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Habitual physical activity and motor cortical neurophysiology: A systematic review with meta-analyses of transcranial magnetic stimulation measures

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Abstract

Acute exercise transiently modulates motor cortical function, but whether habitual physical activity is associated with longer-term changes remains unclear. We conducted a systematic review with meta-analyses of observational studies, searching MEDLINE, Web of Science, PsycINFO, SPORTDiscus, and CINAHL from inception to February 2026. The review was reported according to PRISMA guidelines. We included studies assessing associations between habitual physical activity and resting TMS-derived measures of corticospinal excitability (CSE), inhibitory processes, and facilitatory processes in healthy adults. Pearson correlations were pooled using multilevel random-effects meta-analyses. Twenty-one studies (769 participants) met the inclusion criteria. We recovered previously unreported association estimates using statistical information from the articles, open datasets, and data requests to authors. Results showed no evidence of a robust association between habitual physical activity and CSE, short-interval intracortical inhibition (SICI), intracortical facilitation (ICF), and short-interval intracortical facilitation (SICF). Equivalence testing supported the conclusion that the associations between habitual physical activity and both CSE and inhibitory processes were practically negligible. Facilitation findings were inconclusive, and other TMS-derived measures were examined in only one or two studies. Subgroup analyses showed no statistical difference between self-reported and device-based physical activity measures. Meta-regressions showed no evidence of a moderation by sex, age, or study quality. PROSPERO registration: CRD420251016029.

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Introduction

The primary motor cortex (M1) plays a key role in the control of voluntary movement by integrating inputs from multiple cortical and subcortical regions and contributing to motor output through descending corticospinal signals that drive skeletal muscle activity (Strick et al., 2021). In the short term, corticospinal excitability (CSE) is dynamically modulated during action preparation and selection, reflecting the influence of distributed neural circuits involved in action control (Derosiere & Duque, 2020). Beyond these short-term modulations, M1 circuits exhibit plasticity and can be modified through experience and motor practice (Pascual-Leone et al., 2005).

Physical activity, which includes exercise, sport, active transport, household chores, and occupational activities (Bull et al., 2020), may influence M1 plasticity. Evidence from systematic reviews and meta-analyses indicates that acute exercise can modulate several neurophysiological measures of motor system function, including CSE as well as intracortical inhibitory and facilitatory circuits (Mellow et al., 2020; Youssef et al., 2024). These acute effects, typically observed within minutes following exercise, may be mediated by transient neurochemical changes, including increases in circulating catecholamines and neurotrophic factors (Rasmussen et al., 2009; Skriver et al., 2014). Whether repeated exposure to physical activity is associated with longer-term adaptations in resting M1 neurophysiology remains unclear.

Although the association between habitual physical activity, reflecting typical levels of physical activity accumulated across daily life (Bull et al., 2020), and resting M1 neurophysiology has not been systematically reviewed, several lines of evidence provide a rationale for investigating this relationship. Repeated exposure to physical activity may induce longer-lasting adaptations in neural systems involved in motor control and plasticity, potentially resulting in differences in resting neurophysiological measures (El-Sayes et al., 2019a). For example, habitual physical activity has been associated with alterations in neural systems supporting plasticity, including increases in circulating neurotrophic factors such as brain-derived neurotrophic factor (BDNF) (Rasmussen et al., 2009). Moreover, neurophysiological responses to acute exercise appear to vary according to habitual physical activity levels (Cirillo et al., 2009; Lulic et al., 2017), raising the possibility that habitual physical activity may be associated not only with responsiveness to acute exercise but also with the baseline state of the motor system. However, whether habitual physical activity is associated with resting TMS-derived measures remains unclear.

In humans, M1 neurophysiology can be probed non-invasively using transcranial magnetic stimulation (TMS). Single-pulse TMS allows assessment of CSE through motor-evoked potentials (MEPs), whereas paired-pulse TMS protocols probe inhibitory and facilitatory cortical circuits, including short-interval intracortical inhibition (SICI), long-interval intracortical inhibition (LICI), intracortical facilitation (ICF), and short-interval intracortical facilitation (SICF) (Kujirai et al., 1993; Ziemann et al., 1996). Inhibitory processes can also be assessed using the contralateral silent period (cSP) and ipsilateral silent period (iSP), which predominantly reflect cortical inhibition and interhemispheric inhibition, respectively, although the cSP also includes contributions from spinal mechanisms (Hupfeld et al., 2020). Despite growing interest in the neurobiological effects of physical activity, the relationship between habitual physical activity and these TMS-derived measures has not been systematically reviewed. Therefore, the aim of this study was to conduct a systematic review with meta-analysis examining the association between habitual physical activity and TMS-derived measures of motor neurophysiology. This focus on habitual physical activity distinguishes the present review from studies examining the acute effects of a single exercise bout on TMS-derived measures (Mellow et al., 2020; Youssef et al., 2024).

Methods

Search Strategy

This systematic review was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). Potentially eligible studies were identified through systematic searches of MEDLINE (via PubMed), PsycINFO, Web of Science, SPORTDiscus, and CINAHL. The search strategy combined terms related to physical activity (e.g., physical activity, physical education, training, physical fitness, exercise, cycling, treadmill, single bout) and TMS (e.g., TMS, transcranial magnetic stimulation, motor-evoked potential, stimulus-response curve, input-output curve, intracortical inhibition, intracortical facilitation, silent period) (see Suppl. Material 1 for the full search strategy). The search included all articles published in English available from inception up to March 2025, with no limitation on the start date. In addition, the reference lists of included articles were manually screened to identify potentially relevant studies not captured in the database searches. An updated search was conducted covering the period from April 2025 to February 2026. To enhance transparency, the systematic review was preregistered in the International Prospective Register of Systematic Reviews (PROSPERO) (Farajzadeh et al., 2025). The study was approved by the Office of Research Ethics and Integrity at the University of Ottawa (H-03-26-12745).

Eligibility Criteria

Studies were included if they were written in English, reported original data collected from healthy adults (≥ 18 years), included at least one TMS-derived neurophysiological measure of motor system function and at least one measure of habitual physical activity, and formally quantified the association between these variables by reporting a Pearson's r coefficient or sufficient information to calculate it, irrespective of whether habitual physical activity was a primary exposure of interest. Measures of physical activity could be self-reported (e.g., questionnaire) or device-based (e.g., accelerometry). Eligible study designs included cross-sectional studies, cohort studies, and baseline data from clinical trials.

Studies were excluded if they were published as a review article, book chapter, study protocol, or conference abstract, or assessed laboratory-based measures of physical fitness (e.g., maximal muscle force). Studies assessing only acute changes in TMS-derived measures following an exercise bout, without reporting a measure of habitual physical activity, were excluded.

Study Selection

One author (AF) conducted the initial database search. After removing duplicates, the titles and abstracts of all identified records were screened according to the inclusion and exclusion criteria. Studies that did not meet the eligibility criteria were excluded. In the second stage, two authors (AF, KP) independently screened the full text of the remaining articles. Both reviewers had to agree on the inclusion or exclusion of each study. Any disagreements were resolved through discussion and consensus, with a third reviewer (MPB) consulted when necessary. Reference list screening and forward citation tracking were conducted for all studies retained after the full-text screening stage (Figure 1).

Data Extraction

Data extraction was performed independently by two reviewers (AF, KP). Any discrepancies were resolved through discussion and consensus, with a third reviewer (MPB) consulted when necessary. When insufficient data were reported, the corresponding author was contacted to request additional information.

Data were extracted from the included studies using a standardized extraction form. The extracted information included the first author's name, article title, publication year, study design, sample size, age range, mean age, sex distribution, handedness, type of physical activity measure, duration of physical activity assessment, outcome measures, TMS measures, and results describing the association between physical activity and neurophysiological measures. Five TMS-derived outcome measures were prespecified in the PROSPERO preregistration (CSE, SICI, LICI, ICF, and SICF). During study selection and data extraction, cSP and iSP were added as relevant inhibitory outcomes that fell within the conceptual scope of the review. All habitual physical activity variables and relevant TMS-related information reported by eligible studies were extracted. When studies met all inclusion criteria but did not report the association of interest, the corresponding author was contacted by email to request the relevant information.

Quality Assessment

The methodological quality of each included study was assessed using the Downs and Black checklist (Downs & Black, 1998). This checklist can be applied to both randomized and non-randomized studies and consists of 27 items assessing reporting quality, external validity, internal validity, and statistical power. Total scores range from 0 to 28, with higher scores indicating better methodological quality. Two reviewers (AF, KP) independently assessed study quality, and discrepancies were resolved through discussion and consensus with a third reviewer (MPB).

Statistical Analyses

The meta-analytic approach followed the framework used in our previous systematic reviews and meta-analyses (Goubran et al., 2025; Farajzadeh et al., 2026a; Jabouille et al., 2026), with the specific outcomes and associations determined by the data available from eligible studies. All analyses were conducted with R software (R Core Team, 2024) in RStudio statistical environment using metafor (Viechtbauer, 2023) and meta packages (Schwarzer, 2023). When correlations were not reported, they were computed from available statistics (e.g., t-values, exact p-values, and sample sizes) using custom R scripts (Suppl. Material 2) based on standard relationships between test statistics and correlation coefficients. Because higher values of SICI and LICI indicate weaker inhibition, their correlation coefficients were multiplied by −1 in the meta-analysis so that higher values consistently represented stronger cortical inhibition across all inhibitory measures.

Primary Meta-Analyses

Pearson product–moment correlations from eligible studies were pooled to examine the relationship between habitual physical activity and TMS measures of CSE, inhibitory processes, and facilitatory processes. Prior to analysis, r correlations were Fisher's z-transformed to stabilize variance, and the corresponding sampling variances were calculated.

Meta-analyses were conducted using multilevel random-effects models implemented with the metafor package (Viechtbauer, 2023). This approach accounts for statistical dependence among multiple correlation estimates reported within the same study. A multilevel approach was used because several studies contributed more than one correlation estimate (e.g., different TMS outcomes or measurement conditions), which introduces statistical dependence among effect sizes. Multilevel meta-analysis appropriately accounts for this dependency without requiring aggregation of effect sizes within studies. Specifically, correlation estimates were nested within studies, resulting in a three-level model (level 1: sampling variance, level 2: correlation estimates within studies, level 3: studies). This approach accounts for clustering of estimates within studies through study-level and effect-size-level random effects. However, the sampling covariance between estimates derived from the same participants was not explicitly modeled. Between-study heterogeneity was estimated using the restricted maximum likelihood estimator (Viechtbauer, 2005). Heterogeneity was quantified using the

I^2 statistic, which represents the proportion of total variability in observed effect sizes that is not attributable to sampling error (Higgins and Thompson, 2002). Because a multilevel meta-analytic model was used, I^2 values were decomposed across variance components to estimate the proportion of variability attributable to differences between studies and between effect sizes within studies.

To reduce the risk of inflated type I error rates, confidence intervals for pooled estimates were calculated using a Knapp–Hartung adjustment (Knapp and Hartung, 2003). In addition to pooled correlations and their confidence intervals, prediction intervals were calculated to estimate the range within which the true effect size of a future study is expected to fall based on the current evidence. Unlike confidence intervals, which describe the precision of the pooled estimate, prediction intervals incorporate between-study heterogeneity to reflect the expected variability of effects across future studies.

For visualization purposes, forest plots were produced using the meta package (Schwarzer, 2023) with a RevMan layout. These plots were based on random-effects models equivalent to the multilevel analyses.

Subgroup Meta-Analyses

Subgroup analyses were conducted to examine whether pooled correlations differed across types of inhibitory (SICI, LICI, cSP, and iSP) and facilitatory measures (ICF and SICF), as well as by physical activity assessment method (self-reported vs. device-based). The inhibitory measures (SICI, LICI, cSP, and iSP) probe partially distinct neurophysiological processes and should not be interpreted as interchangeable measures of a single inhibitory mechanism. Thus, the overall pooled estimate for inhibitory measures represents a statistical summary across these measures, whereas the subgroup estimates provide measure-specific associations. Similarly, ICF and SICF reflect distinct forms of intracortical facilitation.

Meta-Regressions

Meta-regression analyses were conducted to examine whether study-level characteristics, including mean age and proportion of women, were associated with the reported correlations.

Sensitivity Analysis

A sensitivity analysis was conducted to examine whether the quality of the studies affected the results.

Publication Bias

Potential publication bias and small-study effects were assessed using contour-enhanced funnel plots and Egger's regression tests. Funnel plots display the Fisher's z-transformed correlations against their standard errors to allow visual inspection of asymmetry around the pooled effect size. Egger's regression test was used as a statistical complement to the visual inspection of funnel plots. Because no direct implementation exists for multilevel meta-analytic models, the test was conducted using a meta-regression approach in which the standard error of the effect size estimate was included as a predictor in the multilevel model (Egger et al., 1997).

Equivalence Testing

When the results of the meta-analysis were not statistically significant, equivalence testing was conducted using the two one-sided tests procedure implemented in the TOSTER package (Lakens & Caldwell, 2025) to determine whether pooled correlations were statistically equivalent to zero within prespecified equivalence bounds. Because no theoretically justified smallest effect size of interest could be identified, equivalence tests were conducted using bounds corresponding to a small correlation ($r = \pm 0.10$) (Lakens, 2017). These bounds were converted to Fisher's z to match the metric used in the meta-analysis. The pooled correlation was considered statistically equivalent to zero and

practically negligible when the 90% confidence interval of the pooled effect fell entirely within the equivalence bounds.

Results

Literature Search

The primary search identified 4,511 potentially relevant articles across five databases (Figure 1), including 1,583 duplicates. After duplicate removal, 2,928 articles were screened, of which 2,736 were excluded as unrelated to physical activity or TMS. The remaining 192 articles underwent full-text eligibility assessment, of which 51 studies assessed both physical activity and TMS measures and were therefore considered potentially eligible.

Although none of these 51 studies directly reported correlation coefficients for the association between physical activity and TMS measures, several provided sufficient statistical information in the article or open datasets, and additional data were obtained upon request to allow computation of the correlation coefficients. We were able to estimate the correlation coefficient in five studies based on open data (Lulic et al., 2017) or reported statistics (Cirillo et al., 2009; McGregor et al., 2011; McGregor et al., 2013; Hand et al., 2022a). We contacted the corresponding authors of the remaining 46 studies to request either the correlation estimate or the raw data required to compute it. At least one reminder email was sent when no response was received. Twenty-five authors responded: two provided correlation coefficients (Houde et al., 2018; Smith et al., 2021), thirteen provided raw data (Hassanlouei et al., 2017; El-Sayes et al., 2019b; Rozand et al., 2019; Hu et al., 2021; Neva et al., 2021; Hand et al., 2022b; Curtin et al., 2023; Wang et al., 2023; Ross et al., 2024; Digonet et al., 2025; Harroum et al., 2025; Hougland et al., 2025; Gamage et al., 2026), three reported no longer having access to the data, six indicated they would follow up, but the requested information was not subsequently received, and one study was excluded because it relied on the same dataset as another included study (Curtin et al., 2023). Ultimately the primary search resulted in 20 included studies.

Reference list screening and forward citation tracking identified seven additional potentially relevant studies, including a dataset from our laboratory (Farajzadeh, 2026). Four were excluded during screening because they did not include both physical activity and TMS measures. Of the three remaining studies assessed for eligibility, two did not test the association of interest and were excluded; the corresponding authors of these studies did not respond to our emails. One additional study was therefore included.

Ultimately, 20 studies from the primary search and one additional study identified through other methods were included, for a total of 21 included studies. These 21 studies represented 39% of the 54 studies assessing both physical activity and TMS measures. The methodological quality scores of the included studies ranged from 11 to 18 out of 28 (mean ± standard deviation of 14.0 ± 1.9) (Table 1).

Descriptive Results

Participants

The 21 studies included in the systematic review comprised 769 participants aged 19-78 years, all of whom were healthy adults. Thirteen studies included only young adults (Cirillo et al., 2009; Lulic et al., 2017; El-Sayes et al., 2019b; Hu et al., 2021; Neva et al., 2021; Hand et al., 2022a; Hand et al., 2022b; Wang et al., 2023; Ross et al., 2024; Digonet et al., 2025; Harroum et al., 2025; Hougland et al., 2025; Farajzadeh, 2026), three included only older adults (Houde et al., 2018; Smith et al., 2021; Gamage et al., 2026), four included both young and older adults (McGregor et al., 2011; Hassanlouei et al., 2017; Rozand et al., 2019; Curtin et al., 2023), and one study included young and middle-aged adults (McGregor et al., 2013).

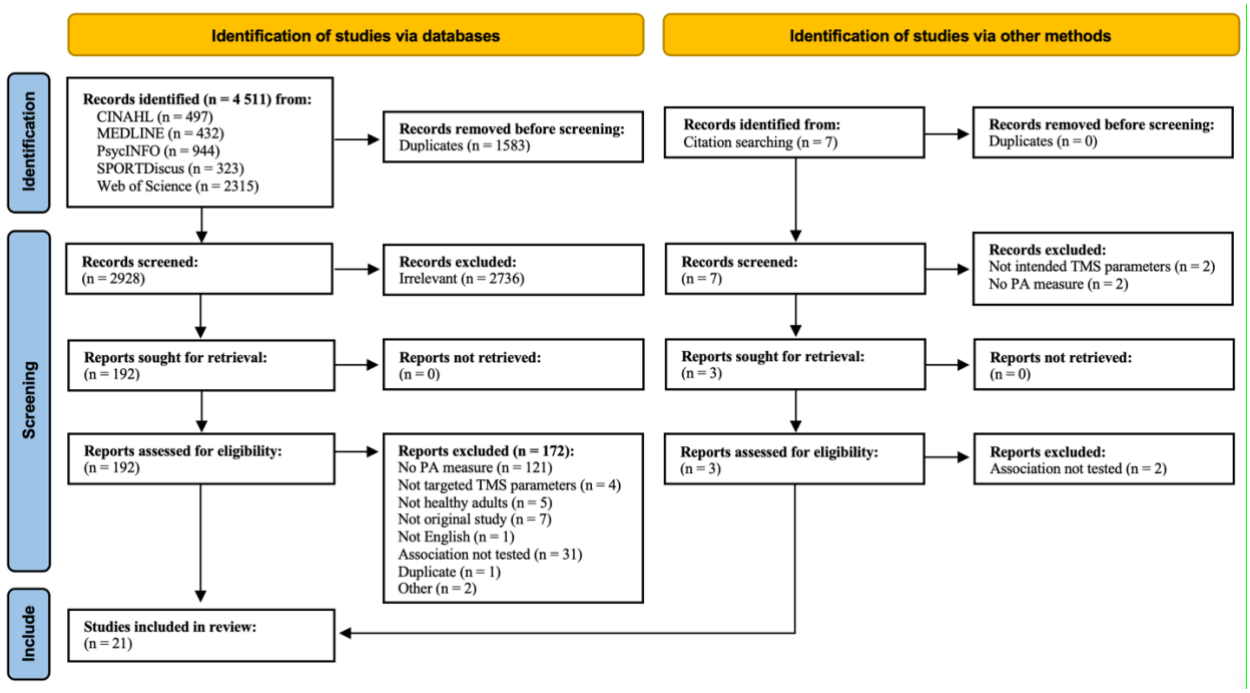


Figure 1 – PRISMA flow diagram of study selection.

Physical Activity

Four studies assessed physical activity using triaxial accelerometers (Hassanlouei et al., 2017; Rozand et al., 2019; Smith et al., 2021; Farajzadeh, 2026), which were worn at the waist (ActiGraph GT3X) (Hassanlouei et al., 2017; Rozand et al., 2019; Farajzadeh, 2026) or the wrist (ActivInsights GENEActiv) (Smith et al., 2021) (Table 1). Seventeen studies assessed physical activity using self-reported measures. Thirteen of these used the International Physical Activity Questionnaire (Cirillo et al., 2009; Lulic et al., 2017; El-Sayes et al., 2019b; Hu et al., 2021; Neva et al., 2021; Hand et al., 2022a; Hand et al., 2022b; Curtin et al., 2023; Ross et al., 2024; Digonet et al., 2025; Harroum et al., 2025; Hougland et al., 2025; Gamage et al., 2026). Other self-report instruments were the Leisure Time Exercise Questionnaire (McGregor et al., 2011), the Physical Activity Questionnaire (Wang et al., 2023), and ad hoc questionnaires (McGregor et al., 2013; Houde et al., 2018).

Regarding the assessment period, accelerometer-based physical activity was assessed over 7 days in one study (Smith et al., 2021), 5 days in one study (Farajzadeh, 2026), and 4 days in two studies (Hassanlouei et al., 2017; Rozand et al., 2019). Self-reported physical activity generally referred to the previous 7 days (Cirillo et al., 2009; McGregor et al., 2011; McGregor et al., 2013; Lulic et al., 2017; El-Sayes et al., 2019b; Hu et al., 2021; Neva et al., 2021; Hand et al., 2022a; Hand et al., 2022b; Curtin et al., 2023; Ross et al., 2024; Digonet et al., 2025; Harroum et al., 2025; Hougland et al., 2025; Gamage et al., 2026), with one study assessing activity over the previous 5 years (Wang et al., 2023) and one not reporting the assessment period (Houde et al., 2018).

Physical activity outcomes included MET-min/week (Cirillo et al., 2009; Lulic et al., 2017; El-Sayes et al., 2019b; Hu et al., 2021; Neva et al., 2021; Hand et al., 2022a; Hand et al., 2022b; Curtin et al., 2023; Ross et al., 2024; Digonet et al., 2025; Harroum et al., 2025; Hougland et al., 2025; Gamage et al., 2026), steps per day (Hassanlouei et al., 2017; Rozand et al., 2019; Farajzadeh, 2026), active time per week (McGregor et al., 2013; Houde et al., 2018; Smith et al., 2021; Wang et al., 2023), and questionnaire scores (McGregor et al., 2011).

Table 1 – Characteristics of included studies and correlations between physical activity and neurophysiological measures

Study	N	Female (%)	Age (mean years)	Age (SD years)	Muscle	PA tool	PA measure	PA Outcome (mean)	PA Outcome (SD)	TMS measure	ISI (ms)	Right-handed (%)	r	SE_z	p	Quality Score
Cirillo (2009)	28	46	24.4	n.a.	FDI	IPAQ	MET-min/wk	Active: 5572	2075	CSE		100	0.26	.20	0.16	12
								Inactive: 491	308	SICI	2		0.08	.20	0.65	
										cSP			0.16	.20	0.38	
McGregor (2011)	24	53	69	n.a.	FDI	GLTEQ	score	Active:124.5	83	iSP		100	0.44	.22	0.03	14
								Inactive:52.4	47							
	12	45	24.3	n.a.				67.58	33.6	iSP			n.a.			
McGregor (2013)	38	57	52.1	n.a.	FDI	Ad-hoc questionnaire	min/week	76.0	33.4	iSP		100	0.48	.2	0.002	16
	21	55	22.1	n.a.				64.7	32.5	iSP			n.a.			
Hassanlouei (2017)	24	50	22.4	2.2	VL	Waist Accelerometer	steps/day	Active: 12326	815	CSE		n.a.	-0.18	.22	0.39	13
								Inactive: 7133	494							
	38	45	70.2	6.1				Active: 13565	1174	CSE			0.02	.17	0.9	
								Inactive: 6381	402							
Lulic (2017)	28	60	21	1.5	FDI	IPAQ	MET-min/wk	High: 7631	6120	CSE		100	0.12	.20	0.54	13
								Low:1305	773	SICI	2		-0.14	.20	0.51	
										SICF	1.2		0.37	.20	0.06	
										SICF	2.5		-0.15	.20	0.48	
										ICF	10		0.009	.20	0.96	
Houde (2018)	26	50	70	n.a.	FDI	Ad-hoc questionnaire	session/wk	≥1: Active		CSE		100	0.225	.21	>0.05	13
								<1: Inactive		cSP			0.124	.21	>0.05	
El-Sayes (2019b)	34	50	21	2	FDI	IPAQ	MET-min/wk	3577	1893	CSE		100	-0.24	.18	0.17	13
										SICI	2		0.08	.18	0.65	
Rozand (2019)	27	48	72	n.a.	FDI	Waist Accelerometer	steps/day	Active: ≥10,000		CSE		100	-0.08	.20	0.69	12
	28	50	24	n.a.				Inactive: <10,000		CSE			0.28	.20	0.14	
Hu (2021)	29	100	19.3	0.6	APB	IPAQ	MET-min/wk	Exercise: 1655	1136	CSE		100	-0.12	.20	0.53	15
								Control: 1111	930	SICI	2.5		0.27	.20	0.15	
										ICF	12		0.11	.20	0.57	
Neva (2021)	23	52	27	5.7	APB	IPAQ	MET-min/wk	3655	2375	CSE		100	-0.16	.22	0.46	16
										CSE			-0.17	.22	0.43	
										CSE			-0.17	.22	0.43	
										CSE			-0.01	.22	0.96	
										CSE			0.11	.22	0.61	
										CSE			-0.04	.22	0.83	
										SICI	3		0.02	.22	0.91	
										SICI	2		0.20	.22	0.36	
Smith (2021)	34	44	66.9	n.a.	FDI	Wrist Accelerometer	h/wk	6.3±0.7		CSE		n.a.	0.185	.18	0.29	18
Hand (2022a)	33	24	32	n.a.	FDI	IPAQ	MET-min/wk	Active: 6488		SICI	2	n.a.	0.37	.18	0.2	11
								Inactive:1209		SICF	1.5		0.02	.18	0.2	
					TA					ICF	10		0.22	.18	0.9	
										SICI	2		0.09	.18	0.6	
										SICF	1.5		0.18	.18	0.6	
										ICF	10		0.09	.18	0.3	
Hand (2022b)	28	25	23	n.a.	FDI	IPAQ	MET-min/wk	Active: 5850		CSE		n.a.	-0.1	.20	0.61	14
								Inactive:1139		SICI	2		0.21	.20	0.28	
										SICF	1.5		-0.14	.20	0.47	
										ICF	10		0.30	.20	0.12	
Curtin (2023)	20	70	25.3	n.a.	FDI	IPAQ	MET-min/wk	5024	4831	ICF		100	-0.18	.24		16
	18	55	64.1	n.a.	FDI			5683	3780	ICF		95	-0.39	.26		
Wang (2023)	40	35	25	n.a.	FDI	PAQ	h/wk	High: 11.6	6.2	CSE		100	0.16	.16	0.32	12
								Low: 0.4	0.6	SICI	2		0.13	.16	0.42	
										ICF	10		0.13	.16	0.42	
Ross (2024)	16	88	27.2	n.a.	APB	IPAQ	MET-min/wk	6663	5611	CSE		81	-0.02	.28	0.94	16
Digonet (2025)	45	51	23.1	3.3	FDI			3274	1865	CSE		100	-0.002	.15	0.9	16
										SICI	3		-0.11	.15	0.4	
Harroum (2025)	30	50	27	6	FDI			4647	5245	CSE		100	-0.27	.19	0.13	16
										CSE			0.03	.19	0.8	
										CSE			-0.27	.19	0.13	
										CSE			0.05	.19	0.93	
										SICI	2		0.11	.19	0.54	
										SICI	2		-0.09	.19	0.6	
Hougland (2025)	15	65	27	n.a.	FDI	IPAQ	MET-min/wk	5237	4028	CSE		100	0.4	.29	0.13	12
	16	65	27	n.a.	VL					CSE			-0.6	.28	0.01	
Farajzadeh (2026)	55	64	32.3	n.a.	FDI	Waist Accelerometer	steps/day	7029		CSE		100	-0.15	.14	0.29	13
										SICI	2		0.05	.14	0.71	
										LICI			-0.05	.14	0.29	
										ICF	12		-0.047	.14	0.76	
Gamage (2026)	54	38	69	5.2	APB	IPAQ	MET-min/wk	3715	2774	SICI	2	100	0.14	.14	0.2	13

Notes. APB = abductor pollicis brevis; CSE = corticospinal excitability; cSP = contralateral silent period; FDI = first dorsal interosseous; ICF = intracortical facilitation; IPAQ = International Physical Activity Questionnaire; iSP = ipsilateral silent period; ISI: interstimulus interval; LICI = long-interval intracortical inhibition; LTEQ = Leisure Time Exercise Questionnaire; Muscle = muscle from which TMS-evoked responses were recorded; N = sample size; n.a. = not available; PA = Physical Activity; PAQ = Physical Activity Questionnaire; r = Pearson's correlation coefficient; SE_z = standard error of the Fisher's z-transformed correlation coefficient calculated as $(N-3)^{-1/2}$; SICF = short-interval intracortical facilitation; SICI = short-interval intracortical inhibition; TA = tibialis anterior; VL = vastus lateralis; % female = percentage of participants who were female; the remaining participants were male.

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Neurophysiological Measures

Eighteen studies assessed TMS measures in upper-extremity muscles (Cirillo et al., 2009; McGregor et al., 2011; McGregor et al., 2013; Lulic et al., 2017; Houde et al., 2018; El-Sayes et al., 2019b; Rozand et al., 2019; Hu et al., 2021; Neva et al., 2021; Smith et al., 2021; Hand et al., 2022b; Curtin et al., 2023; Wang et al., 2023; Ross et al., 2024; Digonet et al., 2025; Harroum et al., 2025; Farajzadeh, 2026; Gamage et al., 2026) (Table 1). Two studies examined both upper- and lower-extremity muscles (Hand et al., 2022a; Hougland et al., 2025), and one examined only lower-extremity muscles (Hassanlouei et al., 2017). Handedness was not reported in four studies (Hassanlouei et al., 2017; Smith et al., 2021; Hand et al., 2022a; Hand et al., 2022b). Fifteen studies included exclusively right-handed participants (Cirillo et al., 2009; McGregor et al., 2011; McGregor et al., 2013; Lulic et al., 2017; Houde et al., 2018; El-Sayes et al., 2019b; Rozand et al., 2019; Hu et al., 2021; Neva et al., 2021; Wang et al., 2023; Digonet et al., 2025; Harroum et al., 2025; Hougland et al., 2025; Farajzadeh, 2026; Gamage et al., 2026). One study included 19 right-handed and one left-handed participants (Curtin et al., 2023), another study included 13 right-handed and three mixed-handed participants (Ross et al., 2024). Seven studies reported restrictions on physical activity before TMS testing. Restrictions ranged from avoiding exercise on the morning (Ross et al., 2024) or day (Cirillo et al., 2009; Hand et al., 2022a; Hand et al., 2022b) of testing to avoiding moderate to vigorous exercise for 12 h (Wang et al., 2023), 24 h (Curtin et al., 2023), or 48 h (Hougland et al., 2025) before testing. However, none of the studies reported the time elapsed since participants' last physical activity bout before TMS assessment.

CSE was assessed in sixteen studies and reported as raw MEP amplitude (Cirillo et al., 2009; Houde et al., 2018; Hu et al., 2021; Neva et al., 2021; Smith et al., 2021; Hand et al., 2022b; Ross et al., 2024; Harroum et al., 2025; Farajzadeh, 2026), input–output curve slope (Wang et al., 2023; Hougland et al., 2025), and area under the recruitment curve (Lulic et al., 2017). In other studies, M-wave-normalized CSE was reported as MEP amplitude (Digonet et al., 2025), area under the curve (El-Sayes et al., 2019b), or MEPmax (Hassanlouei et al., 2017; Rozand et al., 2019), all expressed relative to Mmax. SICI was assessed in twelve studies, using an interstimulus interval (ISI) of 2 ms (Cirillo et al., 2009; Lulic et al., 2017; El-Sayes et al., 2019b; Neva et al., 2021; Hand et al., 2022a; Hand et al., 2022b; Wang et al., 2023; Digonet et al., 2025; Harroum et al., 2025; Farajzadeh, 2026), 2.5 ms (Hu et al., 2021), or 3 ms (Neva et al., 2021; Digonet et al., 2025). LICI was assessed in one study using an ISI of 100 ms (Farajzadeh, 2026). cSP was assessed in two studies (Cirillo et al., 2009; Houde et al., 2018) and iSP in two studies (McGregor et al., 2011; McGregor et al., 2013). ICF was assessed in seven studies, with ISI of 10 ms in four studies (Lulic et al., 2017; Hand et al., 2022a; Hand et al., 2022b; Wang et al., 2023) and 12 ms in three studies (Hu et al., 2021; Curtin et al., 2023; Farajzadeh, 2026). SICF was assessed in three studies using ISIs of 1.2 ms (Lulic et al., 2017), 1.5 ms (Hand et al., 2022a; Hand et al., 2022b), and 2.5 ms (Lulic et al., 2017). Some studies assessed TMS measures using both antero-posterior and postero-anterior current directions (Neva et al., 2021; Harroum et al., 2025).

Association Between Physical Activity and Neurophysiological Measures

None of the studies provided an estimate of the association between physical activity and TMS-derived measures in the published article. Upon request, two authors provided correlation coefficients for CSE (Houde et al., 2018; Smith et al., 2021) and one for cSP (Houde et al., 2018). Thirteen authors provided raw data for CSE (Hassanlouei et al., 2017; Lulic et al., 2017; El-Sayes et al., 2019b; Rozand et al., 2019; Hu et al., 2021; Neva et al., 2021; Hand et al., 2022a; Hand et al., 2022b; Wang et al., 2023; Ross et al., 2024; Digonet et al., 2025; Harroum et al., 2025; Farajzadeh, 2026), ten for SICI (Lulic et al., 2017; El-Sayes et al., 2019b; Hu et al., 2021; Neva et al., 2021; Hand et al., 2022b; Wang et al., 2023; Digonet et al., 2025; Harroum et al., 2025; Farajzadeh, 2026; Gamage et al., 2026), one for LICI (Farajzadeh, 2026), six for ICF (Lulic et al., 2017; Hu et al., 2021; Hand et al., 2022b; Curtin

et al., 2023; Wang et al., 2023; Farajzadeh, 2026), and two for SICF (Lulic et al., 2017; Hand et al., 2022b). In four studies, correlation coefficients were computed from p values or t-statistics and sample sizes for SICI (Cirillo et al., 2009; Hand et al., 2022a), ICF (Hand et al., 2022a), SICF (Hand et al., 2022a), cSP (Cirillo et al., 2009), and iSP (McGregor et al., 2011; McGregor et al., 2013).

Overall, the meta-analysis included twenty-seven Pearson's r correlation coefficients for CSE derived from sixteen studies (Cirillo et al., 2009; Hassanlouei et al., 2017; Lulic et al., 2017; Houde et al., 2018; El-Sayes et al., 2019b; Rozand et al., 2019; Smith et al., 2021; Hu et al., 2021; Neva et al., 2021; Hand et al., 2022a; Hand et al., 2022b; Wang et al., 2023; Ross et al., 2024; Digonet et al., 2025; Harroum et al., 2025; Farajzadeh, 2026), fifteen for SICI from twelve studies (Cirillo et al., 2009; Lulic et al., 2017; El-Sayes et al., 2019b; Hu et al., 2021; Neva et al., 2021; Hand et al., 2022a; Hand et al., 2022b; Wang et al., 2023; Digonet et al., 2025; Harroum et al., 2025; Farajzadeh, 2026; Gamage et al., 2026), nine for ICF from seven studies (Lulic et al., 2017; Hu et al., 2021; Hand et al., 2022a; Hand et al., 2022b; Curtin et al., 2023; Wang et al., 2023; Farajzadeh, 2026), five for SICF from three studies (Lulic et al., 2017; Hand et al., 2022a; Hand et al., 2022b), two for iSP (McGregor et al., 2011; McGregor et al., 2013), two for cSP (Cirillo et al., 2009; Houde et al., 2018), and one for LICI (Farajzadeh, 2026) (Table 1). Of the 61 individual association estimates, 57 (93%) were not statistically significant. This included 26 of 27 (96%) CSE estimates, 14 of 15 (93%) SICI estimates, 9 of 9 (100%) ICF estimates, 5 of 5 (100%) SICF estimates, 2 of 2 (100%) cSP estimates, and 1 of 1 (100%) LICI estimate; both iSP estimates were statistically significant (0% were non-significant).

Meta-Analysis

Corticospinal Excitability

A total of 27 correlation estimates from 16 studies comprising 18 participant samples (766 participants) were included in the meta-analysis examining the association between physical activity and CSE. The multilevel random-effects meta-analysis showed no evidence of an association between physical activity and CSE ($r = -0.03$, 95% CI [−0.10, 0.05], $p = 0.50$) (Figure 2). The prediction interval ranged from −0.10 to 0.05, indicating that future studies are expected to observe correlations ranging from small negative to slightly positive values. Between-study heterogeneity was negligible (total $I^2 = 0.3\%$).

To further evaluate whether the association could be considered practically negligible, an equivalence test was conducted using equivalence bounds corresponding to a small effect size (±0.10). The equivalence test was significant ($Z = 1.95$, $p = 0.026$), and the 90% confidence interval (−0.089 to 0.037) fell within the predefined equivalence bounds, supporting a practically negligible association between physical activity and CSE (Figure 3).

Subgroup analyses comparing physical activity measures (self-reported vs. device-based) showed no significant difference between measure types ($Q = 0.21$, $p = 0.650$) (Suppl. Material 4). The pooled estimate was −0.04 (95% CI [−0.13, 0.05], $k = 21$) for self-reported measures and $r < 0.01$ (95% CI [−0.15, 0.15]; $k = 6$) for device-based measures.

Inhibitory Processes

A total of 20 correlation estimates from 15 studies (656 participants) were included in the meta-analysis examining the association between habitual physical activity and measures of inhibitory processes. The multilevel random-effects meta-analysis showed no evidence of an association between physical activity and inhibitory processes ($r = 0.0008$, 95% CI [−0.11, 0.12], $p = 0.99$) (Figure 4). The prediction interval ranged from −0.30 to 0.30, indicating that future studies are expected to observe correlations ranging from moderately negative to moderately positive values. Between-study heterogeneity was moderate (total $I^2 = 31.2\%$), with nearly all estimated heterogeneity attributable to differences between studies and essentially no heterogeneity among effect sizes within studies.

The equivalence test was significant (Z = 1.81, p = 0.035), and the 90% confidence interval (−0.091 to 0.089) fell within the predefined equivalence bounds, supporting a practically negligible association between physical activity and pooled inhibitory processes (Figure 3).

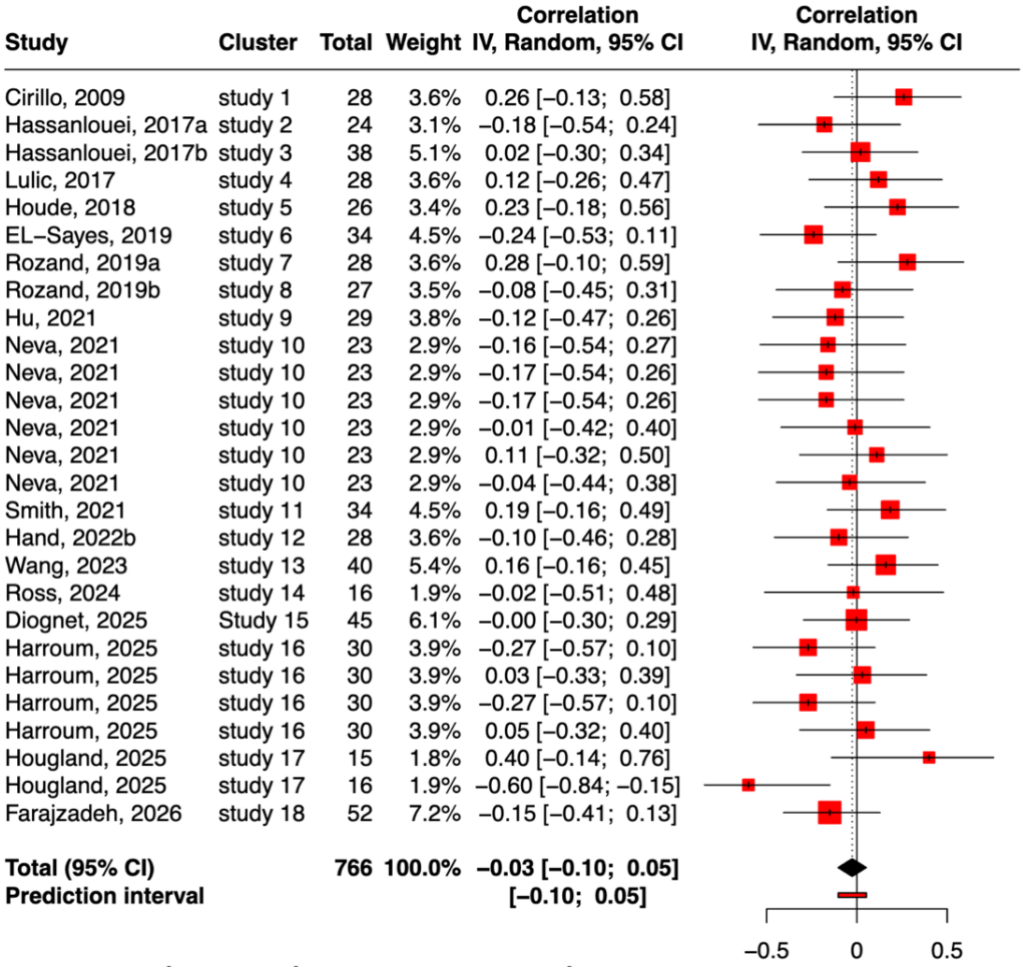


Figure 2 – Forest plot of the association between physical activity and corticospinal excitability. Notes: IV = inverse variance, CI = confidence interval.

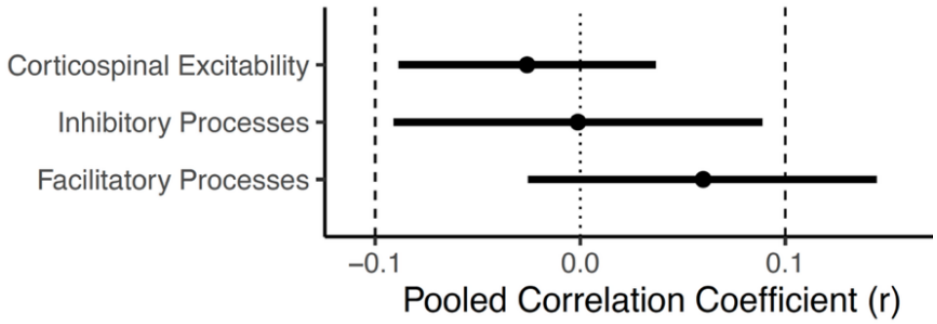


Figure 3 – Equivalence tests. Notes: Thick horizontal lines indicate 90% confidence intervals for equivalence tests. Dashed vertical lines indicate the equivalence bounds (−0.1 and 0.1), and the dotted vertical line indicates the null value (r = 0.0).

Subgroup analyses comparing inhibitory measures (SICI, LICI, cSP, and iSP) showed statistically significant differences (Q = 6.45, p = 0.005) (Figure 4). The association was significant for iSP (r = 0.47, 95% CI [0.22, 0.66]; k = 2), whereas no significant associations were observed for SICI (r = −0.09, 95% CI [−0.19, 0.004]; k = 15), LICI (r = 0.05, 95% CI [−0.28, 0.37]; k = 1), or cSP (r = 0.14, 95% CI [−0.16, 0.42]; k = 2).

Subgroup analyses comparing physical activity measures (self-reported vs. device-based) showed no significant difference between measure types (Q = 0.0009, p = 0.976) (Suppl. Material 4). The pooled estimate was r = 0.003 (95% CI [−0.13, 0.13]; k = 18) for self-reported measures and −0.003 (95% CI [−0.38, 0.38]; k = 2) for device-based measures.

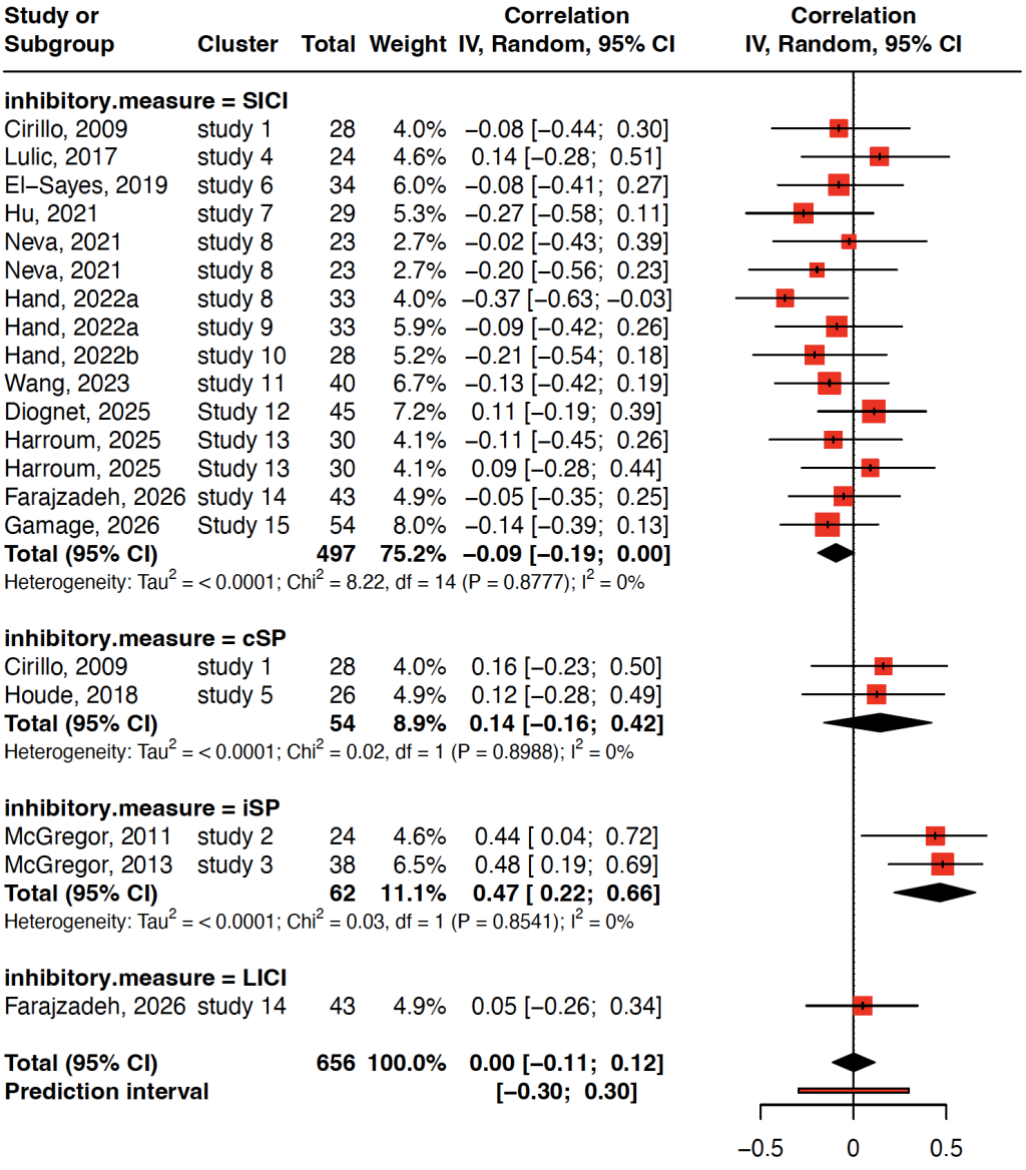


Figure 4 – Forest plot of the association between habitual physical activity and TMS measures of cortical inhibition. Notes: SICI and LICI estimates were multiplied by −1 so that higher values consistently indicate stronger cortical inhibition in this analysis. SICI = short-interval intracortical inhibition, LICI = long-interval intracortical inhibition, cSP = contralateral silent period, iSP = ipsilateral silent period, IV = inverse variance, CI = confidence interval.

Facilitatory Processes

A total of 14 correlation estimates from 7 studies comprising 8 participant samples (412 participants) were included in the meta-analysis examining the association between habitual physical activity and TMS measures of facilitatory processes. The multilevel random-effects meta-analysis indicated no statistically significant association between physical activity and facilitatory processes (r = 0.06, 95% CI [−0.05, 0.17], p = 0.27). The prediction interval ranged from −0.05 to 0.17, indicating that future studies would be expected to observe correlations ranging from slightly negative to small positive values. No meaningful heterogeneity was observed across studies (I^2 = 0.3%), with nearly all variability in the observed correlations attributable to sampling error.

The equivalence test was not significant (Z = −0.78, p = 0.219), and the 90% confidence interval (−0.026 to 0.146) extended beyond the predefined equivalence bounds (Figure 3). Thus, equivalence could not be concluded.

Subgroup analyses comparing facilitatory measures (ICF vs. SICF) showed no significant differences (Q = 0.004, p = 0.953) (Figure 5). Point estimates were similar for ICF (r = 0.06, 95% CI [−0.08, 0.20]; k = 9) and SICF (r = 0.06, 95% CI [−0.13, 0.25]; k = 5).

Subgroup analyses comparing physical activity measures (self-reported vs. device-based) showed no significant difference between measure types (Q = 0.51, p = 0.495) (Suppl. Material 4). The pooled estimate for self-reported measures was r = 0.07 (95% CI [−0.05, 0.19]; k = 13), whereas only one study used a device-based measure (r = −0.05, 95% CI [−0.37, 0.29]; k = 1).

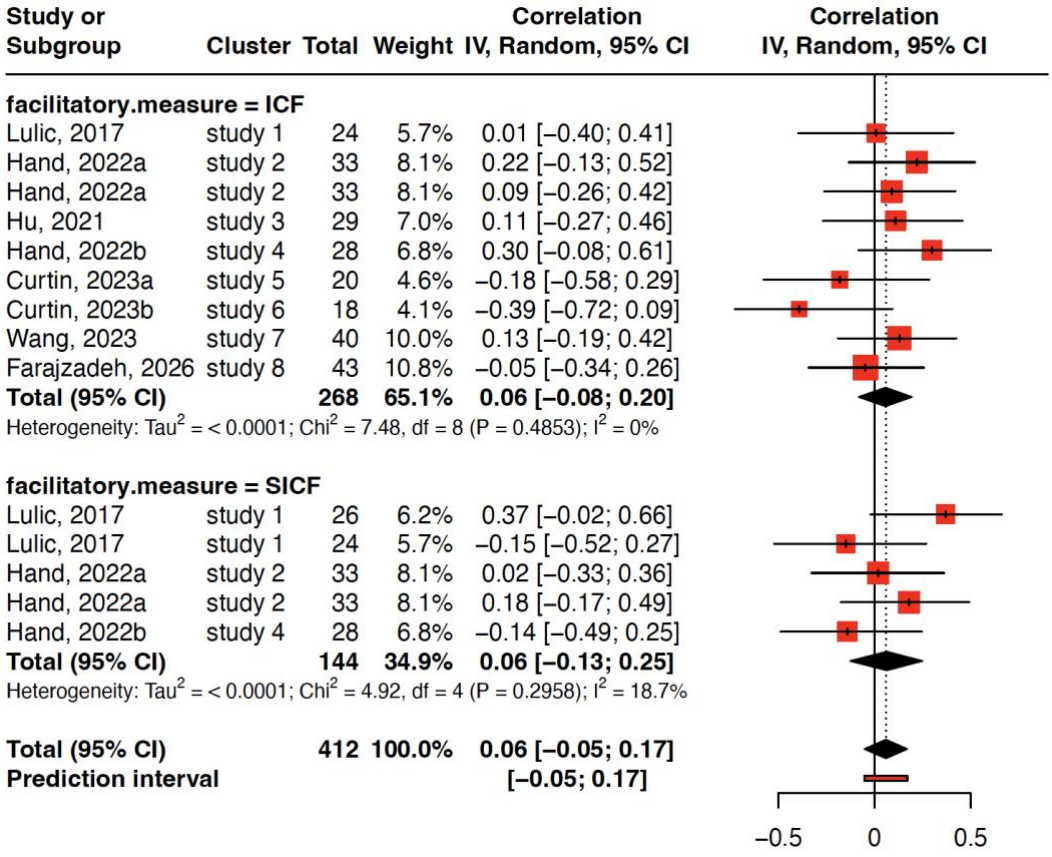


Figure 5 – Forest plot of the association between habitual physical activity and transcranial magnetic stimulation measures of intracortical facilitation. Notes: ICF = intracortical facilitation, SICF = short-interval intracortical facilitation, IV = inverse variance, CI = confidence interval.

Meta-Regressions and Sensitivity Analysis

Meta-regression analyses indicated that the association between habitual physical activity and TMS measures was not significantly moderated by the proportion of women, age, or study quality (all $p > 0.119$).

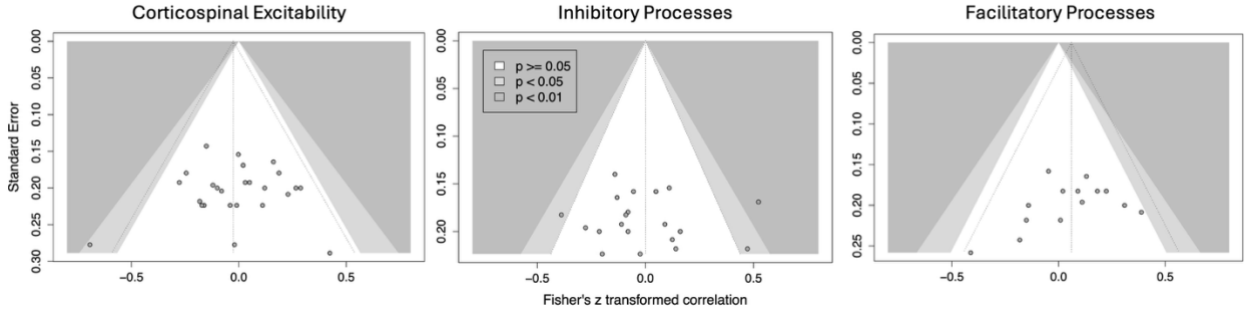


Figure 6 – Funnel Plots

Publication Bias

Potential publication bias and small-study effects were assessed using contour-enhanced funnel plots and Egger's regression tests. Visual inspection of the funnel plots for CSE, inhibitory processes, and facilitatory processes did not reveal substantial asymmetry around the pooled effect sizes (Figure 6).

Egger's regression tests conducted using the meta-regression approach were not statistically significant for any of the meta-analyses. The regression coefficient for the standard error was not significant for CSE ($p = 0.77$), cortical inhibition ($p = 0.74$), or cortical facilitation ($p = 0.18$). These results indicate that smaller studies did not systematically report larger effect sizes.

Discussion

An important strength of this study is that we were able to recover estimates of associations between habitual physical activity and TMS-derived neurophysiology, although none of the original articles reported these associations. By recovering these estimates from reported statistical information, open datasets, and data requests to authors, we performed secondary analyses of previously unanalyzed data and synthesized the resulting associations across studies, generating new empirical evidence on a question that had not previously been examined.

Main Findings

This systematic review with meta-analyses examined the association between habitual physical activity and TMS-derived neurophysiological measures. Overall, the results did not provide evidence of reliable associations across the measures examined. Of the 61 individual association estimates, 57 (93%) were not statistically significant. Specifically, results suggested that the associations between habitual physical activity and both CSE and inhibitory processes were practically negligible. The evidence for facilitatory processes was inconclusive, and the associations varied across the heterogeneous set of TMS-derived inhibitory measures.

For CSE, the pooled correlation was close to zero, with narrow confidence intervals and negligible heterogeneity. Equivalence testing further demonstrated that this effect was statistically equivalent to zero, providing evidence that habitual physical activity is unlikely to be meaningfully associated with CSE. For inhibitory measures, the pooled association was non-significant and practically negligible, with moderate heterogeneity and a wide prediction interval, indicating substantial uncertainty about

the association in future studies. Subgroup analyses revealed differences across inhibitory measures, with a positive association observed for iSP only. However, the iSP estimate was based on only two effect sizes and should therefore be considered hypothesis-generating rather than evidence of a specific association between habitual physical activity and interhemispheric inhibition. Similarly, the available evidence did not support a statistically significant association with facilitatory measures, although equivalence to zero could not be established and small associations cannot be ruled out.

Taken together, these results do not provide evidence of a robust association between habitual physical activity and resting TMS-derived neurophysiological measures. However, the available evidence is insufficient to exclude measure-specific associations, particularly for some inhibitory measures for which very few studies were available.

Acute Exercise Versus Habitual Physical Activity

A recent meta-analysis demonstrated that a single bout of acute aerobic exercise transiently modulates TMS-derived neurophysiological measures (Youssef et al., 2024). Specifically, acute aerobic exercise produced a small increase in intracortical inhibition, reflected by a decrease in SICI (Hedges' g = 0.27), with stronger effects observed at moderate and high exercise intensities, and the effect persisted for up to 30 minutes following exercise. In contrast, increases in CSE were observed only following high-intensity exercise and were generally small in magnitude, while effects on ICF and LICI were not statistically significant. In comparison, the present meta-analysis of habitual physical activity found no reliable association with CSE, SICI, ICF, and SICF.

Together, these results suggest that transient neurophysiological responses to individual bouts of acute exercise do not necessarily accumulate into differences in resting M1 neurophysiology associated with habitual physical activity.

Limitations

Several limitations should be considered when interpreting the results. First, most studies assessing physical activity relied on self-reported questionnaires, which may be subject to recall bias and measurement error compared with device-based approaches such as accelerometry. Second, habitual physical activity assessments varied in the instruments used (e.g., accelerometers and questionnaires), the activity domains assessed (e.g., leisure-time and everyday physical activity), and the reference periods (from the previous week to five years). However, the small number of studies precluded robust analyses of these differences. Third, variability in TMS methodologies across studies (e.g., differences in stimulation parameters, interstimulus intervals, pre-test exercise restrictions, and participant characteristics) may have contributed to heterogeneity in the reported neurophysiological measures. Fourth, for paired-pulse measures, restricted between-participant variability in the derived measures, if present, could attenuate correlations with habitual physical activity. Fifth, because association estimates could only be computed for 39% of the studies assessing both physical activity and TMS measures, these studies may differ systematically from those not included in the meta-analysis, potentially introducing selection bias and limiting the generalizability of the results. Finally, although the multilevel models accounted for clustering of multiple effect-size estimates within studies, the sampling covariance between estimates derived from the same participants was not explicitly modeled. This may have affected the precision of the pooled estimates and, consequently, the equivalence-testing results.

Conclusion

Overall, current evidence does not support a robust association between habitual physical activity and resting TMS-derived measures of CSE, intracortical inhibition (SICI), or intracortical facilitation (ICF and SICF). LICI, cSP, and iSP were examined in only one or two studies, limiting conclusions

about these measures. Although some associations could not be considered equivalent to zero, further research should be pursued only where there is a clear theoretical rationale and with sufficient methodological rigor, including objective assessment of habitual physical activity (e.g., accelerometry), detailed TMS protocols, preregistration, and open sharing of data and analysis scripts. Future studies could also determine whether associations emerge beyond resting TMS-derived measures, for example during motor tasks involving approach–avoidance behavior (Park & Boisgontier, 2025), or whether habitual physical activity is associated with broader motor-network interactions, including those involving regions implicated in the perception of physical effort (Zénon et al., 2015).

Acknowledgments

Author Contributions

Based on the Contributor Roles Taxonomy (CRediT) (Allen et al., 2019), individual author contributions to this work areas follows: AF and MPB conceptualized the study; AF, KP, MPB contributed to study selection, data extraction and study quality assessment; AF, IML, MPB analyzed the data; AF and MPB contributed to data curation; AF and MPB wrote the original draft; KP, IML and ANC reviewed and edited the draft; MPB supervised AF and KP; MPB administered the project and acquired funds to support it. AF, KP, IML, ANC, MPB approved the final version of the manuscript.

Preregistration

The systematic review was preregistered on PROSPERO (CRD420251016029) (Farajzadeh et al., 2025).

Ethics

The study was approved by University of Ottawa Research Ethics Boards (H-03-26-12745) and informed consent was collected in accordance with the Declaration of Helsinki.

Preprint

An earlier version of this preprint was published on SportRχiv (Farajzadeh et al., 2026c).

Data, Scripts, Code, and Supplementary Material

The dataset, analysis code and supplementary material are available in a public repository (https://doi.org/10.5281/zenodo.22069859; Farajzadeh et al., 2026b).

Peer Review

Preprint version 4 of this article has been peer-reviewed and recommended by Peer Community In Neuroscience (https://doi.org/10.24072/pci.neuro.100874; Litvak, 2026). Before submitting to Peer Community In Neuroscience, our manuscript was initially submitted to a nonprofit, society-published scientific journal, where it underwent peer review and was rejected after the first round. We considered the three reviewers' comments useful and addressable. To avoid wasting the effort invested by the reviewers, an increasingly pressing issue in our publishing system, we decided to address their comments. To make this progress transparent, we have made our point-by-point response available on GitHub (https://github.com/Boisgontier-Lab/TMS-MetaAnalysis).

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Conflict of Interest Disclosure

MPB is the founder, representative, and principal manager of Peer Community In (PCI) Health & Movement Sciences and serves as a Recommender for PCI Neuroscience and PCI Registered Reports. KP and IML serve as Recommenders for PCI Health & Movement Sciences. Neither author was involved in the editorial handling, peer-review process, or publication decision for the current article. The authors declare no financial conflicts of interest related to the content of this article.

Use of Artificial Intelligence

ChatGPT (GPT-5; OpenAI) was used to review the manuscript throughout to ensure grammatical correctness and clarity of wording. Artificial intelligence was not used to conduct any data analyses or create any figures. The authors understand all analyses reported in the manuscript, have reviewed the entire manuscript, and take full responsibility for its content.

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