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#### SUPPLEMENTARY MATERIALS

#### Appendix 1

# Evaluation of heavy metal blood concentrations in patients with essential tremor: A preliminary study\*

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### TRG ESSENTIAL TREMOR RATING ASSESSMENT SCALE (TETRAS®) V 3.1

#### **Activities of Daily Living Subscale**

Rate tremor's impact on activities of daily living (0 - 4 scoring).

#### 1. Speaking

- 0 = Normal.
- 1 = Slight voice tremulousness, only when "nervous".
- 2 = Mild voice tremor. All words easily understood.
- 3 = Moderate voice tremor. Some words difficult to understand.
- 4 = Severe voice tremor. Most words difficult to understand.

#### 2. Feeding with a spoon

- 0 = Normal
- 1 = Slightly abnormal. Tremor is present but does not interfere with feeding with a spoon.
- 2 = Mildly abnormal. Spills a little.
- 3 = Moderately abnormal. Spills a lot or changes strategy to complete task such as using two hands or leaning over.
- 4 = Severely abnormal. Cannot feed with a spoon.

#### 3. Drinking from a glass

- 0 = Normal.
- 1 = Slightly abnormal. Tremor is present but does not interfere with drinking from a glass.
- 2 = Mildly abnormal. Spills a little.
- 3 = Moderately abnormal. Spills a lot or changes strategy to complete task such as using two hands or leaning over.
- 4 = Severely abnormal. Cannot drink from a glass or uses straw or sippy cup.

#### 4. Hygiene

- 0 = Normal.
- 1 = Slightly abnormal. Tremor is present but does not interfere with hygiene.
- 2 = Mildly abnormal. Some difficulty but can complete task.
- 3 = Moderately abnormal. Unable to do most fine tasks such as putting on lipstick or shaving unless changes strategy such as using two hands or using the less affected hand.
- 4 = Severely abnormal. Cannot complete hygiene activities independently.

#### 5. Dressing

- 0 = Normal.
- 1 = Slightly abnormal. Tremor is present but does not interfere with dressing.
- 2 = Mildly abnormal. Able to do everything but has difficulty due to tremor.
- 3 = Moderately abnormal. Unable to do most dressing unless uses strategy such as using Velcro, buttoning shirt before putting it on or avoiding shoes with laces.
- 4 = Severely abnormal. Cannot dress independently.

#### 6. Pouring

- 0 = Normal.
- 1 = Slightly abnormal. Tremor is present but does not interfere with pouring.
- 2 = Mildly abnormal. Must be very careful to avoid spilling but may spill occasionally.
- 3 = Moderately abnormal. Must use two hands or uses other strategies to avoid spilling.
- 4 = Severely abnormal. Cannot pour.

#### 7. Carrying food trays, plates or similar items

- 0 = Normal
- 1 = Slightly abnormal. Tremor is present but does not interfere with carrying food trays, plates or similar items.
- 2 = Mildly abnormal. Must be very careful to avoid spilling items on food tray.
- 3 = Moderately abnormal. Uses strategies such as holding tightly against body to carry.
- 4 = Severely abnormal. Cannot carry food trays or similar items.

#### 8. Using Keys

- 0 = Normal
- 1 = Slightly abnormal. Tremor is present but can insert key with one hand without difficulty.
- 2 = Mildly abnormal. Commonly misses target but still routinely puts key in lock with one hand.
- 3 = Moderately abnormal. Needs to use two hands or other strategies to put key in lock.
- 4 = Severely abnormal. Cannot put key in lock.

#### 9. Writing

- 0 = Normal
- 1 = Slightly abnormal. Tremor present but does not interfere with writing.
- 2 = Mildly abnormal. Difficulty writing due to the tremor
- 3 = Moderately abnormal. Cannot write without using strategies such as holding the writing hand with the other hand, holding pen differently or using large pen.
- 4 = Severely abnormal. Cannot write.

## 10. Working. If patient is retired, ask as if they were still working. If the patient is a housewife, ask the question as it relates to housework:

- 0 = Normal.
- 1 = Slightly abnormal. Tremor is present but does not affect performance at work or at home.
- 2 = Mildly abnormal. Tremor interferes with work; able to do everything, but with errors.
- 3 = Moderately abnormal. Unable to continue working without using strategies such as changing jobs or using special equipment.
- 4 = Severely abnormal. Cannot perform any job or household work.

11.	Overall	disability	with	the	$\mathbf{most}$	affected	task	(Name	task,	e.g.
	using co	omputer m	ouse,	wr	iting,	etc)				

Task	

- 0 = Normal.
- 1 = Slightly abnormal. Tremor present but does not affect task.
- 2 = Mildly abnormal. Tremor interferes with task but is still able to perform task.
- 3 = Moderately abnormal. Can do task but must use strategies.
- 4 = Severely abnormal. Cannot do the task.

#### 12. Social Impact

- 0 = None
- 1 = Aware of tremor, but it does not affect lifestyle or professional life.
- 2 = Feels embarrassed by tremor in some social situations or professional meetings.
- 3 = Avoids participating in some social situations or professional meetings because of tremor.
- 4 = Avoids participating in most social situations or professional meetings because of tremor.

Total for	ADL	Subscale	(	(48)	max
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#### Performance subscale

#### instructions

Scoring is 0-4. For most items, the scores are defined only by whole numbers, but 0.5 increments may be used if you believe the rating is between two whole number ratings and cannot be reconciled to a whole number. Each 0.5 increment in rating is specifically defined for the assessment of upper limb postural and kinetic tremor and the dot approximation task (items 4 and 8). All items of the examination, except standing tremor, are performed with the patient seated comfortably. For each item, score the highest amplitude seen at any point during the exam. Instruct patients not to attempt to suppress the tremor, but to let it come out. Maximum total score is 64.

Head tremor: The head is rotated fully left and right and then observed for 10s in mid position. Patient then is instructed to gaze fully to the left and then to the right with the head in mid position. The nose should be used as the landmark to assess and rate the largest amplitude excursions during the examination.

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0 = no tremor
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- 1 = slight tremor (< 0.5 cm)
- 2 = mild tremor (0.5 < 2.5 cm)
- 3 = moderate tremor (2.5-5 cm)
- 4 =severe or disfiguring tremor (> 5 cm)
- 2. Face (including jaw) tremor: Smile, close eyes, open mouth, purse lips. The highest amplitude of the most involved facial anatomy is scored, regardless of whether it occurs during rest or activation. Repetitive blinking or eye fluttering should not be considered as part of facial tremor.
  - 0 = no tremor
  - 1 = slight; barely perceptible tremor
  - 2 = mild: noticeable tremor
  - 3 = moderate: obvious tremor, present in most voluntary facial contractions
  - 4 = severe: gross disfiguring tremor
- 3. Voice tremor: First ask subject to produce an extended "aaah" sound and "eee" sound for 5 seconds each. Then assess speech during normal conversation by asking patients "How do you spend your average day?".
  - 0 = no tremor
  - 1 = slight: tremor during "aaah" and "eee" and no tremor during speech

- 2 = mild: tremor in "aaah" and "eee" and minimal tremor in speech
- 3 = moderate: obvious tremor in speech that is fully intelligible
- 4 = severe: some words difficult to understand

4. Upper limb tremor: Tremor is assessed during three maneuvers: forward horizontal reach posture, lateral "wing beating" posture and finger-nose-finger testing. Each upper limb is assessed and scored individually. The forward horizontal reach posture is held for 5 seconds. The lateral wing beating posture is held for 20 seconds. The finger-nose-finger movement is executed three times. Amplitude assessment should be estimated using the maximally displaced point of the hand at the point of greatest displacement along any single plane. For example, the amplitude of a pure supination-pronation tremor, pivoting around the wrist would be assessed at either the thumb or fifth digit.

Right Left Task		Task
		Forward outstretched postural tremor: Subjects should bring their arms forward, slightly lateral to midline and parallel to the ground for 5 seconds. The wrist should also be straight and the fingers abducted so that they do not touch each other.
their arms parallel to the ground and flex the elbows so that the hands do not quite touch each other and are at the level of the		Lateral "wing beating" postural tremor: Subjects will abduct their arms parallel to the ground and flex the elbows so that the two hands do not quite touch each other and are at the level of the nose. The fingers are abducted so that they do not touch each other. The posture should be held for 20 seconds.
		Kinetic tremor: Subjects extend only their index finger. They then touch a set object or the examiners finger located to the full extent of their reach, which is located at the same height (parallel to the ground) and slightly lateral to the midline. Subjects then touch their own nose (or chin if the tremor is severe) and repeat this back and forth three times. Only the position along the trajectory of greatest tremor amplitude is assessed. This will typically be either at the nose or at the point of full limb extension.

For all three hand tremor ratings

- 0 = no tremor
- 1 = tremor is barely visible
- 1.5 = tremor is visible, but less than 1 cm
- 2 = tremor is 1 < 3 cm amplitude
- 2.5 = tremor is 3 < 5 cm amplitude
- 3 = tremor is 5 < 10 cm amplitude
- 3.5 = tremor is 10 < 20 cm amplitude
- 4 = tremor is > 20 cm amplitude

5. Lower limb tremor: Raise each lower limb horizontally parallel to the ground for 5 seconds. Then perform a standard heel to shin maneuver with each leg, three times. The maximum tremor in either maneuver is scored, and only the limb with the largest tremor is scored. Tremor may exist in any part of the limb, including foot.

Greatest lower limb score	
	0 = no tremor 1 = slight: barely perceptible 2 = mild, less than 1 cm at any point 3 = moderate tremor, less than 5 cm at any point 4 = severe tremor, greater than 5 cm

6. Archimedes spirals: Demonstrate how to draw Archimedes spiral that approximately fills ¼ of an unlined page of standard (letter) paper. The lines of the spiral should be approximately 1.3 cm (0.5 inch) apart. Then ask the subject to copy the spiral. Test and score each hand separately. Use a ballpoint pen. The pen should be held such that no part of the limb touches the table. Secure the paper on the table in a location that is suitable for the patient's style of drawing. Score the tremor in the spiral, not the movement of the limb.

Right	Left	
		0 = normal 1 = slight: tremor barely visible.
		2 = mild: obvious tremor 3 = moderate: portions of figure not recognizable. 4 = severe: figure not recognizable

7. Handwriting: Have patient write the standard sentence "This is a sample of my best handwriting" using the dominant hand only. Patients must write cursively (i.e., no printing). They cannot hold or stabilize their hand with the other hand. Use a ballpoint pen. Secure the paper on the table in a location that is suitable for the patient's style of writing. Score the tremor in the writing, not the movement of the limb.

0 = normal

1 = slight: untidy due to tremor that is barely visible.

2 = mild: legible, but with considerable tremor.

3 = moderate: some words illegible.

4 = severe: completely illegible

8. Dot approximation task: The examiner makes a dot or X and instructs the subject to hold the tip of the pen "as close as possible to the dot (or center of an X) without touching it, (ideally approximately 1 mm) for 10 seconds ". Each hand is scored separately.

Right	Left	
		0 = no tremor 1 = tremor is barely visible 1.5 = tremor is visible, but less than 1 cm 2 = tremor is 1- < 3 cm amplitude 2.5 = tremor is 3- < 5 cm amplitude 3 = tremor is 5- < 10 cm amplitude 3.5 = tremor is 10- < 20 cm amplitude 4 = tremor is > 20 cm amplitude

- 9. Standing tremor: Subjects are standing, unaided if possible. The knees are 10-20 cm apart and are flexed 10-20°. The arms are down at the subject's side. Tremor is assessed at any point on the legs or trunk
  - 0 = no tremor
  - 1 = barely perceptible tremor
  - 2 = obvious but mild tremor, does not cause instability
  - 3 = moderate tremor, impairs stability of stance
  - 4 = severe tremor, unable to stand without assistance

Total for Performance Subscale (64 max)

ACT/INT \_\_\_\_

#### Appendix 2

#### Fahn, Tolosa, Marin Tremor Rating Scale

1-9 Tremor (rate tremor)  1) At rest (in repose). For head and trunk, when lying down  2) With posture holding  UE: arms outstretched, wrists mildly extended, fingers spread apart  LE: legs flexed at hips and knees; foot dorsi-flexed  tongue: when protruded  head and trunk: when sitting or standing  3) with Action(ACT) and Intention(INT):  UE: finger to nose and other actions  LE: toe to finger in flexed posture	
Definitions for 1-9 0 = None 1 = Slight. May be intermittent 2 = Moderate amplitude. May be intermittent 3 = Marked amplitude 4 = Severe amplitude	
1. Face tremor	REST
2. Tongue tremor	REST
	POST
3. Voice tremor	ACT/INT
4. Head tremor	REST
	POST
5. Right upper extremity tremor	REST
	POST
	ACT/INT
6. Left upper extremity tremor	REST
	POST
	ACT/INT
7. Trunk tremor	REST
	POST
8. Right lower extremity tremor	REST
	POST

9. Left lower extremity tremor	EST
Po	OST
ACT	/INT
10. Handwriting	
Have patient write the standard sentence: "This is a sample of my best handwriting", sign his or her the date.  0 = Normal  1 = Mildly abnormal. Slightly untidy, tremulous  2 = Moderately abnormal. Legible, but with considerable tremor.  3 = Marked abnormal. Illegible  4 = Severely abnormal. Unable to keep pencil or pen on paper without holding hand down with other	
11-13. Ask the patient to join both points of the various drawings without crossing the lines. Test eabeginning with the lesser, without leaning the hand or the arm on the table.	ich hand,
Definitions for 11-13  0 = Normal  1 = Slightly tremulous. May cross lines occasionally.  2 = Moderately tremulous or crosses lines frequently.  3 = Accomplishes the task with great difficulty. Many errors.  4 = Unable to complete drawing.	
11. Drawing A	Right
	Left
12. Drawing B	Right
12. Flaming D	Left
13. Drawing C	Right
	Left
14. Pouring	Right
Use firm plastic cups, about 8 cm tall, filled with water to 1 cm from top. Ask patient to pour water	·
from one cup to another. Test each hand separately.  0 = Normal  1 = More careful that a person without tremor, but no water is spilled.  2 = Spills a small amount of water (up to 10% of the total amount).  3 = Spills a considerable amount of water (> 10-50%)  4 = Unable to pour water without spilling most of the water.	Left
15. Speaking This includes spastic dysphonia if present 0 = Normal 1 = Mild voice tremulousness when "nervous" only 2 = Mild voice tremor, constant 3 = Moderate voice tremor 4 = Severe voice tremor. Some words difficult to understand.	

#### 16. Feeding other than liquids

- 0 = Normal
- 1 = Mildly normal. Can bring all solids to mouth, spilling only rarely.
- 2 = Moderately abnormal. Frequent spills of peas and similar foods. May bring head at least halfway to meet food.
- 3 = Markedly abnormal. Unable to cut or uses hands to feed.
- 4 = Severely abnormal. Needs help to feed.

#### 17. Bringing liquids to mouth

- 0 = Normal
- 1 = Mildly abnormal. Can still use a spoon, but not if it is completely full
- 2 = Moderately abnormal. Unable to use spoon; uses cup or glass
- 3 = Markedly abnormal. Can drink from cup or glass, but needs two hands
- 4 = Severely abnormal. Must use a straw.

#### 18 Hygiene

- 0 = Normal
- 1 = Mildly abnormal. Able to do everything, but is more careful than the average person
- 2 = Moderately abnormal. Able to do everything, but with errors; uses electric razor because of tremor
- 3 = Markedly abnormal. Unable to do most fine tasks, such as putting on lipstick or shaving (even with electric razor), unless using two hands.
- 4 = Severely abnormal. Unable to do any fine-movement tasks.

#### 19. Dressing

- 0 = Normal
- 1 = Mildly abnormal. Able to do everything, but is more careful than the average person.
- 2 = Moderately abnormal. Able to do everything, but with errors.
- 3 = Markedly abnormal. Needs some help with buttoning or other activities, such as tying shoelaces.
- 4 = Severely abnormal. Requires assistance even for gross motor activities.

#### 20. Writing

- 0 = Normal
- 1 = Mildly abnormal. Legible. Continues to write letters
- 2 = Moderately abnormal. Legible, but no longer writes letters.
- 3 = Markedly abnormal. Illegible
- 4 = Severely abnormal. Unable to sign checks or other documents requiring a signature.

#### 21.Working

- 0 = Tremor does not interfere with job
- 1 = Able to work, but needs to be more careful than the average person
- 2 = Able to do everything, but with errors. Poorer than usual performance because of tremor
- 3 = Unable to do regular job. May have changed to a different job because of tremor. Tremor limits housework, such as ironing.
- 4 = Unable to do any outside job; housework is very limited.

Non-Dominant Hand	
Drawings A, B, and C and make with the Left Hand Right Hand	
DRAWING A	DRAWING B
DRAWING C	
•	

Dominant Hand	
Handwriting: This is a sample of my best handwriting	
Signature:  Date:	
Drawings A, B, and C and make with the Left Hand Right Hand	
DRAWING A	DRAWING B
DRAWING C	
•	
•	•