for repeated jumping, which showed no differences based on treatment ($\chi^2=3.9250$, $p=0.42$). All testing was performed between 900 and 1200h.

Frequency of arm entries, duration of autogrooming, and the time spent in the open arm proportionate to either arm [defined as (time in open arm) / (time in open arm + time in closed arm)] were examined with mixed model ANOVA with treatment, sex, and a sex*treatment interaction as fixed factors, and a random effect of litter, followed by Dunnett's post hoc tests. Residuals were checked for normality, and when necessary, data were transformed using the square root or quad root transformation. When used, transformations are reported with the results. When transformation was not successful, each sex was compared separately using nonparametric tests (Kruskal-Wallis test). All tests were two-tailed and significance was set at $p < 0.05$. Data were analyzed in SAS 9.1 (SAS Institute, Cary, NC).

The day after EPM testing, all subjects were given an alloparental care test, in which they were exposed to a novel pup [8,30]. All tests were performed between 800 and 1200h. The test is performed in an apparatus consisting of two standard mouse cages joined by a transparent tube (10cm in length). Subjects are placed alone in the testing apparatus for 45 minutes to habituate. At the end of the habituation period, the subject was briefly removed from the apparatus, and unrelated vole pup of 1–4 days of age was placed in the front cage. The subject was then returned to the connector tube, facing the pup. The test was recorded on videotape for ten minutes and stopped immediately if aggressive behavior toward the pup was observed. Behaviors scored using Behavior Tracker included sniffing, licking, and huddling over the pup, as well as autogrooming and pup attacks. Latencies for behaviors not displayed were set to 600s. Chi-square tests were run separately for males and females on frequency of attacks per treatment group. Only non-attacking animals were included for analyses of all other alloparental behaviors. Behaviors were examined with mixed model ANOVA or Kruskal-Wallis tests, as described for EPMs.

We found no treatment differences in frequency of arm entries ($H=4.7465$, $df=4$, $p=0.34$) or autogrooming ($H=8.1319$, $df=4$, $p=0.09$) in the EPM. Mixed model ANOVA for the ratio of time spent in the open arm over time spent in both arms revealed no main effects of treatment ($F_{40,65}=1.89$, $p=0.12$) or sex ($F_{40,65}=0.00$, $p=0.98$), however there was a significant treatment by sex interaction ($F_{40,65}=2.73$, $p=0.036$). Post-hoc analyses indicated that females treated with eticlopride spent significantly more time in the open arm than saline control females ($p=0.0068$; Figure 1). There were no treatment differences from saline among males in relative EPM arm time.

For the alloparental care test, the total number of subjects and attacking subjects are presented in Figure 1. Among non-attacking subjects, there were no significant effects of any treatment on individual behaviors during the alloparental care test. For time spent autogrooming (quad root transformed), mixed model ANOVA revealed no main effects of treatment ($F_{39,58}=1.00$, $p=0.42$) or sex ($F_{39,58}=1.31$, $p=0.26$). While there was a significant sex by treatment interaction on autogrooming ($F=2.69$, $p=0.04$), interpretation is difficult due to the fact that none of the within sex comparisons to controls were significant (data presented in Table 1). There were no differences in time spent sniffing the pup ($H=5.028$, $df=4$, $p=0.28$), non-huddling contact [$F(39,48)=1.48$, $p=0.87$], or huddling ($H=3.928$, $df=4$, $p=0.42$). There was a significant main effect of sex on time spent licking the pup (square root transformed; $F_{39,58}=6.29$, $p=0.015$), with males grooming the pups on average more than females (228 ± 13.71 sec compared to 185.72 ± 18.21 sec, respectively).

Chi-square tests of the proportion of attacking individuals for each treatment group to saline controls were non-significant for males (eticlopride: $\chi^2=0.05$, $p=1.00$; quinpirole: $\chi^2=0.94$, $p=0.37$; SCH23390: $\chi^2=1.62$, $p=0.49$, $\chi^2=1.35$, $p=0.51$). Chi-square comparisons of attacking females to saline controls were significant for eticlopride ($\chi^2=5.865$, $p=0.037$; Figure 2), but no other treatments (quinpirole: $\chi^2=1.49$, $p=0.37$; SCH23390: $\chi^2=0.53$,

$p=0.67$; SKF38393: $\chi^2=1.18$, $p=0.38$). Five out of 13 control females displayed infanticidal behavior, whereas none of the 11 eticlopride treated animals attacked the stimulus pup.

Taken together, these results suggest that a single manipulation of dopamine receptor activity during the late neonatal period can have long-term effects on prairie vole behavior, and that these effects can be sex-specific. Females treated neonatally with the D2-receptor antagonist eticlopride exhibited reduced anxiety-like behavior as indicated by proportionally more time spent in the open arms of an EPM (Figure 1). These same females were also less infanticidal, as none attacked pups in an alloparental care test (Figure 2), compared to a 38% attack rate in control females. However, these females did not differ from the non-attacking controls on any individual alloparenting behaviors.

Our finding that eticlopride increases open arm exploration in the EPM is similar to previous work showing that acute treatment with sulpiride, another D2 antagonist, also reduces anxiety-like behavior in the EPM in mice [31,38]. However, these studies only tested male subjects. Our present findings of changes in females rather than males suggest that there may be sex-differences in dopaminergic regulation of anxiety-related behaviors, and also suggest that these sex differences could be species-specific.

Our data are also consistent with previous studies that have found that measures of anxiety are negatively correlated with maternal behavior in rats. Olazabal and Young [26] found that alloparental responsiveness in female prairie voles is negatively correlated with anxiety-like behaviors, including performance on the elevated plus maze. Specifically, infanticidal behavior was positively correlated with anxiety-like behavior in the elevated plus maze. One interpretation of our findings is that neonatal eticlopride is associated with reduced anxiety in adult females, leading to more exploration in the elevated plus maze and the elimination of infanticidal behavior.

The effects of early dopamine manipulations have been studied in a number of animal models, although the majority of these studies involve chronic treatments in older (i.e. juvenile rather than infant) animals [13,16,21,41]. A prominent model explored in this literature examines treatments of young rats with chronic neonatal quinpirole (a D2-like receptor agonist), resulting in a supersensitization of D2-like receptors and enduring cognitive, motor, and neurochemical abnormalities that persist through adulthood [11–13]. The critical period for these effects occurs between postnatal days (PND) 1 and 11, suggesting that early postnatal development of dopaminergic circuits is sensitive to pharmacological interventions.

We hypothesize that the behavioral effects discussed may be explained by alterations in brain DA receptors, specifically in the striatum. The nucleus accumbens has been identified as a key region for D2 receptor regulation of social behavior in adult prairie voles [17,23]. Eticlopride primarily binds in the rat striatum [24], and the striatum undergoes a significant amount of development during the late neonatal period including a number of alterations in both morphology and density of dopaminergic synapses, with a peak of dopaminergic synaptic density in the striatum at the end of the first postnatal week [2]. It is possible that during this period of intense organization that the striatum is particularly sensitive to pharmacological manipulations.

Chronic treatment with the D2 antagonist spiroperidol from birth to PND32 led to a decrease in D2 receptors in rats, with only a small decrease in D1 receptors [22]. It is possible that our single treatment with a D2 antagonist may also have led to a down regulation of D2 receptors, although it is important to consider that chronic treatments may have different and even opposite effects compared to acute exposure. There are a number of alternative possibilities worth considering. Developmental manipulation of a specific neurotransmitter

system may instead have effects on other, related systems. For example, early exposure to either OT or OTA on the first day of birth can cause sexually dimorphic and site-specific changes in OT- and AVP-immunoreactivity [40] and AVP V1a (but not OT) receptor distribution [7] that persist into adulthood. Additionally, chronic neonatal treatment with the D2 agonist quinpirole affects nerve growth factor and baseline corticosterone levels in rats [11].

The present study demonstrates that a single exposure to a D2 antagonist during development can have persistent effects on social and anxiety behavior into adulthood in the prairie vole. We hypothesize that these behavioral effects may be mediated by a decrease in D2 receptors. However, this conflicts with data in humans showing that patients with generalized social anxiety disorder have lower striatal D2 receptor density [33,34] (although these results are not always replicated [32]). The present findings may be of clinical interest as prescription use of antipsychotics (which act as D2 antagonists) in young patients is rapidly rising [10,27,36], and there is a clinical need for studies on the developmental consequences of these drugs [19]. Non-prescription use of anti-psychotics by children also poses a risk, and often case studies are not followed up for long-term effects [1]. Future research should focus on developmental consequences of these particular drugs on prairie vole social behaviors.

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References

1. Antia SX, Sholevar EH, Baron DA. Overdoses and ingestions of second-generation antipsychotics in children and adolescents. *J Child Adolesc Psychopharmacol*. 2005; 15:970–85. [PubMed: 16379518]
2. Antonopoulos J, Dori I, Dinopoulos A, Chiotelli M, Parnavelas JG. Postnatal development of the dopaminergic system of the striatum in the rat. *Neuroscience*. 2002; 110:245–56. [PubMed: 11958867]
3. Aragona BJ, Liu Y, Curtis T, Stephan FK, Wang ZX. A critical role for nucleus accumbens dopamine in partner-preference formation in male prairie voles. *J Neurosci*. 2003; 23:3483–90. [PubMed: 12716957]
4. Aragona BJ, Liu Y, Yu YJ, Curtis JT, Detwiler JM, Insel TR, Wang ZX. Nucleus accumbens dopamine differentially mediates the formation and maintenance of monogamous pair bonds. *Nat Neurosci*. 2006; 9:133–9. [PubMed: 16327783]
5. Bales KL, Carter CS. Sex differences and developmental effects of oxytocin on aggression and social behavior in prairie voles (*Microtus ochrogaster*). *Horm Behav*. 2003; 44:178–84. [PubMed: 14609540]
6. Bales KL, Carter CS. Developmental exposure to oxytocin facilitates partner preferences in male prairie voles (*Microtus ochrogaster*). *Behav Neurosci*. 2003; 117:854–9. [PubMed: 12931969]
7. Bales KL, Plotsky PM, Young LJ, Lim MM, Grotte ND, Ferrer E, Carter CS. Neonatal oxytocin manipulations have long-lasting, sexually dimorphic effects on vasopressin receptors. *Neuroscience*. 2007; 144:38–45. [PubMed: 17055176]
8. Bales KL, van Westerhuyzen JA, Lewis-Reese AD, Grotte ND, Lanter JA, Carter CS. Oxytocin has dose-dependent developmental effects on pair-bonding and alloparental care in female prairie voles. *Horm Behav*. 2007; 52:274–9. [PubMed: 17553502]
9. Boone, EM.; Sanzenbacher, LL.; Stanfill, SD.; Bales, KL.; Carter, CS. Oxytocin injections in early life reversed negative behavioral effects of repeated handling. Program No.468.12.2009 Neuroscience Meeting Planner; Chicago, IL: Society for Neuroscience; 2009.

10. Brambilla F, Garcia CS, Fassino S, Daga GA, Favaro A, Santonastaso P, Ramaciotti C, Bondi E, Mellado C, Borriello R, Monteleone P. Olanzapine therapy in anorexia nervosa: psychobiological effects. *Int Clin Psychopharmacol.* 2007; 22:197–204. [PubMed: 17519642]
11. Brown RW, Flanigan TJ, Thompson KN, Thacker SK, Schaefer TL, Williams MT. Neonatal quinpirole treatment impairs Morris water task performance in early postweanling rats: relationship to increases in corticosterone and decreases in neurotrophic factors. *Biol Psychiatry.* 2004; 56:161–8. [PubMed: 15271584]
12. Brown RW, Gass JT, Kostrzewa RM. Ontogenetic quinpirole treatments produce spatial memory deficits and enhance skilled reaching in adult rats. *Pharmacol Biochem Behav.* 2002; 72:591–600. [PubMed: 12175456]
13. Brown RW, Thompson KN, Click IA, Best RA, Thacker SK, Perna MK. The effects of eticlopride on Morris water task performance in male and female rats neonatally treated with quinpirole. *Psychopharmacology (Berl).* 2005; 180:234–40. [PubMed: 15696328]
14. Carter CS. Developmental consequences of oxytocin. *Physiol Behav.* 2003; 79:383–97. [PubMed: 12954433]
15. Carter CS, Getz LL. Monogamy and the prairie vole. *Sci Am.* 1993; 268:100–6. [PubMed: 8516669]
16. Chase TD, Carrey N, Brown RE, Wilkinson M. Methylphenidate differentially regulates c-fos and fosB expression in the developing rat striatum. *Brain Res Dev Brain Res.* 2005; 157:181–91.
17. Gingrich B, Liu Y, Cascio C, Wang ZX, Insel TR. Dopamine D2 receptors in the nucleus accumbens are important for social attachment in female prairie voles (*Microtus ochrogaster*). *Behav Neurosci.* 2000; 114:173–83. [PubMed: 10718272]
18. Insel TR, Preston S, Winslow JT. Mating in the monogamous male: Behavioral consequences. *Physiol Behav.* 1995; 615–27. [PubMed: 7777594]
19. Jensen PS, Buitelaar J, Pandina GJ, Binder C, Haas M. Management of psychiatric disorders in children and adolescents with atypical antipsychotics: a systematic review of published clinical trials. *Eur Child Adolesc Psychiatry.* 2007; 16:104–20. [PubMed: 17075688]
20. Jung AB, Bennett JP Jr. Development of striatal dopaminergic function. I. Pre- and postnatal development of mRNAs and binding sites for striatal D1 (D1a) and D2 (D2a) receptors. *Brain Res Dev Brain Res.* 1996; 94:109–20.
21. Kostrzewa RM. Dopamine receptor supersensitivity. *Neurosci Biobehav Rev.* 1995; 19:1–17. [PubMed: 7770190]
22. Kostrzewa RM, Saleh MI. Impaired ontogeny of striatal dopamine D1 and D2 binding sites after postnatal treatment of rats with SCH-23390 and spiroperidol. *Brain Res Dev Brain Res.* 1989; 45:95–101.
23. Liu Y, Wang ZX. Nucleus accumbens oxytocin and dopamine interact to regulate pair bond formation in female prairie voles. *Neuroscience.* 2003; 121:537–44. [PubMed: 14568015]
24. Martelle JL, Nader MA. A review of the discovery, pharmacological characterization, and behavioral effects of the dopamine D2-like receptor antagonist eticlopride. *CNS Neurosci Ther.* 2008; 14:248–62. [PubMed: 18801115]
25. Moody CA, Spear LP. Ontogenetic differences in the psychopharmacological responses to separate and combined stimulation of D1 and D2 dopamine receptors during the neonatal to weanling age period. *Psychopharmacology (Berl).* 1992; 106:161–8. [PubMed: 1347951]
26. Olazabal DE, Young LJ. Variability in “spontaneous” maternal behavior is associated with anxiety-like behavior and affiliation in naive juvenile and adult female prairie voles (*Microtus ochrogaster*). *Dev Psychobiol.* 2005; 47:166–78. [PubMed: 16136562]
27. Olfson M, Blanco C, Liu L, Moreno C, Laje G. National trends in the outpatient treatment of children and adolescents with antipsychotic drugs. *Arch Gen Psychiatry.* 2006; 63:679–85. [PubMed: 16754841]
28. Olivera, A. Honors Thesis. Florida State University; 2006.
29. Pfeifer L, Bales KL, Carter CS. Neonatal administration of oxytocin affects alloparental behavior in male prairie voles. *Horm Behav.* 2001; 40:344.
30. Roberts RL, Zullo AS, Carter CS. Perinatal steroid treatments alter alloparental and affiliative behavior in prairie voles. *Horm Behav.* 1996; 30:576–82. [PubMed: 9047281]

31. Rodgers RJ, Nikulina EM, Cole JC. Dopamine D1 and D2 receptor ligands modulate the behaviour of mice in the elevated plus-maze. *Pharmacol Biochem Behav.* 1994; 49:985–95. [PubMed: 7886117]
32. Schneier FR, bi-Dargham A, Martinez D, Slifstein M, Hwang DR, Liebowitz MR, Laruelle M. Dopamine transporters, D2 receptors, and dopamine release in generalized social anxiety disorder. *Depress Anxiety.* 2009; 26:411–8. [PubMed: 19180583]
33. Schneier FR, Liebowitz MR, bi-Dargham A, Zea-Ponce Y, Lin SH, Laruelle M. Low dopamine D(2) receptor binding potential in social phobia. *Am J Psychiatry.* 2000; 157:457–9. [PubMed: 10698826]
34. Schneier FR, Martinez D, bi-Dargham A, Zea-Ponce Y, Simpson HB, Liebowitz MR, Laruelle M. Striatal dopamine D(2) receptor availability in OCD with and without comorbid social anxiety disorder: preliminary findings. *Depress Anxiety.* 2008; 25:1–7. [PubMed: 17252580]
35. Sickles AE, Stehouwer DJ, Van HC. Dopamine D1 and D2 antagonists block L-dopa-elicited air-stepping in neonatal rats. *Brain Res Dev Brain Res.* 1992; 68:17–22.
36. Spettigue W, Buchholz A, Henderson K, Feder S, Moher D, Kourad K, Gaboury I, Norris M, Ledoux S. Evaluation of the efficacy and safety of olanzapine as an adjunctive treatment for anorexia nervosa in adolescent females: a randomized, double-blind, placebo-controlled trial. *BMC Pediatr.* 2008; 8:4. [PubMed: 18234120]
37. Stribley JM, Carter CS. Developmental exposure to vasopressin increases aggression in adult prairie voles. *Proc Natl Acad Sci USA.* 1999; 96:12601–4. [PubMed: 10535968]
38. Wall PM, Blanchard RJ, Yang M, Blanchard DC. Infralimbic D2 receptor influences on anxiety-like behavior and active memory/attention in CD-1 mice. *Prog Neuropsychopharmacol Biol Psychiatry.* 2003; 27:395–410. [PubMed: 12691774]
39. Wang Z, Yu G, Cascio C, Lui Y, Gingrich B, Insel TR. Dopamine D2 receptor-mediated regulation of partner preferences in female prairie voles (*Microtus ochrogaster*): a mechanism for pair bonding? *Behav Neurosci.* 1999:602–11. [PubMed: 10443786]
40. Yamamoto Y, Cushing BS, Kramer KM, Epperson PD, Hoffman GE, Carter CS. Neonatal manipulations of oxytocin alter expression of oxytocin and vasopressin immunoreactive cells in the paraventricular nucleus of the hypothalamus in a gender specific manner. *Neuroscience.* 2004; 125:947–55. [PubMed: 15120854]
41. Yoshida ST, Baella SA, Stuebner NM, Crawford CA, McDougall SA. Effects of a partial D2-like receptor agonist on striatal dopamine autoreceptor functioning in preweanling rats. *Brain Res.* 2006; 1073–1074:269–275.

Figure 1.

Proportion of time spent in either plus maze arms, defined as $[(\text{time in open arm})/(\text{time in open arm} + \text{time in closed arm})]$, for each female (A) and male (B) subjects. Sample sizes are presented in parentheses. * Indicates statistically significant differences compared to saline controls.

Figure 2. Attacking and non-attacking female (A) and male (B) subjects in the alloparental care test. Eticlopride treated females attack less than saline control females ($\chi^2=5.85$, $*p=0.037$).

Table 1

Time in seconds spent autogrooming in the alloparental care test by sex and treatment (Means $\pm$ standard error).

Seconds spent autogrooming in the alloparental care test					
	Saline	Eticlopride	Quinpirole	SCH23390	SKF38393
Males	36.5 ± 14.1	15.09 ± 4.5	35.0 ± 11.7	21.7 ± 6.0	21.5 ± 8.4
Females	11.9 ± 5.0	25.1 ± 5.1	38.4 ± 24.1	45.2 ± 17.2	9.8 ± 3.0