A Systematic Review of the Effects of Handwriting Interventions on Adults with Parkinson's Disease

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INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disorder caused by a loss of dopaminergic neurons in the basal ganglia that is characterized by a number of motor deficits (Nackaerts et. al, 2017a). Self-generated and well-learned movements such as handwriting are controlled by the basal ganglia (Nackaerts et. al, 2016a). Due to the neuronal deficits PD causes in the basal ganglia, handwriting difficulties may emerge. These deficits include, most commonly, micrographia or the progressive decrease of handwriting amplitude. PD also presents with timing deficits, breakdown of movement, and irregularities in handwriting (Nackaerts et. al, 2016a). As the disease progresses, these deficits may become even more prominent. Dopaminergic medications are traditionally used to treat PD. However, since motor symptoms respond equally to medication and accommodations, motor rehabilitation and verbal or visual cueing are often utilized in conjunction (Nackaerts, 2017b).

Occupational therapists working with this population have incorporated a variety of methods into their interventions in an attempt to facilitate greater ease and legibility in handwriting. These interventions include fine-motor hand exercise programs, practice-based programs, and visual and auditory cueing (Bryant, Rintala, Lai, DeBakey & Protas, 2010). Improvement in handwriting skills can increase quality of life and independence, as well as decrease frustration, for those with PD (Collett et al., 2017). A systematic review of available research was completed in order to assess the efficacy of these interventions for both short and long-term outcomes. Eleven studies were identified as relevant to include in this review. The researchers recommend that therapists working with this population utilize the data gathered when planning handwriting interventions.

Terminology

Parkinson's disease: a neurodegenerative disorder characterized by a number of motor deficits caused by the loss of dopaminergic neurons in the basal ganglia

Micrographia: an impairment of a fine motor skill manifesting mainly as a progressive reduction in amplitude during a writing task (Nackaerts et. al, 2017b)

METHODS

Identification of Relevant Studies

A protocol (see Appendix A.) was used to identify all relevant studies. The protocol describes search methodology including search terms, databases, and inclusion/exclusion criteria.

Relevant electronic databases were searched in February 2018 and included Google Scholar, EBSCO Host, PubMed, OT Search, OT Seeker, and ProQuest. The search plan and Boolean sentence was developed by two researchers for each database. The search was then conducted independently by two additional reviewers. Following the electronic

search, the reviewers manually reviewed all studies' titles or abstracts to determine their relevance. A hand search was also conducted to identify studies not catalogued in the databases. Once the reference lists were individually compiled, the reviewers attempted to reach consensus in order to finalize the final list of studies from each database that would be included for this review. Any discrepancies between individual lists were resolved through discussion with a third reviewer.

Searches were limited to English language, peer-reviewed, quantitative studies. Specific inclusion criteria included adults over the age of 18 with Parkinson's disease. Intervention terms included "handwriting", "writing", "penmanship", "agraphia", and/or "dysgraphia". Neurological disorders that resemble Parkinson's disease were also excluded.

Appraising Study Validity

Two reviewers independently read each article and appraised the study's validity using criteria to assess the quality and level of evidence. The quality of evidence was measured using a modified version of the GRADES criteria (Dijkers, 2013). The level of evidence was assessed using an adapted version of the criteria developed by Sackett, Rosenberg, Muir Gray, Haynes & Richardson (1996). Two reviewers compared their findings for each article and settled any discrepancies with a third-party reviewer.

Pertinent information from each article was consolidated into the Study Description Table (see Table 2.), which includes information on design type, level of evidence, quality level, population, intervention, comparisons, number of subjects, outcomes, measurements, mean, statistical significance and clinical significance. If studies did not provide clinical significance, the information was substituted with a calculated minimally detectable difference (MDD) or the minimal clinically important difference (MCID).

Terminology

Quality of evidence: a measure of rigor in a study's methodology (Crocker, Lehtonen, McDonald, Miele, & Potvin, 2016)

Level of evidence: a measure of rigor in a study's design (Crocker, Lehtonen, McDonald, Miele, & Potvin, 2016)

Clinical significance: a detectable measure of change in a clinical setting (Potvin, 2018)

Minimally detectable change (MDC): the smallest amount of change that can be measured (Potvin, 2018)

Minimally clinically important difference (MCID): the smallest amount of change that has some significance in a patient's life. (Potvin, 2018)

RESULTS

The database searches initially retrieved 615 articles. Eleven of these articles met the pre-established inclusion criteria. This flowchart (see Figure 1) details the study identification process. Level of evidence in the included articles ranged from levels 1-3. Five of the articles were randomized control trials (level 1 evidence) and six were quasi-experimental study designs (level 2-3 evidence). The methodological quality of the articles ranged from low to high, with most of the studies being of low quality. One article, the Collett et al. (2017) randomized control trial (RCT), was rated as being high quality, 9/10. The quality of evidence table (see Table 1.) provides further details regarding each study. The researchers compiled the studies based on the following primary outcomes: handwriting speed, handwriting size (including length and amplitude), motor skills, grip strength, and self-perceived handwriting ability.

Five studies addressed handwriting speed and velocity. Four of these studies were level one

randomized control trials, and one study was a level two quasi-experimental study. Only Collett et al. (2017) had a sample size larger than 50. Two studies were statistically significant: Nackaerts et al. (2016b) and Nackaerts et al. (2017a). In these studies, handwriting amplitude training did not increase writing velocity in those with Parkinson's disease. An increase in handwriting amplitude correlates with a decrease in handwriting speed (Nackaerts et al., 2016b; Nackaerts et al., 2017a). Collett et al. (2017) evaluated handwriting speed using a handwriting intervention group and an exercise intervention group. No improvements in handwriting speed following the handwriting training were noted. Ziliotto et al. (2015) found statistically insignificant differences in handwriting velocity between a group receiving handwriting rehabilitation and its comparison.

Nine of the eleven studies addressed handwriting size as a primary outcome, with size defined as handwriting length, area, or amplitude. Four of these studies were level 1 RCTs. Collett et al. (2017) was the only study with a high quality of evidence. The study authors found increases in handwriting size from baseline to follow-up; however, they did not report statistical significance. One randomized control trial, Nackaerts et al. (2016b), found a statistically significant impact on handwriting when using visual cues. Heremans et al. (2017), a level 2 study, and Bryant et al. (2010), a level 3 study, found statistical significance from baseline to post-training in those with Parkinson's disease following intensive writing training. The remaining studies that evaluated handwriting size as an outcome either did not find the outcome to be statistically significant or did not report it.

Motor skills were addressed by one study, Nackaerts et al. (2018), a RCT (level 1 evidence) with a low quality of evidence. According to the study, there were no statistically significant results found between the group receiving six weeks of handwriting intervention and the group receiving stretching and breathing exercises (Nackaerts et al., 2018).

Bryant et al. (2017), a quasi-experimental study (level 3 evidence), addressed the outcome of grip strength. The quality of evidence was moderate. Researchers found that six weeks of home-based hand resistance exercises resulted in a statistically significant increase in grip strength as measured by a dynamometer (Bryant et al., 2017).

Collett et al. (2017) assessed participants' self-perception of handwriting difficulty under a variety of circumstances. The study was of high quality, with a high level of evidence and a large sample size (n=109). Results indicated that participants in the handwriting group perceived their own handwriting difficulties to diminish whereas the subjects in the exercise group perceived an increase in difficulty in handwriting. These perceived difficulties did not align with reported improvements in handwriting.

In addition to statistical significance, the researchers of this systematic review also wanted to analyze the clinical significance of handwriting interventions for those with Parkinson's disease. Clinical significance was either explicitly referenced in the included studies or the researchers determined the clinical significance through given or calculated effect size. The researchers calculated the minimal detectable difference by halving the standard deviation for studies that did not include an effect size. For handwriting size, handwriting speed, and motor skills, the researchers determined there was low clinical significance. When evaluating grip strength as an outcome, clinical

significance was moderate. One outcome, self-perception of handwriting difficulty, has high clinical significance as an outcome of handwriting intervention. It should be noted that six of the studies that were found to be statistically significant did not present evidence for clinical significance.

PRACTICE RECOMMENDATIONS

Nine studies addressed handwriting size as an outcome with a Grade B score. The studies with positive results ranged from level 1-3 (Dijkers, 2013) with a low quality of evidence, a low degree of clinical significance, and a moderate benefit to burden ratio. Three of the nine studies examining handwriting size found statistically significant results (Bryant et al., 2010; Heremans et al., 2016; Nackaerts et al., 2016b). Due to the low quality of evidence, grade, and degree of clinical significance, the interventions addressed in these studies are not recommended as a primary form of evidence-based treatment. The moderate burden to benefit ratio as well as the lack of potentially malignant effects, however, indicates the interventions can be applied should patients specifically request them.

Five studies addressed writing speed or velocity and were given a Grade B. The studies collectively had a low quality of evidence, a low degree of clinical significance, and a burden that exceeded expected amounts of benefits. Only one of the five studies found statistically positive and significant results (Nackaerts et al., 2016b). Based on these findings, the interventions are not recommended to increase handwriting speed for patients with PD.

One level 1 study addressed motor skills as an outcome. The study did not yield positive results and was given a Grade B (Nackaerts et al., 2018). The study had moderate quality of evidence, no reported clinical significance, and a moderate benefit to burden ratio. Based on the limited results of this study, the researchers are unable to recommend handwriting interventions as an appropriate means for improving motor skills.

Grip strength was measured in one study. This level 3 study yielded positive results and was given a Grade C (Bryant et al., 2017). The study had moderate quality of evidence, moderate clinical significance, and a moderate benefit to burden ratio. Based on this study the researchers suggest that clinicians may consider implementing home-based hand resistance exercises to improve grip strength.

The final outcome addressed in this review was self-perception of handwriting performance. This outcome was from a level 1 study that did not yield positive results and was given a grade C (Collett et al., 2017). The study had high quality of evidence, high clinical significance, and a high benefit to burden ratio. Based on this study the researchers recommend that implementing bi-weekly workbook, hand exercises, and writing activities are appropriate interventions to improve the self-perception of handwriting skills. However, the researchers recommend patients be informed that this study does not support an improvement in handwriting speed or size.

CLINICAL IMPLICATIONS

Of the nine studies that address handwriting size, three found statistically significant results, two for the use of visual cues (Bryant et al., 2010; Nackaerts et al., 2016b) and one for the use of an intensive writing program (Heremans et al., 2016). The clinical implications are not strong or determinable for these studies.

Handwriting interventions were found to be ineffective in improving writing speed and motor skills and only limited evidence suggested handwriting interventions may

improve grip strength or handwriting size. One study found that an intensive handwriting intervention resulted in positive performance perceptions but did not provide evidence regarding improved handwriting size or speed. Writing interventions are not harmful, and despite the lack of clear, beneficial outcomes, may be used if consistent with patients' values and needs.

CLINICAL TIPS

Currently, there are few studies regarding handwriting interventions for patients with PD. Three of the five outcomes addressed in this systematic review came from a single study. While several studies showed weak evidence for the use of cueing and an intensive writing program, overall there is a lack of evidence to support handwriting interventions for PD patients. Nackaerts et al. (2016a) found slight evidence regarding short term effects of visual cueing (increased amplitude even after cues were removed) suggesting transferability of the intervention method. More research is necessary to further examine the differences between short and long-term handwriting interventions with and without cueing.

There was no evidence that handwriting interventions improved speed. In fact, although Bryant et al. (2010) found the use of parallel lines improved handwriting size, the authors stated that these improvements came at the cost of handwriting speed. Additionally, Bryant et al. (2010) found that the use of grid lines was less effective than parallel lines in increasing handwriting size and was less preferred by patients. Results from Collett et al. (2017), indicate that handwriting interventions may have a positive impact on patient perceptions of performance. Despite limited evidence supporting improvements in size and speed, patients with PD may still seek handwriting interventions. These interventions are not associated with any known adverse effects and tend to be low cost. Therefore, patient preference should be considered when planning interventions.

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Appendix A. Systematic Review Protocol

Systematic Review Team Members: Jennifer Buchanan, Wanda Rybak, Vivian Stange, Julia Wing, Veronica Yeh

Topic: Efficacy of handwriting intervention in adults with Parkinson's disease

PICO question			
P - Parkinson's Disease	**I - Handwriting**	**C - N/A**	**O – N/A**

SEARCH STRATEGY

List of the Databases to be Search:

Databases included in SR search	**Planned the search**		**Will conduct the search**	
	Person 1	**Person 2**	**Person 1**	**Person 2**
OT Search	Jenny	Vivian	~~Julia~~	~~Veronica~~
Google Scholar	Jenny	Wanda	Vivian	Veronica
PubMed	all	all	Julia	Jenny
OT Seeker	Julia	Veronica	~~Vivian~~	~~Wanda~~
ProQuest	Wanda	Veronica	Vivian	Julia
Academic Search Premier (EBSCO)	Julia	Vivian	Jenny	Wanda

List of Search Terms:

PubMed	**Parkinson Disease**	**Parkinson Disease**	**Handwriting, writing, Agraphia**	**Handwriting**	
OT Seeker	**NA**	**Parkinson***	**NA**	**Handwriting***	
ProQuest	**Parkinson Disease**	**N/A**	**Handwriting, Agraphia**	**N/A**	
Academic Search Premier (EBSCO)	**Parkinson's Disease, *Parkinsonian disorders***	**Parkinson***	**Writing, Agraphia**	**Handwriting, Writing, Dysgraphia**	

Note: [List here the peculiarities of each database that the person searching it should keep in mind. For example, how are subject heading searched or how to do a manual search]
***EBSCO:** You cannot simply cut and paste boolean sentence.
Step 1: Boolean statement should look like (X) AND (A OR B OR C)
Step 2: Enter first part of statement into boxes (X)
Step 3: Search
Step 4: Save and name search
Step 5: Start new search for second part of boolean (A OR B OR C)
Step 6: Search and save it
Step 7: Start new search
Step 8: Select search history
Step 9: Select box next to each and select search with AND
Step 10: Save and name
Subject heading v keywords do not make a difference in results yielded, search all as keywords

***Google Scholar**: Under advanced search:
Step 1: In box labeled "with the exact phrase," type **Parkinson's disease** (no quotation marks).
Step 2: In box labeled "with at least one of the words," type **Handwriting writing penmanship dysgraphia** (no punctuation)
Step 3: Under "where my words occur," select "in the title of the article"
Step 4: Conduct search. Should yield 60 results.

OT Seeker: There are no subject headings in OT Seeker. Keywords (e.g. handwriting and writing) cannot be grouped together. The keywords "Parkinson*" and "handwriting*" were searched under the Advanced Search function and 0 results were found. A search using the keyword "Parkinson*" was completed and yielded 141 results. The results were manually searched by two students to locate an article that might involve a handwriting intervention. No results were found.

ProQuest:
Step One: Go to Advanced Search
Step Two: Paste Boolean Sentence into box labeled "Subject Heading (all)"
Step Three: Run Search

Boolean Sentence for each database:

Database Name	Boolean Sentence
~~**OT Search**~~	~~**Parkinson$ AND Writing**~~
Google Scholar	**Parkinson's disease AND handwriting OR writing OR penmanship OR dysgraphia (*Do not put this in the search bar; see above instructions*)**
PubMed	**(Parkinson disease OR Parkinsonian Disorders) AND (handwriting OR writing OR Agraphia)**
~~**OT Seeker**~~	~~***Parkinson* AND Handwriting****~~
ProQuest	**(*Parkinson Disease*) AND (*Handwriting* OR *Agraphia*)**
EBSCO	**(*Parkinson**) AND (*Writing* OR *Dysgraphia* OR Agraphia)**

***OT seeker and OT search were scanned using subject heading "Parkinson" and yielded no results**

ARTICLE INCLUSION and EXCLUSION CRITERIA

Inclusion Criteria			
Population	**Intervention and Comparison**	**Outcome**	**Other**
Adults 18+	Any of these terms get included: Handwriting, writing, agraphia, dysgraphia, penmanship		Peer reviewed journals
Parkinson's Disease			English
			Quantitative studies

Exclusion Criteria			
Population	**Intervention and Comparison**	**Outcome**	**Other**
N/A	N/A	N/A	N/A

JUSTIFICATION: Write a brief justification for each inclusion and exclusion criteria included in the table above.

-Adults 18+: PICO question criteria
-Peer-reviewed journals: usually results in higher quality evidence and is required by assignment
-English: accessible to searchers
-Quantitative Studies: higher level of evidence
-Parkinson's Disease: PICO question criteria
-Handwriting, writing, agraphia, dysgraphia, penmanship: This PICO question criteria can be phrased in a variety of ways; those listed are all acceptable.

Figure 1. Flowchart

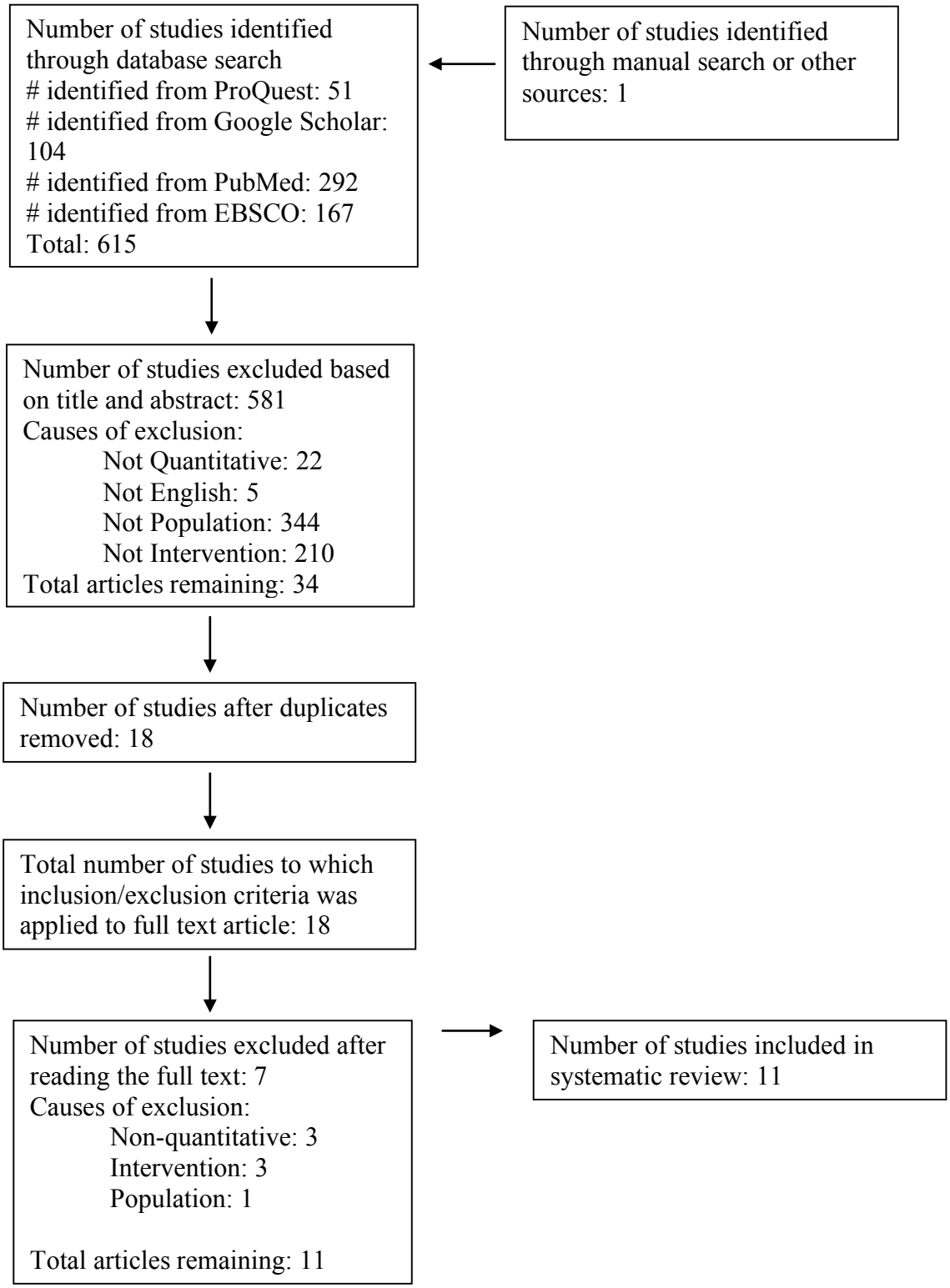

Table 1. Quality and Level of Evidence Table

		Quality Criteria											
Citation	**Type of design**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**Quality Level**	**Evidence Level**
Bryant et al. (2010)	6 = One-Group pretest-posttest design	0	1	0	0	0	0	1	1			3/8, Low	Level III
Bryant et al. (2017)	6 = One-Group pretest-posttest design	0	1	0	0	1	1	0	0			3/8, Low	Level III
Collett et al. (2017)	2 = Large (n>100) randomized clinical trial	1	1	1	1	1	1	0	1	1	1	9/10, High	Level I
Heremans et al. (2016)	5= Nonequivalent pretest-posttest control group design	0	1	1	0	0	0	1	1	1	1	6/10, Moderate	Level II
Nackaerts et al. (2017a)	3= Randomized Control Trial	0	0	1	1	0	0	0	0	0	0	2/10, Low	Level I
Nackaerts et al. (2016a)	3 = Randomized Clinical trial	0	0	1	1	0	0	0	1	0	0	3/10, Low	Level I
Nackaerts et al. (2018)	3 = Randomized Clinical trial	0	0	1	1	0	0	0	0	0	0	2/10, Low	Level I

Nackaerts et al. (2016b)	5 = Nonequivalent pretest-posttest control group design	0	1	1	0	0	0	0	0	0	1	3/10, Low	Level I
Nackaerts et al. (2017b)	3 = Randomized Clinical trial	0	0	1	1	0	1	0	1	0	0	4/10, Low	Level I
Potgieser et al. (2015)	5 = Nonequivalent pretest-posttest control group design	0	1	1	0	0	0	0	0	0	1	3/10, Low	Level II
Ziliotto et al. (2015)	5 = Nonequivalent pretest-posttest control group design	0	1	1	0	0	0	0	0	0	1	3/10, Low	Level II

Table 2. Study Description Table

Included Studies

Study	Design Type	Level of Evidence and Quality Level	Population (including age)	Intervention(s)	Comparison(s)	n in each group	Outcome(s)	Measurement (include units; direction of change)	Mean (SD)	Statistical significance	Clinical significance
Bryant et al. (2010)	Quasi experimental One-group pretest post-test design	Level III, 2/8	Males, PD & Micrographia Age: 72.20 (8.16)	Practice writing words using grid and parallel lined paper	Comparison to self at baseline	n=11	Writing length: Parallel line (pre-post practice) Writing length: Grid line (pre-post practice) Writing length: Parallel line vs. grid line after practice	PlanWheel XLU (cm; 0-∞; ↑= +) PlanWheel XLU (cm; 0-∞; ↑= +) PlanWheel XLU (cm; 0-∞; ↑= +)	Pre: 17.83 (3.93) Post: 23.36 (5.82) Pre: 17.83 (3.93) Post: 22.65 (4.04) Parallel: 23.36 (5.82) Grid: 22.65 (4.04)	p=0.008 p=0.003 p>0.05	MDD*=1.965
Bryant et al. (2017)	Quasi experimental pre-post design	Level III, 4/8	8 male subjects with PD and 9 male subjects with ET. Average age 65.3 (6.0)	6 weeks of home-based hand resistance exercise	Comparison to self at baseline	n=17	Size of writing (words)	Area measuring tool in Adobe Acrobat 9 (cm ^2, 0- ∞; ↑= +) Area measuring tool in Adobe	PD Group Pre: 2.39(0.62) Post: 2.98(1.38) Pre: 1.42(0.49)	p=0.238 p=0.575	MDD*=0.31 MDD*=0.245

							Size of writing (sentence) Grip strength	Acrobat 9 (cm ^2, 0- ∞; ↑= +) Smedley digital hand dynamometer (kg, 0- ∞; ↑= +)	Post: 1.42 (n/a) Pre: 34.14(7.74) Post: 37.34(5.69) ET Group Pre: 2.78(1.10) Post: 3.08(1.56) Pre: 1.89(0.76) Post: 2.21(1.21) Pre: 31.90(8.16) Post: 34.08(9.46)	p=0.031 p=0.282 p=0.160 p=0.091	MDD*=3.87 MDD*=1.39 MDD*=0.945 MDD*=4.08
Collett et al. (2017)	RCT	Level I, 9/10	61 male and 44 female participants with idiopathic PD Exercise group age: 66(9); Handwriting group age: 67(7)	Both groups had 60-minute sessions 2x/ week x 6 months; Handwriting intervention: workbook, hand exercises, and writing activities.	Both groups had 60-minute session 2x/ week x 6 months Exercise intervention: 30 minutes of aerobic training followed by 30 minutes	Exercise (n=54) Handwriting (n=51)	Handwriting Speed	Clock (seconds, 0- ∞; ↑= -)	SPEED-Pre Exercise: 18.7(5.2) Handwriting: 21.3(7.6) SPEED-3mo post: Exercise: 19.5(0.6) Handwriting: 20(0.6) SPEED-6mo post:	--- --- ---	MDD*=2.6 MDD*=3.8 Cohen d=0.10 (-0.33-0.52)

					of resistance training.		Handwriting Size	Ruler (mm^2; 0- ∞; ↑= +)	Exercise: 19.6(0.7) Handwriting: 19.5(0.7) SPEED- 12mo post: Exercise: 18.8(0.6) Handwriting: 19.1(0.6) SIZE-Pre Exercise: 43.1(23.8) Handwriting: 52.3(29.4) SIZE-3 mo post Exercise 49(2.9) Handwriting 55.3(2.9) SIZE-6 mo post Exercise: 50.5(2.6) Handwriting 53(2.7) SIZE-12 mo post Exercise: 51.3(2.9) Handwriting: 56.7(3)	--- --- --- --- ---	MDD*: 11.9 MDD*:14.7 Cohen d=0.32(-0.11-0.74)

							Reduction in amplitude of handwriting	Ratio of first "the" to the second "the" recorded as a percentage (0-100, ↑= +)	REDUCTION IN AMPLITUDE -Pre Exercise: 78.4(40.7) Handwriting : 89.0(39.2) REDUCTION IN AMPLITUDE 3 mo post: Exercise: 66.7(5.3) Handwriting : 77.1(5.3) REDUCTION IN AMPLITUDE 6 mo post: Exercise: 81.2(5) Handwriting : 75.2(5.1) REDUCTION IN AMPLITUDE 12 mo post: Exercise: 78.9(6.1) Handwriting : 86.3(6.4) SELF REPORTED PERCEIVED ---	--- --- --- p=0.02	MDD*: 20.35 MDD*: 19.6 Cohen d=0.11(-0.31-0.53) Odds Ratio (95% CI)

							Self-reported Perceived handwriting difficulties	Item 2.7 on the Movement Disorder Society (MDS)–Unified Parkinson's Disease Rating Scale (UPDRS), a 0–4 scale (0: normal: no problems, 4: severe: most or all words cannot be read)			0.55 (0.34 to 0.91)
Heremans et al. (2016)	Quasi-experimental- 2 groups pre-post with f/u	Level II, 6/10	24 males with PD P-FOG age 63.4 (8.9) P+FOG age 64.7(8.6)	6-week intensive writing training 30 minutes per day 5 days a week	N/A (comparison is between PD with and without FOG post intervention)	n=35 +FOG (n=16) -FOG (n=19)	Amplitude between groups at post Amplitude between groups during retention tests Amplitude from baseline to post-training in	Custom-written Matlab R2011b software (% of target size) (0-100, ↑= +) Custom-written Matlab R2011b software (% of target size) (0-100, ↑= +)	--- --- ---	p=0.03 p<0.01 p<0.01	--- --- ---

							PD without FOG Amplitude from baseline to post-training in PD with FOG	Custom-written Matlab R2011b software (% of target size) (0-100, ↑= +) Custom-written Matlab R2011b software (% of target size) (0-100, ↑= +)	--- ---	p=0.04	---
Nackaerts et al. (2017a)	RCT	Level I, 2/10	38 participants, right-handed with PD	Intensive amplitude training	Stretch and relaxation of upper limbs	EXP, n=18 Control, n=20	Stroke Duration Writing Velocity Normalized jerk	(s 0- ∞, ↑= +) (cm/s 0- ∞, -↑= +) (fluency 0- ∞, ↑= +)	--- --- ---	p=0.004 (Automatization only) p=0.001 (Transfer task only) No changes (Automatization only) p<0.001 (Transfer task only) p=0.027 (Automatization only) p=0.012 (Transfer task only)	--- --- ---

Nackaerts et al. (2016a)	RCT	Level I, 3/10	Adults w/ and w/o PD	Intensive amplitude training	Stretch and relaxation programs	n=18 n=20	Amplitude of handwriting, writing size	Mean writing size (cm, 0-∞, ↑= +) Writing velocity (seconds, 0-∞, ↑= +)) SOS test (i) fluency of letter formation; (ii) fluency in connections between letters; (iii) regularity of letter height; (iv) space between words; and (v) straightness of the sentences) (0-10, ↑= +) Use of visual cues (Y/N)	Experimental: 2.1 (0.4) Control: 3.0 (2.9) Experimental: 364.8 (126.7) Control: 395.7 (112.4) Experimental: 3.5 (1.9) Control: 3.4 (2)	p=0.192 p=0.431 p=0.813 p=0.003	MDD*=0.2 MDD*=63.35 MDD*=.95

								Use of target zone(Y/N)		p<0.001	
Nackaerts et al. (2018)	RCT	Level I, 2/10	Adults with PD	Six weeks of handwriting intervention	Stretching and breathing exercises	EXP, n=13 PLB, n=14	Fine Motor Skills Motor skills Motor Skills	MAM-16 (0-64;) MDS-UPDRS-III (0-132) MDS-UPDRS-III UL (0-56)	55.1 (5.0) 27.2 (14.1) 13.6 (6.9)	p=0.104 p=0.231 p=0.401	MDD* = 2.5 MDD*=7.05 MDD*=3.45
Nackaerts et al. (2016b)	Quasi-experimental	Level I, 3/10	Adults w/ and w/o PD	Visual feedback w/ varying sizes	No visual feedback	n=15	Handwriting size and speed (quality)	Writing amplitude (mm, 0- ∞, ↑= +) Variability of amplitude (mm, 0- ∞, ↑= +) Speed (letters/5	0.6cm: 80% (11%) (w/cue), 86 % (15%) (w/o) 1.0cm: 72% (11%) (w/cue), 65% (11%) (w/o) ---	PD/control (p=0.005) healthy (p<0.001) PD (p=0.044) Healthy (p=0.012) PD (p<0.001),	MDD* w/o cue: 6.5% w/cue: 7.5%

								min, 0- ∞, ↑= +)	PD 323(range: 236-439), healthy 509 (range=465-551)	healthy (p<0.001)	
Nackaerts et al. (2017b)	RCT	Level I, 3/10	Adults with and w/o PD	Short term training with continuous visual cues (tablet)	Intermittent intelligent verbal feedback (pen)	n=10 PD (6 cues, 4 feedback) n=9 healthy controls (4 cues, 5 feedback)	Writing amplitude of specific letters	Difference between the local minima and maxima of each individual stroke (in cm, 0- ∞, ↑= +) Letter "e" Letter "l" 8-like movements	No mean reported (No SD reported) (t=0.450) (t=4.148) (t=1.849)	 p=0.659 p=0.001 p=0.082	--- --- --- ---
Potgieser et al. (2015)	Quasi-experimental, non-equivalent	Level II, 3/10	Adults with and without PD	Withdrawal of visual feedback during writing	Visual feedback during writing	PD group, n=25; Control group, n=25	Handwriting size	Horizontal length of sentence (cm; 0- ∞, ↑= +)	Control w/ feedback: 12.7(2.3) w/o: 14(2.8) PD w/ feedback: 11.5(2.7) w/o: 13.2(2.9)	w/ feedback: p=0.11 w/o feedback: p=0.44	MDD*=1.15 MDD*=0.9

								Summed horizontal word length without interspacing (cm; 0- ∞, ↑= +)	Control w/ feedback: 9.3(1.8) w/o: 10.2(2.1) PD w/ feedback: 8.4(2.0) w/o: 9.2(2.1)	w/ feedback: p=0.08 w/o feedback: p=0.09	
Ziliotto et al. (2015)	Quasi-experimental, nonequivalent	Level II, 3/10	Adults with PD	External Cueing (auditory and visual)	No external cueing	n=30	Graphological characteristics of handwriting	Letter size (0- ∞, ↑= +): Vertical amplitude (mm, ↑= +) and width (cm, ↑= +) Vertical amplitude (mm, ↑= +) and width (cm, ↑= +) Decreasing size of letters: First 'e' amplitude (mm, ↑= +) Last 'e' amplitude (mm, ↑= +)	w/ handwriting rehab (HR) 12.7 (5.1) 13.0 (2.8) w/o HR 13.0 (4.8) 13.8 (2.7) w/ HR 3.7 (1.2) 3.5 (1.4) w/o HR 3.8 (1.3) 3.6 (1.4)	p=0.059 p=0.23 p=0.17 p=0.46 p=0.003 p=0.18 p=0.61 p=1.0	MDD*=2.55 MDD*=1.4 MDD*=2.4 MDD*=1.35 MDD*=0.6 MDD*=0.7 MDD*=0.65 MDD*=0.7

								First 'e' amplitude (mm, ↑= +) Last 'e' amplitude (mm, ↑= +) Direction of handwriting (number of cases and percentage): Ascending (↑= +) Horizontal (↑= +) Descending (↑= +) Ascending (↑= +) Horizontal (↑= +) Descending (↑= +) Surface area of the signature (cm2, ↑= +) Superior margin (mm, ↑= +)	w/ HR 0 (0) 27 (90.0) 3 (10.0) w/o HR 0 (0) 27 (90.0) 3 (10.0) w/ HR 7.2 (6.6) w/o HR 9.0 (6.2) w/ HR 10.7 (7.1) w/o HR 8.8 (6.9) w/HR 5.3 (1.7) w/o HR 6.6 (1.5) w/ HR 83 (28.1) w/o HR 68.9 (28.0)	p=0.19 p=0.70 p=0.19 p=0.15 p=0.92 p=0.97 p=0.01 p=1.0 p=0.001 p=0.46 p=0.45 p=0.02 p=0.22	MDD*=0 MDD*=45 MDD*=5 MDD*=0 MDD*=45 MDD*=5 MDD*=3.3 MDD*=3.1 MDD*=3.55 MDD*=3.45 MDD*=0.85 MDD*=0.75 MDD*=14.05

								Force exerted (calculated w/ software, 1--7, ↑= +) Velocity (number of letters/Minute, ↑= +)		p=0.34	MDD*=14

Key: ET= Essential Tremor, EXP = Experimental Group, FOG = Freezing of Gate, MAM-Manual Ability Measure, PD = Parkinson's Disease, PLB = Placebo Group, MDD* is calculated using ½ SD, --- = Data not provided, mo = months, RCT = Randomized Controlled Trial