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Reducing Attention Deficits After Stroke Using Attention Process Training

A Randomized Controlled Trial

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Background and Purpose—Impaired attention contributes to poor stroke outcomes. Attention process training (APT) reduces attention deficits after traumatic brain injury. There was no evidence for effectiveness of APT in stroke patients. This trial evaluated effectiveness of APT in improving attention and broader outcomes in stroke survivors 6 months after stroke.

Methods—Participants in this prospective, single-blinded, randomized, clinical trial were 78 incident stroke survivors admitted over 18 months and identified via neuropsychological assessment as having attention deficit. Participants were randomly allocated to standard care plus up to 30 hours of APT or standard care alone. Both groups were impaired ($z \leq -2.0$) across measures of attention at baseline, with the exception of Paced Auditory Serial Addition Test, which was below average ($z \leq -1.0$). Outcome assessment occurred at 5 weeks and 6 months after randomization. The primary outcome was Integrated Visual Auditory Continuous Performance Test Full-Scale Attention Quotient.

Results—APT resulted in a significantly greater ($P<0.01$) improvement on the primary outcome than standard care. Difference in change on the Cognitive Failures Questionnaire approached significance ($P=0.07$). Differences on other measures of attention and broader outcomes were not significant.

Conclusion—APT is a viable and effective means of improving attention deficits after incident stroke. **(*Stroke*. 2009;40: 3293-3298.)**

Key Words: attention ■ rehabilitation ■ neuropsychology ■ randomized clinical trial ■ stroke

Cognitive deficits occur in more than half of stroke survivors[1] and are more important determinants of broader outcomes than physical disability.[2–8] Impaired attention is the "most prominent" stroke-related neuropsychological change,[1] with rates of up to 46% to 92% reported in acute stroke survivors.[9,10]

Impaired attention can reduce cognitive productivity when other cognitive functions are intact[11] and is key to learning motor skills.[12] Robertson et al[13] reported that sustained attention 2 months after stroke predicts functional recovery at 2 years. Nys[9] found cognitive impairment 1 week after stroke predicts quality of life 6 months after stroke (Stroke Impact Scale), with visual hemi-inattention contributing significantly. Distractibility and attention are also associated with poststroke balance and functional impairment[14] and daily living (Stroke Impact Scale), including both physical and social outcomes.[15] Attention deficits are linked to greater functional impairment and falls in community-dwelling stroke survivors.[16]

In a randomized, controlled trial of 84 stroke survivors, attention retraining improved driving performance.[18] Unfortunately, this study was specific to visual neglect and did not have sufficient statistical power. In a study of 16 stroke survivors and 13 controls, attention retraining improved attention, neglect, and speed,[17] but was nonrandomized, small, lacked follow-up, and controls were unmatched. Computerized attention training programs were tested in a randomized, controlled trial of 27 patients with left hemisphere damage, with most attributable to stroke;[18] these improved alertness and sustained attention, but the sample was small, daily life impact was not assessed, and inclusion of traumatic brain injury (TBI) participants and differences in the inter-

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For a more detailed description of APT, please see Sohlberg MM, Mateer CA. Management of attention disorders. In: Sohlberg MM, Mateer CA, eds. *Cognitive Rehabilitation: An integrative neuropsychological approach*. New York, Guilford Press; 2001:125–161.

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vention between groups impacted reliability of the findings. Both trials[17,18] also were not blinded in assessment of outcomes. A Cochrane review[19] based on 2 small, controlled trials[18,20] suggests that attention deficits after stroke be treated to improve alertness and sustained attention, concluding that randomized controlled trials with larger samples and blinded outcome assessment are needed. Early identification and rehabilitation of attention deficits after stroke are endorsed by the American Heart Association.[21]

Most studies of poststroke attention rehabilitation examines specific attention deficits.[22–24] One broad attention rehabilitation program validated in neurological samples is Attention Process Training (APT).[25] APT is a theoretically based, hierarchical, multilevel treatment, including sustained, selective, alternating, and divided attention[25] typically administered by neuropsychologists, occupational therapists, speech language therapists, and other rehabilitation specialists, as is appropriate within their scope of practice. APT has been examined in small, nonrandomized evaluations in TBI samples[25–29,34] and is the basis of rehabilitation packages for mild deficits (APT-II)[30] and for children treated with radiation after cancer.[31–33] In a meta-analysis of TBI studies (total n=359) Park and Ingles[34] found attention improved significantly after specific skills training in prepost studies. Several reports indicate APT also improves other cognitive areas (eg, memory) after TBI[28,29] and link attention training and improved real-world outcomes,[35] independent living, and return to work.[24] Unfortunately, there is no robust research on APT poststroke.

This study evaluated in a large poststroke sample, APT efficacy in improving performance on tests of attention, and its impact on broader outcomes (eg, quality of life). The primary aim was to determine if, in stroke survivors identified with attention deficits, APT would improve attention at 6-months poststroke as measured by the Integrated Visual Auditory Continuous Performance Test (IVA-CPT).[36] Secondary aims were to determine impact of APT on attention at 5-week follow-up (ie, postintervention); secondary aims were to determine impact of APT on disability, everyday cognition, and quality of life at 5 weeks and 6 months after stroke, as compared with standard care.

Subjects and Method

Participants

Participants were survivors of incident stroke (all pathological subtypes) admitted to 2 Auckland New Zealand hospitals over 18 months who experienced an attention deficit as determined during neuropsychological screening assessment (see Procedure). Stroke diagnosis was via standard WHO criteria.[37] Individuals were excluded if they could not give informed consent; experienced severe cognitive deficits precluding participation (Mini Mental Status Exam [MMSE] <20), were medically unstable, were not fluent in English as required for standardized assessment, or had another condition that could impact results (eg, dementia). Stroke survivors were approached within 2 weeks after stroke.

Procedure

The study was approved by the regional ethics committee and is registered with Australian Clinical Trials Register (ACTRN12607000045415). The

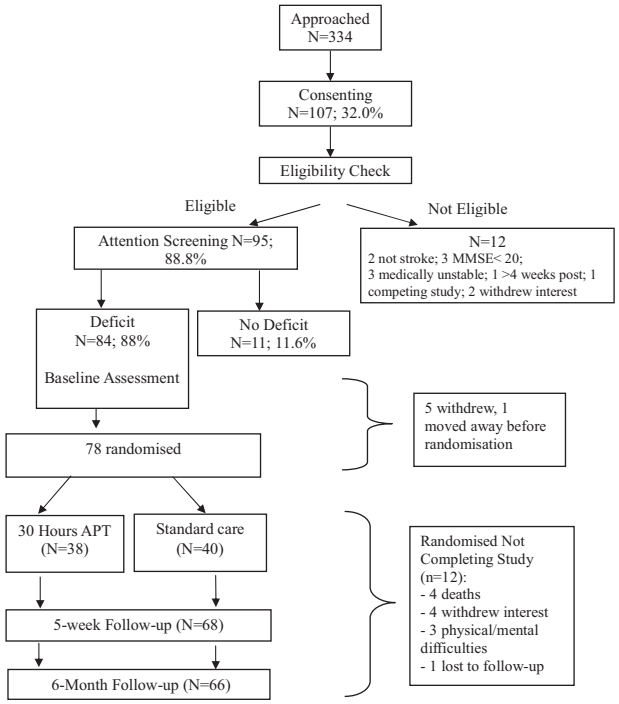

Figure. Study design and recruitment.

Figure summarizes recruitment and patient flow. Screening was conducted at the time of recruitment to establish attention deficit using the Bells Test,[38] the IVA-CPT,[36] Trail Making Test A and B,[39] and 2 slowest Paced Auditory Serial Addition Test trials.[40] These tests were selected because, taken together, they assess the 4 aspects of attention (ie, sustained, selective, divided, alternating) and both visual and auditory modalities of attention targeted by APT. Attention deficit was defined as performance >1 SD below the normative mean (ie, below average) on any test. Those with an attention deficit (n=84; 88%) then completed standardized tests of wider outcomes (ie, Medical Outcomes Study 36-item short-form questionnaire;[41–43] modified Rankin scale;[44] General Health Questionnaire-28;[45] and Cognitive Failures Questionnaire[46]). All measures included have adequate reliability, low practice effects, and good sensitivity to clinical conditions with attention deficits.[39] The high rate of attention deficit found in this sample may reflect self-selection bias with those experiencing such deficits being more likely to agree to participation. The majority of participants (n=72; 92%) performed at >2.0 SD below the normative mean on at least 1 attention test.

After baseline assessment participants were randomly assigned to APT or standard care. Randomization was concealed using an online internet randomization service whose procedures ensure enrollment and check eligibility before allowing randomization. Stratified minimization randomization was used to ensure the balance for possible prognostic factors (ie, age [<70, 70 and older], gender, ethnicity [European, non-European], Barthel Index [≤18, >18]) across the groups.[47] Implementation of the randomization sequence was via secured online contacting of the treating clinician, who had no access to assessment data. Randomization information was not accessible to any other study staff during the study.

Assessments were repeated at 5 weeks and 6 months by a trained assessor blind to randomization. Administration and scoring were via standard procedures. Assessments took up to 2.5 hours and were well-tolerated, occurring over 2 sessions if required. The primary outcome was IVA-CPT Full-Scale Attention Quotient (FSAQ), which combines auditory and visual attention scores. The IVA-CPT is a typical computerized continuous performance test during which participants must click a button each time they see or hear the number 1, and they must not click when they see or hear the number 2. Accuracy in responding to targets (1) provides indices of attention, whereas accuracy of responding to nontargets is used as an indication

of impulsive responding. Sample size was determined via power calculations, with achieved sample of 78 allowing 80% power at $P=0.05$ to detect a 10-point difference in change and >90% power to detect a 15-point (1 SD) difference in change on the IVA-CPT FSAQ with 10% loss to follow-up.

Participants in the APT group received up to 30 hours of individual APT conducted for 1 hour on weekdays for 4 weeks (mean=13.5 hours, SD=9.44). Because of issues such as fatigue, a 30-hour maximum was set and hours of APT treatment received were recorded. Participants discharged from hospital before 30 hours was achieved continued to receive APT sessions in the community. All APT sessions were administered by a registered clinical neuropsychologist, who was the only member of the study team (eg, named investigators, statisticians, data management, assessors) who did not remain blind to randomization status throughout the study.

Analyses

For the primary outcome, intention-to-treat analyses were used, and the last value carried forward replaced missing 6-month values. Change in IVA-CPT FSAQ z-scores from baseline to 5 weeks and to 6 months were analyzed using mixed models. In 4 cases in which baseline data were missing (2 fatigued; 2 unable to comprehend task), mean z-score across other available attention indices was substituted. Alpha for statistical significance was $P<0.05$.

Results

Seventy-eight participants were randomized. Table 1 provides descriptive information for APT and standard care groups, revealing that randomization achieved good balance. Table 2 presents mean performances at baseline for the groups and significance of differences (*t* tests) in change from baseline between groups. Both groups were impaired across attention tests at baseline, except for Paced Auditory Serial Addition Test trials, which were below average (z-score=−1.0-−2.0). However, only 18 standard care and 21 APT participants completed the Paced Auditory Serial Addition Test. The remaining participants were too impaired to complete the task, with the result being elevated means.

There were significant differences between groups in change experienced on 5-week follow-up IVA-CPT FSAQ ($P=0.0003$) and Auditory Attention ($P=0.010$), and some evidence for the IVA-CPT Visual Attention scale ($P=0.052$) in favor of the APT group. Difference in change was not significant for any of the other attention or broader assessments administered; however, the Cognitive Failures Questionnaire at 6 months approached significance ($P=0.069$). As can be seen in Table 2, the direction of change at 6 months for all measures was what one would anticipate if APT had a positive effect.

Differences between groups on IVA-CPT FSAQ at baseline approached significance ($P=0.064$). Unadjusted mixed model results for the primary outcome (n=78) showed that APT group change in IVA-CPT FSAQ z-score was on average 2.03 points greater than standard care change at follow-up ($P=0.0009$). After adjustment for stratification factors (center, age, sex, ethnicity, Barthel) and baseline IVA-CPT, the APT group change in IVA-CPT FSAQ z-score averaged 1.61 points greater than that of the standard care group at follow-up ($P=0.004$). Sensitivity analyses conducted with participants missing IVA-CPT values excluded (N=68) showed that the APT groups change in IVA-CPT FSAQ z-score was on average 1.96 points greater than that of the standard care group ($P=0.002$).

Table 1. Demographics of Participants in APT and Standard Care Groups

Characteristic	APT (N=38)	Standard Care (N=40)
Age		
Mean (SD)	70.2 (15.6)	67.7 (15.6)
Gender, N (%)		
Male	23 (60.5)	24 (60)
Female	15 (39.5)	16 (40)
Ethnicity, N (%)		
European	31 (81.6)	30 (75)
Māori	2 (5.3)	7 (17.5)
Pacific Island	4 (10.5)	3 (7.5)
Indian	1 (2.6)	…
Education, N (%)		
Primary	2 (5.3)	5 (12.5)
Secondary	25 (65.8)	25 (62.5)
Polytechnic	5 (13.2)	2 (5)
University	6 (15.8)	8 (20)
Barthel Index		
Mean (SD)	14.9 (5.3)	14.0 (5.9)
MMSE		
Mean (SD)	26.5 (2.8)	26.7 (2.6)
Stroke type		
Ischemic	31 (81.6)	37 (92.5)
Intracerebral hemorrhage	3 (7.9)	1 (2.5)
Subarachnoid hemorrhage	2 (5.3)	…
Unknown	2 (5.3)	2 (5)
Hemisphere of lesion		
Left	14 (43.8)	25 (58.1)
Right	15 (46.9)	17 (39.5)
Other	3 (9.1)	1 (2.3)
Time after stroke		
Mean (SD)	18.48 (11.95)	18.58 (7.62)

MMSE indicates Mini Mental Status Exam.

Discussion

APT has a significant positive effect on attention, measured by the IVA-CPT, after incident stroke. Differences in change suggest APT was related to improvement across other measures, although not significantly so. That a significant difference between groups was not seen on other attention measures may be attributable to the ability of IVA-CPT to detect change. For example, the IVA-CPT can differentiate controls from individuals with mild TBI or adulthood attention deficit hyperactivity disorder.[48] Unlike other attention tests, the IVA-CPT was not designed to merely identify attention deficits, but rather to evaluate the subtle impact of treatment regimens in children with attention deficits.[49] Furthermore, the IVA-CPT full-scale attention score combines scores from visual and auditory modalities, whereas all other measures used involve only 1 modality.

Table 2. Performance of APT and Standard Care Groups Across Measures at Baseline and Difference Between Groups in Change From Baseline at Each Follow-Up

	Baseline				Difference Between Groups in Change at 5 Weeks				Difference Between Groups in Change at 6 Months			
	APT		SC			95% CI				95% CI		
	Mean	SD	Mean	SD	Mean‡	Lower	Upper	*P*	Mean	Lower	Upper	*P*
Attention measures												
IVA-CPT (z-score)												
Full attention*	−4.93	3.44	−3.52	2.99	2.76	1.31	4.21	0.000	2.49	1.24	3.74	0.0004
Auditory attention	−4.01	3.17	−3.35	2.79	1.96	0.48	3.45	0.011	0.83	−0.47	2.13	0.208
Visual attention	−4.44	3.78	−3.44	3.43	1.56	−0.01	3.12	0.052	1.41	0.02	2.80	0.054
Trail-making (z-score)												
A	−2.60	3.85	−3.97	5.53	0.01	−1.64	1.65	0.995	0.55	−1.17	2.28	0.524
B	−2.41	3.04	−3.01	3.70	−0.29	−1.84	1.26	0.707	0.12	−1.50	1.75	0.881
PASAT (z-score)†												
2.4 sec	−1.63	0.90	−1.58	0.54	0.46	−0.05	0.97	0.074	0.47	−0.04	0.98	0.070
2.0 sec	−1.24	0.80	−1.30	1.05	0.54	−0.08	1.17	0.085	0.15	−0.45	0.74	0.609
Bell (raw)												
Left	11.94	4.77	12.35	4.79	0.92	−0.38	2.21	0.194	1.59	−0.02	3.20	0.072
Center	4.31	1.11	4.30	1.49	−0.18	−0.76	0.40	0.546	0.016	−0.36	0.69	0.556
Right	13.49	2.87	13.30	2.83	−0.54	−1.82	0.75	0.408	0.47	−0.68	1.62	0.451
Broader outcomes												
SF-36												
PCS	32.30	10.11	33.59	10.70	1.84	−2.40	6.08	0.389	3.21	−2.43	8.84	0.260
MCS	46.22	11.30	42.48	11.34	−3.14	−8.53	2.25	0.249	0.31	−5.38	5.99	0.914
MRS total score	2.58	1.24	2.55	1.34	…	…	…	…	−0.29	−0.75	0.17	0.261
CFQ total score	23.50	13.07	28.0	10.81	…	…	…	…	6.14	−0.50	12.78	0.070
GHQ-28	6.53	4.58	7.95	4.91	…	…	…	…	−0.27	−2.78	2.25	0.832

*Primary outcome measure.
†Baseline n=21 (APT); n=18 (standard care).
‡Difference in change: positive values favor APT except for MRS and GHQ-28.
… indicates not administered at 5 weeks.
CFQ indicates Cognitive Failures Questionnaire; MRS, modified Rankin scale; SC, standard care; MCS, Mental Component Score; PCS, Physical Component Score.

APT aims to improve attention, and improving attention has been associated with improved broader outcomes.[15,16] However, in this study, significant improvement in attention as measured by IVA-CPT was not reflected in statistically significant improvement in wider outcomes, although differences across the measures trended in the direction of benefit. It is possible that the 6-month follow-up period was not long enough for changes in attention to impact these more distant measures of outcome, although there was a trend toward better overall recovery in the APT group on Medical Outcomes Study 36-item short-form questionnaire modified Rankin scale and Mental Component Score (MCS) scores. In support of this possibility, the only broader outcome measure for which differences between the groups approached significance (Cognitive Failures Questionnaire) is that which most closely maps onto underlying neuropsychological impairments in attention.

Previous studies of APT in brain-injured patients report significant improvements on the Paced Auditory Serial Addition Test, which was not found with the poststroke sample examined here. It is possible that this discrepancy is attributable to differences in the populations used (eg, stroke populations are often older than TBI populations; some were too impaired to be assessed); alternatively, it is possible that earlier findings are an example of publication bias or selective reporting. The present study was not powered to detect changes on secondary outcome measures. Detailed comparison of the current trial with other research is difficult because of the scarcity of previous trials that have predominantly focused on TBI participants, been small in size, and are frequently nonrandomized with unblinded assessment of participants.[25–27,30,34]

Strengths of the study are: (1) to our knowledge it was the first full-scale randomized, controlled trial to evaluate impact of APT on attention in stroke survivors; (2) it had a relatively large sample (n=78) statistically powered to address the primary hypothesis on effectiveness of the intervention on attention, as measured by the IVA-CPT; (3) it had a very low attrition rate; and (4) the number of patients with missing data was low. The main limitations of the study were: (1) relatively strict inclusion criteria limit generalizability to wider samples; (2) although statistically powered to address

the primary research question, sample size is too small to reliably assess other important secondary outcomes (eg, Paced Auditory Serial Addition Test, Cognitive Failures Questionnaire); (3) the number of *t* tests performed may have led to chance findings; and (4) because of the nature of the intervention, it was not possible to blind the treating neuropsychologist or participants and this may have influenced outcomes. Long-term sustainability of the treatment effect beyond 6 months after randomization also remains to be evaluated. Notwithstanding these limitations, APT had a highly positive effect on attention in the population studied, suggesting early intervention may be beneficial. Whether this intervention is cost-effective and leads to the improvement in other important and related area of cognition (eg, memory) and wider functional outcomes (eg, caregiver burden) should be a subject of further research.

Conclusion

In conclusion, early identification and rehabilitation of attention should be part of poststroke rehabilitation. Although the results are encouraging, further studies are required with larger samples and longer follow-up to identify characteristics of those most likely to benefit from APT and to ascertain the optimal delay before treatment. However, the positive findings for attention in this trial demonstrate that APT is a valuable intervention for patients with attention deficit after stroke.

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Disclosures

None.

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