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Sustained favorable effects of cognitive training in children with acquired brain injuries

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Abstract. The overall aim of the present study was to assess in greater detail the sustained effects of a broad-based cognitive training programme on the neuropsychological performance of children with acquired brain injury.
In particular, the long term (6 months) effects on cognitive functions, as well as how various moderators (gender, age at the time of injury/diagnosis, time since injury/diagnosis, age at the training) might influence outcome were investigated.
A group of 38 children, 9–16 years of age, with various types of acquired brain injury had earlier been randomly assigned into treatment and control groups. These two groups had first been assessed directly after completion of the training and were now reassessed 6 months later. The treatment group exhibited significantly more persistent improvements with respect to complex tasks of attention and memory in comparison to the control group. In contrast there were no differences on simple reaction time tests.
We conclude that the long term effects on cognitive functions of this broad-based neuro-cognitive training is encouraging. These positive results should be further investigated in larger more specific diagnostic groups and in different settings.

Keywords: Cognitive training, training effects, acquired brain injuries, children

1. Introduction

Deficits in attention, memory and information processing skills present during development impede learning and the acquisition of new skills and knowledge, resulting in the global cognitive dysfunction commonly observed in the long- term follow- up of children with acquired brain injuries [2–5,12–14]. The effectiveness of cognitive rehabilitation of adults suffering traumatic brain injury has been demonstrated in a large number of studies described in comprehensive review articles [9,11,12]. In contrast, little research on the efficacy of cognitive rehabilitation in children has been performed.

In children with Attention Deficit Disorder (ADHD) specific training focused on attention or working memory has demonstrated positive effects on neuropsychological parameters [20,21,27]. In addition, children with brain malignancies who underwent a broader type of programme, characterized by process-specific and strategy training, exhibited positive changes in measures of attention [7].

Another comparable broad based programme for interactive cognitive intervention, the Amsterdam Memory and Attention Training for Children (Amat-c) [16]

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produced favorable results in a controlled study involving 20 children treated for cancer [17]. Furthermore, application of this same programme independently in an open study on 3 Swedish children with traumatic brain injuries [18] resulted in improved cognitive performance. Recently, evaluation of a slightly modified version of the Amat-c in a randomized controlled study on 38 Swedish children with acquired brain injury demonstrated improvement in tasks involving complex memory and attention, whereas no effect was shown on simple measures of reaction time [19].

A general drawback associated with previous investigations on cognitive intervention in children with acquired brain injury has been that these have not sufficiently assessed the effects of training over a prolonged period, or other variables that could influence outcome. Thus, the specific questions to be explored in this study were:

How does cognitive training with the Amat-c method affect specific neuropsychological functions over time (6 months)? How do other moderators as; age at the time of injury or diagnosis of illness; time since injury/diagnosis; gender and age at the time of training influence outcome?

2. Material and methods

2.1. Participants

Children with acquired brain injuries due to trauma, infection or malignancy, who participated in this study, were followed at the Neuropaediatric and Oncology Unit at Astrid Lindgren's Children's Hospital, Stockholm, the Folke Bernadotte Unit (Academic Hospital, Uppsala) and the University Children's Hospital of Lund between 1999 and 2003. The initial criteria for inclusion were: 9–17 years of age at the beginning of the intervention, 1–5 years after the injury/end of treatment for malignancy.

The children who fulfilled these criteria then underwent a neuropsychological examination and those with an IQ > 70 and a performance of 1 SD or more below average for age on 20% of attention and memory tests included in the neuropsychological test battery were invited to participate in the study:

After obtaining parental consent, 40 children were assigned consecutively in a random fashion to either treatment or control group.

Two children in the treatment group had a relapse of their tumors and their cognitive training had to be interrupted prematurely. The two groups did not differ significantly with respect to pre- treatment variables such as age at the time of injury; the time which had elapsed since the injury or termination of treatment; gender; age at the time of training; pre-test measures of IQ and the attention factor within the WISC III. (Table 1). There was an imbalance between the two groups in terms of diagnosis with more children suffering from brain tumors in the control group ($p < 0.02$).

2.2. Treatment procedure

The Amat-c [19] involves a combination of daily practice and games on the one hand, and exercises in specific attention and memory techniques on the other. There are two versions of this training programme, one for children 9 to12 years of age, and one for adolescents aged 13 or older.

In addition to attention and memory exercises, the Amat-c programme consists of therapeutic approaches to behavior modification, focused on learning strategies in daily life, and on the accomplishment of school tasks. The exercises are performed for 30 minutes 6 days per week for a period of 17 weeks, and gradually increase in difficulty. Children perform these exercises together with a coach (teacher or parent) at school or at home. Written instructions according to the Amat-c manual, together with keeping of a diary complement the exercises. The child and his/her coach visit the hospital once a week for feedback and reinforcement. This session is also considered as a therapeutic intervention in addition to the specific training tasks, enabling the child to share her/his cognitive, emotional and behavioural experiences. More specific description of the Amat-c method is provided in earlier studies [18,19].

2.3. Neuropsychological test battery

The general intellectual ability of the children was assessed prior to the intervention and at time of follow-up i.e., 6 months after the training was completed employing the Wechsler Intelligence Scales for Children (WISC-III) [30].

2.3.1. Assessment of sustained attention

The computerized *Visual and Auditory Reaction Time Tests* [1] were utilized to evaluate the children's reaction times for simple auditory and visual stimuli.

In the *Vigilance Test of the Gordon Diagnostic System* [15] the child was shown a series of digits on a screen and told to respond only when a particular combination of numbers appeared. Results are expressed in correct answers.

Table 1
Characteristics of the groups

	Treatment group $n = 18$	Control group $n = 20$
Mean age at the time of injury or diagnosis of disease (yrs)	11.7 (2.3)	12.05 (2.6)
Mean time elapsed since injury or termination of treatment (yrs)	2.2 (1.0)	2.6 (1.2)
Boys/girls	12/6	10/10
Diagnosis		
TBI (GCS >8)	7	6
TBI (GCS<8)	5	3
Encephalitis	1	1
Anoxia	1	0
Brain malignancies	4	10
Medical treatment		
Irradiation therapy	4	6
Chemotherapy	4	6
Pretest Full IQ	95	94
Verbal comprehension	101	100
Perceptual organization	96	98
Freedom of Distractability	82	82
Speed of processing	80	85

a) TBI = Traumatic Brain Injury.
b) GCS = Glasgow Coma Scale.

2.3.2. Assessment of selective attention

The *Stroop Colour and Word Test* [27] consists of three stimuli cards where color words are written first in black, then as signs in different colors and last in words describing colors printed with ink in a color that is incongruent with the word. Stroop scores were calculated as the number of correct words.

The *Binary Choice Test* [1] is a computerized measure of choice reaction time whose results are expressed as the number of correct responses.

The Coding Test was administered according to standard manual [23].

The Trail Making Test (*TMT*) [27] includes two parts, A and B, the results are expressed in time of completion (sec).

2.3.3. Assessment of memory

The scores for the *Digit Span* were calculated according to the standard manual [30].

In the *15 Word Test* [27] the children had to listen to simple unrelated words presented 5 times. The task was after each presentation to repeat as many words as possible by free recall. In addition, the total number of words remembered in connection with delayed free recall 40 minutes later was scored separately.

In accordance with the *Rey-Osterrieth Complex Figure Recall* [27] the children were asked to reproduce a complex geometrical design 30 minutes after having copied it and without knowing in advance that they would be requested to do this. The accuracy score is the number of elements remembered and reflects the amount of information retained for this period of time.

The Rivermead Behavioural Memory Test (RBMT) [31] involves a number of practical tasks, such as remembering a name associated with a photograph; remembering a hidden belonging; remembering an appointment and a story; face and picture recognition; remembering a new route; both immediately and after a 10 minute delay; delivering a message during the task of route recall task; orientation in time and place; and knowing today's date. The total score is the sum of the individual test scores.

This study was approved by the Ethical Committee of Karolinska Institute.

3. Procedure

All of the children and their parents had earlier been informed about the evaluation of two different interactive activities to be performed both for 30 min 6 days per week for a period of 17 weeks. The one activity performed by the treatment group was directed by three of the authors (IvH, BB and KA); while the activity in the control group was chosen freely by the parent, teacher and child. The freely chosen activity had the conditions that it should be interactive, like in games, sports, home work and conversations. However, no computer games or television activities were accepted.

After parents' consent the children had been randomly assigned to the two groups (treatment and control group).

The children in the treatment group had trained together with a teacher or parent according to instructions from the manual of Amat-c. Once a week, a psychologist (I.v H.) or a teacher (K.A.or B.B) saw the child and his/her coach at the hospital for instructions, feedback and reinforcement. Both groups of children had recorded their activities in a diary. The children in the control group sent their, registered activities, weekly to the authors at the hospital and were contacted weekly by telephone. This weekly telephone contact was only informative and did not specifically consist of any coaching. All children had earlier been assessed before and directly after the intervention. In the present study, the children were reassessed six months after completing the training. The same test-battery was employed on each occasion.

3.1. Statistical analysis

The test results obtained 6 months after completion of the training were subjected to statistical analysis using the raw scores for all parameters and, an analysis of variance (ANOVA) procedure for repeated measurements.

Post-hoc analysis was performed using the Least Significant Differences (LSD). In order to analyze the influence of variables such as age at the time of injury or diagnosis of illness; time since injury/diagnosis; gender and age at the time of training on positive outcome, multiple logistic regression analysis was carried out.

4. Results

4.1. Attention

Six months following completion of the training, the treatment group demonstrated consistent gains, as compared to controls, in sustained attention; measured by the Gordon Diagnostic System, Vigilance Test correct answers ($p < 0.0003$) and commission errors ($p < 0.04$).

The test results on selective attention assessed by the Binary Choice Reaction Time Test, correct answers, also showed significant sustained gains in the treatment group as compared to controls ($p < 0.002$). (P values indicate the level of significance according to Anova analysis) (Table 2).

4.2. Memory

The treatment group showed sustained improvements on memory tests according to 15 Word Learning Test-recall ($p < 0.0002$), the Rivermead Behavioral Memory Test ($p < 0.0002$); and the Rey-Osterrieth Complex Figure recall ($p < 0.0002$); as compared to the children in the control group.

Post-hoc analysis revealed an additional improvement in the treatment group during the time of this 6 months follow-up with regards to the measures of selective attention Stroop 1, ($p < 0.01$) and Coding ($p < 0.05$), as well as in the auditory verbal learning assessed by the 15 Word Learning Test ($p < 0.04$).

No significant differences between the two groups were observed with respect to the simple visual and auditory reaction time; both groups exhibiting general improvements.

Both groups demonstrated an improvement on general cognitive measures (WISC-III), without any identified significant difference between the groups. In contrast, the freedom of distractibility factor and the verbal comprehension factors within the WISC-III revealed significant improvements ($p < 0.05$; $p < 003$) in the treatment group as compared to controls, whereas the perceptual organization and speed of processing factors did not show any significant difference between the groups.

For logistic regression analysis improvement of at least 1 SD in two of the three variables, freedom of distractibility factor in the WISC-III, the Rey- Osterrieth Complex Figure Recall and the Rivermead Behavioural Memory Test was defined as a positive effect of the training. Such analysis revealed no significant influence of age at the time of injury/illness; the time elapsed since injury or illness; gender; age at the time of training.

The imbalance of diagnosis between the two groups was controlled for by multiple regression analysis, which indicated that diagnosis partly might account for the effect ($p < 0.02$). However, using a stratified Mann-Whitney test analysis for diagnosis the statistically significant treatment effect was confirmed ($p < 0.04$).

5. Discussion

The essential finding of this follow up study is that the treatment group maintained a significant improvement especially on complex attention and memory tasks 6

Table 2
Neuropsychological test results Treatment group = 18

TEST	Treatment group = 18			Control group = 20			$p < 0.05$
	PRE-TRAINING	POST TRAINING	POST 6 MONTHS	PRE TRAINING	POST TRAINING	POST 6 MONTHS	
Auditory RT[1]	359 (319–442)	340 (313–442)	319 (293–363)	400 (347–356)	350 (304–397)	348 (299–405)	n.s.
Visual RT[1]	368 (350–454)	354 (324–405)	375 (347–419)	400 (373–356)	373 (334–397)	370 (347–419)	n.s.
Gordon[2] correct answers	39 (35–43)	43 (40–45)	45 (42–45)	42 (39–43)	43 (41–44)	43 (41–49)	0.0003
Gordon[2] Commission errors	5 (2–7)	3 (1–6)	1 (1–5)	3 (0–6)	2 (1–4)	2 (1–6)	0.04
Binary Choice RT[3] (ms)	426 (335–482)	359 (304–458)	375 (337–426)	429 (379–480)	412 (335–457)	403 (371–433)	n.s.
Binary Choice correct answers	53 (42–58)	57 (55–60)	57 (55–58)	55 (54–58)	56 (51–58)	57 (55–58)	0.002
TMT[4] A(s)	40 (28–60)	29 (24–41)	34 (28–41)	31 (27–37)	32 (25–46)	36 (28–48)	n.s.
TMT[4] B(s) (88–139)	110 (58–89)	72 (58–87)	70 (67–137)	89 (58–119)	88 (65–110)	90	0.03
Stroop 1 nr of words	53 (41–70)	68 (54–81)	76 (60–83)	71 (60–90)	73 (57–90)	80 (71–92)	n.s.
Stroop 2 nr of words	45 (37–52)	53 (41–63)	51 (44–61)	45 (36–56)	50 (41–56)	55 (43–58)	n.s.
Stroop 3 nr of words	24 (20–40)	32 (25–45)	32 (27–46)	27 (18–34)	26 (20–38)	31 (21–40)	0.004
Coding (WISC–III)	38 (29–43)	41 (34–54)	44 (38–53)	43 (32–49)	39 (29–51)	44 (34–56)	0.009
Digit Span (WISC-III)	11.5 (8–13)	14 (12–15)	13 (11–16	10 (9–12)	11 (9–13)	11 (9–13)	n.s
15 words[5]	36 (32–47)	45 (39–55)	48 (45–60)	43 (35–50)	46 (41–50)	48 (44–54)	0.005
15 words[6] delayed recall	9 (7–11)	11 (8–14)	13 (11–14)	9 (7.5–11)	10 (8–12)	10 (9–13)	0.012
RCFT[7] delayed recall	11 (9–22)	18 (15–26)	22 (17–27)	19 (10–22)	16 (10–25)	17 (12–22)	0.00002
RBMT[8] total score	52 (47–57)	64 (60–66)	65 (59–72)	60 (52–62)	58 (51–62)	53 (49–59)	0.00002

The scores given are averages (ranges) of raw scores. P values indicate the level of significance according to Anova analysis prior to, immediately and 6 months after completion of training.
[1]Auditory Reaction Time in milliseconds.
[1]Visual Reaction Time in milliseconds.
[2]Gordon Diagnostic System.
[3]Binary Choice Reaction Time in milliseconds.
[4]Trail Making Test A time in seconds.
Trail Making Test B time in seconds.
[5]15 Words Test Immediate recall nr of words.
[6]15 Words Delayed recall nr of words.
[7]Rey-Osterrieth Complex Figure delayed recall nr of remembered segments. [8]Rivermead Behavioural Memory Test total score.

months after completion of the cognitive training with the Amat-c programme reported about earlier [2]. No significant difference between the treatment and control groups was found with respect to the simple reaction time tests, despite a generally improved performance. Furthermore, selective attention and verbal working memory continued to improve significantly in the treatment group following completion of the training.

The results can be interpreted as indicating that Amat-c does not train speed of performance, but rather enhances the ability to develop strategies and deal correctly with a task. Improvements in speed of processing have been reported to be less consistent than improvements in non-speed tasks in adults [2,24]. The general improvement in speed on the reaction time tests observed here both in treatment and control groups might be explained by the influence of development and the effect of practice.

Other studies have reported that meta-cognitive and self-regulatory strategies play an important role in improving inattentive behaviour [36]. These strategies are also included in the Amat-c programme. The ultimate goal of any rehabilitation program is to facilitate effective and independent functioning of the children within their own environment. In order to achieve this goal the cognitive components to be trained must be integrated into functional tasks and practiced in real-life situations. In addition, the involvement of both parents and teachers in the training procedures provides them with a better understanding for the rehabilitation strategies and the problem solving strategies of the individual child. These factors have been reported to be important for achieving positive outcome [26]. Braga [6] demonstrated the superiority of family-centered, community-based rehabilitation programmes over institutional training. This finding implies that rehabilitation activities that are incorporated naturally into daily life can be performed more often. It seems likely that there are similar elements in the Amat-c programme that contribute to its positive outcome.

The interaction with a coach who provides feedback and the weekly sessions with skilled professionals that are an integrated part of the Amat-c training may be of further value. These aspects can correct faulty training and actively teach the children strategies for improving functions, while at the same time building their self-confidence. Results from studies on adults suggest that the therapeutic intervention, which occurs in addition to the specific training tasks employed, is an important determinant of the effectiveness of treatment [24,32].

In the present study both groups showed a preserved age-related level of intelligence, indicating normal cognitive development. Research suggests [3], however, that the specific neuropsychological functions which are particularly vulnerable to impairment as a result of acquired brain injuries may not be detected by the full scale IQ score.

More specific neuropsychological tests appear to be required in order to assess the subtle neuropsychological deficits often reported after acquired brain injuries.

The significantly greater improvement in the treatment group as compared to controls with respect to the verbal comprehension factor in the WISC- III observed here was unexpected and might indicate that the Amat-c also may transfer to non trained tasks. The verbal comprehension factor is included among the so-called "crystallized skills," i.e. general knowledge and word knowledge which have been reported to be more amenable to rehabilitation following brain injury than are the "fluid skills", i.e. perceptual organizational factor and speed of processing [4]. Indeed, the indices of the perceptual organization and the speed of processing did not improve significantly in our treatment group.

In several studies, young age at injury, severity of injury and nature of injury has been found to have an influence on the outcome following brain injury [10,33]. However, in the present study, possibly due to small groups and heterogeneity, no influence of these variables on the outcome of the treatment could be demonstrated. The fact that the children in the control group did not show the typical practice effects on some subtests after repeated testing could possibly be explained by the imbalance between the groups with regards to diagnosis with more children having malignant brain tumors in the control group. It is important to consider that children with treated malignant tumors do not have static lesions and this may account for some of the findings. However, in order to control for this we used a stratified Mann-Whitney test which confirmed the statistical significant treatment effect. Another approach to evaluate the efficacy of the training could have been a cohort design where it would be possible to match a treated child to an untreated control according to multiple dimensions that might influence outcome. However, the great lack of randomized controlled studies within this research field for children made us choose the present research design, where we focused more on the cognitive dysfunctions than on the aetiology for this. In future studies it will be of interest to expand our findings and to relate the responsiveness to Amat-c treatment also to localization of brain damage and to the type of treatment of e.g. brain tumours.

The results from this follow up study are encouraging and suggest that this form of broad based cognitive training may help. Interventions with children are recommended to address family issues as the family often experience stress associated with their child's impairment. It has also been shown that treatment conducted at home or at school could facilitate generalization of learning [35].

It seems likely that the elements described above which are integrated in the cognitive training programme used in the present study programme contribute to its positive outcome.

The everyday routines of parent or teacher-child interaction, at home or at school may provide a better understanding for the rehabilitation strategies and the problem solving strategies of the individual child. In addition, the weekly sessions with skilled professionals may be of further great value. However, it will be important to further study the effects of this training programme in larger more specific diagnostic groups, as well as to what extent these test effects may positively transfer to the children's everyday life in school and at home.

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