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Brain gym exercises and mirror box therapy in hemispatial neglect post-stroke: A randomised clinical trial

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Abstract---Background: Hemispatial neglect or unilateral neglect is a failure to report, respond, or orient to stimuli that are presented contralateral to a brain lesion, provided that this failure is not due to elementary sensory or motor disorders. There is a complete lack of awareness of one half of space, at which point, patients behave as if that half of the world does not exist. The estimated prevalence of hemispatial neglect after unilateral stroke is 30%. In this study, the differential treatment using brain gym exercises alone or in combination with Mirror Box therapy for hemispatial neglect post-stroke shall be analysed. Methods: This is a single blinded parallel randomised clinical trial consisting of 2 experimental. 121 participants who met the inclusion criteria were distributed randomly in 3 groups using systematic random sampling. Effect of mirror box therapy for one experimental group and brain gym exercises for second experimental group were calculated after 6 months post treatment. Statistical analysis of outcome measures was done before and after treatment using paired t-test and Anova. Results: 40 patients were randomised to MBT group (n=40), 40 to BGT group (n=40) and 40 to CG (n=40) after excluding the dropouts. There was improvement in scores of outcome measures: Catherine bergogo scale, Kessler foundation neglect assessment process (mean difference=), star cancellation test, single letter cancellation test, double letter cancellation test, albert's test, and bell's test for groups MBT, MBBGT and BGT (95% CI, p<0.0001) before and after treatment, however, comparing group MBT, MBBGT and BGT, there was no significant improvement in scores. Conclusion: Within the groups: there was significant improvement in hemispatial neglect outcome measures in Group-A, B and C after treatment suggesting that brain gym exercises

alone have significant effect on hemispatial neglect post stroke. Between groups: the results were non-significant suggesting brain gym exercises alone, mirror box therapy alone and BG and MBT in combination have similar effects on hemispatial neglect outcome measures.

Keywords---mirror box therapy, brain gym therapy, MBBGT, confidence interval.

Introduction

Hemispatial neglect or unilateral neglect is a failure to report, respond, or orient to stimuli that are presented contralateral to a brain lesion, provided that this failure is not due to elementary sensory or motor disorders¹⁻³. There is a complete lack of awareness of one half of space, at which point, patients behave as if that half of the world does not exist. Unilateral neglect is common among patients who have hemiplegia as a result of stroke. The estimated prevalence of hemispatial neglect after unilateral stroke is 30%. The reported incidence of unilateral neglect in a right hemisphere lesion found in stroke patients varies widely from 8% to 90%, in part because of cross-study differences such as evaluation methods or severity of inattention^{4,5}. Mesulam described neglect as an 'attentional network syndrome and, apart from the arousal nature in the frontal area and the visual encoding over the temporo-occipito-parietal area of the brain, the spatial attention theory, based on the right hemisphere specializing in adult spatial attention control, provides clinical evidence that severe contralesional neglect occurs almost exclusively after a right hemisphere lesion^{6,7}. A left neglect syndrome is most commonly observed in right non dominant brain-damaged patients⁸.

Hemispatial neglect patients have impairments of memory, orientation, language, and attention. Dependency rate and overall functional disability are greater among patients with cognitive impairments than in patients with intact cognitive functioning. Moreover, fall risks associated with the sensory neglect are also higher leading to further complications. Certain treatment techniques have been effective in treating hemispatial neglect that include: Prism adaptation, eye patching, visual scanning techniques, visuo-motor feedback and mirror box therapy. In this study, the differential treatment using brain gym exercises alone or in combination with Mirror Box therapy for hemispatial neglect post-stroke shall be analysed.

Materials and Methods

Study design and ethical approval

This was an interventional PROBE design (prospective, open blinded endpoint) randomised clinical trial consisting of three experimental groups. In this clinical trial presentation, Consolidated standards of Reporting Trials (CONSORT) guidelines were used.

Participants

Participants were recruited via neurologist referral from a hospital as well as their private OPD setting. The study included the participants aged 50 to 70, both male and females with subacute brain stroke affecting parietal lobe. Participants with previous history of stroke, any neurological visual or vestibular disorders, any compressive vascular disorders, brain infections, systemic illnesses, psychiatric disorders and with widespread mental deterioration were excluded from the study. The sample size was determined using the clinical superiority design formula with minimal detectable change (MDC 95%).

Randomization

121 participants who met the inclusion criteria were distributed randomly in 3 groups using systematic random sampling with 40 patients each in MBT, BGT and MBBGT groups.

Procedure

Each subject underwent a pre-intervention assessment of hemispatial neglect using outcome measures scales: Catherine bergogo scale, Kessler foundation neglect assessment process, albert test, star cancellation test, single letter cancellation test, double letter cancellation test and bell's test.

Intervention

Group A received exercises including: cross crawls, grounder, balance buttons, hook ups, neck rolls, owl, arm activation, gravity glider, rocker, lazy 8's, alphabet 8's and double doodle. Each movement was performed 3 sets of 10 repetitions each with rest breaks in between for half an hour in total. Group B patients sat near a table on which a mirror box was placed vertically. The affected hand was hidden behind the mirror and the unaffected hand was placed in front of the mirror. Patients were asked to see only the unaffected hand in the mirror. Patients were instructed to perform flexion and extension movements of the nonparetic wrist and fingers while looking into the mirror. Thus, they were seeing the reflection of the unaffected hand as the movement of the affected hand in the mirror. During the session, while they were moving the nonparetic hand, they were asked to do the same movements in the paretic hand. Group A, B and C all received conventional exercises including using affected limb in front of the mirror for ADL's as much as possible for atleast 10 minutes, eye patching for 10 minutes and visual scanning for 10 minutes with total treatment of 30 minutes. Patients received treatment for half an hour a day 5 days a week for 4 weeks. Treatment was given for 1 month and post treatment readings were noted. All patients gave written informed consent. The study was approved by institutional ethical committee.

Outcome measures

Catherine bergogo scale

The CBS is comprised of 10 everyday tasks that the therapist observes during performance of self-care activities. The CBS uses a 4-point rating scale to indicate the severity of neglect for each item. The clinician observes the patient performing self-care activities and provides a score for each of the 10 items according to observations of neglect behaviors.

Kessler foundation neglect assessment process

The KF-NAP consists of 10 categories: limb awareness, personal belongings, dressing, grooming, gaze orientation, auditory attention, navigation, collisions, eating, and cleaning after meal. Each is scored from 0 to 3, with higher scores indicating more severe neglect. The final score is the sum of all category scores, ranging from 0 to 30. If a category is impossible to score due to the patient's condition (e.g., not able to use a wheelchair, eating restrictions), it is not included in the final score. In this case, the final score is calculated by averaging scores in the valid categories: $(\text{sum score} \div \text{number of scored categories}) \times 10 = \text{final score}$.

Star cancellation test

In the Star Cancellation Test, the stimuli are 52 large stars, 13 letters, and 10 short words interspersed with 56 smaller stars. The patient must cross out with a pencil all the small stars on an 8.5" x 11" piece of paper. Two small stars in the centre are used for demonstration. The page is placed at the patient's midline. The maximum score that can be achieved on the test is 54 points (56 small stars in total minus the 2 used for demonstration). A cutoff of < 44 indicates the presence of USN.

Single letter cancellation test

The test consists of one 8.5 x 11 sheet of paper containing 6 lines with 52 letters per line. The stimulus letter H is presented 104 times. The page is placed at the patient's midline. The patient is told to put a line through each H that is found on the page. The time taken to complete the test is recorded. The score is calculated by subtracting the number of omissions (H's that were not crossed out) from the possible perfect score of 104 (0 to 53 on the left and 0 to 51 on the right). Higher scores indicate better performance. Presence of USN can be inferred by calculating the frequency of errors to the left or to the right from the center of the page.

Double letter cancellation test

The patient is asked to look at an 8.5"x11" sheet of paper containing 6 lines with 52 letters per line. Together, the stimuli letters C and E are presented 105 times. The patient is instructed to put a mark through all the letters C and E. The time taken to complete the test is recorded. The score is calculated by subtracting the number of omissions (Cs and Es that were not crossed out) from the possible

perfect score of 105. Higher scores indicate better performance. The timing and total number of errors should be noted

Albert's test

A series of 40 black lines, each about 2 cm long, are randomly oriented on a sheet of white 11 x 8.6-inch size paper in 6 rows. The test sheet is presented to the patient at their midline. Some of the lines are pointed out to him/her, including those to the extreme right and extreme left. The examiner asks the patient to cross out all of the lines and demonstrates what is required by crossing out the 5 central lines him/herself. The presence or absence of USN is based on the number of lines left uncrossed on each side of the test sheet. If any lines are left uncrossed, and more than 70% of uncrossed lines are on the same side as motor deficit, USN is indicated.

Bell's test

In the Bells Test, the patient is asked to circle with a pencil all 35 bells embedded within 280 distractors (houses, horses, etc.) on an 11 x 8.5 – inch page. All drawings are black. The page is placed at the patient's midline. The total number of circled bells is recorded as well as the time taken to complete. The maximum score is 35. An omission of 6 or more bells on the right or left half of the page indicates USN.

Statistical analysis

The Statistical Program for Social Sciences (SPSS, v21) was used to evaluate the collected data. Initially normality of the data was tested using Shapiro-Wilk and Kolmogorov Smirnov statistics in which albert's test, star cancellation test and single letter cancellation test passed the normality while Catherine bergogo scale, Kessler foundation of neglect assessment process, double letter cancellation test and bell's test did not pass the normality testing. Hence, for former 3 scales-parametric testing of paired-t for within the group testing and ANOVA for between the group testing was applied. And for later 4 scales, non-parametric testing of Kruskal Wallis and Wilcoxon Signed rank tests were applied. A probability value of less than 0.05 was considered significant.

Results

For Group A (Mirror Box therapy + conventional exercises) comparison of outcome measures within groups pre-post readings shows significant improvement in scores for Albert's test (MD=7.35), Star cancellation test (MD=17.98), single letter cancellation test (MD=23.90), Catherine Bergogo scale (MD=8.48), Kessler Foundation Neglect Assessment Process (MD=8.8), Double Letter Cancellation test and Bell's Test.

For Group B (Brain Gym exercises + conventional exercises) comparison of outcome measures within groups pre-post readings shows significant improvement in scores for Albert's test (MD=7.10), Star cancellation test (MD=17.85), single letter cancellation test (MD=24.58), Catherine Bergogo scale

(MD=10.23), Kessler Foundation Neglect Assessment Process (MD=8.5), Double Letter Cancellation test and Bell's Test.

For Group C (Conventional Exercises) comparison of outcome measures within groups pre-post readings shows significant improvement in scores for Albert's test (MD=7.73), Star cancellation test (MD=19.40), single letter cancellation test (MD=34.33), Catherine Bergogo scale (MD=8.45), Kessler Foundation Neglect Assessment Process (MD=8.93), Double Letter Cancellation test and Bell's Test with 95% confidence interval and $p < 0.0001$.

However, comparison between groups suggested no significant improvement in scores for Albert's Test (F value= 0.286), Star Cancellation test (F value=0.988), single letter cancellation test (F test value=10.045), Catherine bergogo scale (Chi-Square value= 4.832), Kessler foundation neglect assessment process (Chi-Square test value=0.265), double letter cancellation test (Chi Square test value=0.264) and bell's test (Chi-Square test value=0.249) with 95% confidence interval and $p < 0.0001$.

Discussion

Within the groups: there was a significant improvement in hemispatial neglect outcome measures in Group-A, B and C after treatment suggesting that brain gym exercises along with conventional exercises have significant effect on hemispatial neglect post stroke. Between groups: the results were non-significant suggesting brain gym exercises, mirror box therapy and conventional therapy have similar effects on hemispatial neglect outcome measures. In recent years, the mirror neuron system (MNS) activation has been employed in brain rehabilitation from stroke, especially for motor function and language functions⁹⁻¹¹. The neural mechanisms underlying MNS activation therapy are unknown. It is proposed that the activation of MNS led to brain plasticity, potentially mediated by glutamatergic and neurotrophic mechanisms – which were found to be important in activity dependent brain plasticity¹²⁻¹⁵. In addition, right inferior parietal lobule belongs to the MNS, the activation of which might facilitate the functioning of this brain region, and therefore improve the relative spatial perception or attention function^{16,17}. Moreover, crossline activities also stimulates both dominant as well as non-dominant hemisphere further helping in stimulating the neglected side of the brain^{18,19}. The mirror neurons are activated when the brain attempts to observe, imagine, and execute an action, and they are known to participate in the new motor skills²⁰⁻²¹.

Conclusion

Brain gym exercises are an effective treatment technique along with conventional physiotherapy intervention in hemispatial neglect patients. There was a significant improvement in outcome measures including Albert's Test, Star Cancellation Test, Single Letter Cancellation Test, Double Letter Cancellation Test, Bell's Test, Catherine Bergogo Scale and Kessler Foundation of Neglect Assessment Process. However, Other treatment options including conventional exercises and Mirror Box Therapy also showed similar effects.

Funding sources and conflict of interest

For this study there were no funding sources and conflict of interests.

Credit authorship and contribution statement

PA: investigation, resources, data curation, writing original draft. SM: conceptualization, methodology, formal analysis, writing- review and editing, visualization, supervision.

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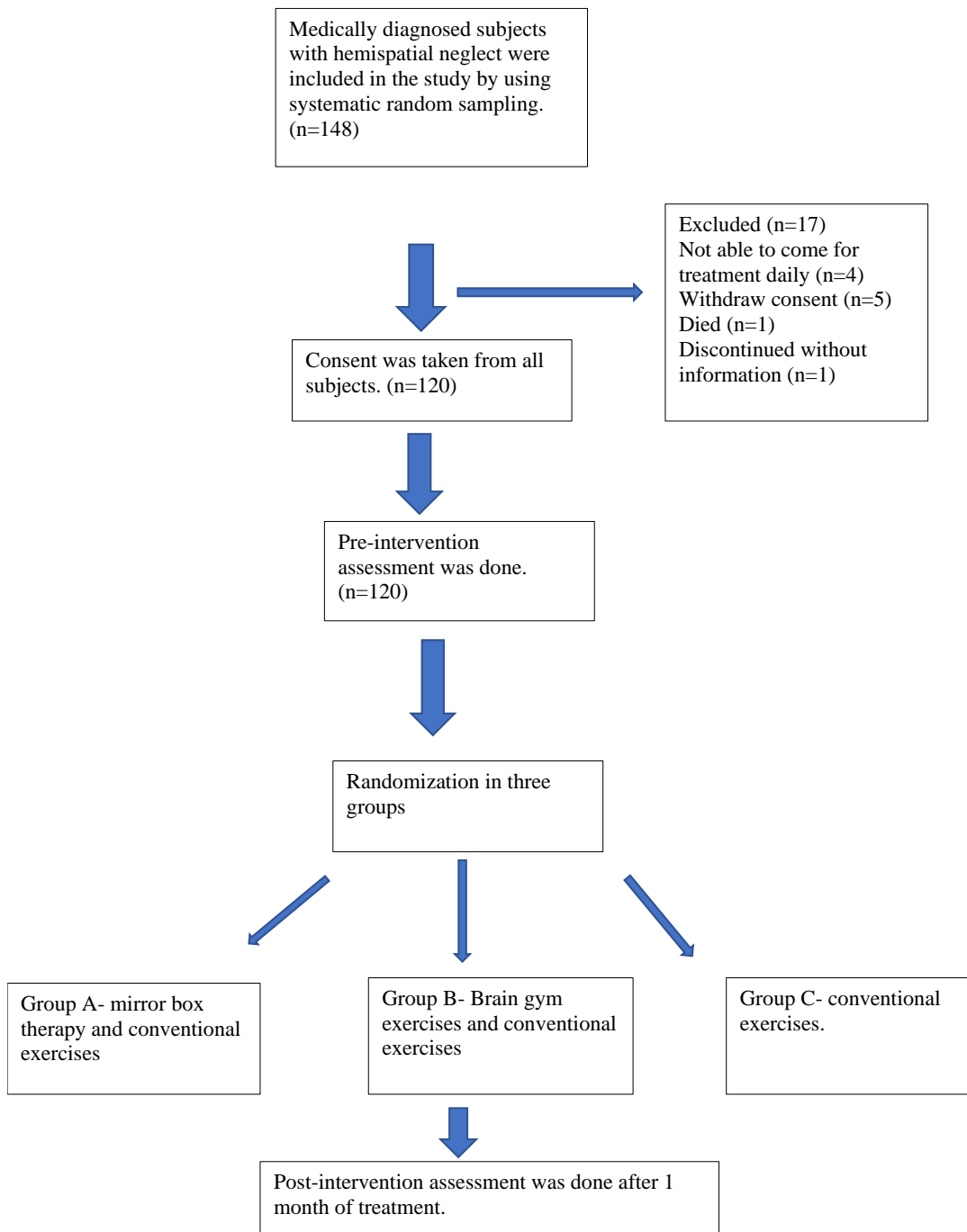
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Figure 1: CONSORT flowchart diagram



Tables

Table 1: Normality testing
Tests of Normality

	Kolmogorov-Smirnov ^a			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Catherine bergogo scale	.117	120	.000	.971	120	.011
KFNAP	.115	120	.001	.971	120	.011
Albert test	.073	120	.182	.986	120	.265
Star cancellation test	.080	120	.056	.986	120	.240
single letter cancellation test	.069	120	.200*	.983	120	.122
double letter cancellation test	.124	120	.000	.965	120	.003
bell's test	.093	120	.013	.977	120	.041

Table 2A: ANOVA Testing between the groups for albert's test, star cancellation test, single letter cancellation test

ANOVA						
		Sum of Squares	df	Mean Square	F	Sig.
albert test	Between Groups	6.650	2	3.325	.286	.752
	Within Groups	1359.475	117	11.619		
	Total	1366.125	119			
star cancellation test	Between Groups	61.317	2	30.658	.988	.375
	Within Groups	3629.850	117	31.024		
	Total	3691.167	119			
single letter cancellation test	Between Groups	2709.217	2	1354.608	10.045	.000
	Within Groups	15777.775	117	134.853		
	Total	18486.992	119			

Table 2B: Multiple comparisons

Multiple Comparisons							
Dependent Variable	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
albert test	1.00	2.00	.25000	.76222	.948	-1.6399	2.1399

		3.00	-.32500	.76222	.913	-2.2149	1.5649
	2.00	1.00	-.25000	.76222	.948	-2.1399	1.6399
		3.00	-.57500	.76222	.753	-2.4649	1.3149
	3.00	1.00	.32500	.76222	.913	-1.5649	2.2149
		2.00	.57500	.76222	.753	-1.3149	2.4649
star cancellation test	1.00	2.00	-.12500	1.24548	.995	-3.2131	2.9631
		3.00	1.45000	1.24548	.510	-1.6381	4.5381
	2.00	1.00	.12500	1.24548	.995	-2.9631	3.2131
		3.00	1.57500	1.24548	.452	-1.5131	4.6631
	3.00	1.00	-1.45000	1.24548	.510	-4.5381	1.6381
		2.00	-1.57500	1.24548	.452	-4.6631	1.5131
single letter cancellation test	1.00	2.00	.67500	2.59666	.967	-5.7632	7.1132
		3.00	10.40000*	2.59666	.001	3.9618	16.8382
	2.00	1.00	-.67500	2.59666	.967	-7.1132	5.7632
		3.00	9.72500*	2.59666	.001	3.2868	16.1632
	3.00	1.00	-10.40000*	2.59666	.001	-16.8382	-3.9618
		2.00	-9.72500*	2.59666	.001	-16.1632	-3.2868

*. The mean difference is significant at the 0.05 level.

Table 2C: Paired t- test for within the group testing for Albert test, star cancellation test and SLCT

Albert Test	Group A		Group B		Group C	
	PRE	POST	PRE	POST	PRE	POST
Mean	15.20	7.85	14.95	7.85	15.55	7.83
S.D.	2.564	2.402	2.459	2.402	2.801	2.427
Mean Difference	7.35		7.10		7.73	
T Paired Test	14.388		14.830		12.457	
P value	0.000		0.000		0.000	
Table Value at 0.05 df 19	2.02		2.02		2.02	
Result	Significant		Significant		Significant	
Star Cancellation Test	Group A		Group B		Group C	
	PRE	POST	PRE	POST	PRE	POST
Mean	28.88	46.85	29.00	46.85	27.43	46.83
S.D.	3.818	4.371	4.045	4.371	4.242	4.349
Mean Difference	17.98		17.85		19.40	
T Paired Test	20.402		20.176		22.124	
P value	0.000		0.000		0.000	
Table Value	2.02		2.02		2.02	

at 0.05 df 19						
Result	Significant		Significant		Significant	
Single letter cancellation test	GROUP A		Group B		Group C	
	PRE	POST	PRE	POST	PRE	POST
Mean	62.45	86.35	61.78	86.35	52.13	86.45
S.D.	8.446	7.526	8.657	7.526	8.398	7.575
Mean Difference	23.90		24.58		34.33	
T Paired Test	11.724		17.080		17.409	
P value	0.000		0.000		0.000	
Table Value at 0.05 df 19	2.02		2.02		2.02	
Result	Significant		Significant		Significant	

Table 3A: Wilcoxon signed rank test for CBS, KFNAP, DLCT, Bell's test

catherine bergego scale	Group A		Group B		Group C	
	PRE	POST	PRE	POST	PRE	POST
Mean	19.45	10.97	21.20	10.97	19.35	10.9
S.D.	3.05	2.74	2.11	2.74	3	2.7
Mean Difference	8.48		10.23		8.45	
Z -test Wilcoxon Signed Ranks Test _a	-5.450		-5.526		-6.166	
Z test (Sign test)	-6.085		-5.450		-6.085	
Result	.000		.000		.000	
Kessler	Group A		Group B		Group C	
	PRE	POST	PRE	POST	PRE	POST
Mean	20.62	11.82	20.62	12.121	20.65	11.72
S.D.	2.11	2.3	2.13	2.52	2.12	2.35
Mean Difference	8.8		8.5		8.93	
Z -test Wilcoxon Signed Ranks Test _a	-5.45		-5.52		-5.52	
Z test (Sign test)	-6.08		-6.17		-6.17	
Result	.000		.000		.000	
Double letter	Group A		Group B		Group C	

Constellation Test						
	PRE	POST	PRE	POST	PRE	POST
Mean	15.2	31.45	15.2	31.45	15.67	31.53
S.D.	2.56	4.54	2.56	4.54	2.35	4.57
Mean Difference						
Z -test Wilcoxon Signed Ranks Test _a	-5.51		-5.51		-5.45	
Z test (Sign test)	-6.166		-6.166		-6.085	
Result	.000		.000		.000	
Bells'test	Group A		Group B		Group C	
	PRE	POST	PRE	POST	PRE	POST
Mean	12.65	24.72	12.65	24.72	12.46	24.76
S.D.	4.53	3.91	4.53	3.91	4.56	3.96
Mean Difference						
Z -test Wilcoxon Signed Ranks Test _a	-5.446		-5.466		-5.307	
Z test (Sign test)	-6.085		-6.085		-5.918	
Result	.000		.000		.000	

Table 3B: Kruskal wallis test for CBS, KFNAP, DLCT, Bell's test

	Group	N	Mean Rank	Test Statistics ^{a,b}	
Difference KFNAP	1	39	61.15		Difference
	2	40	57.73	Chi-Square	.265
	3	40	61.15	Df	2
	Total	119		Asymp. Sig.	.876

	group	N	Mean Rank	Test Statistics ^{a,b}	
Difference CBS	1.00	39	55.81		difference
	2.00	40	70.31	Chi-Square	4.832
	3.00	41	55.39	Df	2
	Total	120		Asymp. Sig.	.089

	Gro up	N	Mean Rank	Test Statistics ^{a,b}
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double letter cancellation test difference	1.00	40	58.65	Chi-Square	.264
	2.00	40	59.10	df	2
	3.00	39	62.31	Asymp. Sig.	.876
	Total	119			

	Group	N	Mean Rank	Test Statistics ^{a,b}	
bell's test difference	1.00	40	61.10		bell's test difference
	2.00	40	61.10	Chi-Square	.249
	3.00	39	57.74	df	2
	Total	119		Asymp. Sig.	.883