

The sound of Parkinson's disease: a model of audible bradykinesia

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Supplementary files

Appendix 1: Cut-off frequencies for each motor task:

Motor task	Cut-off frequencies (Hz)
Finger tapping	2000
Pronation-supination	1400
Toe tap	2600
Leg agility	2000

Appendix 2: Equations to ascertain audible bradykinesia features

For all equations, time slot 1 is defined as the first half of the audio signal, time slot 2 is defined as the second half of the audio signal.

The threshold to find the peaks with the peak-finder algorithm used the following formula (Eq. (1)):

$$(1) \text{ Th} = \text{mean preprocessed signal} + (n * \text{standard deviation of preprocessed signal})$$

The total number of taps (T_n) was calculated by counting the number of peak locations, which represents the number of taps. The mean change of the number of taps (ΔT_n) over time was calculated by extracting the number of peaks within time slot 1 (T_{n1}) from the number of peaks in time slot 2 (T_{n2}) (Eq. (2)).

$$(2) \Delta T_n = T_{n1} - T_{n2}$$

To determine the average tapping speed (T_s), the number of taps per second were calculated first, hereafter the mean of the number of taps per second was measured (Eq. (3)).

$$(3) T_s = \text{mean}(\text{taps per second})$$

The variation coefficient was defined as the standard deviation of the peaks divided by the mean of the peaks (Eq. (4)). Where σ was the standard deviation and μ was the mean. The variation coefficient (VC) of the tapping speed (VT_s) was measured with the following equation (Eq. (5)).

$$(4) VC = \sigma / \mu$$

$$(5) VT_s = \sigma T_s / \mu T_s$$

The tapping interval was the interval from one peak location to the next peak location. The mean change of the tapping interval was calculated by extracting the tapping interval of time slot 1 (TI_{n1}) from the tapping interval of time slot 2 (TI_{n2}) (Eq. (6)).

$$(6) \Delta TI = TI_{n2} - TI_{n1}$$

The mean change of the average amplitude (ΔTA) was calculated by extracting the average amplitude of time slot 1 ($TAn1$) from the average amplitude of time slot 2 ($TAn2$) (Eq. (7)).

$$(7) \Delta TA = TAn2 - TAn1$$

The mean change of the maximum tapping amplitude (ΔMTA) was calculated by extracting the maximum amplitude of time slot 1 ($MTAn1$) from the maximum amplitude of time slot 2 ($MTAn2$) (Eq. (8)).

$$(8) \Delta MTA = MTAn2 - MTAn1$$

To calculate the hesitations and freezes (F_n) a threshold (ThF) was created. The threshold consisted of the average of all tapping intervals plus two times the SD of the tapping interval on top of this average (Eq. (9)). When the tapping interval was above this threshold, the tapping interval was scored as a hesitation or freeze (F_n).

$$(9) ThF = TI + 2 * TISD$$

Appendix 3: Overview of measured features

Symbol	Feature description	Tapping characteristics	Category
1. Tn	Total number of taps	Speed	2
2. ΔTn	The mean change of the number of taps	Speed	2
3. Ts	Average tapping speed	Speed	2
4. VTs	VC in tapping speed	Speed	2
5. TI	Average tapping interval	Speed	2
6. TISD	SD tapping interval	Speed	2
7. ΔTI	The mean change of tapping interval	Speed	2
8. TA	Average tapping amplitude	Amplitude	1
9. VTA	VC in the tapping amplitude	Amplitude	1
10. ΔTA	The mean change of the tapping amplitude	Decrement in amplitude	3
11. ΔMTA	The mean change of maximum tapping amplitude	Decrement in amplitude	3
12. Fn	Total number of freezes	Hesitations/Halts	4

Legend: Total number of taps (Tn), Mean change of the number of taps over time (ΔTn), Average tapping speed (number of taps/second) (Ts), Variation coefficient (VC), Variation coefficient of the tapping speed (VTs), Tapping interval (TI), standard deviation of the tapping interval (TISD), and mean change of tapping interval (ΔTI), Average tapping amplitude (TA), mean change of the tapping amplitude (ΔTA), variation coefficient of the average tapping amplitude (VTA), Mean change of the maximum tapping amplitude (ΔMTA), Hesitations and freezes (Fn).

Appendix 4: The mean value of each feature and corresponding minimum and maximum values, the number of times the features were selected by LASSO and the mean estimated coefficient each time a feature was selected for each motor task in experiment 1.

Features	Finger Tapping			Pronation Supination		
	Mean (Min-Max)	Selected	Mean Coeff	Mean (Min-Max)	Selected	Mean Coeff
Age	63 (33-86)	28	-0.0358	63 (33-86)	20	-0.0189
Tn	67 (9-117)	37	-0.0098	57 (8-104)	69	-0.0121
ΔTn	6 (-11-33)	11	0.0111	3 (-15-16)	21	0.0191
Ts	2.42 (0.31-4.14)	3	0.5065	2.06 (0.52-3.52)	2	-0.2087
VTs	0.38 (0.12-1.95)	57	2.3303	0.36 (0.12-1.11)	23	1.2582
TI	0.50 (0.25-3.56)	4	1.7261	0.55 (0.29-1.25)	1	0.0341
TISD	0.35 (0.01-7.56)	4	4.1707	0.2 (0.01-1.23)	1	-0.604
ΔTI	0.14 (-0.11- 2.06)	3	0.3951	0.07 (-0.70-1.52)	2	0.9575
TA	0.005 (0.001-0.024)	22	-59.1958	0.037 (0.001-0.145)	78	-9.9076
VTA	47.93 (11.65-215.87)	27	-0.0155	51.4 (10.88-136.44.31)	10	0.0077
ΔTA	-0.001 (-0.014-0.004)	58	304.2296	-0.004 (-0.024-0.025)	16	-9.3153
ΔMTA	0.003 (-0.093-0.034)	26	30.1054	0.011 (-0.024-0.085)	64	17.7261
Fn	3 (0-9)	22	-0.0567	2 (0-10)	59	-0.0955

Features	Toe Tapping			Leg Agility		
	Mean (Min-Max)	Selected	Mean Coeff	Mean (Min-Max)	Selected	Mean Coeff
Age	63 (33-86)	28	-0.0363	63 (33-86)	51	-0.0205
Tn	55 (9-90)	46	-0.0107	59 (17-112)	42	-0.0211
ΔTn	8 (-3-48)	11	-0.0415	2 (-16-24)	85	0.0614
Ts	1.99 (0.36-3.17)	14	-0.3063	2.15 (0.64-3.93)	2	-0.3395
VTs	0.47 (0.00-1.90)	73	1.4157	0.29 (0.07-1.420.73)	76	1.5984
TI	0.58 (0.32-2.49)	8	1.0354	0.54 (0.26-1.04)	16	-4.1476
TISD	0.37 (0.02-3.45)	12	2.3523	0.15 (0.01-2.731)	12	3.1934
ΔTI	0.24 (-0.16-2.19)	0		-0.006 (-2.947-0.739)	0	
TA	0.013 (0.001-0.057)	31	-14.5226	0.047 (0.002-0.208)	21	-2.9158
VTA	51.1 (20.51-113.86)	8	-0.0196	42.1 (12.3-190.5)	50	0.0117
ΔTA	-0.004 (-0.019-0.004)	50	43.3591	-0.003 (-0.019-0.021)	89	-62.2501
ΔMTA	0.007 (-0.022-0.043)	16	-2.741	0.006 (-0.045-0.058)	32	-39.4979
Fn	2.5 (0-8)	9	0.0002	4 (0-18)	100	-0.4936

Legend: Age in years, Total number of taps (Tn), Mean change of the number of taps over time (ΔTn), Average tapping speed (number of taps/second) (Ts), Variation coefficient of the tapping speed (VTs), Tapping interval (TI), standard deviation of the tapping interval (TISD), and mean change of tapping interval (ΔTI), Average tapping amplitude (TA), mean change of the tapping amplitude (ΔTA), variation coefficient of the average tapping amplitude (VTA), Mean change of the maximum tapping amplitude (ΔMTA), Hesitations and freezes (Fn).

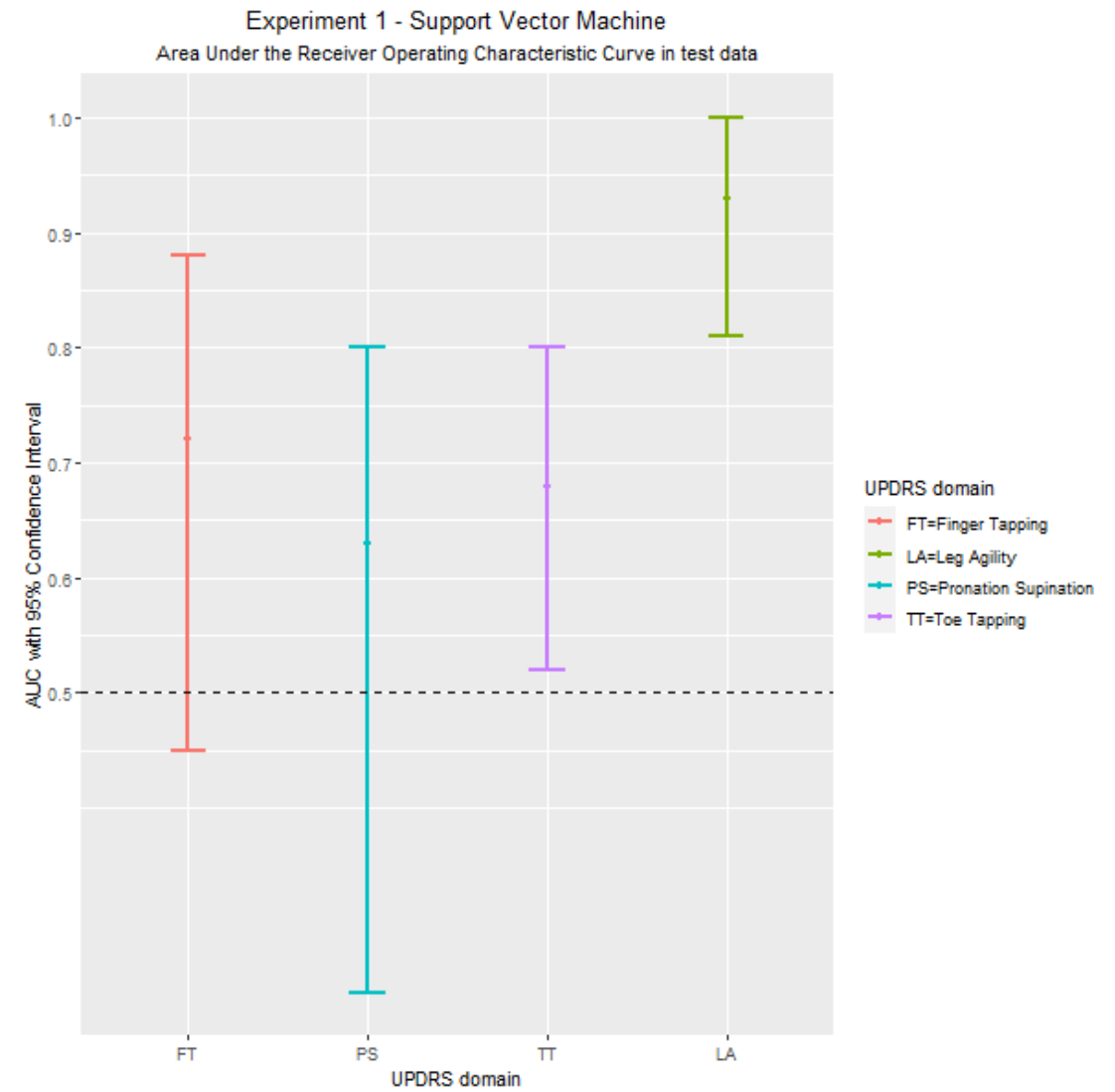
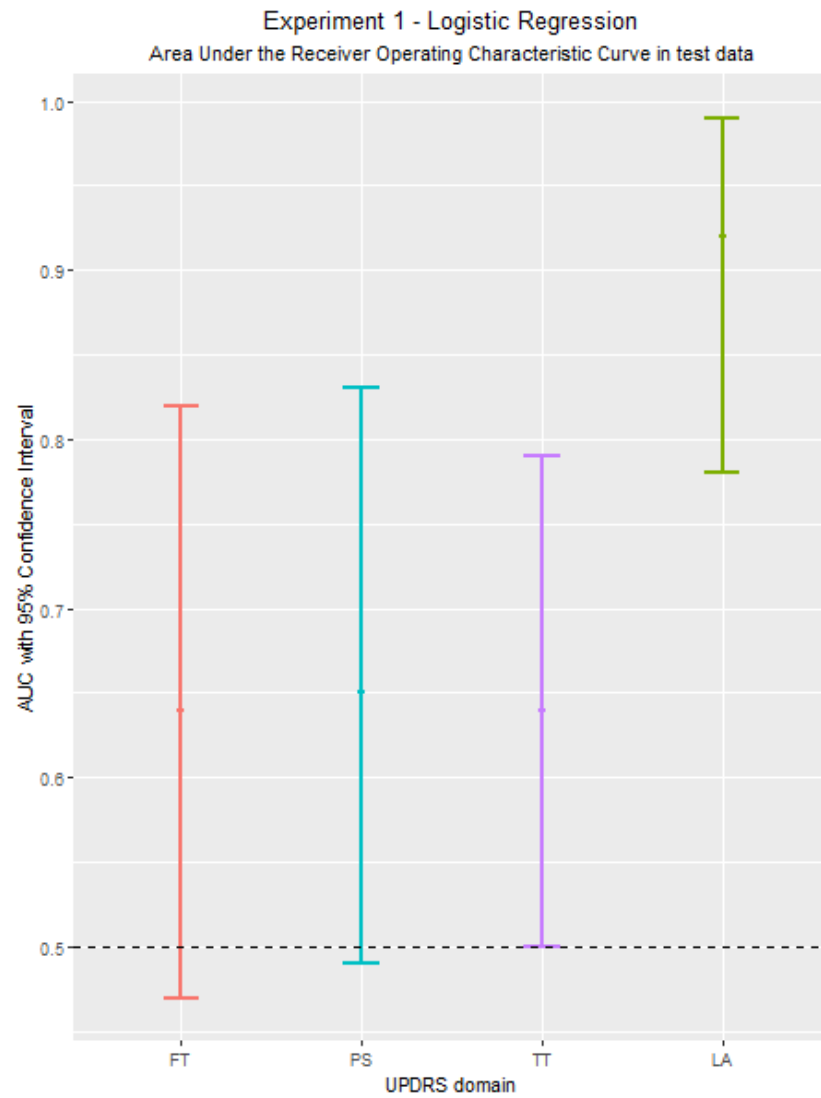
Appendix 5: The mean value of each feature and corresponding minimum and maximum values, the number of times the features were selected by LASSO and the mean estimated coefficient each time a feature was selected for each motor task in experiment 2.

Features	Finger Tapping			Pronation Supination		
	Mean (Min-Max)	Selected	Mean Coeff	Mean (Min-Max)	Selected	Mean Coeff
Age	63 (33-86)	29	0.0318	63 (33-86)	45	0.0395
Tn	62 (9-117)	32	-0.0145	52 (15-83)	13	-0.0284
ΔTn	6 (-6-33)	7	-0.0214	4 (-6-16)	30	0.0503
Ts	2.32 (0.31-4.14)	6	-0.1293	1.93 (0.52-3.00)	0	
VTs	0.43 (0.13-1.95)	67	1.9363	0.4 (0.15-1.15)	81	4.1831
TI	0.55 (0.25-3.56)	2	-0.2884	0.59 (0.35-1.25)	2	1.849
TISD	0.47 (0.01-7.56)	7	-1.3743	0.23 (0.01-1.23)	89	4.4254
ΔTI	0.18 (-0.11-2.06)	0		0.08 (-0.70-1.52)	0	
TA	0.004 (0.001-0.018)	9	-121.1394	0.03 (0.001-0.096)	16	-12.9135
VTA	47.01 (11.65-215.87)	20	0.0053	57.6 (21.28-136.44)	20	0.0159
ΔTA	-0.001 (-0.008-0.001)	4	-209.6158	-0.004 (-0.024-0.013)	5	63.5452
ΔMTA	0.003 (-0.001-0.015)	6	8.3115	0.014 (-0.013-0.085)	23	-12.3028
Fn	3 (0-9)	10	-0.1484	2 (0-8)	21	0.1843

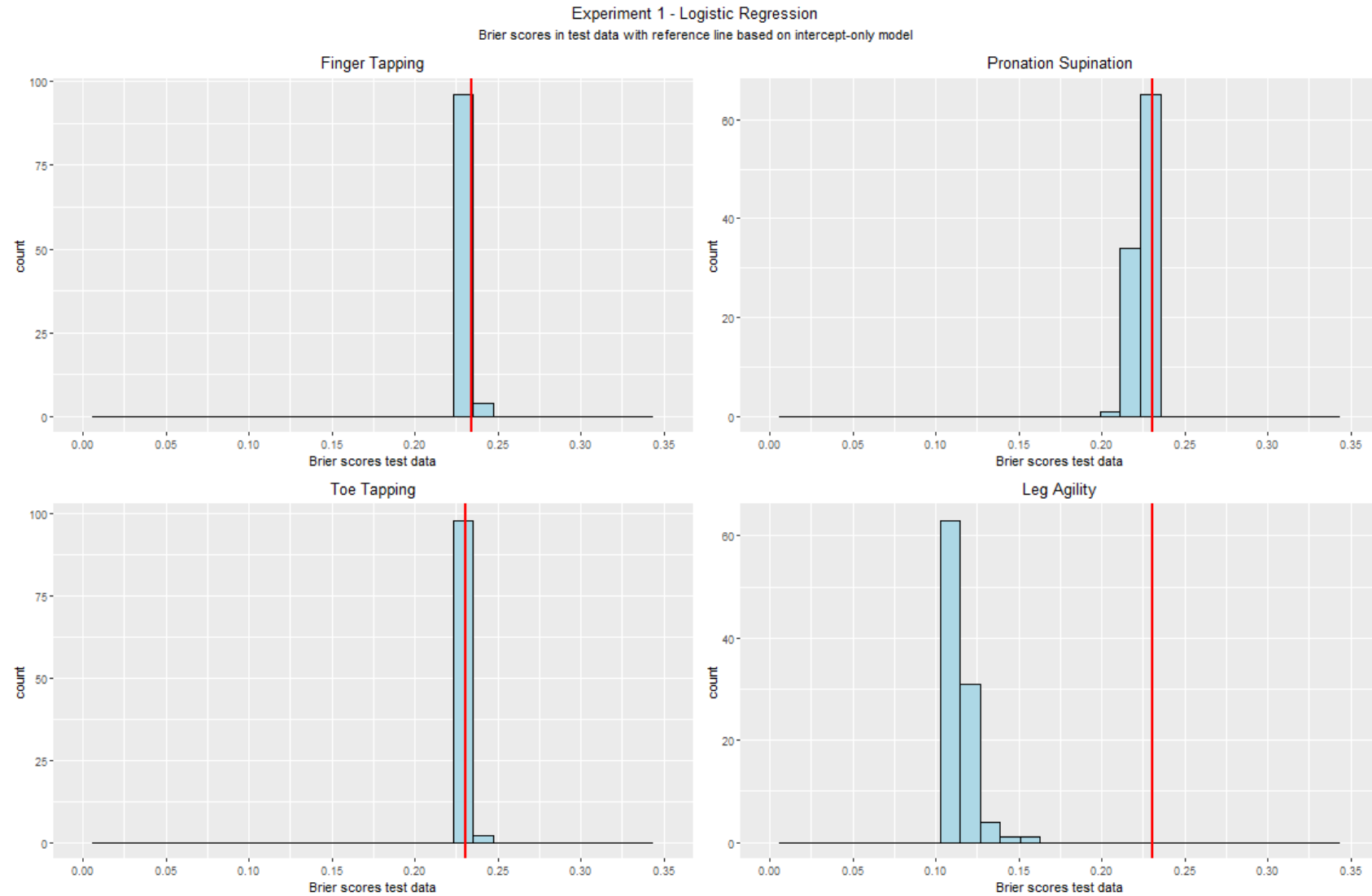
Features	Toe Tapping			Leg Agility		
	Mean (Min-Max)	Selected	Mean Coeff	Mean (Min-Max)	Selected	Mean Coeff
Age	63 (33-86)	14	-0.0111	63 (33-86)	11	-0.0637
Tn	51 (9-85)	82	-0.0274	55 (17-89)	0	
ΔTn	8 (-3-29)	67	0.0505	3 (-16-24)	15	0.0275
Ts	1.86 (0.36-3.04)	7	-1.0483	2.02 (0.64-3.21)	16	1.1776
VTs	0.55 (0.14-1.90)	64	1.5625	0.33 (0.11 – 1.42)	60	3.5157
TI	0.63 (0.34-2.49)	2	-2.3331	0.58 (0.31-1.79)	0	
TISD	0.48 (0.02-3.45)	25	0.5987	0.21 (0.01-2.73)	50	1.7566
ΔTI	0.3 (-0.16-2.19)	7	0.4461	-0.014 (-2.947-0.739)	7	0.7878
TA	0.011 (0.001-0.057)	83	-60.7319	0.044 (0.002-0.208)	43	-29.0704
VTA	52.65 (20.51-113.86)	36	0.0197	45.53 (12.31-190.52)	13	0.003
ΔTA	-0.003 (-0.018-0.004)	2	378.5769	-0.005 (-0.019-0.021)	10	37.3176
ΔMTA	0.006 (-0.022-0.043)	35	59.4609	0.007 (-0.035-0.058)	23	-23.8498
Fn	2 (0-7)	13	0.2703	2 (0-5)	3	0.0055

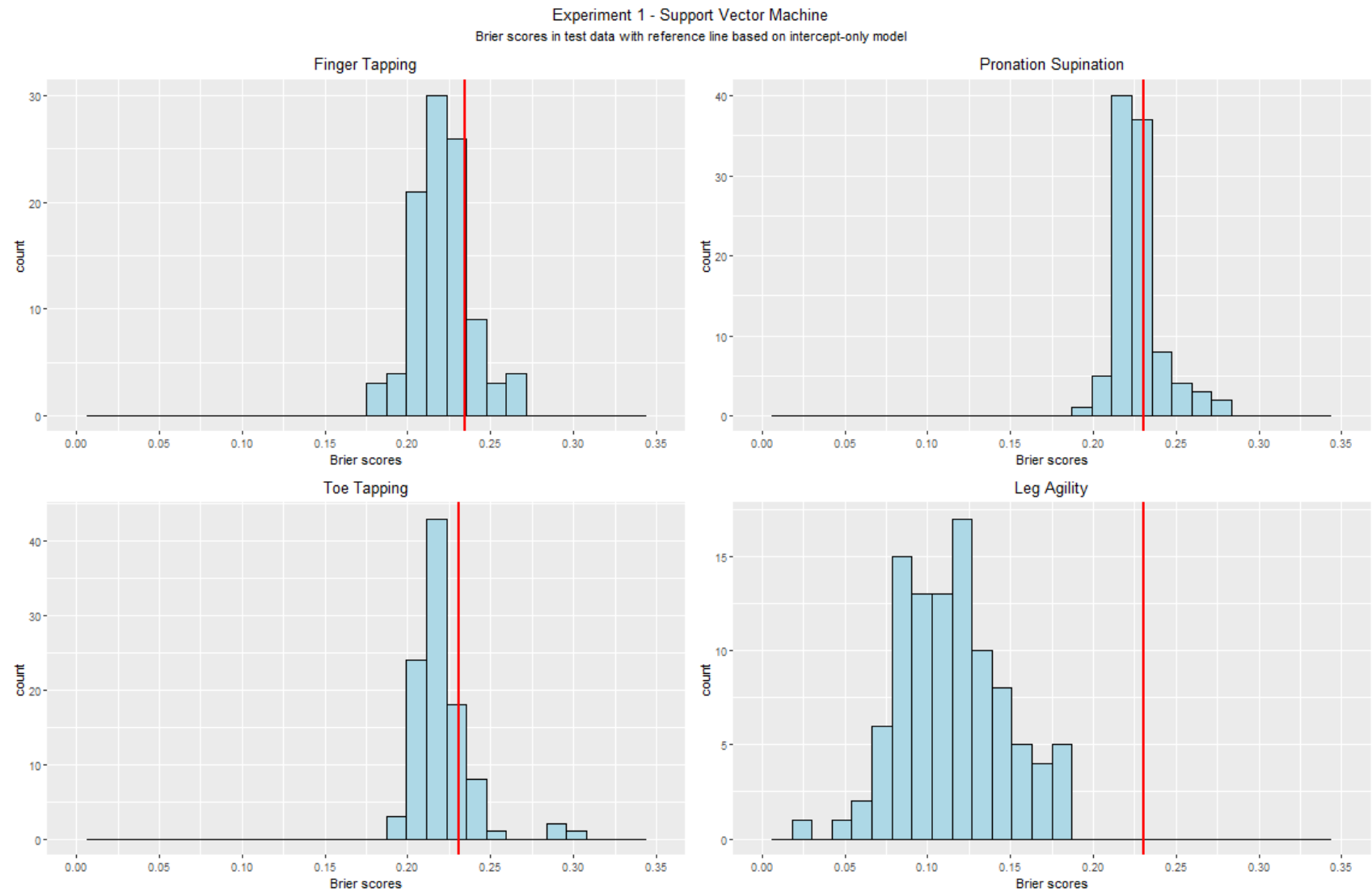
Legend: Age in years, Total number of taps (Tn), Mean change of the number of taps over time (ΔTn), Average tapping speed (number of taps/second) (Ts), Variation coefficient of the tapping speed (VTs), Tapping interval (TI), standard deviation of the tapping interval (TISD), and mean change of tapping interval (ΔTI), Average tapping amplitude (TA), mean change of the tapping amplitude (ΔTA), variation coefficient of the average tapping amplitude (VTA), Mean change of the maximum tapping amplitude (ΔMTA), Hesitations and freezes (Fn).

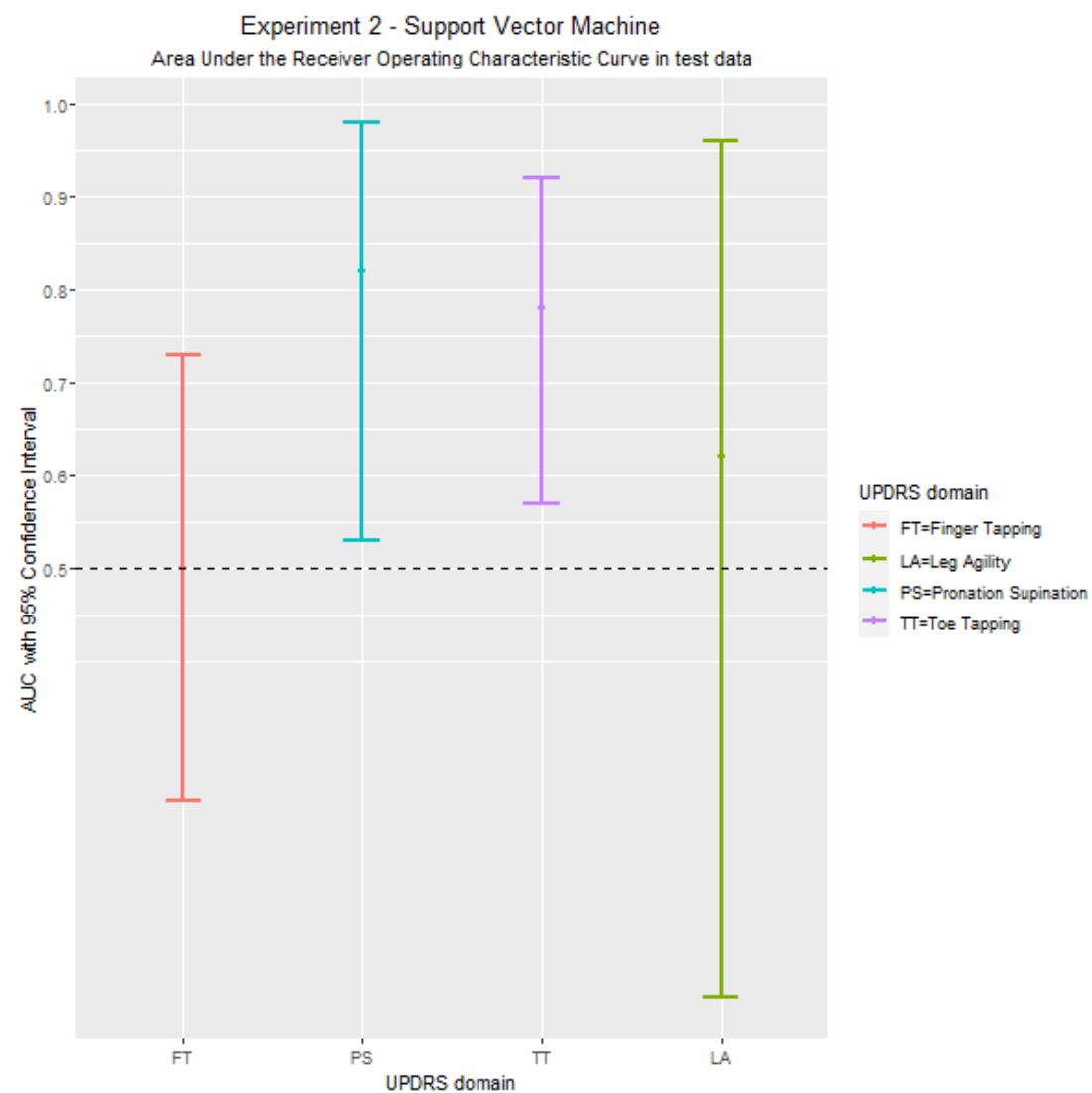
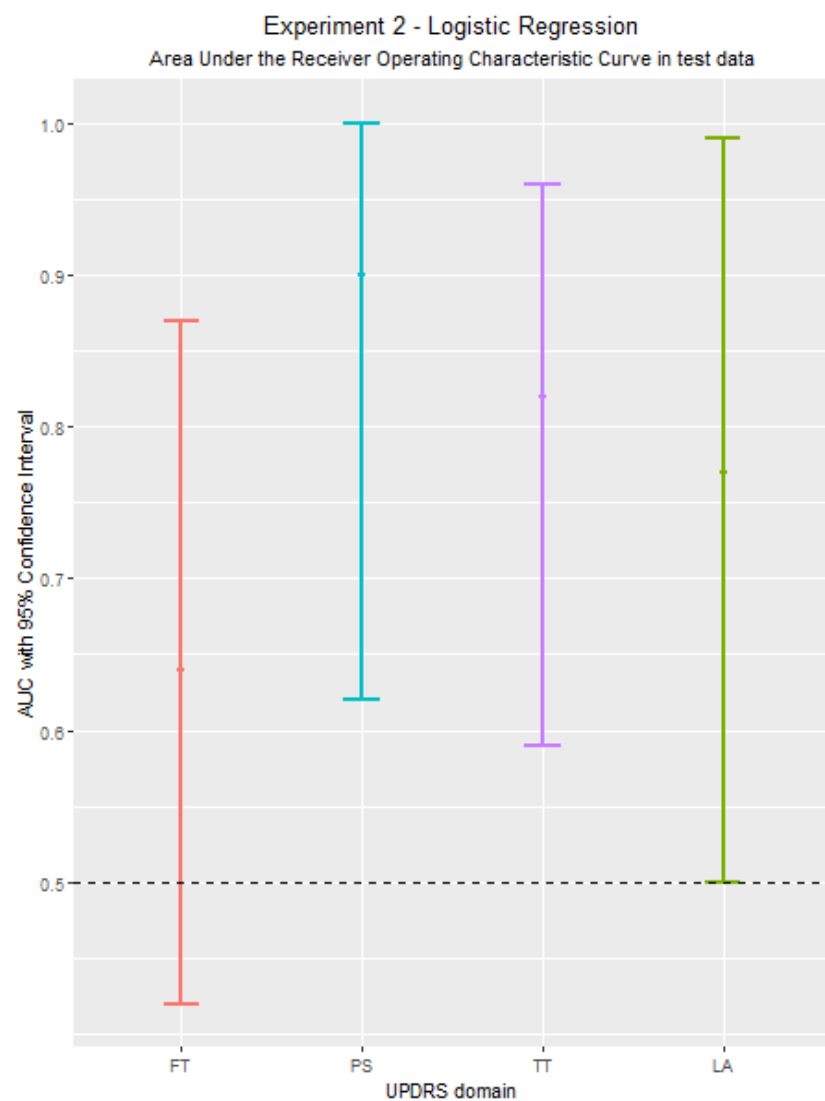
Appendix 6: Error bars of the AUC in the test data for each motor task and each model in experiment 1



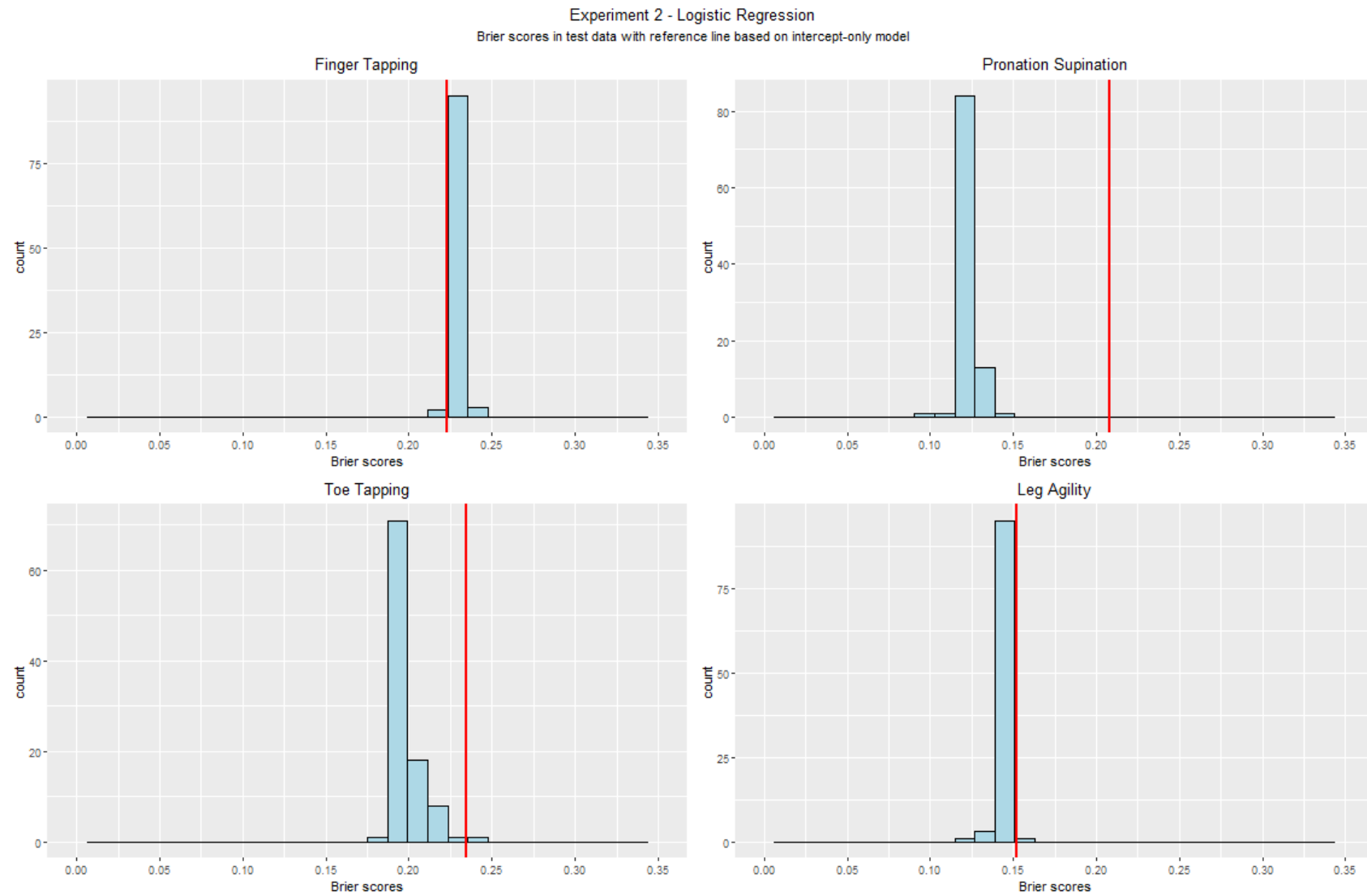
Appendix 7: Brier scores calculated on the test data presented in histograms, together with the Brier score of the intercept-only model for experiment 1. A Brier score of 0 is perfectly accurate, a score of 0.25 is chance and a score of 1 is perfectly inaccurate.





Appendix 8: Error bars of the AUC in the test data for each motor task and each model in experiment 2

Appendix 9: Brier scores calculated on the test data presented in histograms, together with the Brier score of the intercept-only model for experiment 2. A Brier score of 0 is perfectly accurate, a score of 0.25 is chance and a score of 1 is perfectly inaccurate.



Experiment 2 - Support Vector Machine
Brier scores in test data with reference line based on intercept-only model

