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Comparative Behavioral and Neurochemical Studies With Striatal Kainic Acid- or Quinolinic Acid-Lesioned Rats

LÁSZLÓ VÉCSEI[1] AND M. FLINT BEAL

Neurology Services, Massachusetts General Hospital and the Department of Neurology, Harvard Medical School, Boston, MA

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VÉCSEI, L. AND M. F. BEAL. *Comparative behavioral and neurochemical studies with striatal kainic acid- or quinolinic acid-lesioned rats.* PHARMACOL BIOCHEM BEHAV **39**(2) 473–478, 1991.—In the present studies the effects of kainic acid (KA)- or quinolinic acid (QA)-induced striatal lesions were compared in different behavioral tests in rats. Both KA- and QA-lesioned animals had ipsilateral barrel-rotation (BR). The KA-lesioned rats, however, had contralateral, while the QA-lesioned rats had both ipsi- and contralateral turning activity. The KA-lesioned animals showed increased open-field activity as well as increased percentage of entries, and time spent in the open arms of Montgomery's conflict test. Learning of an active avoidance response was strongly inhibited by both striatal QA- or KA-induced striatal lesions. The QA-lesioned animals showed less pronounced behavioral changes than KA-lesioned animals in most of the tests, and had a smaller loss of body weight. There was no significant difference in the extent of the KA- and QA-induced substance P (SP) and GABA depletions in striatum, however, the depletions with QA lesions were slightly greater. These findings show that KA-induced striatal lesions produce more pronounced behavioral effects than QA lesions of similar size. It is possible that the differential effects of KA versus QA on striatal interneurons may result in its more marked behavioral effects.

Behavior GABA Kainic acid Quinolinic acid Rats Substance P

HUNTINGTON'S disease is a progressive degenerative disorder of the central nervous system, which primarily affects the neostriatum, but also affects other extrapyramidal and cortical areas to a lesser extent (13, 16, 37). The clinical manifestations of this illness consist of involuntary choreiform movements of the body, and progressive intellectual deterioration with impairment of learning, memory and judgement (17). The cognitive symptoms often precede the appearance of the associated motor abnormalities (25).

Olney and co-workers (29) showed that kainic acid (KA) is a powerful neurotoxic analogue of glutamate, which causes neuronal degeneration. The neurochemical and histological sequelae of KA injections into the caudate-putamen (CP) are remarkably similar to the neurochemical and histologic findings in the CP of patients suffering from Huntington's disease. It has, therefore, been suggested that intrastriatal injections of KA serve as an animal model for this condition (10,24).

Despite the cell loss in the striatum of patients suffering from Huntington's disease, there is a marked increase in the striatal concentration of somatostatin-like immunoreactivity (SLI) (1, 2, 28). Graded doses of KA (or ibotenic acid) cause a proportional decrease in the concentration of SLI (3). The increased SLI in Huntington's disease is, therefore, not reproduced by KA lesions in rats.

Schwarcz et al. (36) demonstrated that quinolinic acid (QA), an endogenous metabolite of tryptophan present in human brain, could produce excitotoxin lesions in striatum. Subsequently, Beal et al. (4) found that lesions due to QA closely resemble those of Huntington's disease, since they result in marked depletions of both GABA and substance P, with relative sparing of somatostatin/neuropeptide Y neurons. They concluded that QA or a similar compound could be responsible for neuronal degeneration in Huntington's disease.

Based on these morphological and neurochemical findings, the aim of the present studies was to compare the acute behavioral effects, exploration of a new environment, and learning of a new paradigm in striatal KA- or QA-lesioned rats.

METHOD

Animals

Male Sprague-Dawley rats (Charles River) weighing 200–230 g were housed in cages (2–4 animals/cage) with ad lib access to chow and water. A 12:12-h light-dark cycle was maintained

[1]Requests for reprints should be addressed to László Vécsei, M.D., Ph.D., Department of Neurology, University Medical School, Pécs, Rt ut 2. 7623-Hungary.

(light on 0600 h), and temperature and humidity were controlled.

Surgery

The animals were anesthetized with pentobarbital (Anthony Products Co., Arcadia, CA), 50 mg/kg intraperitoneal, and were placed in a Kopf stereotactic apparatus (David Kopf Instruments, Tujunga, CA). Compounds were dissolved in saline and neutralized to pH 7.4. Injections were made with a 10 μl Hamilton syringe fitted with a 30-gauge blunt-tipped needle into the left striatum at the coordinates 0.5 mm anterior to bregma, 2.6 mm lateral to midline and 4.5 mm ventral to dura. QA (Sigma, St. Louis, MO) (240 nmol) or KA (Sigma, St. Louis, MO) (7 nmol), were injected in 1 μl over 2 min, the needle left in place for an additional 2 min, and then slowly withdrawn. The doses of QA and KA were selected on the findings of earlier studies (7). In these dose-response investigations it was demonstrated that KA injected in 7 nmol and QA injected in 240 nmol depleted the substance P (SP) and GABA concentrations in the striatum with approximately similar potency. The sham-lesioned animals were injected with 1 μl saline.

Behavioral Studies

The behavioral studies started 9–10 days after the surgery and were performed between 2000–2300 h since the activity of rodents is higher during the dark cycle. The observer for the activity measurements was not blind to the experimental conditions.

Acute Behavioral Effects of KA- or QA-Induced Striatal Lesions in Rats

Three h after surgery each of the animals were placed in individual plastic cages and their behavior during a 15-min observation period was videorecorded (VHS Movie, VX-306, Olympus, Olympus Optical Co. Ltd., Tokyo, Japan). Recent findings suggest that 3 h after surgery, the behavior of the rats is stabilized (26). The activity [rearing, barrel rotation (BR), turning] was carefully evaluated in separate sessions using the videotapes.

Exploratory Activity

The animals were placed in an open-field box (100 by 100 cm, 40 cm high), white wooden box, the floor consisting of 25 equally sized squares measuring 20 by 20 cm each. The activity during a three-min session was videorecorded. During the experimental sessions, the testing room was illuminated with dimmed white light. Their behavior was characterized by the total number of squares (horizontal activity), the total number of rearings (vertical activity), the number of groomings and the number of defecation boluses produced during the 3-min session (39). The videotapes were evaluated in separate sessions.

Elevated Plus Maze Test

The experimental device was an elevated (1 m above ground) plus-formed maze, which was placed in a dimly room. The four arms were 40 cm long and 10 cm wide, with mesh wire floors. Two opposing arms were surrounded by black 10 cm high walls (closed arms), while the other arms were devoid of walls (open arms). The testing was immediately preceded by the open-field test. The placement of the animal in an unfamiliar environment prior to the test increases the total number of entries (30), increasing the sensitivity of the test (19). Thereafter, the rat was placed in the centre of the maze, facing a closed arm. The investigator was situated approximately 2 m from the center of the maze. Entry into an arm was defined as the animal placing all four paws in that arm. The cumulative time spent in, as well as the number of entries made into the open or closed arms, were recorded during a five-minute test session. The open-arm data were then expressed as percent of the total time spent in, and of the total number of entries made into both the closed and open arms. The plus-maze was carefully wiped with a wet towel after each tested animal.

Active Avoidance Behavior

Active avoidance conditioning was performed in a bench jumping conditioning apparatus (Lafayette Instrument, IN). The conditional stimulus (CS) was the light of a 40-W electric bulb, while the unconditional stimulus (US) was an electric shock of 0.2 mA (1 s) delivered through the grid floor of the apparatus to the paws of the rat (38,39). Each day 10 trials were performed, with a mean intertrial interval of 60 s.

Neurochemical Studies

After the behavioral studies the animals were killed by decapitation, their brains promptly removed and placed on ice, and coronal sections, 2.5 mm in thickness were made with razor blades (Zivic-Miller Lab., Allison Park, PA). The frontal poles were removed and the second coronal cut passed through the anterior commissure. Both striata were dissected and placed in chilled 0.1 M HCl and stored frozen until assay.

Measurements of Substance P-Like Immunoreactivity (SPI) and GABA Concentrations of Striatum

Striatal samples were boiled in 1 ml of 0.1 N HCl for 10 min and centrifuged, and aliquots of supernatant were lyophilized. Extracts were reconstituted in neutral buffer and assayed for SPI. The SP antisera was generously provided by Dr. John A. Kessler. Assay buffer was 0.1 M sodium phosphate, pH 7.4, containing 0.01 M EDTA, 0.05 M NaCl, 0.02% sodium azide, and 0.1% bovine serum albumin. Iodinated SP was obtained from New England Nuclear. Assay tubes containing standards (1 to 20 fmol) or samples (0.1 ml) were incubated at 4°C for 24 h (0.5 ml final volume) before the addition of 0.1 ml appropriately diluted guinea pig serum (Pel Freeze Biologicals, Rogers, AR) and goat anti-guinea pig gamma globulin (Biotek, Shawnee Mission, KA). After 24 h incubation, the assay tubes were centrifuged and radioactivity in the pellet was determined. The sensitivity of the assay, defined as the concentration of SP which resulted in binding of labeled SP 2 SD below the mean binding in the absence of SP, was 1 fmol/tube. The ED_{50} (defined as the concentration of SP required to displace 50% of [^{125}I] SP specifically bound to antiserum) in the RIA was 6.2 fmol. The nonspecific binding was 6.1%. The intraassay coefficient of variation was less than 10%, and interassay coefficients of variation in six assays for two internal standards were 6.7 and 8.5% (5).

For rapid analysis of GABA, the pH was adjusted to 6.0 with 36% methanol, 0.1 M phosphate buffer, allowing a total run time of 12 min. Under these conditions, ethanolamine migrates after GABA (6). Proteins were measured on the pellets using a fluorimetric assay.

The neurochemical measurements were compared with the unlesioned (control) side (SPI: 342 ± 47 fmol/mg protein,

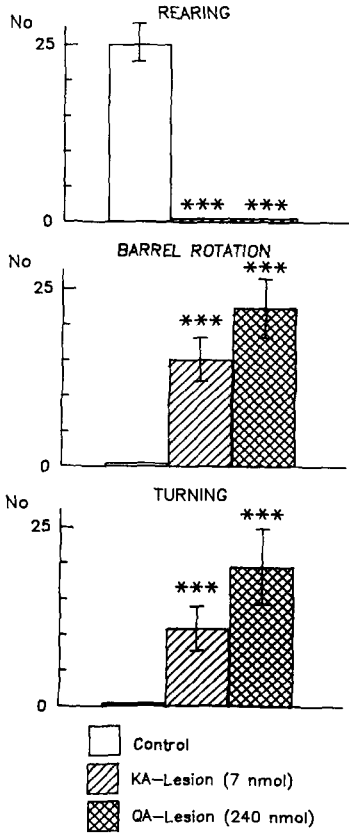

FIG. 1. Acute behavioral effects of unilateral kainic or quinolinic acid injections in the rat striatum. Vertical lines represent the standard errors of the mean (n = 8–10 animals/group). ***$p<0.01$ (Student's t-test). Both kainic- and quinolinic acid-lesioned rats showed significantly decreased rearing and increased barrel rotation and turning, but the two groups did not differ from each other.

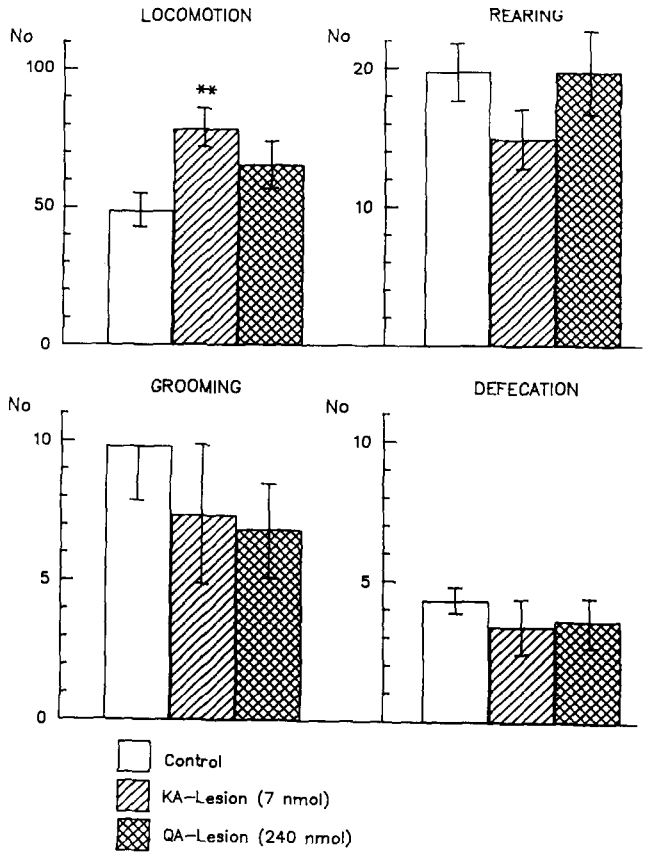

FIG. 2. Open-field activity of striatal kainic or quinolinic acid-lesioned rats. Vertical lines represent the standard errors of the mean (n = 8–10 animals/group). **$p<0.02$ (Student's t-test). Kainic acid significantly increased the locomotor activity of the rats during the 3-min observation period, however, the increased locomotor activity in the quinolinic acid group was not significantly different from controls.

GABA: 28.7 ± 4.3 nmol/mg protein) and expressed as the percentage of control. We have previously found that the right (control) values do not differ from saline controls.

Statistical Analysis

The behavioral and neurochemical data were evaluated by analysis of variance (ANOVA) followed by Student's t-test (two tailed).

RESULTS

The acute behavioral effects of unilateral KA or QA injections are presented in Fig. 1. During the 15-min observation period the animals showed several behavioral phenomena. These often started with chewing. The head was then drawn posteriorly to the right side by clonic-tonic movements. Then, the whole body twisted about its long axis in such a manner that the dorsal aspect rotated towards the injection side. Soon the rostral end twisted over completely and the caudal end followed, producing a complete BR. During and at the end of an episode of BR, the animal chewed and made clonic movements of the right forepaw and neck. The direction of the BR was always ipsilateral. The lesioned animals showed no rearing activity, while the saline-injected rats had normal exploration, $F(2,25) = 187.5$, $p<0.01$, ANOVA. Both excitotoxins induced BR, $F(2,25) = 15.47$, $p<0.01$, ANOVA, and turning, $F(2,25) = 8.08$, $p<0.01$, ANOVA. All of the KA-lesioned animals had contralateral, while the QA-lesioned rats had contra- and ipsilateral (approx. 50–50%) turning. The magnitude of KA- or QA-induced BR or turning activity did not differ significantly from each other.

The open-field activities of the KA- and QA-lesioned animals are presented in Fig. 2. The KA-lesioned rats had higher locomotor activity [$F(2,25) = 5.12$, $p<0.02$, ANOVA; $p<0.02$, Student's t-test] compared to the controls. Although QA lesions resulted in increased locomotion during the 3-min observation period, the change was not significant. The rearing, grooming and defecation activities did not differ between the treatment groups.

In elevated plus maze test the KA-lesioned animals spent more time [$F(2,25) = 13.34$, $p<0.01$, ANOVA; $p<0.01$, Student's t-test] and entered more frequently [$F(2,25) = 3.61$, $p<0.05$, ANOVA; $p<0.05$, Student's t-test] in the open arms of the equipment as compared to the controls, while QA lesions did not significantly influence these parameters. The KA lesions slightly but not significantly, $F(2,25) = 1.89$, p = NS, increased the total entries into the open and closed arms of the equipment (Fig. 3).

Both KA and QA lesions inhibited the learning performance

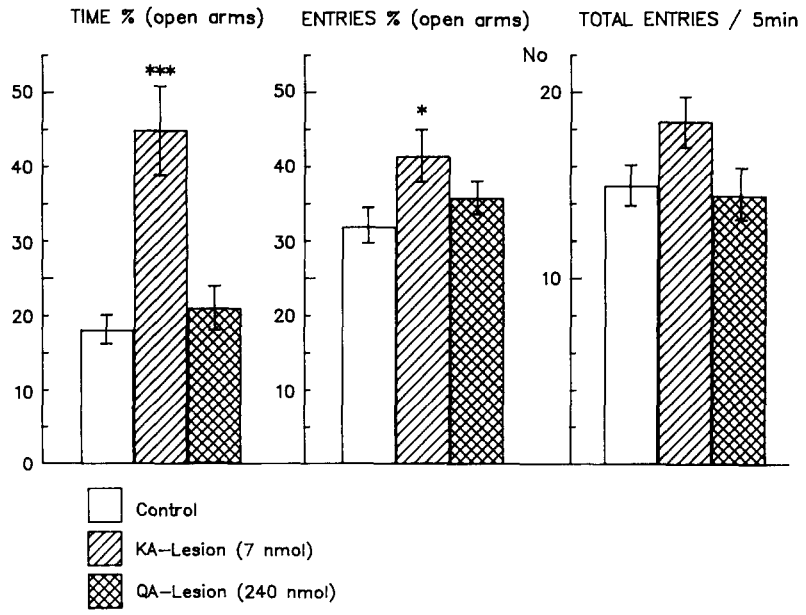

FIG. 3. Effect of striatal kainic or quinolinic acid injection on elevated plus maze test in rats. Vertical lines represent the standard errors of the mean (n = 8–10 animals/group). *$p<0.05$; ***$p<0.01$ (Student's t-test). The kainic acid-lesioned animals spent significantly more time and entered more frequently in the open arms of the equipment. Kainic acid slightly, but not significantly, increased the total number of entries. Quinolinic acid lesions had no significant effects.

of the rats in an active avoidance learning paradigm, $F(2,20) = 24.43$, $p<0.01$, ANOVA (Fig. 4). Differences were observed from the first day of training between both lesioned and control groups. While the control group showed acquisition over the five-day training period, performance did not change significantly for the rats which received neurotoxin lesions.

Both KA and QA lesions inhibited the normal body weight increases of the animals [4th day: $F(2,25) = 78.06$, $p<0.01$, 6th

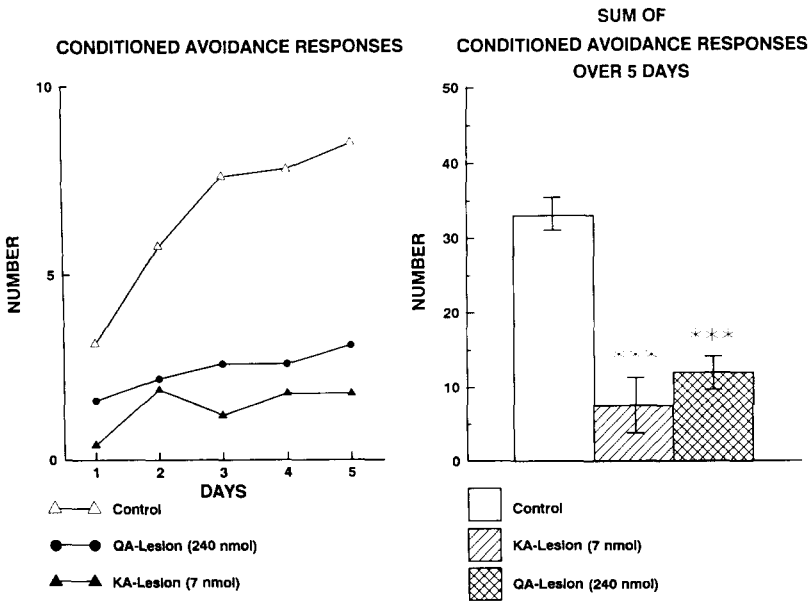

FIG. 4. Active avoidance learning of striatal kainic- or quinolinic acid-lesioned rats. Vertical lines represent the standard errors of the mean (n = 7 animals/group). ***$p<0.01$ (Student's t-test). The performance of both KA- and QA-lesioned animals was significantly attenuated to a comparable extent.

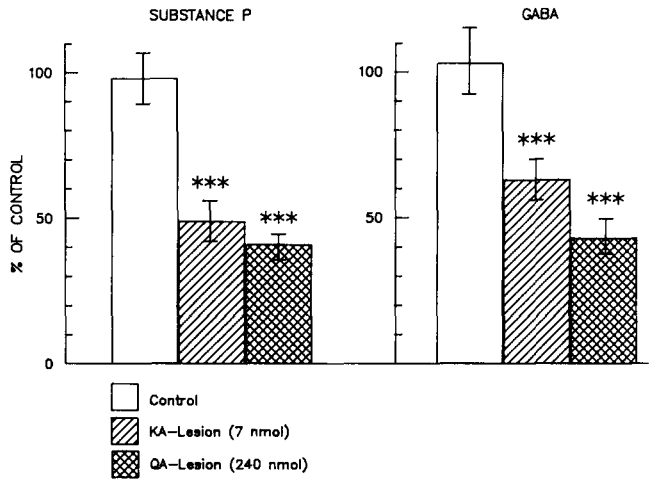

FIG. 5. Effects of unilateral striatal kainic or quinolinic acid lesion on substance P and GABA concentrations in rats. Vertical lines represent the standard errors of the mean (n = 8–10 animals/group). ***$p<0.01$ (Student's t-test). Both kainic and quinolinic acid resulted in significant depletions of substance P and GABA of approximately 50%. The decreases in SP and GABA did not significantly differ between the 2 groups.

day: $F(2,25) = 40.9$, $p<0.01$, 9th day: $F(2,25) = 34.96$, $p<0.01$, 22nd day: $F(2,25) = 8.43$, $p<0.01$, ANOVA], but the effect of KA lesion was more pronounced (data not shown). The mean body weights of controls, KA-lesioned and QA-lesioned animals on day 4 were 252 ± 4 g, 185 ± 4 g, and 206 ± 6 g respectively. On day 22 the mean body weights of the 3 groups were 319 ± 6 g, 289 ± 7 g and 320 ± 5 g, respectively.

The effects of KA and QA striatal lesions on SPI and GABA are presented in Fig. 5. Both excitotoxins significantly depleted the striatal SPI, $F(2,25) = 19.66$, $p<0.01$, ANOVA, and GABA, $F(2,25) = 11.92$, $p<0.01$, ANOVA, levels. The QA- and KA-induced neurochemical changes did not differ significantly from each other (Fig. 5).

DISCUSSION

In the present experiments intrastriatal injections of both KA and QA resulted in clonic-tonic movements of the contralateral limbs and episodic BR. This behavior could be quantified reliably for several h (26). Some authors have attributed BR to seizures (22,41), whereas others have not observed epileptic EEG changes in cortex, hippocampus and amygdala during chlorpromazine methiodide and somatostatin-induced BR (8,9). Marrannes and Wauquier (26), however, reported that BR and clonic forepaw movements seen 3–6 h after intrastriatal injection of QA respond to anticonvulsants, but are not sensitive to drugs used in the symptomatic treatment of Huntington's disease. It is of interest that KA lesions consistently induced contralateral turning, while QA lesions induced turning in either direction. The differences in the direction of turning behavior of QA- or KA-lesioned rats may be related to the different effects of the excitotoxins on striatal neurotransmitters (see details below).

Previous studies in rats with striatal KA and ibotenic acid lesions have demonstrated that the major behavioral consequences of the lesions are a persistent nocturnal hyperactivity with relatively normal daytime activity (21,27). Recently, Sanberg et al. (35) investigated the locomotor abnormalities of QA-lesioned animals using the computerized Digiscan system (34). They found that although chorea, as such, is not recognizable in QA-lesioned rats, they do show an abnormal locomotion which is characterized by an increase in swing time and decrease in stance time as compared to control rats. Thus the lesioned rats put their paws on the ground for shorter periods of time and swing them farther than normal rats. This has been suggested to be analogous to the locomotion pattern observed in patients with Huntington's disease (20). Furthermore, they found locomotor hyperactivity after bilateral QA striatal lesions in rats.

In the present studies KA-lesioned animals had more pronounced exploratory activity in the open-field box, and these animals spent more time in the open arms of the elevated plus maze test, as compared to the control or QA-lesioned rats. In the open-field test behavior is studied in a situation of conflict between a reinforced drive (exploration of the new environment) and an aversive stimulus (unconditional aversion that rats have for new unknown environments). However, there are two major problems in examining exploratory behavior in rodents: 1) the problem of novelty and fear; and 2) the problem of separating locomotor activity from exploration. A problem with any test of exploration is that an animal will walk round an area to explore it, or to escape from it, or both (12). There is no way to separate out these factors (15). Clearly, then, the fear level (arousal) of the animal (determined by the novelty of the situation, light level, past history of the animal) will be a strong determinant of his response to any test in which exploration is measured, and may be a confounding factor. In our experiments the KA-lesioned animals spent more time in the open arms of the elevated plus maze test suggesting that their fear level does not account for their increased exploration. The increase in activity in the open field and plus maze in the KA lesions rats may indicate a decrease in the suppression by novel environments or "fear levels."

Another similarity to Huntington's disease which exists in the motor activity of excitotoxin-lesioned rats is that, as compared to controls, their locomotor activity is markedly potentiated during arousal. Huntington's disease patients also show much greater choreiform movements during their awake period and when aroused (32,33).

Both KA- and QA-lesioned animals had impaired learning activity in the active avoidance test. The suggestion that the learning and memory deficits found in the present experimental animals and in Huntington's disease (25) may be associated with striatal pathology is consistent with a large number of reports which have implicated the caudate and putamen in complex psychological functions (14,18). Furthermore, these deficits have been shown to be reversible with striatal transplants (11,21).

Postoperatively the mean body weight of the lesioned rats was reduced as compared to sham-operated controls, thus further strengthening the parallels between these animal models and Huntington's disease for which such deficits are also observed (31). The initial weight loss of the lesioned animals was probably related in part to the debilitating effect of the lesioning process (35).

Our present findings show that KA-lesioned animals exhibit more profound changes in most behavioral tests as compared to QA-lesioned rats, despite the fact that the extent of the SP and GABA depletions in the two groups did not differ significantly from each other. Several factors could account for the differences. Our previous studies showed that somatostatin-neuropeptide Y neurons are relatively resistant to lesions with NMDA agonists, however, they are preferentially vulnerable to lesions with kainate and quisqualate agonists (7). KA striatal lesions at the dose used in the present study result in significant depletions of both somatostatin and neuropeptide Y concentrations,

whereas QA and NMDA lesions do not (7). Somatostatin and neuropeptide Y are involved in several behavioral processes [see review: (19,40)]. Another factor which could account for differences is the presence of "remote" lesions within other brain regions, which can result from localized striatal injections of KA (23). Therefore, the more wide-spread and less specific neurochemical changes of KA striatal lesions may be responsible for the more marked behavioral abnormalities.

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REFERENCES

1. Aronin, N.; Cooper, P. E.; Lorenz, L. J.; Bird, E. D.; Sagar, S. M.; Leeman, S. E.; Martin, J. B. Somatostatin is increased in the basal ganglia in Huntington's disease. Ann. Neurol. 13:519–526; 1983.
2. Beal, M. F.; Bird, E. D.; Langlais, P. J.; Martin, J. B. Somatostatin is increased in the nucleus accumbens in Huntington's disease. Neurology 34:663–666; 1984.
3. Beal, M. F.; Marshall, P. E.; Bird, E. D.; Landis, D. M. D.; Martin, J. B. Excitotoxin lesions do not mimic the alteration of somatostatin in Huntington's disease. Brain Res. 361:135–145; 1985.
4. Beal, M. F.; Kowall, N. W.; Ellison, D. W.; Mazurek, M. F.; Swartz, K. J.; Martin, J. B. Replication of the neurochemical characteristics of Huntington's disease by quinolinic acid. Nature 321: 168–171; 1986.
5. Beal, M. F.; Mazurek, M. F. Substance P-like immunoreactivity is reduced in Alzheimer's disease cerebral cortex. Neurology 37:1205–1209; 1987.
6. Beal, M. F.; Kowall, N. W.; Swartz, K. J.; Ferrante, R. J.; Martin, J. B. Systemic approaches to modifying quinolinic acid striatal lesions in rats. J. Neurosci. 8:3901–3908; 1988.
7. Beal, M. F.; Kowall, N. W.; Swartz, K. J.; Ferrante, R. J.; Martin, J. B. Differential sparing of somatostatin-neuropeptide Y and cholinergic neurons following striatal excitotoxin lesions. Synapse 3:38–47; 1989.
8. Burke, R. E.; Fahn, S.; Wagner, H. R.; Smeal, M. Chlorpromazine methiodide-induced barrel rotation: an antimuscarinic effect. Brain Res. 250:130–142; 1982.
9. Burke, R. E.; Fahn, S. Electroencephalographic studies of chlorpromazine and somatostatin-induced barrel rotation in rats. Exp. Neurol. 79:704–713; 1983.
10. Coyle, J. F.; Schwarcz, R. Lesion of striatal neurons with kainic acid provides a model of Huntington's chorea. Nature 263:244–246; 1976.
11. Deckel, A. W.; Moran, T. H.; Coyle, J. T.; Sanberg, P. R.; Robinson, R. G. Anatomical predictors of behavioral recovery following fetal striatal transplants. Brain Res. 365:249–258; 1986.
12. Denenberg, V. H. Open-field behavior in the rat: What does it mean? Ann. NY Acad. Sci. 159:852–859; 1969.
13. Dulap, C. B. Pathological changes in Huntington's chorea with special reference to the corpus striatum. Arch. Neurol. 18:867–943; 1927.
14. Fibiger, H. C.; Phillips, A. G. Retrograde amnesia after electrical stimulation of the substantia nigra: mediation by the dopaminergic nigraneostriatal bundle. Brain Res. 116:23–33; 1976.
15. File, S. E.; Pellow, S. Behavioral pharmacology of minor tranquilizers. Pharmacol. Ther. 35:265–290; 1987.
16. Forno, L. S.; Jose, C. Huntington's chorea: a pathological study. Adv. Neurol. 1:453–470; 1973.
17. Garron, D. C. Behavioral aspects of Huntington's chorea. Adv. Neurol. 1:729–735; 1973.
18. Glick, S. D.; Greenstein, S. Comparative learning and memory deficits following hippocampal and caudate lesions in mice. J. Comp. Physiol. Psychol. 82:188–194; 1973.
19. Heilig, M. Neuropeptide Y and behaviour: An experimental study in the rat. Lund: Studentlitteratur; 1989:1–157.
20. Hruska, R. E.; Sibergeld, E. K. Abnormal locomotion in rats after bilateral intrastriatal injection of kainic acid. Life Sci. 25:181–194; 1979.
21. Isacson, O.; Brundin, P.; Kelly, P.; Gage, F. H.; Björklund, A. Functional neuronal replacement by grafted striatal neurons in the ibotenic acid-lesioned rat striatum. Nature 311:458–460; 1984.
22. Kasting, N. W.; Veale, W. L.; Cooper, R. E. Convulsive and hypothermic effects of vasopressin in the brain of the rat. Can. J. Physiol. Pharmacol. 58:316–319; 1980.
23. Kohler, C.; Schwarcz, R. Comparison of ibotenate and kainate neurotoxicity in rat brain. A histological study. Neuroscience 8:819–835; 1983.
24. McGeer, E. G.; McGeer, P. L. Duplication of biochemical changes of Huntington's chorea by intrastriatal injection of glutamic and kainic acids. Nature 263:517–519; 1976.
25. Maida, E.; Scnaberth, G. Organic dementia as a first symptom of infantile Huntington's chorea. Wien. Klin. Wochenschr. 88:775–776; 1976.
26. Marrannes, R.; Wauquier, A. Episodic barrel rotations induced by intrastriatal injections of quinolinic acid in rats. Inhibition by anticonvulsants. Pharmacol. Biochem. Behav. 31:153–162; 1988.
27. Mason, S. T.; Sanberg, P. R.; Fibiger, H. C. Kainic acid lesions of striatum dissociate amphetamine and apomorphine stereotype: Similarities to Huntington's chorea. Science 201:352–355; 1978.
28. Nemeroff, C. B.; Youngblood, W. W.; Manberg, P. J.; Prange, A. J.; Kizer, J. S. Regional brain concentrations of neuropeptides in Huntington's chorea and schizophrenia. Science 221:972–975; 1983.
29. Olney, J. W.; Rhee, V.; Ho, O. L. Kainic-acid: A powerful neurotoxic analogue of glutamate. Brain Res. 77:507–512; 1974.
30. Pellow, S.; Chopin, P.; File, S. E.; Briley, M. Validation of open: closed arm entries in an elevated plus-maze as a measure of anxiety in the rat. J. Neurosci. Methods 14:149–167; 1985.
31. Podolsky, S.; Leopold, N. A. Abnormal glucose tolerance and arginine tolerance tests in Huntington's disease. Gerontology 23:55–63; 1977.
32. Sanberg, P. R.; Johnston, G. A. Glutamate and Huntington's disease. Med. J. Aust. 2:460–465; 1981.
33. Sanberg, P. R.; Coyle, J. T. Scientific approaches to Huntington's disease. CRC Crit. Rev. Clin. Neurobiol. 1:1–44; 1984.
34. Sanberg, P. R.; Hagenmeyer, S. H.; Henault, M. A. Automated measurement of multivariate locomotor behavior in rodents. Neurobehav. Toxicol. Teratol. 7:87–94; 1985.
35. Sanberg, P. R.; Calderon, S. F.; Giordano, M.; Tew, J. M.; Norman, A. B. The quinolinic acid model of Huntington's disease: Locomotor abnormalities. Exp. Neurol. 105:45–53; 1989.
36. Schwarcz, R.; Whetsell, W. O.; Mangano, R. M. Quinolinic acid: An endogenous metabolite that produces axon sparing lesion in rat brain. Science 219:316–318; 1983.
37. Shoulson, I.; Chase, T. N. Huntington's disease. Annu. Rev. Med. 26:419–426; 1975.
38. Telegdy, G.; Hadnagy, J.; Lissák, K. The effects of gonads on conditioned avoidance behavior of rats. Acta Physiol. Hung. 339: 439–446; 1968.
39. Vécsei, L.; Telegdy, G.; Schally, A. V.; Coy, D. H. Effects of beta(Tyr^9)melanotropin-(9–18) decapeptide on passive and active avoidance behavior and on open-field activity of rats. Peptides 2:389–391; 1981.
40. Vécsei, L. Behavioral, pharmacological and neurochemical studies of somatostatin, cysteamine and pantethine. Lund: Studentlitteratur; 1989:1–273.
41. Wurpel, J. N. D.; Dundore, R. L.; Barbella, Y. R.; Balaban, C. P.; Keil, L. C.; Severs, W. B. Barrel rotation evoked by intracerebroventricular vasopressin injections in conscious rats. II Visual/vestibular interactions and efficacy of antiseizure drugs. Brain Res. 365:30–41; 1986.