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Protocol status: Working We use this protocol and it's working

Rating scale for parkinsonian motor signs in macaques and other non-human primates

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ABSTRACT

This protocol details rating scale for parkinsonian motor signs in macaques and other non-human primates.

ATTACHMENTS

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PROTOCOL REFERENCES

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GUIDELINES

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Appendix 1: Description of individual score criteria

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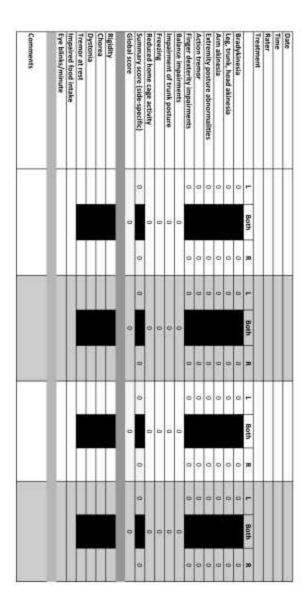
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Eye blinks/minute	ř	Tremor at rest (present/absent)	Oystonia Sut (present/absent) mu boo	(/absent)	Rigidity Mu	The following items do no	Reduced home cage Pov activity hor	Freezing Dis	Impairment of trunk Tru posture (su	Balance impairments clin	Finger dexterity Diffingairments pic	Action tremor that	Extremity posture durin abnormalities digits wrist	Arm akinesia mo	Leg, trunk, head Pov akinesia leg	100 m
	Change in amount and type of food eaten		Substained and abnormal muscle contractions. Note body part(s) affected.	Involuntary large amplitude movements (e.g. arm swings).	Muscle stiffness	ot count for the total scor	Poverty of movement in home cage	Disruption of ongoing movement (usually gait)	Trunk postural impairment (such as stooping)	Problems normally climbing a perch	Difficulty with grasping or picking movements	Oscillatory movements that appear with movement	d postures, such as: not fully extended g locomotion, curled , flexed elbow and/or	Amount of arm movements	Poverty of movement in legs, trunk or head	STOWNISSO OF THE VESTIGATION
N/a	Regular intake of chow, fruits, vegetables, and treats	N/a	N/a		Normal tone	The following items do not count for the total score, but are helpful to fully describe the parkinsonian state:	Normal activity in home cage	No freezing episodes	Head above shoulder level, slight back curve, gaze unrestricted	No impairment	Normal ability to move fingers	No tremor	No abnormal postures	Normal amount of movement	Normal number of movements	and the special of the section of
n/a	Eats treats, fruits and veggies, but reduced regular chow intake	n/a	n/a	n/a	Slight rigidity, 1-2 limbs	e the parkinsonian state:	reactive	Few (<3) or short (<5 s) episodes	Head tilted forward; slightly hunched, Head at shoulder level, noticeable gaze at or below horizon hunched over, gaze below horizon	Single episode of imbalance (e.g., clumsy mounting and dismounting perch) during a 15 minute observation period	Some failures to pick up small items	Tremor appears < 10% of time when monkey is moving	Abnormal postures appear occassionally	Slightly reduced number of movements	Slightly reduced number of movements	observation time
n/a	Eats small amounts of regular chow or soft chow. Eats treats or drinks liquids if offered	n/a	n/a	n/a	Moderate rigidity, 2-4 limbs		Spends most time not moving, still reactive	Several episodes (3-5 per 15 minutes), lasting >5s	f, Head at shoulder level, noticeable hunched over, gaze below horizon	Some episodes of imbalance (loses balance moving to or from perch, use Frequent epis of the cage wall for support), with falling other episodes of normal balance	Fine finger movements fail 50% of the time	Appears with 10-50% of movements	Abnormal postures appear intermittently	Moderately reduced number of movements (reaches ocassionally)	Moderately reduced number of movements	Monroson Support Controls times
n/a	Cannot take any food without external help or medication	n/a	n/a	n/a	Severe rigidity, 2-4 limbs		Does not react, does not move	Many episodes (>5 per 15 minutes) lasting > 5s	Head below shoulder level, gaze at floor	Frequent episodes of losing balance, falling	Not able to use fingers for fine reaching (only gross hand movements).		Abnormal postures appear frequently	Severely reduced number of movements (no reaches)	No movement during observation time	secure discussion of the secure
Single number	Item is compared to animal's baseline	Binary Item (yes or no); tremor at rest is rarely present in parkinsonian macaques	Binary item (yes or no)	Binary item (yes or no)	Examined by physical examination		Item is compared to animal's baseline				Item is compared to animal's baseline	Action tremor is not per se a parkinsonian sign, but is often present with significant effort or exertion	*	Item is compared to animal's baseline	Item is compared to animal's baseline	irem is compared to ailman's pasemie

Appendix 2: Example scoring sheet (4 days)



Description of rating scale

1 Parkinsonian motor signs in macaques closely resemble findings in humans. To quantify the degree of parkinsonism in our animals, we use the rating scale reproduced on the next two pages. There are a variety of such scales available, each differing slightly by areas of emphasis. 1-3

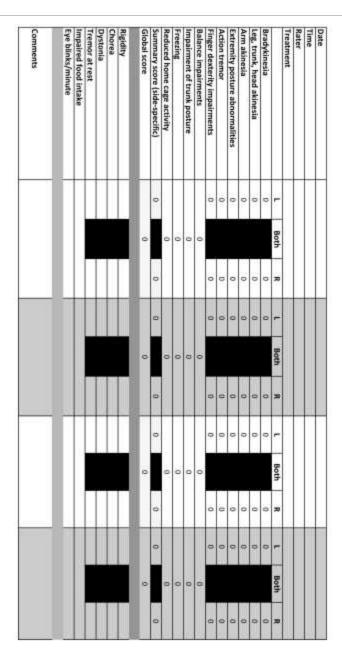
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- 2 The scale emphasizes akinesia, bradykinesia and gait instability.
 - The definition of the individual scale components is provided in appendix 1, and a sample scoring sheets (for 4 observations) is provided in appendix 2.
 - The quantification of the chosen parkinsonian signs can be done based on observation only and can be applied to archival footage (such as video segments). Many of these items can be rated separately for either side (to generate scores for the right (R) or left (L) sides).

Appendix 1: Description of individual score criteria

Eye blinks/minute	impaired food intake	(present/absent)	Dystonia (present/absent)	(present/absent)	Rigidity	The following items d	Reduced frome cage activity	Freezing	Impairment of trusk posture	Balance impairments	Finger dectarity impairments	Action tremor	Extremity posture abnormalities	Arm akinesia	akinesia	Bradykinesia	
	Ounge in ansuurt and type of food exten		Substained and abnormal muscle contractions. Note body partisl affected.	emplitude movements (e.g. arm raings)	Musde stiffness	o mot count for the total sur	home coge	Disruption of ongoing movement [usually gain]	Trunk postural impairment (such as stooping)	Problems normally climbing a perch	Difficulty with grasping or picking movements.	Occidatory movements that appear with movement	Floor postures, such as: limbs not fully extended during locomotion, curied dipits, floor above and/or wrist	Amount of arm movements	legs, trunk or head	Stowness of movements.	Definition
24/4	degular intoke of chow, fruits, vegetables, and treats	N/W	TN/s		Plannal tone	The following terms do not count for the total score, but are helpful to fully describe the parkinsonian state	Normal activity in home cays	No bearing apriories	Head above shoulder level, sight back curve, gase unrestricted	No inquatment	Normal addity to move fingers	No tremor	No abnormal postures	Normal amount of movement	Normal number of receivers	Parmai speed of moverments	.0
Ne	Easts breach, fruits and seggest, but reduced regular thow intake	n/a	2/2	N/a	Staffer rigidley, 3-2 lends	be the parkinsonian state:	less sportaneous activity, less mactive	Faw (<1) or short (<5 t) spicodes	Head 55ed forward; slightly frunched, seed at shoulder level, noticeable gaze of at Selses horizon. hindhed over, gaze Selses horizon.	Single upnote of imbalance (e.g., clumsy mounting and dismounting people during a 35 minute observation period	Some failures to pick up small drains	from appears < 10% of time when monkey is mosking.	Abnormal pattures appear occasionally	Mighilly reduced number of movements	Signify reduced number of requereents	Noticoubly slower , 15-20% time of observation time	1
75/10	Eats small amounts of regular chow or soft chee. Eats wests or strinks liquids if offered.	nda	nda	n/a	Middenite egithly, 2-4 lends		Spends most time not moving, still reactive	Several opisodos (3-5 per 15 minutes), lasting >5s.	Lifesal at shoulder level, noticeable hundred over, gaze below hurson	Some episodes of embalance (boats balance moving to or from perch, we of the cage wall for support, with other episodes of normal balance	Fire flager remements fail 50% of the time	Appears with 10-50% of movements	Absormal postures appear interestinantly	Moderately reduced number of movements (reaches occasionally)	Moderately reduced number of requerements	Platicionality skywart, 20-50% tome	*
N/A	Cernot take any food without external help or medication	n/a	n/a	n/a	Severe rigidity, 2-4 lends		Does not react, does not maye	Many optiodes (>5 per 15 minutes) batting > 5+	Head below shoulder level, gaze at fluor	Frequent episodes of losing belance, falling	Not able to use fragers for fine reaching (only gross hand movements).	Present >50% time of movements	Abnormal postures appear frequently	Severely reduced oursion of movements (no reachos):	time	Noticeably slower >50% time	-
Single number	Pen is compared to unimar's baseline	Barary Both (NES or not); tremor at risk is namely present in personantian managers	Binary lam (yes or oo)	Brury turn (yes or red)	Examined by physical examination		Them is correpained to assertal's handline				Them is compared to animal's baseline	Action freezor is not per se a parkinsoran sign, but is often present with significant offert or usertien	*	Tem is compared to unimal's baseline	Hem is compared to arienal's boseline	Hern to compared to animal's baseline	Notice

Appendix 2: Example scoring sheet (4 days)



- 3 Other parkinsonian signs, such as tremor at rest, are inconstant (or not existent) in most non-human primates.
 - Rigidity, another cardinal sign of parkinsonism, is present in many animals, but, because it can only be tested by examination or instrumented studies (torque motor responses), was not included in the main list of items of our scale.
 - These items, in addition to others such as chorea or dystonia, are included in a secondary list, used for documentation purposes only.

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- The 10 primary items of the scale each contribute maximally 3 points (adding up to 30 points total, with overall scores being used for items that are rated separately for the right and left side).
 - We use the summary score to classify animals into those which are mildly parkinsonian (5-10/30 points), moderately parkinsonian (10-20/30 points), and severely parkinsonian (> 20 points).

Use of scale

- It is a challenge to obtain a high-quality record of the animal's spontaneous behavior, as observations in a specialized cage or direct observations by an observer tend to influence the animal's behavior. We therefore typically use the scale to observe animals in their home cages, either in person or (more commonly) on video tape.
- To obtain reliable scores with low variance, the external conditions under which the animal's behavior is examined should remain constant.
 - Among these are the time of day of the observation, the cage position and proximity to other animals in the animal housing area, the lighting, the presence (or absence) of food items, and the presence or absence of auditory or other stimuli that may distract the animals or otherwise interfere with behavior.
- Prior to the induction of parkinsonism, the animal should undergo at least 5 baseline observations against which the subsequent behavioral observations can be judged. 10-20 minutes of observation times will provide adequate sampling of behaviors.