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Virtual Remediation Versus Methylphenidate to Improve Distractibility in Children With ADHD: A Controlled Randomized Clinical Trial Study

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Abstract

Objective: Virtual environments have been used to assess children with ADHD but have never been tested as therapeutic tools. We tested a new virtual classroom cognitive remediation program to improve symptoms in children with ADHD. **Method:** In this randomized clinical trial, 51 children with ADHD (7-11 years) were assigned to a virtual cognitive remediation group, a methylphenidate group, or a psychotherapy group. All children were evaluated before and after therapy with an ADHD Rating Scale, a Continuous Performance Test (CPT), and a virtual classroom task. **Results:** After therapy by virtual remediation, children exhibited significantly higher numbers of correct hits on the virtual classroom and CPT. These improvements were equivalent to those observed with methylphenidate treatment. **Conclusion:** Our study demonstrates for the first time that a cognitive remediation program delivered in a virtual classroom reduces distractibility in children with ADHD and could replace methylphenidate treatment in specific cases. *(J. of Att. Dis. XXXX; XX(X) XX-XX)*

Keywords

ADD/ADHD, cognitive remediation, virtual reality

Introduction

ADHD is one of the most common childhood and adolescent psychiatric disorders with prevalence rates ranging from 5% to 7% worldwide (Thomas, Sanders, Doust, Beller, & Glasziou, 2015). It is characterized by difficulties with attention, hyperactivity, and impulsivity, and results in significant impairment in social, cognitive, academic, behavioral, and familial functioning (Loe & Feldman, 2007). Attention disturbances are a core symptom of children with ADHD, notably distractibility and inability to stay on task. In particular, increased distractibility could explain why children with ADHD may have difficulties at school because environmental stimuli may distract them.

Multimodal approaches are recommended for the treatment for ADHD with combinations of pharmacological and psychological treatments (Catala-Lopez et al., 2017; Sibley, Kuriyan, Evans, Waxmonsky, & Smith, 2014; Taylor et al., 2004). Pharmacological treatments are efficacious (Banaschewski et al., 2006; Feldman & Reiff, 2014; National Institute for Health and Care Excellence [NICE], 2008) and often used but they may be limited in various situations and have possible adverse effects, poor adherence, or lead to negative medication-related attitudes from parents and clinicians (Banaschewski et al., 2006; Sonuga-Barke et al., 2013). In clinical studies, approximately 30% of participants have an inadequate response to treatment with a single stimulant (Hodgkins, Shaw, McCarthy, & Sallee, 2012). Nonpharmacological treatments should, therefore, also be considered. Cognitive remediation (also called cognitive training) is an important emerging form of treatment for psychiatric disorders that aims at minimizing the daily impact of cognitive deficits by optimizing and improving cognitive functioning (Ben-Yishay, 2008). Cognitive remediation has been investigated as a potential nonpharmacological treatment for ADHD (Azami et al., 2016; Chacko et al., 2014; Cortese et al., 2015; Gray et al.,

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2012; Green et al., 2012; Rapport, Orban, Kofler, & Friedman, 2013; Van der Oord, Ponsioen, Geurts, Ten Brink, & Prins, 2014). Findings generally suggest improved functioning with such treatment (i.e., in targeted cognitive skills and/or ADHD symptoms; Dickstein, Cushman, Kim, Weissman, & Wegbreit, 2015). Although the recent systematic review and meta-analysis from Catala-Lopez et al. (2017) concluded that evidence for the efficacy of cognitive training in ADHD was lacking, two previous systematic reviews concluded that the effects of cognitive training were significant with unblinded measures whereas they became nonsignificant with blinded ratings (Cortese et al., 2015; Sonuga-Barke et al., 2013).

In the field of neurocognition, the use of virtual reality for cognitive remediation, especially in the domain of schizophrenia (Franck et al., 2013), has become more and more popular within the past few years. Such programs offer several advantages including a more realistic, lifelike environment that may allow participants to "forget" they are being assessed, increase participation, and improve learning. Moreover, virtual reality systems can provide multimodal stimuli such as visual and auditory stimuli and can also be used to evaluate a patient's multimodal integration and aid the rehabilitation of cognitive abilities. The use of virtual reality may be particularly beneficial for children who often show great interest and considerable success in computers, consoles, or videogame tasks (Bioulac et al., 2017). Previous studies have already used virtual reality in children with ADHD to assess performance (Adams, Finn, Moes, Flannery, & Rizzo, 2009; Areces, Rodriguez, Garcia, Cueli, & Gonzalez-Castro, 2016; Bioulac et al., 2012; Clancy, Rucklidge, & Owen, 2006; Diaz-Orueta, Fernandez-Fernandez, Morillo-Rojas, & Climent, 2016; Diaz-Orueta et al., 2014; Iriarte et al., 2016; Muhlberger et al., 2016; Negut, Jurma, & David, 2017; Parsons, Bowerly, Buckwalter, & Rizzo, 2007; Pollak, Shomaly, Weiss, Rizzo, & Gross-Tsur, 2010; Pollak et al., 2009; Rizzo et al., 2006; Shriki et al., 2010). In particular, they investigated the impact of this new technology for assessing ADHD cognitive performance, notably on attentional processes and executive functions. Most of the studies used a virtual classroom environment and found that children with ADHD made more omissions and more commission errors (Adams et al., 2009; Areces et al., 2016; Bioulac et al., 2012; Diaz-Orueta et al., 2016; Diaz-Orueta et al., 2014; Iriarte et al., 2016; Muhlberger et al., 2016; Negut et al., 2017; Parsons et al., 2007; Pollak et al., 2010; Pollak et al., 2009; Rizzo et al., 2006). Interestingly, they showed that virtual reality provides information on clinical symptoms (i.e., head movements; Muhlberger et al., 2016; Rizzo et al., 2006) and can also be an effective tool to test the impact of pharmacological treatment (Diaz-Orueta et al., 2016; Muhlberger et al., 2016; Pollak et al., 2010). A recent review of the literature concluded that virtual reality can be effective in providing optimal rehabilitation of children with ADHD (for diagnosis, training, monitoring, assessment, and treatment; Bashiri, Ghazisaeedi, & Shahmoradi, 2017). Moreover, it can be used to give hope to children with ADHD as a method for improving their coping skills. This work utilizing a self-face recognition paradigm design has the potential for providing an emotionally positive experience that is therapeutically beneficial in children with ADHD (Shiri, Tenenbaum, Sapir-Budnero, & Wexler, 2014).

Collaborative studies (Bioulac et al., 2012; Rizzo et al., 2006) have evaluated performance in children with ADHD using virtual classroom tasks. On one hand, performance was impaired as the task became more complex by adding distractors (Rizzo et al., 2006). On the other hand, virtual classroom tasks have been shown to be reliable for testing ADHD children's ability to sustain performance over time (Bioulac et al., 2012). To be able to attribute enough attention to a virtual classroom task, children have to inhibit various potential distracters in the classroom (e.g., teachers' and other children's movements, paper airplanes, and so on). The effort made to resist a distracter may increase the cognitive load of the task so the participant's attention may be difficult to maintain over time.

Although virtual reality and virtual classrooms have been shown to provide added value for performance assessments in children with ADHD, they could be an opportunity for providing remediation of children with ADHD (Bashiri et al., 2017). The aim of the present study was to create and evaluate the efficacy of a cognitive remediation program embedded within a previously tested virtual classroom (Bioulac et al., 2012) that aimed to reduce cognitive distractibility in ADHD children.

Participants and Method

Participants

The sample consisted of children with ADHD aged between 7 and 11 years recruited among outpatients referred for a psychiatric examination to the Child and Adolescent Psychiatry Department, Bordeaux University Hospital, France. Clinical diagnosis of ADHD was made by a psychiatrist using *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; *DSM-IV*; American Psychiatric Association, 1994) criteria after several interviews with the child and his parents. Children with ADHD were excluded if they presented hyperactive/impulsive ADHD subtype, comorbid autism, mental retardation, or IQ score < 85. All parents and children provided written informed consent and the local ethics committee (consultative committee for the protection of persons participating in biomedical research [CPP {Comité de Protection des Personnes-ethical research committees} Bordeaux]) approved the study (clinical trial NCT018271170).

Assessment Procedures

Evaluation of ADHD symptoms. Severity of ADHD was evaluated with the ADHD Rating Scale (ADHD-RS; Zhang, Faries, Vowles, & Michelson, 2005), a self-report inventory adapted from the *DSM-IV* criteria for ADHD consisting of 18 questions regarding a child's behavior over the past 6 months. Patients were selected if they had a score >28. The parents' version of the ADHD-RS was used.

Virtual classroom task assessment. We used the virtual classroom task developed by Rizzo et al. (Rizzo, et al., 2006; Rizzo & Buckwalter, 1997; Rizzo et al., 1999; Rizzo, Buckwalter, & Van der Zaag, 2002). This software was developed by the Integrated Media Systems Center at the University of Southern California in Los Angeles (Rizzo et al. with Digital Media Works Inc.; http://www.dmv.ca/). It was adapted for French-speaking patients by our team (Bioulac et al., 2012). The virtual classroom was a head-mounted display (HMD) virtual system for the assessment of attention processes. Each participant sat in front of a desk. Then, the physician fitted the HMD to the child's head and the system presenting the virtual classroom was activated. Participants saw the interior of the classroom in the HMD. The scenario consisted of a standard rectangular classroom environment containing three rows of desks, a teacher's desk at the front, a blackboard across the front wall, a female virtual teacher between the desk and blackboard, on the left side wall a large window looking out on to a playground with buildings, vehicles and people, and on each end of the wall opposite the window a pair of doorways through which activity occurs. The virtual teacher gave the information to the participants. They were instructed to view a series of letters on the blackboard and to press a mouse button as quickly as possible, only when they viewed the letter "K" preceded by the letter "A." Many distracters were presented in the classroom during the task including auditory distracters (pencils dropping, footsteps, etc.), visual distracters (paper airplane flying across the classroom, etc.), and mixed distracters (auditory and visual distracters) such as a car rumbling by the outside window. The experiment comprised five blocks (for a period of 100 s each) with 20 targets (AK). Five hundred stimuli were presented during the whole task (500 s). During the virtual classroom task, we recorded for every block the number of correct hits (number of cases where a response occurred together with the target "AK") and commission errors (number of cases where a response occurred together with a nontarget).

Continuous Performance Test (CPT II) assessments. We used the CPT II, one of the most useful measures for assessing ADHD (Conners & Staff, 2000; Epstein et al., 2003; Rosvold & Delgado, 1956). Participants had to react to target letters on the computer screen, except the letter X. The experiment comprised six blocks (for a period of 140 s). Each block contained 54 targets (except Block 1, 53 targets) and six nontargets. The task lasted for 14 min, and participants observed computer-generated letters presented at interstimulus intervals of 1, 2, and 4 s, with a display time of 250 ms. Results are described with four indicators as follows: correct hits (number of cases where a response occurs in presence of a target), commission errors (number of cases where a response occurred together with a nontarget), mean reaction time (hit reaction time), and variability of hit reaction time (measured by standard deviation). These indicators were also recorded for every block and group.

Procedure

The children were randomly assigned to virtual classroom cognitive remediation (virtual cognitive remediation group), psychostimulant treatment (methylphenidate group), or psychotherapy placebo training (psychotherapy group). In the virtual classroom cognitive remediation group, the children had to execute a letter detection task while inhibiting attention to various distracters (e.g., pencils dropping, footsteps, intercom announcements, and so on). Sessions were made increasingly effortful with more and more distractors (twelve 30-min sessions, twice a week for 6 weeks). Children were then progressively trained to resist paying attention to the distractors presented in the virtual classroom. In the psychotherapy group, this supportive psychotherapy was individual. The psychotherapy condition controlled for nonspecific therapeutic effects of a group intervention, including session and treatment duration (30 min per week for 6-8 weeks, 12 sessions), therapist attention, support and encouragement, and psychoeducation. The most typical areas covered included primary symptoms of ADHD, emotional symptoms, and impact on everyday life (notably on self-esteem). In the methylphenidate group, children were treated with long-acting methylphenidate (QUASYM®) and had a clinical interview once every 2 weeks for 8 weeks. The posology was adapted according to the clinical response and the tolerance of the molecule. The maximal posology prescribed was 1 mg/kg. All children were evaluated pre- and postintervention with the ADHD-RS, the virtual classroom task described previously (Bioulac et al., 2012), and the CPT. During the virtual classroom task, the number of correct hits and commission errors was recorded, as were omissions and commissions during the CPT.

Statistical Analysis

Descriptive statistics of the sample included frequencies and percentages of categorical variables, together with means and standard deviations of continuous variables. Data analyses were performed using SPSS software (Version 18, PASW Statistics) and Prism software (Version

6, GraphPad). To determine whether the virtual classroom cognitive remediation program was more efficient on distractibility than psychotherapy placebo training or psychostimulant treatment, the overall effects between the three groups were compared using ANOVA (single-factor ANOVA with *F*-test statistics). Tukey's tests were used to correct post hoc multiple comparisons and to determine which groups significantly differed from each other. For each analysis, effects were considered significant when the *p* value was equal to or less than .05.

Results

Description of Population

Our sample comprised 51 children (*M* age = 8.9 ± 1.2 years, 10 females). Most children with ADHD presented mixed subtype (88%), whereas 30% presented a comorbid anxious disorder and/or 40% presented an oppositional defiant disorder. Children were randomly assigned to either the virtual classroom cognitive remediation group ($n = 16$), the methylphenidate group ($n = 16$), or the psychotherapy group ($n = 19$; Figure 1). The mean age of the groups was different, $F(2, 48) = 4.43$, $p = .017$: virtual classroom cognitive remediation group, *M* age = 9.5 ± 1.2 years; methylphenidate group, *M* age = 8.4 ± 0.99 years; and psychotherapy group, *M* age = 8.8 ± 1.07 years (significant difference between virtual classroom cognitive remediation and methylphenidate groups, $p = .014$). The sex ratio differed between the groups with two females in the virtual classroom cognitive remediation group, eight in the psychotherapy group, and none in the other ($p = .005$). At baseline, there were no significant differences on the ADHD-RS total between the three groups, $F(2, 48) = 0.42$, *ns*.

ADHD-RS assessment. There were significant differences between the groups on ADHD-RS total, $F(2, 45) = 20.98$, $p < .0001$; ADHD-RS inattention, $F(2, 45) = 21.24$, $p < .0001$; and ADHD-RS hyperactivity, $F(2, 45) = 7.47$, $p < .002$ from before to after therapy. The methylphenidate group exhibited lower ADHD-RS total ($p < .0001$), ADHD-RS inattention ($p < .0001$), and ADHD-RS hyperactivity ($p = .001$) compared with the other two groups (respectively, ADHD-RS total, $p < .0001$; ADHD-RS inattention, $p < .0001$; ADHD-RS hyperactivity, $p = .05$).

No children in the virtual classroom cognitive remediation group reported any cybersickness-related side effects. All participants in the virtual classroom cognitive remediation group completed training.

Virtual Classroom Assessment

On the virtual classroom task, there were significant differences for the entire group between the number of correct hits, $F(2, 47) = 14.56$, $p < .0001$, and the number of commissions, $F(2, 47) = 3.01$, $p = .05$, from before to after therapy. After therapy, the number of correct hits in the virtual classroom cognitive remediation group was significantly higher than in the psychotherapy group ($p < .0001$) and was similar to that in the methylphenidate group. After therapy, the number of commissions in the virtual classroom cognitive remediation group was significantly lower than in the methylphenidate group ($p < .0001$), whereas the number of commissions in the methylphenidate and psychotherapy groups were equivalent. No patients decreased their scores in the methylphenidate group ($n = 16$), one patient decreased his score in the virtual classroom cognitive remediation group ($n = 16$), and six patients decreased their scores in the psychotherapy group ($n = 19$).

CPT Task Assessment

On the CPT task, there were significant differences for the entire group between omissions, $F(2, 45) = 3.48$, $p = .03$, and a trend to significance for the number of commissions, $F(2, 47) = 2.79$, $p = .07$, from before to after therapy. After therapy, there was no difference between the number of omissions in the virtual classroom cognitive remediation group and in the methylphenidate group. However, there were significant differences in the number of commissions between the virtual classroom cognitive remediation group and in the methylphenidate group ($p = .05$).

Table 1 shows the descriptive results on the variables (ADHD-RS, virtual classroom task, and CPT) before and after therapy and Figure 2 shows the number of correct hits on the virtual classroom task in the three groups before and after therapy.

Discussion

Our findings show for the first time that cognitive training delivered in a virtual environment improves attentional performance and decreases distractibility and impulsivity significantly. After the therapy and during the virtual classroom task, the number of correct hits in the virtual classroom cognitive remediation group was equivalent to that in the methylphenidate group (pharmacological reference treatment; NICE, 2008). After cognitive remediation in the virtual classroom, children with ADHD were less affected by distracters, as assessed by the number of correct hits on the task. Moreover, they were less impulsive after the virtual classroom cognitive remediation, as assessed by the number of commissions. With the classical neuropsychological evaluation (CPT II task) and after therapy, there was no difference in the number of omissions between the virtual classroom cognitive remediation group and the methylphenidate group, although there were significant differences in the number of commissions between the virtual classroom

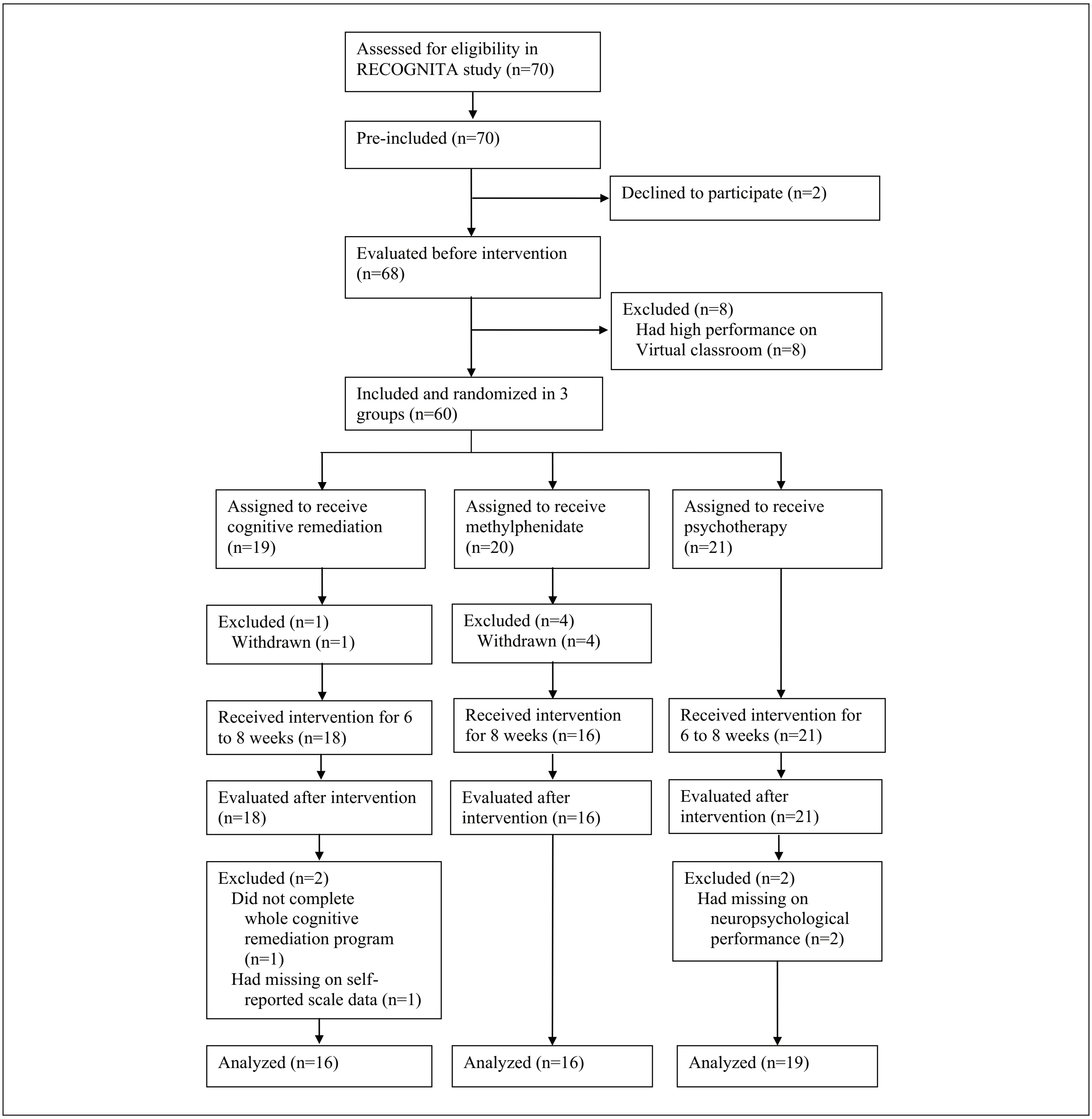

Figure 1. Patient progress through the phases of the study comparing cognitive remediation, methylphenidate treatment, and psychotherapy for the treatment of children with ADHD.

cognitive remediation group and the methylphenidate group.

Interestingly, our study confirms the possibility of conducting cognitive remediation in virtual reality and its acceptability by children. Indeed, none of the children in the virtual reality group reported any cybersickness-related side effects and all participants enrolled in the virtual classroom cognitive remediation group completed training. Although participants in the virtual classroom cognitive remediation group increased their performance on objective measures (virtual classroom task and CPT task), their behavioral ratings (ADHD-RS) did not improve likewise. Transferring skills or benefits acquired during cognitive remediation to daily life is challenging, a transfer occurring during the neuropsychological task (CPT) but not on subjective measurements of daily life behavior (ADHD-RS). In the future, it

Table 1. Descriptive Results on the Various Variables: ADHD-RS, Virtual Classroom Task, and CPT Before and After Therapy.

	Cognitive remediation group *N* = 16		Methylphenidate group *N* = 16		Psychotherapy group *N* = 19		Significance		
	M	*SD*	*M*	*SD*	*M*	*SD*	*F*	*p*	Pairwise
Sex (number of participants)									
Female	2	—	0	—	8	—	—	.005	—
Age (years)	9.5	1.29	8.4	0.99	8.8	1.07	$F(2, 48) = 4.43$	.017	
ADHD-RS before therapy									
Total	40.19	7.94	37.63	8.02	39.26	8.05	$F(2, 48) = 4.21$	*ns*	—
Inattention	23.31	3.32	19.69	5.31	22.26	3.85	$F(2, 48) = 3.1$	*ns*	—
Hyperactivity	16.88	7.20	17.94	5.06	17.0	5.44	$F(2, 48) = 0.15$	*ns*	—
ADHD-RS after therapy									
Total	35.13	10.45	15.93	6.82	30.18	7.85	$F(2, 45) = 20.98$	<.0001 <.0001	MED < VCCR MED < PPT
Inattention	20.06	6.08	8.0	5.43	17.88	4.87	$F(2, 45) = 21.24$	<.0001 <.0001	MED < VCCR MED < PPT
Hyperactivity	15.06	6.82	7.93	2.89	12.29	4.89	$F(2, 45) = 7.47$	.001 .05	MED < VCCR MED < PPT
Virtual classroom task before therapy									
Correct hits	57.50	15.76	56.19	15.13	57.68	14.29	$F(2, 48) = 0.04$	*ns*	—
Commissions	20.06	13.37	17.94	10.82	19.00	11.91	$F(2, 48) = 0.12$	*ns*	—
Virtual classroom task after therapy									
Correct hits	75.94	14.73	80.0	14.17	54.28	16.04	$F(2, 47) = 14.56$	<.0001	VCCR > PPT VCCR = MED
Commissions	9.06	10.73	17.44	9.99	14.0	8.38	$F(2, 47) = 3.01$	.05	VCCR < MED MED = PPT
CPT before therapy									
Omissions	25.13	21.51	25.07	21.41	35.76	26.87	$F(2, 43) = 1.09$	*ns*	—
Commissions	23.27	7.85	26.71	5.22	23.35	5.02	$F(2, 43) = 1.49$	*ns*	—
CPT after therapy									
Omissions	27.31	27.0	20.14	18.55	42.78	27.40	$F(2, 45) = 3.48$	.03	MED < PPT VCCR = MED
Commissions	20	5.55	25.29	7.55	22.5	5.29	$F(2, 45) = 2.79$	.05	VCCR < MED MED = PPT

Note. ADHD-RS = ADHD Rating Scale; CPT = Continuous Performance Test; MED = methylphenidate group; VCCR = virtual classroom cognitive pemediation; PPT = psychotherapy placebo training; pre = before therapy; post = after therapy; correct hits = number of correct hits on the virtual classroom task.

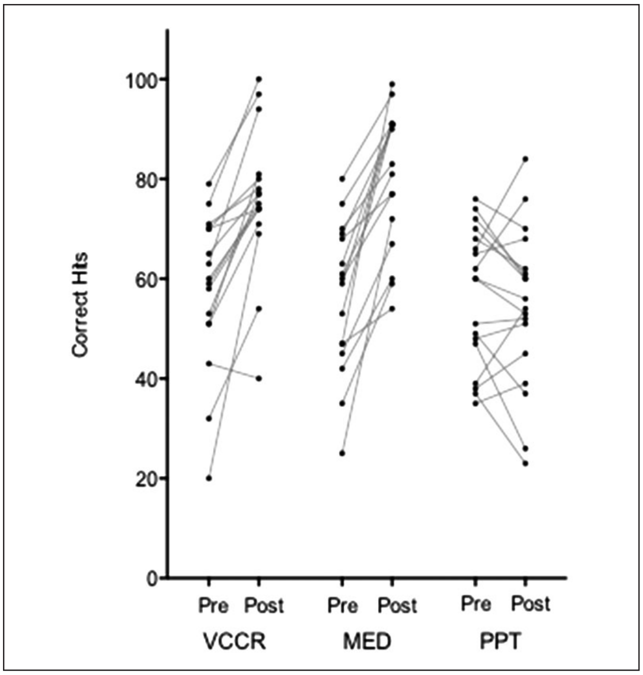

Figure 2. Number of correct hits on virtual classroom task in three groups before and after therapy.
Note. VCCR = virtual classroom cognitive remediation; MED = methylphenidate group; PPT = psychotherapy placebo training; pre = before therapy; post = after therapy; correct hits = number of correct hits on virtual classroom task.

would be important to train participants on ecological tasks or in a more ecological environment. Indeed, only the environment was a daily life environment (the classroom) in this study but not the "task to be done," that is, pressing a button as quickly as possible. We hypothesize that generalization to performance in everyday activities would be more effective if participants were to be trained on an ecological task such as packing one's school bag. Another concern is the possible existence of a subgroup of responders to cognitive remediation. One participant in the virtual classroom cognitive remediation group did not respond, so a larger sample of participants would help in identifying specific phenotypes of responders. A third issue is the concomitant delivery of cognitive remediation, that is, in combination with a pharmacological treatment.

Because virtual therapy is highly identifiable, a dual procedure was impossible, so our protocol did not match the "gold standard" for therapeutic studies, that is, placebo-controlled randomized double-blind design (Sonuga-Barke et al., 2013). Therefore, to allow for the many therapeutic aspects of cognitive remediation such as a good patient–therapist relationship, psychoeducation, and strengthening of self-efficacy expectations (nonspecific effects), we decided to use a pharmacological reference treatment and an active control condition. The control group did not involve "empty treatment" (Mayer, Wyckoff, Fallgatter, Ehlis, & Strehl, 2015) but induced identical nonspecific (placebo) effects that helped to differentiate between the specific effects of cognitive remediation and nonspecific effects. The next step will be to test this cognitive program in a larger sample and to add an arm with cognitive remediation in combination with pharmacological treatment. Indeed, cognitive remediation requires regular and intense repeated sessions during a limited time. Hence, attendance in the intervention program implies that the children were ready to accept the constraints placed on their family organization as well their parents. Future studies might focus on integrating rehabilitation programs into support at home and assessing the impact that this has on adherence.

The present study has some limitations. First, our group was rather small, so we were unable to take gender, comorbidity, and *DSM-IV* subtypes into account for statistical analysis. Furthermore, the participants were recruited in an ADHD outpatient clinic, a setting where patients are likely to be more severely ill, which would explain the high comorbidity. In addition, the use of other questionnaires such as the Behavior Rating Inventory Executive Function (BRIEF), an instrument that assesses executive functioning, would allow changes in daily life behaviors to be explored more closely (Mahone et al., 2002). Finally, these promising findings are tempered by the fact that neither the evaluators, participants, nor parents were blinded owing to the nature of the trial.

Conclusion

This study is the first to conduct an experiment using cognitive remediation in virtual reality for children with ADHD. The findings suggest that a cognitive remediation program delivered in a virtual classroom reduces distractibility in children with ADHD to a level similar to that with methylphenidate treatment. Further research is, thus, needed to develop such technological alternatives to pharmaceutical treatments. Virtual reality-based ecologically relevant assessment and training tasks are needed to understand their impact on generalization to performance in everyday activities, their effects on symptom reduction, and on their contribution to general functional improvement. These preliminary findings pave the way for the development of cognitive remediation methods that leverage the use of ecologically relevant simulation tools and offer significant potential for improving clinical care for children with ADHD.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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