The International Journal of Psychosocial Rehabilitation
Volume 21, Number 1
January 2017 to December 2017

Place of cognitive remedition therapy in the management of autism spectrum disorder

Melek Hajri1,2
Zeineb Abbes1,2
Houda Ben Yahia1
Mariem Boudali1.2
Meriem Hamza 2,3,
Asma Bouden1,2,
Ali Mrabet2,4,
Isabelle Amado5.

Child and Adolescent Psychiatry Department- Razi University Hospital – Manouba -Tunisia

1: Child and adolescent psychiatry department, Razi Hospital, Manouba, Tunisia
2: El Manar Tunis University, Faculty of Medicine of Tunis, Tunisia.
3: Child and adolescent psychiatry department, Mongi Slim Hospital, Marsa, Tunisia
4: Military Center for Health and Environment Protection / General Directorate of Military Health. Tunisia
5: Psychiatrist; Director, Reference Center for Cognitive Remediation and Rehabilitation (C3RP), Sainte Anne Hospital, Paris

Citation:
Hajri A, Abbes Z, Yahia HB, Boudali M, Hamza M, Bouden A, Mrabet A, Amado I. (2017)
Place of cognitive remedition thearpy in the management of autism spectrum disorder.
International Journal of Psychosocial Rehabilitation. Vol 21 (1) 55-66

Abstract

Background : Autism Spectrum Disorder (ASD) is known to be associated with Cognitive impairment, especially executive dysfunction. Cognitive Remediation Therapy (CRT) is a novel rehabilitation method aiming to produce improvement in cognitive processes. CRT has been used in patients with schizophrenia. Taking into account the overlap between ASD and schizophrenia, the aim of our study was to adapt and apply the cognitive remediation program CRT for children and adolescents with autism spectrum disorder, and evaluate its effectiveness on the executive functions, clinical symptoms and school performance.
Methods: A cross-sectional study conducted with children and adolescents with autism spectrum disorder according to the DSM-5 criteria. The program called CRT was provided at the rate of one session (duration = 45 minutes) per week. The patients were evaluated before the beginning of the intervention and one week after its end. The evaluated parameters were intellectual abilities, cognitive flexibility, inhibition, working memory, planning, clinical symptoms and school results.

Results: Twenty-five subjects were included. 16 patients completed the program. After cognitive remediation, children showed significant improvement in intellectual abilities ($p<10-3$), scores of phonemic flexibility ($p = 0.027$), working memory ($p = 0.003$ for the forward digit-span and $p = 0.003$ for the backward digit-span), clinical symptoms ($p<10-3$) and school results ($p = 0.001$).
Conclusion : The cognitive remediation is a promising technique that can be effective in the management of children with autism spectrum disorder.
Key words : Autism, Child, Cognitive remediation, Cognitive Remediation Therapy, Executive function.

Introduction:

Autism Spectrum disorders arouse increasing interest by their prevalence estimated at 1%(Won, Mah, & Kim, 2013), and their impact on social relationships, psychological health and individual's academic progress. The significant development in the field of cognitive neuropsychology stresses the existence of cognitive deficits in patients with ASD. These cognitive deficits primarily concern executive functions (EF). EF is a relatively new concept that reflects 'highly advanced' mechanisms comprising many components of cognitive processes(Stuss & Levine, 2002; Watanabe et al., 2005). In patients with ASD, executive dysfunctioning involve cognitive flexibility, inhibition, working memory and planning (Ozonoff, Pennington, & Rogers, 1991; Pellicano, Maybery, Durkin, & Maley, 2006). These executive dysfunctions could, on one hand explain some autistic symptoms such as repetitive behaviors(Robinson, Goddard, Dritschel, Wisley, & Howlin, 2009; White, 2013), as well communication and social interactions disorders(Barendse et al., 2013; Bennetto, Pennington, & Rogers, 1996). On the other hand, they could explain school difficulties found in these children.

In this context, cognitive remediation (CR) is a new therapeutic strategy that aims to improve cognitive functions deficits. This postulate is based on the hypothesis of cerebral plasticity. The use of this therapeutic technique dates back to several years, among various clinical populations with cognitive deficits. Such is the case of victims of craniocerebral trauma or stroke. The first use in psychiatry interested patients with schizophrenia, given the cognitive deficits associated with the disease(Heinrichs & Zakzanis, 1998). This treatment strategy has given promising results in this population, as demonstrated by several studies(Penades et al., 2006; S. Tan et al., 2015; Wykes, Huddy, Cellard, McGurk, & Czobor, 2011; Wykes et al., 2007; Wykes, Reeder, Corner, Williams, & Everitt, 1999). CR programs dedicated to children suffering from attention deficit disorder with hyperactivity (ADHD) have also been developed, and have given interesting results(Hamza, 2014). Several projects have been developed on the training of subjects with ASD using computer programs over the past ten years (Grynszpan, Martin, & Nadel, 2007). These programs target different skills relating mostly to social cognition (Bernard-Opitz, Sriram, & Nakhoda-Sapuan, 2001). The social nature of these training contrast with CR programs usually used in schizophrenia(Grynszpan et al., 2011) where the exercises essentially/ primarily target neurocognitive functions.

Thus, to this day and to our knowledge, our study is among the first to be interested in the CR strictly speaking in children with ASD. In a study conducted by Weiner et al in 2010, the authors applied a part of Cognitive Remediation Therapy program (CRT) on two adult subjects with Asperger syndrome. An improvement in tests of working memory, flexibility and self-esteem in one of the subjects was observed.

The objectives of our study is to apply and adapt the CRT program for children with ASD, and to evaluate its effectiveness on executive functions, clinical symptoms and school performance. We used a version of the CRT modified and adapted to children, it demonstrated evidence in children with ADHD(Hamza, 2014).

Methods:
The study was performed by the 12SP20 Research Unit ("Cognitive processes in psychiatric disorders") - Faculty of Medicine of Tunis.
It was a cross-sectional study involving children and adolescents with ASD according to DSM-5.

The inclusion criteria are:

-Diagnosis of ASD according to the Diagnostic and Statistical Manual, 5th (DSM-5): participants were screened with a psychiatric interview using DSM-5 criteria to confirm diagnosis.
-Cognitive difficulties reported by parents.
-On a stable dose and type of medication, for at least one month prior to inclusion.
-Age between 6 and 21.
-Regular school curriculum.

Participants are not included if they had:

-a history of seizures or any other neurological disorder
-a history of a chronic medical condition
-mental retardation

Outcome assessments
The main study outcomes (executive functioning, clinical symptoms and school results) were measured at baseline and one week after achievement of treatment.
Intellectual efficiencies were assessed using Raven Progressive Matrices (CPM) which evaluates general non-verbal intellectual abilities as well as the ability of deductive reasoning (Raven, 2000).

Cognitive flexibility was assessed using verbal and semantic fluency tests: participants are asked to say as many words as possible from a category in a given time (usually 60 seconds). This category can be semantic (such as animals) or phonemic.

In our study, we chose the letter "m" "م" in Arabic. In fact, neuropsychological research performed by Aguibi and Bouaziz in 1998 showed that this letter is productive among children aged from 6 to 12. Besides, we adjusted the time to 2minutes.

As for semantic fluency, we chose both "clothes" and "animals" as stated in a prior Tunisian study (Bellaj, Salhi, Le Gall, & Roy, 2015).
For each semantic or phonemic category, we accounted words number. A one point credit was awarded for each correct response.

Inhibition was assessed using either the Hayling Sentence Completion Task, or the Colors and Animals Attention Test (CAAT), for those who couldn't perform the first test.

The Hayling test includes two parts, A and B. In both parts, we recorded the response time (in seconds) and the produced word. For the response time, we calculated the "Additional Thinking Time" (ATT) which is the difference between the latencies in parts A and B (B-A). Correct responses number and error score were also calculated (Wang et al., 2013). We used a child version of HSCT elaborated by Bellaj et al in 1999 .It is not still published. However, we obtained authors' approval in order to use this test.

Working memory: was assessed by the mean of forward and backward digit span.This test consists in recalling without delay series of digits of increasing sizes presented auditively at a rate of one digit per second in direct order then in indirect order. This test allows to assess verbal working memory. It did not need adaptation.

Planning: We evaluated planning by the mean of The Rey-Osterrieth Complex Figure (ROCF). This tool consists in copying then drawing from memory a complex geometric figure after a delay of three minutes (ROCF: A or B)

(Watanabe et al., 2005). The duration of the test is open for both the copy and the reproduction. The order and accuracy in which the figure is copied and drawn from recall are taken into account. Concerning the rating, it is in type and digital.
We used a point scoring system which is based on the presence and accuracy of the 18 units of the ROCF.

Clinical symptoms: They were assessed using The Childhood Autism Rating Scale (CARS). It is a behavior-observation instrument aiming to differentiate children with autism from those with other developmental disorders and to quantify severity of most autism symptomatology. This brief questionnaire contains 15 items, assessing social communication and behavioral flexibility, which are captured on a graded scale (from non-autistic to severely autistic) by a clinician or other nominally trained observer (Breidbord & Croudace, 2013).

School performance: was evaluated by school results.

Interventions

Cognitive remediation therapy
CRT was set out in the Frontal/Executive program (Delahunty and Morice, 1996) (Delahunty & Morice, 1993, 1996).
By aiming executive functions, the program tried to ameliorate cognitive functioning in subjects with schizophrenia. It is an individual treatment mostly using pencil and paper tasks and relying on cognitive strategy instruction. It is implemented once a week for between 45 and 90 minutes. The duration of the intervention generally ranges between four and six months.

In the program three modules are included, and delivered in the following order: cognitive flexibility, working memory and planning (Delahunty, Morice, & Frost, 1993; Penadés & Catalán, 2012).

The sessions are divided between the various modules as follows: 8 sessions of cognitive flexibility, 8 sessions of memory and 8 planning sessions. However, this duration could be adapted to each child's level.

Novel techniques are applied, including errorless learning and scaffolding. The later is a learning technique where the therapist tries to coach the subject to answer to problems considering their cognitive limitations.

Exercises turn into a chance not only to apply cognitive strategies but besides to acquire new ones. All the learning procedure occurs during an errorless learning approach with the use of tasks of progressive complexity and with a fixed problem, as much as possible, at the speed of the patients. Afterwards, more practice is required to attain the over-learning of the novel cognitive strategies. The identical procedure implemented across the modules will be utilized to answer everyday issues of planning, working memory, and to some extent cognitive flexibility (Delahunty & Morice, 1993; Delahunty, Reeder, Wykes, Morice, & E., 2002).

An adaptation of certain tasks to children was made making them simpler and "funnier". Furthermore, for non-francophone children, exercises in Arabic were included and those made with French alphabet letters were changed by turning letters into images(Hamza, 2014).

Statistical analysis:
Data were entered and analyzed using statistical logiciel. Comparisons of two independent quantitative variables were performed using parametric or non-parametric tests as the Mann-Whitney test. Comparisons of several independent quantitative variables were performed using non-parametric Kruskal-Wallis test or the Pearson's chi-squared test.

Ethical considerations:
The informed parental consent was obtained, after exposing to them the management modalities in the CR program and explained the experimental nature of the study.

Results:

25 patients were included, 18 had reached the end of the program. Among them, 16 patients achieved the neuropsychological assessments tests after CRT, thus constituting our final sample. Their average age was 10.87 (±3.55) years. The mean number of sessions performed was 22.38(±1.99).

ü Intellectual efficiency

After achievement of CR program, we noticed a statistically positive significant correlation between IQ before after CRT (rho= 0.95; p<10-3). IQ was 27.6 and reached 28.5 after completion of this program. (MD=1.21±2.32). CI 95%= [-1.28;2.55].

-Mental flexibility

The average score in "animals" category raised from 13.16 before CRT to 17 after it (Mean difference=3.06 ± 6.11) (p=0.064). Regarding the "clothes" category, the average score was 10.47 before CRT and 12 after finishing the program(MD=1.42 ±3.87)(p=0.191). As for phonemic fluency, the average score increased from 4.27 in baseline to 7 after it (MD=2.78 ±4.19).This improvement was significant (p=0.027).

Concerning repetitive errors,in "animals" category, the average score increased from 0.56 before CRT to 0.94 after it (MD=0.375 ± 1.58) (p=0.359). More repetitive errors were noticed in "clothes" category after CRT (0.87) in comparison with baseline average score (0.6) (MD=0.28 ± 1.72).This variation was not significant(p=0.547). Patients made also more repetitive errors in phonemic fluency which average score raised from 0.07 before CRT to 0.2after completion of the program (MD=0.14 ±0.53).This variation was not significant (p=0.336).

As for intrusive errors, scores in "animals" category varied from 0.44 to 0.25 after CRT program achievement (MD=-0.18±1.51). This was not a significant variation (p=0.628). In the "clothes" category, the average score raised from 0.93 to 1.2 after finishing the program (MD=0.00 ± 1.41) (p=1.00). Fewer errors were made (1.87 before CRT and 0.87 after it) in phonemic fluency after CRT. This was not a significant improvement (p=0.236) (MD=-0.50±1.50) (Table 1).

-Inhibition

Ten patients were assessed by the means of the CAAT, and six by the means of Hayling Sentence Completion Task.

As for patients who performed Hayling Sentence Completion Task, the latency for sentences in part A was shorter after completion of CRT (32,8 seconds) than before it (38,25 seconds) (MD=-14.33±20.5) (p=0.350). As for part B, the latency was longer after CRT (41 seconds) than at baseline (35 seconds) (MD= 1.33± 3.21) (p=0.54).As for ATT (TB-TA), it non significatntly raises from 20.33 before CRT to 22 at post treatment (MD=-5.33 ±11.93) (p=0.52).Patients gave more correct responses after the program (14,8) than before it (10,33) (MD=1±4.35) (p=0.729). Besides, Hayling score was 10.33 at baseline and 14.8 after completion of the program (MD=0.00 ±4.58) (p=1.00).

Concerning the CAAT, patients showed improvement on interference score which increased from 4.1before CRT to 5.8 (MD=2.05±4.13)after achievement of the program. This improvement was not significant (p=0.279) (Table 1).

-Working memory

Significant improvement (p=0.003) on forward digit span was observed. In fact, the average score raised from 3.38 before CRT to 4 after completion of the program. Concerning backward digit-span, patients displayed significant improvement (p=0.003): the average score was 2.21 before CRT and 3.09 after achievement of the program.

-Planning

In copy condition

Concerning ROCF-A, higher scores were noticed after completion of the progam (40.67) in comparison with baseline (35.83) (MD=-4.83 ± 29.31). This improvement was not significant (p=0.703).

As for ROCF-B, the mean score raised from 23.69 to 27.94 after CRT (MD= -4.25±.6.86). This improvement was not significant (p=.0.123).
A shorter time to copy was observed after CRT (192.1 ± 111.6 seconds than before it (205.6 ±137.5 seconds) (MD= -31.5 ± 104.72). This variation was not
significant (p=0.693).

In recall condition

For ROCF-A, the mean score was 11.5 before CRT and reached 17.75 after achievement of the program (MD=-6.25 ± 12.71). This variation was not significant (p=0.398).
Regarding ROCF-B, higher score was noticed after CRT (10.78) in comparison with baseline (10.71) (MD=-0.071 ±8.53) with p=0.983.
A longer time of reproduction was observed after CRT (120 ± 69.13 seconds) than before it (89 ± 58.93 seconds) (MD= 31.00± 51.4). This variation was not significant (p=0.162) (Table 1).

-Clinical Symptoms

After completion of CRT program, patients displayed lower scores (26.81) comparing with baseline average score (27.87). This was a statistically positive significant correlation (rho=0.876; p<10-3). MD equaled -1.06±2.95, with CI 95%= [-2.636;0.511] (Table 1).

Table 1: Comparison of flexibility, inhibition and planning results before CRT and after it

					Mean Difference	Standard Deviation	Confidence interval		P
							Min	Max	
Flexibility	**Verbal fluency**	**Semantic fluency**	**Animals**	**Score**	3.063	6.11	-0.196	6.321	**0.064**
				Repetition	0.375	1.586	0.397	-0.470	**0.359**
				Intrusion	-0.188	1.515	0.379	-0.995	**0.628**
			Clothes	**Score**	1.429	3.877	-0.810	3.667	**0.191**
				Repetition	0.286	1.729	-0.713	1.284	**0.547**
				Intrusion	0.000	1.414	-0.817	0.817	**1.00**
		Phonemic fluency	**Letter « m » "م"**	**Score**	2.786	4.191	0.366	5.206	**0.027**
				Repetition	0.143	0.535	-0.166	0.451	**0.336**

				Intrusion	-0.500	1.506	-1.370	0.370	**0.236**
Inhibition	**Hayling test**	**TA**			-14.333	20.551	-65.384	36.718	**0.35**
		TB			1.333	3.215	-6.652	9.319	**0.54**
		ATT=TB-TA			-5.333	11.930	-34.970	24.303	**0.52**
		Inhibition score			0.000	4.583	-11.384	11.384	**1**
		Correct responses			1.000	4.359	-9.828	11.828	**0.729**
	CAAT	**X**			2.05	4.13			**0.279**
Planning	**ROCF**	**Copy condition**	**Score**	**ROCF-A**	**-4.83**	**29.31**	**-35.597**	**25.931**	**0.703**
				ROCF-B	**-4.25**	**6.86**	**-9.99**	**1.49**	**0.123**
			Time	**ROCF-A**	**53.00**	89.816	**53.000**	**89.816**	**0.257**
				ROCF-B	**-26.00**	112.732	**-165.97**	**113.97**	**0.633**
		Recall condition	**Score**	**ROCF-A**	**-6.25**	12.71	**-26.47**	**13.97**	**0.398**
				ROCF-B	**-0.07**	8.53	**-7.96**	**7.81**	**0.983**
			Time	**ROCF A**	**-13.00**	66.46	**-610.19**	**584.19**	**0.828**
				ROCF-B	**-38.20**	51.30	**-101.89**	**25.49**	**0.171**

-School Results

The mean score increased 10.57/20 before CRT to 11.08/20 after it, showing a statistically significant positive correlation (p=0.001). MD equaled -0.08±1.44 with CI 95% = [-1.00; 0.834].

Discussion:

In our study, after an average duration of 25.5 weeks of CR and 22.38 sessions conducted, we found that patients who reached the end of the intervention showed significant improvement in the intelligence, working memory, clinical symptoms and school results. At the level of cognitive flexibility, we noted a significant improvement in scores of phonemic fluency. Only few studies were interested in CR among children, and fewer with those with ASD. Thus, we will compare our results with those of patients with schizophrenia, considering the continuum between these two conditions, highlighted by some researchers (Eack et al., 2013; Kastner et al., 2015; Reichelt, Rodgers, & Clapcote, 2012).

Regarding the intelligence, our results join those of a meta-analysis listing 16 studies including 805 patients with schizophrenia, conducted by Grynszpan et al in 2011 (Grynszpan et al., 2011), to assess the effectiveness of a computerized program of CR (Computer-assisted cognitive remediation CACR). A significant improvement of the global cognition was objectified.This is a perfect illustration of the CR objectives, which aims to improve cognitive skills by modifying information processing strategies, while adjusting to the strengths and weaknesses of each individual. These modifications refer to cerebral plasticity.

At the level of cognitive flexibility, our results corroborate those of the literature(!!! INVALID CITATION !!!; Penades et al., 2006; B. L. Tan & King, 2013; Ueland & Rund, 2005; Wykes et al., 1999). Indeed, Wykes et al conducted in 1999 a study describing a randomized trial of an intensive CR program Involving individual daily sessions of 1 hour for up to 3 months (Wykes et al., 1999). Results showed a significant improvement in flexibility

measured with the Wisconsin Card Sorting Test (WCST)(Hill, 2004). This advocates for a relevant effect of the CR on cognition. This improvement in flexibility could'nt be attributable to practice, as the CR program encompasses many exercices that were dissimilar to the content of the neurocognitive tests.

Patients learned to engage information-processing strategies, which can be used in a variety of tasks. One other possible explanation to cognitive improvement is therapeutic contact. In fact, CR was designed to be active.

Moreover, in our study, we noted an increase in number of repetition and intrusion errors in "clothes" category. This could be explained by the fact that the child, when seeking to provide more answers corresponding to the category, made more errors.

At the level of inhibition, patients assessed by the mean of the Hayling test displayed mixed results: improvement in parameters related to time and increase of correct responses number, however, error score increased, thus constituting a negative result. Those assessed by the mean of CAAT showed a non significant improvement. In fact, although extending their thinking time, patients made more errors at the end, reflecting a cognitive rigidity.

Inhibition has been involved in several researchs. Hamza et al conducted a study in 2014, involving children and adolescents with ADHD who received CRT program. Patients were evaluated using The Attentional Network Test (ANT) (Fan, McCandliss, Sommer, Raz, & Posner, 2002) administered prior to the intervention and one week after finishing it. At post treatment, patients committed fewer errors in incongruent situations, with a significant improvement of the conflict effect, signing a better inhibition control(Hamza, 2014).

In a study carried out by Choi et al in 2005, authors examined some of the factors associated with a positive response to CR, among them treatment intensity. Higher treatment intensity was associated with greater cognitive improvement(Choi & Medalia, 2005).

In our study, CRT was provided at the rate of one session per week. Higher intensity couldn't be realized, as children had a regular school curriculum, and most of them were living far from the hospital.

Regarding the working memory, we observed a significant improvement in the forward and backward digit-span. Indeed, in our CR program(CRT), an entire module was dedicated to memory, which is also solicited in many tasks in other modules (manipulation of shapes, numbers and letters, sequential search, change of number, double counting ..). According to literature about CR, the stimulation of a deficient cognitive function causes an improvement of the same function(Medalia & Lim, 2004).

Our findings are in line with literature data (Grynszpan et al., 2011; B. L. Tan & King, 2013; Ueland & Rund, 2005; Wykes et al., 1999). In fact, Tan and King conducted a study evaluating the effects of CR on neurocognition and functioning among patients with schizophrenia(B. L. Tan & King, 2013). 36 participants benefited from a computer program of CR. The results objectified a significant improvement in the forward and backward digit-span, assessed by the Wechsler Adult Intelligence Scale (WAIS)-Digit Span Forward and Backward(Wechler, 1981). This improvement in working memory is particularly interesting. Indeed,this cognitive function is highly related to social functioning in patients with schizophrenia(Green, Kern, Braff, & Mintz, 2000). Moreover, literature findings showed that working memory was amenable to improve through a shorter duration of treatment. Besides, Rose and collaborators found that an improvement in memory scores was significantly associated with the improvement in self-esteem, which would generate a dynamic of success(Rose et al., 2008).

As for planning, a non significant improvement was observed in our study. This executive function was studied in literature. In a Meta-analyses of randomized controlled trials of social cognitive remediation carried out by Pilling et al in 2002, no benefit of CRT on planning was found. Authors insist on efforts that should be directed to wider psychological and environmental interventions that take account of the cognitive deficits present in schizophrenia(Pilling et al., 2002).

Concerning clinical symptoms, we also observed a significant improvement in the CARS ($p<10-3$). Indeed, unlike computer programs, the CRT is an individual relational therapy involving highly enriching dynamic interactions between the subject and the therapist.

However, in a study made by Penades et al in 2006, it was observed that although CR has a relevant effect on cognition, its impact on symptoms is little. It should be stressed that symptoms and neuropsychological functioning in chronic functioning are not related and follow different courses (Penades et al., 2006).

In our patients, a significant improvement in school performance was objectified ($p=0.001$) at the end of the CRT program. Indeed, the benefits of CR translate to practical gains for the participants. In fact, school tasks include reasoning and problem solving exercises that have already been trained throughout the CRT program. This improvement in school results could also be due to improved self-esteem. Indeed, CRT is designed to ensure maximum success for the participants. The therapist constantly strives to encourage participants so that the therapy represents for them a positive and rewarding experience.

The CR effect on social functioning has been approached by various authors(Choi & Medalia, 2005; Penades et al., 2006; B. L. Tan & King, 2013; Wykes et al., 2011). In a study conducted by Tan et al in 2013, participants who achieved CR program displayed significantly greater improvement and better vocational skills (B. L. Tan & King, 2013). In fact, CR could lead to significant positive impact on functioning when provided in the context of a psychiatric rehabilitation program(McGurk, Twamley, Sitzer, McHugo, & Mueser, 2007; Wykes et al., 2011).

Limitations :

The current study had some limitations, so the results should be interpreted with caution. The first issue was that of small sample size, which made it difficult to extrapolate results. In addition, we didn't include a control group because of ethical considerations: the control group would have had to come to the hospital weekly in order to practice games, at the expense of their school hours and multidisciplinary care sessions including occupational and speech therapy. Another limitation is that it is unclear how many training sessions are optimal for patients with ASD with executive dysfunction.

It appears from our study that CR, a promising therapeutic strategy, has demonstrated its benefit in the management of children with ASD. Clinicians are required to conduct further researches to better document its effects, and the conditions enabling to reach an optimal level of effectiveness (program type, sessions frequency, duration of the management, training modality). Further studies are also required to determine the clinical and neuropsychological patients' profile for whom the CR will be the most beneficial.

Acknowledgements
We thank the patients participating in this study, as well as their parents.

Disclosure statement
The Authors declare that there is no conflict of interest.

Author's contributions
MH, ZA, HBY, MBD and MH conceived the trial. MH authored the first version of this article, which was then revised and optimized by AM, AB and IA.

References

Barendse, E. M., Hendriks, M. P., Jansen, J. F., Backes, W. H., Hofman, P. A., Thoonen, G., . . . Aldenkamp, A. P. (2013). Working memory deficits in high-functioning adolescents with autism spectrum disorders: neuropsychological and neuroimaging correlates. J Neurodev Disord, 5(1), 14. doi: 10.1186/1866-1955-5-14

Bellaj, T., Salhi, I., Le Gall, D., & Roy, A. (2015). Development of executive functioning in school-age Tunisian children. Child Neuropsychol, 1-36. doi: 10.1080/09297049.2015.1058349

Bennetto, L., Pennington, B. F., & Rogers, S. J. (1996). Intact and impaired memory functions in autism. Child Dev, 67(4), 1816-1835.

Bernard-Opitz, V., Sriram, N., & Nakhoda-Sapuan, S. (2001). Enhancing social problem solving in children with autism and normal children through computer-assisted instruction. J Autism Dev Disord, 31(4), 377-384.

Breidbord, J., & Croudace, T. J. (2013). Reliability generalization for Childhood Autism Rating Scale. J Autism Dev Disord, 43(12), 2855-2865. doi: 10.1007/s10803-013-1832-9

Choi, J., & Medalia, A. (2005). Factors associated with a positive response to cognitive remediation in a community psychiatric sample. Psychiatr Serv, 56(5), 602-604. doi: 10.1176/appi.ps.56.5.602

Delahunty, A., & Morice, R. (1993). The Frontal Executive Program. A Neurocognitive Rehabilitation Program for Schizophrenia, Revised Edition. Albury, NSW, Australia: Department of Health.

Delahunty, A., & Morice, R. (1996). Rehabilitation of frontal/executive impairments in schizophrenia. Aust N Z J Psychiatry, 30(6), 760-767.

Delahunty, A., Morice, R., & Frost, B. (1993). Specific cognitive flexibility rehabilitation in schizophrenia. Psychol Med, 23(1), 221-227.

Delahunty, A., Reeder, C., Wykes, T., Morice, R., & E., N. (2002). Revised Cognitive Remediation Therapy Manual. London: Institute of Psychiatry.

Eack, S. M., Bahorik, A. L., McKnight, S. A., Hogarty, S. S., Greenwald, D. P., Newhill, C. E., . . . Minshew, N. J. (2013). Commonalities in social and non-social cognitive impairments in adults with autism spectrum disorder and schizophrenia. Schizophr Res, 148(1-3), 24-28. doi: 10.1016/j.schres.2013.05.013

Fan, J., McCandliss, B. D., Sommer, T., Raz, A., & Posner, M. I. (2002). Testing the efficiency and independence of attentional networks. J Cogn Neurosci, 14(3), 340-347. doi: 10.1162/089892902317361886

Green, M. F., Kern, R. S., Braff, D. L., & Mintz, J. (2000). Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the "right stuff"? Schizophr Bull, 26(1), 119-136.

Grynszpan, O., Martin, J., & Nadel, J. (2007). Exploring the influence of task assignment and output modalities on computerized training for autism. Interaction Studies, 8(2), 224–266.

Grynszpan, O., Perbal, S., Pelissolo, A., Fossati, P., Jouvent, R., Dubal, S., & Perez-Diaz, F. (2011). Efficacy and specificity of computer-assisted cognitive remediation in schizophrenia: a meta-analytical study. Psychol Med, 41(1), 163-173. doi: 10.1017/S0033291710000607

Hamza, M. (2014). Place of cognitive remediation in attention deficit hyperactivity disorder. (MD), Faculty of Medicine of Tunis, Tunis.

Heinrichs, R. W., & Zakzanis, K. K. (1998). Neurocognitive deficit in schizophrenia: a quantitative review of the evidence. Neuropsychology, 12(3), 426-445.

Hill, E. (2004). Evaluating the theory of executive dysfunction in autism. Developmental Review, 24(2), 189-233.

Kastner, A., Begemann, M., Michel, T. M., Everts, S., Stepniak, B., Bach, C., . . . Ehrenreich, H. (2015). Autism beyond diagnostic categories: characterization of autistic phenotypes in schizophrenia. BMC Psychiatry, 15(1), 115. doi: 10.1186/s12888-015-0494-x

McGurk, S. R., Twamley, E. W., Sitzer, D. I., McHugo, G. J., & Mueser, K. T. (2007). A meta-analysis of cognitive remediation in schizophrenia. Am J Psychiatry, 164(12), 1791-1802. doi: 10.1176/appi.ajp.2007.07060906

Medalia, A., & Lim, R. (2004). Treatment of cognitive dysfunction in psychiatric disorders. J Psychiatr Pract, 10(1), 17-25.

Ozonoff, S., Pennington, B. F., & Rogers, S. J. (1991). Executive function deficits in high-functioning autistic individuals: relationship to theory of mind. J Child Psychol Psychiatry, 32(7), 1081-1105.

Pellicano, E., Maybery, M., Durkin, K., & Maley, A. (2006). Multiple cognitive capabilities/deficits in children with an autism spectrum disorder: "weak" central coherence and its relationship to theory of mind and executive control. Dev Psychopathol, 18(1), 77-98. doi: 10.1017/S0954579406060056

Penadés, R., & Catalán, R. (2012). Cognitive Remediation Therapy (CRT): Improving Neurocognition and Functioning in Schizophrenia. In T. H. J. Burne (Ed.), Schizophrenia in the 21st Century: InTech.

Penades, R., Catalan, R., Salamero, M., Boget, T., Puig, O., Guarch, J., & Gasto, C. (2006). Cognitive remediation therapy for outpatients with chronic schizophrenia: a controlled and randomized study. Schizophr Res, 87(1-3), 323-331. doi: 10.1016/j.schres.2006.04.019

Pilling, S., Bebbington, P., Kuipers, E., Garety, P., Geddes, J., Martindale, B., . . . Morgan, C. (2002). Psychological treatments in schizophrenia: II. Meta-analyses of randomized controlled trials of social skills training and cognitive remediation. Psychol Med, 32(5), 783-791.

Raven, J. (2000). Manual for Raven's Progressive Matrices and Vocabulary Scales: Research supplement no. 3, 2000 ed: Oxford Psychologists Press.

Reichelt, A. C., Rodgers, R. J., & Clapcote, S. J. (2012). The role of neurexins in schizophrenia and autistic spectrum disorder. Neuropharmacology, 62(3), 1519-1526. doi: 10.1016/j.neuropharm.2011.01.024

Robinson, S., Goddard, L., Dritschel, B., Wisley, M., & Howlin, P. (2009). Executive functions in children with autism spectrum disorders. Brain Cogn, 71(3), 362-368. doi: 10.1016/j.bandc.2009.06.007

Rose, D., Farrier, D., Doran, A.-M., Sporle, T., Bogner, D., & Wykes, T. (2008). What do clients think of cognitive remediation therapy: a consumer led investigation of satisfaction and side effects. Am J Psychiatr Rehab, 11, 181-204.

Stuss, D., & Levine, B. (2002). ADULT CLINICAL NEUROPSYCHOLOGY: Lessons from Studies of the Frontal Lobes. Annu. Rev. Psychol., 53, 401-433.

Tan, B. L., & King, R. (2013). The effects of cognitive remediation on functional outcomes among people with schizophrenia: a randomised controlled study. Aust N Z J Psychiatry, 47(11), 1068-1080. doi: 10.1177/0004867413493521

Tan, S., Zou, Y., Wykes, T., Reeder, C., Zhu, X., FudeYang, . . . Zhou, D. (2015). Group cognitive remediation therapy for chronic schizophrenia: A randomized controlled trial. Neurosci Lett. doi: 10.1016/j.neulet.2015.08.036

Ueland, T., & Rund, B. R. (2005). Cognitive remediation for adolescents with early onset psychosis: a 1-year follow-up study. Acta Psychiatr Scand, 111(3), 193-201. doi: 10.1111/j.1600-0447.2004.00503.x

Wang, K., Song, L. L., Cheung, E. F., Lui, S. S., Shum, D. H., & Chan, R. C. (2013). Bipolar disorder and schizophrenia share a similar deficit in semantic inhibition: a meta-analysis based on Hayling Sentence Completion Test performance. Prog Neuropsychopharmacol Biol Psychiatry, 46, 153-160. doi: 10.1016/j.pnpbp.2013.07.012

Watanabe, K., Ogino, T., Nakano, K., Hattori, J., Kado, Y., Sanada, S., & Ohtsuka, Y. (2005). The Rey-Osterrieth Complex Figure as a measure of executive function in childhood. Brain Dev, 27(8), 564-569. doi: 10.1016/j.braindev.2005.02.007

Wechler, D. (1981). Wechsler Adult Intelligence Scale – Revised. New York: The Psychological corporation.

White, S. J. (2013). The Triple I Hypothesis: taking another('s) perspective on executive dysfunction in autism. J Autism Dev Disord, 43(1), 114-121. doi: 10.1007/s10803-012-1550-8

Won, H., Mah, W., & Kim, E. (2013). Autism spectrum disorder causes, mechanisms, and treatments: focus on neuronal synapses. Front Mol Neurosci, 6, 19. doi: 10.3389/fnmol.2013.00019

Wykes, T., Huddy, V., Cellard, C., McGurk, S. R., & Czobor, P. (2011). A Meta-Analysis of Cognitive Remediation for Schizophrenia: Methodology and Effect Sizes. Am J Psychiatry, 168(5).

Wykes, T., Newton, E., Landau, S., Rice, C., Thompson, N., & Frangou, S. (2007). Cognitive remediation therapy (CRT) for young early onset patients with schizophrenia: an exploratory randomized controlled trial. Schizophr Res, 94(1-3), 221-230. doi: 10.1016/j.schres.2007.03.030

Wykes, T., Reeder, C., Corner, J., Williams, C., & Everitt, B. (1999). The effects of neurocognitive remediation on executive processing in patients with schizophrenia. Schizophr Bull, 25(2), 291-307.