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Use of fluoxetine for the treatment of stereotypical pacing behavior in a captive polar bear

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- Polar bear activities were videotaped and scored, using 4 behavioral categories, to assess the effects of fluoxetine administration.
- Fluoxetine treatment terminated stereotypical pacing behavior, facial tic, and huffing/coughing behavior without affecting typical polar bear behaviors.
- Pharmacologic manipulation of the serotonergic system may be 1 method to safely eliminate stereotypical behaviors in captive polar bears.

A 24.5-year-old 257-kg female polar bear (*Ursus maritimus*) had stereotypical pacing behavior. The bear was born at the zoo in November 1969 and had been at the zoo throughout its life. The first report of pacing behavior was when the bear was 2.5 years old; it had been separated from its parents and moved to a different enclosure. Records maintained by the zookeepers indicated that an unspecified tranquilizer was not effective in reducing the pacing. Twenty days after separation, the young bear was returned to the original enclosure and was reunited with its parents, and the pacing stopped. Observations by the zookeepers indicated that the bear resumed pacing 2 months after it was reunited with its parents and that it had had the pacing behavior for the past 22 years. Furthermore, the zookeepers recorded that the bear paced a considerable amount every day of the year. The bear also had a facial tic and huffing/coughing behavior. The facial tic involved a sudden and recurrent twitch of the facial (masseter and temporal) muscles. The huffing/coughing behavior was defined as a sudden forced expulsion of air from the lungs through partially closed vocal cords. The facial tic and huffing/coughing behavior were displayed simultaneously and also were associated with a change of direction during a pacing cycle.

Starting in 1988, the bear received ivermectin[a] (300 µg/kg of body weight, PO, q 30 d) for treatment of ectoparasites considered responsible for chronic, intermittent, recurring alopecia and associated pruritus. In July 1994, the bear was considered healthy by means of visual examination; obvious clinical abnormalities were not identified.

Housing—The polar bear enclosure was an 836-m^2 area. Approximately a tenth of this area was partitioned into a concrete holding area, whereas three fourths of the area was composed of concrete that was partially covered with boulders, rocks, tree trunks, wood chips, and pebbles. A concrete pool constituted the remainder of the enclosure. The pool contained approximately 170,000 L of processed tap water to which 227 g of dry chlorine was added (as needed) to control algae growth. During warmer months, the enclosure was cleaned daily by use of a hose, but during colder months, fecal material was removed daily by use of a shovel. The enclosure had direct sunlight and shaded areas. For the past several years and for the duration of fluoxetine treatment, the enclosure housed the affected bear and an unrelated female polar bear.

Diet—The bears had access to a commercially available omnivore chow ad libitum.[b] Each day, bears also were fed smelt, herring, chicken heads, or horse tails to which 50 mg of menhaden fish oil had been added. Fruits, vegetables, and invertebrates were offered regularly in various ways and forms.

Observations and behavioral scoring—Polar bear behavior was videotaped for 9 daylight hours (from 7:00 AM to 4:00 PM) about every third day during a 300-day period (94 videotaping days). Equipment was placed on the upper deck, which allowed approximately 85% of the enclosure to be videotaped, including 4 pacing runways used by the bear. A daily log was kept, and pertinent information was recorded. Qualitative statements regarding the facial tic and huffing/coughing behavior were documented.

To assess the effect of treatment on stereotypical and typical polar bear behaviors, polar bear behavior recorded on the videotapes was scored according to 5 categories. For the purposes of scoring, stereotypical mobility was determined as pacing behavior, which was easily discriminated from other activities. Pacing was defined as the repeated production of 1 type of motor act (walking). Nonstereotypical mobility was defined as any gross locomotor act that was not repeated or, when repeated, had flexibility (ie, rubbing, swimming, walking, running, eating, and grooming). Awake immobility was defined as the lack of gross locomotor acts in the awake bear. Sleeping was inferred when the bear was recumbent with its head down; it was impossible to discern whether the bear's eyes were open or closed. The "off" category was used when the bear was not visible on the videotapes.

The amount of continuous time spent engaging in a particular behavior (duration of bout) before engaging in another behavior and the number of times a bout of behavior was observed (number of bouts) in each 9-hour recording session were scored. The total

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amount of time spent in each category during a 9-hour recording session was calculated and converted to a percentage score for that observation day.

Fluoxetine administration—Three contiguous observation periods were included: pretreatment phase (32 days; first day of pretreatment phase = day 0), treatment phase (105 days), and posttreatment phase (163 days). During the treatment phase of the experiment, 20-mg fluoxetine[c] capsules were hidden in herring and administered to the bear in the morning. Observations by the zookeepers indicated that the bear consumed the herring that contained the drug. To maintain consistency, the polar bear was hand-fed 4 or 5 herring every morning during all 3 observation periods.

Initially, an empirical dosage of 1.32 mg of fluoxetine/kg was administered for 7 days. After consultation with an expert (who believed that the initial dosage might have been too high), we switched to a dosage determined by means of an allometric scale[1] (0.62 mg/kg) for 77 days. The dosage was increased to 1.0 mg/kg for the final 21 days of the treatment phase to facilitate cessation of pacing.

Immobilization and blood sample collection—The bear was immobilized 3 times by use of tiletamine-zolazepam[d] (4.5 mg/kg) for routine blood sample collection on days 83, 138, and 178. An ECG and pulse oximetry values were recorded continuously during each immobilization. The bear was allowed to recover without administration of a reversal agent. A CBC and serum biochemical analyses were conducted, using an automated system.[e] Aliquots of serum were collected, frozen, and stored at −80 C for later drug metabolite analysis.

Fluoxetine and metabolite analysis—Serum concentrations of fluoxetine, norfluoxetine, and trifluoromethylphenol were assayed by use of an extractive derivatization with pentafluorobenzenesulfonyl chloride and were subsequently analyzed on a gas chromatograph equipped with a fused silica capillary column, an electron-capture detector, and a printer/integrator, using methodology reported elsewhere.[2]

At the lower dosage of 0.62 mg/kg/d, serum concentration of fluoxetine (S enantiomer, 69.2 ng/ml) and norfluoxetine (S enantiomer, 47.1 ng/ml) were comparable. At the higher dosage of 1.0 mg/kg/d, norfluoxetine concentration (S enantiomer, 82.0 ng/ml) was much greater than fluoxetine concentration (S enantiomer, 41.4 ng/ml).

Stereotypical pacing behavior—During the pretreatment phase (days 0 to 32), the bear paced for a mean of 68.6% of each day. A typical day consisted of 22 pacing bouts, each of which lasted a mean of 16.84 minutes. There was a great deal of variability in duration of pacing bouts, with bouts ranging from < 1 minute to 150 minutes in duration. Pacing bouts were composed of a mean of 78 cycles. Each pacing cycle, up and back along the length of a wall once, took 13 seconds to complete and was fixed and rigid with little variation. The bear would place its paws in the same spot and in the same temporal sequence from cycle to cycle. Although pacing was performed on 4 pathways, 1 particular pathway was favored. Pacing was performed mainly on shaded pathways and most frequently was done in the morning.

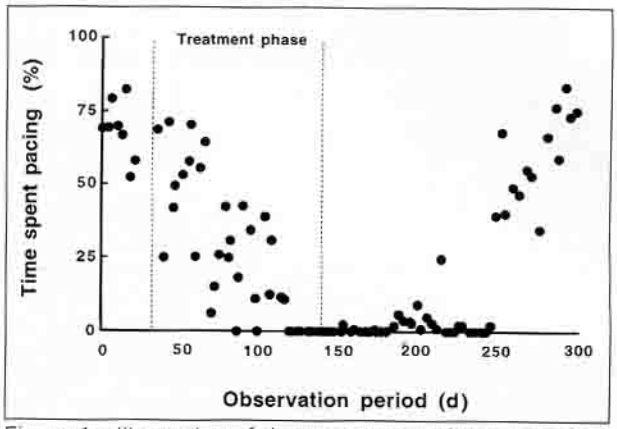

Figure 1—Illustration of the percentage of time a captive polar bear spent pacing during a 300-day period. Percentage of time was determined for a 9-hour recording session during 94 observation periods. Treatment phase indicates the period during which fluoxetine was administered.

During the first part of the treatment phase (days 33 to 73), the pacing behavior was similar to that during the pretreatment phase, requiring 13 seconds to complete a pacing cycle. However, between days 74 to 90 (6 to 10 weeks into the treatment phase), we observed a decrease in the number of pacing bouts, and the mean duration for a bout of pacing decreased to 9.1 minutes (42 cycles).

Pacing bouts during the later part of the treatment phase (days 90 to 116), just prior to cessation of pacing, became progressively shorter. The pacing cycle itself deteriorated, and we observed frequent interruptions of the pacing cycle. Eighty-four days after initiation of treatment (day 117), pacing ceased, and the cessation was maintained (Fig 1). From the initiation of treatment until pacing had completely ceased, there was a 0.6035% reduction in pacing/d, as determined by means of linear regression analysis.

Resumption of pacing was first observed 14 days after the cessation of fluoxetine treatment. However, pacing was not observed on each day until 104 days after cessation of treatment. The mean amount of time spent pacing for the last 8 observations in the posttreatment phase was 65.2% and was not significantly different than the mean amount of time spent pacing for the first 8 observations in the pretreatment phase. The last 8 posttreatment observations were similar to the first 8 pretreatment observations, with 13 sec/pacing cycle, a mean duration of 21 min/pacing bout, and a mean of 97 pacing cycles/pacing bout.

The facial tic and huffing/coughing behavior were concurrent with pacing and were not observed when the bear was not pacing. They were observed at a particular time of the pacing cycle, usually when the bear changed direction. The facial tic and huffing/coughing behavior were apparent during the pretreatment phase

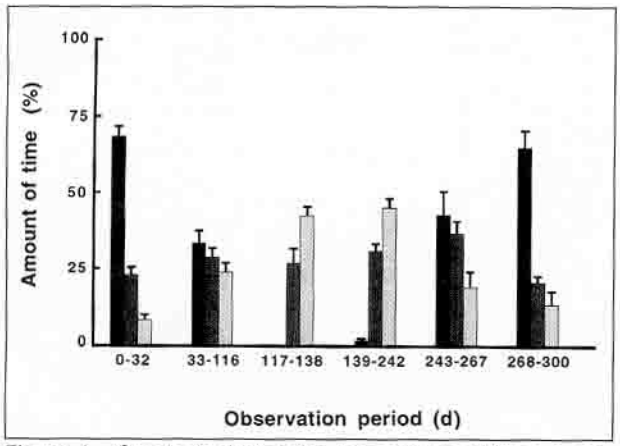

Figure 2—Graph depicting the percentage of time a captive polar bear spent on various activities. Days 0 to 32 corresponded to the pretreatment phase, days 33 to 116 corresponded to the treatment phase when pacing was still evident, days 117 to 138 corresponded to the later part of the treatment phase when pacing had been eliminated, days 139 to 242 corresponded to the posttreatment phase from when the drug was discontinued until the bear resumed pacing on a daily basis, days 243 to 267 corresponded to the later part of the posttreatment phase when pacing was observed daily, and days 268 to 300 corresponded to the last 8 observations. Values reported are mean ± SEM. ■ = pacing; ■ = nonstereotypical mobility; ▒ = immobility.

and the initial part of the treatment phase, but were not evident when the stereotypical pacing behavior ceased. The facial tic and huffing/coughing behavior returned in the posttreatment phase with the resumption of the stereotypical pacing behavior.

Nonstereotypical mobility and immobility—The bear had nonstereotypical mobility a mean of 29.1% of the time during the 300-day period. Nonstereotypical mobility scores were fairly consistent and ranged from a high during the late posttreatment phase (days 243 to 267) of 37.8% to a low during the last 8 sessions (days 268 to 300) of 21.0%. The amount of time that the bear spent immobile varied considerably and tended to be inversely proportional to the amount of time spent pacing (Fig 2).

Daily behavioral routine—During the pretreatment phase (days 0 to 32) and the last 8 sessions of the posttreatment phase (days 268 to 300), we observed that a bout of pacing was most frequently followed by a bout of swimming, which then was followed by another pacing bout. The pace-swim-pace pattern was disrupted for some period of time by introducing food or a novel object into the enclosure. However, after the food was consumed or the novelty of the object abated (30 to 60 minutes), the pattern was reestablished. Although many captive polar bears have stereotypical swimming behaviors,[3] the bear described here did not exhibit any clearly identifiable or consistent stereotypical swimming behavior.

During the 300-day period, the amount of time spent engaged in nonstereotypical mobility remained relatively constant; however, the types of locomotor behavior the bear engaged in did vary. Although practically all of the typical locomotor behaviors observed during periods of high amounts of pacing were swimming and feeding, during the late part of the treatment phase when the bear did not pace, it was observed to spend more time walking about the enclosure, gazing outside of the enclosure, and playing with various objects in the enclosure.

During the early part of the treatment phase (days 33 to 116) and the early part of the posttreatment phase (days 139 to 242), the bear was observed sleeping for bouts of 30 minutes. The amount of time the bear spent sleeping during these 2 phases accounted for < 5% of its time. Sleeping was never observed during the 9-hour recording session during other phases.

Laboratory analysis—Results of CBC and serum biochemical analyses were within reference ranges, except for the cholesterol concentration on day 83 (15.6 nmol/L; reference range, 7.18 ± 1.14 nmol/L).

Stereotypical behavior is defined as the excessive, invariant, and repeated production of 1 type of motor act in which an obvious goal or function is not apparent.[4,5] Stereotypical behaviors are commonly found in human beings[6,7] and among various domestic[7-12] and nondomestic captive[13-16] animal species. A large proportion (55 to 100%) of captive polar bears have been reported to exhibit stereotypical behaviors, most often expressed as pacing.[17-19] In fact, pacing is so common among polar bears that the Dutch language contains the verb "ijsberen" (to polar bear), which is translated as walking up and down restlessly.[3] Similar to the bear reported here, afflicted polar bears may spend most of their waking time performing stereotypical behaviors, and for this reason, such behaviors are believed to constitute a major animal health issue. The most important finding was that fluoxetine administration caused dramatic reduction and eventual elimination of the chronic stereotypical behavior in this captive polar bear. The bear remained active and consistently had high degrees of nonstereotypical locomotor behavior throughout the observation period. Furthermore, the bear did not appear to suffer adverse effects from the treatment and had typical polar bear behavior during the later part of the treatment phase and also after cessation of treatment.

Past attempts by zoo professionals to reduce stereotypical behavior in bears have focused almost exclusively on enrichment programs.[3,20-23] Although enrichment programs have decreased the amount of time that some bears engaged in stereotypical behaviors,[20,21,23] the decrease often was only observed for hours or days. Furthermore, even intensive enrichment programs have failed to completely eliminate stereotypical behavior in bears.[20-23] In the bear described here, pharmacologic manipulation of the serotonergic system, in concert with the enrichment programs already in place, completely eliminated stereotypical behaviors.

Causes of stereotypical behaviors are most likely heterogeneous in origin. One suggested cause of stereotypical behaviors in captive animals is that they are housed in impoverished environments that lack natu-

ralistic cues and features.[4,5,10,14,17,19] We agree with this general assertion. However, on the basis of this bear's response to treatment, it was likely that there was an endogenous neurochemical (serotonin) abnormality that was expressed as stereotypical behavior. Descriptions of stereotypical behaviors in captive and domestic animals have numerous commonalities with the descriptions of **obsessive-compulsive disorder (OCD)** in human beings.[24-29] There is evidence that a common link between stereotypical behaviors in animals and OCD in human beings may be the serotonergic system.[12,24-33] Fluoxetine and its major metabolite, norfluoxetine, function as potent and selective 5-hydroxytryptamine reuptake inhibitors.[34] Although fluoxetine is not more efficacious than established tricyclic compounds, its high degree of selectivity reduces adverse effects associated with the use of tricyclic compounds. Fluoxetine has been used successfully for the treatment of stereotypical disorders[35] such as OCD, Tourette's syndrome, anorexia nervosa, bulimia, and trichotillomania in human beings as well as stereotypical paw licking in dogs.[36]

Pathologic repetition can develop at various functional levels.[4] The bear described here had repetitive behaviors at the motor execution level (facial tic and huffing/coughing), the motor program level (pacing), and, perhaps to some degree, at the planning level (pace-swim-pace routine). When repetitive behaviors develop at more than one of these levels, failure in a control system is believed to be responsible.[4] Analysis of the data reported here indicated that the serotonin reuptake inhibitor, fluoxetine, could be effective for treatment of problems at all functional levels and further supported the involvement of the serotonergic system in stereotypical behaviors.

Although serum fluoxetine and metabolite concentrations were within the ranges reported as therapeutic for human beings,[34] there was a switch in the predominant metabolite from fluoxetine at the low dosage to norfluoxetine at the high dosage. This suggested that, similar to the situation in human beings, fluoxetine itself may not substantially contribute to the therapeutic response and that the active pharmacologic agent may be the metabolite norfluoxetine. Clearance of all metabolites was confirmed within 4 weeks of drug withdrawal, which was expected on the basis of the elimination half-life of metabolites in human beings. The relatively rapid resumption of pacing and the reappearance of the facial tic and huffing/coughing behavior is similar to the return of symptoms observed after drug withdrawal in human beings with OCD or Tourette's syndrome.

We believe that it is essential to understand the neurobiologic aspects of stereotypical behaviors if we are to improve practices of husbandry that will abolish or minimize the causes and not just treat the symptoms of CNS dysfunction. We should determine the lowest dosage that can be used to maintain animals that are free of stereotypical behaviors and should document the effectiveness of fluoxetine treatment in polar bears and other captive species exhibiting stereotypical behaviors. Further, we advocate that pharmacologic treatment of stereotypical behavior be used in conjunction with improvements in naturalistic enclosure design and environmental enrichment programs.

[a]Ivomec, Merck Agvet, Merck Frosst Canada Inc, Kirkland, Quebec, Canada.

[b]Omnivore chow, Unifeed, United Grain Growers Ltd, Calgary, Alberta, Canada.

[c]Prozac, Eli Lilly Co, Indianapolis, Ind.

[d]Telazol, Fort Dodge Laboratories, Fort Dodge, Iowa.

[e]Kodak Ektachem, Eastman Kodak Co, Rochester, NY.

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