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

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We use this protocol and it's working

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Abstract

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

Attachments



[p5g9bu5cf.pdf](#)

449KB

Guidelines

Appendix 1: Description of individual score criteria

	Definition	0	1	2	3	Notes
Bradykinesia	Slowness of movements	Normal speed of movements	Noticeably slower, .15-20% time of observation time	Noticeably slower, 20-50% time	Noticeably slower >50% time	Item is compared to animal's baseline
Leg, trunk, head akinesia	Poverty of movement in legs, trunk or head	Normal number of movements	Slightly reduced number of movements	Moderately reduced number of movements	No movement during observation time	Item is compared to animal's baseline
Arm akinesia	Amount of arm movements	Normal amount of movement	Slightly reduced number of movements	Moderately reduced number of movements (reaches occasionally)	Severely reduced number of movements (no reaches)	Item is compared to animal's baseline
Extremely posture abnormalities	Fixed postures, such as: limbs not fully extended during locomotion, curled digits, flexed elbow and/or wrist	No abnormal postures	Abnormal postures appear occasionally	Abnormal postures appear intermittently	Abnormal postures appear frequently	
Action tremor	Oscillatory movements that appear with movement	No tremor	Tremor appears < 10% of time when monkey is moving	Appears with 10-50% of movements	Present >50% time of movements	Action tremor is not <i>per se</i> a parkinsonian sign, but is often present with significant effort or exertion
Finger dexterity impairments	Difficulty with grasping or picking movements	Normal ability to move fingers	Some failures to pick up small items	Fine finger movements fail 50% of the time	Not able to use fingers for fine reaching (only gross hand movements).	Item is compared to animal's baseline
Balance impairments	Problems normally climbing a perch	No impairment	Single episode of imbalance (e.g.: clumsy mounting and dismounting perch) during a 15 minute observation period	Some episodes of imbalance (loses balance moving to or from perch, use of the cage wall for support), with other episodes of normal balance	Frequent episodes of losing balance, falling	
Impairment of trunk posture	Trunk postural impairment (such as stooping)	Head above shoulder level, slight back curve, gaze unrestricted	Head tilted forward, slightly hunched (gaze at or below horizon)	Head at shoulder level, noticeable hunched over, gaze below horizon	Head below shoulder level, gaze at floor	
Freezing	Disruption of ongoing movement (usually gait)	No freezing episodes	Few (<3) or short (<5 s) episodes	Several episodes (3-5 per 15 minutes), lasting >5s	Many episodes (>5 per 15 minutes) lasting > 5s	
Reduced home cage activity	Poverty of movement in home cage	Normal activity in home cage	Less spontaneous activity, less reactive	Spends most time not moving, still reactive	Does not react, does not move	Item is compared to animal's baseline
The following items do not count for the total score, but are helpful to fully describe the parkinsonian state:						
Rigidity	Muscle stiffness	Normal tone	Slight rigidity, 1-2 limbs	Moderate rigidity, 2-4 limbs	Severe rigidity, 2-4 limbs	Examined by physical examination
Chorea (present/absent)	Involuntary/large amplitude movements (e.g. arm swings)		n/a	n/a	n/a	Binary item (yes or no)
Dystonia (present/absent)	Subsustained and abnormal muscle contractions. Note body part(s) affected.	N/a	n/a	n/a	n/a	Binary item (yes or no)
Tremor at rest (present/absent)		N/a	n/a	n/a	n/a	Binary item (yes or no), tremor at rest is rarely present in parkinsonian macaques
Impaired food intake	Change in amount and type of food eaten	Regular intake of chow, fruits, vegetables, and treats	Eats treats, fruits and veggies, but reduced regular chow intake	Eats small amounts of regular chow or soft chow. Eats treats or drinks liquids if offered	Cannot take any food without external help or medication	Item is compared to animal's baseline
Eye blinks/minute		N/a	n/a	n/a	n/a	Single number

Appendix 2: Example scoring sheet (4 days)

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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
- 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

	Definition	0	1	2	3	Notes
Brachycephalia	Slowness of movements	Normal speed of movements	Noticeably slower, ~15-20% time of observation time	Noticeably slower, ~20-50% time	Noticeably slower, >50% time	Item is compared to animal's baseline
Leg, trunk, head abducts	Poverty of movement in legs, trunk or head	Normal number of movements	Slightly reduced number of movements	Modestly reduced number of movements	No movement during observation time	Item is compared to animal's baseline
Arm abducts	Amount of arm movements	Normal amount of movement	Slightly reduced number of movements	Modestly reduced number of movements (reactive occasionally)	Severely reduced number of movements (no reaction)	Item is compared to animal's baseline
Extremely posture abnormalities	Fixed postures, such as limbs not fully extended during locomotion, curled digits, flexed elbow and/or wrist	No abnormal postures	Abnormal postures appear occasionally	Abnormal postures appear intermittently	Abnormal postures appear frequently	
Action tremor	Oscillatory movements that appear with movement	No tremor	Tremor appears < 10% of time when monkey is moving	Agrees with 10-50% of movements	Present >50% time of movements	Action tremor is not per se a parkinsonian sign, but is often present with significant effort or exertion
Finger dexterity impairments	Difficulty with grasping or picking movements	Normal ability to move fingers	Some failures to pick up small items	Fine finger movements fail 50% of the time	Not able to use fingers for fine reaching (only gross hand movements)	Item is compared to animal's baseline
Balance impairments	Problems normally climbing a perch	No impairment	Single episode of imbalance (e.g., clumsy moving and dismounting perch) during a 15 minute observation period	Some episodes of imbalance (jumps balance moving to or from perch, set of the cage wall for support, with other episodes of normal balance)	Frequent episodes of losing balance, falling	
Impairment of trunk posture	Trunk postural impairment (such as stooping)	Head above shoulder level, slight back curve, gaze unobstructed	Head tilted forward, slightly hunched (gaze at or below horizon)	Head at shoulder level, noticeable hunched over, gaze below horizon	Head below shoulder level, gaze at floor	
Freezing	Disruption of ongoing movement (usually gait)	No freezing episodes	Free (<3) or short (<5 s) episodes	Several episodes (3-5 per 15 min)	Many episodes (>5 per 15 minutes) lasting > 5s	
Reduced home cage activity	Poverty of movement in home cage	Normal activity in home cage	Less spontaneous activity, less reactive	Spent most time not moving, still reactive	Spent not react, does not move	Item is compared to animal's baseline
The following items do not count for the total score, but are helpful to fully describe the parkinsonian state:						
Rigidity	Muscle stiffness	Normal tone	Slight rigidity, 1-2 limbs	Moderately rigidity, 2-4 limbs	Severe rigidity, 2-4 limbs	Comment by physical examination
Chorea (present/absent)	Involuntary large amplitude movements (e.g. arm, tail, leg)	n/a	n/a	n/a	n/a	Binary item (yes or no)
Dystonia (present/absent)	Subtle and/or abnormal muscle contractions. Note body part(s) affected.	n/a	n/a	n/a	n/a	Binary item (yes or no)
Tremor at rest (present/absent)		n/a	n/a	n/a	n/a	Binary item (yes or no). Tremor at rest is rarely present in parkinsonian macaques
Impaired food intake	Change in amount and type of food eaten	Regular intake of chow, fruits, vegetables, and treats	Less intake, fruits and veggies, but not regular chow intake	Less usual amounts of regular chow or with chow. Eats treats or drinks liquids if offered.	Cannot take any food without behavioral help or medication	Item is compared to animal's baseline
Eye blinks/minute		n/a	n/a	n/a	n/a	Single number

Appendix 2: Example scoring sheet (4 days)

Date												
Time												
Rater												
Treatment												
Bradykinesia	L	Both	R	L	Both	R	L	Both	R	L	Both	R
Leg, trunk, head akinesia	0	0	0	0	0	0	0	0	0	0	0	0
Arm akinesia	0	0	0	0	0	0	0	0	0	0	0	0
Extremity posture abnormalities	0	0	0	0	0	0	0	0	0	0	0	0
Action tremor	0	0	0	0	0	0	0	0	0	0	0	0
Finger dexterity impairments	0	0	0	0	0	0	0	0	0	0	0	0
Balance impairments	0	0	0	0	0	0	0	0	0	0	0	0
Impairment of trunk posture	0	0	0	0	0	0	0	0	0	0	0	0
Freezing	0	0	0	0	0	0	0	0	0	0	0	0
Reduced home cage activity	0	0	0	0	0	0	0	0	0	0	0	0
Summary score (side-specific)	0	0	0	0	0	0	0	0	0	0	0	0
Global score	0	0	0	0	0	0	0	0	0	0	0	0
Rigidity												
Chorea												
Dystonia												
Tremor at rest												
Impaired food intake												
Eye blinks/minute												
Comments												

- 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.



- 4 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

- 5 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.
- 6 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.
- 7 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.

Protocol references

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