The Cognitive Remediation Therapy Program Among Children with ADHD: Tunisian experience

La remédiation cognitive dans le Trouble Déficit de l'Attention Hyperactivité: expérience Tunisienne

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RÉSUMÉ

Introduction: Le Trouble Déficit de l'Attention avec Hyperactivité (TDAH) est associé à des deficits attentionnels et exécutifs. La remédiation cognitive est une stratégie d'intervention qui a pour cible ces fonctions déficitaires.
But: Adapter et appliquer le programme de remédiation cognitive CRT (Cognitive Remediation Therapy) auprès des patients présentant un TDAH et d'en évaluer l'efficacité.
Méthodes: Etude expérimentale portant sur des enfants et adolescents présentant un TDAH dont le diagnostic a été confirmé par le K-SADS-PL. Le programme de remédiation a été conduit sur une période moyenne de 14 semaines à raison d'une séance par semaine de 40 minutes chacune. Les patients ont été évalués à l'aide de l'Attentionnel Network Test avant le début de l'intervention et une semaine après la fin.
Résultats : Parmi les 30 patients inclus, 14 étaient arrivés au terme de la prise en charge. Neuf patients ont accompli le test attentionnel post CRT. Leur moyenne d'âge était de 9 ans. Le nombre moyen des séances effectuées était de 14,5. En post CRT, les patients ont présenté un raccourcissement global des temps de réaction (p=0,004) avec un nombre moindre d'erreurs d'omissions. Ils ont également commis moins d'erreurs dans les situations incongruentes en post programme, avec une amélioration significative de l'effet de conflit (p=0,009) signant un meilleur contrôle exécutif.
Conclusion: La remédiation cognitive est une prometteuse modalité dans la prise en charge du TDAH. D'autres recherches sont nécessaires pour mieux documenter ses effets et les conditions optimales requises pour sa mise en place.

Mots-clés
Remédiation cognitive, Déficit de l'attention avec hyperactivité, Enfant

SUMMARY

Background: Attention-Deficit Hyperactivity Disorder (ADHD) is associated with neuropsychological deficits including executive and attentional impairments. The cognitive remediation therapy is a new promising technique designed to improve the neurocognitive abilities damaged in ADHD.
Aim: Adapt and apply the cognitive remediation program CRT (Cognitive Remediation Therapy) for children and adolescents with ADHD and to evaluate its effectiveness on attentional and executive abilities.
Methods: Children and adolescents with ADHD, diagnosed using the K-SADS-PL questionnaire was involved in the study. The CRT program was administered for an average period of fourteen weeks with a rate of one session per week of 40 minutes each. The Attentional Network Test was administered prior to the intervention and one week after.
Results: Of the 30 patients included, 14 had reached the end of the program. Among them, nine patients passed the attentional test post CRT, thus constituting our final sample. Their average age was 9 years. The mean number of sessions performed was 14.5. Post CRT, the mean of patient's response time was found to be shorter (p=0,004) and the frequency of omissions errors was also lesser than that found at the initial assessment. Patients also committed fewer errors in incongruent situations in post program, with a significant improvement of the conflict effect (p= 0.009) signing a better executive control.
Conclusions: Cognitive remediation is a promising new modality in the treatment of ADHD. Further research is needed to better document its effects and the optimal conditions required for setting it up.

Key-words
Cognitive remediation therapy, Attention deficit hyperactivity disorder, Child.

Since the description of George Still in 1902, the Attention Deficit Hyperactivity Disorder (ADHD) has continued to be of growing scientific and clinical interest: firstly, by the prevalence of the disorder, estimated to 3-7%, by the American Psychiatric Association (1); secondly, by its incidence on academic learning, social relationships, psychological health and in a long-term view, on the individual outcome. All over the years, the theoretical concepts of this disorder, as well as its etiopathogenic hypotheses, evolved. Since the late 90s, neurobiological (2), genetic (3), and recently neuropsychological research were developed leading to various theoretical models (4-6). Hence, neuropsychological studies have been conducted showing cognitive deficits associated with ADHD, in attentional and executive functions, and mainly demonstrating an inhibition, planning and working memory deficit (7-9).

The need to develop new treatments in ADHD was encouraged by the uncertain response to medication and limited long-term benefits. In addition, non-pharmacological interventions generate more interest from parents of children and adolescents with ADHD, possibly due to the reluctance to psychoactive substances and to the putative effect of these treatments on children development (10). This opened therapeutic issues to non-pharmacological treatments targeted to improve the neurocognitive dysfunctional abilities in ADHD, such as cognitive remediation therapy.

Originally, studies on brain plasticity raised the development of cognitive training, which allows functional recovery and structural-functional reorganization of neural networks underlying cognitive functions (11). Cognitive remediation therapy presents currently a growing interest among ADHD children and adolescents. Overall, the studies to date showed promising results regarding the effectiveness of cognitive remediation therapy in ADHD (12, 13), although intervention methods are widely disparate from one study to another in the type of program (computerized versus paper and pencil programs) as well as in the number of sessions, duration of the program and neuropsychological evaluations that has been assessed.

The purpose of this preliminary work was to adapt and apply the cognitive remediation program CRT (Cognitive Remediation Therapy) for children and adolescents with ADHD, and to evaluate its effectiveness on attentional and executive abilities. Our hypotheses state that patients with ADHD will benefit from CRT treatment, to improve attention and executive abilities.

METHODS

The informed consent of parents and children who participated to this study was obtained, after setting out the terms of being part in the cognitive remediation program and after giving all explanations concerning the experimental nature of the study.

Participants:

Participants (n=30) aged from 7 to 15 years were recruited in clinical population, at the child and adolescent psychiatry department of Razi hospital, using the Conners Scale (parents and teachers) in its Arabic version (for details see Figure 1). To confirm the ADHD diagnosis, a psychiatric interview and the semi-structured clinical interview, the Kiddie-SADS Present and Lifetime Version (K-SADS-PL) (14) were conducted.

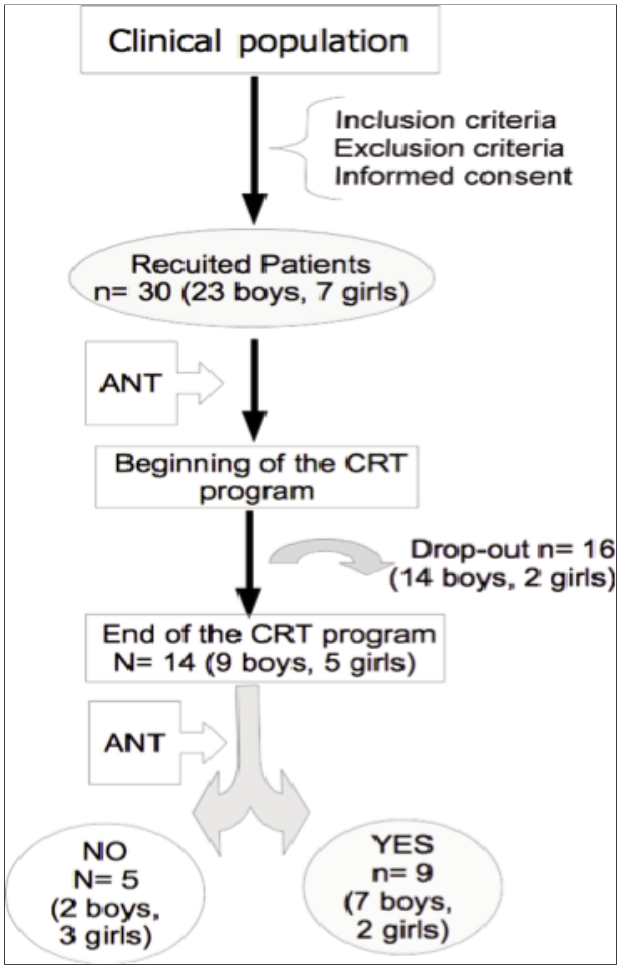

Figure 1: The progress of the study

Participants were free from any somatic and neurological disease and had a quotient of development evaluated by the Raven's colored progressive matrices (15) superior to 90.

Patients receiving pharmacological treatment were included with a stable medication status during the study (molecule, posology).

Neuropsychological measure:
Assessment of attentional functions was carried using the Attentional Network Test (ANT), a measure that allow independent assessment of the efficiency of the three attention networks (alerting, orienting, and executive control) within the context of a quick and simple computerized task (16). The ANT is a combination of a flanker task and a cued reaction time task. Participants indicate the direction of a central arrow that is flanked by four arrows (two per side) pointing in the same direction as the central arrow (congruent condition) or in the opposite direction (incongruent condition); in the neutral condition, straight lines flank the central arrow.
Arrows are preceded by one of three types of cues (center cue, double cue, spatially informative cue; all of which are temporally informative) or no cue (a temporally uninformative condition). The center and double cues indicate that the arrow stimulus will occur soon, and the spatially informative cue is 100% predictive of target location (17). The ANT provides two measures of performance, response time (RT) and error rate (ER), and the three network scores are calculable within each of these measures.

Intervention:
The cognitive remediation program used in the study is the French version of «Cognitive Remediation Therapy-CRT". The CRT is a paper / pencil remediation method administered face-to-face therapist / patient, which includes three modules: cognitive flexibility, memory and planning. These various modules are performed using booklets that fully exhibit the method and target different cognitive functions such as attention, executive function, memory, reasoning and problem solving (18, 19). Since the CRT was originally intended for adults, in our study, some of the proposed tasks couldn't be retained because of their difficulty. Moreover, among the selected exercises some have been adjusted to the child's level by making them easier and playful while keeping the same basic principle.

Design and procedure:
The CRT program was administered for an average period of fourteen weeks spread over the different modules at a rate of one session per week of 40 minutes each. At each session-end, the therapist talk to the parents for few minutes to inform them about the exercises that have been practiced, the skills trained and how parents could implement those skills in everyday life for their children.
Assessment of attentional abilities was carried before the beginning of the program and one week after the achievement of the CRT program.
Among the 30 patients initially included, 14 had reached the end of the program. Among them, only nine performed the final assessment, the others didn't come back despite the formal convocation, for the final assessment. Children' parents that have been lost at the follow-up were also contacted by phone to explain the reasons of their absence to the post program assessment (Figure 1).

Statistical method:
The comparison of ANT results in pre and post CRT program was performed using the paired-samples t test with SPSS (Statistical Package for the Social Science) in its 20th version.

Ethical Statements
The study was conducted in the child and adolescent psychiatry department of Razi Hospital within the research unit UR12SP20: "Processus cognitifs dans la pathologie psychiatrique" dependent on the Ministry of Health and Higher Education of Tunis and Razi Hospital. No funding was received for the study.
Informed consent was obtained from all individual participants included in the study.
All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

RESULTS

Participants:
The clinical and socio-demographic characteristics of the population are displayed in Table 1. Participants lost to follow up had a mean age of 9,46 years. Most of them abandoned the CRT program between the 5th and the 10th session. According to parents, the drop out was mainly due to the geographical remoteness, the constraining schedules of sessions and the low motivation of the participants.

Table 1: Socio-demographic and clinical features

	Initial population (n = 30)	Final population (n = 9)
Age (mean, sd)	9,5 (2,04)	9,1 (1,63)
Gender (n)		
Male	23 (76,7%)	7 (77,8%)
Female	7 (23,3%)	2 (22,2%)
ADHD subtype (n)		
Combined type	21 (70%)	5 (55,6%)
Inattentive type	9 (30%)	4 (44,4%)
Medicated patients (n)	8 (26,6%)	4 (44,4%)
Methylphenidate	4	3
Atomoxetine	4	1
CRT Sessions Attended (mean, sd)	11,35 (5,5)	14,5 (2,5)
Cognitive flexibility	4,14 (1,2)	4,5 (1)
Memory	3,59 (2,57)	5,5 (0,8)
Planning	3,88 (2,43)	4,5 (1,2)

Attentional assessment:
Compared to the initial, preprogram performance, the participants showed better results on the Attentional Network Test in post CRT program: the mean response time was found to be shorter (p=0,004) and the number of errors was also (p=0,46) compared to the initial assessment. Patients also committed fewer errors in the incongruent condition (p=0,001), with a significant improvement of the conflict effect (p=0,009) (Table 2).

Table 2: Results on the Attentional Network Test

	Pre CRT Mean	Post CRT Mean	P
Reaction time (ms):			
Hits RT	1020	876	0,004
RT/ Condition			
Incongruent	1135,51	962,46	0,001
Central cue	978,38	868,88	0,017
No cue	1059,27	925,27	0,000
Errors (n):			
Overall errors	144	113	0,46
Wrong responses	86	70	0,45
Omissions	49	38	0,351
Perseverations	9	5	-
Errors/Incongruent condition (n):			
Wrong responses	73	58	0,429
Omissions	26	19	-
Attention Networks (ms):			
Conflict	204,26	134,14	0,009
Orientation	- 6,04	35,84	-
Alerting	79,44	108,8	0,36

RT= Reaction Time = Mean reaction time for each clue and flanker condition; Hits= Number of correct responses; Hits RT = Median RT for correct responses; Omissions = RT = 0 ms; Perseverations = 0 ms < RT < 300 ms; Wrong responses= All other error responses than omissions and perseverations; Overall errors= Number of overall errors; Attention Networks: Conflict = RT for incongruent flanker – RT for congruent flanker, Alerting = RT for no cue – RT for double cue, Orienting = RT for central cue – RT for orienting cue.

DISCUSSION

Despite the limited number of children who achieved the CRT program, the results of this preliminary study suggest that CRT had a positive impact on attentional process with an improvement in sustained attention attested by the fact that patient's response time was found to be shorter (p=0,004) and the frequency of omissions errors was lesser than that found at the initial assessment. A significant improvement in executive control shown by improvement of the conflict effect (p= 0.009) was also found. No improvement was found in the orienting and alerting attentional networks. This could be due to the fact that the CRT program mainly targets executive functions. Worth noting that these results cannot be due to a learning effect since the evaluations were performed at an average of 4 months apart, and that the allocation of the trials in the ANT is random.
In our study, an average of 14,5 sessions were carried at a rate of one session per week of 40 minutes each. This rate was conditioned by the geographical remoteness and the schedules of children, who came out of school hours, and the parents accompanying them. In the literature, interventions were held on a maximum of 16 weeks in which 16 to 64 sessions were conducted and lasted between 20 and 60 minutes (12). To date, the sufficient number of training sessions and the duration of the intervention required to be effective is not yet established in children. For anorexia nervosa, Tchanturia et al. (2014) report module, which includes 10 sessions. The aim is to do one or two sessions per week, each session should last approximately 30–40 minutes (20).
The comparative pre/post CRT results of the ANT showed that the participants displayed better-sustained attention after the program. This was evidenced by shorter RT hits (p=0,004) and lesser omission errors (p=0,351). In the studies of Parent (2010) and Tamm et al. (2013) who conducted a computerized cognitive remediation and training program among ADHD children, the omission errors were analyzed to assess sustained attention using respectively the Conners' continuous performance test (CCPT-II) and the Quotient ADHD System. These two neuropsychological tools evaluate attention similarly to the ANT. In the former, 26 ADHD children were trained with a program targeting response inhibition at a rate of 3 sessions per week during 12 weeks. Only 15 participants were selected for analysis. The results showed that the number of omission errors was lower after the training, but with no significant differences comparing to controls (12). In the latter, 45 children were trained using the Pay Attention! program. The intervention took place over 8 weeks with 2 sessions per week of 30 minutes each. On the Quotient continuous performance task, the results showed a small effect in the intervention group to make more errors of omission. The authors argued that the program might have had an unintended negative effect. Hence the patients might be slowed too much and therefore failed to respond quickly enough resulting in an increasing number of errors of omission (21).
In our study, the ANT results post CRT program showed that the participants responded faster in the incongruent condition (p=0,001) reducing the number of wrong responses (p=0,429) with a significant improvement of the conflict effect (p=0,009). These results sign a better executive control ability including a greater inhibition capacity. This executive function was targeted by many exercises selected from the different modules. In the literature, the results of various studies indicate that the overall training of a specific cognitive function leads to an improvement of that function (11) and may be generalized to some others given the neuroanatomical connections (22). Response inhibition happens to be the most

consistently evaluated executive function in the studies that have investigating the efficiency of cognitive remediation therapy in ADHD children. In some studies (12, 13), this function was directly targeted by the remediation while in others (21, 23), the effect on response inhibition was assessed after working memory or attention training. Results were discordant across studies that used different training process with dissimilarity in the program used as well as in the duration and frequency of sessions, the cognitive functions assessed and the neuropsychological tools used (24).

The results of this first pilot study tend to support that cognitive remediation therapy (CRT) may improve executive functions in children with ADHD.

However, further studies are warranted to confirm this result with larger samples. The noticeable loss of participants during the program was mainly due to the remoteness, the constraining schedules of sessions and the low motivation of the participants. This leads to discuss the possibility of implementation of this type of program proximal to the child's environment (home or school). This initiative has been adopted in some studies and the programs used were computerized, so that the child could carry out the activities at school or at home (12, 21). In our study, CRT being a paper / pencil method, the therapist can select in advance the session exercises and provide them to the parents in order to be done at home under their supervision and within a preset time. Indeed, CRT even if it could be a less feasible program, is considered as a real cognitive remediation method, and is fully personalized to the child level and performance. However, the efficiency of this treatment has to be more documented, as a professional support remains relevant to establish favorable conditions to the proper functioning of such intervention.

In the following studies, it's also necessary to reconsider the motivational aspects. Motivation was referred in various theoretical models explaining the pathogenesis of ADHD (25). In cognitive remediation programs, the motivation of participants is generally provided by repetitive gratifications and feedback on performance. In Shalev's study (2007) this was represented by a winning points system allowing the child access to higher difficulty levels (26). In Parent's study (2010) the reward was a gift card gained after the accomplishment of a certain number of sessions. In our study, it was essentially the therapist that provided the positive reinforcement by encouraging actively the participants. Several researchers investigated the impact of motivation on the efficiency of training programs. Prins et al. (2011) showed that adding game elements to standard computerized working memory training significantly enhance motivation and performance of children with ADHD as well as improve training efficacy. Furthermore, adjusting the difficulty level of the exercises to the patient's age and performance has been identified as an important element for the effectiveness of these programs (27). This may have been lacking in our study. Hence the patients who dropped out were relatively older (mean age 11.5 years), and referring to their parents' arguments, reported low motivation. The difficulty of the exercises was perhaps not well adjusted to satisfy these participants. In the future, in order to adapt the CRT program to child and adolescents it would be interesting to create modules adjusted for each age group by adding playful exercises for younger children and adjusting the difficulty level of tasks designed for adolescents.

Beside attention abilities, other cognitive functions are trained in the CRT program including flexibility, memory and planning. So the perspective for the next recruitment of patients, is to enlarge the neuropsychological evaluation including verbal executive tasks such as a verbal fluency test (phonemic and semantic), visuospatial organization with the Rey-Osterrieth Complex Figure Test (28), verbal inhibition with the Hayling sentence completion test (29) in its Arabic version, and a memory span test. In addition to neuropsychological assessment, it is also necessary to evaluate the clinical symptomatology after cognitive remediation, especially since some studies support a relative dissociation between cognition and symptoms and where symptoms can but do not need to arise as a consequence of cognitive deficits (30). It's also necessary in the subsequent studies to include more un-medicated ADHD children. In fact, it has been reported in several studies that in addition to the effects on clinical ADHD symptoms, methylphenidate and atomoxetine also improve executive function (31, 32). However, there is a possibility of a reciprocal interaction between cognitive remediation therapy and medication, one can enhance the effect of the other.

CONCLUSION

Using the CRT program constituted an innovative and promising issue in the treatment of ADHD. However, further work is necessary to better document its effect, as well as the conditions governing its application to reach an optimum level of efficiency.

With the perspective of a larger sample in future work, future studies could aim to identify the clinical and neuropsychological profile of the patients for whom the CRT will be the most beneficial taking into account the age, the ADHD subtype, the severity of clinical symptoms and of cognitive impairment.

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