Behavioral Evaluation of the Stargazer Mutant Rat in a Tactile Startle Paradigm

The stargazer rat displays abnormal behavior characterized by pronounced arching of the neck, head tics, and hyperactivity. Thus, stargazer rats may provide a behavioral model of Tourette syndrome (TS). The responsiveness of these rats to tactile startle stimuli was examined. Littermate controls showed significant prepulse inhibition and habituation over repeated startle sessions. Stargazer rats did not exhibit startle responses, even under conditions of haloperidol-induced reduction of abnormal behavior. These data disagree with the hypothesis that stargazer rats would have increased responsiveness to startle stimuli due to their hyperactive dopamine systems. However, the reduction of head tics by haloperidol suggests stargazer rats are a model of TS. Thus, the mechanisms by which dopaminergic hyperactivity enhances either head tics or startle responsiveness appear distinct.

The DSM-IV (American Psychiatric Association, 1994) characterizes Tourette’s disorder (commonly known as Tourette syndrome; TS) as recurrent, involuntary, repetitive, rapid movements (tics) that include multiple vocal tics. TS was once considered to be a rare illness, with poor prognosis and intellectual and psychological deterioration. During the last 15 years the marked increase in basic research on and clinical knowledge of TS resulted in large part because of the increased public awareness of TS through the well-funded Tourette Syndrome Association, as well as public service announcements from that same association. Recent findings in the areas of pharmacological treatment and biochemical, genetic, neurological, and psychological studies have advanced our understanding of TS (Brunn & Budman, 1992; Jankovic, 1992; A. K. Shapiro, E. S. Shapiro, Young, & Feinberg, 1988; E. S. Shapiro & A. K. Shapiro, 1986). It is commonly believed the tic disorders, transient tics of childhood, chronic multiple motor tics, and TS represent a continuum, with transient tics of childhood being the least severe condition and TS being the most severe. The classification of these disorders is based on the age of onset, symptomatology, and clinical course (E. S. Shapiro & A. K. Shapiro, 1986).

The intensity, frequency, and location of these symptoms can vary over weeks or months. The tics experienced occur especially with the head and face, although other body parts, such as the lower and upper limbs and the torso, may experience tics as well. The vocal tics include clicks, grunts, yelps, barks, sniffs, coughs, and words. Coprolalia, the irresistible urge to utter obscenities, occurs in about 30% of the cases. Other associated features include echokinesis (the imitation of others’ movements), palilalia (the repetition of one’s own last words or phrases), men-
Behavorial Evaluation of the Stargazer Rat

Kazlauskas and Kelland

Psi Chi Journal of Undergraduate Research Fall 1997 91

tal coprolalia, obsessive thoughts of doubting, and compulsive impulses to touch something or to perform complicated movements (Jankovic, 1992; A. K. Shapiro et al., 1988; E. S. Shapiro & A. K. Shapiro, 1986). The symptoms are sudden, abrupt, and explosive. The movements may be simple, such as an eye blink, or as complex as jumping up and down (E. S. Shapiro & A. K. Shapiro, 1986). The age of onset is between 2 and 15 years, and it is three times more common in boys than girls. Its course is usually lifelong, although the patient may have brief periods of remission. There are no known predisposing factors for this disorder, and it has been shown to be unrelated to social class or history of other mental disorders in the family or individual (American Psychiatric Association, 1994).

There is strong evidence that environmental stimuli affect the presence of TS symptoms. The symptoms significantly increase under stress, with either anxiety or pleasurable anticipation, and with the family. They have been known to decrease significantly while sleeping, in the presence of strangers (including doctors, which often creates a problem for diagnosis), while repairing an object, during nonanxious absorption in a task, and when at school or at work (A. K. Shapiro et al., 1988). The symptoms of TS can be voluntarily suppressed for a few minutes to an hour at a time, but are then typically followed by a rebound in symptomatology.

The symptoms of TS can be successfully managed in many patients with medication. Beginning in the 1960s, haloperidol was the drug of choice for treating TS patients, and it has been found to be quite effective at low doses. However, many patients discontinue the use of the drug because of its many side effects, including akathisia, akinesia, developing phobias, becoming irritable and fearful, cognitive impairment, dysphoric symptoms, and tardive dyskinesia. These side effects intervene to limit the drug's usefulness (A. K. Shapiro et al., 1988; E. S. Shapiro & A. K. Shapiro, 1986). Another drug that appears to be at least as effective as haloperidol is pimozide. The major side effects are similar to those seen with haloperidol, but the drug is less sedating. The mode of action for these drugs appears to be preferential inhibition of postsynaptic dopamine (DA) receptors (Erenberg, 1992; A. K. Shapiro et al., 1988). Another drug that has been used in the treatment of TS is clonidine (an alpha-2-adrenergic agonist). This drug not only reduces the simple motor and phonic tics, but it has also been useful in improving attentional problems and ameliorating complex motor and phonic symptoms. The major side effect found with the use of clonidine is sedation (LeWitt, 1992; A. K. Shapiro et al., 1988).

Presently, the etiology for TS has not been identified. Preliminary evidence suggests the site of the disturbance may be the basal ganglia (E. S. Shapiro & A. K. Shapiro, 1986). The basal ganglia are a site of DA transmission, and DA antagonists are the drugs of choice for treating TS. By examining the regions of the brain where there may be increased dopaminergic activity, the specific pathways involved in TS might be identified. One line of research has investigated the role of the pedunculopontine tegmental nucleus (PPN) and its effect on increased dopaminergic activity. M. D. Kelland and colleagues (M. D. Kelland, Chiodo, & Freeman, 1990; M. D. Kelland, Freeman, Rubin, & Chiodo, 1993) have confirmed that electrical stimulation of the PPN excites nigrostriatal DA neurons (see also Scarnati, Campana, & Pacitti, 1984; Scarnati, Proia, Campana, & Pacitti, 1986), and have demonstrated that PPN stimulation excites mesoaccumbens DA neurons in a similar fashion (M. D. Kelland et al., 1990; M. D. Kelland et al., 1993). These studies provided evidence for both monosynaptic and polysynaptic excitatory inputs. Thus, it seems clear that increased dopaminergic activity resulting from increased PPN activity could be involved in the development of TS.

One problem with the above-mentioned studies, however, is that they were conducted on normal rats. An animal model of TS is needed that would allow for an examination of the role of the PPN and other theories regarding the cause of TS. A new mutant rat called the stargazer has been derived from the Zucker strain (homozgous stg/stg). These rats display abnormal behavior characterized by pronounced arching of the neck ("stargazing") and head ticks, rapid circling, and conspicuous hyperactivity (Brock & Ashby, 1996; Brock, Truett, Ross, & Kloster, 1995; Truett, Brock, Lidl, & Kloster, 1994). Preliminary tests have concluded stargazer rats possess a genetically mediated dysfunction of their central dopaminergic system, which links their abnormal behavior to an overstimulation of the dopaminergic system. Therefore these rats may be a suitable animal model for TS. Their heterozygous stg/+ littermates display normal spontaneous behaviors and provide an ideal control group (Brock & Ashby, 1996; Brock et al., 1995; Truett et al., 1994).

Because stargazer rats demonstrate abnormal behavior related to a hypothesized dopaminergic hyperactivity, we have chosen to examine the behavior of these rats in a behavioral model known to be sensitive to the level of dopaminergic activity in the brain: responsiveness to acoustic startle reflex paradigms (Bolino et al., 1992; Davis et al., 1990; Geyer, Swerdlow, Mansbach, & Braff, 1990; Mansbach, Geyer,
& Braff, 1988; Swerdlow, Braff, & Geyer, 1990; Swerdlow, Braff, Masten, & Geyer, 1990; Swerdlow, Koob, Geyer, Mansbach, & Braff, 1988; Swerdlow, Mansbach, et al., 1990; Young, Randall, & Wilcox, 1991). However, because stargazer rats are deaf (Brock & Ashby, 1996; Brock et al., 1995; Truett et al., 1994), we utilize tactile startle pulses rather than acoustic startle stimuli. Because this paradigm addresses the sensory responsiveness of stargazer rats to external (tactile) stimuli, it may be directly related to the well-established observation that environmental stimuli have an influence on the symptoms of TS patients.

The specific purpose of the present study is to address whether the hyperdopaminergic nature of stargazer rats manifests itself in startle reflex paradigms in a predictable way. Specifically, compounds which increase dopamine levels in rats increase responsiveness to startle pulses and interfere with habituation to repeatedly presented startle stimuli; these phenomena have been suggested as a model of schizophrenia (Geyer et al., 1990; Swerdlow et al., 1988). However, the stargazer rat has been proposed as a model of TS, not schizophrenia, and TS does not involve any psychotic symptoms. Thus, we hypothesize that the stargazer rat will demonstrate normal responses to tactile startle pulses and subsequent habituation to repeated administration of startle pulses.

Method

Animals

In this study we examined stargazer rats (homozygous stg/stg; stg group) and unaffected littermates (heterozygous stg/+; LM group) provided by Dr. Charles R. Ashby, Jr., of the Brookhaven National Laboratory (Upton, NY). Rat pups were bred in the vivarium and phenotyped at 14 days of age as stargazers or littermates, based upon the demonstration of stargazing behavior. After weaning, the rats were housed in pairs (stargazer with littermate), in rooms maintained at 25°C, 40% humidity, a 12-hr light/dark cycle (light, 0700–1900 hrs), with food and water available ad libitum (Brock & Ashby, 1996). After being shipped to Saint Anselm College the rats were allowed to accommodate for 7 days, being maintained on a 12-hr light/dark cycle (light, 0800–2000 hrs), with food and water ad lib. All behavior measurements were performed during the light cycle, from 0800 to 1200 hrs.

Tactile Startle Experiments

Rats were tested in an SR-LAB stabilimeter chamber to detect startle responses (San Diego Instruments, San Diego, CA). The testing chambers consist of a Plexiglas cylinder 8.2 cm in diameter resting on a 12.5 x 25.5 cm Plexiglas frame, and the entire assembly is located within a ventilated enclosure. The tactile stimulus consisted of a pressurized air puff directed into the testing chamber by a copper tube. A standard regulator allowed for control of the air pressure (20 to 50 psi). A piezoelectric accelerometer mounted below the Plexiglas frame detected and transduced motion within the cylinder. An IBM-compatible 286 computer and interface assembly controlled the delivery of tactile stimuli and digitized and recorded 250 1-ms readings from the stabilimeter, starting at the onset of the air puff. The peak amplitude of these readings was used as the dependent variable. Calibration procedures were performed between experiments to ensure consistent levels of air pressure and equivalent sensitivities of the stabilimeters. The rats were placed into the startle apparatus and exposed to 100 dB[A] background noise for 5 min. The background noise continued throughout the session to mask the noise of the air puffs.

The rats were then exposed to two types of stimuli: (a) a 40-ms tactile pulse of either 20 or 50 psi; or (b) a 40-ms prepulse of 20 or 50 psi presented 100 ms prior to the onset of a second 40-ms tactile stimulus, the latter stimulus being the point from which data were collected. The startle pulse and the prepulse-pulse pair were administered 15 times each in an alternating fashion with 15 sec between the stimuli. All rats were tested at 20 psi on Days 1, 5, and 7. Each group was later tested one time at 50 psi.

Results

Effect of Haloperidol on the Incidence of Head Tics (Stargazing)

In the test examining the effects of haloperidol on the tactile startle response of stargazer rats, the animals received an intraperitoneal injection of haloperidol (0.3 mg/kg) 2 hr prior to initiating the tactile startle procedure (utilizing 20 psi during the tactile startle testing). Haloperidol (Research Biochemicals International, Natick, MA) was prepared for injection by dissolving in a minimal amount of glacial acetic acid and then diluting with distilled water. During the last 5 min of the 2-hr treatment period with haloperidol the rats were videotaped in an open field for later analysis of the incidence of head tics (as compared to 5 min of videotaped behavior preceding haloperidol administration). The occurrence of head tics was tallied for that 5-min period.

Effects of Time on the Response of Stargazers Versus Control Rats to Tactile Startle Pulses

On Days 1, 5, and 7, the rats were tested for their responsiveness to tactile startle pulses at 20 psi. The
Bar graphs demonstrating the responsiveness of control versus stargazer rats to tactile startle stimuli.

Control rats demonstrate habituation to repeated presentation of the startle stimuli as well as a significant reduction in the startle response following administration of a prepulse.

Stargazer rats demonstrate neither of these phenomena, most likely due to the fact that they are not being startled by the stimuli (note the dramatic reduction in the value of the y axis).

groups consisted of six stargazer rats and seven littermate controls, and the repeated-measures multivariate analysis of variance (MANOVA) revealed significant main effects for group, $F(2, 10) = 26.8, p < .01$; day, $F(4, 8) = 21.3, p < .01$; and the interaction between group and day, $F(4, 8) = 23.4, p < .01$. Specifically, over the three testing sessions the relative startle amplitude for the control rats significantly declined, from $M = 1397.5 \pm 197.5$ on Day 1 to $M = 866.5 \pm 138.7$ on Day 7, $F(2, 22) = 5.6, p < .05$ (see Figure 1), and from $M = 288.4 \pm 52.4$ on Day 1 to $M = 109.6 \pm 22.0$ on Day 7 following the prepulse/pulse pair, $F(2, 22) = 9.5, p < .01$ (see Figure 1). In contrast, the stargazers did not show a significant reduction in their responsiveness to tactile startle stimuli over time. For tactile startle alone there was no significant reduction in level of startle: $M = 41.1 \pm 1.8$ on Day 1 versus $39.0 \pm 1.6$ on Day 7 (see Figure 1). Similar results were obtained for the prepulse/pulse pair: $M = 46.2 \pm 52.4$ on Day 1 versus $37.5 \pm 2.6$ on Day 7 (see Figure 1).

The most important result from these data is the apparent failure of the stargazer rats to exhibit startle responses at all (see also tests of the effects of 20 vs. 50 psi tactile pulses with no rat in the chamber, described below). There were significant differences between the responsiveness of the stargazers and that of the control rats for both startle alone and the prepulse/pulse pair, $F(2, 11) = 49.5$ and 18.0, respectively, $p s < .01$ (see Figure 1). Because only the control rats responded differently over time to tactile startle pulses, there was also a significant interaction between type of rat and day of testing for both startle alone and the prepulse/pulse pair, $F(4, 22) = 5.6, p < .01$ and 7.8, respectively, $p s < .05$ and .01, respectively (see Figure 1).

Effects of 20 Versus 50 psi Tactile Stimuli
Following completion of the preceding phase the rats were tested for their responsiveness to tactile startle stimuli at 50 psi, the factorial MANOVA revealing significant main effects for group, $F(2, 21) = 44.9, p < .01$; pressure, $F(2, 21) = 5.9, p < .01$; and the interaction between group and pressure, $F(2, 21) = 4.6, p < .05$. As compared to the effects at 20 psi on Day 7 (see above), there was a significant increase in the response of control rats to startle pulses at 50 psi, $M = 1720.6 \pm
FIGURE 2

Bar graphs demonstrating the responsiveness of control versus stargazer rats to tactile startle stimuli at either 20 or 50 psi.

Control rats demonstrate increased responsiveness to the high-pressure tactile stimuli.

Stargazer rats also appear to demonstrate increased responses. However, the increases are not significant, and similar results are obtained when no rat is in the chamber (see text).

Note: The values at 20 psi are those obtained on Day 7 in the preceding experiment.

210.5, $F(1, 22) = 11.0, p < .01$ (see Figure 2). Likewise, there was a significant increase in the effect following the prepulse/pulse pair, $M = 401.0 \pm 96.9$, $F(1, 22) = 9.5, p < .01$ (see Figure 2).

Although 50 psi tactile startle pulses increased the measured response of stargazer rats for both startle alone and the prepulse/pulse pair ($M = 74.7 \pm 9.9$ and $72.6 \pm 10.1$, respectively; see Figure 2), the differences were not significant. In order to determine whether the data from stargazer rats at either 20 or 50 psi actually represented startle responses, we tested the measured response of empty chambers at these air pressure levels. The results provided values of $M = 31.5 \pm 0.7$ at 20 psi and $M = 69.6 \pm 0.9$ at 50 psi, values that are nearly identical to those obtained when stargazer rats are in the chambers. Thus, the data obtained during tactile startle experiments with stargazer rats appear to equate to the effects of the tactile stimulus itself.

Again there was a significant difference in the responsiveness of the control versus stargazer rats for both startle alone and the prepulse/pulse pair, $F_s(1, 22) = 85.0$ and 13.7, respectively, $ps < .01$ (see Figure 2), and there were also significant interaction effects, $F_s(1, 22) = 9.3$ and 5.6, respectively, $ps < .01$ and .05, respectively (see Figure 2). Specifically, the interaction effect demonstrates that the rat must be responding in the first place in order for the air pressure to modulate the response of the rat.

Effects of Haloperidol on the Incidence of Head Tics and Responsiveness to Tactile Startle Stimuli

Haloperidol has previously been shown to reduce the incidence of head tics in stargazer rats (Brock & Ashby, 1996; Brock et al., 1995). In the present study we administered haloperidol in order to determine whether a reduction in head tics would unveil sensory responsiveness to tactile stimuli. As expected, haloperidol significantly reduced the number of head tics exhibited by the stargazer rats from $M = 58.2 \pm 4.4$ preceding drug administration to $M = 18.7 \pm 4.1$ postdrug, $t(5) = 5.7, p < .01$, (see Figure 3).

However, haloperidol did not alter the responsiveness of stargazer rats to tactile startle stimuli; factorial MANOVA revealed a significant main effect for
group, $F(2, 21) = 34.9, p < .01$, but not for either the main effect of drug, $F(2, 21) = 0.5$, or the interaction between group and drug, $F(2, 21) = 0.6$. Specifically, in the presence of haloperidol control rats still responded to the tactile startle stimuli as before: $M = 866.5 \pm 128.4$ predrug versus $M = 688.9 \pm 153.5$ postdrug for startle alone and $M = 109.6 \pm 20.4$ predrug versus $M = 95.2 \pm 34.0$ for the prepulse/pulse pair (see Figure 4).

The responsiveness of stargazer rats was also unchanged: $M = 39.0 \pm 1.6$ predrug versus $M = 38.2 \pm 5.8$ postdrug for startle alone and $M = 37.5 \pm 2.6$ predrug versus $M = 36.6 \pm 2.3$ postdrug for the prepulse/pulse pair (see Figure 4). Again there was a significant difference between the control versus stargazers rats in terms of their responsiveness to both tactile startle pulses alone and the prepulse/pulse pair, $F_{s}(1, 22) = 46.1$ and 9.1, respectively, $ps < .01$ (see Figure 4).

**Discussion**

Previous literature on the responsiveness of rats to startle and prepulse inhibition has focused on the use of acoustic startle (for review see: Geyer et al., 1990; Swerdlow et al., 1988). Further, M. D. Kelland and colleagues (M. D. Kelland, 1995; M. D. Kelland et al., 1995) have shown that over repeated testing sessions habituation to acoustic startle pulses occurs. However, because stargazer rats are deaf, tactile startle was used as an alternative means to evaluate these animals as a putative model for TS. In agreement with the literature on acoustic startle, the littermate control rats used in this experiment exhibited startle responses to tactile stimulation. Likewise, these startle responses were subject to paired-pulse habituation, and over the three testing sessions these rats showed a significant reduction of their startle responses for both the startle alone as well as the prepulse/pulse pair condition. To further verify the validity of the tactile startle paradigm, the air pressure in the chambers was increased from 20 psi to 50 psi. Comparing the effects of 50 psi to the third session at 20 psi, there was a significant increase in the response of these control rats. Thus, it can be concluded that, because tactile stimulation results are quite similar to those obtained with acoustic startle, the former technique may be substituted for the latter when studying the deaf stargazer rats.

The stargazer rats were then tested under the tactile stimulation conditions. There is strong evidence in the literature to support the notion that environmental stimuli affect the presence of TS symptoms. One effect is an increase in symptoms when the patient is experiencing anxiety or stress (A. K. Shapiro et al., 1988). Therefore, it was assumed that if stargazer rats were tested under anxiety-producing or stressful situations (i.e., tactile startle) they would be hyperresponsive, a phenomenon akin to the increased symptomatology in TS patients. Previous research has also shown that DA agonists increase responses to acoustic stimuli and decrease the ability of prepulses to inhibit sensory responsiveness (Davis et al., 1990; Geyer et al., 1990; Mansbach et al., 1988; Swerdlow, Braff, & Geyer, 1990; Swerdlow, Braff, Masten, & Geyer, 1990; Swerdlow et al., 1988; Swerdlow, Mansbach, et al., 1990; Young et al., 1991). If the abnormal behavior of stargazer rats results from hyperdopaminergic activity (Brock & Ashby, 1996; Brock et al., 1995), then it is again expected that stargazer rats would be hyperresponsive to tactile stimuli. However, the present data suggest our assumptions about their level of responsiveness were incorrect, because the stargazer rats did not startle at all. Therefore, both the model and our assumptions regarding the neurobiology and the symptomatology of TS require closer examination.

The possibility that the lack of startle responses was due to hyperactivity in general, so much so the
stargazer rats could not focus on the environmental stimuli, was then tested. The rats were given haloperidol, a drug that reduces the incidence of head tics and hyperactivity in stargazer rats (Brock & Ashby, 1996; Brock et al., 1995) and that is commonly used to treat the symptoms of TS (A. K. Shapiro et al., 1988; E. S. Shapiro & A. K. Shapiro, 1986). It was believed that if the drug reduced the symptoms the stargazer rats displayed, then the rats would have the ability to startle. The drug significantly reduced the head tics and hyperactivity in the abnormal rats, but failed to uncover any sensory responsiveness. Thus, the occurrence of head tics may be unrelated to sensory responsiveness.

Another possibility regarding the lack of startle relates to the effect environmental stimulation has on persons with TS. An alternative to the suggestion that tactile startle is a stressful event is that the chambers represent a novel situation. The literature suggests when those suffering from TS encounter new environments their symptoms will diminish and may even temporarily disappear (A. K. Shapiro et al., 1988). Therefore the lack of startle may be due to the fact that the chamber is a strange situation for the stargazers and they cannot respond properly or in a similar fashion to other rats without these symptoms. This explanation does not seem plausible, however, because after repeated test sessions the stargazer rats should have acclimated to the startle chambers.

The idea that the stargazer rat is a model for TS needs to be examined more closely. It seems this strain of rats is a good model for TS for several reasons. First, researchers (Brock & Ashby, 1996; Brock et al., 1995) have found these rats do seem to have a hyperactive dopaminergic system, which is the same system the literature suggests underlies TS in humans (A. K. Shapiro et al., 1988; M. D. Kelland et al., 1990; M. D. Kelland et al., 1993). Further, haloperidol significantly reduced the head tics and hyperactivity of the stargazer rats, as is the case with drugs in the treatment of patients with TS. However, the lack of startle of the stargazer rat contradicts the literature regarding the increase of dopaminergic activity and the acoustic startle. A more plausible explanation for the lack of startle is that the source of the dopaminergic abnormality is different. Much of the literature on acoustic startle is related to schizophrenia (Bolino et al., 1992; Davis et al., 1990;
Geyer et al., 1990; Keith, Mansbach, & Geyer, 1991; M. D. Kelland, 1995; M. D. Kelland et al., 1995; Mansbach, 1991; Mansbach et al., 1988; Swerdlow, Braff, & Geyer, 1990; Swerdlow, Braff, Masten, & Geyer, 1990; Swerdlow et al., 1988; Swerdlow, Mansbach, et al., 1990; Young et al., 1991). Schizophrenia and TS are both the result of increased dopaminergic function and can be treated with the same drugs (e.g., haloperidol); however, they are fundamentally different disorders. The increased dopaminergic function may be caused by completely separate pathways. Theories have suggested that reduced cortical glutamate causes a dopaminergic abnormality that results in schizophrenia (Carlsson, 1988; Grace, 1991), whereas PPN-induced increases in dopaminergic activity may underlie TS.

An alternative explanation is that the DA hyperactivity models are different. In the previous studies, rats tested in the acoustic startle chambers were administered a DA agonist, whereas the stargazer rats have a genetically caused abnormality. Therefore, the mechanisms that underlie the abnormality in the stargazer rats may be significantly different. To wit, peripheral drug administration potentially results in relatively high levels of the drug throughout the entire milieu of the central nervous system. In contrast, the genetic abnormality must exert its effects within the constraints of endogenous physiological limitations. Based on these differences, the stargazer rat is probably a good model for TS, but the tactile startle paradigm may not be a good measure to evaluate these rats.

If the startle paradigm is not a good measure for evaluation, is there an alternative behavioral model with which to assess the stargazer rat? Another characteristic of some patients with TS, not discussed to this point, is obsessive-compulsive disorder (OCD). Some individuals manifest symptoms of both OCD and tic disorder, thereby receiving a dual diagnosis. The incidence of OCD in TS patients is quite high (up to 63%; Cath et al., 1992). The tics of TS can be distinguished from compulsions in that the latter are performed in a complex way and in response to an obsession and according to a set of rigidly followed rules, whereas tics are typically less complex and are not aimed at decreasing the anxiety and tension caused by the obsession (Cath et al., 1992; A. K. Shapiro et al., 1988). A behavioral model of OCD in rats in which chronic treatment with quinpirole produces a behavioral sensitization with compulsive and rigid locomotion along few paths in a region of an open field, as well as motor rituals when objects are placed in this open field, was described (Eilam & Szechtman, 1995; Szechtman, Talangbayan, Canaran, Dai, & Eilam; 1994). The quinpirole treatment also causes these rats to be hyperactive (Eilam & Szechtman, 1995; Szechtman et al., 1994), which may parallel the hyperactivity of the stargazer rats observed in the present study (data not quantified; see also Brock & Ashby, 1996; Brock et al., 1995; Truett et al., 1994). Further research should be directed toward setting up a similar open field maze containing objects and evaluating the stargazer rats in this new OCD behavioral paradigm. However, it is important to keep in mind that this procedure may not be appropriate either, since OCD is not the defining characteristic of TS; rather, head tics are the major defining characteristic.

In conclusion, it is believed that the stargazer mutant rat may still be a suitable model for TS. As stated earlier, the increased dopaminergic activity and the outward symptoms displayed by these rats (head tics), appear to make them a good animal model for the study of TS. These data add to the limited literature about this rat strain. The testing procedures used (similar to acoustic startle) are commonly administered as a model of schizophrenia. Therefore, it has been established that the stargazer rat is a nonschizophrenogenic model. Further investigation of the stargazer rat will help to elucidate the precise nature of its abnormality, as well as to address further the applicability of the model to TS.

References


