A new method of monitoring motor activity in baboons

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Movement activity of a normal baboon and of a baboon with induced Parkinsonism by unilateral administration of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) was recorded by the Walter Reed Activity Monitor (or actigraph). Mean activity in the lesioned baboon was 41% less than that of the nonlesioned baboon measured over a 14-day period. In addition, the daily maximum activity value was significantly less in the MPTP-treated baboon. Moreover, resting and sleeping periods were 30% greater in the lesioned animal. The akinesia and resting and sleeping periods were displayed by the lesioned baboon throughout the day, whereas the control baboon showed them only at night. The data representing summarized movement activity are in accordance with observations of bradykinesia, hypokinesia, and akinesia of the MPTP-treated baboon. The actigraph was well tolerated by the animal because its small size and weight made it largely unobtrusive. We suggest that the actigraph is an appropriate device for measuring motor activity in nonhuman primates.

It is well known that the most debilitating feature of Parkinson's disease is the inability to rapidly and easily perform the most ordinary volitional motor activities. The bradykinesia (slowness of volitional movements), hypokinesia (diminished involuntary movements), and akinesia (inability to carry out involuntary movements) have also been seen in the animal model of Parkinson's disease after 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) treatment (Adams & Victor, 1989). Hence, locomotor activity is one of the parameters for measuring the level of response to treatment in MPTP-lesioned animals.

There are many different procedures for measuring motor activity in nonhuman primates (Bankiewicz et al., 1988; Dubach, Schmidt, Martin, German, & Bowden, 1988; Fine et al., 1988; Lange et al., 1992; Mavridis, De-

gryse, Lategan, Marien, & Colpaert, 1991; Rouillard, Be-
dard, & Di Paolo, 1990; Schneider et al., 1992; Tryon,
1991, pp. 60-63). One procedure is to observe the animal
and count the activity. This allows differentiation into the
various types of movement, such as climbing activity, lo-
comotion and gait, gross upper and lower limb move-
ment, fine motor skills, bradykinesia, dyskinesia (abnor-
mal involuntary movements), posture, resting and intention
tremor, balance, grooming ability, involuntary arrest dur-
ing attempted movements, and eating ability (Schneider
et al., 1992). However, this procedure has the disadvan-
tage of being very labor intensive (at least two observers
are required for objective scoring), limited measuring
time, and, in particular, the difficulty of measuring in the
dark cycle. Continuous counting of motor activity is also
possible in activity cages equipped with photocells (Lange
et al., 1992), but these cages have a limited number of sets
of infrared photocells, so that activities can be missed.
Additionally, if the room housing the animal is used for
other experiments, measurements can be taken only at
certain times.

In addressing the concerns noted above and to allow
for continuous collection of data up to 30 days, an acti-
graph designed for human use was attached to the upper

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arm of a control baboon and of an MPTP-treated baboon. For baboons, attachment to the wrist would mean almost immediate attempts to rip (or bite and chew) the actigraph off. Hence, the upper arm was chosen to be less accessible and therefore less vulnerable to tampering by the animal. Since movement recordings are relative and the locations of actigraph placement are the same for both animals (control and lesioned), then direct comparisons may be made as to relative movement activity between the two.

METHOD

Locomotor activity was monitored by the Walter Reed Activity Monitoring System (commonly known as an *actigraph*; see Redmond & Hegge, 1985), which consists of a small battery-powered movement device ($4 \times 6.5 \times 1.5$ cm, 75 g) and a read-out unit interfaced with a personal computer (PC). Movement is detected by a piezoelectric accelerometer contained within the measuring device, and the resulting electronic signal is processed, digitized, and stored in its memory. The actigraph is initialized on the read-out unit via software in the PC to establish identification, date, time, and epoch length prior to use. Once initialized, the actigraph is removed from the read-out unit and worn as an ambulatory monitor by means of Velcro straps on the wrist or other limbs. It is worth noting that the actigraph may be initialized to record at a future time and date, which allows transporting it to distant locations for use. The actigraph was run in zero crossing mode, so that the number of counts per epoch reflect the number of signal (transduced from the sensor) excursions above and below the referenced threshold. The output of counts is a relative measure of movement activity. The length of time an actigraph may be worn is dependent on epoch length. An epoch length of 1 min, for example, allows continuous data collection of at least 11 days. The data are retrieved via the read-out unit and transferred directly to the PC for analysis by software algorithms to distinguish between wakefulness and sleep. Empirically determined threshold values set the criteria below which sleep is assumed, and the actigraph record is scored on an epoch-to-epoch basis accordingly (Tryon, 1991, pp. 161–166).

The Walter Reed actigraph is uniaxial. Although the movement behavior of the animals extends through all three physical planes, the difference among the axes diminishes at longer epoch lengths. Redmond et al. (1985) have pointed out that, according to the study of Webster, Messin, Mullaney, and Kripke (1982), the signal from one axis was about as good as that of another and that movement seldom occurs solely in the single axis, but counter movements involving the other axis almost always occur in the same epoch.

The control baboon (*Papio anubis*), a 20-kg male adult, was anesthetized with an intramuscular injection of 8 mg/kg of Saffan (alfadolone and alfaxalone acetate, Pitman-Moore, Harefield, Uxbridge, Middlesex UB9 6LS, UK) in order to attach the actigraph to his upper left arm above the elbow with two Velcro straps and with tape completely wrapped around the actigraph (Figure 1). In a second male baboon (26 kg), a unilateral lesion was made by administration of MPTP, a dopaminergic neurotoxin, via the right internal carotid artery as previously described (Guttman et al., 1988), 10 months before the behavioral test. The lesion was confirmed by a dopamine reuptake site using single photon emission computed tomography (SPECT) and iodine-123 labeled RTI-55 (3β -(4-[123I]iodophenyl)tropan-2 β -carboxylic acid methyl ester) as a ligand (Shaya et al., 1992). The actigraph was placed on the baboon's left arm as described above. The animals were kept under the same conditions. Measurements were taken over a 14-day period. The neurobehavior of both baboons was recorded on videotape. Two neurologists blind to the nature of the experiment independently observed the neurobehavior of the MPTP-treated baboon.

Figure 1. Baboon with an attached actigraph on its left upper arm completely wrapped with tape.

Differences were tested using an unpaired two-tail Student's *t* test. Differences were considered significant at $p < .05$. All data are shown in mean $\pm$ standard error of the mean.

RESULTS

Because of their small size and low weight, the actigraphs were well tolerated by the animals. The 24-h activity session was delineated for each day and showed different patterns (data collection epochs of 2-min duration) between the normal and the lesioned baboon (Figure 2). The control baboon had sleep or resting periods only in the dark (night) cycle, but the Parkinsonian baboon showed these periods throughout the day. To determine the changes between the lesioned and the nonlesioned animal, the mean activity value, the maximum activity value, and sleep and wake epochs were counted (see Table 1). The mean activity value was reduced in the MPTP-lesioned baboon by 41.1%. Measuring the maximum activity over each day's period within the 14 days, a significant difference of 65.6% was found between the nonlesioned and the lesioned baboon. The lesioned baboon had 69.9% more sleep or resting epochs than did the control baboon. Sleep-to-wake ratio (counted in minutes) displayed a significant difference between the 2 animals. The lesioned animal showed a 43.7% increase.

Both neurologists concurred in their neurobehavioral observations. Both found a generalized bradykinesia with diminished spontaneous movements, especially on the left side and associated with abnormal posturing of the left arm without apparent loss of strength. A circling behavior with rotation toward the side of the lesion was also

Figure 2. The 24-h activity sessions in (a) a normal baboon and (b) a MPTP-treated baboon. Activity values represent relative activity counts per 2.4 min, abscissa, time of day.

noted. Tremor was not noted. There was no neurobehavioral abnormality on the control baboon.

DISCUSSION

The neurologists' observations of behavior such as hypokinesia, bradykinesia, and akinesia are in accordance with the significant differences in the mean activity value, maximum activity value, and resting epochs measured by the actigraph.

In the MPTP-treated baboon, the actigraph measured sleeping epochs that included phases of akinesia and sleep. Those were distributed throughout the daytime. The control baboon, on the other hand, was active during the light cycle so that there were no phases of akinesia. This was in accordance with the neurobehavioral observations.

The advantages of the actigraph over other locomotor measuring procedures for nonhuman primates are the following: (1) its small size, (2) its acceptable tolerance by the animal, (3) the possibility of measuring the activity in a continuous period up to 30 days by summarizing activity within 2-min periods, (4) the possibility of establishing the starting time independently from that at which the actigraph is actually attached to the animal,

and (5) the prospect of examining further the behavioral and physiological correlates of the activity.

It is critical to use caution when applying the actigraph to the animal's upper arm. To prevent venous and lymphatic stasis and local injuries, the straps should not be applied too tightly. Because the posture of the baboon's upper arm remains mostly in a flexion position, the actigraph was kept in position even when the straps were somewhat loose. In one baboon, the actigraph was attached for up to 2 months. Differences between the right and left limbs may be observed by attaching actigraphs on both extremities. In an ongoing study, actigraphs are being well tolerated on both upper arms for over 2 weeks.

Although the actigraph is an objective measuring device of locomotor activity, it cannot replace visual observation for verifying the MPTP lesion; a neurologist and a dopamine-uptake study will still be necessary. Furthermore, turning behavior, dyskinesias (Van Hilten et al., 1993), ataxia, and tremor cannot be determined by the actigraph. Nevertheless, an objective measure of the influence on locomotor activity after special treatment in induced Parkinsonism may be obtained by using the actigraph, which can be very helpful in tracking subtle changes in the

Table 1
Differences in Movement Activity of a Unilateral MPTP-Lesioned Baboon and a Control Baboon

	Baboon				Student's <i>t</i> Test (Unpaired Two-Tail)		
	Control		MPTP-Treated		<i>n</i>	<i>t</i>	<i>p</i>
	<i>M</i>	<i>SEM</i>	<i>M</i>	<i>SEM</i>			
Maximum activity value	682.9	±24.3	448.3	±7.9	14	4.88	.00014
Mean activity value	105.5	±10.0	62.2	±8.4	14	2.39	.028
Sleep epochs	613.1	±53.3	877.3	±64.9	14	2.41	.028
Sleep-to-wake ratio	0.8	±0.08	1.7	±0.4	14	3.55	.003

frequency and temporal distribution of movement and activity. The actigraph could be useful for locomotor activity studies in nonhuman primates in other movement disorders, such as Huntington's disease (Hantraye, Riche, Maziere, & Isacon, 1990).

Recently, it has been shown in humans (Van Hilten et al., 1993) that this type of activity monitoring can be used as an objective quantitative assessment in Parkinson's disease, since data from clinical scores and activity measured by the activity monitor were well correlated. Human monitoring is feasible throughout the 24-h day while at home (and therefore hospitalization is not necessary) to indicate progress of the disease or in the case of drug treatment to monitor any potential improvement by the observation of whether movement activity is normal, sufficient, and so on. Furthermore, Parkinson's disease is not the only pathology amenable to monitoring by actigraph. The actigraph could be used to monitor activity in other diseases, such as attention-deficit hyperactivity disorder, Tourette's syndrome, and so on. Movement in one part of the body can involuntarily cause movement of the limb.

In conclusion, this report suggests that the actigraph, which has been approved and well tolerated in humans for over 10 years, is also well tolerated in baboons. Neurobehavioral examination and in vivo radiolabeled ligand imaging of the dopamine reuptake sites remain necessary for the verification and assessment of the extent of MPTP-induced nigro-striatal lesions. However, the actigraph is very helpful in evaluating the effects of such lesions and those of subsequent treatments on the locomotor activity and its diurnal variation in baboons.

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