SUPPLEMENTAL INFORMATION:

No significant changes in synaptic density and gray matter volume following motor learning

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Supplement 1. Detailed description of the Bimanual Tracking Task (BTT)

The Bimanual Tracking Task

The goal of the BTT was to accurately track a target moving along a target line presented on a screen with a cursor by rotating two dials to control the vertical and horizontal movements with the left and right index finger, respectively (see main manuscript, **Figure 1A,B**) (Sisti et al. 2011, Fujiyama et al. 2016, Zivari Adab et al. 2020). Consequently, moving both dials at the exact same speed (frequency ratio L:R of 1:1, both hands rotating rightwards) would result in a line tilted 45° to the upper right corner, whereas other frequency ratios would lead to steeper lines (e.g., 3:1) or flatter lines (e.g., 1:3). The BTT was performed while participants were seated in an upright position in front of the task setup and a 15-inch laptop placed on a table in front of them (see main manuscript, **Figure 1A**). The task setup consisted of two hand rests spaced approximately 48 cm apart, and circular dials (diameter = 6 cm) in front of them with a hollow (diameter = 1.5 cm), in which participants placed the fingertip of their index fingers after adjusting the distance between handle and dial to each individual's hand size.

The Training Paradigm

The 4-week training paradigm was compromised of 4 training sessions per week lasting 30 minutes each, separated into 6 blocks of 5 minutes with a brief self-paced break between blocks to avoid fatigue. Trials lasted 9 to 54 sec consisting of 2 sec with display of the target line, 5–50 sec of movement execution (depending on the trial), and 2 sec in which the feedback was displayed. Trials were compiled in a way to always add up to 5-minute training blocks. After thorough instruction and a 2-minute familiarization session, participants performed the total of 16 training sessions in their home environment with daily online follow-up and occasional contact by phone to ensure training adherence. After screening, participants were stratified by sex and pseudo-randomly assigned to either the complex training group or the simple training group.

Complex Training Group

Participants in the complex training group would constantly be kept challenged throughout the training paradigm by a staircase-level-design with participants being exposed to progressively more difficult tasks with increasing level number (280 different tasks, combined and arranged to 5-minute levels in the coarse order: straight lines [in-phase → anti-phase] → simple curves → zig-zags → waves → complex figures with various combinations of the stated conditions; also the speed of the tracing would vary between trials). Starting in the first level with the simplest task variant (1:1 lines), participants would progress one level (>65%), stay on the same level (40–65%), or regress one level (<40%) based on the average score of all trials in the previous 5-minute block.

Simple Training Group

Participants in the simple training group were only exposed to the simplest task condition, the 1:1 frequency ratio line in all four possible directions (2 sec of preparation, 10 sec of movement, 2 sec of feedback), with both hands moving at the same speed. The plasticity induced by the complex bimanual task training program was compared with this practice of a simple task variant that is considered to be part of the intrinsic motor repertoire and does not require learning (control group).

Progress Tests

To ensure comparability of the training progress between individuals despite individualized training program and two different training paradigms (complex vs. simple), participants were presented with a 5-minute standardized progress test at six different times throughout the 4-week training paradigm: at baseline, at the beginning of each of the four training weeks (when it would replace the first 5-minute block of the training day) and after finalizing the training paradigm. This progress test consisted of a subset of trained tasks (1:1, 1:3, zig-zag, waves) and untrained tasks (complex line-art flamingo with several straight and bended lines) (see main manuscript, **Figure 1C**, as well as mirrored counterparts, total of 18 tasks). The first and the last progress test were performed under supervision in the laboratory.

Score Calculation

Participants' performance was scored on each trial with a percentage ranging from 0–100%, reflecting their overall accuracy in terms of speed, movement direction, and distance from the target. Participants received on-screen feedback of this score after each trial. The score was calculated online as described earlier (see (Zivari Adab et al. 2020), their Fig. 1D, here with a trajectory sampling rate of 20 Hz) to obtain the preliminary percentage P, but was additionally multiplied with a distance factor D to obtain the final score S. This was done to penalize perfectly parallel but distant tracking of the target line and therefore encourage participant's overall accuracy and offer more room for improvement. The distance factor D was determined by calculating the distance between the participant's cursor and the target line for each data point (see (Zivari Adab et al. 2020), their Fig. 1D) and averaging this distance over the whole trial as average distance $\bar{d}$ (expressed in units, with 1 unit = distance that can be covered in 200 ms). This average distance was then divided by 5 units (distance that can be covered in 1000 ms), a value that showed in pilot experiments to have the best sensitivity to progress while offering reasonably small bottom and ceiling effects, and subtracted from 1:

$$D = \left(1 - \frac{\bar{d}}{5}\right)$$

Finally, the distance factor D was multiplied with the percentage of points P that were reached in the correct order (see score calculation in (Zivari Adab et al. 2020), their Fig. 1D) to obtain the final score:

$$S = P \cdot D$$

Consequently, very small average distances $\bar{d}$ would lead to a distance factor D close to 1, resulting to nearly no deduction from the obtained percentage P, whereas very large distances $\bar{d}$ would lead to a distance factor D close to 0, and would therefore considerably lower the obtained percentage P. Lastly, since participants should not be discouraged during early learning, the final distance factor was limited to range between 1 (maximum) and 0.1 (minimum).

Slope of Linear Regression as Overall Learning Outcome

The learning progress was quantified as the linear slope of the progress test scores over time. This was done by estimating a linear regression using the average scores at each of the progress tests as dependent variable and the time spent on the BTT (BTT$_{time}$; during trainings and measurements, measured in minutes, see **Supplemental Figure 1**) as the independent variable. Since participants in the here presented sample also participated in magnetic resonance imaging (MRI) and transcranial magnetic stimulation (TMS) experiments where they were presented with 1:1, 1:3 and 3:1 lines for functional measurements, exposure to the BTT during measurements has been included in the independent variable. An overview of the training weeks, points of measurement, training sessions

(30 min each) and progress tests can be seen in **Supplemental Figure 1**. The slope of a linear regression was chosen since it takes into account the initial task performance as well as the progress in performance as the training advances. Furthermore, the linear regression was chosen over a logarithmic or power regression due to its much better ability to fit the data of this learning process over an extended period of time. To obtain a more detailed picture of the skill level and coordinative requirements of different subsets of tasks, linear slopes were calculated for the average scores on specified sets of BTT subtasks (e.g., all lines: $BTTslope_{11}$ derived from $BTTscore_{11}$; complex task variants: $BTTslope_{complex}$ derived from $BTTscore_{complex}$).
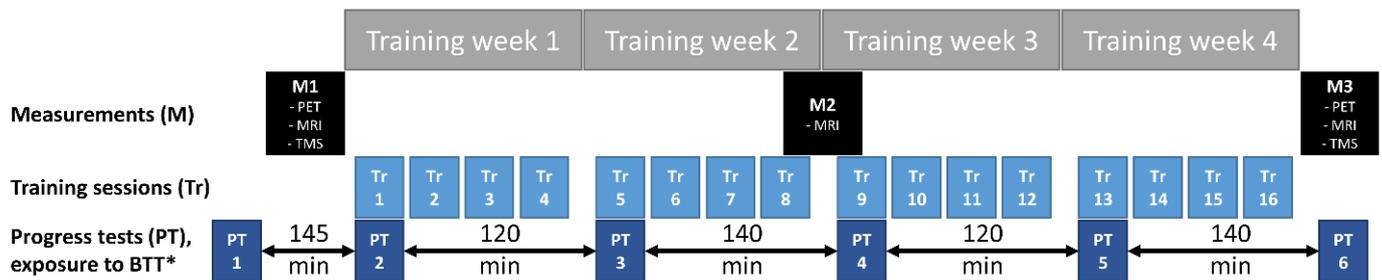
Supplemental Figure 1. *Overview of the four bimanual tracking task (BTT) training weeks. Each training session (Tr1–16) lasted 30 minutes, and trainings 1, 5, 9, and 13 started with a progress test instead of the first 5-minute block. During the measurements (M1–3), participants were exposed to the 1:1, 1:3 and 3:1 frequency ratio task variant during the magnetic resonance imaging (MRI, 20 min of BTT) and transcranial magnetic stimulation (TMS, 120 min of BTT), but not during the positron emission tomography (PET) measurement. Furthermore, participants were not shown any more difficult task variants during these times. Therefore, the exposure to the BTT in minutes is approximately equally spaced between progress tests (PT1–6).*

Supplement 2. Detailed results of the behavioral analysis.

Supplement 2A: Behavioral analysis of BTTscore₁₁ by time spent on the BTT.

→ Initial (and final) model (quadratic transformation of dependent variable necessary due to left skewed distribution of the residuals without transformation):

```
MODEL INFO:
Observations: 132
Dependent Variable: (Score11^2)
Type: Mixed effects linear regression

MODEL FIT:
AIC = 2284.496, BIC = 2301.793
Pseudo-R² (fixed effects) = 0.598
Pseudo-R² (total) = 0.674

FIXED EFFECTS:
-------------------------------------------------------------------------
                          Est.      2.5%      97.5%   t val.    d.f.
------------------------- --------- --------- --------- -------- ---------
(Intercept)               2559.017  1920.413  3197.621   7.854   69.151
BTTtime                      8.105     6.784     9.427  12.023  110.000
GROUP[complex]             -19.062  -922.185   884.060  -0.041   69.151
BTTtime:GROUP[complex]      -1.792    -3.661     0.077  -1.880  110.000
-------------------------------------------------------------------------


-------------------------------
                          p
------------------------- -------
(Intercept)               0.000
BTTtime                   0.000
GROUP[complex]            0.967
BTTtime:GROUP[complex]    0.063
-------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
-------------------------------------
   Group     Parameter     Std. Dev.
----------- ------------- -----------
 SubjectID  (Intercept)     597.471
 Residual                  1230.999
-------------------------------------

Grouping variables:
-----------------------------
   Group     # groups   ICC
----------- ---------- -------
 SubjectID     22       0.191
-----------------------------


Type III Analysis of Variance Table with Satterthwaite's method
                  Sum Sq    Mean Sq NumDF   DenDF  F value  Pr(>F)
BTTtime        346603981  346603981     1 110.000 228.7274 < 2e-16 ***
GROUP               2593       2593     1  69.151   0.0017 0.96712
BTTtime_min:GROUP 5353332    5353332     1 110.000   3.5327 0.06282 .
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

→ Stepwise simplification attempt:

  o Removing the non-significant BTTtime:GROUP interaction (p=0.0628) led to a higher AIC (AIC 2284.5 → 2286.0), hence no effect was removed and the initial transformed model is the final model.

Supplement 2B: Behavioral analysis of BTTscore_{complex} by time spent on the BTT.

→ Initial (and final) model:

```
MODEL INFO:
Observations: 132
Dependent Variable: ScoreComplex
Type: Mixed effects linear regression

MODEL FIT:
AIC = 981.299, BIC = 998.596
Pseudo-R² (fixed effects) = 0.672
Pseudo-R² (total) = 0.879

FIXED EFFECTS:
--------------------------------------------------------------------------
                         Est.    2.5%    97.5%   t val.    d.f.      p
----------------------- ------- -------- -------- ------- --------- -------
(Intercept)              2.513  -4.376    9.402    0.715   31.224   0.480
BTTtime                  0.062   0.053    0.070   14.485  110.000   0.000
GROUP[complex]           4.632  -5.110   14.375    0.932   31.224   0.359
BTTtime:GROUP[complex]   0.026   0.014    0.038    4.309  110.000   0.000
--------------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
   Group      Parameter    Std. Dev.
----------- ------------- -----------
 SubjectID   (Intercept)    10.177
 Residual                    7.773
------------------------------------

Grouping variables:
----------------------------
   Group     # groups   ICC
----------- ---------- -------
 SubjectID     22       0.632
----------------------------

Type III Analysis of Variance Table with Satterthwaite's method
               Sum Sq Mean Sq NumDF  DenDF  F value    Pr(>F)
BTTtime         37145   37145     1 110.000 614.7201 < 2.2e-16 ***
GROUP              52      52     1  31.224   0.8685    0.3585
BTTtime_min:GROUP 1122    1122     1 110.000  18.5638 3.589e-05 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

→ Stepwise simplification attempt of the model:

- o Main effect BTTtime ($p < 0.0001$) and interaction BTTtime:GROUP ($p < 0.0001$) were significant, consequently the main effect GROUP ($p = 0.3585$) could not be removed. The initial model is the final model.

Due to the (non-significant) interaction with GROUP, both training groups have been analyzed individually, and progress test results have additionally been compared between groups. Consequently, n = 11 per group necessitates the non-parametric Wilcoxon signed rank test (WSRT).

Results from independent two-sided WSRT with H_A: $\tilde{x}_{Simple} \neq \tilde{x}_{Complex}$, with $\tilde{x}$ being the median score of the progress test (PTs).

contrast	difference in location	95% CI	W-value	p-value	significance
(GROUP_simple - GROUP_complex) | PT1	4.7004	-13.3858 – 25.1696	68	0.6522	
(GROUP_simple - GROUP_complex) | PT2	-4.1213	-29.2559 – 13.0940	53	0.6522	
(GROUP_simple - GROUP_complex) | PT3	6.6796	0.3379 – 13.9891	93	0.0336	
(GROUP_simple - GROUP_complex) | PT4	8.1369	3.7834 – 11.7806	111	0.0004	*
(GROUP_simple - GROUP_complex) | PT5	5.7596	1.4798 – 10.7983	96	0.0192	
(GROUP_simple - GROUP_complex) | PT6	5.4251	1.9658 – 8.5209	104	0.0032	*

Asterisks indicate results p < α, with Bonferroni correction for 5 tests (α = 0.05/6 = 0.0083).
Abbreviations: CI = confidence interval; PT = progress test.

Results from paired one-sided WSRT with H_A: $\Delta\tilde{x} < 0$, with $\Delta\tilde{x}$ being the difference in median score between the two progress tests (PTs). Significant results indicate an increase in performance from the earlier to the later PT. Fitting with the one-sided hypothesis, only an upper limit of the confidence interval (CI) is reported.

contrast	median	95% CI upper limit	V-value	p-value	significance
(PT1 - PT2) | GROUP_simple	-5.4701	7.6884	28	0.3501	
(PT2 - PT3) | GROUP_simple	-30.9958	-21.3067	0	0.0005	*
(PT3 - PT4) | GROUP_simple	-2.9873	-1.2017	4	0.0034	*
(PT4 - PT5) | GROUP_simple	-0.6265	0.4715	25	0.2598	
(PT5 - PT6) | GROUP_simple	-0.7129	1.1835	22	0.1826	

Asterisks indicate results p < α, with Bonferroni correction for 5 tests (α = 0.05/5 = 0.01).
Abbreviations: CI = confidence interval; PT = progress test.

contrast	median	95% CI upper limit	V-value	p-value	significance
(PT1 - PT2) | GROUP_complex	-10.5953	-2.3883	9	0.0161	
(PT2 - PT3) | GROUP_complex	-16.0616	-7.8566	3	0.0024	*
(PT3 - PT4) | GROUP_complex	-1.9641	1.3324	26	0.2886	
(PT4 - PT5) | GROUP_complex	-1.9255	1.0869	21	0.1602	
(PT5 - PT6) | GROUP_complex	-0.3187	1.0313	26	0.2886	

Asterisks indicate results p < α, with Bonferroni correction for 5 tests (α = 0.05/5 = 0.01).
Abbreviations: CI = confidence interval; PT = progress test.

Due to the interaction with GROUP, both training groups have been analyzed individually, and progress test results have additionally been compared between groups. Consequently, n = 11 per group necessitates the non-parametric Wilcoxon signed rank test (WSRT).

Results from independent two-sided WSRT with H_A: $\tilde{x}_{Simple} \neq \tilde{x}_{Complex}$, with $\tilde{x}$ being the median score of the progress test (PTs).

contrast	difference in location	95% CI	W-value	p-value	significance
(GROUP_simple - GROUP_complex) | PT1	-1.1520	-5.8066 – 0.2156	42	0.2426	
(GROUP_simple - GROUP_complex) | PT2	-3.1767	-10.9479 – 1.6761	37	0.1330	
(GROUP_simple - GROUP_complex) | PT3	-9.7647	-26.3927 – 1.7084	35	0.1014	
(GROUP_simple - GROUP_complex) | PT4	-18.1970	-33.6005 – -0.0482	30	0.0473	
(GROUP_simple - GROUP_complex) | PT5	-23.9316	-38.3335 – -8.4981	14	0.0014	*
(GROUP_simple - GROUP_complex) | PT6	-17.7092	-28.3083 – -7.6662	16	0.0024	*

Asterisks indicate results p < α, with Bonferroni correction for 5 tests (α = 0.05/6 = 0.0083).
Abbreviations: CI = confidence interval; PT = progress test.

Results from paired one-sided WSRT with H_A: $\Delta\tilde{x} < 0$, with $\Delta\tilde{x}$ being the difference in median score between the two progress tests (PTs). Significant results indicate an increase in performance from the earlier to the later PT. Fitting with the one-sided hypothesis, only an upper limit of the confidence interval (CI) is reported.

contrast	median	95% CI upper limit	V-value	p-value	significance
(PT1 - PT2) | GROUP_simple	-3.4854	-1.0751	7	0.0093	*
(PT2 - PT3) | GROUP_simple	-9.3034	-3.9747	2	0.0015	*
(PT3 - PT4) | GROUP_simple	-9.4724	-4.6363	3	0.0024	*
(PT4 - PT5) | GROUP_simple	-6.4128	-3.9643	0	0.0005	*
(PT5 - PT6) | GROUP_simple	-8.9991	-6.0129	0	0.0005	*

Asterisks indicate results p < α, with Bonferroni correction for 5 tests (α = 0.05/5 = 0.01).
Abbreviations: CI = confidence interval; PT = progress test.

contrast	median	95% CI upper limit	V-value	p-value	significance
(PT1 - PT2) | GROUP_complex	-6.5339	-3.1114	0	0.0005	*
(PT2 - PT3) | GROUP_complex	-14.9490	-8.7999	1	0.0010	*
(PT3 - PT4) | GROUP_complex	-12.4372	-8.1699	1	0.0010	*
(PT4 - PT5) | GROUP_complex	-12.3501	-4.4731	0	0.0005	*
(PT5 - PT6) | GROUP_complex	-4.9277	-1.3962	7	0.0093	*

Asterisks indicate results p < α, with Bonferroni correction for 5 tests (α = 0.05/5 = 0.01).
Abbreviations: CI = confidence interval; PT = progress test.

Supplement 3. Detailed results of the VOI-based PET analyses.

Supplement 3A: VOI-based analysis of motor learning-related differences in SUVR.

> SUVR CB

→ Full model:

```
MODEL INFO:
Observations: 44
Dependent Variable: SUVR
Type: Mixed effects linear regression

MODEL FIT:
AIC = 21.656, BIC = 32.361
Pseudo-R² (fixed effects) = 0.006
Pseudo-R² (total) = 0.572

FIXED EFFECTS:
-------------------------------------------------------------------------
                          Est.    2.5%   97.5%  t val.    d.f.       p
----------------------- -------- ------- ------- -------- -------- -------
(Intercept)              5.628   5.452   5.804   62.680   33.239   0.000
GROUP[complex]           0.045  -0.204   0.294    0.357   33.239   0.723
TIMING[pre]              0.030  -0.133   0.194    0.366   22.000   0.718
GROUP[complex]:TIMING[pre]-0.015 -0.246   0.217   -0.123   22.000   0.903
-------------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
   Group      Parameter    Std. Dev.
----------- ------------- -----------
 SUBJECT     (Intercept)    0.225
 Residual                   0.195
------------------------------------

Grouping variables:
----------------------------
   Group     # groups   ICC
----------- ---------- -------
 SUBJECT        22     0.569
----------------------------

Type III Analysis of Variance Table with Satterthwaite's method
               Sum Sq   Mean Sq NumDF DenDF F value Pr(>F)
GROUP        0.0043748 0.0043748     1    22  0.1145 0.7383
TIMING       0.0059180 0.0059180     1    22  0.1548 0.6977
GROUP:TIMING 0.0005825 0.0005825     1    22  0.0152 0.9029
```

→ Stepwise simplification of the model:
1. remove GROUP:ROIname interaction (p=0.9029; AIC 21.7 → 19.7)
2. remove GROUP main effect (p=0.7383; AIC 19.7 → 17.8 for REML = FALSE)

→ Final model (REML = TRUE):

```
MODEL INFO:
Observations: 44
Dependent Variable: SUVR
Type: Mixed effects linear regression

MODEL FIT:
AIC = 25.476, BIC = 32.613
Pseudo-R² (fixed effects) = 0.001
Pseudo-R² (total) = 0.571

FIXED EFFECTS:
----------------------------------------------------------------
                 Est.    2.5%   97.5%  t val.    d.f.       p
---------------- ------- -------- ------- -------- -------- -------
(Intercept)      5.650   5.523   5.778   86.770   31.687   0.000
TIMING[pre]      0.023  -0.095   0.141    0.384   21.000   0.705
----------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
   Group      Parameter    Std. Dev.
----------- ------------- -----------
 SUBJECT     (Intercept)    0.231
 Residual                   0.200
```

```
-------------------------------------

Grouping variables:
----------------------------
   Group    # groups   ICC
---------- ---------- -------
 SUBJECT       22      0.571
----------------------------

Type III Analysis of Variance Table with Satterthwaite's method
        Sum Sq  Mean Sq NumDF DenDF F value Pr(>F)
TIMING 0.005918 0.005918     1    21  0.1477 0.7046
```

> SUVR DLPFC

→ Full model:

```
MODEL INFO:
Observations: 44
Dependent Variable: SUVR
Type: Mixed effects linear regression

MODEL FIT:
AIC = 53.462, BIC = 64.167
Pseudo-R² (fixed effects) = 0.027
Pseudo-R² (total) = 0.592

FIXED EFFECTS:
------------------------------------------------------------------------
                         Est.    2.5%   97.5%  t val.    d.f.       p
---------------------- -------- ------- ------- -------- -------- -------
(Intercept)             7.371   7.117   7.625   56.924   32.919   0.000
GROUP[complex]         -0.129  -0.488   0.229   -0.707   32.919   0.485
TIMING[pre]             0.053  -0.180   0.286    0.446   22.000   0.660
GROUP[complex]:TIMING[pre]-0.006 -0.335  0.323   -0.036   22.000   0.972
------------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
   Group      Parameter    Std. Dev.
---------- ------------- ------------
 SUBJECT    (Intercept)     0.327
 Residual                   0.278
------------------------------------

Grouping variables:
----------------------------
   Group    # groups   ICC
---------- ---------- -------
 SUBJECT       22      0.580
----------------------------

Type III Analysis of Variance Table with Satterthwaite's method
             Sum Sq  Mean Sq NumDF DenDF F value Pr(>F)
GROUP       0.051275 0.051275     1    22  0.6621 0.4245
TIMING      0.027464 0.027464     1    22  0.3547 0.5576
GROUP:TIMING 0.000098 0.000098    1    22  0.0013 0.9719
```

→ Stepwise simplification of the model:
   1. remove GROUP:ROIname interaction (p=0.9719; AIC 53.5 → 51.5)
   2. remove TIMING main effect (p=0.5576; AIC 51.5 → 49.8 for REML = FALSE)

→ Final model (REML = TRUE):

```
MODEL INFO:
Observations: 44
Dependent Variable: SUVR
Type: Mixed effects linear regression

MODEL FIT:
AIC = 54.693, BIC = 61.830
Pseudo-R² (fixed effects) = 0.022
Pseudo-R² (total) = 0.615

FIXED EFFECTS:
-----------------------------------------------------------------
                   Est.    2.5%   97.5%  t val.    d.f.       p
---------------- -------- ------- ------- -------- -------- -------
(Intercept)       7.398   7.161   7.634   61.280   20.000   0.000
GROUP[complex]   -0.132  -0.467   0.202   -0.776   20.000   0.447
```

```
------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
-------------------------------------
   Group      Parameter     Std. Dev.
----------- ------------- -----------
 SUBJECT     (Intercept)     0.348
 Residual                    0.281
-------------------------------------

Grouping variables:
----------------------------
   Group     # groups    ICC
----------- ---------- -------
 SUBJECT        22       0.606
----------------------------

Type III Analysis of Variance Table with Satterthwaite's method
        Sum Sq  Mean Sq NumDF DenDF F value Pr(>F)
GROUP 0.047368 0.047368     1    20  0.6019 0.4469
```

> SUVR hMT/V5+

→   Full model:

```
MODEL INFO:
Observations: 44
Dependent Variable: SUVR
Type: Mixed effects linear regression

MODEL FIT:
AIC = 52.438, BIC = 63.143
Pseudo-R² (fixed effects) = 0.029
Pseudo-R² (total) = 0.441

FIXED EFFECTS:
-------------------------------------------------------------------------
                          Est.    2.5%   97.5%  t val.    d.f.       p
----------------------- -------- ------- ------- -------- -------- -------
(Intercept)              7.261   7.023   7.499  59.823   37.296   0.000
GROUP[complex]          -0.037  -0.373   0.300  -0.213   37.296   0.833
TIMING[pre]              0.144  -0.111   0.400   1.109   22.000   0.279
GROUP[complex]:TIMING[pre]-0.104 -0.465  0.257  -0.566   22.000   0.577
-------------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
-------------------------------------
   Group      Parameter     Std. Dev.
----------- ------------- -----------
 SUBJECT     (Intercept)     0.262
 Residual                    0.306
-------------------------------------

Grouping variables:
----------------------------
   Group     # groups    ICC
----------- ---------- -------
 SUBJECT        22       0.424
----------------------------

Type III Analysis of Variance Table with Satterthwaite's method
              Sum Sq  Mean Sq NumDF DenDF F value Pr(>F)
GROUP       0.034979 0.034979     1    22  0.3747 0.5467
TIMING      0.093797 0.093797     1    22  1.0047 0.3271
GROUP:TIMING 0.029884 0.029884     1    22  0.3201 0.5773
```

→   Stepwise simplification of the model:
      1. remove GROUP:ROIname interaction (p=0.5773; AIC 52.4 → 50.8)
      2. remove GROUP main effect (p=0.5467; AIC 50.8 → 49.1 for REML = FALSE)

→   Final model (REML = TRUE):

```
MODEL INFO:
Observations: 44
Dependent Variable: SUVR
Type: Mixed effects linear regression

MODEL FIT:
```

```
AIC = 55.394, BIC = 62.531
Pseudo-R² (fixed effects) = 0.012
Pseudo-R² (total) = 0.432


FIXED EFFECTS:
-----------------------------------------------------------------
                  Est.    2.5%   97.5%  t val.     d.f.       p
----------------- ------- ------- ------- -------- -------- -------
(Intercept)        7.243   7.070   7.417  81.785   35.575   0.000
TIMING[pre]        0.092  -0.094   0.278   0.972   21.000   0.342
-----------------------------------------------------------------


p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
   Group      Parameter    Std. Dev.
----------- ------------- -----------
 SUBJECT     (Intercept)     0.271
 Residual                    0.315
------------------------------------


Grouping variables:
----------------------------
   Group     # groups   ICC
----------- ---------- ------
 SUBJECT        22      0.425
----------------------------


Type III Analysis of Variance Table with Satterthwaite's method
         Sum Sq   Mean Sq NumDF DenDF F value Pr(>F)
TIMING 0.093797 0.093797     1    21  0.9453  0.342
```

> SUVR PMd

→ Full model:

```
MODEL INFO:
Observations: 44
Dependent Variable: SUVR
Type: Mixed effects linear regression

MODEL FIT:
AIC = 47.306, BIC = 58.011
Pseudo-R² (fixed effects) = 0.066
Pseudo-R² (total) = 0.683

FIXED EFFECTS:
------------------------------------------------------------------------
                         Est.     2.5%   97.5%  t val.     d.f.       p
---------------------- -------- -------- ------- -------- -------- -------
(Intercept)              6.747    6.501   6.994  53.650   30.632   0.000
GROUP[complex]          -0.144   -0.492   0.205  -0.808   30.632   0.426
TIMING[pre]              0.124   -0.079   0.327   1.200   22.000   0.243
GROUP[complex]:TIMING[pre]-0.115 -0.403   0.172  -0.788   22.000   0.439
------------------------------------------------------------------------


p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
   Group      Parameter    Std. Dev.
----------- ------------- -----------
 SUBJECT     (Intercept)     0.339
 Residual                    0.243
------------------------------------

Grouping variables:
----------------------------
   Group     # groups   ICC
----------- ---------- ------
 SUBJECT        22      0.661
----------------------------

Type III Analysis of Variance Table with Satterthwaite's method
              Sum Sq  Mean Sq NumDF DenDF F value Pr(>F)
GROUP        0.091137 0.091137    1    22  1.5433 0.2272
TIMING       0.048767 0.048767    1    22  0.8258 0.3733
GROUP:TIMING 0.036635 0.036635    1    22  0.6204 0.4393
```

→ Stepwise simplification of the model:
1. remove GROUP:ROIname interaction (p=0.4393; AIC 47.3 → 45.9)
2. remove TIMING main effect (p=0.3798; AIC 45.9 → 44.7 for REML = FALSE)

→ Final model (REML = TRUE):

```
MODEL INFO:
Observations: 44
Dependent Variable: SUVR
Type: Mixed effects linear regression

MODEL FIT:
AIC = 49.602, BIC = 56.739
Pseudo-R² (fixed effects) = 0.052
Pseudo-R² (total) = 0.687

FIXED EFFECTS:
------------------------------------------------------------------
                    Est.    2.5%   97.5%  t val.    d.f.       p
----------------- -------- ------- ------- ------- -------- -------
(Intercept)         6.810   6.574   7.045  56.655   20.000   0.000
GROUP[complex]     -0.201  -0.534   0.132  -1.184   20.000   0.250
------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
   Group     Parameter    Std. Dev.
----------- ------------- ----------
 SUBJECT    (Intercept)      0.357
 Residual                    0.251
------------------------------------

Grouping variables:
----------------------------
   Group    # groups   ICC
----------- ---------- -------
 SUBJECT       22       0.669
----------------------------

Type III Analysis of Variance Table with Satterthwaite's method
        Sum Sq  Mean Sq NumDF DenDF F value Pr(>F)
GROUP 0.088298 0.088298     1    20   1.403 0.2501
```

> SUVR SM1

→ Full model:

```
MODEL INFO:
Observations: 44
Dependent Variable: SUVR
Type: Mixed effects linear regression

MODEL FIT:
AIC = 48.920, BIC = 59.625
Pseudo-R² (fixed effects) = 0.031
Pseudo-R² (total) = 0.678

FIXED EFFECTS:
-----------------------------------------------------------------------
                         Est.    2.5%   97.5%  t val.    d.f.       p
---------------------- -------- ------- ------- ------- -------- -------
(Intercept)              6.460   6.207   6.712  50.212   30.429   0.000
GROUP[complex]          -0.144  -0.500   0.213  -0.790   30.429   0.435
TIMING[pre]              0.036  -0.169   0.242   0.344   22.000   0.734
GROUP[complex]:TIMING[pre]-0.009  -0.300   0.281  -0.064   22.000   0.950
-----------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
   Group     Parameter    Std. Dev.
----------- ------------- ----------
 SUBJECT    (Intercept)      0.349
 Residual                    0.246
------------------------------------

Grouping variables:
----------------------------
   Group    # groups   ICC
----------- ---------- -------
 SUBJECT       22       0.668
----------------------------

Type III Analysis of Variance Table with Satterthwaite's method
            Sum Sq  Mean Sq NumDF DenDF F value Pr(>F)
```

```
GROUP        0.048325 0.048325   1   22  0.7991 0.3810
TIMING       0.010814 0.010814   1   22  0.1788 0.6765
GROUP:TIMING 0.000246 0.000246   1   22  0.0041 0.9497
```

→ Stepwise simplification of the model:
1. remove GROUP:ROIname interaction (p=0.9497; AIC 48.9 → 46.9)
2. remove TIMING main effect (p=0.6765; AIC 46.9 → 45.1 for REML = FALSE)

→ Final model (REML = TRUE):

```
MODEL INFO:
Observations: 44
Dependent Variable: SUVR
Type: Mixed effects linear regression

MODEL FIT:
AIC = 49.899, BIC = 57.035
Pseudo-R² (fixed effects) = 0.028
Pseudo-R² (total) = 0.700

FIXED EFFECTS:
----------------------------------------------------------------------
                   Est.    2.5%   97.5%   t val.    d.f.       p
---------------- -------- ------- ------- -------- -------- -------
(Intercept)        6.478   6.236   6.719   52.573   20.000   0.000
GROUP[complex]    -0.149  -0.490   0.193   -0.852   20.000   0.404
----------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
   Group      Parameter    Std. Dev.
---------- ------------- -----------
 SUBJECT    (Intercept)     0.369
 Residual                   0.247
------------------------------------

Grouping variables:
----------------------------
   Group     # groups    ICC
---------- --------- -------
 SUBJECT       22       0.691
----------------------------

Type III Analysis of Variance Table with Satterthwaite's method
       Sum Sq  Mean Sq NumDF DenDF F value Pr(>F)
GROUP 0.044297 0.044297   1    20  0.7265 0.4041
```

> SUVR (pre)SMA

→ Full model:

```
MODEL INFO:
Observations: 44
Dependent Variable: SUVR
Type: Mixed effects linear regression

MODEL FIT:
AIC = 53.640, BIC = 64.345
Pseudo-R² (fixed effects) = 0.038
Pseudo-R² (total) = 0.700

FIXED EFFECTS:
-----------------------------------------------------------------------------
                          Est.    2.5%   97.5%   t val.    d.f.       p
--------------------- -------- ------- ------- -------- -------- -------
(Intercept)              6.967   6.697   7.236   50.671   29.855   0.000
GROUP[complex]          -0.141  -0.522   0.240   -0.725   29.855   0.474
TIMING[pre]              0.093  -0.120   0.305    0.853   22.000   0.403
GROUP[complex]:TIMING[pre]-0.044 -0.345   0.257   -0.289   22.000   0.776
-----------------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
   Group      Parameter    Std. Dev.
---------- ------------- -----------
 SUBJECT    (Intercept)     0.378
 Residual                   0.255
------------------------------------

Grouping variables:
```

```
----------------------------
  Group     # groups   ICC
---------- --------- -------
 SUBJECT      22      0.688
----------------------------

Type III Analysis of Variance Table with Satterthwaite's method
             Sum Sq  Mean Sq NumDF DenDF F value Pr(>F)
GROUP        0.054033 0.054033   1    22  0.8337 0.3711
TIMING       0.054604 0.054604   1    22  0.8425 0.3686
GROUP:TIMING 0.005402 0.005402   1    22  0.0833 0.7755
```

> → Stepwise simplification of the model:
> > 1. remove GROUP:ROIname interaction (p=0.7755; AIC 53.6 → 51.7)
> > 2. remove GROUP main effect (p=0.3711; AIC 51.7 → 50.5 for REML = FALSE)

> → Final model (REML = TRUE):

```
MODEL INFO:
Observations: 44
Dependent Variable: SUVR
Type: Mixed effects linear regression

MODEL FIT:
AIC = 56.744, BIC = 63.880
Pseudo-R² (fixed effects) = 0.006
Pseudo-R² (total) = 0.699

FIXED EFFECTS:
-------------------------------------------------------------------
                  Est.    2.5%   97.5%  t val.     d.f.      p
---------------- ------- ------- ------ -------- -------- -------
(Intercept)       6.896   6.698  7.095  68.201   28.267  0.000
TIMING[pre]       0.070  -0.084  0.225   0.895   21.000  0.381
-------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
  Group      Parameter    Std. Dev.
---------- ------------- -----------
 SUBJECT    (Intercept)     0.396
 Residual                   0.261
------------------------------------

Grouping variables:
----------------------------
  Group     # groups   ICC
---------- --------- -------
 SUBJECT      22      0.697
----------------------------

Type III Analysis of Variance Table with Satterthwaite's method
        Sum Sq  Mean Sq NumDF DenDF F value Pr(>F)
TIMING 0.054604 0.054604   1    21  0.8012 0.3809
```

Supplement 3B: Correlation between baseline / changes in SV2A binding and motor learning outcome.

→ Pooled group analysis (n = 22)

		SUVR$_{PRE}$					
		CB	DLPFC	hMT/v5+	PMd	SM1	(pre)SMA
BTT_SlopeScore11	r	0.0632	0.0446‡	-0.0371	0.0575	0.0107	0.0023
	p	0.7798	0.8437	0.8699	0.7995	0.9623	0.9920
BTT_SlopeScoreComplex	r	0.1725	-0.0672‡	-0.0776	-0.0665	-0.0789	0.0060
	p	0.4427	0.7664	0.7313	0.7687	0.7271	0.9788

‡ = Spearman correlation due to non-normality

		SUVR$_{DIFF}$					
		CB	DLPFC	hMT/v5+	PMd	SM1	(pre)SMA
BTT_SlopeScore11	r	0.0287	0.0377	0.0931	0.0224	0.0927	0.0255
	p	0.8992	0.8678	0.6804	0.9213	0.6816	0.9102
BTT_SlopeScoreComplex	r	-0.2316	-0.2583	-0.1488	-0.1280	-0.1759	-0.1862
	p	0.2998	0.2459	0.5087	0.5702	0.4336	0.4067

→ Analysis for group 'complex training' (n = 11)

		SUVR$_{PRE}$					
		CB	DLPFC	hMT/v5+	PMd	SM1	(pre)SMA
BTT_SlopeScore11	r	0.0273‡	0.0091‡	-0.1909‡	0.0273‡	-0.0091‡	-0.0636‡
	p	0.9366	0.9788	0.5739	0.9366	0.9788	0.8525
BTT_SlopeScoreComplex	r	0.2625	0.2909‡	0.2287	0.3755	0.3025	0.3829
	p	0.4355	0.3855	0.4988	0.2551	0.3659	0.2451

‡ = Spearman correlation due to non-normality

		SUVR$_{DIFF}$					
		CB	DLPFC	hMT/v5+	PMd	SM1	(pre)SMA
BTT_SlopeScore11	r	0.1636‡	0.0091‡	0.3727‡	0.3545‡	0.1727‡	0.2818‡
	p	0.6307	0.9788	0.2589	0.2847	0.6115	0.4011
BTT_SlopeScoreComplex	r	0.0858	0.0186	-0.0921	-0.1494	-0.1041	-0.1805
	p	0.8019	0.9567	0.7876	0.6611	0.7608	0.5954

‡ = Spearman correlation due to non-normality

→ Analysis for group 'simple training' (n = 11)

		SUVR$_{PRE}$					
		CB	DLPFC	hMT/v5+	PMd	SM1	(pre)SMA
BTT_SlopeScore11	r	0.3057	0.3613	0.3652	0.1916	0.2958	0.3527
	p	0.3606	0.2750	0.2695	0.5724	0.3772	0.2875
BTT_SlopeScoreComplex	r	0.1000	-0.2206	-0.1414	-0.1301	-0.2736	-0.0965
	p	0.7698	0.5146	0.6783	0.7031	0.4157	0.7777

		SUVR$_{DIFF}$					
		CB	DLPFC	hMT/v5+	PMd	SM1	(pre)SMA
BTT_SlopeScore11	r	0.1455‡	-0.0436	-0.1248	-0.0196	-0.0352	-0.0345
	p	0.6696	0.8988	0.7147	0.9544	0.9181	0.9197
BTT_SlopeScoreComplex	r	-0.2818‡	-0.4416	-0.3424	-0.3360	-0.2777	-0.3179
	p	0.4011	0.1740	0.3027	0.3125	0.4084	0.3407

‡ = Spearman correlation due to non-normality

Supplement 4. Detailed results of the VOI-based gray matter analyses.

Supplement 4A: VOI-based analysis of motor learning-related differences in GM.

> GMV CB

→ Full model:

```
MODEL INFO:
Observations: 66
Dependent Variable: GMV
Type: Mixed effects linear regression

MODEL FIT:
AIC = 1165.412, BIC = 1185.119
Pseudo-R² (fixed effects) = 0.668
Pseudo-R² (total) = 0.992

FIXED EFFECTS:
-----------------------------------------------------------------------
                             Est.      2.5%      97.5%   t val.    d.f.
----------------------- ---------- ---------- ---------- -------- --------
(Intercept)              17565.061   484.588  34645.534   2.016   22.014
GROUP[complex]             626.146 -2926.056   4178.347   0.345   22.679
TIMING[mid]                102.727  -432.506    637.961   0.376   44.000
TIMING[post]              -116.182  -651.415    419.052  -0.425   44.000
eTIV                         0.052     0.037      0.068   6.644   22.000
GROUP[complex]:TIMING[mid] -420.364 -1177.298    336.571  -1.088   44.000
GROUP[complex]:TIMING[post] 189.455  -567.480    946.389   0.491   44.000
-----------------------------------------------------------------------


------------------------------
                             p
----------------------- -------
(Intercept)              0.056
GROUP[complex]           0.733
TIMING[mid]              0.709
TIMING[post]             0.673
eTIV                     0.000
GROUP[complex]:TIMING[mid] 0.282
GROUP[complex]:TIMING[post]0.626
------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
  Group     Parameter    Std. Dev.
---------- ------------- ----------
 SUBJECT   (Intercept)   4201.783
 Residual                 640.437
------------------------------------

Grouping variables:
---------------------------
  Group    # groups    ICC
--------- ---------- -------
 SUBJECT     22       0.977
---------------------------


Type III Analysis of Variance Table with Satterthwaite's method
             Sum Sq  Mean Sq NumDF DenDF F value    Pr(>F)
GROUP          38239    38239     1    22  0.0932    0.7630
TIMING        142287    71144     2    44  0.1735    0.8413
eTIV        18104667 18104667     1    22 44.1405 1.113e-06 ***
GROUP:TIMING 1071541   535770     2    44  1.3062    0.2811
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

→ Stepwise simplification of the model:
1. remove GROUP:TIMING interaction (p=0.2811; AIC 1165.4 → 1163.9)
2. remove TIMING main effect (p=0.8495; AIC 1163.9 → 1160.3 for REML = FALSE)

→ Final model (REML = TRUE):

```
MODEL INFO:
Observations: 66
Dependent Variable: GMV
Type: Mixed effects linear regression

MODEL FIT:
AIC = 1135.643, BIC = 1146.592
Pseudo-R² (fixed effects) = 0.635
Pseudo-R² (total) = 0.992
```

```
FIXED EFFECTS:
--------------------------------------------------------------------------
                       Est.       2.5%       97.5%    t val.    d.f.       p
----------------- ----------- ---------- ---------- ------- -------- -------
(Intercept)        17560.576   -815.947   35937.099   1.873   19.000   0.077
GROUP[complex]       549.176  -3244.151    4342.504   0.284   19.000   0.780
eTIV                   0.052      0.036       0.069   6.174   19.000   0.000
--------------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
-----------------------------------
  Group      Parameter    Std. Dev.
--------- ------------- -----------
 SUBJECT   (Intercept)    4522.721
 Residual                  661.624
-----------------------------------

Grouping variables:
---------------------------
  Group   # groups   ICC
--------- --------- -------
 SUBJECT     22      0.979
---------------------------


Type III Analysis of Variance Table with Satterthwaite's method
        Sum Sq  Mean Sq NumDF DenDF F value    Pr(>F)
GROUP    35245    35245     1    19  0.0805    0.7797
eTIV  16687503 16687503     1    19 38.1214 6.215e-06 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

> GMV DLPFC

→ Full model:

```
MODEL INFO:
Observations: 66
Dependent Variable: GMV
Type: Mixed effects linear regression

MODEL FIT:
AIC = 1047.789, BIC = 1067.495
Pseudo-R² (fixed effects) = 0.613
Pseudo-R² (total) = 0.974

FIXED EFFECTS:
----------------------------------------------------------------------------------
                            Est.       2.5%      97.5%   t val.     d.f.       p
----------------------- ---------- ---------- ---------- -------- -------- -------
(Intercept)               256.602  -4575.769   5088.974    0.104   22.044   0.918
GROUP[complex]            349.968   -670.153   1370.088    0.672   24.085   0.508
TIMING[mid]                20.182   -244.238    284.602    0.150   44.000   0.882
TIMING[post]              -51.545   -315.966    212.875   -0.382   44.000   0.704
eTIV                        0.013      0.009      0.018    5.970   22.000   0.000
GROUP[complex]:TIMING[mid] -303.727  -677.674     70.220   -1.592   44.000   0.119
GROUP[complex]:TIMING[post]-135.273  -509.220    238.674   -0.709   44.000   0.482
----------------------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
-----------------------------------
  Group      Parameter    Std. Dev.
--------- ------------- -----------
 SUBJECT   (Intercept)    1178.885
 Residual                  316.394
-----------------------------------

Grouping variables:
---------------------------
  Group   # groups   ICC
--------- --------- -------
 SUBJECT     22      0.933
---------------------------


Type III Analysis of Variance Table with Satterthwaite's method
             Sum Sq Mean Sq NumDF DenDF F value    Pr(>F)
GROUP         16042   16042     1    22  0.1602    0.6928
TIMING       232471  116236     2    44  1.1611    0.3225
eTIV        3568024 3568024     1    22 35.6428 5.225e-06 ***
GROUP:TIMING 254697  127349     2    44  1.2722    0.2903
```

```
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

→ Stepwise simplification of the model:
1. remove GROUP:TIMING interaction (p=0.2903; AIC 1047.8 → 1046.3)
2. remove GROUP main effect (p=0.6928; AIC 1046.3 → 1044.4 for REML = FALSE)

→ Final model (REML = TRUE):

```
MODEL INFO:
Observations: 66
Dependent Variable: GMV
Type: Mixed effects linear regression

MODEL FIT:
AIC = 1019.995, BIC = 1033.133
Pseudo-R² (fixed effects) = 0.587
Pseudo-R² (total) = 0.972

FIXED EFFECTS:
----------------------------------------------------------------------
                      Est.      2.5%      97.5%   t val.    d.f.      p
----------------- ---------- ---------- ---------- -------- -------- -------
(Intercept)         424.852  -4636.871   5486.574    0.165   20.020   0.871
TIMING[mid]        -131.682   -328.511     65.147   -1.311   42.000   0.197
TIMING[post]       -119.182   -316.011     77.647   -1.187   42.000   0.242
eTIV                  0.013      0.009      0.018    5.674   20.000   0.000
----------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
  Group      Parameter    Std. Dev.
---------- ------------- -----------
 SUBJECT    (Intercept)    1240.916
 Residual                   333.071
------------------------------------

Grouping variables:
---------------------------
  Group    # groups    ICC
--------- ---------- -------
 SUBJECT      22       0.933
---------------------------


Type III Analysis of Variance Table with Satterthwaite's method
        Sum Sq Mean Sq NumDF DenDF F value    Pr(>F)
TIMING  232471  116236     2    42  1.0478    0.3597
eTIV   3572096 3572096     1    20 32.1995 1.489e-05 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

> GMV hMT/V5+

→ Full model:

```
MODEL INFO:
Observations: 66
Dependent Variable: GMV
Type: Mixed effects linear regression

MODEL FIT:
AIC = 1005.384, BIC = 1025.091
Pseudo-R² (fixed effects) = 0.254
Pseudo-R² (total) = 0.983

FIXED EFFECTS:
----------------------------------------------------------------------------
                             Est.      2.5%      97.5%   t val.    d.f.      p
----------------------- ---------- ---------- ---------- -------- -------- ------
(Intercept)               4255.702  -784.057   9295.462    1.655   22.015   0.112
GROUP[complex]             182.250  -866.056   1230.556    0.341   22.696   0.736
TIMING[mid]                -67.091  -226.983     92.801   -0.822   44.000   0.415
TIMING[post]               -51.727  -211.619    108.165   -0.634   44.000   0.529
eTIV                         0.006     0.002      0.011    2.714   22.000   0.013
GROUP[complex]:TIMING[mid]  -74.545  -300.667    151.576   -0.646   44.000   0.522
GROUP[complex]:TIMING[post]  32.455  -193.667    258.576    0.281   44.000   0.780
----------------------------------------------------------------------------

p values calculated using Satterthwaite d.f.
```

```
RANDOM EFFECTS:
------------------------------------
  Group      Parameter    Std. Dev.
---------- ------------- -----------
 SUBJECT    (Intercept)   1239.652
 Residual                  191.320
------------------------------------

Grouping variables:
---------------------------
  Group    # groups   ICC
--------- ---------- -------
 SUBJECT      22      0.977
---------------------------


Type III Analysis of Variance Table with Satterthwaite's method
              Sum Sq Mean Sq NumDF DenDF F value  Pr(>F)
GROUP          3678    3678     1    22  0.1005 0.75425
TIMING       123891   61945     2    44  1.6924 0.19585
eTIV         269619  269619     1    22  7.3660 0.01267 *
GROUP:TIMING  33109   16554     2    44  0.4523 0.63911
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

→ Stepwise simplification of the model:
  1. remove GROUP:TIMING interaction (p=0.6391; AIC 1005.4 → 1002.3)
  2. remove GROUP main effect (p=0.75425; AIC 1002.3 → 1000.4 for REML = FALSE)

→ Final model (REML = TRUE):

```
MODEL INFO:
Observations: 66
Dependent Variable: GMV
Type: Mixed effects linear regression

MODEL FIT:
AIC = 977.873, BIC = 991.011
Pseudo-R² (fixed effects) = 0.234
Pseudo-R² (total) = 0.983

FIXED EFFECTS:
-------------------------------------------------------------------------
                     Est.       2.5%      97.5%   t val.     d.f.      p
----------------- ---------- ---------- ---------- -------- -------- -------
(Intercept)        4341.264   -931.420   9613.948    1.614   20.007   0.122
TIMING[mid]        -104.364   -221.268     12.541   -1.750   42.000   0.087
TIMING[post]        -35.500   -152.405     81.405   -0.595   42.000   0.555
eTIV                  0.006      0.002      0.011    2.584   20.000   0.018
-------------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
  Group      Parameter    Std. Dev.
---------- ------------- -----------
 SUBJECT    (Intercept)   1303.291
 Residual                  197.825
------------------------------------

Grouping variables:
---------------------------
  Group    # groups   ICC
--------- ---------- -------
 SUBJECT      22      0.977
---------------------------


Type III Analysis of Variance Table with Satterthwaite's method
        Sum Sq Mean Sq NumDF DenDF F value  Pr(>F)
TIMING  123891   61945     2    42  1.5829 0.21739
eTIV    261299  261299     1    20  6.6770 0.01773 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

> GMV PMd

→ Full model:

```
MODEL INFO:
Observations: 66
Dependent Variable: GMV
Type: Mixed effects linear regression
```

```
MODEL FIT:
AIC = 1054.140, BIC = 1073.847
Pseudo-R² (fixed effects) = 0.393
Pseudo-R² (total) = 0.978

FIXED EFFECTS:
-------------------------------------------------------------------------
                            Est.       2.5%       97.5%  t val.    d.f.
-------------------------- ---------- ----------- ----------- -------- --------
(Intercept)              6752.388    516.846   12987.929   2.122   22.024
GROUP[complex]          -1458.477  -2761.398    -155.556  -2.194   23.115
TIMING[mid]                -45.182   -295.350     204.986  -0.354   44.000
TIMING[post]                47.091   -203.077     297.259   0.369   44.000
eTIV                         0.009      0.003       0.014   2.977   22.000
GROUP[complex]:TIMING[mid] -193.727   -547.518     160.064  -1.073   44.000
GROUP[complex]:TIMING[post] -75.455   -429.246     278.336  -0.418   44.000
-------------------------------------------------------------------------


------------------------------
                           p
-------------------------- -------
(Intercept)             0.045
GROUP[complex]          0.039
TIMING[mid]             0.725
TIMING[post]            0.714
eTIV                    0.007
GROUP[complex]:TIMING[mid] 0.289
GROUP[complex]:TIMING[post]0.678
------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
  Group      Parameter    Std. Dev.
--------- ------------- -----------
 SUBJECT   (Intercept)   1529.975
 Residual                 299.340
------------------------------------

Grouping variables:
---------------------------
  Group    # groups   ICC
--------- --------- -------
 SUBJECT      22     0.963
---------------------------

Type III Analysis of Variance Table with Satterthwaite's method
           Sum Sq Mean Sq NumDF DenDF F value   Pr(>F)
GROUP      498257  498257     1    22  5.5606 0.027673 *
TIMING     316722  158361     2    44  1.7673 0.182697
eTIV       794045  794045     1    22  8.8617 0.006958 **
GROUP:TIMING 104889  52444     2    44  0.5853 0.561223
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

> → Stepwise simplification of the model:
>   1. remove GROUP:TIMING interaction (p=0.56122; AIC 1054.1 → 1051.3)
>   2. remove TIMING main effect (p=0.19062; AIC 1051.3 → 1050.6 for REML = FALSE)

> → Final model (REML = TRUE):

```
MODEL INFO:
Observations: 66
Dependent Variable: GMV
Type: Mixed effects linear regression

MODEL FIT:
AIC = 1032.024, BIC = 1042.972
Pseudo-R² (fixed effects) = 0.358
Pseudo-R² (total) = 0.977

FIXED EFFECTS:
----------------------------------------------------------------------------
                    Est.        2.5%       97.5%   t val.    d.f.       p
---------------- ---------- ----------- ----------- -------- -------- -------
(Intercept)      6753.024      45.038   13461.010    1.973   19.000   0.063
GROUP[complex]  -1548.204   -2932.883    -163.525   -2.191   19.000   0.041
eTIV                0.009       0.002       0.015    2.766   19.000   0.012
----------------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
```

```
   Group      Parameter    Std. Dev.
--------- ------------- -----------
 SUBJECT   (Intercept)   1646.800
 Residual                 314.939
---------------------------------

Grouping variables:
--------------------------
  Group    # groups   ICC
--------- ---------- -------
 SUBJECT      22      0.965
--------------------------

Type III Analysis of Variance Table with Satterthwaite's method
       Sum Sq Mean Sq NumDF DenDF F value  Pr(>F)
GROUP  476330  476330     1    19  4.8024 0.04108 *
eTIV   759100  759100     1    19  7.6533 0.01229 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

> GMV SM1

→ Full model:

```
MODEL INFO:
Observations: 66
Dependent Variable: GMV
Type: Mixed effects linear regression

MODEL FIT:
AIC = 1027.053, BIC = 1046.760
Pseudo-R² (fixed effects) = 0.287
Pseudo-R² (total) = 0.976

FIXED EFFECTS:
-------------------------------------------------------------------------------
                           Est.      2.5%      97.5%   t val.    d.f.       p
----------------------- ---------- ---------- ---------- -------- -------- -------
(Intercept)              7987.663  2727.933  13247.393    2.976   22.021   0.007
GROUP[complex]           -426.452 -1524.157    671.254   -0.761   23.003   0.454
TIMING[mid]               -51.818  -252.036    148.400   -0.507   44.000   0.615
TIMING[post]              -70.545  -270.763    129.672   -0.691   44.000   0.493
eTIV                         0.007     0.002      0.012    2.856   22.000   0.009
GROUP[complex]:TIMING[mid] -139.818 -422.969    143.332   -0.968   44.000   0.338
GROUP[complex]:TIMING[post] -25.364 -308.514    257.787   -0.176   44.000   0.861
-------------------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
----------------------------------
   Group      Parameter    Std. Dev.
--------- ------------- -----------
 SUBJECT   (Intercept)   1291.402
 Residual                 239.572
----------------------------------

Grouping variables:
--------------------------
  Group    # groups   ICC
--------- ---------- -------
 SUBJECT      22      0.967
--------------------------

Type III Analysis of Variance Table with Satterthwaite's method
             Sum Sq Mean Sq NumDF DenDF F value    Pr(>F)
GROUP         43386   43386     1    22  0.7559 0.393993
TIMING       170328   85164     2    44  1.4838 0.237893
eTIV         468100  468100     1    22  8.1558 0.009189 **
GROUP:TIMING  61036   30518     2    44  0.5317 0.591321
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

→ Stepwise simplification of the model:
  1. remove GROUP:TIMING interaction (p=0.5913; AIC 1027.1 → 1024.1)
  2. remove GROUP main effect (p=0.393993; AIC 1024.1 → 1022.8 for REML = FALSE)

→ Final model (REML = TRUE):

```
MODEL INFO:
Observations: 66
Dependent Variable: GMV
Type: Mixed effects linear regression
```

```
MODEL FIT:
AIC = 999.205, BIC = 1012.342
Pseudo-R² (fixed effects) = 0.245
Pseudo-R² (total) = 0.976


FIXED EFFECTS:
-----------------------------------------------------------------------------
                     Est.      2.5%      97.5%   t val.     d.f.       p
----------------- ---------- --------- ---------- -------- -------- -------
(Intercept)        7790.361  2206.765  13373.958    2.735   20.009   0.013
TIMING[mid]        -121.727  -268.375     24.920   -1.627   42.000   0.111
TIMING[post]        -83.227  -229.875     63.420   -1.112   42.000   0.272
eTIV                  0.007     0.002      0.012    2.672   20.000   0.015
-----------------------------------------------------------------------------


p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
  Group      Parameter    Std. Dev.
--------- ------------- -----------
 SUBJECT    (Intercept)   1377.958
 Residual                  248.155
------------------------------------


Grouping variables:
--------------------------
  Group    # groups   ICC
--------- ---------- -------
 SUBJECT      22      0.969
--------------------------


Type III Analysis of Variance Table with Satterthwaite's method
       Sum Sq Mean Sq NumDF DenDF F value  Pr(>F)
TIMING 170328   85164     2    42  1.3830 0.26202
eTIV   439586  439586     1    20  7.1383 0.01465 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

> GMV (pre)SMA

→   Full model:

```
MODEL INFO:
Observations: 66
Dependent Variable: GMV
Type: Mixed effects linear regression

MODEL FIT:
AIC = 1014.603, BIC = 1034.310
Pseudo-R² (fixed effects) = 0.330
Pseudo-R² (total) = 0.975


FIXED EFFECTS:
-----------------------------------------------------------------------------------
                            Est.       2.5%      97.5%   t val.     d.f.       p
----------------------- ---------- ---------- ---------- -------- -------- -------
(Intercept)               4323.242   -278.500   8924.985    1.841   22.024   0.079
GROUP[complex]            -221.256  -1182.944    740.433   -0.451   23.130   0.656
TIMING[mid]               -133.000   -318.818     52.818   -1.403   44.000   0.168
TIMING[post]                 4.818   -181.000    190.636    0.051   44.000   0.960
eTIV                         0.007      0.003      0.011    3.260   22.000   0.004
GROUP[complex]:TIMING[mid]  -18.545   -281.332    244.241   -0.138   44.000   0.891
GROUP[complex]:TIMING[post] -93.091   -355.877    169.695   -0.694   44.000   0.491
-----------------------------------------------------------------------------------


p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
  Group      Parameter    Std. Dev.
--------- ------------- -----------
 SUBJECT    (Intercept)   1129.003
 Residual                  222.342
------------------------------------


Grouping variables:
--------------------------
  Group    # groups   ICC
--------- ---------- -------
 SUBJECT      22      0.963
--------------------------
```

```
Type III Analysis of Variance Table with Satterthwaite's method
             Sum Sq Mean Sq NumDF DenDF F value   Pr(>F)
GROUP         14068   14068     1    22  0.2846 0.599071
TIMING       235342  117671     2    44  2.3803 0.104339
eTIV         525409  525409     1    22 10.6281 0.003586 **
GROUP:TIMING  26706   13353     2    44  0.2701 0.764554
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

→ Stepwise simplification of the model:
1. remove GROUP:TIMING interaction (p=0.7646; AIC 1014.6 → 1011.1)
2. remove GROUP main effect (p=0.599071; AIC 1011.1 → 1009.4 for REML = FALSE)

→ Final model (REML = TRUE):

```
MODEL INFO:
Observations: 66
Dependent Variable: GMV
Type: Mixed effects linear regression

MODEL FIT:
AIC = 986.679, BIC = 999.817
Pseudo-R² (fixed effects) = 0.301
Pseudo-R² (total) = 0.975

FIXED EFFECTS:
--------------------------------------------------------------------------
                   Est.       2.5%      97.5%   t val.     d.f.       p
---------------- ---------- ---------- ---------- -------- -------- -------
(Intercept)      4221.162   -613.001   9055.326    1.711   20.010   0.102
TIMING[mid]      -142.273   -277.581     -6.965   -2.061   42.000   0.046
TIMING[post]      -41.727   -177.035     93.581   -0.604   42.000   0.549
eTIV                0.007      0.003      0.011    3.085   20.000   0.006
--------------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
  Group     Parameter    Std. Dev.
--------- ------------- -----------
 SUBJECT   (Intercept)   1192.113
 Residual                 228.967
------------------------------------

Grouping variables:
---------------------------
  Group    # groups   ICC
--------- ---------- -------
 SUBJECT      22      0.964
---------------------------

Type III Analysis of Variance Table with Satterthwaite's method
        Sum Sq Mean Sq NumDF DenDF F value  Pr(>F)
TIMING  235342  117671     2    42  2.2445 0.11854
eTIV    498961  498961     1    20  9.5175 0.00584 **
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

> aCT CB

→ Analysis not available since volume- (and not surface-)based segmentation

> aCT DLPFC

→ Full model:

```
MODEL INFO:
Observations: 66
Dependent Variable: aCT
Type: Mixed effects linear regression

MODEL FIT:
AIC = -156.124, BIC = -136.417
Pseudo-R² (fixed effects) = 0.100
Pseudo-R² (total) = 0.705

FIXED EFFECTS:
--------------------------------------------------------------------------
```

```
                              Est.     2.5%   97.5%    t val.    d.f.      p
------------------------- -------- -------- ------- -------- -------- -------
(Intercept)                  2.466    2.174   2.759   16.537   22.262   0.000
GROUP[complex]              -0.021   -0.089   0.047   -0.617   34.659   0.541
TIMING[mid]                 -0.004   -0.043   0.035   -0.182   44.000   0.856
TIMING[post]                -0.007   -0.046   0.032   -0.353   44.000   0.726
eTIV                        -0.000   -0.000   0.000   -0.682   22.000   0.502
GROUP[complex]:TIMING[mid]  -0.042   -0.097   0.013   -1.493   44.000   0.142
GROUP[complex]:TIMING[post] -0.019   -0.074   0.036   -0.663   44.000   0.511
------------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
  Group      Parameter    Std. Dev.
---------- ------------- -----------
 SUBJECT    (Intercept)     0.067
 Residual                   0.047
------------------------------------

Grouping variables:
---------------------------
  Group    # groups    ICC
--------- ---------- -------
 SUBJECT      22       0.672
---------------------------

Type III Analysis of Variance Table with Satterthwaite's method
              Sum Sq   Mean Sq NumDF DenDF F value Pr(>F)
GROUP        0.0039918 0.0039918    1    22  1.8380 0.1889
TIMING       0.0068998 0.0034499    2    44  1.5885 0.2157
eTIV         0.0010104 0.0010104    1    22  0.4652 0.5023
GROUP:TIMING 0.0048640 0.0024320    2    44  1.1198 0.3355
```

→ Stepwise simplification of the model:
   1. remove GROUP:TIMING interaction (p=0.3355; AIC -156.1 → -157.9)
   2. remove TIMING main effect (p=0.2318; AIC -157.9 → -159.0 for REML = FALSE)

→ Final model (REML = TRUE):

```
MODEL INFO:
Observations: 66
Dependent Variable: aCT
Type: Mixed effects linear regression

MODEL FIT:
AIC = -117.778, BIC = -106.830
Pseudo-R² (fixed effects) = 0.068
Pseudo-R² (total) = 0.702

FIXED EFFECTS:
-------------------------------------------------------------------
                    Est.     2.5%   97.5%   t val.    d.f.       p
---------------- -------- -------- ------- ------- -------- -------
(Intercept)         2.463    2.149   2.776   15.392   19.000   0.000
GROUP[complex]     -0.042   -0.106   0.023   -1.260   19.000   0.223
eTIV               -0.000   -0.000   0.000   -0.634   19.000   0.534
-------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
  Group      Parameter    Std. Dev.
---------- ------------- -----------
 SUBJECT    (Intercept)     0.072
 Residual                   0.049
------------------------------------

Grouping variables:
---------------------------
  Group    # groups    ICC
--------- ---------- -------
 SUBJECT      22       0.680
---------------------------

Type III Analysis of Variance Table with Satterthwaite's method
        Sum Sq   Mean Sq NumDF DenDF F value Pr(>F)
GROUP 0.0038719 0.0038719    1    19  1.5873 0.2230
eTIV  0.0009801 0.0009801    1    19  0.4018 0.5337
```

> aCT hMT/V5+

→ Full model:

```
MODEL INFO:
Observations: 66
Dependent Variable: aCT
Type: Mixed effects linear regression

MODEL FIT:
AIC = -165.890, BIC = -146.183
Pseudo-R² (fixed effects) = 0.018
Pseudo-R² (total) = 0.886

FIXED EFFECTS:
------------------------------------------------------------------------
                          Est.    2.5%   97.5%  t val.    d.f.      p
----------------------- -------- ------- ------- -------- -------- -------
(Intercept)              2.392   1.987   2.797  11.577   22.078   0.000
GROUP[complex]           0.023  -0.064   0.110   0.516   25.744   0.611
TIMING[mid]             -0.010  -0.039   0.020  -0.650   44.000   0.519
TIMING[post]            -0.005  -0.035   0.024  -0.344   44.000   0.732
eTIV                    -0.000  -0.000   0.000  -0.305   22.000   0.763
GROUP[complex]:TIMING[mid] -0.012 -0.054  0.030  -0.554   44.000   0.582
GROUP[complex]:TIMING[post] 0.002 -0.040  0.044   0.101   44.000   0.920
------------------------------------------------------------------------


p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
  Group      Parameter    Std. Dev.
---------- ------------- -----------
 SUBJECT   (Intercept)     0.098
 Residual                  0.035
------------------------------------

Grouping variables:
---------------------------
  Group    # groups   ICC
--------- ---------- -------
 SUBJECT     22      0.884
---------------------------

Type III Analysis of Variance Table with Satterthwaite's method
                Sum Sq    Mean Sq NumDF DenDF F value Pr(>F)
GROUP        0.00026632 0.00026632    1    22  0.2125 0.6493
TIMING       0.00292288 0.00146144    2    44  1.1663 0.3210
eTIV         0.00011640 0.00011640    1    22  0.0929 0.7634
GROUP:TIMING 0.00062287 0.00031143    2    44  0.2485 0.7810
```

→ Stepwise simplification of the model:
1. remove GROUP:TIMING interaction (p=0.7810; AIC -165.9 → -169.4)
2. remove GROUP main effect (p=0.6493; AIC -169.4 → -171.2 for REML = FALSE)

→ Final model (REML = TRUE):

```
MODEL INFO:
Observations: 66
Dependent Variable: aCT
Type: Mixed effects linear regression

MODEL FIT:
AIC = -121.583, BIC = -108.445
Pseudo-R² (fixed effects) = 0.007
Pseudo-R² (total) = 0.890

FIXED EFFECTS:
--------------------------------------------------------------------
                  Est.    2.5%   97.5%  t val.    d.f.      p
----------------- ------- ------- ------- -------- -------- -------
(Intercept)       2.403   1.978   2.827  11.091   20.034   0.000
TIMING[mid]      -0.016  -0.037   0.006  -1.431   42.000   0.160
TIMING[post]     -0.004  -0.026   0.017  -0.375   42.000   0.710
eTIV             -0.000  -0.000   0.000  -0.286   20.000   0.778
--------------------------------------------------------------------


p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
  Group      Parameter    Std. Dev.
---------- ------------- -----------
 SUBJECT   (Intercept)     0.103
 Residual                  0.036
```

```
-----------------------------------

Grouping variables:
--------------------------
  Group    # groups   ICC
--------- ---------- -------
 SUBJECT     22       0.889
--------------------------


Type III Analysis of Variance Table with Satterthwaite's method
         Sum Sq    Mean Sq NumDF DenDF F value Pr(>F)
TIMING 0.00292288 0.00146144   2    42  1.1009 0.3420
eTIV   0.00010874 0.00010874   1    20  0.0819 0.7777
```

> aCT PMd

→   Full model:

```
MODEL INFO:
Observations: 66
Dependent Variable: aCT
Type: Mixed effects linear regression

MODEL FIT:
AIC = -143.266, BIC = -123.559
Pseudo-R² (fixed effects) = 0.238
Pseudo-R² (total) = 0.859

FIXED EFFECTS:
--------------------------------------------------------------------------
                            Est.    2.5%    97.5%   t val.    d.f.      p
---------------------- -------- -------- -------- -------- -------- -------
(Intercept)               2.812   2.408    3.217   13.632   22.132   0.000
GROUP[complex]           -0.098  -0.187   -0.009   -2.168   28.349   0.039
TIMING[mid]              -0.015  -0.054    0.023   -0.784   44.000   0.438
TIMING[post]              0.002  -0.036    0.041    0.117   44.000   0.908
eTIV                     -0.000  -0.000    0.000   -0.803   22.000   0.431
GROUP[complex]:TIMING[mid] -0.025  -0.079  0.029   -0.911   44.000   0.367
GROUP[complex]:TIMING[post]-0.008  -0.062  0.046   -0.279   44.000   0.781
--------------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
-----------------------------------
  Group     Parameter    Std. Dev.
--------- ------------- -----------
 SUBJECT   (Intercept)     0.096
 Residual                  0.046
-----------------------------------

Grouping variables:
--------------------------
  Group    # groups   ICC
--------- ---------- -------
 SUBJECT     22       0.815
--------------------------

Type III Analysis of Variance Table with Satterthwaite's method
               Sum Sq    Mean Sq NumDF DenDF F value  Pr(>F)
GROUP        0.0139019 0.0139019   1    22  6.6204 0.01735 *
TIMING       0.0108018 0.0054009   2    44  2.5720 0.08782 .
eTIV         0.0013538 0.0013538   1    22  0.6447 0.43060
GROUP:TIMING 0.0018287 0.0009144   2    44  0.4354 0.64974
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

→   Stepwise simplification of the model:
  1. remove GROUP:TIMING interaction (p=0.64974; AIC -143.3 → -146.4)
  2. remove TIMING main effect (p=0.09184; AIC -146.4 → -145.6 for REML = FALSE)
    → AIC of simplified model is NOT BETTER → keep TIMING in final model

→   Final model (REML = TRUE):

```
MODEL INFO:
Observations: 66
Dependent Variable: aCT
Type: Mixed effects linear regression

MODEL FIT:
AIC = -93.467, BIC = -78.140
Pseudo-R² (fixed effects) = 0.213
```

```
Pseudo-R² (total) = 0.864

FIXED EFFECTS:
------------------------------------------------------------------------
                      Est.      2.5%     97.5%   t val.     d.f.       p
----------------- -------- --------- --------- -------- -------- -------
(Intercept)          2.818     2.383     3.253   12.703   19.053   0.000
GROUP[complex]      -0.109    -0.199    -0.020   -2.391   19.000   0.027
TIMING[mid]         -0.028    -0.056     0.000   -1.953   42.000   0.057
TIMING[post]        -0.002    -0.030     0.026   -0.111   42.000   0.912
eTIV                -0.000    -0.000     0.000   -0.746   19.000   0.465
------------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
  Group     Parameter     Std. Dev.
--------- ------------- -----------
 SUBJECT    (Intercept)      0.104
 Residual                    0.047
------------------------------------

Grouping variables:
---------------------------
  Group    # groups    ICC
--------- ---------- -------
 SUBJECT      22      0.828
---------------------------

Type III Analysis of Variance Table with Satterthwaite's method
          Sum Sq   Mean Sq NumDF DenDF F value Pr(>F)
GROUP  0.0128269 0.0128269     1    19  5.7176 0.0273 *
TIMING 0.0108018 0.0054009     2    42  2.4075 0.1024
eTIV   0.0012491 0.0012491     1    19  0.5568 0.4647
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

> aCT SM1

→ Full model:

```
MODEL INFO:
Observations: 66
Dependent Variable: aCT
Type: Mixed effects linear regression

MODEL FIT:
AIC = -199.071, BIC = -179.364
Pseudo-R² (fixed effects) = 0.200
Pseudo-R² (total) = 0.948

FIXED EFFECTS:
---------------------------------------------------------------------------
                           Est.      2.5%     97.5%   t val.     d.f.       p
----------------------- -------- --------- --------- -------- -------- -------
(Intercept)                2.609     2.224     2.995   13.263   22.043   0.000
GROUP[complex]             0.009    -0.073     0.090    0.210   24.024   0.835
TIMING[mid]               -0.010    -0.030     0.011   -0.906   44.000   0.370
TIMING[post]              -0.012    -0.032     0.009   -1.094   44.000   0.280
eTIV                      -0.000    -0.000    -0.000   -2.355   22.000   0.028
GROUP[complex]:TIMING[mid] -0.010   -0.039     0.020   -0.645   44.000   0.522
GROUP[complex]:TIMING[post] 0.003   -0.027     0.032    0.173   44.000   0.863
---------------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
  Group     Parameter     Std. Dev.
--------- ------------- -----------
 SUBJECT    (Intercept)      0.094
 Residual                    0.025
------------------------------------

Grouping variables:
---------------------------
  Group    # groups    ICC
--------- ---------- -------
 SUBJECT      22      0.935
---------------------------

Type III Analysis of Variance Table with Satterthwaite's method
              Sum Sq   Mean Sq NumDF DenDF F value  Pr(>F)
```

```
GROUP        0.0000152 0.0000152   1   22  0.0246 0.87680
TIMING       0.0024350 0.0012175   2   44  1.9674 0.15193
eTIV         0.0034324 0.0034324   1   22  5.5467 0.02785 *
GROUP:TIMING 0.0004610 0.0002305   2   44  0.3725 0.69119
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

→ Stepwise simplification of the model:
1. remove GROUP:TIMING interaction (p=0.69119; AIC -199.1 → -202.3)
2. remove GROUP main effect (p=0.87680; AIC -202.3 → -204.3 for REML = FALSE)

→ Final model (REML = TRUE):

```
MODEL INFO:
Observations: 66
Dependent Variable: aCT
Type: Mixed effects linear regression

MODEL FIT:
AIC = -153.095, BIC = -139.957
Pseudo-R² (fixed effects) = 0.184
Pseudo-R² (total) = 0.948

FIXED EFFECTS:
----------------------------------------------------------------------
                   Est.    2.5%    97.5%   t val.    d.f.       p
----------------- -------- ------- ------- -------- -------- -------
(Intercept)        2.614   2.211   3.016   12.722   20.019   0.000
TIMING[mid]       -0.014  -0.030   0.001   -1.866   42.000   0.069
TIMING[post]      -0.010  -0.025   0.005   -1.331   42.000   0.190
eTIV              -0.000  -0.000  -0.000   -2.243   20.000   0.036
----------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
------------------------------------
  Group      Parameter    Std. Dev.
---------- ------------- -----------
 SUBJECT   (Intercept)      0.099
 Residual                   0.026
------------------------------------

Grouping variables:
---------------------------
  Group    # groups   ICC
--------- ---------- -------
 SUBJECT     22       0.937
---------------------------

Type III Analysis of Variance Table with Satterthwaite's method
          Sum Sq   Mean Sq NumDF DenDF F value  Pr(>F)
TIMING 0.0024350 0.0012175     2    42  1.8467 0.17033
eTIV   0.0033177 0.0033177     1    20  5.0324 0.03636 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

> aCT (pre)SMA

→ Full model:

```
MODEL INFO:
Observations: 66
Dependent Variable: aCT
Type: Mixed effects linear regression

MODEL FIT:
AIC = -123.693, BIC = -103.986
Pseudo-R² (fixed effects) = 0.142
Pseudo-R² (total) = 0.857

FIXED EFFECTS:
--------------------------------------------------------------------------
                            Est.    2.5%    97.5%   t val.    d.f.      p
-------------------------- ------- ------- ------- -------- -------- -------
(Intercept)                 3.290   2.803   3.778   13.221   22.117   0.000
GROUP[complex]             -0.069  -0.175   0.038   -1.263   27.629   0.217
TIMING[mid]                -0.014  -0.058   0.029   -0.649   44.000   0.520
TIMING[post]                0.009  -0.034   0.053    0.425   44.000   0.673
eTIV                       -0.000  -0.000   0.000   -1.349   22.000   0.191
GROUP[complex]:TIMING[mid]  0.002  -0.060   0.063    0.060   44.000   0.952
GROUP[complex]:TIMING[post]-0.018  -0.080   0.043   -0.584   44.000   0.562
--------------------------------------------------------------------------
```

```
p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
-----------------------------------
  Group      Parameter     Std. Dev.
---------- ------------- -----------
 SUBJECT    (Intercept)     0.117
 Residual                   0.052
-----------------------------------

Grouping variables:
--------------------------
  Group    # groups    ICC
--------- ---------- -------
 SUBJECT      22       0.833
--------------------------

Type III Analysis of Variance Table with Satterthwaite's method
               Sum Sq   Mean Sq NumDF DenDF F value Pr(>F)
GROUP        0.0056815 0.0056815    1    22  2.0924 0.1621
TIMING       0.0027167 0.0013583    2    44  0.5002 0.6098
eTIV         0.0049438 0.0049438    1    22  1.8207 0.1910
GROUP:TIMING 0.0013758 0.0006879    2    44  0.2533 0.7773
```

→ Stepwise simplification of the model:
1. remove GROUP:TIMING interaction (p=0.7773; AIC -123.7 → -127.2)
2. remove TIMING main effect (p=0.6132; AIC -127.2 → -130.2 for REML = FALSE)

→ Final model (REML = TRUE):

```
MODEL INFO:
Observations: 66
Dependent Variable: aCT
Type: Mixed effects linear regression

MODEL FIT:
AIC = -92.056, BIC = -81.108
Pseudo-R² (fixed effects) = 0.124
Pseudo-R² (total) = 0.868

FIXED EFFECTS:
------------------------------------------------------------------
                  Est.    2.5%   97.5%  t val.    d.f.       p
---------------- ------- ------- ------- ------- -------- -------
(Intercept)       3.289   2.765   3.813  12.296   19.000   0.000
GROUP[complex]   -0.074  -0.182   0.034  -1.344   19.000   0.195
eTIV             -0.000  -0.000   0.000  -1.254   19.000   0.225
------------------------------------------------------------------

p values calculated using Satterthwaite d.f.

RANDOM EFFECTS:
-----------------------------------
  Group      Parameter     Std. Dev.
---------- ------------- -----------
 SUBJECT    (Intercept)     0.126
 Residual                   0.053
-----------------------------------

Grouping variables:
--------------------------
  Group    # groups    ICC
--------- ---------- -------
 SUBJECT      22       0.849
--------------------------

Type III Analysis of Variance Table with Satterthwaite's method
       Sum Sq   Mean Sq NumDF DenDF F value Pr(>F)
GROUP 0.0050749 0.0050749    1    19  1.8071 0.1947
eTIV  0.0044159 0.0044159    1    19  1.5724 0.2251
```

Supplement 4B: Association between baseline / changes in GM and motor learning outcome.

→ Pooled group analysis (n = 22)

VOI	Model				GMV / aCT				eTIV			
	p	F [DF]	mult. R²	adj. R²	β	SE	t	p	β	SE	t	p
TIMING PRE												
BTTscore_11 ~ GMV + eTIV												
CB	0.2261	1.6090 [2, 19]	0.1449	0.0548	-1.78E-06	1.24E-06	-1.4340	0.1679	4.22E-08	7.97E-08	0.5290	0.6029
DLPFC	0.4929	0.7344 [2, 19]	0.0717	-0.0259	-2.85E-06	4.52E-06	-0.6310	0.5356	-1.34E-08	7.62E-08	-0.1760	0.8619
hMT/V5+	0.5713	0.5766 [2, 19]	0.0572	-0.0420	1.42E-06	4.52E-06	0.3150	0.7566	-5.95E-08	5.69E-08	-1.0450	0.3092
PMd	0.1290	2.2850 [2, 19]	0.1939	0.1090	5.50E-06	3.01E-06	1.8270	0.0835	-9.52E-08	5.16E-08	-1.8450	0.0807
SM1	0.5940	0.5355 [2, 19]	0.0533	-0.0462	-6.06E-07	4.19E-06	-0.1450	0.8865	-4.62E-08	5.73E-08	-0.8060	0.4301
(pre)SMA	0.4831	0.7561 [2, 19]	0.0737	-0.0237	3.06E-06	4.63E-06	0.6630	0.5155	-7.14E-08	5.81E-08	-1.2300	0.2338
BTTscore_11 ~ aCT + eTIV												
DLPFC	0.5205	0.6759 [2, 19]	0.0664	-0.0318	0.0357	0.0666	0.5360	0.5980	-4.56E-08	4.97E-08	-0.9190	0.3700
hMT/V5+	0.5889	0.5446 [2, 19]	0.0542	-0.0453	0.0098	0.0500	0.1950	0.8470	-5.00E-08	4.92E-08	-1.0150	0.3230
PMd	0.3816	1.0140 [2, 19]	0.0964	0.0013	0.0405	0.0421	0.9630	0.3480	-4.02E-08	4.92E-08	-0.8170	0.4240
SM1	0.5218	0.6732 [2, 19]	0.0661	-0.0321	-0.0300	0.0565	-0.5310	0.6020	-6.31E-08	5.44E-08	-1.1600	0.2600
(pre)SMA	0.5923	0.5384 [2, 19]	0.0536	-0.0459	0.0067	0.0413	0.1630	0.8720	-4.83E-08	5.09E-08	-0.9490	0.3550
BTTscore_complex ~ GMV + eTIV												
CB	0.6028	0.5199 [2, 19]	0.0518	-0.0479	2.13E-07	1.17E-06	0.1810	0.8580	3.32E-08	7.52E-08	0.4420	0.6640
DLPFC	0.3924	0.9830 [2, 19]	0.0937	-0.0016	3.82E-06	4.00E-06	0.9550	0.3510	-5.29E-09	6.75E-08	-0.0780	0.9380
hMT/V5+	0.5902	0.5423 [2, 19]	0.0540	-0.0455	1.11E-06	4.06E-06	0.2740	0.7870	3.72E-08	5.11E-08	0.7280	0.4750
PMd	0.3978	0.9680 [2, 19]	0.0924	-0.0030	-2.69E-06	2.87E-06	-0.9400	0.3590	6.62E-08	4.91E-08	1.3490	0.1930
SM1	0.5552	0.6070 [2, 19]	0.0600	-0.0388	1.67E-06	3.74E-06	0.4450	0.6610	3.26E-08	5.12E-08	0.6380	0.5310
(pre)SMA	0.5958	0.5322 [2, 19]	0.0530	-0.0466	9.93E-07	4.19E-06	0.2370	0.8150	3.75E-08	5.26E-08	0.7120	0.4850
BTTscore_complex ~ aCT + eTIV												
DLPFC	0.3350	1.1590 [2, 19]	0.1087	0.0149	0.0652	0.0584	1.1170	0.2780	5.30E-08	4.35E-08	1.2180	0.2380
hMT/V5+	0.3349	1.1590 [2, 19]	0.1088	0.0150	0.0486	0.0435	1.1170	0.2780	4.65E-08	4.28E-08	1.0850	0.2920
PMd	0.4442	0.8471 [2, 19]	0.0818	-0.0147	-0.0307	0.0380	-0.8090	0.4290	3.65E-08	4.45E-08	0.8220	0.4210
SM1	0.1067	2.5240 [2, 19]	0.2099	0.1267	0.0913	0.0466	1.9590	0.0649	8.28E-08	4.48E-08	1.8470	0.0804
(pre)SMA	0.6065	0.5134 [2, 19]	0.0512	-0.0486	0.0053	0.0370	0.1430	0.8880	4.60E-08	4.57E-08	1.0060	0.3270
DIFFERENCE POST – PRE												
BTTscore_11 ~ GMV + eTIV												
CB	0.5510	0.6151 [2, 19]	0.0608	-0.0380	2.35E-06	5.66E-06	0.4150	0.6831	-5.30E-08	4.94E-08	-1.0730	0.2969
DLPFC	0.5036	0.7114 [2, 19]	0.0696	-0.0282	-7.23E-06	1.22E-05	-0.5950	0.5587	-4.34E-08	5.02E-08	-0.8650	0.3979
hMT/V5+	0.5103	0.6972 [2, 19]	0.0683	-0.0296	-1.06E-05	1.85E-05	-0.5720	0.5738	-5.09E-08	4.88E-08	-1.0430	0.3099
PMd	0.5885	0.5453 [2, 19]	0.0542	-0.0452	-2.65E-06	1.33E-05	-0.1990	0.8445	-4.84E-08	5.02E-08	-0.9640	0.3470
SM1	0.5985	0.5274 [2, 19]	0.0525	-0.0471	-1.10E-06	1.46E-05	-0.0750	0.9412	-5.04E-08	4.92E-08	-1.0240	0.3187
(pre)SMA	0.4630	0.8021 [2, 19]	0.0778	-0.0192	-1.11E-05	1.53E-05	-0.7250	0.4770	-4.69E-08	4.88E-08	-0.9610	0.3488
BTTscore_11 ~ aCT + eTIV												
DLPFC	0.4867	0.7480 [2, 19]	0.0729	-0.0245	-0.0535	0.0822	-0.6510	0.5229	-4.49E-08	4.94E-08	-0.9090	0.3749
hMT/V5+	0.5317	0.6531 [2, 19]	0.0643	-0.0341	-0.0515	0.1042	-0.4940	0.6270	-5.27E-08	4.91E-08	-1.0730	0.2970
PMd	0.5930	0.5372 [2, 19]	0.0535	-0.0461	-0.0127	0.0817	-0.1560	0.8780	-4.86E-08	5.05E-08	-0.9630	0.3476
SM1	0.5509	0.6154 [2, 19]	0.0608	-0.0380	-0.0655	0.1576	-0.4150	0.6827	-4.99E-08	4.90E-08	-1.0180	0.3216
(pre)SMA	0.5451	0.6266 [2, 19]	0.0618	-0.0368	-0.0277	0.0630	-0.4400	0.6648	-4.89E-08	4.91E-08	-0.9960	0.3316
BTTscore_complex ~ GMV + eTIV												
CB	0.5651	0.5883 [2, 19]	0.0583	-0.0408	-2.05E-06	5.08E-06	-0.4030	0.6910	4.65E-08	4.43E-08	1.0500	0.3070
DLPFC	0.5378	0.6409 [2, 19]	0.0632	-0.0354	-5.60E-06	1.09E-05	-0.5120	0.6140	4.97E-08	4.51E-08	1.1020	0.2840
hMT/V5+	0.6021	0.5212 [2, 19]	0.0520	-0.0477	3.15E-06	1.68E-05	0.1880	0.8530	4.44E-08	4.41E-08	1.0070	0.3270
PMd	0.5805	0.5597 [2, 19]	0.0556	-0.0437	3.93E-06	1.19E-05	0.3290	0.7460	4.13E-08	4.50E-08	0.9190	0.3700
SM1	0.5446	0.6276 [2, 19]	0.0619	-0.0367	-6.36E-06	1.31E-05	-0.4870	0.6320	4.44E-08	4.39E-08	1.0110	0.3250
(pre)SMA	0.4745	0.7756 [2, 19]	0.0754	-0.0218	-9.86E-06	1.37E-05	-0.7200	0.4800	4.74E-08	4.38E-08	1.0830	0.2920
BTTscore_complex ~ aCT + eTIV												
DLPFC	0.5940	0.5354 [2, 19]	0.0533	-0.0462	-0.0186	0.0744	-0.2500	0.8060	4.62E-08	4.48E-08	1.0320	0.3150
hMT/V5+	0.5692	0.5805 [2, 19]	0.0575	-0.0416	0.0360	0.0937	0.3850	0.7050	4.59E-08	4.42E-08	1.0380	0.3120
PMd	0.5996	0.5256 [2, 19]	0.0524	-0.0473	-0.0153	0.0733	-0.2090	0.8370	4.64E-08	4.53E-08	1.0250	0.3180
SM1	0.6128	0.5026 [2, 19]	0.0502	-0.0497	-0.0001	0.1421	-0.0010	1.0000	4.43E-08	4.42E-08	1.0020	0.3290
(pre)SMA	0.5218	0.6733 [2, 19]	0.0661	-0.0321	-0.0321	0.0563	-0.5690	0.5760	4.60E-08	4.39E-08	1.0480	0.3080

BTTscore$_{11}$ ~ GMV + eTIV

CB	0.6002	0.5244 [2, 19]	0.0523	-0.0474	-3.23E-08	7.17E-06	-0.0050	0.9964	-5.04E-08	4.92E-08	-1.0240	0.3187
DLPFC	0.4220	0.9030 [2, 19]	0.0868	-0.0093	-1.16E-05	1.37E-05	-0.8470	0.4075	-5.04E-08	4.83E-08	-1.0430	0.3102
hMT/V5+	0.5944	0.5347 [2, 19]	0.0532	-0.0463	2.87E-06	2.06E-05	0.1390	0.8906	-5.01E-08	4.93E-08	-1.0170	0.3220
PMd	0.5382	0.6402 [2, 19]	0.0631	-0.0354	-6.31E-06	1.35E-05	-0.4680	0.6450	-4.80E-08	4.92E-08	-0.9760	0.3410
SM1	0.4381	0.8623 [2, 19]	0.0832	-0.0132	1.42E-05	1.77E-05	0.8000	0.4335	-4.65E-08	4.87E-08	-0.9560	0.3512
(pre)SMA	0.4825	0.7574 [2, 19]	0.0738	-0.0236	-1.90E-05	2.86E-05	-0.6650	0.5143	-5.33E-08	4.89E-08	-1.0910	0.2889

BTTscore$_{11}$ ~ aCT + eTIV

DLPFC	0.1906	1.8110 [2, 19]	0.1601	0.0717	-0.1376	0.0881	-1.5620	0.1349	-4.78E-08	4.64E-08	-1.0300	0.3158
hMT/V5+	0.5974	0.5293 [2, 19]	0.0527	-0.0469	0.0097	0.1008	0.0960	0.9242	-5.05E-08	4.92E-08	-1.0260	0.3177
PMd	0.5553	0.6068 [2, 19]	0.0600	-0.0389	-0.0370	0.0938	-0.3950	0.6972	-4.46E-08	5.12E-08	-0.8710	0.3948
SM1	0.5596	0.5987 [2, 19]	0.0592	-0.0397	0.0602	0.1604	0.3750	0.7118	-5.05E-08	4.91E-08	-1.0300	0.3160
(pre)SMA	0.4944	0.7313 [2, 19]	0.0714	-0.0262	-0.0739	0.1180	-0.6260	0.5390	-5.20E-08	4.88E-08	-1.0660	0.3000

BTTscore$_{complex}$ ~ GMV + eTIV

CB	0.5382	0.6402 [2, 19]	0.0631	-0.0354	-3.27E-06	6.39E-06	-0.5110	0.6150	4.45E-08	4.39E-08	1.0150	0.3230
DLPFC	0.5739	0.5719 [2, 19]	0.0567	-0.0425	4.54E-06	1.25E-05	0.3630	0.7210	4.43E-08	4.40E-08	1.0060	0.3270
hMT/V5+	0.6086	0.5098 [2, 19]	0.0509	-0.0489	2.15E-06	1.85E-05	0.1160	0.9090	4.45E-08	4.42E-08	1.0070	0.3260
PMd	0.5406	0.6354 [2, 19]	0.0626	-0.0359	6.07E-06	1.21E-05	0.5020	0.6210	4.20E-08	4.41E-08	0.9520	0.3530
SM1	0.6077	0.5114 [2, 19]	0.0510	-0.0488	2.09E-06	1.62E-05	0.1290	0.8990	4.49E-08	4.44E-08	1.0110	0.3250
(pre)SMA	0.5796	0.5614 [2, 19]	0.0558	-0.0435	-8.65E-06	2.59E-05	-0.3340	0.7420	4.30E-08	4.42E-08	0.9720	0.3430

BTTscore$_{complex}$ ~ aCT + eTIV

DLPFC	0.5993	0.5261 [2, 19]	0.0524	-0.0472	0.0177	0.0839	0.2110	0.8350	4.39E-08	4.41E-08	0.9950	0.3320
hMT/V5+	0.6119	0.5041 [2, 19]	0.0503	-0.0495	0.0047	0.0905	0.0520	0.9590	4.42E-08	4.42E-08	1.0010	0.3290
PMd	0.6123	0.5034 [2, 19]	0.0503	-0.0496	0.0032	0.0845	0.0380	0.9700	4.38E-08	4.61E-08	0.9490	0.3540
SM1	0.5915	0.5400 [2, 19]	0.0537	-0.0458	0.0384	0.1442	0.2660	0.7930	4.42E-08	4.41E-08	1.0030	0.3280
(pre)SMA	0.5130	0.6916 [2, 19]	0.0678	-0.0302	0.0635	0.1059	0.5990	0.5560	4.57E-08	4.38E-08	1.0420	0.3100

BTTscore$_{11}$ ~ GMV + eTIV

CB	0.5505	0.6160 [2, 19]	0.0609	-0.0379	2.35E-06	5.64E-06	0.4170	0.6816	-5.28E-08	4.93E-08	-1.0700	0.2979
DLPFC	0.5952	0.5333 [2, 19]	0.0531	-0.0465	1.49E-06	1.15E-05	0.1300	0.8981	-5.19E-08	5.05E-08	-1.0280	0.3169
hMT/V5+	0.4125	0.9281 [2, 19]	0.0890	-0.0068	-1.98E-05	2.27E-05	-0.8750	0.3927	-4.91E-08	4.83E-08	-1.0170	0.3219
PMd	0.5816	0.5576 [2, 19]	0.0554	-0.0439	3.22E-06	1.28E-05	0.2510	0.8046	-5.16E-08	4.94E-08	-1.0450	0.3089
SM1	0.4179	0.9139 [2, 19]	0.0877	-0.0082	-1.46E-05	1.70E-05	-0.8590	0.4010	-4.62E-08	4.86E-08	-0.9520	0.3530
(pre)SMA	0.5596	0.5987 [2, 19]	0.0592	-0.0397	-5.92E-06	1.58E-05	-0.3750	0.7120	-4.76E-08	4.96E-08	-0.9600	0.3490

BTTscore$_{11}$ ~ aCT + eTIV

DLPFC	0.4954	0.7291 [2, 19]	0.0712	-0.0264	0.0477	0.0766	0.6230	0.5408	-5.44E-08	4.92E-08	-1.1070	0.2821
hMT/V5+	0.4323	0.8767 [2, 19]	0.0844	-0.0118	-0.1145	0.1401	-0.8170	0.4240	-5.68E-08	4.90E-08	-1.1580	0.2611
PMd	0.5879	0.5463 [2, 19]	0.0543	-0.0451	0.0181	0.0891	0.2030	0.8409	-5.01E-08	4.92E-08	-1.0180	0.3214
SM1	0.4441	0.8474 [2, 19]	0.0818	-0.0147	-0.1203	0.1537	-0.7820	0.4437	-4.96E-08	4.85E-08	-1.0240	0.3186
(pre)SMA	0.5958	0.5323 [2, 19]	0.0530	-0.0466	-0.0087	0.0711	-0.1220	0.9041	-4.98E-08	4.95E-08	-1.0050	0.3275

BTTscore$_{complex}$ ~ GMV + eTIV

CB	0.6128	0.5026 [2, 19]	0.0502	-0.0497	3.66E-09	5.08E-06	0.0010	0.9990	4.43E-08	4.45E-08	0.9960	0.3320
DLPFC	0.4520	0.8282 [2, 19]	0.0801	-0.0166	-7.98E-06	1.02E-05	-0.7860	0.4410	5.20E-08	4.46E-08	1.1670	0.2580
hMT/V5+	0.6096	0.5080 [2, 19]	0.0507	-0.0491	2.10E-06	2.07E-05	0.1010	0.9200	4.41E-08	4.42E-08	0.9990	0.3300
PMd	0.6052	0.5157 [2, 19]	0.0514	-0.0483	-1.81E-06	1.15E-05	-0.1570	0.8770	4.50E-08	4.44E-08	1.0140	0.3230
SM1	0.4798	0.7636 [2, 19]	0.0744	-0.0230	-1.08E-05	1.53E-05	-0.7040	0.4900	4.74E-08	4.38E-08	1.0820	0.2930
(pre)SMA	0.5273	0.6619 [2, 19]	0.0651	-0.0332	-7.76E-06	1.41E-05	-0.5500	0.5890	4.79E-08	4.43E-08	1.0820	0.2930

BTTscore$_{complex}$ ~ aCT + eTIV

DLPFC	0.5640	0.5904 [2, 19]	0.0585	-0.0405	-0.0282	0.0692	-0.4080	0.6880	4.43E-08	4.45E-08	1.0520	0.3060
hMT/V5+	0.5542	0.6089 [2, 19]	0.0602	-0.0386	0.0572	0.1272	0.4490	0.6580	5.20E-08	4.46E-08	1.0660	0.3000
PMd	0.5919	0.5392 [2, 19]	0.0537	-0.0459	-0.0211	0.0798	-0.2640	0.7950	4.41E-08	4.42E-08	0.9950	0.3320
SM1	0.5926	0.5379 [2, 19]	0.0535	-0.0460	-0.0362	0.1399	-0.2590	0.7990	4.50E-08	4.44E-08	1.0100	0.3250
(pre)SMA	0.3711	1.0450 [2, 19]	0.0990	0.0042	-0.0631	0.0621	-1.0150	0.3230	4.74E-08	4.38E-08	1.1340	0.2710

→ Analysis for group 'complex training' (n = 11)

VOI	Model				GMV / aCT				eTIV			
	p	F [DF]	mult. R^2	adj. R^2	β	SE	t	p	β	SE	t	p
TIMING PRE												
BTTscore$_{11}$ ~ GMV + eTIV												
CB	0.2023	1.9650 [2, 8]	0.3294	0.1617	-2.54E-06	1.95E-06	-1.2980	0.2306	4.27E-08	1.40E-07	0.3050	0.7681
DLPFC	0.2505	1.6540 [2, 8]	0.2926	0.1157	-8.81E-06	8.11E-06	-1.0860	0.3090	2.05E-08	1.43E-07	0.1430	0.8895
hMT/V5+	0.3961	1.0420 [2, 8]	0.2067	0.0083	-5.17E-06	1.20E-05	-0.4310	0.6778	-8.39E-08	1.03E-07	-0.8180	0.4371
PMd	0.2740	1.5290 [2, 8]	0.2765	0.0956	8.16E-06	8.26E-06	0.9880	0.3520	-1.60E-07	9.15E-08	-1.7480	0.1190
SM1	0.4142	0.9861 [2, 8]	0.1978	-0.0027	-2.38E-06	7.70E-06	-0.3080	0.7660	-9.82E-08	9.13E-08	-1.0760	0.3130
(pre)SMA	0.0809	3.5000 [2, 8]	0.4666	0.3333	2.26E-05	1.11E-05	2.0440	0.0753	-2.82E-07	1.07E-07	-2.6450	**0.0295***
BTTscore$_{11}$ ~ aCT + eTIV												
DLPFC	0.4188	0.9723 [2, 8]	0.1955	-0.0055	-0.0314	0.1164	-0.2700	0.7940	-1.15E-07	8.28E-08	-1.3940	0.2010
hMT/V5+	0.4342	0.9275 [2, 8]	0.1882	-0.0147	0.0003	0.0680	0.0050	0.9960	-1.11E-07	8.17E-08	-1.3600	0.2110
PMd	0.4300	0.9397 [2, 8]	0.1902	-0.0122	0.0120	0.0850	0.1410	0.8920	-1.08E-07	8.45E-08	-1.2770	0.2370
SM1	0.3695	1.1300 [2, 8]	0.2203	0.0254	-0.0517	0.0901	-0.5740	0.5820	-1.35E-07	8.98E-08	-1.4990	0.1720
(pre)SMA	0.4299	0.9399 [2, 8]	0.1903	-0.0121	-0.0114	0.0802	-0.1420	0.8910	-1.12E-07	8.17E-08	-1.3700	0.2080
BTTscore$_{complex}$ ~ GMV + eTIV												
CB	0.5366	0.6735 [2, 8]	0.1441	-0.0698	1.25E-06	1.17E-06	1.0680	0.3170	-5.56E-08	8.37E-08	-0.6650	0.5250
DLPFC	0.4983	0.7608 [2, 8]	0.1598	-0.0502	5.36E-06	4.68E-06	1.1450	0.2850	-6.00E-08	8.26E-08	-0.7260	0.4880
hMT/V5+	0.8928	0.1151 [2, 8]	0.0279	-0.2150	1.55E-06	7.04E-06	0.2210	0.8310	1.19E-08	6.01E-08	0.1990	0.8470
PMd	0.4738	0.8212 [2, 8]	0.1703	-0.0370	-5.60E-06	4.68E-06	-1.1960	0.2660	5.36E-08	5.19E-08	1.0330	0.3320
SM1	0.1739	2.1950 [2, 8]	0.3543	0.1929	7.42E-06	3.66E-06	2.0290	0.0770	-2.02E-08	4.34E-08	-0.4660	0.6540
(pre)SMA	0.4602	0.8565 [2, 8]	0.1764	-0.0295	-8.92E-06	7.29E-06	-1.2240	0.2560	8.75E-08	7.02E-08	1.2470	0.2480
BTTscore$_{complex}$ ~ aCT + eTIV												
DLPFC	0.4120	0.9927 [2, 8]	0.1988	-0.0014	0.0817	0.0615	1.3290	0.2210	3.13E-08	4.38E-08	0.7160	0.4940
hMT/V5+	0.5866	0.5706 [2, 8]	0.1248	-0.0939	0.0363	0.0374	0.9690	0.3610	2.23E-08	4.49E-08	0.4960	0.6330
PMd	0.8446	0.1725 [2, 8]	0.0413	-0.1983	-0.0197	0.0490	-0.4010	0.6990	1.50E-08	4.87E-08	0.3070	0.7670
SM1	0.7335	0.3223 [2, 8]	0.0745	-0.1568	0.0350	0.0520	0.6740	0.5190	3.60E-08	5.18E-08	0.6950	0.5070
(pre)SMA	0.9110	0.0943 [2, 8]	0.0230	-0.2212	0.0042	0.0466	0.0910	0.9300	2.04E-08	4.75E-08	0.4300	0.6780
DIFFERENCE POST – PRE												
BTTscore$_{11}$ ~ GMV + eTIV												
CB	0.3664	1.1410 [2, 8]	0.2220	0.0275	8.08E-06	1.37E-05	0.5890	0.5720	-9.52E-08	8.43E-08	-1.1290	0.2920
DLPFC	0.4293	0.9416 [2, 8]	0.1906	-0.0118	-2.85E-06	1.88E-05	-0.1510	0.8833	-1.10E-07	8.20E-08	-1.3390	0.2174
hMT/V5+	0.3950	1.0460 [2, 8]	0.2073	0.0091	-1.25E-05	2.85E-05	-0.4380	0.6729	-1.15E-07	8.11E-08	-1.4170	0.1943
PMd	0.3984	1.0350 [2, 8]	0.2055	0.0069	-9.24E-06	2.22E-05	-0.4170	0.6874	-1.15E-07	8.13E-08	-1.4160	0.1945
SM1	0.4341	0.9279 [2, 8]	0.1883	-0.0146	-4.96E-07	2.05E-05	-0.0240	0.9810	-1.11E-07	8.16E-08	-1.3620	0.2100
(pre)SMA	0.4013	1.0260 [2, 8]	0.2041	0.0051	-1.04E-05	2.62E-05	-0.3990	0.7004	-1.11E-07	8.08E-08	-1.3710	0.2075
BTTscore$_{11}$ ~ aCT + eTIV												
DLPFC	0.4140	0.9866 [2, 8]	0.1978	-0.0026	-0.0403	0.1302	-0.3100	0.7647	-1.09E-07	8.13E-08	-1.3450	0.2156
hMT/V5+	0.3566	1.1760 [2, 8]	0.2272	0.0340	-0.1038	0.1634	-0.6350	0.5430	-1.18E-07	8.03E-08	-1.4660	0.1809
PMd	0.4289	0.9427 [2, 8]	0.1907	-0.0116	-0.0188	0.1199	-0.1570	0.8792	-1.10E-07	8.17E-08	-1.3490	0.2144
SM1	0.4310	0.9367 [2, 8]	0.1897	-0.0128	-0.0282	0.2308	-0.1220	0.9058	-1.12E-07	8.17E-08	-1.3680	0.2084
(pre)SMA	0.4235	0.9586 [2, 8]	0.1933	-0.0083	-0.0198	0.0883	-0.2250	0.8280	-1.11E-07	8.14E-08	-1.3630	0.2100
BTTscore$_{complex}$ ~ GMV + eTIV												
CB	0.5465	0.6523 [2, 8]	0.1402	-0.0747	-8.01E-06	7.64E-06	-1.0490	0.3250	4.37E-09	4.70E-08	0.0930	0.9280
DLPFC	0.8842	0.1250 [2, 8]	0.0303	-0.2121	-2.85E-06	1.09E-05	-0.2610	0.8000	2.15E-08	4.75E-08	0.4520	0.6630
hMT/V5+	0.8667	0.1457 [2, 8]	0.0351	-0.2061	-5.49E-06	1.67E-05	-0.3300	0.7500	1.85E-08	4.74E-08	0.3900	0.7070
PMd	0.5956	0.5532 [2, 8]	0.1215	-0.0981	1.17E-05	1.23E-05	0.9520	0.3690	2.52E-08	4.53E-08	0.5560	0.5940
SM1	0.8884	0.1201 [2, 8]	0.0291	-0.2136	-2.88E-06	1.19E-05	-0.2420	0.8150	1.98E-08	4.73E-08	0.4180	0.6870
(pre)SMA	0.9147	0.0902 [2, 8]	0.0220	-0.2224	-1.80E-07	1.54E-05	-0.0120	0.9910	2.01E-08	4.74E-08	0.4250	0.6820
BTTscore$_{complex}$ ~ aCT + eTIV												
DLPFC	0.8963	0.1110 [2, 8]	0.0269	-0.2163	-0.0153	0.0760	-0.2020	0.8450	2.08E-08	4.74E-08	0.4390	0.6720
hMT/V5+	0.9094	0.0961 [2, 8]	0.0234	-0.2207	-0.0105	0.0973	-0.1080	0.9170	1.95E-08	4.78E-08	0.4080	0.6940
PMd	0.8968	0.1104 [2, 8]	0.0268	-0.2164	0.0139	0.0696	0.1990	0.8470	1.94E-08	4.75E-08	0.4100	0.6930
SM1	0.9117	0.0935 [2, 8]	0.0228	-0.2214	0.0109	0.1342	0.0820	0.9370	2.04E-08	4.75E-08	0.4290	0.6790
(pre)SMA	0.8716	0.1398 [2, 8]	0.0337	-0.2078	-0.0160	0.0512	-0.3120	0.7630	2.03E-08	4.72E-08	0.4310	0.6780

BTTscore$_{11}$ ~ GMV + eTIV

CB	0.3260	1.2940 [2, 8]	0.2444	0.0555	-9.38E-06	1.22E-05	-0.7710	0.4628	-1.31E-07	8.28E-08	-1.5810	0.1526
DLPFC	0.0908	3.2880 [2, 8]	0.4511	0.3139	-3.84E-05	1.96E-05	-1.9570	0.0860	-1.36E-07	6.83E-08	-1.9930	0.0814
hMT/V5+	0.4322	0.9333 [2, 8]	0.1892	-0.0135	-3.27E-06	3.37E-05	-0.0970	0.9250	-1.12E-07	8.23E-08	-1.3630	0.2099
PMd	0.2554	1.6270 [2, 8]	0.2891	0.1114	-2.07E-05	1.94E-05	-1.0650	0.3178	-1.09E-07	7.64E-08	-1.4220	0.1927
SM1	0.4317	0.9346 [2, 8]	0.1894	-0.0132	2.87E-06	2.67E-05	0.1080	0.9168	-1.10E-07	8.27E-08	-1.3250	0.2218
(pre)SMA	0.1004	3.1050 [2, 8]	0.4370	0.2963	-1.35E-04	7.20E-05	-1.8800	0.0969	-1.44E-07	7.02E-08	-2.0550	0.0740

BTTscore$_{11}$ ~ aCT + eTIV

DLPFC	0.0554	4.2460 [2, 8]	0.5149	0.3936	-0.2738	0.1180	-2.3210	**0.0488***	-1.08E-07	6.31E-08	-1.7080	0.1260
hMT/V5+	0.4340	0.9281 [2, 8]	0.1883	-0.0145	-0.0044	0.1444	-0.0310	0.9762	-1.11E-07	8.16E-08	-1.3620	0.2102
PMd	0.3479	1.2080 [2, 8]	0.2320	0.0400	-0.0859	0.1272	-0.6750	0.5190	-9.79E-08	8.18E-08	-1.1970	0.2650
SM1	0.4138	0.9872 [2, 8]	0.1979	-0.0025	-0.0670	0.2152	-0.3110	0.7635	-1.14E-07	8.16E-08	-1.3960	0.2001
(pre)SMA	0.2025	1.9630 [2, 8]	0.3291	0.1614	-0.2588	0.1997	-1.2960	0.2310	-1.26E-07	7.50E-08	-1.6740	0.1327

BTTscore$_{complex}$ ~ GMV + eTIV

CB	0.9147	0.0902 [2, 8]	0.0220	-0.2224	1.01E-07	7.33E-06	0.0140	0.9890	2.04E-08	4.99E-08	0.4080	0.6940
DLPFC	0.5198	0.7109 [2, 8]	0.1509	-0.0613	1.43E-05	1.29E-05	1.1020	0.3030	2.94E-08	4.50E-08	0.6540	0.5320
hMT/V5+	0.7375	0.3164 [2, 8]	0.0732	-0.1584	1.27E-05	1.91E-05	0.6650	0.5250	2.44E-08	4.66E-08	0.5230	0.6150
PMd	0.4464	0.8937 [2, 8]	0.1826	-0.0217	1.38E-05	1.10E-05	1.2540	0.2450	1.85E-08	4.34E-08	0.4260	0.6810
SM1	0.9147	0.0901 [2, 8]	0.0220	-0.2225	-4.23E-08	1.55E-05	-0.0030	0.9980	2.01E-08	4.81E-08	0.4180	0.6870
(pre)SMA	0.8783	0.1319 [2, 8]	0.0319	-0.2101	1.43E-05	5.00E-05	0.2860	0.7820	2.36E-08	4.88E-08	0.4850	0.6410

BTTscore$_{complex}$ ~ aCT + eTIV

DLPFC	0.7222	0.3390 [2, 8]	0.0781	-0.1523	0.0601	0.0861	0.6980	0.5050	1.94E-08	4.61E-08	0.4210	0.6850
hMT/V5+	0.8379	0.1808 [2, 8]	0.0432	-0.1960	0.0350	0.0830	0.4210	0.6850	2.08E-08	4.69E-08	0.4430	0.6700
PMd	0.6608	0.4365 [2, 8]	0.0983	-0.1270	0.0601	0.0730	0.8230	0.4340	1.09E-08	4.69E-08	0.2320	0.8230
SM1	0.7722	0.2670 [2, 8]	0.0625	-0.1718	0.0725	0.1232	0.5880	0.5730	2.32E-08	4.67E-08	0.4960	0.6330
(pre)SMA	0.6390	0.4739 [2, 8]	0.1059	-0.1176	0.1058	0.1221	0.8660	0.4120	2.60E-08	4.59E-08	0.5670	0.5860

BTTscore$_{11}$ ~ GMV + eTIV

CB	0.2397	1.7170 [2, 8]	0.3003	0.1254	1.10E-05	9.74E-06	1.1320	0.2904	-1.13E-07	7.58E-08	-1.4860	0.1757
DLPFC	0.2190	1.8470 [2, 8]	0.3159	0.1449	2.12E-05	1.73E-05	1.2220	0.2566	-1.35E-07	7.74E-08	-1.7440	0.1192
hMT/V5+	0.3912	1.0580 [2, 8]	0.2091	0.0114	-1.70E-05	3.69E-05	-0.4600	0.6579	-1.11E-07	8.06E-08	-1.3720	0.2073
PMd	0.3416	1.2320 [2, 8]	0.2355	0.0444	1.58E-05	2.24E-05	0.7030	0.5017	-1.03E-07	8.01E-08	-1.2800	0.2365
SM1	0.4300	0.9396 [2, 8]	0.1902	-0.0122	-3.75E-06	2.68E-05	-0.1400	0.8921	-1.10E-07	8.22E-08	-1.3350	0.2188
(pre)SMA	0.4325	0.9323 [2, 8]	0.1890	-0.0137	2.49E-06	2.81E-05	0.0890	0.9314	-1.12E-07	8.19E-08	-1.3650	0.2094

BTTscore$_{11}$ ~ aCT + eTIV

DLPFC	0.1971	2.0030 [2, 8]	0.3337	0.1671	0.1524	0.1153	1.3220	0.2228	-1.16E-07	7.40E-08	-1.5670	0.1557
hMT/V5+	0.3162	1.3340 [2, 8]	0.2501	0.0626	-0.1748	0.2152	-0.8120	0.4401	-1.19E-07	7.90E-08	-1.5050	0.1707
PMd	0.3766	1.1060 [2, 8]	0.2166	0.0208	0.0752	0.1397	0.5380	0.6049	-1.03E-07	8.15E-08	-1.2690	0.2402
SM1	0.4239	0.9571 [2, 8]	0.1931	-0.0086	0.0531	0.2421	0.2190	0.8318	-1.12E-07	8.15E-08	-1.3760	0.2061
(pre)SMA	0.4115	0.9943 [2, 8]	0.1991	-0.0011	0.0377	0.1145	0.3290	0.7504	-1.14E-07	8.14E-08	-1.3960	0.2001

BTTscore$_{complex}$ ~ GMV + eTIV

CB	0.6845	0.3976 [2, 8]	0.0904	-0.1370	-4.56E-06	5.88E-06	-0.7750	0.4600	2.07E-08	4.58E-08	0.4530	0.6630
DLPFC	0.4912	0.7780 [2, 8]	0.1628	-0.0464	-1.18E-05	1.02E-05	-1.1600	0.2800	3.35E-08	4.54E-08	0.7370	0.4820
hMT/V5+	0.4475	0.8907 [2, 8]	0.1821	-0.0223	-2.49E-05	1.99E-05	-1.2510	0.2460	2.10E-08	4.34E-08	0.4850	0.6410
PMd	0.8619	0.1514 [2, 8]	0.0364	-0.2044	-4.62E-06	1.33E-05	-0.3460	0.7380	1.76E-08	4.76E-08	0.3700	0.7210
SM1	0.8709	0.1407 [2, 8]	0.0339	-0.2075	-4.87E-06	1.55E-05	-0.3150	0.7610	2.21E-08	4.75E-08	0.4640	0.6550
(pre)SMA	0.9097	0.0958 [2, 8]	0.0233	-0.2208	-1.72E-06	1.63E-05	-0.1050	0.9190	2.06E-08	4.76E-08	0.4330	0.6770

BTTscore$_{complex}$ ~ aCT + eTIV

DLPFC	0.6774	0.4091 [2, 8]	0.0927	-0.1340	-0.0563	0.0713	-0.7900	0.4520	2.19E-08	4.57E-08	0.4800	0.6440
hMT/V5+	0.6609	0.4363 [2, 8]	0.0983	-0.1271	-0.1028	0.1249	-0.8230	0.4340	1.56E-08	4.59E-08	0.3390	0.7430
PMd	0.7489	0.2998 [2, 8]	0.0697	-0.1628	-0.0517	0.0806	-0.6400	0.5400	1.48E-08	4.70E-08	0.3150	0.7610
SM1	0.7794	0.2572 [2, 8]	0.0604	-0.1745	-0.0791	0.1384	-0.5720	0.5830	2.16E-08	4.66E-08	0.4640	0.6550
(pre)SMA	0.6335	0.4836 [2, 8]	0.1078	-0.1152	-0.0561	0.0640	-0.8770	0.4060	2.40E-08	4.55E-08	0.5270	0.6130

Note: Significant p-values are marked with an asterisk and printed in bold.

→ Analysis for group 'simple training' (n = 11)

VOI	Model				GMV / aCT				eTIV			
	p	F [DF]	mult. R²	adj. R²	β	SE	t	p	β	SE	t	p
TIMING PRE												
BTTscore₁₁ ~ GMV + eTIV												
CB	0.8045	0.2235 [2, 8]	0.0529	-0.1839	6.33E-07	1.60E-06	0.3950	0.7030	3.42E-09	8.45E-08	0.0400	0.9690
DLPFC	0.4441	0.8999 [2, 8]	0.1837	-0.0204	5.20E-06	4.30E-06	1.2090	0.2610	-2.49E-08	6.71E-08	-0.3710	0.7200
hMT/V5+	0.6799	0.4051 [2, 8]	0.0919	-0.1351	2.61E-06	3.66E-06	0.7120	0.4970	8.81E-09	6.00E-08	0.1470	0.8870
PMd	0.3869	1.0720 [2, 8]	0.2113	0.0142	3.80E-06	2.84E-06	1.3400	0.2170	-1.29E-08	5.84E-08	-0.2210	0.8310
SM1	0.8101	0.2162 [2, 8]	0.0512	-0.1859	-1.62E-06	4.30E-06	-0.3770	0.7160	4.38E-08	6.66E-08	0.6570	0.5290
(pre)SMA	0.8395	0.1789 [2, 8]	0.0428	-0.1965	-1.00E-06	3.79E-06	-0.2650	0.7980	3.51E-08	5.88E-08	0.5970	0.5670
BTTscore₁₁ ~ aCT + eTIV												
DLPFC	0.2928	1.4380 [2, 8]	0.2644	0.0805	0.0985	0.0623	1.5810	0.1520	4.17E-08	4.82E-08	0.8640	0.4120
hMT/V5+	0.6226	0.5031 [2, 8]	0.1117	-0.1103	0.0760	0.0911	0.8340	0.4280	3.12E-08	5.23E-08	0.5970	0.5670
PMd	0.3885	1.0670 [2, 8]	0.2105	0.0131	0.0560	0.0419	1.3360	0.2180	4.19E-08	5.02E-08	0.8350	0.4280
SM1	0.8685	0.1436 [2, 8]	0.0346	-0.2067	-0.0029	0.0658	-0.0440	0.9660	2.80E-08	6.00E-08	0.4670	0.6530
(pre)SMA	0.5552	0.6338 [2, 8]	0.1368	-0.0790	0.0404	0.0415	0.9740	0.3590	5.45E-08	5.78E-08	0.9440	0.3730
BTTscore_complex ~ GMV + eTIV												
CB	0.3589	1.1680 [2, 8]	0.2260	0.0325	-1.55E-06	1.76E-06	-0.8800	0.4040	1.37E-07	9.26E-08	1.4750	0.1780
DLPFC	0.5088	0.7360 [2, 8]	0.1554	-0.0557	1.07E-06	5.30E-06	0.2030	0.8450	6.28E-08	8.28E-08	0.7580	0.4700
hMT/V5+	0.5176	0.7158 [2, 8]	0.1518	-0.0602	-3.52E-07	4.29E-06	-0.0820	0.9370	7.67E-08	7.04E-08	1.0900	0.3080
PMd	0.4077	1.0060 [2, 8]	0.2009	0.0011	2.45E-06	3.46E-06	0.7060	0.5000	4.69E-08	7.13E-08	0.6580	0.5290
SM1	0.5075	0.7392 [2, 8]	0.1560	-0.0550	-1.06E-06	4.92E-06	-0.2160	0.8350	8.35E-08	7.62E-08	1.0960	0.3050
(pre)SMA	0.2723	1.5380 [2, 8]	0.2777	0.0971	4.73E-06	3.99E-06	1.1840	0.2700	4.58E-08	6.19E-08	0.7390	0.4810
BTTscore_complex ~ aCT + eTIV												
DLPFC	0.2633	1.5840 [2, 8]	0.2837	0.1046	0.0907	0.0745	1.2170	0.2580	8.55E-08	5.77E-08	1.4820	0.1770
hMT/V5+	0.4844	0.7947 [2, 8]	0.1657	-0.0428	0.0401	0.1070	0.3750	0.7170	7.51E-08	6.15E-08	1.2210	0.2570
PMd	0.4370	0.9196 [2, 8]	0.1869	-0.0163	0.0307	0.0516	0.5940	0.5690	8.10E-08	6.18E-08	1.3100	0.2260
SM1	**0.0191***	6.7660 [2, 8]	0.6284	0.5356	0.1586	0.0495	3.2060	**0.0125***	1.34E-07	4.51E-08	2.9760	**0.0177***
(pre)SMA	0.1718	2.2130 [2, 8]	0.3562	0.1952	0.0693	0.0434	1.5960	0.1490	1.18E-07	6.05E-08	1.9440	0.0879
DIFFERENCE POST – PRE												
BTTscore₁₁ ~ GMV + eTIV												
CB	0.5976	0.5494 [2, 8]	0.1208	-0.0990	-4.64E-06	5.23E-06	-0.8860	0.4010	5.26E-08	5.84E-08	0.9010	0.3940
DLPFC	0.1082	2.9750 [2, 8]	0.4265	0.2832	-2.95E-05	1.26E-05	-2.3390	**0.0475***	7.69E-08	4.67E-08	1.6460	0.1384
hMT/V5+	0.7208	0.3412 [2, 8]	0.0786	-0.1518	-1.43E-05	2.31E-05	-0.6190	0.5530	3.31E-08	5.36E-08	0.6170	0.5540
PMd	0.5346	0.6779 [2, 8]	0.1449	-0.0688	-1.69E-05	1.66E-05	-1.0170	0.3390	6.80E-08	6.40E-08	1.0630	0.3190
SM1	0.7961	0.2347 [2, 8]	0.0554	-0.1807	-9.86E-06	2.34E-05	-0.4220	0.6840	3.12E-08	5.41E-08	0.5760	0.5810
(pre)SMA	0.3999	1.0300 [2, 8]	0.2048	0.0060	-2.02E-05	1.54E-05	-1.3090	0.2270	4.32E-08	5.06E-08	0.8540	0.4180
BTTscore₁₁ ~ aCT + eTIV												
DLPFC	0.3055	1.3800 [2, 8]	0.2566	0.0707	-0.1404	0.0908	-1.5460	0.1610	5.45E-08	5.06E-08	1.0780	0.3130
hMT/V5+	0.8612	0.1523 [2, 8]	0.0366	-0.2042	0.0168	0.1226	0.1370	0.8950	2.95E-08	5.45E-08	0.5410	0.6040
PMd	0.6654	0.4288 [2, 8]	0.0968	-0.1290	-0.0863	0.1161	-0.7430	0.4780	5.12E-08	6.05E-08	0.8460	0.4220
SM1	0.4180	0.9746 [2, 8]	0.1959	-0.0051	-0.2647	0.2089	-1.2680	0.2410	4.21E-08	5.08E-08	0.8280	0.4310
(pre)SMA	0.4816	0.8017 [2, 8]	0.1670	-0.0412	-0.1106	0.0980	-1.1280	0.2920	4.12E-08	5.18E-08	0.7970	0.4490
BTTscore_complex ~ GMV + eTIV												
CB	0.4047	1.0150 [2, 8]	0.2024	0.0030	-4.33E-06	6.04E-06	-0.7180	0.4930	9.59E-08	6.74E-08	1.4230	0.1930
DLPFC	0.5177	0.7157 [2, 8]	0.1518	-0.0602	-1.50E-06	1.86E-05	-0.0810	0.9380	7.64E-08	6.89E-08	1.1090	0.3000
hMT/V5+	0.4848	0.7937 [2, 8]	0.1656	-0.0430	9.94E-06	2.67E-05	0.3730	0.7190	7.12E-08	6.19E-08	1.1500	0.2830
PMd	0.4800	0.8056 [2, 8]	0.1676	-0.0404	-7.93E-06	1.99E-05	-0.3990	0.7000	9.22E-08	7.65E-08	1.2040	0.2630
SM1	0.4283	0.9445 [2, 8]	0.1910	-0.0112	-1.65E-05	2.62E-05	-0.6290	0.5470	7.74E-08	6.07E-08	1.2740	0.2380
(pre)SMA	0.3999	1.0300 [2, 8]	0.2048	0.0060	-1.38E-05	1.87E-05	-0.7350	0.4830	8.35E-08	6.14E-08	1.3610	0.2110
BTTscore_complex ~ aCT + eTIV												
DLPFC	0.4951	0.7685 [2, 8]	0.1612	-0.0485	0.0363	0.1170	0.3100	0.7640	6.74E-08	6.51E-08	1.0350	0.3310
hMT/V5+	0.4195	0.9703 [2, 8]	0.1952	-0.0059	0.0900	0.1359	0.6620	0.5260	7.58E-08	6.04E-08	1.2560	0.2450
PMd	0.4182	0.9741 [2, 8]	0.1958	-0.0052	-0.0886	0.1328	-0.6670	0.5230	9.66E-08	6.92E-08	1.3960	0.2000
SM1	0.4639	0.8467 [2, 8]	0.1747	-0.0316	-0.1228	0.2566	-0.4780	0.6450	7.99E-08	6.24E-08	1.2820	0.2360
(pre)SMA	0.4996	0.7578 [2, 8]	0.1593	-0.0509	-0.0334	0.1194	-0.2790	0.7870	7.76E-08	6.30E-08	1.2310	0.2530

DIFFERENCE MID – PRE

$BTTscore_{11}$ ~ GMV + eTIV

CB	0.8690	0.1429 [2, 8]	0.0345	-0.2069	-2.54E-07	9.65E-06	-0.0260	0.9800	2.98E-08	6.14E-08	0.4860	0.6400
DLPFC	0.8275	0.1939 [2, 8]	0.0462	-0.1922	6.08E-06	1.93E-05	0.3150	0.7610	2.38E-08	5.67E-08	0.4190	0.6860
hMT/V5+	0.8693	0.1426 [2, 8]	0.0344	-0.2070	1.90E-07	2.42E-05	0.0080	0.9940	2.91E-08	5.47E-08	0.5320	0.6090
PMd	0.6390	0.4739 [2, 8]	0.1059	-0.1176	1.45E-05	1.81E-05	0.8000	0.4470	1.85E-08	5.41E-08	0.3420	0.7410
SM1	0.4285	0.9439 [2, 8]	0.1909	-0.0113	3.12E-05	2.51E-05	1.2440	0.2490	2.72E-08	4.99E-08	0.5450	0.6010
(pre)SMA	0.8674	0.1448 [2, 8]	0.0349	-0.2063	1.53E-06	2.33E-05	0.0660	0.9490	2.92E-08	5.45E-08	0.5350	0.6070

$BTTscore_{11}$ ~ aCT + eTIV

DLPFC	0.8683	0.1437 [2, 8]	0.0346	-0.2067	0.0059	0.1260	0.0470	0.9640	2.89E-08	5.46E-08	0.5290	0.6110
hMT/V5+	0.8668	0.1455 [2, 8]	0.0351	-0.2061	-0.0117	0.1548	-0.0760	0.9410	2.97E-08	5.50E-08	0.5400	0.6040
PMd	0.6523	0.4509 [2, 8]	0.1013	-0.1234	0.1324	0.1716	0.7720	0.4620	7.45E-09	5.96E-08	0.1250	0.9040
SM1	0.0829	3.4550 [2, 8]	0.4634	0.3293	0.7229	0.2859	2.5290	**0.0353***	-1.37E-08	4.40E-08	-0.3110	0.7636
(pre)SMA	0.7750	0.2632 [2, 8]	0.0617	-0.1728	0.0567	0.1174	0.4830	0.6420	2.78E-08	5.38E-08	0.5180	0.6190

$BTTscore_{complex}$ ~ GMV + eTIV

CB	0.5171	0.7170 [2, 8]	0.1520	-0.0599	-1.03E-06	1.10E-05	-0.0940	0.9280	7.69E-08	6.98E-08	1.1030	0.3020
DLPFC	0.2264	1.7990 [2, 8]	0.3102	0.1378	2.70E-05	1.99E-05	1.3590	0.2110	5.03E-08	5.85E-08	0.8600	0.4150
hMT/V5+	0.5194	0.7119 [2, 8]	0.1511	-0.0611	1.00E-07	2.75E-05	0.0040	0.9970	7.39E-08	6.22E-08	1.1890	0.2690
PMd	0.4296	0.9407 [2, 8]	0.1904	-0.0120	1.30E-05	2.09E-05	0.6230	0.5500	6.44E-08	6.24E-08	1.0310	0.3320
SM1	0.1558	2.3670 [2, 8]	0.3718	0.2147	4.49E-05	2.68E-05	1.6760	0.1320	7.12E-08	5.33E-08	1.3350	0.2190
(pre)SMA	0.4764	0.8146 [2, 8]	0.1692	-0.0385	-1.10E-05	2.62E-05	-0.4180	0.6870	7.36E-08	6.13E-08	1.2010	0.2640

$BTTscore_{complex}$ ~ aCT + eTIV

DLPFC	0.1831	2.1150 [2, 8]	0.3458	0.1823	0.1942	0.1258	1.5430	0.1610	6.79E-08	5.45E-08	1.2450	0.2480
hMT/V5+	0.5192	0.7121 [2, 8]	0.1511	-0.0610	-0.0038	0.1761	-0.0220	0.9830	7.41E-08	6.26E-08	1.1850	0.2700
PMd	0.5193	0.7120 [2, 8]	0.1511	-0.0611	0.0032	0.2022	0.0160	0.9880	7.34E-08	7.02E-08	1.0450	0.3260
SM1	0.4931	0.7734 [2, 8]	0.1620	-0.0474	0.1400	0.4331	0.3230	0.7550	6.56E-08	6.67E-08	0.9840	0.3540
(pre)SMA	0.5188	0.7132 [2, 8]	0.1513	-0.0608	0.0065	0.1353	0.0480	0.9630	7.38E-08	6.20E-08	1.1900	0.2680

DIFFERENCE POST – MID

$BTTscore_{11}$ ~ GMV + eTIV

CB	0.5418	0.6622 [2, 8]	0.1420	-0.0724	-5.88E-06	5.87E-06	-1.0020	0.3460	4.17E-08	5.29E-08	0.7880	0.4530
DLPFC	0.1488	2.4400 [2, 8]	0.3789	0.2236	-2.26E-05	1.07E-05	-2.1060	0.0683	4.60E-08	4.44E-08	1.0340	0.3312
hMT/V5+	0.6604	0.4371 [2, 8]	0.0985	-0.1269	-2.05E-05	2.72E-05	-0.7540	0.4720	3.11E-08	5.27E-08	0.5890	0.5720
PMd ##	0.2994	1.4070 [2, 8]	0.2603	0.0753	-1.97E-05	1.26E-05	-1.5630	0.1570	6.00E-08	5.16E-08	1.1620	0.2790
SM1	0.3285	1.2830 [2, 8]	0.2429	0.0537	-2.92E-05	1.97E-05	-1.4840	0.1760	3.34E-08	4.83E-08	0.6910	0.5090
(pre)SMA	0.3925	1.0540 [2, 8]	0.2085	0.0106	-1.99E-05	1.50E-05	-1.3260	0.2210	4.36E-08	5.05E-08	0.8620	0.4140

$BTTscore_{11}$ ~ aCT + eTIV

DLPFC	0.3830	1.0840 [2, 8]	0.2133	0.0166	-0.1100	0.0815	-1.3490	0.2140	4.56E-08	5.07E-08	0.8990	0.3950
hMT/V5+	0.8340	0.1857 [2, 8]	0.0443	-0.1945	0.0514	0.1782	0.2890	0.7800	3.27E-08	5.57E-08	0.5880	0.5730
PMd	0.4301	0.9394 [2, 8]	0.1902	-0.0122	-0.1268	0.1022	-1.2410	0.2500	4.09E-08	5.08E-08	0.8040	0.4450
SM1	0.0566	4.2000 [2, 8]	0.5122	0.3903	-0.3970	0.1418	-2.7990	**0.0232***	2.50E-08	3.88E-08	0.6460	0.5365
(pre)SMA	0.4192	0.9712 [2, 8]	0.1954	-0.0058	-0.0957	0.0757	-1.2650	0.2410	3.75E-08	5.02E-08	0.7470	0.4770

$BTTscore_{complex}$ ~ GMV + eTIV

CB	0.3942	1.0480 [2, 8]	0.2076	0.0095	-5.17E-06	6.84E-06	-0.7560	0.4720	8.50E-08	6.16E-08	1.3790	0.2050
DLPFC	0.3358	1.2550 [2, 8]	0.2388	0.0485	-1.38E-05	1.44E-05	-0.9600	0.3650	8.42E-08	5.97E-08	1.4120	0.1960
hMT/V5+	0.4719	0.8261 [2, 8]	0.1712	-0.0360	1.39E-05	3.16E-05	0.4400	0.6710	7.26E-08	6.13E-08	1.1840	0.2700
PMd	0.3761	1.1080 [2, 8]	0.2169	0.0211	-1.29E-05	1.57E-05	-0.8200	0.4360	9.41E-08	6.44E-08	1.4610	0.1820
SM1 ##	0.0765	3.6060 [2, 8]	0.4741	0.3426	-4.40E-05	1.99E-05	-2.2170	0.0575	8.04E-08	4.89E-08	1.6460	0.1383
(pre)SMA	0.4794	0.8071 [2, 8]	0.1679	-0.0401	-7.48E-06	1.86E-05	-0.4020	0.6980	7.94E-08	6.28E-08	1.2640	0.2420

$BTTscore_{complex}$ ~ aCT + eTIV

DLPFC	0.4029	1.0210 [2, 8]	0.2033	0.0041	-0.0721	0.0995	-0.7240	0.4900	8.47E-08	6.18E-08	1.3700	0.2080
hMT/V5+	0.3161	1.3350 [2, 8]	0.2502	0.0627	0.1968	0.1914	1.0280	0.3340	8.78E-08	5.98E-08	1.4690	0.1800
PMd	0.4282	0.9448 [2, 8]	0.1911	-0.0111	-0.0779	0.1239	-0.6290	0.5470	8.12E-08	6.16E-08	1.3180	0.2240
SM1	0.4378	0.9175 [2, 8]	0.1866	-0.0167	-0.1312	0.2221	-0.5910	0.5710	7.26E-08	6.07E-08	1.1960	0.2660
(pre)SMA	0.5031	0.7495 [2, 8]	0.1578	-0.0527	-0.0237	0.0939	-0.2530	0.8070	7.60E-08	6.23E-08	1.2210	0.2570

Note: ## = impaired normality of residuals (Shapiro-Wilk test: 0.014 < p < 0.031); significant p-values are marked with an asterisk and printed in bold.

Supplement 5. Results correlation SV2A and gray matter.

> CB

```
MODEL INFO:
Observations: 22
Dependent Variable: GMV[pre]
Type: OLS linear regression

MODEL FIT:
F(2,19) = 21.260, p = 0.000
R² = 0.691
Adj. R² = 0.659

Standard errors:OLS
----------------------------------------------------------------------
                       Est.        2.5%       97.5%    t val.       p
----------------- ----------- ------------ ---------- -------- -------
(Intercept)        41845.467     3377.826  80313.108    2.277   0.035
SUVR[pre]          -4465.959   -10822.775   1890.857   -1.470   0.158
eTIV                   0.054        0.036      0.071    6.492   0.000
----------------------------------------------------------------------

ANOVA TABLE (TYPE II TESTS):

Response: GMV[pre]
              Sum Sq Df F value    Pr(>F)
SUVR[pre]   41478981  1  2.1622    0.1578
eTIV       808621461  1 42.1518 3.206e-06 ***
Residuals  364487859 19
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

> DLPFC

```
MODEL INFO:
Observations: 22
Dependent Variable: GMV[pre]
Type: OLS linear regression

MODEL FIT:
F(2,19) = 16.260, p = 0.000
R² = 0.631
Adj. R² = 0.592

Standard errors:OLS
----------------------------------------------------------------------
                       Est.        2.5%       97.5%    t val.       p
----------------- ----------- ------------ ---------- -------- -------
(Intercept)        -6342.356   -18072.912   5388.200   -1.132   0.272
SUVR[pre]            920.319     -423.883   2264.521    1.433   0.168
eTIV                   0.013        0.008      0.018    5.631   0.000
----------------------------------------------------------------------

ANOVA TABLE (TYPE II TESTS):

Response: GMV[pre]
             Sum Sq Df F value    Pr(>F)
SUVR[pre]   3257211  1  2.0535    0.1681
eTIV       50293817  1 31.7077 1.982e-05 ***
Residuals  30137246 19
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

> hMT/V5+

```
MODEL INFO:
Observations: 22
Dependent Variable: GMV[pre]
Type: OLS linear regression

MODEL FIT:
F(2,19) = 3.263, p = 0.061
R² = 0.256
Adj. R² = 0.177

Standard errors:OLS
----------------------------------------------------------------------
                       Est.        2.5%       97.5%    t val.       p
----------------- ---------- ----------- ----------- -------- -------
(Intercept)         4592.498  -8344.784   17529.780    0.743   0.467
SUVR[pre]            -39.340  -1508.941    1430.261   -0.056   0.956
```

```
eTIV                        0.006      0.001      0.012    2.521   0.021
----------------------------------------------------------------

ANOVA TABLE (TYPE II TESTS):

Response: GMV[pre]
            Sum Sq Df F value  Pr(>F)
SUVR[pre]     5595  1  0.0031 0.95590
eTIV      11323851  1  6.3533 0.02082 *
Residuals 33864899 19
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

> PMd

```
MODEL INFO:
Observations: 22
Dependent Variable: GMV[pre]
Type: OLS linear regression

MODEL FIT:
F(2,19) = 2.804, p = 0.086
R² = 0.228
Adj. R² = 0.147

Standard errors:OLS
----------------------------------------------------------------
                       Est.       2.5%      97.5%   t val.       p
----------------- ---------- ----------- ----------- -------- -------
(Intercept)        8032.185  -7571.551  23635.921    1.077   0.295
SUVR[pre]          -214.734  -2083.261   1653.793   -0.241   0.812
eTIV                  0.008      0.001      0.015    2.318   0.032
----------------------------------------------------------------

ANOVA TABLE (TYPE II TESTS):

Response: GMV[pre]
            Sum Sq Df F value  Pr(>F)
SUVR[pre]   197736  1  0.0579 0.81249
eTIV      18368799  1  5.3746 0.03174 *
Residuals 64936401 19
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

> SM1

```
MODEL INFO:
Observations: 22
Dependent Variable: GMV[pre]
Type: OLS linear regression

MODEL FIT:
F(2,19) = 3.967, p = 0.036
R² = 0.295
Adj. R² = 0.220

Standard errors:OLS
----------------------------------------------------------------
                       Est.        2.5%      97.5%   t val.       p
----------------- ---------- ----------- ----------- -------- -------
(Intercept)        2390.812  -10927.456  15709.080    0.376   0.711
SUVR[pre]           710.579    -877.365   2298.522    0.937   0.361
eTIV                  0.008       0.002      0.013    2.810   0.011
----------------------------------------------------------------

ANOVA TABLE (TYPE II TESTS):

Response: GMV[pre]
            Sum Sq Df F value  Pr(>F)
SUVR[pre]  1746279  1  0.8772 0.36072
eTIV      15715169  1  7.8942 0.01119 *
Residuals 37823740 19
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

> (pre)SMA

```
MODEL INFO:
Observations: 22
Dependent Variable: GMV[pre]
Type: OLS linear regression

MODEL FIT:
```

```
F(2,19) = 4.064, p = 0.034
R² = 0.300
Adj. R² = 0.226


Standard errors:OLS
------------------------------------------------------------------
                     Est.       2.5%      97.5%   t val.       p
---------------- ---------- ----------- ----------- -------- -------
(Intercept)       3396.325  -6613.178   13405.828    0.710   0.486
SUVR[pre]          126.383  -1061.350    1314.116    0.223   0.826
eTIV                 0.007      0.002        0.012    2.844   0.010
------------------------------------------------------------------


ANOVA TABLE (TYPE II TESTS):

Response: GMV[pre]
             Sum Sq Df F value  Pr(>F)
SUVR[pre]     82714  1  0.0496 0.82614
eTIV       13490163  1  8.0896 0.01037 *
Residuals  31684389 19
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Supplement 5B: Association between baseline aCT and SUVR.

> CB

→ Analysis not available since volume- (and not surface-)based segmentation

> DLPFC

```
MODEL INFO:
Observations: 22
Dependent Variable: aCT[pre]
Type: OLS linear regression

MODEL FIT:
F(2,19) = 2.601, p = 0.100
R² = 0.215
Adj. R² = 0.132

Standard errors:OLS
-----------------------------------------------------------
                    Est.    2.5%   97.5%   t val.       p
----------------- -------- ------- ------ -------- -------
(Intercept)         1.828   1.072  2.584    5.062   0.000
SUVR[pre]           0.087   0.000  0.174    2.103   0.049
eTIV               -0.000  -0.000  0.000   -0.678   0.506
-----------------------------------------------------------

ANOVA TABLE (TYPE II TESTS):

Response: aCT[pre]
            Sum Sq Df F value Pr(>F)
SUVR[pre] 0.029129  1  4.4238 0.0490 *
eTIV      0.003029  1  0.4600 0.5058
Residuals 0.125108 19
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

> hMT/V5+

```
MODEL INFO:
Observations: 22
Dependent Variable: aCT[pre]
Type: OLS linear regression

MODEL FIT:
F(2,19) = 0.187, p = 0.831
R² = 0.019
Adj. R² = -0.084

Standard errors:OLS
-----------------------------------------------------------
                    Est.    2.5%   97.5%   t val.       p
----------------- -------- ------- ------ -------- -------
(Intercept)         2.103   0.942  3.264    3.791   0.001
SUVR[pre]           0.036  -0.095  0.168    0.578   0.570
eTIV               -0.000  -0.000  0.000   -0.117   0.908
-----------------------------------------------------------

ANOVA TABLE (TYPE II TESTS):

Response: aCT[pre]
            Sum Sq Df F value Pr(>F)
SUVR[pre] 0.004803  1  0.3346 0.5698
eTIV      0.000198  1  0.0138 0.9078
Residuals 0.272743 19
```

> PMd

```
MODEL INFO:
Observations: 22
Dependent Variable: aCT[pre]
Type: OLS linear regression

MODEL FIT:
F(2,19) = 1.454, p = 0.259
R² = 0.133
Adj. R² = 0.041

Standard errors:OLS
-----------------------------------------------------------
                    Est.    2.5%   97.5%   t val.       p
----------------- -------- ------- ------ -------- -------
(Intercept)         2.236   1.106  3.366    4.142   0.001
```

```
SUVR[pre]              0.089   -0.046    0.224    1.375   0.185
eTIV                  -0.000   -0.000    0.000   -0.860   0.401
--------------------------------------------------------


ANOVA TABLE (TYPE II TESTS):

Response: aCT[pre]
           Sum Sq Df F value Pr(>F)
SUVR[pre]  0.03391  1  1.8918 0.1850
eTIV       0.01325  1  0.7390 0.4007
Residuals  0.34058 19
```

> SM1

```
MODEL INFO:
Observations: 22
Dependent Variable: aCT[pre]
Type: OLS linear regression

MODEL FIT:
F(2,19) = 2.285, p = 0.129
R² = 0.194
Adj. R² = 0.109

Standard errors:OLS
-----------------------------------------------------------
                   Est.    2.5%    97.5%   t val.      p
----------------- -------- -------- -------- -------- -------
(Intercept)        2.702    1.701    3.704    5.647   0.000
SUVR[pre]         -0.011   -0.131    0.108   -0.200   0.844
eTIV              -0.000   -0.000   -0.000   -2.105   0.049
-----------------------------------------------------------

ANOVA TABLE (TYPE II TESTS):

Response: aCT[pre]
            Sum Sq Df F value  Pr(>F)
SUVR[pre]  0.000449  1  0.0398 0.84390
eTIV       0.049878  1  4.4309 0.04883 *
Residuals  0.213883 19
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

> (pre)SMA

```
MODEL INFO:
Observations: 22
Dependent Variable: aCT[pre]
Type: OLS linear regression

MODEL FIT:
F(2,19) = 4.340, p = 0.028
R² = 0.314
Adj. R² = 0.241

Standard errors:OLS
-----------------------------------------------------------
                   Est.    2.5%    97.5%   t val.      p
----------------- -------- -------- ------- -------- -------
(Intercept)        2.257    1.284    3.231    4.853   0.000
SUVR[pre]          0.145    0.029    0.260    2.620   0.017
eTIV              -0.000   -0.000    0.000   -1.325   0.201
-----------------------------------------------------------

ANOVA TABLE (TYPE II TESTS):

Response: aCT[pre]
            Sum Sq Df F value  Pr(>F)
SUVR[pre]  0.108222  1  6.8620 0.01687 *
eTIV       0.027672  1  1.7546 0.20101
Residuals  0.299654 19
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Supplement 5C: Association between POST-PRE differences in GMV and SUVR.

> CB

```
MODEL INFO:
Observations: 22
Dependent Variable: GMV[diff]
Type: OLS linear regression

MODEL FIT:
F(3,18) = 0.426, p = 0.737
R² = 0.066
Adj. R² = -0.089

Standard errors:OLS
-------------------------------------------------------------------
                        Est.       2.5%      97.5%   t val.      p
----------------- ----------- ---------- ---------- -------- -------
(Intercept)        -1908.177  -6739.008  2922.654   -0.830   0.417
SUVR[diff]           772.907  -1038.379  2584.192    0.896   0.382
GROUP[complex]       175.593   -778.830  1130.017    0.387   0.704
eTIV                   0.002     -0.003     0.006    0.795   0.437
-------------------------------------------------------------------


ANOVA TABLE (TYPE II TESTS):

Response: GMV[diff]
             Sum Sq Df F value Pr(>F)
SUVR[diff]   911419  1  0.8037 0.3818
GROUP        169423  1  0.1494 0.7036
eTIV         716088  1  0.6315 0.4372
Residuals  20412224 18
```

> DLPFC

→ Note: 1 data point excluded to obtain normality of residuals

```
MODEL INFO:
Observations: 21
Dependent Variable: GMV[diff]
Type: OLS linear regression

MODEL FIT:
F(3,17) = 0.181, p = 0.908
R² = 0.031
Adj. R² = -0.140

Standard errors:OLS
-------------------------------------------------------------------
                        Est.       2.5%      97.5%   t val.      p
----------------- ----------- ---------- ---------- -------- -------
(Intercept)         -515.207  -2200.219  1169.805   -0.645   0.527
SUVR[diff]           -57.929   -496.707   380.850   -0.279   0.784
GROUP[complex]         7.629   -332.795   348.053    0.047   0.963
eTIV                   0.000     -0.001     0.002    0.580   0.569
-------------------------------------------------------------------

ANOVA TABLE (TYPE II TESTS):

Response: GMV[diff]
            Sum Sq Df F value Pr(>F)
SUVR[diff]   10558  1  0.0776 0.7840
GROUP          304  1  0.0022 0.9628
eTIV         45829  1  0.3368 0.5693
Residuals  2313340 17
```

> hMT/V5+

```
MODEL INFO:
Observations: 22
Dependent Variable: GMV[diff]
Type: OLS linear regression

MODEL FIT:
F(3,18) = 0.227, p = 0.877
R² = 0.036
Adj. R² = -0.124

Standard errors:OLS
-------------------------------------------------------------------
                       Est.       2.5%      97.5%   t val.       p
---------------- ---------- ---------- ---------- -------- -------
(Intercept)         123.090  -1329.631   1575.811    0.178   0.861
SUVR[diff]         -131.146   -481.273    218.980   -0.787   0.442
GROUP[complex]       46.405   -248.275    341.085    0.331   0.745
eTIV                -0.000     -0.002      0.001   -0.281   0.782
-------------------------------------------------------------------

ANOVA TABLE (TYPE II TESTS):

Response: GMV[diff]
          Sum Sq Df F value Pr(>F)
SUVR[diff]  65947  1  0.6193 0.4416
GROUP       11656  1  0.1095 0.7446
eTIV         8392  1  0.0788 0.7821
Residuals 1916819 18
```

> PMd

```
MODEL INFO:
Observations: 22
Dependent Variable: GMV[diff]
Type: OLS linear regression

MODEL FIT:
F(3,18) = 0.600, p = 0.623
R² = 0.091
Adj. R² = -0.061

Standard errors:OLS
-------------------------------------------------------------------
                       Est.       2.5%      97.5%   t val.       p
---------------- ---------- ---------- ---------- -------- -------
(Intercept)        -886.374  -2867.018   1094.271   -0.940   0.360
SUVR[diff]          261.278   -336.758    859.315    0.918   0.371
GROUP[complex]     -107.001   -518.882    304.880   -0.546   0.592
eTIV                 0.001     -0.001      0.003    1.030   0.317
-------------------------------------------------------------------

ANOVA TABLE (TYPE II TESTS):

Response: GMV[diff]
          Sum Sq Df F value Pr(>F)
SUVR[diff] 173023  1  0.8425 0.3708
GROUP       61176  1  0.2979 0.5919
eTIV       217932  1  1.0612 0.3166
Residuals 3696625 18
```

> SM1

```
MODEL INFO:
Observations: 22
Dependent Variable: GMV[diff]
Type: OLS linear regression

MODEL FIT:
F(3,18) = 0.036, p = 0.991
R² = 0.006
Adj. R² = -0.160

Standard errors:OLS
------------------------------------------------------------------
                       Est.       2.5%      97.5%    t val.      p
---------------- --------- ---------- ---------- -------- -------
(Intercept)         -23.787  -1914.425   1866.851   -0.026   0.979
SUVR[diff]          -79.434   -642.366    483.498   -0.296   0.770
GROUP[complex]      -24.541   -403.705    354.623   -0.136   0.893
eTIV                 -0.000     -0.002      0.002   -0.056   0.956
------------------------------------------------------------------


ANOVA TABLE (TYPE II TESTS):

Response: GMV[diff]
          Sum Sq Df F value Pr(>F)
SUVR[diff]  15739  1  0.0879 0.7703
GROUP        3311  1  0.0185 0.8933
eTIV          553  1  0.0031 0.9563
Residuals 3223592 18
```

> (pre)SMA

```
MODEL INFO:
Observations: 22
Dependent Variable: GMV[diff]
Type: OLS linear regression

MODEL FIT:
F(3,18) = 0.196, p = 0.898
R² = 0.032
Adj. R² = -0.130

Standard errors:OLS
------------------------------------------------------------------
                       Est.       2.5%      97.5%    t val.      p
---------------- --------- ---------- ---------- -------- -------
(Intercept)        -386.035  -2130.460   1358.389   -0.465   0.648
SUVR[diff]           75.018   -427.369    577.404    0.314   0.757
GROUP[complex]      -96.988   -453.829    259.853   -0.571   0.575
eTIV                  0.000     -0.001      0.002    0.482   0.636
------------------------------------------------------------------

ANOVA TABLE (TYPE II TESTS):

Response: GMV[diff]
          Sum Sq Df F value Pr(>F)
SUVR[diff]  15552  1  0.0984 0.7573
GROUP       51525  1  0.3261 0.5750
eTIV        36720  1  0.2324 0.6356
Residuals 2844345 18
```

Supplement 5D: Association between POST-PRE differences in aCT and SUVR.

> CB

→ Analysis not available since volume- (and not surface-)based segmentation

> DLPFC

```
MODEL INFO:
Observations: 22
Dependent Variable: aCT[diff]
Type: OLS linear regression

MODEL FIT:
F(3,18) = 0.616, p = 0.614
R² = 0.093
Adj. R² = -0.058

Standard errors:OLS
----------------------------------------------------------
                   Est.    2.5%   97.5%  t val.       p
---------------- -------- -------- ------- -------- -------
(Intercept)       -0.083  -0.408   0.242  -0.536   0.599
SUVR[diff]        -0.038  -0.124   0.047  -0.945   0.357
GROUP[complex]    -0.019  -0.083   0.046  -0.601   0.556
eTIV              0.000  -0.000   0.000   0.480   0.637
----------------------------------------------------------

ANOVA TABLE (TYPE II TESTS):

Response: aCT[diff]
          Sum Sq Df F value Pr(>F)
SUVR[diff]0.004672  1  0.8936 0.3570
GROUP     0.001886  1  0.3607 0.5556
eTIV      0.001205  1  0.2305 0.6370
Residuals 0.094110 18
```

> hMT/V5+

```
MODEL INFO:
Observations: 22
Dependent Variable: aCT[diff]
Type: OLS linear regression

MODEL FIT:
F(3,18) = 0.583, p = 0.634
R² = 0.089
Adj. R² = -0.063

Standard errors:OLS
----------------------------------------------------------
                   Est.    2.5%   97.5%  t val.       p
---------------- -------- -------- ------- -------- -------
(Intercept)        0.077  -0.176   0.330   0.643   0.529
SUVR[diff]        -0.036  -0.097   0.025  -1.250   0.227
GROUP[complex]     0.006  -0.045   0.057   0.248   0.807
eTIV              -0.000  -0.000   0.000  -0.731   0.474
----------------------------------------------------------

ANOVA TABLE (TYPE II TESTS):

Response: aCT[diff]
          Sum Sq Df F value Pr(>F)
SUVR[diff]0.005048  1  1.5626 0.2273
GROUP     0.000199  1  0.0615 0.8070
eTIV      0.001724  1  0.5338 0.4744
Residuals 0.058149 18
```

> PMd

```
MODEL INFO:
Observations: 22
Dependent Variable: aCT[diff]
Type: OLS linear regression

MODEL FIT:
F(3,18) = 0.463, p = 0.712
R² = 0.072
Adj. R² = -0.083

Standard errors:OLS
-----------------------------------------------------------
                     Est.    2.5%   97.5%   t val.       p
----------------- -------- ------- ------- -------- -------
(Intercept)        -0.162  -0.490   0.167   -1.034   0.315
SUVR[diff]          0.027  -0.072   0.126    0.578   0.570
GROUP[complex]     -0.011  -0.079   0.057   -0.342   0.736
eTIV                0.000  -0.000   0.000    1.076   0.296
-----------------------------------------------------------


ANOVA TABLE (TYPE II TESTS):

Response: aCT[diff]
          Sum Sq Df F value Pr(>F)
SUVR[diff]0.001889  1  0.3345 0.5702
GROUP     0.000660  1  0.1168 0.7364
eTIV      0.006541  1  1.1580 0.2961
Residuals 0.101681 18
```

> SM1

```
MODEL INFO:
Observations: 22
Dependent Variable: aCT[diff]
Type: OLS linear regression

MODEL FIT:
F(3,18) = 0.017, p = 0.997
R² = 0.003
Adj. R² = -0.163

Standard errors:OLS
-----------------------------------------------------------
                     Est.    2.5%   97.5%   t val.       p
----------------- -------- ------- ------- -------- -------
(Intercept)        -0.018  -0.193   0.157   -0.214   0.833
SUVR[diff]         -0.003  -0.055   0.049   -0.125   0.902
GROUP[complex]      0.003  -0.033   0.038    0.157   0.877
eTIV                0.000  -0.000   0.000    0.074   0.942
-----------------------------------------------------------

ANOVA TABLE (TYPE II TESTS):

Response: aCT[diff]
           Sum Sq Df F value Pr(>F)
SUVR[diff]0.0000238  1  0.0155 0.9023
GROUP     0.0000378  1  0.0246 0.8771
eTIV      0.0000084  1  0.0055 0.9419
Residuals 0.0276617 18
```

> (pre)SMA

→ <u>Note</u>: 1 data point excluded to obtain normality of residuals

```
MODEL INFO:
Observations: 21
Dependent Variable: aCT[diff]
Type: OLS linear regression

MODEL FIT:
F(3,17) = 0.085, p = 0.967
R² = 0.015
Adj. R² = -0.159

Standard errors:OLS
----------------------------------------------------------
                    Est.    2.5%   97.5%  t val.      p
----------------- -------- ------- ------- -------- -------
(Intercept)        0.062  -0.245   0.369    0.423   0.677
SUVR[diff]        -0.000  -0.088   0.087   -0.012   0.991
GROUP[complex]     0.011  -0.052   0.075    0.366   0.719
eTIV              -0.000  -0.000   0.000   -0.361   0.723
----------------------------------------------------------

ANOVA TABLE (TYPE II TESTS):

Response: aCT[diff]
          Sum Sq Df F value Pr(>F)
SUVR[diff]0.000001  1  0.0001 0.9909
GROUP     0.000633  1  0.1339 0.7189
eTIV      0.000616  1  0.1304 0.7225
Residuals 0.080323 17
```

Supplement 6. Explorative whole-brain analysis of SV2A tracer binding and voxel-based morphometry (VBM).

An exploratory whole-brain analysis of PET and GM data was conducted using SPM12 (Statistical Parametric Mapping v7771, Wellcome Trust Centre for Human Neuroimaging, University College, London, UK) in MATLAB (vR2022a, MathWorks, Natick, MA) to complement the VOI-based approach, addressing the lack of prior *in vivo* evidence on motor-related synaptic density changes and potential effects outside the selected VOIs. Given its exploratory nature, no multiple comparison correction was applied (peak $p_{height,uncorr} < 0.01$), with a cluster threshold of $k_{ext} \geq 120$ voxels (~0.4 cm^3) (Vanhaute et al. 2020). Results were visualized in MRIcroGL (Rorden & Brett 2000) and labeled using the Neuromorphometrics, Brainnetome (Fan et al. 2016), Buckner's cerebellar 7-network (Buckner et al. 2011), and Diedrichsen anatomical cerebellar (Diedrichsen et al. 2009) atlases using the Anatomy toolbox v3 (Eickhoff et al. 2005), with simplified labeling excluding fractions below 5% for clarity.

Explorative voxel-wise whole-brain analysis of SynVesT-1. To do so, first, the motion corrected and summed SUV maps were divided by the average SUV of the reference region (centrum semiovale) to obtain SUVR images. Following the Diffeomorphic Anatomical Registration Through Exponentiated Lie Algebra (DARTEL) procedure (Ashburner 2007), a study-specific average template based on the PRE T1 scan of all 22 subjects was created. Then, individual MR (PRE) and PET (PRE and POST) images were normalized to Montreal Neurological Institute (MNI, MNI152NLin2009cAsym) space using the DARTEL flow fields, and smoothed by an additional Gaussian kernel of 11.1 mm FWHM to obtain a total smoothing value of about 12 mm (combination of 11.1 mm smoothing applied during this step and 4.5 mm smoothing applied during image reconstruction, see main manuscript section *2.3 Anatomical and PET imaging acquisition and reconstruction*). SUV ratios (SUVR) of parametric [^{18}F]SynVesT-1 images were calculated using the centrum semiovale as reference region (Rossano et al. 2020, Sadasivam et al. 2021) (see **Supplemental Figure 2** for overview).

Explorative voxel-wise whole-brain analysis of changes in SUVR associated with motor training was performed in SPM12. Statistical analyses were masked with an explicit binary GM mask (averaged GM segmentations, smoothed with a 12 mm FWHM Gaussian kernel, including only values > 0.2). First, the influence of TIME (with GROUP as a covariate of no interest) and the effect of the GROUP × TIME interaction on SUVR were analyzed. Second, the association between SynVesT-1 tracer binding at baseline (SUVR$_{PRE}$) and BTT training progress (BTTslope$_{11}$, BTTslope$_{complex}$), as well as between SUVR$_{DIFF}$ and BTT training progress were investigated.
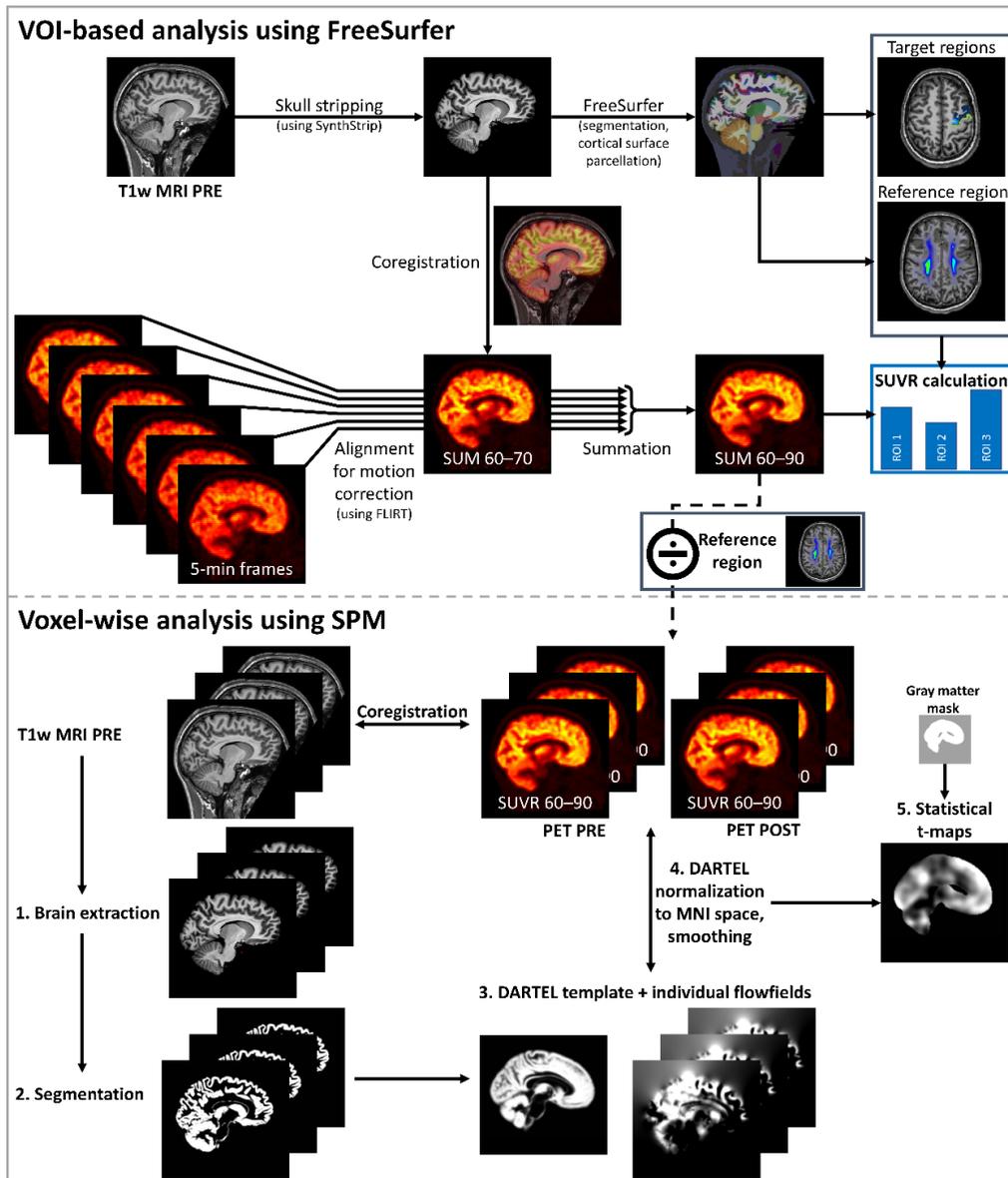
Supplemental Figure 2. *Overview of (pre)processing steps of positron emission tomography (PET) analysis. The top panel shows the volume-of-interest (VOI)-based analysis using FreeSurfer, the bottom panel the steps for the voxel-wise whole-brain analysis in SPM12. Abbreviations: PRE = pre/baseline measurement; POST = post measurement after 4 weeks of bimanual motor training; SUV(R) = standardized uptake value (ratio); T1w = T1-weighted anatomical magnetic-resonance image.*

Explorative whole-brain GM analysis using voxel-based morphometry. Longitudinal VBM was performed following the procedure described earlier (Eshaghi et al. 2014) (see **Supplemental Figure 3** for overview). First, a within-subject serial longitudinal coregistration of PRE, MID, and POST MRIs was performed to rigidly coregister all images of one individual and construct an unbiased median template of the three time points (from now on referred to as 'within-subject template'). Subsequently, non-rigid registration of each time point to the within-subject template was performed using high-dimensional warping. During this step, deformation fields (mapping the deformation of each time point to the within-subject template, i.e., the amount of volume change) were acquired, based on which the Jacobian (tensor) determinant maps (showing the expansion or contraction of each voxel with regard to the within-subject template) were calculated. Next, segmentation of the within-subject template into GM, WM and cerebrospinal fluid was performed, and the Jacobian

determinant was multiplied voxel-wise with the obtained GM segmentation of the within-subject template, resulting in images that show the probabilistic GM volume at each time point (here called 'pseudo time points' of the GM volume estimate). Subsequently, the DARTEL procedure (Ashburner 2007) was followed to create a study-specific average template based on the within-subject templates of all 22 subjects, and to spatially normalize all pseudo time points into MNI space based on the DARTEL flow fields. During this step, a Gaussian smoothing (FWHM of 8 mm) was applied. Based on these spatially normalized pseudo time points, difference images between pseudo time points (PRE vs. POST, PRE vs. MID, MID vs. POST) were calculated in a voxel-wise manner to run the statistical analysis.
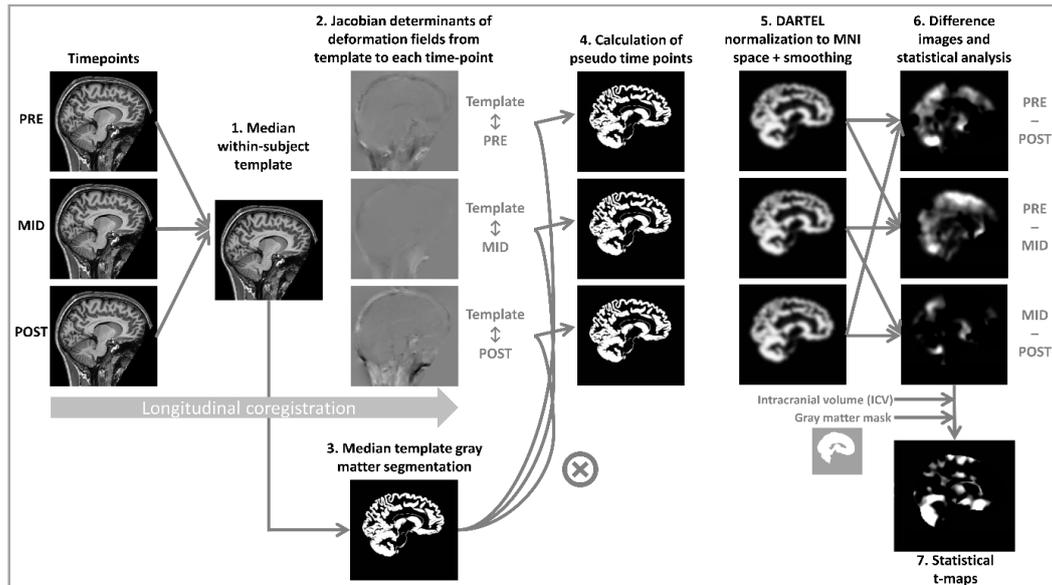
Supplemental Figure 3. *Overview of (pre)processing steps for voxel-based morphometry (VBM) to estimate the GM volumetric changes between the three time points baseline (PRE), after 2 weeks (MID) and after 4 weeks (POST) of bimanual motor training.*

VBM-based changes in GM associated with motor learning were investigated using SPM12. Statistical analysis was performed with intracranial volume (ICV; calculated based on the within-subject template) as covariate of no interest and masked with an explicit binary GM mask (averaged GM segmentations, smoothed with a 12 mm FWHM Gaussian kernel, including only values > 0.2). The change between measurements (PRE vs. POST, PRE vs. MID, MID vs. POST) was investigated with GROUP and ICV as covariates of no interest. In addition, the influence of GROUP on that change (i.e., the interaction effect between GROUP and TIME) was investigated with ICV as covariates of no interest.

PET whole-brain results.

Results of the whole-brain PET analysis are displayed in **Supplemental Figure 4**–**Supplemental Figure 6**. An overview of all significant peaks exceeding the cluster extend k_{ext} and their location in MNI space are reported in brief in **Supplemental Table 1**.

Analysis revealed a decrease in SynVesT-1 uptake in the left temporal lobe (temporal pole and middle/inferior temporal gyrus) associated with motor learning (see **Supplemental Figure 4**). However, there were no regions that showed a significant increase in SynVesT-1 uptake or an interaction effect between the scan TIMING (PRE vs. POST) and the training GROUP (simple vs. complex). An additional one-sample t-test of the $SUVR_{DIFF}$ images for each training group separately revealed that this effect was driven by the complex training group.
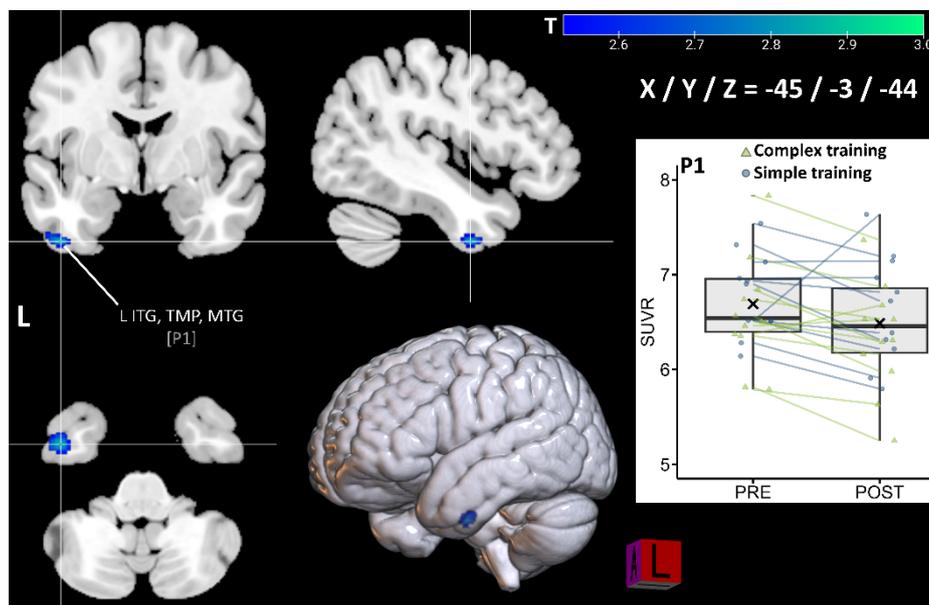
Supplemental Figure 4. *Decrease of SynVesT-1 tracer uptake in left inferior temporal gyrus (ITG), temporal pole (TMP) and middle temporal gyrus (MTG) associated with bimanual motor learning. Boxplot of the standard uptake value ratio (SUVR) of the cluster P1 (box indicating the interquartile range, bar the median, and "×" the mean; also refer to Supplemental Table 1). L indicates the left side.*

Investigating the association between SynVesT-1 uptake at PRE and the subsequent motor learning progress revealed that there were brain regions in which SynVesT-1 uptake at PRE was linked to the motor learning slope (see **Supplemental Figure 5**). When looking at $BTTslope_{11}$, (i.e., learning progress on the easy 1:1 subtask), SynVesT-1 uptake in the right middle temporal gyrus showed a positive link with learning progress, whereas uptake in the left and right posterior cerebellum (crus I and II) were negatively associated (see **Supplemental Figure 5**, top panel). However, a negative correlation with the 1:1 subtask learning progress could also be based on an initial high score on the 1:1 task that some participants displayed (see main manuscript, **Figure 4A**), and a consequently less steep learning slope. Hence, a follow-up analysis was conducted, looking into the association between the PRE SynVesT-1 uptake and the 1:1 score from the first progress test (conducted at PRE), which revealed a positive association in the same cerebellar region. This suggests that the effect was driven by participants with an initially high score on the 1:1 subtask, limiting the learning slope due to a ceiling

effect. When investigating only the complex subtasks of the BTT, SynVesT-1 uptake sub-regions of the left and right cerebellum (crus I, II and lobule VIIb) and the right inferior occipital gyrus (including hMT/V5+) at PRE showed a positive association with motor learning progress. In contrast, the right inferior temporal gyrus, (occipital) fusiform gyrus and inferior occipital gyrus showed a negative association between SynVesT-1 uptake and motor learning progress on the complex subtasks (see **Supplemental Figure 5**, bottom panel).
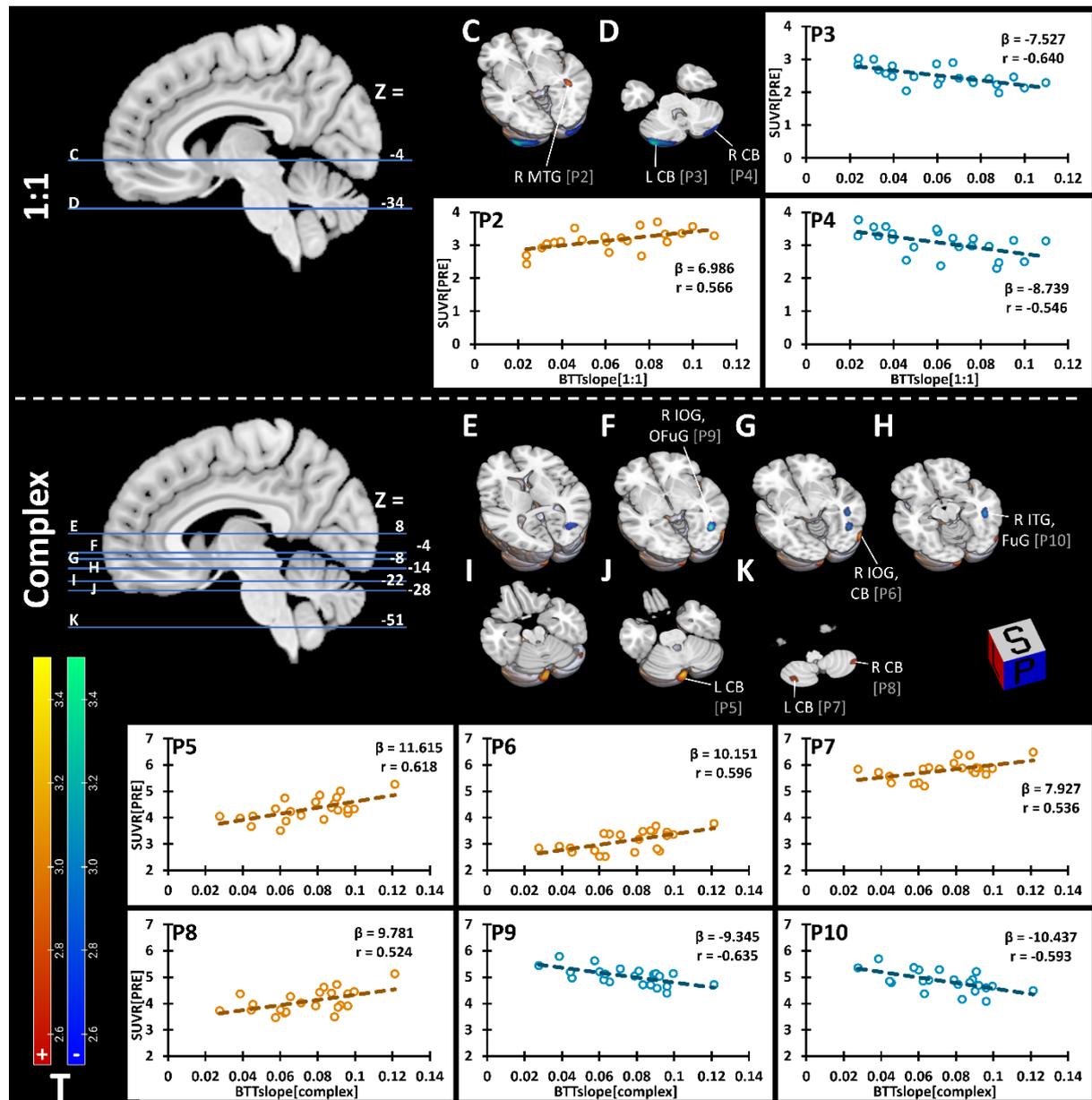
Supplemental Figure 5. *Brain regions showing associations between SynVesT-1 tracer uptake at baseline and subsequent motor learning progress (i.e., the learning slope) on the bimanual tracking task (BTT). The top panel shows the associations with the motor learning slope for the 1:1 frequency ratio subtask, and the bottom panel the associations with the complex subtasks. Red–orange colors indicate areas with a positive association (i.e., higher SynVesT-1 tracer uptake at baseline was associated with more learning), blue–green colors indicate regions with a negative association (i.e., higher SynVesT-1 tracer uptake at baseline was associated with less learning or vice versa). The scatterplots show the individual data points for each cluster (P2–P10, see also Supplemental Table 1). Abbreviations: CB = cerebellum; FuG = fusiform gyrus; IOG = inferior occipital gyrus; ITG = inferior temporal gyrus; L = left; MTG = middle temporal gyrus; OFuG = occipital fusiform gyrus; P = posterior; R = right; S = superior.*

The associations of the change in SynVesT-1 uptake from PRE to POST (i.e., $SUVR_{DIFF}$) and the motor learning progress on the complex subtasks are displayed in **Supplemental Figure 6**. There were no regions that showed an association between the change in SynVesT-1 uptake and the learning progress on all BTT progress test tasks combined, or only the 1:1 subtask. Furthermore, analysis did not reveal any brain regions that showed a positive association between the change in SynVesT-1 uptake and the learning progress on the complex BTT subtasks. However, negative associations between the change in SynVesT-1 uptake and the motor learning slope on the complex subtasks were observed for the left hemisphere in the angular gyrus, supramarginal gyrus, superior and middle occipital gyrus, superior temporal gyrus, superior parietal lobule, occipital pole and cuneus, as well as in the right hemisphere cerebellum (lobule VIIIb and X), right superior parietal lobule, precuneus, parietal operculum, putamen, pallidum, and the thalamus. This means, that more decrease in SynVesT-1 uptake was associated with a higher learning progress or vice versa.
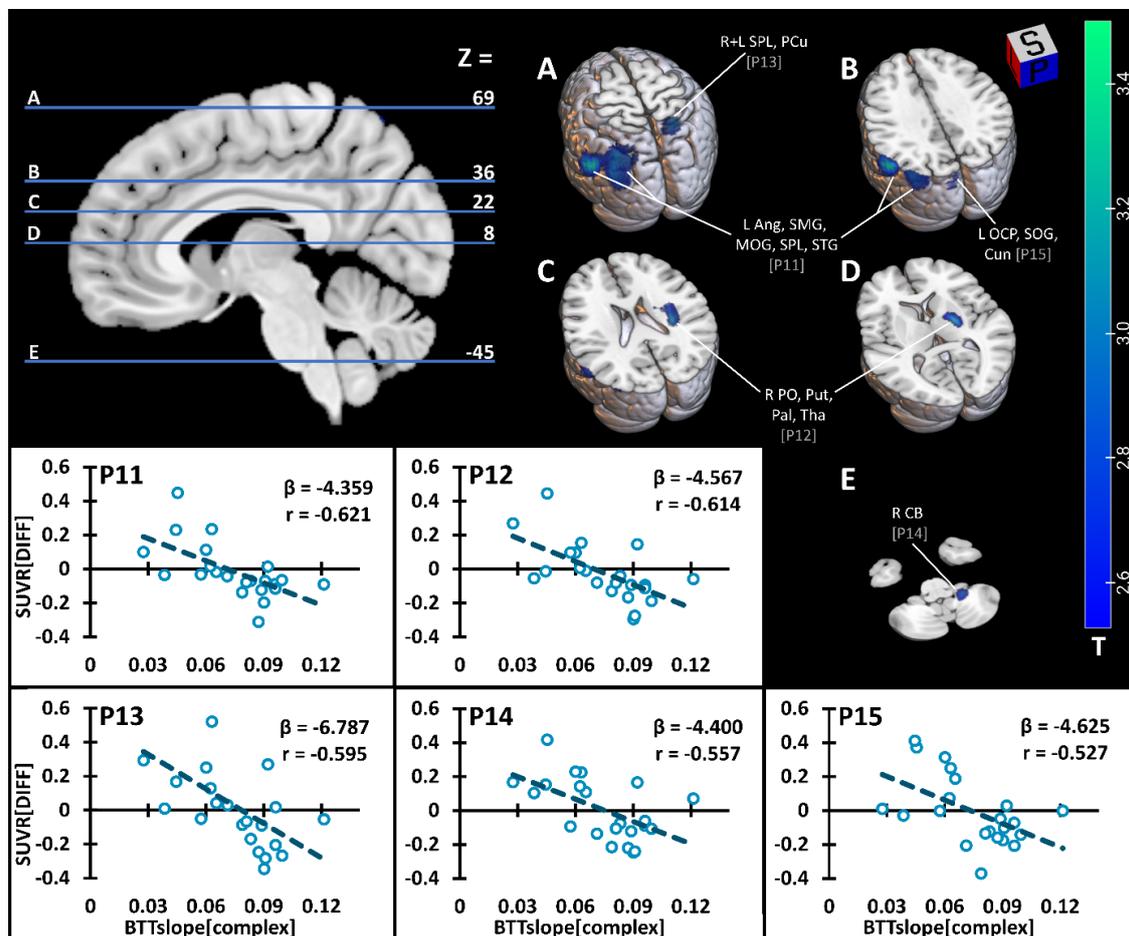
Supplemental Figure 6. Brain regions showing associations between the change in SynVesT-1 tracer uptake between baseline and post measurement and the motor learning progress (i.e., the learning slope) on the complex subtasks of the bimanual tracking task (BTT). Several regions showed a negative association between the change in SynVesT-1 tracer uptake and the complex subtasks learning progress (i.e., decrease in SynVesT-1 tracer uptake was associated with more learning or vice versa), but neither a positive association for the complex subtasks, nor any associations with the 1:1 subtask were shown. The scatterplots show the individual data points for each cluster (P11–P15; see also Supplemental Table 1). Abbreviations: AnG = angular gyrus; CB = cerebellum; Cun = cuneus; L = left; MOG = middle occipital gyrus; OCP = occipital pole; P = posterior; Pal = pallidum; PCu = precuneus; PO = parietal operculum; Put = putamen; R = right; S = superior; SMG = supramarginal gyrus; SOG = superior occipital gyrus; SPL = superior parietal lobule; STG = superior temporal gyrus; Tha = thalamus.

Cluster				Peak		MNI coordinates			Extended local maxima labelling		
Index	equiv k	p(unc)	Cluster labels	T	p(unc)	x	y	z	Neuromorphometrics Atlas [Cerebellar atlas Diedrichsen et al.]	Brainnetome Atlas	Buckner 7 Networks Atlas
[A] Differences in SUVR PRE vs. POST											
• **PRE>POST**											
P1	**180**	0.838	A20r_L (93.8%) A20il_L (4.4%) A21r_L (1.5%) N/A (0.3%)	2.84	0.005	-45	-3	-44	<u>L ITG inferior temporal gyrus</u> (44.3%) N/A (33.8%) L TMP temporal pole (9.0%) L MTG middle temporal gyrus (6.7%) L Cerebral White Matter (6.2%)	A20r_L (63.4%) N/A (23.6%) A20rv_L (5.4%)	-
[B] Correlation SUVR[PRE] ~ Motor learning SLOPE											
• **SLOPE[11]**											
→ Positive correlation											
P2	**208**	0.665	N/A (99.1%) rpSTS_R (0.6%) aSTS_R (0.3%)	3.05	0.003	40	-34	-4	<u>R Cerebral White Matter</u> (82.4%) R MTG middle temporal gyrus (7.4%)	N/A (70.5%) cHipp_R (11.4%) rpSTS_R (9.2%)	-
→ Negative correlation											
P3	**863**	0.348	Network7 (55.0%) N/A (23.6%) Network6 (19.9%) Network5 (1.5%)	3.69	0.001	-46	-78	-40	<u>N/A</u> (71.6%) L Cerebellum Exterior (28.4%) [L crus I (23.0%), L crus II (6.0%)]	-	<u>N/A</u> (55.7%) Network 7 (33.4%) Network 6 (9.1%)
				3.36	0.002	-38	-87	-38	<u>N/A</u> (75.7%) L Cerebellum Exterior (24.3%) [L crus I (10.0%), L crus II (6.0%)]	-	<u>N/A</u> (58.8%) Network 7 (39.4%)
P4	**305**	0.590	Network7 (75.4%) N/A (24.6%)	2.90	0.004	24	-92	-34	<u>N/A</u> (63.3%) R Cerebellum Exterior (36.7%) [R crus II (51.0%)]	-	<u>Network 7</u> (54.5%) N/A (45.5%)
				2.81	0.005	40	-86	-38	<u>N/A</u> (76.3%) R Cerebellum Exterior (23.7%) [N/A]	-	<u>N/A</u> (59.7%) Network 7 (39.7%)
• **SLOPE[Complex]**											

			→ Positive correlation								
P5	556	0.457	Network6 (48.1%) Network7 (39.3%) N/A (12.6%)	3.50	0.001	-8	-87	-28	L Cerebellum Exterior (52.3%) N/A (47.4%) [L crus II (84.0%), L crus I (8.0%)]	-	Network 6 (45.3%) N/A (33.3%) Network 7 (21.4%)
P6	401	0.533	N/A (51.4%) iOccG_R (36.6%) Network7 (7.1%) Network6 (2.4%) V5/MT+_R (2.2%) Network5 (0.1%) mOccG_R (0.1%)	3.31	0.002	50	-84	-8	N/A (69.8%) R IOG inferior occipital gyrus (30.1%)	N/A (60.1%) iOccG_R (25.8%) V5/MT+_R (10.8%)	-
				2.99	0.004	46	-78	-22	N/A (69.7%) R Cerebellum Exterior (17.7%) R IOG inferior occipital gyrus (10.3%) [N/A]	N/A (83.4%) iOccG_R (11.5%)	N/A (69.6%) Network 7 (16.8%) Network 6 (11.5%)
P7	144	0.728	Network6 (100.0%)	2.83	0.005	-38	-64	-50	L Cerebellum Exterior (91.9%) [L lobule VIIb (50.0%), L crus II (40.0%)]	-	Network 6 (87.1%) Network 3 (6.8%) Network 4 (6.1%)
P8	154	0.717	Network7 (61.4%) Network6 (19.7%) N/A (18.9%)	2.74	0.006	46	-63	-51	R Cerebellum Exterior (52.1%) N/A (47.9%) [R crus II (59.0%), R lobule VIIb (6.0%)]	-	Network 7 (39.4%) N/A (31.3%) Network 6 (29.2%)
			→ Negative correlation								
P9	581	0.447	N/A (71.4%) V5/MT+_R (12.5%) A37lv_R (8.3%) A37mv_R (5.4%) iOccG_R (1.2%) mOccG_R (0.6%) vmPOS_R (0.6%)	3.65	0.001	36	-69	-4	R Cerebral White Matter (82.9%) R IOG inferior occipital gyrus (8.8%) R OFuG occipital fusiform gyrus (8.2%)	N/A (43.6%) A37mv_R (22.9%) V5/MT+_R (19.9%) oOccG_R (6.0%) A37lv_R (5.2%)	-
				2.78	0.006	27	-75	8	R Cerebral White Matter (95.5%)	N/A (71.7%) vmPOS_R (12.6%) mOccG_R (11.0%) cCunG_R (11.0%)	-
P10	237	0.642	A37lv_R (43.5%) N/A (35.7%) A20cv_R (8.6%) A20iv_R (6.4%) A37elv_R (5.8%)	3.28	0.002	46	-39	-14	R Cerebral White Matter (71.1%) R ITG inferior temporal gyrus (16.4%) R FuG fusiform gyrus (11.6%)	N/A (45.9%) A37lv_R (27.8%) A20cv_R (9.8%) A37elv_R (7.1%)	-

[C] Correlation SUVR[DIFF] ~ Motor learning SLOPE

P	cluster	r	region	t	p	x	y	z	region	region	
P11	1995	0.526	N/A (57.6%) A39rv_L (13.8%) A40c_L (13.0%) A39c_L (7.5%) A39rd_L (7.1%) A7c_L (0.6%) A22c_L (0.2%) lsOccG_L (0.1%) A7r_L (0.0%)	3.51	0.001	-60	-63	36	N/A (77.8%) L AnG angular gyrus (20.5%)	N/A (67.3%) A40c_L (16.4%) A39rv_L (16.2%)	-
				3.21	0.002	-40	-74	52	N/A (75.6%) L AnG angular gyrus (24.4%)	N/A (68.4%) A39rd_L (24.1%) A39rv_L (6.6%)	-
				3.18	0.002	-64	-54	34	N/A (75.3%) L SMG supramarginal gyrus (20.6%)	N/A (64.8%) A40c_L (33.2%)	-
				3.18	0.002	-46	-80	39	N/A (79.9%) L AnG angular gyrus (20.6%)	N/A (68.4%) A39rv_L (25.3%) A39c_L (6.3%)	-
				3.17	0.002	-36	-80	50	N/A (78.0%) L AnG angular gyrus (19.6%)	N/A (68.5%) A39c_L (12.9%) A39rd_L (11.8%) A39rv_L (6.8%)	-
				3.10	0.003	-56	-66	42	N/A (76.0%) L AnG angular gyrus (24.0%)	N/A (67.2%) A39rv_L (14.8%) A40c_L (14.8%)	-
				3.08	0.003	-44	-87	30	N/A (80.7%) L MOG middle occipital gyrus (19.3%)	N/A (69.0%) A39c_L (29.2%)	-
				2.89	0.004	-24	-81	51	N/A (70.5%) L SPL superior parietal lobule (16.7%) L AnG angular gyrus (7.5%)	N/A (62.6%) lsOccG_L (17.6%) A39c_L (8.9%) A7c_L (8.7%)	-
				2.76	0.006	-14	-74	63	N/A (70.9%) L SPL superior parietal lobule (28.6%)	N/A (69.9%) A7c_L (21.2%) A7r_L (8.8%)	-
				2.55	0.010	-68	-54	16	N/A (76.6%) L STG superior temporal gyrus (15.8%)	N/A (62.6%) A22c_L (15.9%) A37dl_L (8.9%) A40c_L (6.2%)	-

P	Cluster	Value	Region (%)	Peak	p	x	y	z	Anatomical label (%)	Label (%)	Network
P12	**849**	0.695	N/A (49.9%) GP_R (28.2%) dlPu_R (9.9%) G_R (5.0%) A40rv_R (4.2%) dIg_R (1.8%) vmPu_R (0.9%) A1/2/3tonIa_R (0.1%)	3.45	0.001	32	-24	22	R Cerebral White Matter (80.7%) R PO parietal operculum (11.6%)	N/A (76.2%) G_R (11.5%) A40rv_R (11.5%)	-
				3.22	0.002	24	-8	8	R Cerebral White Matter (54.8%) R Putamen (28.5%) R Pallidum (11.0%) R Thalamus Proper (5.7%)	N/A (36.7%) dlPu_R (28.3%) GP_R (24.6%) mPMtha_R (7.2%)	-
P13	**236**	0.856	A7r_R (39.8%) N/A (39.3%) A7c_R (20.8%)	3.30	0.002	20	-64	69	N/A (62.5%) R SPL superior parietal lobule (37.3%)	N/A (62.6%) A7r_R (33.5%)	-
				2.77	0.006	9	-64	68	N/A (61.8%) R SPL superior parietal lobule (27.0%) R PCu precuneus (9.9%)	N/A (60.6%) A7r_R (24.3%) A7m_R (6.2%) A7c_R (5.2%)	-
				2.72	0.007	12	-58	72	N/A (59.2%) R SPL superior parietal lobule (37.4%)	N/A (59.3%) A7r_R (31.6%) A5m_R (6.0%)	-
				2.70	0.007	-2	-64	64	N/A (66.7%) L PCu precuneus (14.3%) L SPL superior parietal lobule (10.8%) R PCu precuneus (8.1%)	N/A (61.4%) A7m_L (16.1%) A7r_L (7.7%) A7m_R (7.2%)	-
				2.60	0.009	4	-69	62	N/A (65.6%) R PCu precuneus (18.4%) R SPL superior parietal lobule (10.8%)	N/A (59.2%) A7m_R (20.0%) A7c_R (9.9%) A7r_R (5.7%)	-
P14	**166**	0.885	Network5 (48.0%) Network3 (26.5%) Network4 (16.7%) Network7 (8.3%) Network2 (0.5%)	2.98	0.004	21	-44	-45	R Cerebellum White Matter (46.5%) R Cerebellum Exterior (39.9%) N/A (12.6%) [R lobule X (42.0%), R lobule VIIIb (25.0%)]	-	Network5 (39.2%) Network3 (22.5%) Network7 (15.4%) Network4 (13.8%) Network2 (6.2%)
P15	**146**	0.894	N/A (99.4%) msOccG_L (0.4%)	2.76	0.006	-12	-104	22	N/A (80.8%) L OCP occipital pole (16.3%)	N/A (73.5%) OPC_L (19.4%)	-

equivk	p(unc)	x	y	z	PRE	POST	
					OPC_L (0.2%)	msOccG_L (6.2%)	
2.72	0.007	-8	-94	36	N/A (77.2%) L SOG superior occipital gyrus (13.7%) L Cun cuneus (7.4%)	N/A (72.0%) msOccG_L (28.0%)	-
2.71	0.007	-6	-105	16	N/A (78.9%) L OCP occipital pole (20.5%)	N/A (72.9%) OPC_L (18.0%) cCunG_L (8.1%)	-
2.70	0.007	-10	-99	30	N/A (80.4%) L SOG superior occipital gyrus (11.2%) L OCP occipital pole (5.4%)	N/A (73.3%) msOccG_L (21.8%)	-
2.58	0.009	-22	-94	33	N/A (75.7%) L SOG superior occipital gyrus (22.2%)	N/A (66.9%) msOccG_L (13.4%) lsOccG_L (9.0%) mOccG_L (6.8%)	-

Abbreviations: equivk = cluster extent (number of voxels, with each voxel 1.5×1.5×1.5 mm^3); L = left; N/A = not available; PRE = pre/baseline measurement; POST = post measurement after 4-week motor training intervention; R = right; SUVR = standardized uptake value ratio; unc = uncorrected.

Supplement 6C: Results VBM.

VBM whole-brain results

The results of the VBM analysis comparing GM volume between the three time points (PRE, MID and POST) are displayed in **Supplemental Figure 7** and **Supplemental Figure 8**. A detailed overview of all significant clusters exceeding the cluster extend k$_{ext}$ are reported in **Supplemental Table 2**. There were no regions of overlap between the results of the PET analysis (PRE vs. POST) and the VBM analysis (at any time point). Nevertheless, the results of the VBM analysis are being reported in the following.

Comparing PRE and POST measurement, analysis revealed a decrease in GM in subsections of the left and right cerebellum (left: crus I; right: lobule VI, crus I), and an increase in GM for the right inferior frontal gyrus and frontal operculum, as well as the right temporal pole, inferior frontal gyrus and orbital gyrus (see **Supplemental Figure 7**, top panel). When investigating the timing of GM changes more in detail, especially the period from PRE to MID measurement revealed changes, with GM increases (1) around the right temporal pole (right temporal pole, medial and posterior orbital gyrus, inferior temporal gyrus), (2) in the right entorhinal area, amygdala and hippocampus, (3) in the left and right frontal cortex (left: frontal pole, anterior and medial orbital gyrus, superior and medial frontal gyrus, anterior cingulate gyrus, gyrus rectus ; right: frontal pole, medial frontal cortex, gyrus rectus, orbital gyrus), (4) in the left inferior frontal gyrus and opercular region (left precentral gyrus, opercular/ triangular/ orbital part of the inferior frontal gyrus, central/ frontal operculum, lateral orbital gyrus), and (5) in the left sensorimotor region (left pre- and postcentral gyrus). A decrease between PRE and MID has been observed in the left superior and middle occipital gyrus (see

Supplemental Figure 7, middle panel). In contrast, no changes in GM could be observed between week 2 and 4 of motor training, i.e., between MID and POST measurement.
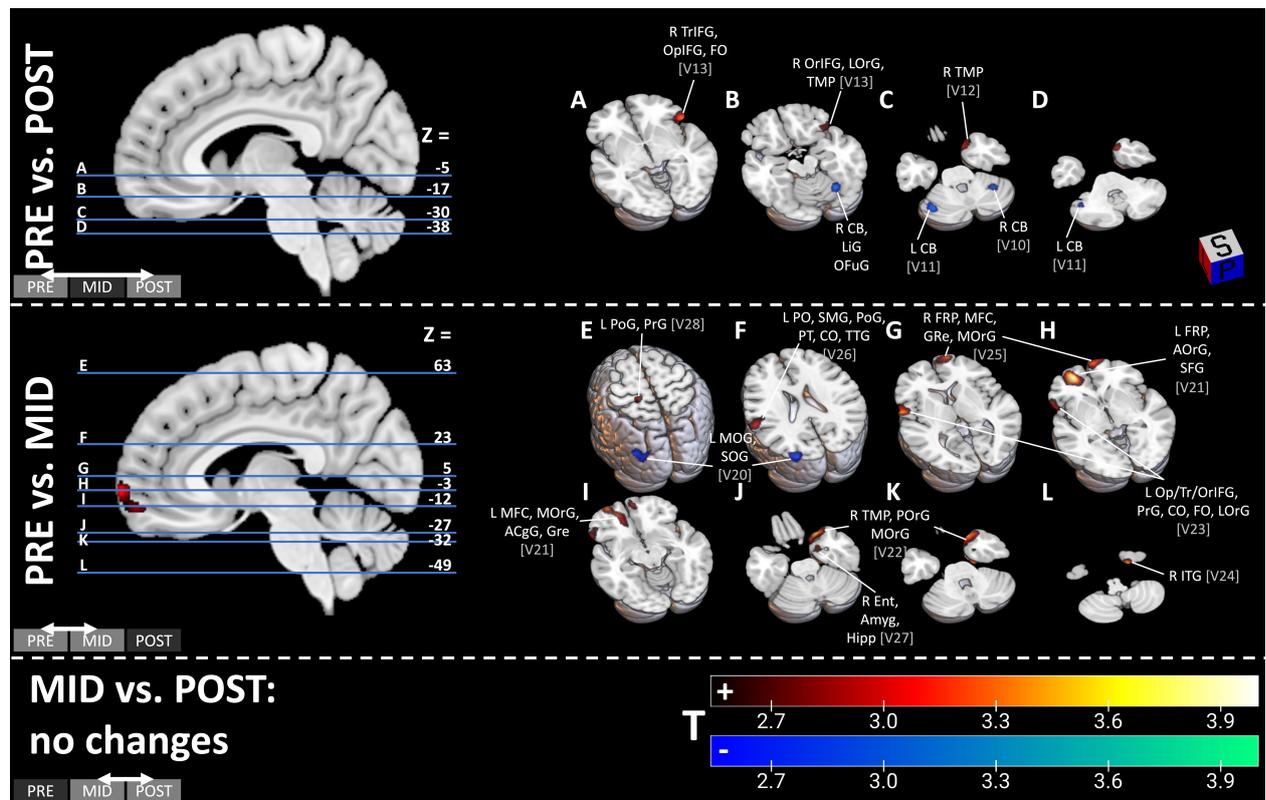
Supplemental Figure 7. Voxel-based morphometry (VBM) results investigating changes in gray matter associated with motor learning. Red–yellow colors indicate increases in gray matter, blue–green colors indicate decreases. Top panel: comparison of measurement at baseline (PRE) and measurement after 4 weeks of motor learning (POST). Middle panel: comparison of PRE and measurement after first 2 weeks of motor learning (MID). Bottom panel: no results for the comparison of MID and POST measurement. [V] indicate the cluster index of the VBM analysis (see Supplemental Table 2). Abbreviations: ACgG = anterior cingulate gyrus; Amyg = amygdala; AOrG = anterior orbital gyrus; CB = cerebellum; CO = central operculum ; Ent = entorhinal area; FO = frontal operculum; FRP = frontal pole; GRe = gyrus rectus; Hipp = hippocampus; ITG = inferior temporal gyrus; L = left; LiG = lingual gyrus; LOrG = lateral orbital gyrus; MFC = medial frontal cortex; MOG = middle occipital gyrus; MOrG = medial orbital gyrus; OFuG = occipital fusiform gyrus; OpIFG = opercular part of the inferior frontal gyrus; P = posterior; PO = parietal operculum; PoG = postcentral gyrus; POrG = posterior orbital gyrus; PrG = precentral gyrus; PT = planum temporale; R = right; S = superior; SFG = superior frontal gyrus; SMG = supramarginal gyrus; SOG = superior occipital gyrus; TMP = temporal pole; TrIFG = triangular part of the inferior frontal gyrus; TTG = transverse temporal gyrus.

Investigating the influence of GROUP on GM changes with motor training revealed differences between all time points (PRE vs. POST, PRE vs. MID, MID vs. POST; see **Supplemental Figure 8**). Because the analysis of a GROUP effect on a difference image between two time points actually tests the interaction effect GROUP×TIME, the magnitudes of the beta estimates were reported to facilitate the interpretation of each effect (see **Supplemental Figure 8**, green/purple triangles next to each region). Overall, it appears that beta estimates were larger between MID and POST than between PRE and MID measurement, and that the effects were largely stronger for the complex training as compared to the simple training group.

When comparing PRE and POST measurement (see **Supplemental Figure 8**, top panel), GM intensity increased for the complex and decreased for the simple training group in the right fusiform gyrus and inferior temporal gyrus, as well as in two regions of the left cerebellum (left crus I and II; left lobule VIIb and VIIIa), with higher absolute beta estimates for the complex as compared to the simple

training group. The opposite effect, i.e., a GM intensity decrease for the complex and increase for the simple training group, could be observed in (1) the left middle occipital and angular gyrus, (2) the left frontal region (superior frontal gyrus, frontal pole), (3) the right frontal region (superior and middle frontal gyrus, and frontal pole), (4) the right hippocampal and temporal pole area (right entorhinal area, hippocampus, amygdala, parahippocampal gyrus, fusiform gyrus and temporal pole), and (5) the right cerebellum (lobule VI), lingual gyrus and occipital fusiform gyrus. Notably, while most absolute beta estimates were bigger for the complex training group, the opposite was true for the right middle/superior frontal gyrus and frontal pole, and in the right hippocampal peak voxels.

As compared to the full four-week training period (PRE vs. POST measurement), beta estimates for the PRE vs. MID measurement were overall smaller, and absolute estimates were overall larger for the complex training group (see **Supplemental Figure 8**, middle panel). GM intensity increases for the complex and decreases for the simple training group were located in the right pre- and postcentral gyrus (mainly driven by changes in the complex training group), the left middle cingulate gyrus and supplementary motor cortex, as well as the left operculum and inferior frontal gyrus region (left central/ frontal operculum, opercular/ triangular/ orbital part of the inferior frontal gyrus, precentral gyrus). Decreases in GM intensity for the complex and increases for the simple training group have been observed in the right and left superior and middle occipital gyrus (including the left occipital pole; both effects more driven by the complex training group), and in the left supramarginal and angular gyrus.

For the comparison of the MID and POST measurement, overall effects were stronger than between the PRE and MID measurement and absolute beta estimates for all peak voxels were higher for the complex as compared to the simple training group (see **Supplemental Figure 8**, bottom panel). GM intensity increased for the complex and decreased for the simple training group in the right occipital region (right superior/ middle/ inferior occipital gyrus, occipital pole) and in the left and right lingual gyrus. In contrast, GM intensity decreased for the complex and increased for the simple training group in the right frontal lobe (right superior and middle frontal gyrus, frontal pole), the left frontal lobe (frontal pole, superior frontal gyrus), the right entorhinal area, temporal pole and amygdala, as well as the right cerebellum (right lobule IX, VIIIb).
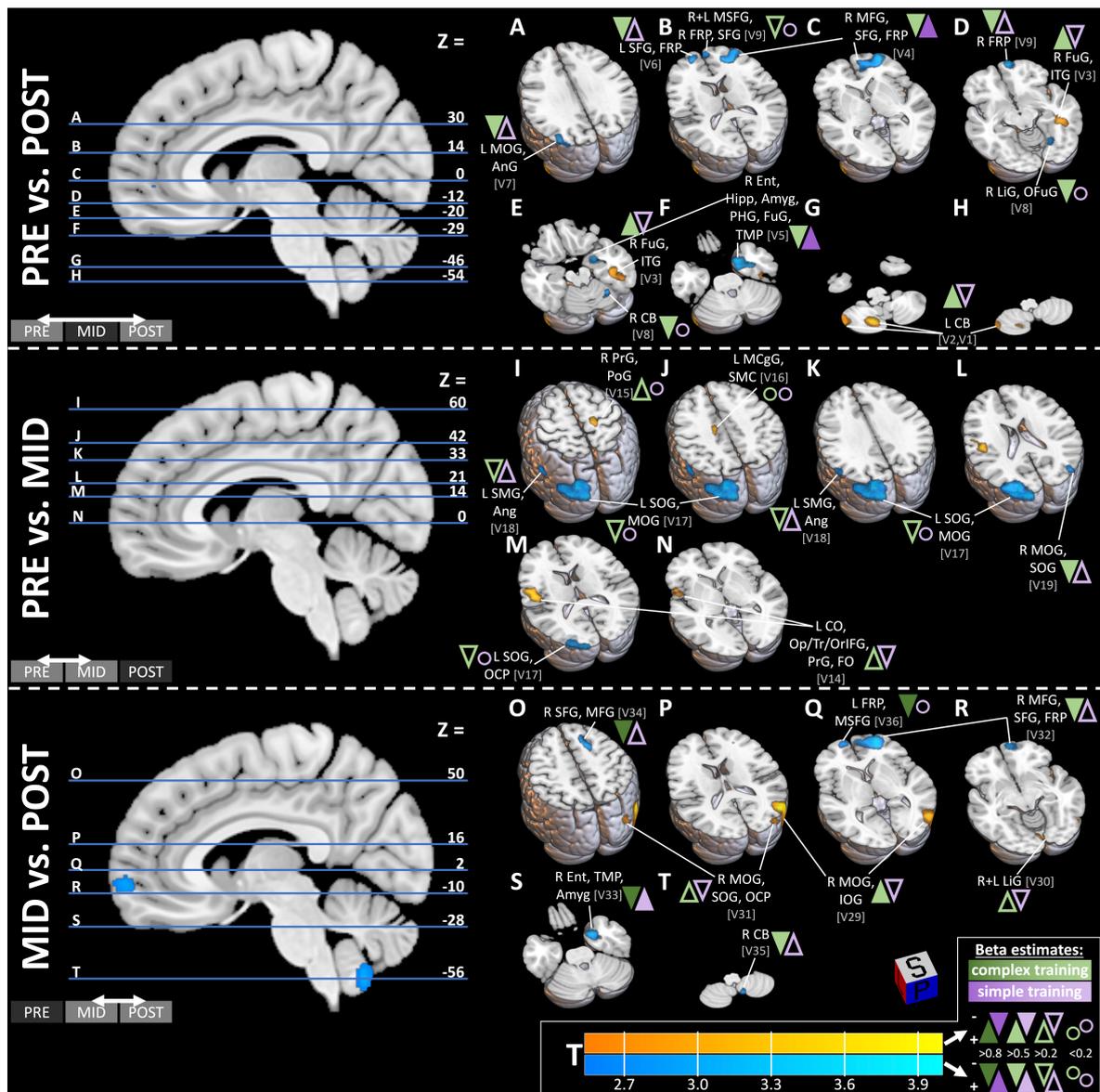
Supplemental Figure 8. Voxel-based morphometry (VBM) results investigating changes in gray matter associated with motor learning for the complex and the simple learning group. Because the limited interpretability of a group comparison based on difference images due to the interaction effect (orange and blue t-values), the magnitude of the beta estimates and effect directions per group are reported in green and purple. Top panel: comparison of measurement at baseline (PRE) and after four weeks of motor learning (POST). Middle panel: comparison of PRE and measurement after first 2 weeks of motor learning (MID). Bottom panel: comparison of MID and POST measurement. [V] indicate the cluster index of the VBM analysis (see Supplemental Table 2). <u>Abbreviations</u>: Amyg = amygdala; AnG = angular gyrus; CB = cerebellum; CO = central operculum ; Ent = entorhinal area; FO = frontal operculum; FRP = frontal pole; FuG = fusiform gyrus; Hipp = Hippocampus; IOG = inferior occipital gyrus; ITG = inferior temporal gyrus; L = left; LiG = lingual gyrus; MCgG = middle cingulate gyrus; MFC = medial frontal cortex; MOG = middle occipital gyrus; MSFG = superior frontal gyrus medial segment; OCP = occipital pole; OFuG = occipital fusiform gyrus; OpIFG = opercular part of the inferior frontal gyrus; PHG = parahippocampal gyrus; PoG = postcentral gyrus; PrG = precentral gyrus; R = right; SFG = superior frontal gyrus; SMC = supplementary motor cortex; SMG = supramarginal gyrus; TMP = temporal pole; TrIFG = triangular part of the inferior frontal gyrus.

Supplemental Table 2. Explorative SPM12 whole-brain analysis of the associations between VBM and motor learning. Results of longitudinal changes **[A]** PRE vs. POST, **[B]** PRE vs. MID, and **[C]** MID vs. POST are being reported. Cutoff for all analyses was peak $p_{height} < 0.01$ (i.e., SPM[T_{19}] with T = 2.59483), $k_{ext} > 120$ and intracranial volume as covariate, hence cluster and peak statistics are being reported. The cluster indices V refer to the visualizations in Supplemental Figure 7 and 8. Cluster labelling has been performed using the Brainnetome atlas (Fan et al. 2016) and the functional 7-networks atlas by Buckner et al. (2011), and the fraction of each cluster that belongs to a certain label is stated in percent. Furthermore, extended local maxima labelling has been performed (additionally including Neuromorphometrics and the anatomical

cerebellar atlas by Diedrichsen et al. (2009) labels) and simplified and fractions <5.0% are not reported for the purpose of readability; the location of the actual peak coordinate is underlined. All significant peaks within a cluster are reported.

cluster				peak					MNI coordinates		Extended local maxima labelling
Index	equivk	p(unc)	Cluster label	T	p(unc)	x	y	z	Neuromorphometrics Atlas [Cerebellar atlas Diedrichsen et al.]	Brainnetome Atlas	Buckner 7 Networks Atlas
[A] PRE vs. POST											
• Intensity increase COMPLEX > SIMPLE GROUP or intensity decrease in SIMPLE > COMPLEX GROUP											
V1	461	0.318	Network 3 (54.5%) Network 4 (45.1%) Network 6 (0.4%)	3.99	<0.001	-18	-68	-46	L Cerebellum Exterior (72.4%) L Cerebellum White Matter (27.6%) [L lobule VIIIa (63.0%), L lobule VIIb (28.0%)]	-	Network4 (47.0%) Network3 (32.9%) Network6 (11.0%)
V2	679	0.227	Network 6 (54.6%) Network 7 (38.5%) N/A (6.8%)	3.89	<0.001	-54	-58	-42	N/A (59.5%) L Cerebellum Exterior (40.5%) [L crus I (50.0%), L crus II (7.0%)]	-	Network7 (34.1%) Network6 (33.9%) N/A (31.2%)
				2.92	0.004	-50	-58	-54	N/A (69.5%) L Cerebellum Exterior (30.5%) [L crus II (19.0%), L lobule VIIb (7.0%)]	-	N/A (52.5%) Network6 (45.5%)
V3	814	0.187	A37lv_R (53.1%) A20rv_R (18.5%) N/A (13.4%) A20cv_R (11.2%) A37elv_R (2.1%) A20iv_R (1.7%)	3.23	0.002	40	-36	-16	R Cerebral White Matter (55.3%) R FuG fusiform gyrus (33.2%) R ITG inferior temporal gyrus (8.9%)	A37lv_R (40.0%) N/A (29.8%) A20rv_R (13.4%) TL_R (5.2%) A20cv_R (5.1%)	-
				3.16	0.003	40	-27	-22	R FuG fusiform gyrus (43.5%) R Cerebral White Matter (35.7%) R ITG inferior temporal gyrus (14.3%)	A20rv_R (36.2%) A37lv_R (16.8%) N/A (16.5%) A20cv_R (12.2%) cHipp_R (7.9%) TL_R (6.3%)	-
• Intensity increase SIMPLE > COMPLEX GROUP or intensity decrease in COMPLEX > SIMPLE GROUP											

V4	**3044**	0.018	A46_R (28.2%) N/A (28.1%) A10l_R (21.9%) A9/46v_R (12.0%) A11m_R (5.9%) A14m_R (2.6%) A9/46d_R (1.1%) A10m_R (0.2%)	3.64	0.001	33	58	2	R MFG middle frontal gyrus (58.7%) N/A (16.7%) R Cerebral White Matter (10.2%) R SFG superior frontal gyrus (8.8%)	A10l_R (39.2%) A46_R (35.7%) A9/46v_R (13.0%) N/A (12.0%)	-
				3.45	0.001	24	44	18	R Cerebral White Matter (76.2%) R MFG middle frontal gyrus (17.9%) R SFG superior frontal gyrus (5.8%)	N/A (60.6%) A46_R (27.5%) A9/46d_R (10.2%)	-
				3.31	0.002	15	68	-12	N/A (45.4%) R FRP frontal pole (39.2%) R Cerebral White Matter (8.1%)	N/A (40.9%) A11m_R (31.6%) A10l_R (27.1%)	-
V5	**740**	0.208	rHipp_R (18.3%) lAmyg_R (13.6%) N/A (13.1%) A38m_R (11.3%) TI_R (10.2%) A20rv_R (8.9%) mAmyg_R (8.6%) A28/34_R (7.9%) A35/36r_R (7.3%) cHipp_R (0.8%)	3.49	0.001	27	-4	-28	R Cerebral White Matter (35.1%) R Ent entorhinal area (20.9%) R Hippocampus (15.1%) R Amygdala (14.5%) R PHG parahippocampal gyrus (9.4%)	rHipp_R (24.5%) A35/36r_R (17.9%) N/A (14.7%) lAmyg_R (12.3%) mAmyg_R (9.0%) TI_R (6.8%) A20rv_R (5.8%) A28/34_R (5.2%)	-
				3.41	0.001	34	-9	-28	R Cerebral White Matter (51.7%) R FuG fusiform gyrus (21.0%)	A20rv_R (31.7%) N/A (22.4%) rHipp_R (12.9%) A35/36r_R (11.9%) cHipp_R (9.2%) lAmyg_R (5.2%)	-

									Region A	Region B	
									R Hippocampus (11.7%) R PHG parahippocampal gyrus (5.3%)		
				3.38	0.002	24	4	-30	R Ent entorhinal area (33.1%) N/A (22.6%) R TMP temporal pole (20.1%) R Cerebral White Matter (16.1%) R Amygdala (5.7%)	A38m_R (27.2%) N/A (25.2%) TI_R (17.8%) mAmyg_R (9.1%) lAmyg_R (5.2%)	-
V6	242	0.474	A10m_L (60.4%) A9l_L (26.2%) N/A (11.8%) A46_L (1.6%)	3.27	0.002	-15	63	15	L Cerebral White Matter (30.1%) L SFG superior frontal gyrus (29.1%) L FRP frontal pole (18.9%) N/A (18.8%)	A10m_L (37.2%) N/A (26.0%) A46_L (17.3%) A9l_L (14.5%) A10l_L (5.0%)	-
V7	259	0.458	A39rv_L (62.1%) A39c_L (37.9%)	3.12	0.003	-44	-75	30	L MOG middle occipital gyrus (34.8%) L AnG angular gyrus (32.2%) N/A (22.4%) L Cerebral White Matter (10.6%)	A39rv_L (61.0%) A39c_L (23.0%) N/A (16.0%)	-
				2.8	0.006	-38	-84	26	L MOG middle occipital gyrus (62.7%) N/A (30.5%) L Cerebral White Matter (6.9%)	A39c_L (74.1%) N/A (21.9%)	-

						x	y	z			
V8	188	0.532	Network4 (62.1%) Network2 (37.0%) A37mv_R (4.8%) rLinG_R (1.7%)	3.08	0.003	21	-63	-18	R Cerebellum Exterior (76.0%) R LiG lingual gyrus (12.5%) R OFuG occipital fusiform gyrus (8.1%) [R lobule VI (92.3%), R lobule V (2.9%)]	N/A (70.9%) rLinG_R (15.7%) A37mv_R (13.4%)	Network4 (42.6%) Network2 (29.9%) N/A (20.9%)
V9	182	0.540	A10m_R (62.0%) A9l_R (14.2%) N/A (23.8%)	2.81	0.006	3	64	10	N/A (36.3%) R MSFG superior frontal gyrus medial segment (25.1%) R FRP frontal pole (16.7%) L MSFG superior frontal gyrus medial segment (10.8%) R Cerebral White Matter (7.0%)	A10m_R (55.8%) N/A (25.2%) A10m_L (17.5%)	-
				2.76	0.006	12	57	20	R Cerebral White Matter (46.6%) R SFG superior frontal gyrus (26.3%) R MSFG superior frontal gyrus medial segment (25.3%)	A10m_R (44.4%) N/A (23.2%) A9l_R (19.8%) A46_R (7.9%)	-
• Intensity decrease (both GROUPs)											
V10	504	0.296	Network4 (62.5%) Network6 (23.4%) Network2 (8.6%) A37mv_R (7.7%)	3.41	0.001	33	-56	-30	R Cerebellum Exterior (81.6%) R Cerebellum White Matter (17.9%) [R lobule VI	-	Network6 (58.5%) Network4 (36.9%)

			Network	t	p	x	y	z	Region		Network
			rLinG_R (4.0%) Network 3 (0.3%) Network 1 (0.1%)	3.34	0.002	22	-63	-18	R Cerebellum Exterior (71.5%) R LiG lingual gyrus (11.5%) R OFuG occipital fusiform gyrus (10.9%) [R lobule VI (91.1%)]	N/A (66.5%) A37mv_R (19.3%) rLinG_R (14.1%)	Network4 (44.1%) Network2 (24.6%) N/A (24.4%)
				3.16	0.003	26	-57	-26	R Cerebellum Exterior (82.5%) R Cerebellum White Matter (15.2%) [R lobule VI (95.0%)]	N/A (94.9%) A37mv_R (5.1%)	Network4 (39.5%) Network2 (27.4%) Network6 (25.2%)
V11	258	0.459	Network 6 (68.5%) Network 4 (31.5%)	3.25	0.002	-40	-60	-33	L Cerebellum Exterior (89.2%) L Cerebellum White Matter (10.8%) [L crus I (89.0%)]	-	Network6 (71.5%) Network4 (20.6%) Network7 (7.9%)
				3.09	0.003	-40	-50	-39	L Cerebellum Exterior (85.8%) L Cerebellum White Matter (13.5%) [L crus I (53.0%), L crus II (7.0%)]	-	Network6 (63.6%) Network4 (35.8%)
• Intensity increase (both GROUPs)											
V12	274	0.445	A38m_R (72.8%) N/A (27.2%)	3.44	0.001	24	15	-34	N/A (54.1%) R TMP temporal pole (42.0%)	A38m_R (51.3%) N/A (43.6%)	-

V	size	val	Region (peak)	T	p	x	y	z	Anatomical region	Anatomical region	
V13	864	0.175	N/A (31.7%) A12/47l_R (27.6%) A12/47o_R (12.7%) A45r_R (11.9%) A45c_R (8.5%) A44op_R (4.8%) A38l_R (2.3%) A44v_R (0.6%)	3.41	0.001	56	21	-3	N/A (57.1%) R TrIFG triangular part of the inferior frontal gyrus (13.4%) R OpIFG opercular part of the inferior frontal gyrus (11.8%) R FO frontal operculum (10.8%)	N/A (45.2%) A45c_R (14.1%) A44op_R (11.8%) A45r_R (9.5%) A44v_R (7.8%) TE1.0/TE1.2_R (6.7%)	-
				3.25	0.002	48	26	-12	N/A (45.9%) R OrIFG orbital part of the inferior frontal gyrus (23.0%) R Cerebral White Matter (8.7%) R LOrG lateral orbital gyrus (6.1%) R TMP temporal pole (5.4%)	A12/47l_R (35.3%) N/A (33.6%) A38l_R (10.8%) A12/47o_R (10.4%)	-

V	size	val	Region (peak)	T	p	x	y	z	Anatomical region	Anatomical region	
V14	1346	0.145	A4tl_L (28.1%) N/A (21.5%) A44v_L (19.4%) A1/2/3tonIa_L (17.2%) A6cvl_L (11.5%) A44op_L (0.8%) dIg_L (0.7%) dId_L (0.6%) A45r_L (0.2%)	3.79	0.001	-50	-8	14	L Cerebral White Matter (47.8%) L CO central operculum (46.1%)	N/A (29.8%) A1/2/3tonIa_L (29.7%) A4tl_L (26.7%)	-
				3.59	0.001	-54	6	9	L Cerebral White Matter (33.1%) L OpIFG opercular part of the inferior frontal gyrus (23.8%) L PrG precentral gyrus (23.4%) L CO	A4tl_L (40.5%) A6cvl_L (21.4%) A44v_L (21.3%) N/A (13.6%)	-

						x	y	z			
									central operculum (11.3%) N/A (7.9%)		
		2.75	0.006			-50	20	-3	N/A (35.5%) L FO frontal operculum (23.4%) L TrIFG triangular part of the inferior frontal gyrus (13.9%) L OpIFG opercular part of the inferior frontal gyrus (11.2%) L Cerebral White Matter (6.1%) L OrIFG orbital part of the inferior frontal gyrus (5.1%)	N/A (24.5%) A44op_L (19.9%) A44v_L (18.6%) A12/47l_L (9.7%) A45r_L (9.0%) A45c_L (8.1%)	-
V15	413	0.415	A4t_R (46.9%) N/A (35.7%) A1/2/3tru_R (9.0%) A4ul_R (8.4%)	3.47	0.001	16	-26	60	R Cerebral White Matter (69.2%) R PrG precentral gyrus (18.6%) R PoG postcentral gyrus (9.2%)	N/A (55.8%) A4t_R (17.2%) A1/2/3tru_R (11.6%) A4ul_R (10.7%)	-
V16	139	0.653	A23c_L (65.1%) N/A (26.6%) A6m_L (8.3%)	3.47	0.001	-14	-12	42	L Cerebral White Matter (71.9%) L MCgG middle cingulate gyrus (16.7%) L SMC supplementary motor cortex (9.1%)	N/A (59.8%) A23c_L (26.6%) A6m_L (11.2%)	-

• **Intensity increase SIMPLE > COMPLEX GROUP or intensity decrease in COMPLEX > SIMPLE GROUP**

ID	Size	Value	Regions	t	p	x	y	z	Anatomical region	Region (atlas)	
V17	**2286**	0.064	A39c_L (40.1%) mOccG_L (22.5%) N/A (19.5%) OPC_L (7.7%) lsOccG_L (6.0%) msOccG_L (3.6%) A39rv_L (0.5%) V5/MT+_L (0.1%)	3.62	0.001	-21	-10	16	N/A (67.8%) L OCP occipital pole (22.2%) L SOG superior occipital gyrus (5.2%)	N/A (57.9%) OPC_L (31.9%) mOccG_L (10.3%)	-
				3.56	0.001	-26	-90	27	L SOG superior occipital gyrus (37.8%) N/A (36.1%) L MOG middle occipital gyrus (23.4%)	N/A (26.1%) mOccG_L (24.8%) A39c_L (22.9%) lsOccG_L (15.8%) msOccG_L (10.3%)	-
				3.26	0.002	-34	-92	16	L MOG middle occipital gyrus (47.4%) N/A (47.3%)	mOccG_L (37.6%) N/A (34.2%) A39c_L (28.2%)	-
				3.22	0.002	-40	-82	21	L MOG middle occipital gyrus (67.1%) N/A (26.7%) L Cerebral White Matter (6.2%)	A39c_L (64.3%) N/A (20.3%) A39rv_L (7.6%) mOccG_L (5.9%)	-
V18	**134**	0.660	A40c_L (43.1%) N/A (39.3%) A39rv_L (17.6%)	2.9	0.005	-62	-57	34	N/A (65.6%) L SMG supramarginal gyrus (18.2%) L Ang angular gyrus (15.2%)	N/A (54.3%) A40c_L (35.4%) A39rv_L (10.3%)	-
V19	**138**	0.655	A39c_R (85.3%) mOccG_R (12.2%) N/A (2.6%)	2.84	0.005	39	-81	18	R MOG middle occipital gyrus (65.7%) N/A (16.2%) R Cerebral White Matter (11.8%) R SOG superior occipital	A39c_R (50.0%) mOccG_R (33.7%) N/A (10.5%)	-

gyrus
(5.5%)

• Intensity decrease (both GROUPs)											
V20	**470**	0.3 84	A39c_L (85.2%) mOccG_ L (7.9%) N/A (5.8%) lsOccG_ L (1.1%)	2. 99	0. 00 4	- 3 2	- 87	2 2	L MOG middle occipital gyrus (60.4%) N/A (22.0%) L SOG superior occipital gyrus (12.6%) L Cerebral White Matter (5.0%)	A39c_L (57.6%) mOccG_L (22.4%) N/A (12.4%) lsOccG_L (7.5%)	-
				2. 96	0. 00 4	- 3 9	- 84	2 7	L MOG middle occipital gyrus (54.7%) N/A (39.9%) L Cerebral White Matter (5.3%)	A39c_L (65.1%) N/A (29.4%) A39rv_L (5.5%)	-
• Intensity increase (both GROUPs)											
V21	**1260**	0.1 57	A10l_L (45.1%) N/A (36.1%) A14m_L (14.7%) A13_L (1.6%) A11m_L (1.3%) A12/47o _L (0.7%) A11l_L (0.6%)	4. 35	0	- 2 0	57	-8	L Cerebral White Matter (50.6%) L FRP frontal pole (14.9%) L AOrG anterior orbital gyrus (14.7%) L SFG superior frontal gyrus (13.3%)	A10l_L (55.7%) N/A (28.6%) A11l_L (9.1%)	-
				3. 14	0. 00 3	- 1 0	44	- 1 5	L Cerebral White Matter (48.5%) L MFC medial frontal cortex (22.5%) L MOrG medial orbital gyrus (12.5%) L ACgG anterior	N/A (28.7%) A14m_L (27.7%) A11l_L (16.7%) A11m_L (16.4%) A32sg_L (6.8%)	-

cingulate
gyrus
(9.7%)
L GRe
gyrus
rectus
(6.4%)

V22	667	0.298	A38m_R (68.8%) N/A (27.1%) A38l_R (4.0%) A21r_R (0.1%)	3.94	0	30	22	-30	N/A (60.2%) R TMP temporal pole (28.3%) R POrG posterior orbital gyrus (11.2%)	N/A (49.4%) A38m_R (38.0%) A11l_R (12.4%)	-
				3.21	0.002	21	14	-32	N/A (61.0%) R TMP temporal pole (25.4%) R POrG posterior orbital gyrus (6.1%) R MOrG medial orbital gyrus (5.2%)	N/A (50.3%) A38m_R (32.1%) A11l_R (8.4%)	-
				2.87	0.005	44	24	-24	N/A (55.2%) R TMP temporal pole (33.3%) R POrG posterior orbital gyrus (8.4%)	N/A (42.0%) A38l_R (31.9%) A38m_R (13.9%) A12/47o_R (11.4%)	-
V23	1105	0.184	N/A (29.1%) A4tl_L (18.2%) A12/47l_L (15.6%) A44v_L (14.2%) A45r_L (11.1%) A6cvl_L (9.4%) A45c_L (1.4%) A12/47o_L (0.5%) A44op_L (0.3%)	3.78	0.001	-57	8	6	N/A (32.4%) L OpIFG opercular part of the inferior frontal gyrus (22.7%) L PrG precentral gyrus (17.3%) L Cerebral White Matter (15.5%) L CO central operculum (8.3%)	A4tl_L (32.3%) N/A (26.6%) A44v_L (20.4%) A6cvl_L (14.3%) TE1.0/TE1.2_L (6.1%)	-

			A4hf_L (0.1%)	3.27	0.002	-54	30	-9	N/A (62.9%) L TrIFG triangular part of the inferior frontal gyrus (18.9%) L OrIFG orbital part of the inferior frontal gyrus (14.2%)	N/A (58.9%) A45r_L (23.7%) A12/47l_L (17.0%)	-
				3.22	0.002	-54	20	-3	N/A (57.6%) L TrIFG triangular part of the inferior frontal gyrus (14.7%) L OpIFG opercular part of the inferior frontal gyrus (12.0%) L FO frontal operculum (9.6%)	N/A (49.5%) A44v_L (17.4%) A45r_L (8.7%) A45c_L (8.2%) A44op_L (7.3%)	-
				2.73	0.007	-44	40	-12	L Cerebral White Matter (31.4%) L LOrG lateral orbital gyrus (26.3%) L OrIFG orbital part of the inferior frontal gyrus (16.2%) N/A (16.0%) L TrIFG triangular part of the inferior frontal gyrus (7.9%)	A12/47l_L (34.6%) A12/47o_L (28.8%) N/A (18.3%) A45r_L (16.9%)	-
V24	213	0.568	A20rv_R (69.3%) N/A (30.7%)	3.63	0.001	24	-6	-51	N/A (90.1%) R ITG inferior temporal	N/A (73.7%) A20rv_R (25.4%)	-

gyrus
(5.5%)

V25	650	0.304	A11m_R (54.6%) A10l_R (21.0%) N/A (16.0%) A10m_R (7.8%) A14m_R (0.6%)	3.62	0.001	21	72	0	N/A (68.1%) R FRP frontal pole (29.4%)	N/A (60.8%) A10l_R (31.5%)	-
				3.33	0.002	10	70	-4	N/A (51.7%) R FRP frontal pole (40.3%) R Cerebral White Matter (7.4%)	N/A (44.8%) A11m_R (32.7%) A10m_R (10.0%) A10l_R (9.5%)	-
				3.04	0.003	9	60	-12	R Cerebral White Matter (32.5%) R FRP frontal pole (28.1%) R MFC medial frontal cortex (15.4%) R GRe gyrus rectus (6.5%) R MOrG medial orbital gyrus (6.1%) N/A (5.7%)	A11m_R (56.3%) A14m_R (17.1%) N/A (12.5%) A10l_R (10.1%)	-
V26	398	0.424	A40rv_L (83.6%) A1/2/3tonla_L (11.2%) N/A (4.8%) A41/42_L (0.4%)	3.13	0.003	-62	-26	20	N/A (20.7%) L PO parietal operculum (16.4%) L SMG supramarginal gyrus (16.0%) L PoG postcentral gyrus (14.5%) L PT planum temporale (13.3%) L Cerebral White Matter (9.9%) L CO central	A40rv_L (59.2%) A41/42_L (14.4%) A1/2/3tonla_L (12.8%) N/A (11.4%)	-

operculum
(7.8%)

				2.71	0.007	-4	-18	18	L CO central operculum (42.7%) L Cerebral White Matter (37.6%) L PO parietal operculum (10.8%) L TTG transverse temporal gyrus (7.7%)	A1/2/3tonla_L (45.2%) N/A (24.1%) A40rv_L (23.1%)	-
V27	156	0.632	mAmyg_R (41.7%) rHipp_R (40.3%) lAmyg_R (10.5%) A35/36r_R (4.7%) N/A (1.5%) TI_R (1.1%) A38m_R (0.2%)	3.08	0.003	22	-2	-26	R Ent entorhinal area (35.0%) R Amygdala (21.7%) R Cerebral White Matter (13.3%) R Hippocampus (12.1%) N/A (11.2%)	rHipp_R (24.5%) mAmyg_R (23.6%) N/A (16.3%) lAmyg_R (11.6%) A28/34_R (7.8%) TI_R (6.9%) A38m_R (6.1%)	-
V28	234	0.548	A1/2/3tru_L (78.5%) N/A (20.6%) A7pc_L (0.8%) A4ul_L (0.1%)	2.98	0.004	-18	-34	63	L PoG postcentral gyrus (43.4%) L Cerebral White Matter (38.1%) L PrG precentral gyrus (13.4%)	A1/2/3tru_L (45.8%) N/A (22.5%) A4ul_L (21.8%) A7pc_L (5.7%)	-

[C] MID vs. POST											
• **Intensity increase COMPLEX > SIMPLE GROUP or intensity decrease in SIMPLE > COMPLEX GROUP**											
V29	1847	0.114	V5/MT+_R (52.7%) A39c_R (31.2%) N/A (6.6%) iOccG_R (6.4%) mOccG_R (2.7%)	4.56	0	51	-74	14	N/A (38.9%) R MOG middle occipital gyrus (34.0%) R IOG inferior occipital gyrus (19.5%) R Cerebral	A39c_R (48.5%) V5/MT+_R (26.3%) N/A (23.8%)	-

			A37dl_R (0.5%)						White Matter (6.2%)		
V30	123	0.700	cLinG_L (45.6%) N/A (18.2%) rLinG_L (13.2%) cLinG_R (11.6%) rCunG_L (11.4%)	2.89	0.005	-2	-72	-4	L LiG lingual gyrus (42.1%) N/A (25.5%) R LiG lingual gyrus (19.1%) [N/A]	N/A (33.7%) rCunG_L (21.6%) rLinG_L (17.3%) rCunG_R (14.0%) cLinG_L (6.9%)	N/A (84.4%) Network4 (15.5%)
				2.86	0.005	0	-82	-10	L LiG lingual gyrus (38.0%) N/A (31.9%) R LiG lingual gyrus (22.6%)	cLinG_L (33.9%) cLinG_R (28.8%) N/A (27.7%)	-
V31	134	0.686	mOccG_R (95.7%) N/A (3.8%) OPC_R (0.4%)	2.86	0.005	33	-92	16	N/A (46.4%) R SOG superior occipital gyrus (21.7%) R MOG middle occipital gyrus (13.7%) R Cerebral White Matter (9.8%) R OCP occipital pole (5.1%)	mOccG_R (54.5%) N/A (34.2%) OPC_R (10.4%)	-

• Intensity increase SIMPLE > COMPLEX GROUP or intensity decrease in COMPLEX > SIMPLE GROUP											
V32	1987	0.103	A10l_R (43.7%) N/A (19.4%) A46_R (16.1%) A11m_R (14.4%) A9/46v_R (3.9%) A14m_R (2.3%) A10m_R (0.2%)	3.52	0.001	30	58	2	R MFG middle frontal gyrus (48.3%) R SFG superior frontal gyrus (19.0%) R Cerebral White Matter (12.8%) N/A (10.3%) R FRP frontal pole (6.9%)	A10l_R (46.6%) A46_R (41.5%) N/A (6.4%) A9/46v_R (5.4%)	-

ID	N	value	Peak regions	t	p	x	y	z	Region	Region %	
				3.19	0.002	12	63	-8	R FRP frontal pole (43.6%) R Cerebral White Matter (33.7%) N/A (6.1%) R MFC medial frontal cortex (5.0%)	A11m_R (42.5%) A10l_R (25.6%) N/A (15.8%) A14m_R (13.7%)	-
V33	459	0.424	A38m_R (22.6%) lAmyg_R (17.9%) mAmyg_R (16.1%) rHipp_R (14.2%) N/A (14.2%) TI_R (11.2%) A35/36r_R (2.7%) A28/34_R (0.8%) A20rv_R (0.4%)	3.34	0.002	27	2	-28	R Ent entorhinal area (33.3%) R Cerebral White Matter (32.3%) R TMP temporal pole (12.6%) R Amygdala (11.3%) N/A (6.1%)	N/A (26.1%) A38m_R (18.9%) TI_R (12.0%) lAmyg_R (10.7%) mAmyg_R (10.0%) rHipp_R (9.2%) A35/36r_R (7.7%)	-
V34	432	0.439	A8dl_R (46.9%) N/A (24.0%) A6vl_R (14.8%) A6dl_R (14.4%)	3.15	0.003	20	21	51	R SFG superior frontal gyrus (46.2%) R Cerebral White Matter (44.7%) R MFG middle frontal gyrus (9.1%)	A8dl_R (57.7%) N/A (32.2%)	-
				3.02	0.004	21	12	50	R Cerebral White Matter (58.2%) R SFG superior frontal gyrus (26.2%) R MFG middle frontal gyrus (15.6%)	N/A (45.4%) A8dl_R (21.9%) A6vl_R (20.4%) A6dl_R (12.1%)	-
				2.59	0.009	22	2	51	R Cerebral White Matter (57.9%) R SFG	N/A (45.9%) A6dl_R (21.4%) A6vl_R (21.1%) A6cdl_R (9.8%)	-

										superior frontal gyrus (22.5%) R MFG middle frontal gyrus (18.0%)		
V35	160	0.654	Network 5 (80.5%) Network 2 (14.0%) N/A (3.3%) Network 7 (2.2%)	3.04	0.003	6	-62	-56	R Cerebellum Exterior (61.4%) N/A (31.0%) L Cerebellum Exterior (5.9%) [R lobule IX (76.0%), R lobule VIIIb (20.0%)]	-	Network5 (37.5%) Network2 (19.5%) N/A (19.2%) Network7 (16.7%) Network4 (6.6%)
V36	179	0.633	A14m_L (58.6%) A10m_L (28.6%) N/A (5.9%) A11m_L (4.4%) A10l_L (2.5%)	2.76	0.006	-6	68	0	N/A (43.3%) L FRP frontal pole (34.5%) L Cerebral White Matter (10.7%) L MSFG superior frontal gyrus medial segment (7.8%)	N/A (36.6%) A14m_L (26.8%) A10m_L (22.4%) A11m_L (7.9%)	-

Abbreviations: Abbreviations: equivk = cluster extent (number of voxels, with each voxel 1.5×1.5×1.5 mm³); L = left; N/A = not available; PRE = pre/baseline measurement; POST = post measurement after 4-week motor training intervention; R = right; unc = uncorrected.

Supplement 6D: Brief discussion of exploratory results.

The explorative PET analysis showed decreased SynVesT-1 uptake after training in the left temporal lobe, driven by the complex training group, and pre-training uptake in cerebellar and temporal regions correlating with motor learning progress. Changes in SynVesT-1 uptake negatively correlated with learning progress in widespread cortical, cerebellar, and subcortical areas, indicating greater uptake decreases associated with better performance. Explorative longitudinal VBM analysis revealed GM volume increases in frontal, temporal, and sensorimotor regions and decreases in the cerebellum and occipital cortex, which mainly occurred during the first two weeks of training when investigating both groups pooled. There were no overlapping regions between the longitudinal PET and VBM findings. VBM analysis with an interaction effect of group and timing showed stronger and different gray matter changes for complex versus simple training, especially between mid and post training time points. This might suggest a more general training effect in the first two weeks of the training intervention, and a

more group-specific effect in the second half of the training intervention, when the complex training group is increasingly exposed to the more complex task variants.

Choice of analyses based on behavioral and VOI-based findings of the main manuscript.

Both training groups improved skills over time, with greater gains in the complex group, suggesting that neuroplastic changes occurred in both. Therefore, group was included as a factor in whole-brain analyses comparing baseline to post measurements. For correlations between SV2A uptake and learning progress, participants were pooled to increase statistical power. This pooling also allowed classification by individual learning slopes, reflecting varying degrees of learning across groups (Aggarwal & Ranganathan 2016).

The VOI-based analysis applied in the main manuscript offers advantages such as hypothesis-driven regional specificity, reduced noise, and fewer multiple comparisons. However, its results might miss results outside the pre-selected VOIs, and subtle local variations within the VOIs might remain undetected due to averaging. Given the exploratory nature of this study and the lack of prior in vivo data on synaptic density changes in motor learning, we complemented the VOI analysis with a whole-brain voxel-wise approach for higher spatial resolution and comprehensive coverage. Due to small sample size and expected effect sizes, the voxel-wise results are exploratory and should be interpreted with caution but might still be useful in guiding future research.

Decreased SV2A tracer uptake in left temporal pole after 4 weeks of motor learning.

The exploratory whole-brain analysis revealed decreased SynVesT-1 uptake after 4 weeks of motor learning in a region covering the left temporal pole, inferior, and middle temporal gyrus. These regions are linked to visuospatial processing (Makris et al. 2013), object recognition (Sewards & Sewards), and visually guided behavior (Hamamé et al. 2012, Conway 2018, Lin et al. 2020). In line, fMRI activation decreases have been reported in motor learning studies (Rieckmann et al. 2010, Santos Monteiro et al. 2017), possibly reflecting LTD-like plasticity and synaptic pruning as visuomotor skills become automatic. When comparing to VBM literature, this aligns with models of structural brain changes showing initial growth followed by renormalization (Wenger et al. 2017) which suggests that the present findings of the SV2A decrease at the 4-week follow up measurement might reflect the renormalization phase.

Associations between SV2A tracer uptake at baseline and subsequent motor learning.

Baseline SV2A uptake was linked to subsequent motor learning in both simple and complex BTT subtasks. For the 1:1 subtask, uptake in the right middle temporal gyrus correlated positively with learning progress, whereas posterior cerebellar regions (crus I and II) showed negative correlations, likely driven by higher initial performance on these simple task variants rather than slower learning. For the complex subtasks, positive associations emerged in bilateral cerebellum (crus I, II, lobule VIIb) and right inferior occipital gyrus (hMT/V5+), while negative associations were found in the right inferior temporal, occipital fusiform, and inferior occipital gyri. These findings suggest that cerebellar and occipital regions supporting visual processing, cognitive control, and visuomotor integration (Indovina & Sanes 2001, Claeys et al. 2003, Stoodley et al. 2012, Balsters et al. 2013, Sinanaj et al. 2015) at baseline may facilitate complex motor learning. Especially the hMT/V5+ has been shown to be of relevance to bimanual visuomotor tasks (Ronsse et al. 2011) and the BTT in particular (Santos Monteiro et al. 2017).

Associations between training-related changes in SV2A tracer uptake and motor learning progress.

Changes in SV2A uptake from baseline to post were unrelated to learning progress on the 1:1 subtask, but for complex subtasks, greater decreases were linked to better performance gains. Associated regions included cortical areas (right precuneus, superior temporal gyrus, superior parietal lobe, angular gyrus, parietal operculum, occipital pole, cuneus, superior/middle occipital gyrus), subcortical structures (right putamen, pallidum, thalamus), and the right cerebellum (lobules VIIIb and X). Many of these regions are involved in visuospatial integration (Sommer 2003, Gowen & Miall 2007, Milner et al. 2007, Sepulcre et al. 2012, Makris et al. 2013, Derbie et al. 2021), motor coordination (Cavanna & Trimble 2006, Chakravarthy et al. 2010, Genon et al. 2017), cognitive control (Dadario & Sughrue 2023), and error monitoring (Galléa et al. 2008), processes likely crucial in mastering complex (Van Ruitenbeek et al. 2023), visually guided bimanual movements (Wenderoth et al. 2005, Santos Monteiro et al. 2017). The pattern supports a shift toward automatization and synaptic reorganization with extended practice, potentially via pruning of task-irrelevant connections. Since SV2A tracer uptake in these regions mostly declined from baseline to post, this negative correlation is most likely to be interpreted as more decline in SV2A tracer uptake being linked to a better learning progress. Furthermore, the absence of associations between SV2A tracer uptake changes and motor learning progress for the 1:1 progress test might indicate that especially the most complex tasks elicited neuroplastic changes that were large enough and functionally essential to be linked with each other.

Relationship between PET and VBM findings.

No overlap was found between regions showing SV2A uptake changes (baseline vs. post) and those with GM volume changes across any of the three investigated time periods. A possible explanation might be that volumetric changes can mask synaptic alterations. For example, in a rodent optokinetic motor learning paradigm, synaptic pruning occurred within 24 hours with a reduction in spine volume (−17.8% in cerebellum vs. sham) but no change in spine density (Morizawa et al. 2022), suggesting that regression of spine volume can precede bouton loss detectable with SV2A PET. Similarly, skilled reaching training in rodents increased synapses per neuron in cortical layer V, but concurrent neuropil and cortical volume expansion left synaptic density per volume unchanged (Kleim et al. 2002). Such structural remodeling – whether through spine regression preceding bouton loss or volume increases obscuring synaptic density changes – may conceal associations between SV2A PET and VBM measures.

Alternatively, motor learning–related GM changes could stem from other processes such as gliogenesis, angiogenesis, or dendritic remodeling (Zatorre et al. 2012), distinct from the synaptic changes detected via SV2A PET.

Changes in gray matter associated with motor learning.

Across both groups, GM changes were most evident in the first half of training (PRE vs. MID) and across the whole learning period (PRE vs. POST), but not during the second half alone (MID vs. POST). Early changes were largely group-unspecific, whereas later adaptations did appear to be group-specific, especially for the complex group which was increasingly exposed to the more complex task variants during this period. Overall, there was a trend that anterior regions rather showed GM volume increases, whereas posterior regions (occipital, cerebellum) rather showed decreases.

In sensorimotor areas, early bilateral pre-/postcentral gyrus changes suggested short-lived adaptations to the BTT-related finger movements, possibly reverting later when task demands shifted towards more coordinative and cognitive processing due to higher task complexity. Frontal and opercular regions – linked to rhythm encoding (Konoike et al. 2015), interoception (Luo et al. 2022), visual scene analysis (Herlin et al. 2021), working memory (du Boisgueheneuc et al. 2006), spatial navigation/judgment (Derbie et al. 2021), action selection (Isherwood et al. 2021), reward/punishment processing (O'Doherty et al. 2001, de la Vega et al. 2016), motivation and error monitoring (Holroyd & Yeung 2012, Ullsperger et al. 2014), attention switching (Higo et al. 2011) and multimodal integration (Milner et al. 2007, Sepulcre et al. 2012) – showed predominantly early (first 2 weeks) increases, with effects specific to the complex group in later stages.

Occipital GM changes varied by group and time: regions supporting spatial visualization, navigation, and spatial memory (Roberts et al. 2013, Li et al. 2018, Derbie et al. 2021, Du et al. 2022, Geissmann et al. 2023) decreased in GM volume early in the complex group but increased in the simple group, with a partial reversals later in the training. These patterns may reflect group differences in visual reliance, with the simple group (always being explosed to the simple 1:1 subtask during training) executing more automatized movements. Cerebellar changes showed both decreases and increases depending on hemisphere and time window, with complex-group decreases driving some of the effects.

Limbic GM changes, particularly in the entorhinal cortex, hippocampus, and amygdala, align with their roles in spatial mapping (Hafting et al. 2005, Jacobs et al. 2010), memory integration (Basu & Siegelbaum 2015), and associative learning (Chau & Galvez 2012). Such functions likely supported the spatial, navigational, and sensory–motor associations required for the BTT.

Limitations.

Sample size vs. statistical effect and power. The present study included 22 participants across two training groups. In addition, the employed motor learning intervention was expected to show smaller effects on SV2A tracer uptake or GM as compared to studies in neurodegenerative diseases or fMRI research to study changes in brain activity. It should therefore be considered that the combination of small sample sizes and small effect size leads to a reduced statistical power, which may lead to effects being overlooked but also to a limited generalizability of the findings. To balance the sensitivity and specificity of the explorative whole-brain analyses in the current study, more liberal statistical cut-off values were chosen, which may increase the likelihood of false positives and reduce the study's specificity. Therefore, results of the explorative analysis must be interpreted with care. However,

smaller studies such as the current work can provide valuable preliminary data and insights, serving as a foundation for future larger-scale investigations.

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