Supplementary File

Contents

Table 1. Grade assessment

Certainty assessment							Number of patients		Effect (95% CI)	Certainty	Importance
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Active remote tDCS	Sham remote tDCS			
SDMT											
4	randomised trials	serious[a]	not serious	serious[b]	serious[c]	none	137	114	SMD **of 0.20 (95% CI: [-0.06, 0.45])**	⨁◯◯◯ Very low[a,b,c]	**Higher scores are better.**
PROMIS											
2	randomised trials	not serious	serious[d]	serious[b]	serious[c]	none	69	63	MD **of -2.51 (95% CI: [-8.94, 3.92])**	⨁◯◯◯ Very low[b,c,d]	**Lower scores are better.**
Timed Up & Go											
2	randomised trials	not serious	not serious	serious[b]	serious[c]	none	36	39	SMD **of -0.13 (95% CI: [-0.59, 0.32])**	⨁⨁◯◯ Low[b,c]	**Lower scores are better.**
MSQOL											
2	randomised trials	not serious	not serious	serious[b]	serious[c]	none	50	48	SMD **of 0.22 (95% CI: [-0.31, 0.75])**	⨁⨁◯◯ Low[b,c]	**Higher scores are better.**

CI: confidence interval; **MD:** mean difference; **SMD:** standardized mean difference

Explanations:

a. There is a study that has a high risk of bias

b. There are co-interventions

c. Small sample size and the confidence interval includes benefit and harm

d. Downgraded due to unexplained substantial heterogeneity

Table 2. Detailed risk of bias results with justification

Study	D1		D2		D3		D4		D5		Overall
	decision	justification	decision	justification	decision	justification	decision	justification	decision	justification	
Pilloni 2025	Low		Low		High	9 loss in active vs 3 in sham (intention to treat analysis)	Low		Low		High
Charvet 2018	Low		Low		Low		Low		Some concerns	Unavailable protocol	Low
Pilloni 2024	Low		Low		Low		Low		Low		Low
Charvet 2025	Low		Low		Low		Low		Some concerns	The primary outcome (PROMIS Fatigue Scale) was prespecified, but None of the secondary outcomes were prespecified in the protocol, and there was also no accessible analysis plan.	Some concerns
Pagliari 2025	Low		Low		Low		Low		Low		Low

Table 3. R code used for analysis

R code	library(meta)
	library(readxl)
	library(grid)
	
	# -------------------------
	# Import your dataset
	# -------------------------
	data <- read_excel(file.choose())
	
	# -------------------------
	# Meta-analysis (Random-effects)
	# -------------------------
	meta_res <- metacont(
	  n.e = data$n.e,
	  mean.e = data$mean.e,
	  sd.e = data$sd.e,
	  n.c = data$n.c,
	  mean.c = data$mean.c,
	  sd.c = data$sd.c,
	  studlab = data$studlab,
	  data = data,
	# MD or SMD, based on the outcome
	  sm = "MD",
	  method.tau = "DL",
	  hakn = FALSE,
	  comb.fixed = FALSE,
	  comb.random = TRUE
	)
	
	print(meta_res, digits = 2)
	
	# --------------------------
	# Heterogeneity calculations
	# --------------------------
	het <- data.frame(
	  k = meta_res$k,
	  Q = meta_res$Q,
	  df = meta_res$df.Q,
	  p_Q = meta_res$pval.Q,
	  I2 = meta_res$I2,
	  I2_low = meta_res$lower.I2,
	  I2_high = meta_res$upper.I2,
	  tau2 = meta_res$tau^2,

```
  tau      = meta_res$tau
)
print(het)
write.csv(het, "heterogeneity_stats.csv",
row.names = FALSE)

# ---------------------------
# Dynamic x-axis helper
# ---------------------------
make_xaxis_from_ci <- function(obj, ref = 0,
pad_frac = 0.10) {
  vals <- c(obj$lower, obj$upper,
obj$lower.random, obj$upper.random, ref)
  vals <- vals[is.finite(vals)]

  if (length(vals) == 0) {
    return(list(xlim = NULL, at = NULL))
  }

  rng <- range(vals)
  span <- diff(rng)
  pad <- span * pad_frac
  if (!is.finite(pad) || pad == 0) pad <- 1

  xmin <- rng[1] - pad
  xmax <- rng[2] + pad

  span2 <- xmax - xmin
  step <- if (span2 <= 2) 0.5 else if (span2 <= 5) 1
else if (span2 <= 10) 2 else 5

  lim <- max(abs(xmin - ref), abs(xmax - ref))
  lim <- ceiling(lim / step) * step
  xlim <- c(ref - lim, ref + lim)

  at <- seq(xlim[1], xlim[2], by = step)

  list(xlim = xlim, at = at)
}

# ---------------------------
# Forest plot
# ---------------------------
nice_forest <- function(x, file = NULL, device =
c("png","pdf"),
                        width = 12, height = 7, res = 300) {
```

```
  device <- match.arg(device)

  if (!is.null(file)) {
    if (device == "pdf") {
      pdf(file, width = width, height = height, onefile
= TRUE)
    } else {
      png(file, width = width, height = height, units =
"in", res = res, type = "cairo")
    }
  }

  ax <- make_xaxis_from_ci(x, ref = 0, pad_frac =
0.10)

  forest(
    x,
    layout = "BMJ",

    xlab = "outcome name",
# MD or SMD, based on the outcome
    smlab = "MD",
    lab.e = "Active tDCS",
    lab.c = "Sham tDCS",

    leftcols = c("studlab", "mean.e", "sd.e", "n.e",
"mean.c", "sd.c", "n.c"),
    leftlabs = c("Study", "Mean", "SD", "N", "Mean",
"SD", "N"),

    digits.mean = 2,
    digits = 2,

    overall = TRUE,
    test.overall = TRUE,
    prediction = FALSE,

    overall.hetstat = TRUE,
    print.I2 = TRUE,
    print.I2.ci = FALSE,
    print.Q = TRUE,
    print.pval.Q = TRUE,
    print.tau2 = TRUE,

    plotwidth = grid::unit(80, "mm"),
```

```
    colgap.left = grid::unit(1.5, "mm"),
    colgap.right = grid::unit(1.5, "mm"),
    colgap.studlab = grid::unit(2.5, "mm"),
    colgap. forest.left = grid::unit(6, "mm"),
    colgap.forest.right = grid::unit(3, "mm"),

    calcwidth.hetstat = FALSE,
    calcwidth.tests   = FALSE,

    fontsize = 9,
    spacing  = 0.95,

    col.square = "#1F4E79",
    col.square.lines = "#1F4E79",
    col.inside = "white",
    col.diamond.random = "#111111",
    col.diamond.lines.random = "#111111",

    lwd = 1.2,
    lwd.square = 1.1,
    lwd.diamond = 1.2,

    ff.heading = "bold",
    ff.study = "plain",
    ff.study.label = "bold",
    ff.smlab = "bold",
    ff.xlab = "plain",
    ff.hetstat = "plain",
    ff.test.overall = "bold",

    fs.study = 8.5,
    fs.study.label = 9,
    fs.test.overall = 8.5,

    xlim = ax$xlim,
    at   = ax$at,
    ref  = 0
  )

  if (!is.null(file)) dev.off()
}

# --------------------------
# Leave-one-out analysis
# --------------------------
loo_res <- metainf(meta_res, pooled = "random")
```

```
print(loo_res)

loo_forest <- function(x, file = NULL, device =
c("png","pdf"),
                       width = 9, height = 6, res = 300) {

  device <- match.arg(device)

  if (!is.null(file)) {
    if (device == "pdf") {
      pdf(file, width = width, height = height, onefile
= TRUE)
    } else {
      png(file, width = width, height = height, units =
"in", res = res, type = "cairo")
    }
  }

  ax <- make_xaxis_from_ci(x, ref = 0, pad_frac =
0.10)

  forest(
    x,
    layout = "BMJ",
    smlab = "Leave-One-Out Meta-Analysis",
    type = "square",

    fontsize = 9,
    spacing = 0.95,
    addrows.below.overall = 1,

    plotwidth = grid::unit(80, "mm"),
    colgap.forest.left = grid::unit(6, "mm"),
    colgap.forest.right = grid::unit(3, "mm"),
    calcwidth.hetstat = FALSE,
    calcwidth.tests   = FALSE,

    xlim = ax$xlim,
    at   = ax$at,
    ref  = 0
  )

  if (!is.null(file)) dev.off()
}

# --------------------------
```

```
# Save plots
# ----------------------------
nice_forest(meta_res, file = "forest_plot.pdf",
device = "pdf", width = 12, height = 7)
nice_forest(meta_res, file = "forest_plot.png",
device = "png", width = 12, height = 7, res = 300)

loo_forest(loo_res, file =
"leave_one_out_forest.pdf", device = "pdf", width
= 9, height = 6)
loo_forest(loo_res, file =
"leave_one_out_forest.png", device = "png",
width = 9, height = 6, res = 300)

# ----------------------------
# Save numeric outputs
# ----------------------------
write.csv(meta_res$TE, "effect_sizes.csv",
row.names = FALSE)
write.csv(data.frame(p_overall =
summary(meta_res)$pval), "p_values.csv",
row.names = FALSE)

getwd()
```

Table 4. Measured outcomes in the included trials

Study	Outcomes	Analyzed outcomes	Reasons for the exclusion of other outcomes
Pilloni 2025	Change in withdrawal symptoms, depressed mood, craving, restlessness, MS symptoms severity, and cognitive functions using the SDMT score	cognitive functions using the SDMT score	Only reported in one trial
Charvet 2018	Fatigue using the PROMIS scale	Fatigue using the PROMIS scale	Only reported in one trial
Pilloni 2024	9-HPT for manual dexterity, DMMPUT for manual dexterity, TPDS for sensory function, MGPST for strength, T25FWT for mobility, TUG for mobility, SDMT for cognition, PANAS for affect, MS-QOL for quality of life.	TUG for mobility, SDMT for cognition, and MS-QOL for quality of life.	Only reported in one trial
Charvet 2025	PROMIS Fatigue for fatigue, MFIS for fatigue impact, BICAMS (SDMT, RAVLT, BVMT-R) for cognition	PROMIS Fatigue for fatigue, and SDMT for cognition	Only reported in one trial
Pagliari 2025	Mini-BESTest for balance, Box and Block Test for manual dexterity, TUG for mobility, MoCA for cognition, SDMT for processing speed, STAI for anxiety, BDI for depression, MSQOL-54 for quality of life, RESE for emotional self-efficacy	TUG for mobility, SDMT for cognition, and MS-QOL for quality of life.	Only reported in one trial