

Supplementary Material

Model 1-2: R model specification used in the analysis in the whole sample.

Linear model (1):

```
My.Func.lin <- function(a,MTime,b){a + b * MTime}
```

R code

```
lme.1 <- nlme(  
  BBS ~ My.Func.lin(a, Session, b),  
  data = m.df.long.gr,  
  fixed = list(a + b ~ 1),  
  random = pdCompSymm(a + b) ~ 1 | ID,  
  correlation = corARMA(.5, form = ~Session | ID, p = 1, q = 0),  
  na.action = na.exclude,  
  start = fixef(m.nls)  
)
```

Model summary

```
Nonlinear mixed-effects model fit by maximum likelihood  
Model: BBS ~ My.Func.lin(a, Session, b)  
Data: m.df.long.gr  
      AIC      BIC    logLik  
1796.522 1824.285 -891.2609  
  
Random effects:  
Formula: list(a ~ 1, b ~ 1)  
Level: ID
```

Structure: General positive-definite, Log-Cholesky parametrization

	StdDev	Corr
a	5.1029367	a
b	0.3869307	-0.707

Residual 2.0825171

Correlation Structure: AR(1)

Formula: ~Session | ID

Parameter estimate(s):

Phi
0.3187698

Fixed effects: list(a + b ~ 1)

	Value	Std.Error	DF	t-value	p-value
a	44.99502	0.9768366	359	46.06197	0
b	0.48241	0.0791985	359	6.09114	0

Correlation:

a
b -0.719

Standardized Within-Group Residuals:

Min	Q1	Med
-6.10552678	-0.38998994	0.09381608
Q3	Max	
0.52358753	2.87334355	

Number of Observations: 390

Number of Groups: 30

95% confidence intervals

	lower	est.	upper
a	41.2599478	43.2001180	45.1402883
b	0.3423773	0.4609526	0.5795279

Exponential model (2):

```
My.Func.exp <- function(a,MTime,b, c){a + b * exp(c * MTime)}
```

R code

```
lme.2 <- nlme(  
  BBS ~ My.Func.exp(a, Session, b, c),  
  data = m.df.long.gr,  
  fixed = list(a + b + c ~ 1),  
  random = pdCompSymm(a + b + c) ~ 1 | ID,  
  correlation = corARMA(0.4, form = ~Session|ID, p = 1, q =0),  
  na.action = na.exclude,  
  start = fixef(m.nls)  
)
```

Model summary

Nonlinear mixed-effects model fit by maximum likelihood

Model: BBS ~ My.Func.exp(a, Session, b, c)

Data: m.df.long.gr

	AIC	BIC	logLik
	1687.744	1731.372	-832.8722

Random effects:

Formula: list(a ~ 1, b ~ 1, c ~ 1)

Level: ID

Structure: General positive-definite, Log-Cholesky
parametrization

	StdDev	Corr	
a	4.1960400	a	b
b	9.5529280	-0.198	
c	0.1813014	0.499	0.421
Residual	1.4530890		

Correlation Structure: AR(1)

Formula: ~Session | ID
Parameter estimate(s):
Phi
-0.08364599

Fixed effects: list(a + b + c ~ 1)
Value Std.Error DF t-value p-value
a 52.08854 0.8876217 358 58.68326 0
b -10.27031 1.8249405 358 -5.62775 0
c -0.20882 0.0408072 358 -5.11731 0
Correlation:
a b
b -0.264
c 0.489 0.333

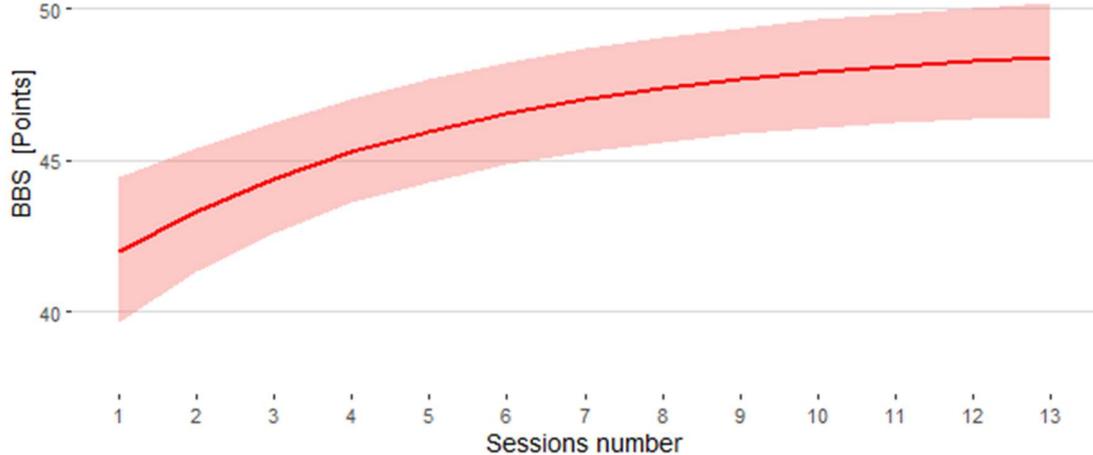
Standardized Within-Group Residuals:
Min Q1 Med
-5.14358990 -0.44233954 0.00637763
Q3 Max
0.53167091 2.95440402

Number of Observations: 390
Number of Groups: 30

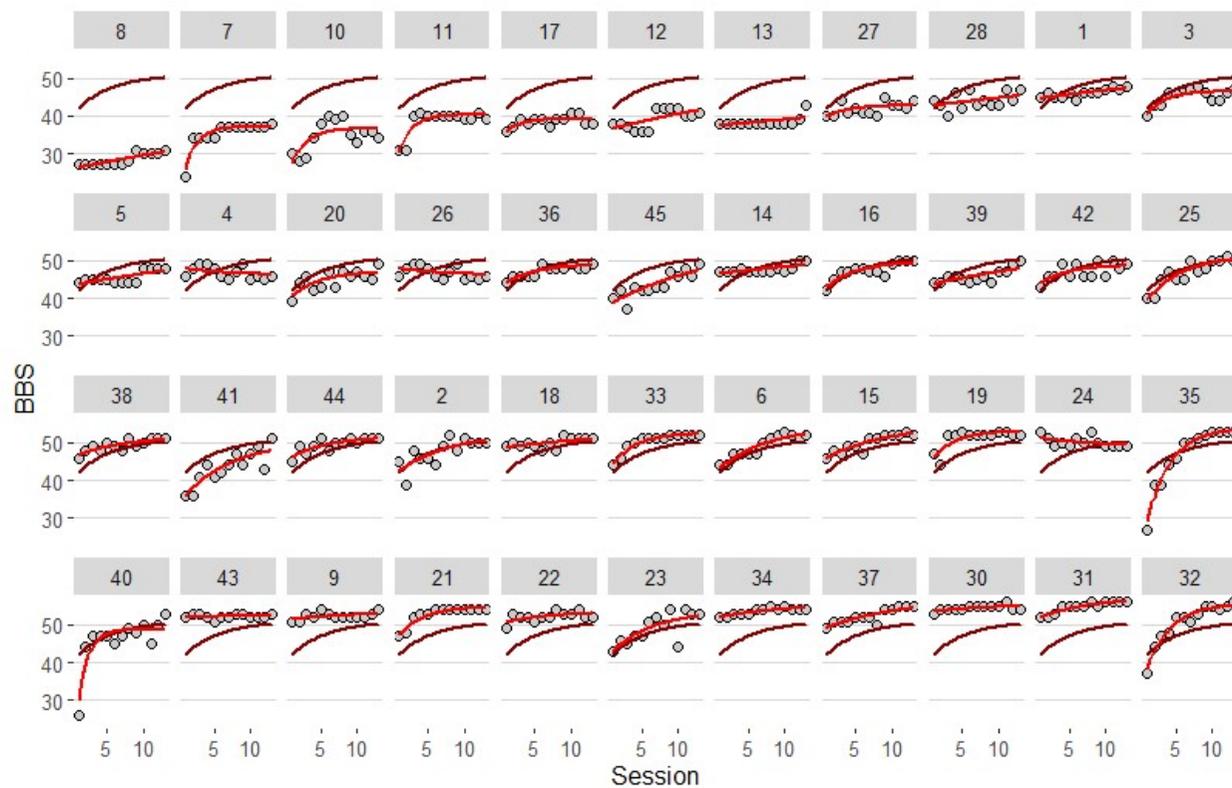
95% confidence intervals
lower est. upper
a 46.971293 48.9865955 51.0018982
b -11.234699 -8.6156474 -5.9965955
c -0.281407 -0.2094444 -0.1374818

Note: parameter "c" represents the rate parameter "alpha"

Supplementary Figure 1a. Model fitting of the exponential mixed model, n = 44

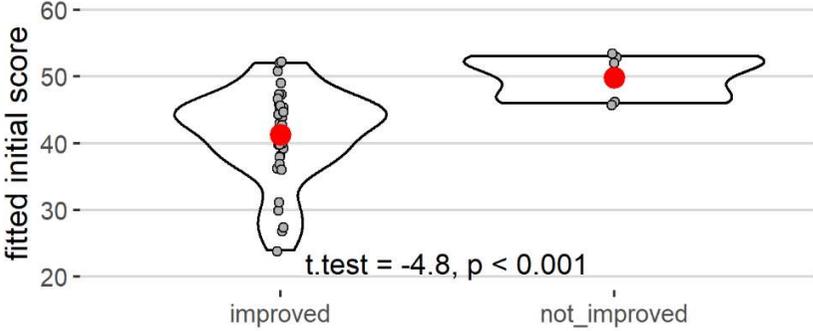


Supplementary Figure 1b. Population's and subject's level fitting of the exponential mixed model, n = 44

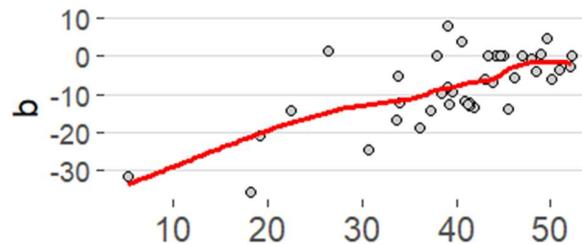
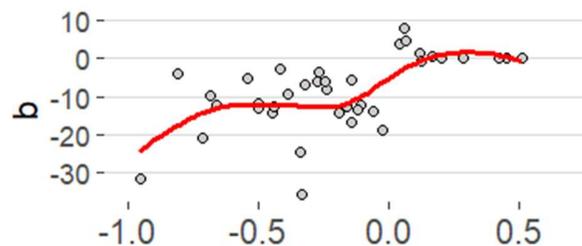
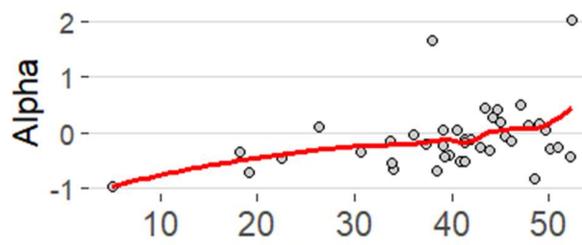
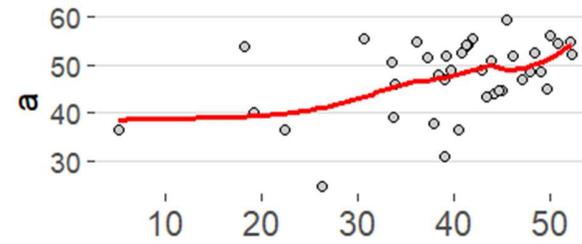
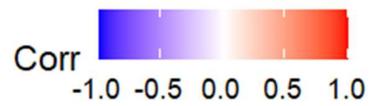
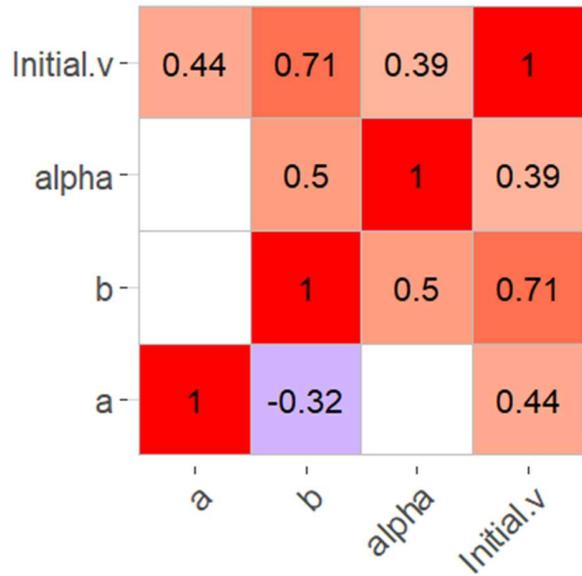


Dark red line: regression line at population level, light red line: regression line at individual level, BBS: Berg Balance Scale

Supplementary Figure 2. BBS scores, n = 44

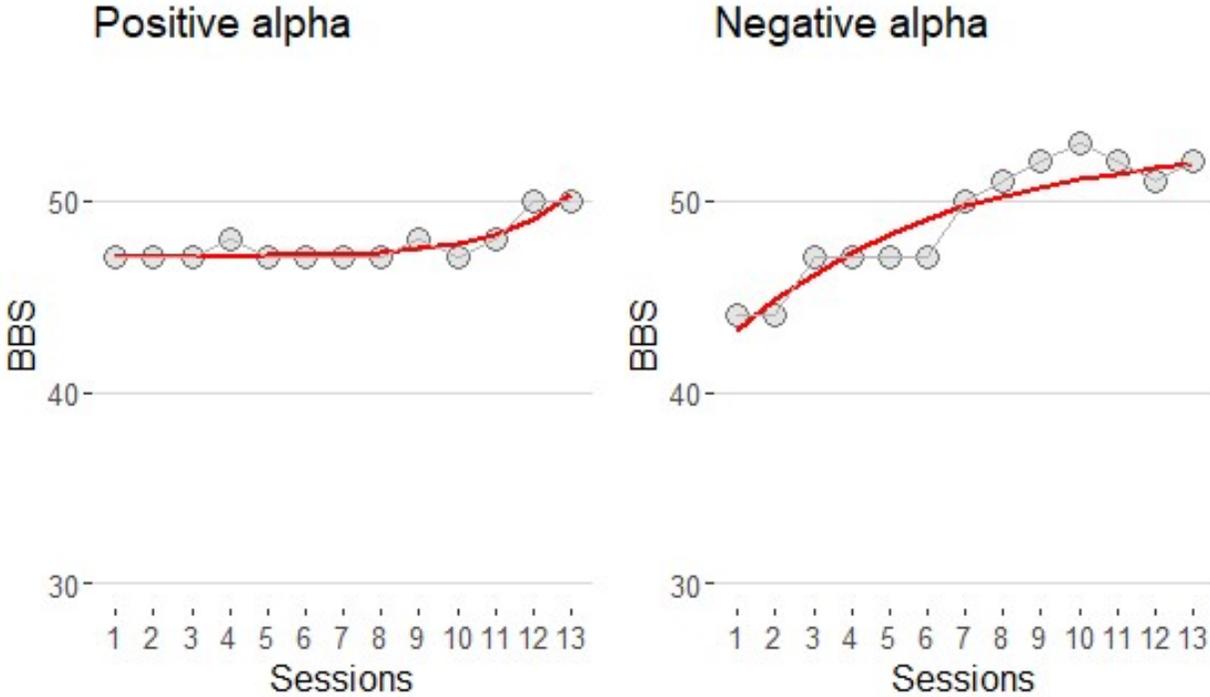


Supplementary Figure 3: bivariate pearson's correlations, n = 44



Initial.v: estimated initial value, a: asymptotic parameter, b: change in the expected value of
estimated BBS from the beginning to the end of treatments, α : rate parameter

Supplementary figure 3: fitted BBS trends for positive and negative α parameter



BBS: Berg Balance Scale

Model 3: R model specification used in the analysis of variability.

```
My.Func.exp <- function(a,MTime,b, c){a + b * exp(c * MTime)}
```

R code

```
lme.var.exp <- nlme(  
  abs.resid ~ My.Func.exp(a, Session, b, c),  
  data = df,  
  fixed = a + b + c ~ 1,  
  random = a + b ~ 1 | ID,  
  correlation = corAR1(form = ~ Session | ID),  
  start = c(a = a0, b = b0, c = c0),  
  method = "ML",  
  na.action = na.exclude,  
  control = nlmeControl(msMaxIter = 300, pnlsMaxIter = 150,  
returnObject = TRUE)  
)
```

```
lme.var.exp.0 <- nlme(  
  abs.resid ~ a,  
  data = df,  
  fixed = a ~ 1,  
  random = a ~ 1 | ID,  
  correlation = corAR1(form = ~ Session | ID),  
  start = list(fixed = c(a = fixef(lme.var.exp)["a"])),  
  method = "ML",  
  na.action = na.exclude,  
  control = nlmeControl(msMaxIter = 300, pnlsMaxIter = 150,  
returnObject = TRUE)  
)
```

Model summary

```
lme.var.exp

Nonlinear mixed-effects model fit by maximum likelihood
Model: abs.resid ~ My.Func.exp(a, Session, b, c)
Data: df.sub
      AIC      BIC    logLik
1510.68  1545.48 -747.344

Random effects:
Formula: list(a ~ 1, b ~ 1)
Level: ID
Structure: General positive-definite, Log-Cholesky
parametrization
      StdDev   Corr
a      0.2759662 a
b      0.0020920 -0.044
Residual 1.0652158

Correlation Structure: AR(1)
Formula: ~Session | ID
Parameter estimate(s):
      Phi
0.2506577

Variance function:
Structure: Power of variance covariate, different strata
Formula: ~Session | ID
Parameter estimates:
      1      2      3      4
-0.24907621  0.17338127 -0.07541306 -0.13883107
      5      6      7      8
-0.29745980 -0.22824239 -0.32760484 -0.30314284
      9     10     11     12
-0.35833195  0.27674840 -0.13078473 -0.09804786
      13     14     15     16
 0.04635818 -0.30433384 -0.16817346 -0.15766689
      17     18     19     20
-0.14596819 -0.16299247 -0.19124527 -0.14887619
      21     22     23     24
-0.61703644 -0.32445674  0.31124694 -0.04661806
```

```

      25          26          27          28
-0.26105171 -0.13883107 -0.08442622 -0.09651209
      30          31          32          33
-0.46219804 -0.66564191 -0.29828813 -0.72154324
      34          35          36          37
-0.47652238 -0.39103144 -0.45628832 -0.11704104
      38          39          40          41
-0.41461807 -0.01153565  0.24097670  0.12034869
      42          43          44          45
-0.16473090 -0.71800459 -0.34199395 -0.07957795

```

```

Fixed effects: a + b + c ~ 1
      Value Std.Error DF   t-value p-value
a  0.4127502 1.1038249 526  0.3739272  0.7086
b  0.8075198 0.9801646 526  0.8238614  0.4104
c -0.0658175 0.1473358 526 -0.4467178  0.6553
Correlation:
a      b
b -0.993
c -0.992  0.975

```

```

Standardized Within-Group Residuals:
      Min      Q1      Med      Q3
-1.8901046 -0.6799129 -0.1099198  0.6896284
      Max
  3.1364829

```

```

Number of Observations: 572
Number of Groups: 44

```

```

95% confidence intervals
      lower      est.      upper
a -1.7500025  0.41275020  2.5755029
b -1.1129421  0.80751979  2.7279817
c -0.3544963 -0.06581752  0.2228613

```

```
lme.var.exp.0
Nonlinear mixed-effects model fit by maximum likelihood
  Model: abs.resid ~ a
  Data: df.sub
      AIC      BIC    logLik
1392.91 1601.669 -648.4551

Random effects:
  Formula: a ~ 1 | ID
              a Residual
StdDev: 0.3021111 1.057047

Correlation Structure: AR(1)
  Formula: ~Session | ID
  Parameter estimate(s):
    Phi
0.2755027
Variance function:
  Structure: Power of variance covariate, different strata
  Formula: ~Session | ID
  Parameter estimates:
      1      2      3      4
-0.23198986 0.19741723 -0.07145936 -0.12094863
      5      6      7      8
-0.32191055 -0.20723058 -0.28114707 -0.30063097
      9     10     11     12
-0.34367116 0.28076794 -0.11228985 -0.07918637
     13     14     15     16
 0.03709865 -0.32581312 -0.14359955 -0.14517158
     17     18     19     20
-0.16206455 -0.14241541 -0.15474443 -0.14592576
     21     22     23     24
-0.60681854 -0.33322289 0.31073811 -0.02686173
     25     26     27     28
-0.22101088 -0.12094863 -0.07343578 -0.09970374
     30     31     32     33
-0.51495126 -0.60999007 -0.27974509 -0.69318067
     34     35     36     37
-0.47897653 -0.33155729 -0.42939134 -0.11164281
```

```

      38      39      40      41
-0.37194979 -0.01215116  0.24249208  0.10359688
      42      43      44      45
-0.15427115 -0.70283531 -0.28800742 -0.06618938
Fixed effects: a ~ 1
      Value Std.Error DF t-value p-value
a  0.9104695 0.06069611 528 15.00046      0

Standardized Within-Group Residuals:
      Min      Q1      Med      Q3
-1.86486352 -0.64141260 -0.07922236  0.70653721
      Max
  3.29298689

Number of Observations: 572
Number of Groups: 44

95% confidence intervals
      lower      est.      upper
a  0.7913383 0.9104695 1.029601

Note: parameter "c" represents the rate parameter "alpha"

```

ANOVA output

```

anova(lme.var.exp.0, lme.var.exp)

      Model df      AIC      BIC      logLik
lme.var.exp.0      1 48 1392.910 1601.669 -648.4551
lme.var.exp      2 52 1389.606 1615.761 -642.8030
      Test L.Ratio p-value
lme.var.exp.0
lme.var.exp      1 vs 2 11.30425  0.0233

```

Model 4: R model specification used in the analysis to compare specific and unspecific treatment.

```
My.Func.exp <- function(a,MTime,b, c){a + b * exp(c * MTime)}
```

R code

```
lme.group <- nlme(  
  BBS ~ My.Func.exp(a, Time, b, c),  
  data = df,  
  fixed = list(a ~ BBS0z, b ~ 1, c ~ Group),  
  random = a ~ 1 | ID,  
  na.action = na.exclude,  
  start = c(fixef(m0_t), 0, -0.05),  
  control = nlmeControl(msMaxIter = 500, pnlsMaxIter = 250,  
  returnObject = TRUE)  
)
```

Model summary

```
lme.group  
  
Nonlinear mixed-effects model fit by maximum likelihood  
Model: BBS ~ My.Func.exp(a, Time, b, c)  
  
Data: df  
  
      AIC      BIC  logLik  
2708.24 2738.684 -1347.12  
  
Random effects:  
Formula: a ~ 1 | ID  
      a.(Intercept) Residual  
StdDev:      3.029173 2.255137  
  
Fixed effects: list(a ~ BBS0z, b ~ 1, c ~ Group)  
              Value Std.Error DF  t-value p-value
```

```

a. (Intercept) 49.05312 0.5643522 525 86.91934 0e+00
a.BBS0z      4.18426 0.4728112 42 8.84975 0e+00
b           -6.35175 0.3828827 525 -16.58927 0e+00
c. (Intercept) -0.09765 0.0226710 525 -4.30737 0e+00
c.GroupT     -0.19102 0.0505407 525 -3.77947 2e-04
Correlation:
      a. (In) a.BBS0 b      c. (In)
a.BBS0z    -0.027
b          -0.415 0.059
c. (Intercept) 0.373 -0.111 -0.384
c.GroupT     0.207 0.093 -0.025 -0.302

Standardized Within-Group Residuals:
      Min      Q1      Med      Q3      Max
-6.74973806 -0.47928481 0.02132345 0.55487254 3.17958846

Number of Observations: 572
Number of Groups: 44

95% confidence intervals
      lower      est.      upper
a. (Intercept) 47.9493083 49.05311785 50.15692744
a.BBS0z      3.2342674 4.18425941 5.13425146
b           -7.1006214 -6.35174578 -5.60287017
c. (Intercept) -0.1419942 -0.09765233 -0.05331044
c.GroupT     -0.2898687 -0.19101686 -0.09216499
    
```

Note: parameter "c" represents the rate parameter "alpha"

Please note that in the above model we included baseline BBS as a covariate on the intercept/asymptote parameter (a), so that between-group comparisons are made conditional on baseline performance. Group differences were then tested on the rate parameter (c), which captures the speed of change over sessions, rather than relying on raw differences that could reflect pre-existing disparities. We also explored adding a within-subject residual

correlation structure (e.g., AR(1)) given the repeated-measures design; however, in this dataset the resulting nonlinear mixed model was not identifiable and failed to converge. Therefore, we retained the more parsimonious model with subject-level random effects and independent residuals, which provided stable estimates and directly addresses the baseline imbalance concern.

Supplementary table 1a. clinical characteristics

	Specific Treatment, n = 14					Unspecific Treatment, n = 14				
	Mean	sd	median	Min	Max	mean	sd	median	min	Max
Age (Years)	56.7	9.9	61.0	37.0	68.0	56.5	14.2	60.0	27.0	62.0
Onset (Years)	18.2	9.2	14.0	4.0	36.0	16.8	10.3	14.5	1.0	38
EDSS (points)	5.7	0.8	6	4.5	6.5	6.5	0.50	6.5	5.5	7
BBS (points)	42.6	6.9	44	26	52	39.3	8.3	42	24	51

Supplementary table 1b. a, b and rate parameter (α) for the Treated and control group

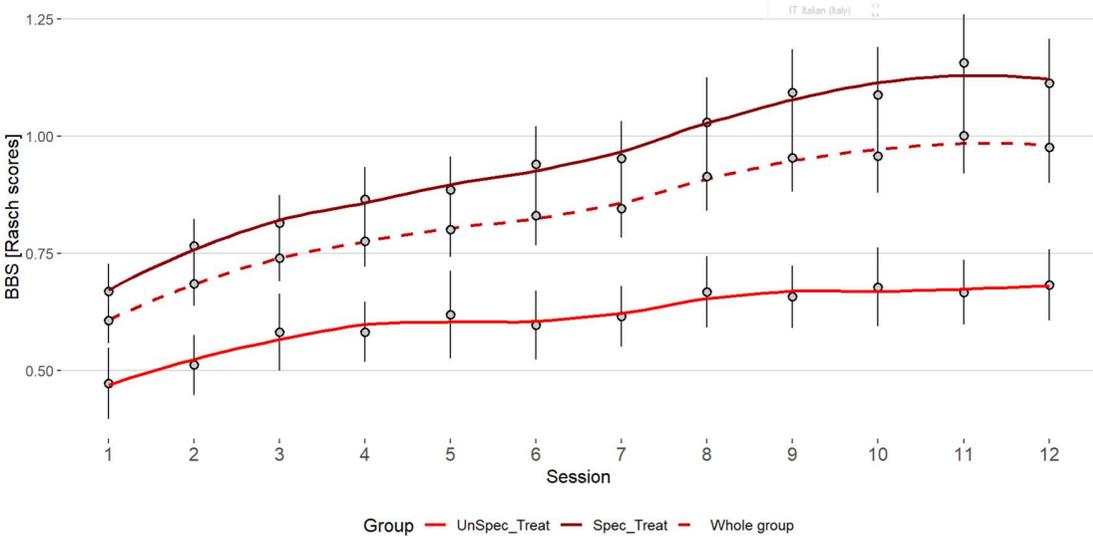
Model fit and random effects**Fixed effects**

Parameter	Estimate	SE	DF	t	p
a.(Intercept)	49.05	0.56	525	86.91	<0.001
a.BBS0z	4.18	0.47	42	8.85	<0.001
b	-6.35	0.38	525	-16.58	<0.001
c.(Intercept)	-0.09	0.02	525	-4.30	<0.001
c.GroupT	-0.19	0.05	525	-3.77	0.0002

Component	Estimate
AIC	2708.24
BIC	2738.68
logLik	-1347.12
Random effect SD (a intercept, ID)	3.02
RMSE	2.25

Rasch analysis

Supplementary fig 5. BBS, rasch scores



Dot and whiskers: Mean and standard error of mean

Models 3-4: R model fitting of BBS rasch values for the exponential and linear models.

```
My.Func.lin <- function(a, Session, b){a + b * Session}

My.Func.exp <- function(a, Session, b, c){a + b * exp(c * Session)}

m.lme.2.lin <- nlme(
  BBS ~ My.Func.lin(a, Session, b),
  data = m.df.long.gr,
  fixed = list(a + b ~ 1),
  random = pdCompSymm(a + b) ~ 1 | ID,
  correlation = corARMA(.5, form = ~ Session | ID, p = 1, q = 0),
  na.action = na.exclude,
  start = fixef(m.nls)
)

m.lme.2.exp <- nlme(
  BBS ~ My.Func.exp(a, Session, b, c),
  data = m.df.long.gr,
  fixed = list(a + b + c ~ 1),
  random = pdCompSymm(a + b) ~ 1 | ID,
  correlation = corARMA(0.4, form = ~ Session | ID, p = 1, q = 0),
  na.action = na.exclude,
  control = nlmeControl(msMaxIter = 400, pnlsMaxIter = 200,
returnObject = TRUE),
  start = fixef(m.nls2)
)
```

Model summary

m.lme.2.lin

Nonlinear mixed-effects model fit by maximum likelihood
Model: BBS ~ My.Func.lin(a, Session, b)

```
Data: m.df.long.gr
      AIC      BIC    logLik
-330.7913 -300.3474 172.3957

Random effects:
Formula: list(a ~ 1, b ~ 1)
Level: ID
Structure: General positive-definite, Log-Cholesky parametrization
      StdDev      Corr
a      0.30056758 a
b      0.03477137 -0.016
Residual 0.14993252

Correlation Structure: AR(1)
Formula: ~Session | ID
Parameter estimate(s):
      Phi
0.2781633

Fixed effects: list(a + b ~ 1)
      Value Std.Error DF t-value p-value
a 0.6197234 0.04829214 527 12.832801 0
b 0.0333877 0.00563691 527 5.923054 0
Correlation:
a
b -0.122

Standardized Within-Group Residuals:
      Min      Q1      Med      Q3      Max
-4.27024533 -0.35833808 -0.03068541 0.30710433 3.70673031

Number of Observations: 572
Number of Groups: 44

m.lme.2.exp
Nonlinear mixed-effects model fit by maximum likelihood
Model: BBS ~ My.Func.exp(a, Session, b, c)
```

```
Data: m.df.long.gr
      AIC      BIC    logLik
-334.6644 -299.8713 175.3322

Random effects:
Formula: list(a ~ 1, b ~ 1)
Level: ID
Structure: General positive-definite, Log-Cholesky parametrization
      StdDev   Corr
a      0.5795263 a
b      0.5842799 -0.867
Residual 0.1500206

Correlation Structure: AR(1)
Formula: ~Session | ID
Parameter estimate(s):
      Phi
0.2858263

Fixed effects: list(a + b + c ~ 1)
      Value Std.Error DF  t-value p-value
a  1.0966616 0.09716064 526 11.287098      0
b -0.5692341 0.09750486 526 -5.838008      0
c -0.1430698 0.02404491 526 -5.950109      0
Correlation:
      a      b
b -0.853
c  0.396 -0.228

Standardized Within-Group Residuals:
      Min      Q1      Med      Q3      Max
-4.47567055 -0.40072177 -0.05244518  0.32770192  3.47966984

Number of Observations: 572
Number of Groups: 44
```

Model performance

```
performance::performance(m.lme.2.lin)
# Indices of model performance
AIC    |   AICc |   BIC |  RMSE | Sigma
-----|-----|-----|-----|-----
-318.0 | -317.8 | -287.6 | 0.132 | 0.150

performance::performance(m.lme.2.exp)
# Indices of model performance
AIC    |   AICc |   BIC |  RMSE | Sigma
-----|-----|-----|-----|-----
-321.9 | -321.6 | -287.1 | 0.133 | 0.150
```

Treatment details

Balance-specific rehabilitation (Spec_Treat).

PwMS allocated to the balance-specific intervention received a structured balance rehabilitation programme targeting both motor and sensory components of postural control. Motor strategy retraining was delivered through progressively challenging static and dynamic activities, with systematic attention to postural alignment (particularly axial segment attitude) and to the participant's ability to detect, quantify, and control centre-of-mass (CoM) position and displacement. Exercises were designed to enhance ankle strategy and expand limits of stability via voluntary CoM shifts, supported by therapist modelling and feedback information. Anticipatory postural adjustments were trained using reaching tasks and manipulation of objects with different sizes and weights. During walking activities, treatment addressed abnormal CoM motion—especially in the frontal plane—and progressed from static balance tasks to exercises embedded within gait practice; trunk and head stability were trained using positional feedback of axial segments. To improve generalisation, more complex conditions were introduced later, including dual-task and open-skill activities (e.g., ball-based tasks). In addition, sensory strategy retraining aimed to promote sensory compensation and habituation by challenging sensory integration and encouraging use of the most impaired sensory system in varied perceptual contexts. For this purpose, balance and gait exercises were performed under altered sensory conditions (e.g., eyes closed, foam surfaces, and modified lenses), and tasks incorporating head movements, eye movements, and combined head–eye movements were added. Sensory conditions were individually selected and progressed according to each participant's pattern of sensory impairment.

Balance-unspecific rehabilitation (UnSpec_Treat).

Participants in the balance-unspecific intervention received conventional therapy, defined as a set of therapeutic approaches delivered according to usual clinical practice and not specifically targeted at balance impairments. Treatment was not structured to systematically retrain CoM control, ankle strategy, anticipatory postural adjustments, or trunk/head stability, nor did it include a planned progression of balance-challenging tasks. Instead, therapy consisted of general rehabilitation activities selected by the treating clinician to address broader functional

goals (e.g., mobility, general conditioning, flexibility, and/or strengthening as clinically indicated), without the explicit use of balance-focused biofeedback/modelling procedures or sensory-compensation/habituation components. As a result, any improvements in balance, if present, were considered secondary to the broader rehabilitative focus of the conventional programme rather than a direct objective of treatment.