1 **Title: Running Head:** Mental practice for the upper-limb

2 **Title:** A systematic review and meta-analysis of the effectiveness of mental practice

3 for the upper-limb after stroke: Imagined or real benefit?

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A systematic review and meta-analysis of the effectiveness of mental practice for the upper-limb after stroke: Imagined or real benefit?

Abstract

Objective: This systematic review sought to determine the effectiveness of mental practice (MP) upon the activity limitations of the upper-limb in people after stroke, and when, in whom and how it should be delivered.

Data sources: Ten electronic databases were searched from November 2009 to May 2020. Search terms included: Arm; Practice; Stroke Rehabilitation; Imagination; Paresis; Recovery of Function; Stroke

Studies from a Cochrane review of MP (up to November 2009) were automatically included. The review was registered with Prospero database of systematic reviews (Reference number: CRD42019126044).

Study selection: Randomised controlled trials of adults after stroke using MP for the upper-limb were included if they compared to usual care, conventional therapy or no treatment and reported activity limitations of the upper-limb as outcomes. Independent screening was carried out by two reviewers.

Data extraction: One reviewer extracted data using a tool based upon the Template for Intervention Description and Replication. Data extraction was independently verified by a second reviewer. Quality was assessed using the PEDro tool.

Data Synthesis: Fifteen studies (n=486) were included and 12 (n=328) underwent meta-analysis. MP demonstrated significant benefit upon upper-limb activities compared to usual treatment (standardised mean difference, SMD: 0.6, 95%

59   confidence intervals, CI: 0.32 to 0.88). Sub-group analyses demonstrated that MP

60   appeared most effective in the first 3 months after stroke (SMD: 1.01, 95% CI: 0.53

61   to1.50) and in people with the most severe upper-limb deficits (weighted mean

62   difference, WMD: 7.33; 95% CI:0.94 to 13.72).

63   **Conclusions:** This review demonstrates that MP appears effective in reducing

64   activity limitations of the upper-limb after stroke particularly in people in the first three

65   months after stroke and in those with the most severe upper-limb dysfunction. There

66   was no clear pattern of the ideal dosage of MP.

67   **Word count: Abstract: 286; Manuscript: 4769**

68   **Keywords**: mental practice; imagery; stroke; systematic review; upper limb

69   **List of abbreviations**:

70   Confidence interval, CI

71   Mental Practice, MP

72   Standardised mean difference, SMD

73   Weighted mean difference, WMD

74

A systematic review and meta-analysis of the effectiveness of mental practice for the upper-limb after stroke: Imagined or real benefit?

Stroke is the single main cause of acquired disability in high income countries.[1] Difficulties in using the arm, wrist and hand (the upper-limb) is the most common deficit after stroke, being reported by at least 70% of stroke survivors.[2] This has a significant impact on daily activities, and has been shown to reduce independence, the likelihood of returning to employment and hobbies, and poorer mental health and quality of life.[3,4]

Mental practice (MP) is one of only a handful of interventions included in evidence based guidelines for the rehabilitation of the upper-limb after stroke. [5,6] It comprises the repeated practice of motor (or kinaesthetic) imagery.[7] During MP participants are typically guided to cognitively rehearse, but not physically perform, movements of the upper-limb often to complete a functional task [8,9] or to consider how one might perform a task (e.g. grip a cup).[10] This can be from a first person perspective (egocentric, through one's own eyes) or a third person perspective (as an observer watching from a distance).[11] Mental practice was initially developed in sports psychology to improve performance, and has been used in both cognitive and physical therapies.[12,13] Whilst the precise mechanisms by which MP may work have not been fully elucidated, it is agreed that mental imagery utilises stored multimodal (motor and sensory) representational formats and/or previous experiences of movements.[14] It has been shown that MP activates many of the same areas of the brain that are stimulated when physically executing a movement.[15,16] These include the premotor cortex, basal ganglia and cerebellum and associative parietal cortex.

99   [7,15] Consequently MP may provide a 'back door' to the motor cortex as it facilitates

100   motor cortex activity and neuroplasticity without physical movement.[15,17–19]

101   Studies indicate that the majority of people can undertake MP within the first six

102   weeks after stroke. This does vary depending upon the test used to assess MP

103   ability,[16,20,21] but the ability to undertake MP after stroke does not appear to be

104   significantly influenced by age.[22] It is also one of very few treatments that can be

105   used by those who have no voluntary movement of their upper-limb. This enables

106   participation in an upper-limb rehabilitative intervention for those who could not

107   undertake exercise based interventions for the upper-limb, such as constraint

108   induced movement therapy or repetitive task practice.[23,24] Conversely, its use in high

109   performance sport indicates that it is suitable to be used by people with good upper-

110   limb function to refine high-level skills after stroke.[7] Crucially, as MP does not require

111   any actual physical movement, it is safe for people after stroke to undertake with

112   only minimal or no supervision. This means that if MP can be shown to be effective,

113   it could provide multiple practice opportunities and be a useful method to supplement

114   the amount of therapist-provided rehabilitation for the upper-limb after stroke and

115   improve outcomes.

116   Several trials of mental practice for the upper-limb after stroke have shown it to be as

117   effective as some forms of physical practice upon impairments, and it appears

118   particularly efficacious if used alongside physical therapy. [8,9,25,26] However, others

119   have reported no differences in activity limitations when compared to usual care

120   interventions, [27] suggesting that its effectiveness cannot be assumed. The most

121   recent Cochrane review of MP for the upper-limb after stroke was published in 2020[8]

122   and found that MP had a significant benefit upon upper-limb motor recovery and

123   activities. Further reviews largely support this finding, [28,29] although the magnitude of

124   the effect appears to differ between studies. Even with the increase in available

125   trials, there is still uncertainty as to whether the changes elicited by MP could

126   specifically reduce activity limitations of the upper-limb, a recognised and shared

127   priority for people after stroke and clinicians[30]. Furthermore, the optimal parameters

128   of use of MP for the upper-limb remain unclear. Specifically, the time period after

129   stroke during which MP might be most effective (when) and the effect of dose upon

130   activity limitations (how much)[31] have not been identified.

131   Therefore, this review seeks to address this shortcoming by:

132   (i)   examining the effectiveness of MP upon outcomes that specifically

133   measure activities and activity limitations,

134   (ii)   describing when and in whom after stroke MP might have most benefit to

135   upper-limb activity outcomes

136   (iii)   investigating if and how the dose affects the effectiveness of MP

137   The lack of clear guidance regarding how and in whom MP should be used

138   clinically may, in part, explain why despite its inclusion in stroke guidelines, MP is

139   reported to be rarely used in practice.[32] The information generated by this review

140   will provide greater clarity for clinicians regarding how they might choose to use

141   MP in practice and identify clear indications of priorities for future research.

142   **Methods**

143   This review follows the Cochrane Reviews of mental practice and utilised the same

144   search criteria.[8] It was registered with Prospero database of systematic reviews

145   (Prospero reference number: CRD42019126044) and followed published checklist

146   and guidance on systematic reviews (PRISMA and Cochrane).[33,34]

147 Electronic searches of the following databases were completed: Cochrane Central

148 Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE , CINAHL,

149 PsycINFO, Scopus, Web of Science, the Physiotherapy Evidence Database (PEDro)

150 (http://www.pedro.org.au/), the specialist rehabilitation research databases CIRRIE

151 (http://cirrie.buffalo.edu) and REHABDATA (www.naric.com). The databases were

152 searched from the point of the last Cochrane review (November 2009) until 4th May

153 2020.

154 Search terms included: Arm; Practice; Stroke Rehabilitation; Imagination; Paresis;

155 Recovery of Function; Stroke

156 The search strategy is documented in appendix 1.

157 ***Screening and Selection***

158 Titles and abstracts were independently screened by two reviewers (RS and KJ).

159 Studies were included if: they were a parallel group randomised controlled trial;

160 participants were over16 years of age with a confirmed diagnosis of stroke (clinical

161 criteria and/or scanning) and had a sensorimotor upper-limb involvement as a result

162 of their stroke; compared a MP intervention, defined as cognitive rehearsal of a

163 movement or task for the upper-limb,[9] to conventional therapy, usual care, a defined

164 placebo intervention or no therapy; and the effects of MP could be delineated from

165 other interventions. Only studies whose full text was available in English and that

166 used outcomes that measured upper-limb activities before and after the intervention

167 were included. Upper-limb activities were defined according to the WHO criteria[35]

168 and included lifting/carrying and putting down (d4300,4301, 4302, 4305) fine hand

169 use (d440) and hand and arm use (d445).

170   After title and abstract screening, the full text of selected studies were retrieved,

171   independently read and assessed for inclusion. Any papers where suitability was

172   unclear were reviewed by two reviewers (RS and KJ) and a decision made through

173   discussion.

174   *Data Extraction*

175   Data was extracted by one reviewer (PB) into a data extraction spreadsheet which

176   was developed based on the Template for intervention description and replication

177   (TIDieR) checklist.[31] Data extraction was checked by a second reviewer (RS).

178   The following data were extracted: citation details; aims; total number of participants;

179   number of groups; number in each group; number lost to attrition in each group;

180   randomisation; blinding; time since stroke; selection criteria; measurement schedule;

181   baseline arm function/score; frequency of MP sessions; duration of each MP

182   session; the length of the entire MP intervention; number of completed sessions;

183   total minutes of completed MP; duration and length of control intervention; baseline,

184   post intervention and follow-up (where available) point estimates and measures of

185   variability on outcome tools that measured activities or activity limitations. Where the

186   manuscript did not present data, the authors were contacted for this information.

187   *Risk of bias (quality) assessment*

188   Two reviewers (RS and KJ) independently assessed the quality of all included

189   studies using the Physiotherapy Evidence Database (PEDro)[36] criteria scores.

190   Where possible, published assessments on the PEDro website were used to indicate

191   the quality of included studies. In the absence of published scores, PEDro scores

192   were independently assigned and then agreed by two reviewers (RS and KJ).

193 Scores indicated poor (less than 2), moderate (3-5) or high quality (6-10) trials.[36] Any

194 discrepancies were resolved by discussion.

Analysis

196 Studies were synthesised narratively and, where possible, meta-analysis of the

197 different continuous measures of upper-limb activity, presenting results as point

198 estimates and 95% confidence intervals (CI) was also undertaken by one reviewer

199 (AC). Funnel plots (plot of effect estimates from studies against a measure of

200 precision) were used to judge risk of publication bias. Weighted mean differences

201 (MD) were calculated where outcomes were measured on the same scale, with

202 standardised weighted mean differences (SMDs) calculated where outcomes were

203 measured on different scales for the same underlying construct.[34] Random-effects

204 models were estimated where SMDs were used to pool outcomes and fixed-effect

205 models where MD were synthesised. Heterogeneity was assessed through visual

206 inspection of forest plots and the calculation of the χ^2 and I^2 statistics. Sub-group

207 analyses explored the influence of time post stroke onset (using Stroke Recovery

208 and Rehabilitation Roundtable, SRRR classification),[37] severity of upper-limb

209 involvement at baseline (i.e. Action Research Arm Test; ARAT 0-20; 21-40; 41-57)

210 and the overall dose of mental practice delivered (minutes per day, calculated by

211 dividing the total number of minutes of MP reported to be delivered by the total

212 length of the MP intervention in days). This was categorised into low (below 25th

213 centile), medium (25-75th centile), high doses (above 75th centile).

214 Results were presented according to the Template for Intervention Description and

215 Replication (TIDieR),[31] and comprised consideration of who and when (including

216 participant gender, the time since stroke using published criteria,[37] the participants'

217 cognitive function, and arm severity at baseline) and what and how much (the

218 viewpoint of MP, the simultaneous inclusion and the nature of other rehabilitative

219 interventions and the overall dose of MP provided).

220

221

222 **Results**

223 Initial searches yielded 1721 articles, which were reduced to 1239 after duplicates

224 were removed (see PRISMA diagram in Figure 1). After title, abstract, and then full

225 text screening, fifteen studies were selected for narrative review and presented in

226 Table 1.[19,26,27,38–49] Four authors were contacted and asked to provide data which

227 would allow meta-analysis;[44,46,47,49] one responded with data, another responded but

228 did not provide the data, two did not respond but the data for one of these two was

229 able to be extracted from Barclay-Goddard et al.'s (2011) Cochrane review.[8] This left

230 12 studies that were suitable for meta-analysis.[19,26,27,38–46] The characteristics and

231 main findings of included studies are presented in Table 1.

232 Figure 1 here

233 Figure 1 PRISMA diagram to show article flow through the review

234 TABLE 1 here

235 Table 1 Characteristics of included studies

236

237 *Quality:*

238   PEDRO scores are displayed in Table 1. Seven studies were either of

239   moderate[19,26,38,39,44–46] or high quality[27,40–43,48,49] whilst one was of poor quality.[47]

240   ***Outcomes:***

241   Nine[19,26,27,38–41,45,49] studies utilised the Action Research Arm Test to indicate upper-

242   limb activity limitations as a primary or secondary outcome tool. The remaining six

243   studies used either the Wolf Motor Function Test,[42,48] Jebsen-Taylor hand test,[43]

244   Arm functional test - Functional Arm ability scale[46] or Motor activity log.[44,47] As these

245   tools captured data predominantly at the level of activities they were collectively

246   pooled for analysis.[19,26,27,38–46] Meta-analysis of these 12 studies revealed the

247   standardised weighted mean difference (SMD) for the overall effectiveness of MP

248   upon measures of activity limitation (shown in Figure 2) was 0.6 (95% confidence

249   intervals, CI: 0.32 to 0.88; n=328; I^2=29%).

250

251   FIGURE 2 HERE

252   Figure 2 Forest plot to show the overall effectiveness of mental practice upon activity

253   limitations of the upper-limb

254

255   ***Who and when?***

256   Fourteen of the 15 included studies presented demographic data and reported the

257   time since stroke (Table 1).[19,26,27,38–46,48,50] There were more males than females

258   (males: 282; females: 183) and participants were a mean of 59.2 (SD: 4.9) years old.

259   Using standard criteria[37], eight studies were conducted in the chronic period[26,38,39,42–

260   45,49], two in the late sub-acute period[27,41] with four being undertaken with people

261 predominantly in the early sub-acute period after stroke.[19,40,46,48] Meta-analysis of 12

262 studies showed that MP had the largest benefit upon activity limitations in the early

263 subacute period (7 days to 3 months) after stroke (SMD:1.01, 95% CI: 0.53 to 1.5; 3

264 studies, n=76; I^2=0%)[19,40,46] followed by the chronic period (6 months and later; SMD:

265 0.65, 95% CI: 0.32 to 0.99; 7 studies, n=151 I^2=0%)[13,26,38,39,42–44] (Figure 3). Changes

266 in activity limitation after MP during the late sub-acute period (3 to 6 months) were

267 small and non-significant (SMD:0.09, 95% CI: -0.3 to 0.48, p=0.65; 2 studies, n=111

268 I^2=0%).[27,41]

269 FIGURE 3 HERE

270 Figure 3 Forest plot to show subgroup analysis (fixed effects) of time after stroke and

271 effectiveness of mental practice upon upper limb activities

272

273 All studies required participants to have no or very mild cognitive deficits in order to

274 take part. Ten from 15 studies screened people for cognitive dysfunction prior to

275 inclusion. [26,27,38,39,41–44,46,49] Eight used the mini or full modified mental state

276 examination [26,38,39,42–44,46,49] with cut-offs of 24 and 70 respectively. One used the

277 mental status questionnaire,[27] whilst another used the Wechsler Memory scale.[41]

278 For those eight studies (n=226) that reported baseline arm function using the

279 ARAT,[19,26,27,38–41,45] most included participants who had moderate arm limitations

280 (median ARAT score: 25 range: 5-49). Only one study included participants who

281 would be classed as having severe arm limitations on the ARAT (mean ARAT score:

282 5)[41]. As presented in Figure 4, meta-analysis showed that MP had the greatest

283 benefit for those with the most severe upper-limb limitations (ARAT scores of 0-20;

284 weighted mean difference, WMD: 7.33, 95% CI: 0.94 to13.72; 3 studies,[39–41] n=82;

285 I^2=0%) followed by those with moderate limitations (ARAT scores from 21-40; WMD:

286 5.13, 95% CI: 2.88 to 7.39, 4 studies, [19,26,27,38] n=115; I^2=0%). However, MP was not

287 effective in improving limitations in those with the most mild upper-limb involvement,

288 although this was only based on one study (ARAT scores from 41-57; WMD: 2.50,

289 95% CI: -4.38 to 9.38, p=0.48; 1 study,[45] n=29).

290 FIGURE 4 HERE

291 Figure 4 Forest plot to show subgroup analysis (random effects) of the effects of

292 initial arm severity, measured using the ARAT, upon the effectiveness of mental

293 practice

294

295 ***What and how much?***

296 Ten studies did not clearly specify which perspective (first or third person) was used

297 during MP. Of the five studies that did, four solely utilised a first person

298 perspective[19,39,41,48] whilst one used both first and third person.[43]

299 In ten of the studies, MP was delivered in addition to conventional therapy/other

300 usual rehabilitation[13,19,26,38–40,42,43,46,49] however there was little included detail of what

301 this comprised.

302 The mean length of the MP intervention was 4.7 weeks (SD: 1.9) with a median of 3

303 sessions (range 2-15) being provided each week. One study compared three

304 different durations of MP intervention so was excluded from this analysis.[50] The

305 mean duration of a typical MP session in the other 14 studies was 28.4 minutes (SD:

306 15.1).[19,26,27,38–48] Dose was calculated to indicate the average amount of MP received

307 per day (total number of minutes of MP divided by the total length of the intervention

14

308 in days). The mean average dose was 20.3 minutes/day (SD: 14) from the 14

309 studies that used a single MP intervention[19,26,27,38–48] (Table 1).

310 For meta-analysis, the data were split into low, medium and high doses using the

311 method of calculation described earlier. Two studies used a low dose of MP (≤6.6

312 minutes/day),[26,43] five used a medium dose (6.7 to 32 minutes/day)[13,38,39,42,44] whilst

313 five used a high dose (≥32.1 minutes/day).[19,27,40,41,46] As shown in Figure 5, a lower

314 dose appeared to confer somewhat greater benefit to upper-limb function (SMD:

315 0.89, 95% CI: 0.04 to1.74; 2 studies,[26,43] n=25; I^2=0%) than a medium (SMD: 0.61,

316 95%: 0.25 to 0.98; 5 studies,[13,38,39,42,44] n=126 I^2=0%) or high dose (SMD: 0.57, 95%

317 CI: 0.05 to 1.08; 5 studies, [19,27,40,41,46] n=177; I^2=60%).

318 FIGURE 5 HERE

319 Figure 5 Forest plot to show subgroup analysis of the effects of dose upon activity

320 limitations

321 Six of the 15 studies provided control treatments to match the time and attention

322 given the intervention group. [19,27,38,43,44,48] They provided additional conventional

323 therapy,[19,44] relaxation recordings,[38,43] additional treatment based on the

324 neurodevelopmental technique,[48] or visual imagery training.[27] The remaining nine

325 studies did not detail the provision of additional control treatment.

326

327

328 **Discussion**

329 This systematic review evaluates the effectiveness of MP for the upper-limb after

330 stroke. It aimed to determine in whom and when after stroke it might have benefit

331   and to identify the dose of MP that might have the greatest effect. The main results

332   of this review were based on largely moderate to high quality trials and indicate that

333   MP can confer significant reductions in upper-limb activity limitations. Heterogeneity

334   in the meta-analyses were low (less than 29%) supporting the validity of these

335   results.

336   An important finding is that the magnitude of reported benefit of MP on upper-limb

337   activity limitations (SMD: 0.60, 95% confidence intervals, CI: 0.32 to 0.88; 12 studies,

338   n=328) exceeds that reported for other recognised upper-limb treatments in

339   comparable studies of people after stroke. These include repetitive task training

340   (SMD: 0.25, 95% CI: 0.01 to 0.49; 11 studies n=749)[24] and constraint induced

341   movement therapy (SMD: 0.24, 95% CI: -0.05 to 0.52; 42 studies, n= 1453)[51].

342   Despite the apparent superiority of MP to other upper-limb interventions, MP is

343   reported to be used much less frequently than either repetitive task training or

344   constraint induced movement therapy in clinical practice.[32] This indicates that further

345   work to support the implementation of MP into routine therapy practice is clearly

346   warranted.

347   The results of the current study are similar to that of the most recent Cochrane

348   review of MP for the upper-limb which reported analogous effect sizes of the overall

349   effectiveness of MP from 15 studies (SMD: 0.66, 95%CI: 0.39 to 0.94; n=397).[9]

350   However, a larger analysis reported a smaller effect (SMD: 0.36, 95% CI: 0.16 to

351   0.55; 18 studies, n=644).[28] The disparity between these two reviews may be

352   attributable to differences in the number of studies and participants included and the

353   analytical approach; Guerra et al. (2017)[28] pooled data from studies measuring both

354   impairment and activity limitations, whilst Barclay-Goddard et al. (2020) did not.[9] The

355   findings could indicate a trend for lower effectiveness of MP on impairments in

356   comparison to activity limitations. However, this supposition is not supported in the

357   analysis of impairment outcomes by Barclay-Goddard et al. (2020) (SMD: 0.59,

358   95%CI: 0.30 – 0.87; 15 studies, n=397)[9] . This warrants further investigation.

359   ***Who? Patient selection and time since stroke***

360   All trials selected participants that had normal or only mild cognitive dysfunction after

361   stroke. The effect of reduced cognition upon the ability to undertake MP after stroke

362   remains uncertain. Several studies have shown that mental imagery after stroke may

363   take longer to complete when compared to healthy and/or younger controls[20,21,52,53]

364   but no studies have provided explicit evidence of the minimal cognitive function

365   required to successfully complete MP. Future studies should therefore consider

366   broadening inclusion criteria to incorporate sub-groups of those after stroke with

367   moderate cognitive deficits to determine if they may benefit from MP.

368   None of the included trials stratified participants at baseline. As well as potentially

369   attenuating the estimates of effectiveness, the absence of stratification leads to

370   difficulty in knowing the optimal time after stroke and the severity of upper-limb

371   limitations that are likely to benefit most from MP. However, the sub-analyses

372   presented in this review suggest that MP delivered in the early subacute and chronic

373   phases after stroke and to those with the most severe arm deficits (scoring 0-20 on

374   the ARAT) may gain the most from MP.

375   Whilst others have found small differences between the effectiveness of MP

376   provided in the first six months after stroke or later[9] (less than 6 months: SMD: 0.48,

377   95% CI: -0.04 to 0.99; 5 studies, n=188; ≥more than 6 months: SMD: 0.75, 95% CI:

378   0.44 to 1.06, 8 studies, n=179),[9] our use of the SRRR criteria allowed more detailed

379   consideration of time periods. This revealed that the early subacute (seven days to

380   three months after stroke) group had the largest change in activity limitations after

381   using MP. The larger magnitude of changes during this early period is perhaps

382   unsurprising as the most rapid and the majority of endogenous plasticity, and thus

383   recovery of motor control, is typically observed in the first few weeks after stroke.[37,54]

384   However, in line with the Barclay et al. (2020) review,[9] a smaller but significant

385   benefit was also seen in people at least 6 months after stroke, suggesting that MP

386   may have different mechanisms of effect depending upon when after stroke it is

387   used. Collectively these results suggest that MP can improve upper-limb function at

388   multiple time points after stroke, and that work to understand the mechanism, and

389   potential differences in mechanisms, depending upon the time period in which it is

390   applied after stroke is warranted.

391   Our finding that those with the most severe deficits exhibited substantial and

392   significant benefit from MP is novel and is particularly noteworthy as this benefit (MD:

393   7.3, 95% CI: 0.94 to 13.7, I^2=0%) exceeds the minimal clinically important difference

394   for the ARAT (5.7).[55] No other reviews of MP for the upper-limb have considered the

395   severity of upper-limb deficits upon the effectiveness of MP.[9,28,56] Our finding

396   indicates that MP could provide a promising treatment for people with severe upper-

397   limb limitations, who typically cannot independently participate in other recognised

398   treatments (such as repetitive task training), as they have little voluntary movement.

399   The strength of this conclusion is limited by the wide confidence intervals, relatively

400   small number of studies in each subgroup, although heterogeneity was low, and

401   because the cut offs used in this analysis were arbitrarily assigned (ARAT scores:

402   severe: 0-20; moderate: 21-40; mild:41-57) to allow comparison. However, we chose

403   not to use more widely recognised ARAT cut off scores (severe: 0-10; moderate: 11-

404   56; mild: 57)[55] as this would mean all but one study[41] would be considered to have

405   moderate limitations and so any subtleties in the response to MP would be missed.

406   Whilst analysing the severity of upper-limb limitations as we did is not standard, it

407   highlights that the effect of MP upon severe activity limitations after stroke is worthy

408   of further study in this group.

409   ***What and How much? Delivery and dose of MP after stroke***

410   In this review there was little indication to determine which perspective (first or third

411   person) used during MP was superior as most studies did not indicate the

412   perspective used. Mental imagery from a first person (egocentric) perspective is

413   generally agreed to be more effective than from a third person perspective and so is

414   more widely used in published research protocols[7] but there is little empirical

415   evidence to support this.[11,43] Few studies also indicated if or how MP training was

416   supervised. This is important as how MP is provided will have important time and

417   cost implications for therapy services, significantly influencing cost effectiveness.

418   Lack of detail regarding how MP is provided is a common criticism of studies

419   reporting MP interventions.[57] This could be remedied by adopting recognised

420   frameworks to deliver MP used in sport (e.g. Physical, Environment, Task, Timing,

421   Learning, Emotion and Perspective, PETTLEP)[11] and by the assiduous use of

422   intervention reporting guidelines in future studies (e.g. TIDieR).[31,57]

423   Interestingly, all but one[41] of the 15 included studies in this review delivered MP as a

424   single massed practice session on each day it was delivered. This contrasts with the

425   superiority of distributed over massed practice seen in motor learning[58] and the

426   findings of a small study in which distributed MP (20 minutes, three times a day,

427   n=13) produced significantly larger gains in upper-limb recovery after stroke when

428   compared to once daily therapy for 60 minutes (n=14).[59] This suggests that future

429   studies should consider delivering shorter but more frequent MP sessions to elicit

430   greater gains in function.

431   The meta-analysis of the dose delivered in this review indicated that a low or

432   medium dose (low: less than 6.6 minutes per day medium: more than>6.7 to less

433   than 32.1 minutes/day) appeared slightly more beneficial than higher doses of MP

434   (more than32.2 minutes). If accurate, this indicates that MP could provide an

435   effective intervention without requiring substantial increases in therapist time and

436   costs. However, this is perhaps unlikely as these findings contradict the accepted

437   linear relationship between upper-limb therapy dose and response,[60] and instead

438   could be explained by the doses of MP delivered in all included studies being below

439   the amount needed to elicit optimal benefit. Other studies indicate that therapy for

440   the upper-limb must be delivered intensively in order to show an optimal benefit, [61,62]

441   which is likely to comprise several hours of intensive daily treatment.[60,63] In studies

442   included in this review, one hour was the maximum daily amount of MP delivered

443   and this was only delivered in two trials.[41,46] Others have shown no significant

444   differences in outcomes between MP delivered for an hour a day when compared to

445   lower doses 20 and 40 minutes/day.[49] This suggests that future trials should

446   compare doses of a few minutes of MP to much more intensive practice akin to that

447   in studies of upper limb rehabilitation that have shown significant benefit. It is also

448   important to note that, both in this study and others, judgements of dose and

449   intensity were estimated solely from the duration that MP was provided. Detailing the

450   numbers of repetitions and the joints and movements targeted of mentally practiced

451   movements provided by the MP script would provide a more accurate estimation of

452   the intensity of training and should be reported in future studies, although it is

453   recognised that an individual's adherence to imagining movements cannot be

454   measured.

Limitations

456   Funnel plots suggest that the findings of this systematic review may be skewed by

457   publication bias, with asymmetrical plots suggesting a lack of small studies showing

458   no benefit from the comparator interventions. Inevitably this can lead to

459   overestimation of the effectiveness of MP. Potential bias in the judgements of which

460   studies were included in the review may also skew results. Whilst data extraction

461   was checked, it was undertaken by one reviewer which may have introduced error.

462   Its wider validity is also restricted by the inclusion of only full-text articles available in

463   English and exclusion of articles that did not measure changes in activity limitations

464   of the upper-limb. The exclusion of studies that measured impairment was primarily

465   because a reduction in activity limitations is recognised to be more meaningful to

466   people after stroke than alterations in impairment.[64] Taken alongside the knowledge

467   that finding ways to effectively rehabilitate the upper-limb after stroke is a recognised

468   priority for both stroke survivors and clinicians[30] the focus upon activity limitations in

469   this review increases its clinical validity and ultimately its usefulness to clinicians and

470   people after stroke.

471   Interestingly, the studies included in this review did not always reflect the 'typical'

472   person who has had a stroke which limits the broader generalisability of the findings.

473   Included studies had relatively young participants with a mean age of 59 (SD: 5)

474   years and preferentially recruited males (there were almost 100 more males than

475   females). In Europe and Australasia, the average age for first stroke is markedly

476   older (around 70 years), stroke is more common in women than men,[65] and findings

21

477 between sexes are not directly transferable as females tend to have poorer

478 functional recovery.[66]

479 A further limitation to the findings of this review is that no studies comprehensively

480 examined compliance and fidelity to the MP intervention; others have reported low

481 patient and therapist compliance to MP,[67] MP interventions are often not clearly

482 defined[57] and few therapists report using MP as part of therapy for the upper-limb

483 after stroke[32] suggesting that the training and practical requirements of implementing

484 MP need to be considered alongside its clinical effectiveness.

485

486 **Conclusions**

487 The results of this systematic review and meta-analysis indicated that MP can

488 significantly improve activity limitations of the upper-limb after stroke and that it

489 appears more effective than several other, more frequently used interventions for the

490 upper-limb. This highlights that work is warranted to explore and support the

491 successful implementation of MP into clinical practice so that more people can

492 benefit from using it as part of their rehabilitation after stroke. The finding that MP

493 provides significant and substantial benefit that markedly exceeds the minimal

494 clinically important difference for the ARAT in those people after stroke with the most

495 severe limitations of the upper-limb is particularly novel and suggests that MP may

496 constitute a promising therapy for this subgroup.

497 Future trials should seek to stratify people based on the severity of upper-limb

498 function and/or their potential for recovery of the upper-limb to aid understanding of

499 who may benefit the most from MP. Further work is also needed to standardise the

500 delivery of MP; including identifying an optimal dose, standardising exactly how MP

501   is being used (first or third person viewpoints) and the number of repetitions of the

502   included movements in the MP intervention. This could be done by use of a detailed

503   intervention reporting tool[31] and established MP intervention structure.[11]

504

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698   Figure 1 NO LEGEND

699   Figure 2

700 Legend: Data in Nilsen et al (2012) are reversed so that improvement is indicated by a
701 higher score.

702
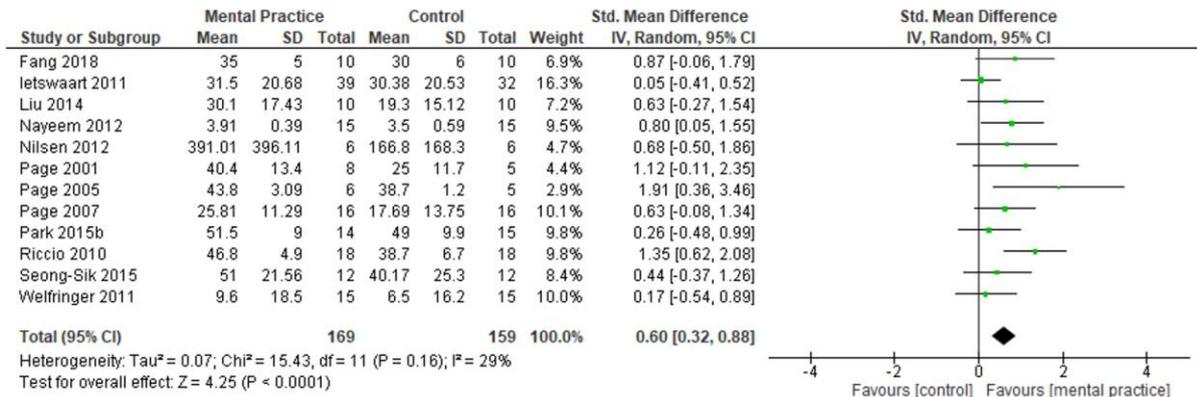
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705 Figure 3

706

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709 Legend: Data in Nilsen et al (2012) are reversed so that improvement is indicated by a
710 higher score.

711   Figure 4

Figure 4 — Mental Practice vs Control (ARAT subgroups), Mean Difference, IV, Fixed, 95% CI

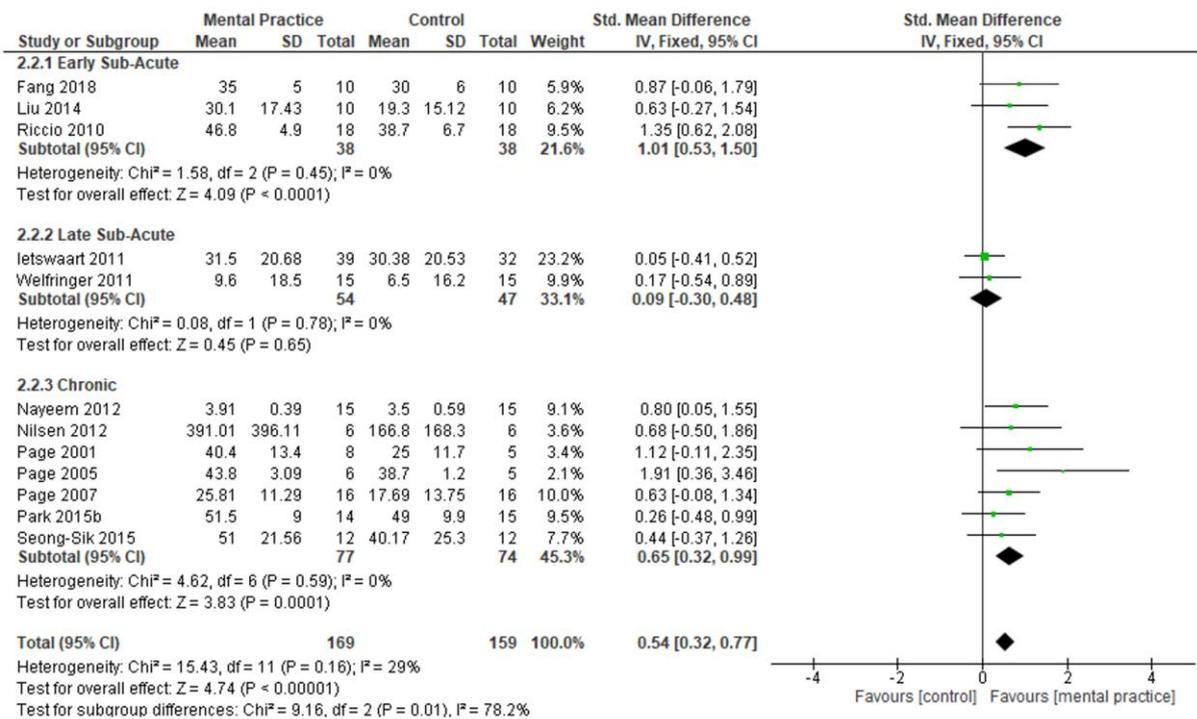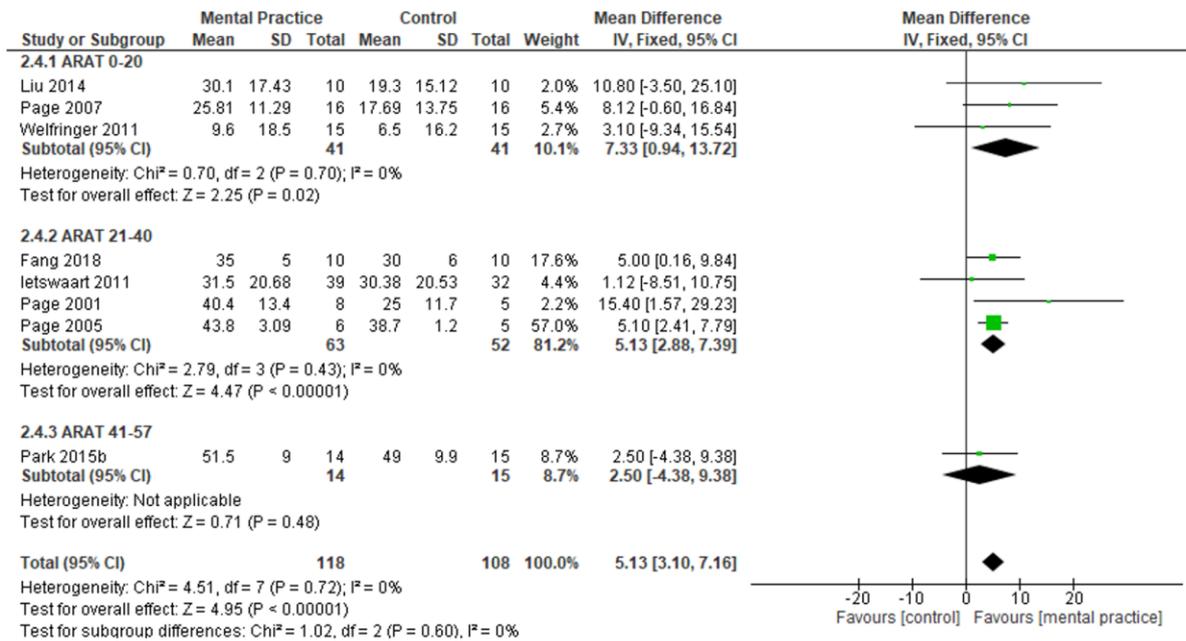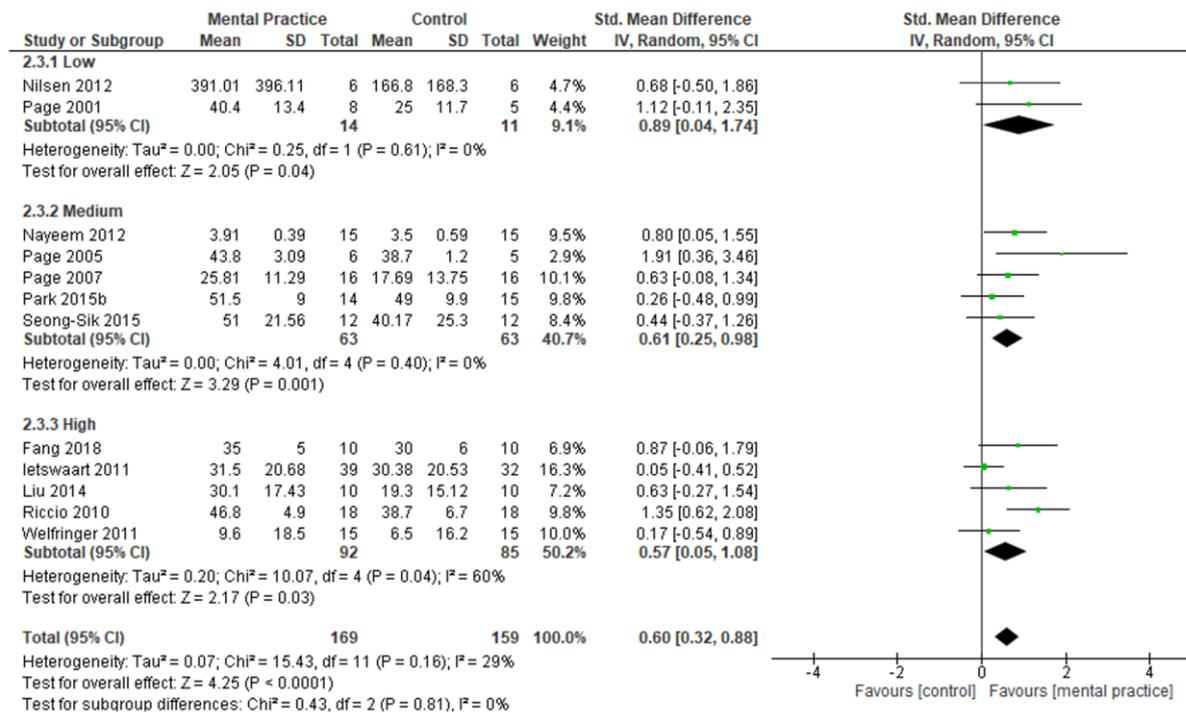| Study or Subgroup	Mental Practice Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.4.1 ARAT 0-20								
Liu 2014	30.1	17.43	10	19.3	15.12	10	2.0%	10.80 [-3.50, 25.10]
Page 2007	25.81	11.29	16	17.69	13.75	16	5.4%	8.12 [-0.60, 16.84]
Welfringer 2011	9.6	18.5	15	6.5	16.2	15	2.7%	3.10 [-9.34, 15.54]
Subtotal (95% CI)			41			41	10.1%	7.33 [0.94, 13.72]
Heterogeneity: Chi² = 0.70, df = 2 (P = 0.70); I² = 0%								
Test for overall effect: Z = 2.25 (P = 0.02)								
2.4.2 ARAT 21-40								
Fang 2018	35	5	10	30	6	10	17.6%	5.00 [0.16, 9.84]
Ietswaart 2011	31.5	20.68	39	30.38	20.53	32	4.4%	1.12 [-8.51, 10.75]
Page 2001	40.4	13.4	8	25	11.7	5	2.2%	15.40 [1.57, 29.23]
Page 2005	43.8	3.09	6	38.7	1.2	5	57.0%	5.10 [2.41, 7.79]
Subtotal (95% CI)			63			52	81.2%	5.13 [2.88, 7.39]
Heterogeneity: Chi² = 2.79, df = 3 (P = 0.43); I² = 0%								
Test for overall effect: Z = 4.47 (P < 0.00001)								
2.4.3 ARAT 41-57								
Park 2015b	51.5	9	14	49	9.9	15	8.7%	2.50 [-4.38, 9.38]
Subtotal (95% CI)			14			15	8.7%	2.50 [-4.38, 9.38]
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.71 (P = 0.48)								
Total (95% CI)			118			108	100.0%	5.13 [3.10, 7.16]
Heterogeneity: Chi² = 4.51, df = 7 (P = 0.72); I² = 0%								
Test for overall effect: Z = 4.95 (P < 0.00001)								
Test for subgroup differences: Chi² = 1.02, df = 2 (P = 0.60), I² = 0%								

Favours [control]   Favours [mental practice]

712

713   Figure 5

Figure 5 — Mental Practice vs Control, Std. Mean Difference, IV, Random, 95% CI

Study or Subgroup	Mental Practice Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.3.1 Low								
Nilsen 2012	391.01	396.11	6	166.8	168.3	6	4.7%	0.68 [-0.50, 1.86]
Page 2001	40.4	13.4	8	25	11.7	5	4.4%	1.12 [-0.11, 2.35]
Subtotal (95% CI)			14			11	9.1%	0.89 [0.04, 1.74]
Heterogeneity: Tau² = 0.00; Chi² = 0.25, df = 1 (P = 0.61); I² = 0%								
Test for overall effect: Z = 2.05 (P = 0.04)								
2.3.2 Medium								
Nayeem 2012	3.91	0.39	15	3.5	0.59	15	9.5%	0.80 [0.05, 1.55]
Page 2005	43.8	3.09	6	38.7	1.2	5	2.9%	1.91 [0.36, 3.46]
Page 2007	25.81	11.29	16	17.69	13.75	16	10.1%	0.63 [-0.08, 1.34]
Park 2015b	51.5	9	14	49	9.9	15	9.8%	0.26 [-0.48, 0.99]
Seong-Sik 2015	51	21.56	12	40.17	25.3	12	8.4%	0.44 [-0.37, 1.26]
Subtotal (95% CI)			63			63	40.7%	0.61 [0.25, 0.98]
Heterogeneity: Tau² = 0.00; Chi² = 4.01, df = 4 (P = 0.40); I² = 0%								
Test for overall effect: Z = 3.29 (P = 0.001)								
2.3.3 High								
Fang 2018	35	5	10	30	6	10	6.9%	0.87 [-0.06, 1.79]
Ietswaart 2011	31.5	20.68	39	30.38	20.53	32	16.3%	0.05 [-0.41, 0.52]
Liu 2014	30.1	17.43	10	19.3	15.12	10	7.2%	0.63 [-0.27, 1.54]
Riccio 2010	46.8	4.9	18	38.7	6.7	18	9.8%	1.35 [0.62, 2.08]
Welfringer 2011	9.6	18.5	15	6.5	16.2	15	10.0%	0.17 [-0.54, 0.89]
Subtotal (95% CI)			92			85	50.2%	0.57 [0.05, 1.08]
Heterogeneity: Tau² = 0.20; Chi² = 10.07, df = 4 (P = 0.04); I² = 60%								
Test for overall effect: Z = 2.17 (P = 0.03)								
Total (95% CI)			169			159	100.0%	0.60 [0.32, 0.88]
Heterogeneity: Tau² = 0.07; Chi² = 15.43, df = 11 (P = 0.16); I² = 29%								
Test for overall effect: Z = 4.25 (P < 0.0001)								
Test for subgroup differences: Chi² = 0.43, df = 2 (P = 0.81), I² = 0%								

Favours [control]   Favours [mental practice]

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715   Legend: Data in Nilsen et al (2012) are reversed so that improvement is indicated by a

716   higher score

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