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Cognitive remediation for adolescents with 22q11 deletion syndrome (22q11DS): A preliminary study examining effectiveness, feasibility, and fidelity of a hybrid strategy, remote and computer-based intervention

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Abstract

Background—22q11DS is a multiple anomaly syndrome involving intellectual and behavioral deficits, and increased risk for schizophrenia. As cognitive remediation (CR) has recently been found to improve cognition in younger patients with schizophrenia, we investigated the efficacy, feasibility, and fidelity of a remote, hybrid strategy, computerized CR program in youth with 22q11DS.

Methods—A longitudinal design was implemented in which 21 participants served as their own controls. Following an eight month baseline period in which no interventions were provided, cognitive coaches met with participants remotely for CR via video conferencing three times a week over a targeted 8 month timeframe and facilitated their progress through the intervention, offering task-specific strategies. A subset of strategies were examined for fidelity. Outcomes were evaluated using a neurocognitive test battery at baseline, pre-treatment and post-treatment.

Results—All participants adhered to the intervention. The mean length of the treatment phase was 7.96 months. A moderately high correlation (intraclass correlation coefficient, 0.73) was found for amount and type of strategies offered by coaches. Participants exhibited significant

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Contributors
Wendy Kates designed and directed the study, conducted the statistical analyses, wrote the results section of the manuscript and edited the remainder of the manuscript. Margaret Mariano and Kerri Tang implemented the intervention. Margaret Mariano wrote the methods and discussion sections of the manuscript and prepared the tables and references. Kerri Tang wrote the introduction of the manuscript. Matthew Kurtz consulted on the project throughout. All authors read, contributed to and have approved the final manuscript.

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Uncited references
IBM Corp, 2012
Wykes et al., 2009

Appendix A. Supplementary data
Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.schres.2015.05.030.

improvements (ES = .36–.55, p ≤ .009) in working memory, shifting attention and cognitive flexibility. All significant models were driven by improvements in pre to post-treatment scores.

Conclusions—Based on our preliminary investigation, a remote, hybrid strategy, computerized CR program can be implemented with 22q11DS youth despite geographic location, health, and cognitive deficits. It appears effective in enhancing cognitive skills during the developmental period of adolescence, making this type of CR delivery useful for youth with 22q11DS transitioning into post-school environments.

Keywords

Schizophrenia; Remote; Cognitive remediation; 22q11DS; Adolescents

1. Introduction

Caused by a microdeletion of chromosome 22 at band q11.2, 22q11.2 deletion syndrome (22q11DS; also known as velo-cardio-facial syndrome) is a common multiple anomaly syndrome, occurring in approximately 1:4000 live births. Cognitive disability is a prominent feature, including impairments in attention, executive function, mathematical ability, visuo-spatial skills, cognitive control (Shapiro et al., 2014) and visual memory (Campbell et al., 2010; Swillen et al., 1997; van Amelsvoort et al., 2004; Zinkstok and van Amelsvoort, 2005). Accordingly, the multiple cognitive challenges of youth with 22q11DS represent an opportunity for cognitive interventions that could, potentially, yield far-reaching effects.

More than 25% of individuals with 22q11DS develop psychosis (Bassett et al., 2003; Green et al., 2009; Murphy et al., 1999). Schizophrenia in 22q11DS has been found to be indistinguishable from the core phenotype of idiopathic schizophrenia (Bassett et al., 2003). Research supports a relationship between early onset psychosis and poor prognosis (Lay et al., 2000; Remschmidt, 2002) suggesting that treatment of deficits early on may be helpful (Mcglashan and Johannessen, 1996). Thus, examining adolescents with 22q11DS could offer a unique opportunity to investigate specific and early interventions related to potential psychotic onset (Armando et al., 2012).

Cognitive remediation (CR) has emerged as an efficacious option for the treatment of schizophrenia, especially when coupled with other psychiatric rehabilitation treatment modalities (Bowie et al., 2012; Wykes et al., 2011). Significant improvements have been reported in attention, memory, problem solving ability, and global cognition (Kern et al., 2009; Wykes et al., 2011). Recent studies suggest that CR is beneficial for early-course vs. long-term (Bowie et al., 2014) patients and adolescents with early-onset schizophrenia (Holzer et al., 2014; Puig, 2014; Ueland and Rund, 2005; Wykes et al., 2007). Studies of successful CR programs support the feasibility of utilizing computer-based interventions with both adult (Kurtz et al., 2007) and adolescent populations (Holzer et al., 2014). Current studies have successfully employed a remote, computer based CR program for stable patients (Ventura et al., 2013) and younger individuals (Fisher et al., 2015) with recent onset psychosis.

Tang et al. (2014) noted the prevalence yet undertreatment of psychiatric disorders in 22q11DS. However, to our knowledge, only one CR study focused on a small sample of individuals with 22q11DS has been published (Harrell et al., 2013), with promising preliminary results, including improvement in a summary score of cognition as well as simple processing speed. Taken together, these findings represent an emerging trend in CR research emphasizing effective treatment approaches examining cognitive improvements following CR intervention, especially for younger individuals with, or at risk for, schizophrenia.

In this study, we implemented a novel, standardized, computer-assisted CR training program with adolescents with 22q11DS. Since interventions that incorporate both strategies and practice have been linked to a more positive functional outcome in people with schizophrenia (Wykes et al., 2011; Wykes and Spaulding, 2011), we used a hybrid model, combining “drill and practice” and “strategy-based” modes of intervention.

Specifically, the goals of the study were to evaluate:

- Changes in cognitive skills over time.
- Feasibility and accessibility of remotely administering the cognitive intervention program to adolescents with 22q11DS.
- Variables associated with participants' ability to progress successfully through the intervention program.
- Fidelity of strategies offered by coaches.

2. Materials and methods

2.1. Participants

Twenty-two adolescents with 22q11DS were recruited through parent support groups and clinicians. Written, informed consent was provided by all participants/parents upon their initial visit and assessment at our lab. The study was IRB approved by the research ethics board of Upstate University, Syracuse, NY. Participant IQs ranged from 63 to 94 (M = 76.85). Participants were included if they were between the ages of 12 and 15 years, had an IQ within 2.5 SD below the mean, internet access, and were available for approximately 3 h per week after school. In order to focus on the efficacy and feasibility of delivering our intervention to study participants without the confound of the presence of prodromal symptoms, exclusion criterion consisted of the presence of prodromal symptoms based on parent report. All participants successfully completed the intervention. However, one participant who received the treatment was dropped from our statistical analyses, because Internet connectivity problems made cognitive coaching in real time impossible with that participant, thereby rendering her data invalid. Therefore, twenty-one participants were included in our statistical analyses. Refer to Table 1 for study demographics and Table 4 for baseline cognitive information.

2.2. Design

Prior to implementing our study we piloted the computerized, on-line cognitive remediation program, Challenging Our Minds (COM) for suitability and remote use with (15) 22q11DS youth not included in the current study. The current study employed a longitudinal design, with participants serving as their own controls to examine the efficacy of the CR program for our participants. Youth were seen at our lab for assessments at three time points: baseline (M = 7.82 months), pre-treatment and post-treatment. At each time point, participants were administered cognitive skills and behavior function assessments as described below. Target intervention length was 8 months.

Immediately after the assessment at the pre-treatment visit, participants were provided with a laptop computer (with built-in camera) to use during the intervention. Throughout the study, a Master's-level trained "cognitive coach" met with each participant via Cisco WebEx web conferencing (Cisco, 2015) three times per week for at least 45 min per session, as recommended by the CR program developer (Bracy, 2010). Participants received $10.00 for each COM session in which they participated.

2.3. IQ and behavior function

A report of psychological functioning that included an IQ test administered within two years was used for each subject to verify IQ. When not available, a Weschler Abbreviated Test of Intelligence—Second Edition (WASI-II) (Wechsler and Hsiao-pin, 2011) was administered prior to the baseline assessment. The Behavior Assessment System for Children, Second Edition Parent Rating Scale (BASC-2 PRS) (Reynolds and Kamphaus, 2004) was administered at each timepoint to appraise behavior function. Mid to high levels of reliability and validity have been demonstrated for this instrument (Reynolds and Kamphaus, 2004) and composite scores based on a variety of behavioral and personality characteristics comprised the following scales used in our analysis: externalizing problems, internalizing problems, behavior symptoms index and adaptive skills. IQ and behavior function were appraised in order to determine their impact on progressing through the intervention. See Tables 1 and 2.

2.4. Cognitive remediation program

Challenging Our Minds (COM) is a cognitive remediation system, developed by neuropsychologist, Dr. Odie Bracy. It is a child-friendly/adolescent version of the computerized CogRehab system (Chen et al., 1997) which was originally developed for adults with brain injury, but which has been used extensively with adults with schizophrenia (Bell et al., 2001; Hogarty et al., 2004; Kurtz et al., 2007) and individuals exhibiting learning disabilities/attention deficits (Bracy et al., 1999).

The COM system is completed on-line. Cognitive tasks are designed as games involving a standardized sequence of computerized cognitive exercises intended to improve skills across several domains including attention, executive function, memory, visual-spatial abilities, problem solving, and communication. Each domain entails several tasks with three progressively difficult levels that participants attempt to "pass" in order to move on to the next task. During the pilot phase, tasks were evaluated for appropriateness of use with

22q11DS youth. If 50% of subjects failed to complete a task due to frustration, it was dropped from our intervention. Ultimately, one level of a task was dropped from the executive track, one task was dropped from the memory track and two tasks were dropped from the communication track. This left 53 tasks for the current study.

During the current intervention, participants were expected to complete all 53 tasks. However, if participants failed to pass the third and most difficult level of any task 3 times in arrow, they were moved on to the next new task in a track. See Table 3 for COM program domains and examples of tasks used within each domain.

2.5. Cognitive coach training and strategy implementation

During each session, Master's level cognitive coaches with degrees in Psychology and Rehabilitation Counseling facilitated participants' progress, demonstrated tasks, and provided structured input, including goal setting and purposeful applications for each task. Prior to the pilot phase, cognitive coaches were trained in person by Dr. Odie Bracy to implement, instruct and suggest strategies, based both on individualized participant needs and COM program instructions. Strategies included visualization, analysis, planning ahead, problem solving, organization, sequencing, association, verbal rehearsal, grouping and chunking of numbers, and encouraging impulse control. During the pilot phase, coaches integrated strategies for each task into a written Instructional Manual Strategies Guide (available by request), adapted from the manual originally developed by Dr. Bracy for the COM program. Coaches also met with the study's Principal Investigator on a bi-weekly basis throughout the intervention phase, to discuss participant progress and proper strategy implementation.

2.6. Effect of CR program on cognitive function

The CNS Vital Signs (CNS-VS) was used to assess cognitive skills. The CNS-VS is a computerized neurocognitive test battery designed as a clinical screening instrument. Stimuli are randomized and each presentation of the CNS-VS is unique, making it particularly useful for serial assessment. (Gualtieri and Johnson, 2006, 2008). The battery consists of several tests adapted from commonly used neuropsychological assessments. Test scores are combined into composite scores, including but not limited to reaction time, cognitive flexibility, executive function, complex attention, and working memory.

Reliability and validity coefficients are analogous to those of other computerized neuropsychological batteries (Gualtieri and Johnson, 2006). Test–retest reliability is moderate to good, with coefficients ranging across all scores from 0.45 to 0.87, and concurrent validity is moderately correlated ($r = .26$ to $.79$, $p \leq .05$) with conventional neuro-psychological tests (Lanting et al., 2012).

2.7. Feasibility

To assess feasibility of the COM program with adolescents with 22q11DS, descriptive information pertaining to session length, completed number of sessions and cancellations over time were compiled and calculated.

2.8. Accessibility of program

Accessibility was determined by the number of locations throughout the United States where participants remotely connected to their coaching session via videoconferencing software and the number of subjects who successfully completed the cognitive training program from their own homes in those locations.

2.9. Evaluation of progress during the COM program

In order to assess progress on COM tasks, we calculated the percentage of tasks for which participants passed all three levels, by both track and overall. We also assessed the extent to which IQ, age, and behavioral function were associated with percentage of tasks completed at the most difficult level.

2.10. Fidelity

In order to examine the extent to which coaches offered similar, task-specific strategies, video-recorded COM sessions depicting coach and subject encounters were observed and evaluated post intervention on a subset of ten subjects. Each of five subjects in the caseload of Coach A was matched with a subject in the caseload of Coach B, based on IQ and BASC-2 PRS (Reynolds and Kamphaus, 2004) parent-rated attentional abilities. One task from each track of the COM program was selected for analysis. The tasks involved varying levels of difficulty and required strategies similar to those offered throughout the COM program. Twenty-one task-specific strategies were potentially introduced during subject-coach encounters.

An independent rater reviewed video-recorded COM sessions of the aforementioned tasks and encounters, referred to a detailed strategy checklist (see Supplement 1) adapted from the strategies guide developed during preliminary phases of the study, and indicated whether or not the coaches introduced a task-specific strategy.

2.11. Data analysis

Outcome measures were statistically examined using IBM SPSS (21). Non-parametric statistics for feasibility data were calculated. Fidelity data were evaluated using chi-square analyses and intraclass correlation coefficients. Standardized scores were used for all performance-based measures and rating scales. Outlier scores were truncated to four standard deviations to reduce skewness (Mahone et al., 2009). In order to determine if outcome measures changed significantly, we conducted paired t-tests for behavior functions, and a repeated measures ANOVA on the ten composite scores provided by the CNS-VS. In order to determine which scores accounted for the significant changes that we observed in these composite scores, we conducted repeated measures analyses of variance on the nine subtests scores from which the composite scores (for which we observed significant change) were derived. Planned, follow-up comparisons were conducted with t-tests in order to determine if the significant change we observed was due to change in baseline to pre-treatment scores, or pre-treatment to post-treatment scores. The Bonferroni correction for multiple comparisons was applied to both repeated measures ANOVAs, and to the follow-up t-tests on the nine subtest scores.

3. Results

3.1. Performance on CNS-VS across time

Based on repeated measures analyses of variance, we observed that participants exhibited significant change (i.e., in Wilks' Lambda scores) on five of the ten composite scores, including cognitive flexibility, executive function, reaction time, working memory, and complex attention (see Table 4). Additionally, we observed significant Wilks' Lambda scores for four out of the nine subtests from which these five composite scores were derived (see Table 5). Specifically, participants demonstrated an increase in correct responses to the Four Part Continuous Performance Task (a 2-back working memory task); a decrease in errors on the Shifting Attention task; and a decrease in response time to correct responses to both the congruent and incongruent conditions of the Stroop task. Importantly, planned, follow-up comparisons of these subtests indicated that although one model (Shifting attention, correct responses) was driven by marginally significant changes from both baseline to pre-treatment scores and pre-treatment to post-treatment scores, the remainder of the significant models were driven exclusively by improvements in pre-treatment to post-treatment scores for the aforementioned tasks (Table 5).

3.2. Feasibility of administration of challenging our minds program to adolescents with 22q11DS

On average, participants completed the treatment in 92.95 sessions (S.D. = 21.24). Session length averaged 49.02 min (S.D. = 9.75) and mean number of cancellations per subject was 8.52 (S.D. = 7.94). There were no significant differences in baseline to pre-treatment wait time (M = 7.82 months, SD = 1.02) or treatment time (M = 7.96 months, SD = 2.04); $t(20) = .23$, $p = .815$.

3.3. Accessibility of program

The 21 participants included in the analysis successfully connected remotely via a web-based videoconferencing program, WebEx, from their own homes, from 15 states across all four time zones within the contiguous United States.

3.4. Progress during the COM program

As noted above, we assessed degree to which participants progressed through the COM program by calculating the percentage of tasks for which participants passed all three levels. Across all tracks, participants were able to pass 61.6% (S.D., 17.1) of tasks at the most difficult level (Level 3). The tracks with the largest percentage of tasks with all three levels completed were Attention (mean, 88.6%; S.D., 10.6) and Problem Solving (mean, 80.0%; S.D., 15.6). The tracks with the lowest percentage of tasks with all three levels completed were Executive Function (mean, 46.8%; S.D., 16.1) and Visual–Spatial Perception (mean, 49.0%; S.D., 25.9). We also sought to determine the extent to which demographic variables and baseline behavioral function predicted progress through the program (using the Spearman rank correlation coefficient due to skewed data distributions). Age was associated with ability to progress through the Executive Function track (rho, .50; p = .02), the Memory track (rho, .56; p = .009) and the Visual–Spatial Perception track (rho, .60; p = .004). Full

Scale IQ was only associated with progression through the Communication track (rho, .48; p = .03). Behavioral function, measured with the BASC-2 PRS, did not predict ability to progress through the program.

3.5. Fidelity of strategies offered

Based on Pearson chi square analyses, we did not observe differences between coaches in the percent of task-specific strategies offered for the following COM tasks: Multiple Simultaneous Attention, X^2 (1, N = 40) = .440 p = .507; Number Recall, Visual, X^2 (1, N = 190) = 1.09, p = .296; Design Completion, X^2 (1, N = 60) = 1.67, p = .196; and Kubos, X^2 (1, N = 40) = .921, p = .337. Coaches did differ significantly in percent of task-specific strategies offered for the attributes and groups task, X^2 (1, N = 84) = 10.12, p = .001 and the follow my instructions task, X^2 (1, N = 40) = 6.40, p = .01. An intraclass correlation (ICC) was conducted to assess consistency of strategies offered (type and amount) between coaches, ICC = .73.

4. Discussion

The present study examined the feasibility of administering a standardized CR intervention program to adolescents with 22q11DS. We found our intervention to be feasible, accessible and efficacious for our target population.

4.1. Performance on CNS-VS across time

As noted in the introduction, 22q11DS is associated with cognitive impairments and risk for psychosis (Bassett et al., 2003; Campbell et al., 2010; Murphy et al., 1999; Swillen et al., 1997; van Amelsvoort et al., 2004; Zinkstok and van Amelsvoort, 2005). Our participants demonstrated outcomes of decreased reaction time and increased accuracy scores in working memory, shifting attention and cognitive flexibility tasks. Previous studies have reported that individuals with 22q11DS show comparable response speed to individuals with nonsyndromal psychosis (Goldenberg et al., 2012), and that processing speed in 22q11DS predicts later symptoms of psychosis (Hooper et al., 2013). Importantly, these relative impairments improved in our sample after implementing our CR intervention. Specifically, 22q11DS subjects responded more quickly and accurately to increasingly complex stimuli in areas related to cognitive flexibility, executive function, reaction time, working memory, and complex attention. Overall, our findings indicated significant post-treatment improvements with small to medium effect-sizes in working memory, shifting attention and cognitive flexibility tasks. These executive abilities are crucial in the development of behavioral flexibility (Miller and Cohen, 2001), classroom learning (Kibby et al., 2004), everyday functioning and decision-making (Martinussen et al., 2005).

4.2. Feasibility of administration of challenging our minds program to adolescents with 22q11DS

We reasoned that a significant increase in cancellations might indicate that tolerability of the intervention was waning due, potentially, to its length or, tediousness. While previous research demonstrated the feasibility of a short-term (12 week) at home CR program for an intervention sample of 13 22q11DS youth (Harrell et al., 2013), the present study extended these findings to a larger intervention sample (21), utilizing a within-group design that permitted excellent adherence over a longer term with limited subject cancelations. This exceeded the previous adherence rates found in studies of CR with 22q11DS adolescents (Harrell et al., 2013) and adolescents with early onset schizophrenia (Puig et al., 2014). While economic compensation may have impacted adherence rates, this suggests that an intensive, long-term, internet-based intervention is feasible for youth with 22q11DS, despite their potential health problems and learning limitations.

4.3. Accessibility of program

All participants successfully connected remotely via a web-based videoconferencing program in their own homes. Due to the relatively rare incidence of 22q11DS and given the need for effective interventions that accommodate the educational and behavioral limitations associated with the disorder, our novel approach of using a trained cognitive coach and videoconferencing technology has implications for increased service provision to youth with 22q11DS who live in rural settings or have limited access to service professionals

4.4. Progress during the COM program

Behavior function as indicated by non significant BASC-2 PSR scores was not a factor in the ability to progress through the COM program, and IQ impacted only the Communication track. Overall, participants completed over 60% of tasks at the most difficult level (Level 3). However, Level 2 was in fact, challenging and sufficient enough to produce improvement in outcome measures suggesting that computer assisted CR therapy can be successfully implemented with 22q11DS youth having lower IQ.

Although Fiszdon et al. (2006) found that while adult patients with lower IQ could benefit from CR, they were not able to generalize skills to untrained tasks. While the principles of several of the tasks in our CR program were similar to the outcome measures (e.g. ability to shift attention, cognitive flexibility), very few of the 53 CR tasks themselves were identical to the CNS-VS outcome measures, supporting the notion that cognitive gains were generalizable beyond the practice effects of the CR program for our adolescent participants. See Supplement 2 for screen-shot examples of COM tasks.

The association between age and completion of several tracks that represent major cognitive challenges associated with 22q11DS (Campbell et al., 2010; Shapiro et al., 2014; Woodin et al., 2001) suggests that older adolescents may be able to complete the intervention with less frustration than their younger peers. Accordingly, our finding aligns with recent studies (Bowie et al., 2012; Kontis et al., 2013) regarding the effects of age on CR in schizophrenia patients, and suggests that adolescence is an appropriate time to employ CR (Bachman et al., 2012; Puig et al., 2013).

4.5. Fidelity of strategies offered

Although the importance of demonstrating comparability of interventions across providers has been well-described (Wolery, 2011), our study was, to the best of our knowledge, one of the first to address the issue of fidelity regarding strategy-based interventions. Overall, we found a moderate to strong correlation between coaches for the amount and type of strategies offered in tasks examined for fidelity indicating consistency in the delivery of strategies offered. For two of the six tasks, strategies offered individually to each subject varied presumably due to the combination of subject needs, coaching style, and learning skills associated with those tasks. Nonetheless, task-specific strategies offered by both coaches (i.e. chunking, context clues, verbalization) were similar to each other and to previous studies (Medalia and Saperstein, 2013; Wykes et al., 2011).

4.6. Study limitations

There are several limitations to the current study. The purpose of the study was to provide preliminary data that would guide us in a future, randomized, controlled trial. Accordingly, our sample size was small and non-randomized, thus limiting generalizability beyond the scope of this study. Furthermore, our study focused on cognitive functions and did not address psychosocial outcomes, which should be a goal of future studies with this population. Additionally, the fact that the IQ assessment was not administered at the same point for all subjects should be included as a limitation. Although we controlled for cognitive developmental changes and behavioral function in our within-group design by including associated baseline measures whereby participants served as their own controls, other potential moderators including motivation, physical and mental health issues, parental and extra educational supports, may have affected our findings. Since our finding regarding higher post-treatment scores for adolescents with 22q11DS suggested gains in knowledge and skills that were similar, but not identical to, our outcome measure, the extent to which these cognitive gains generalized to untrained tasks remains to be explored.

Another limitation is that the tasks used for fidelity analyses were selected to echo a range of strategies potentially offered by cognitive coaches throughout the entire intervention. Furthermore, we did not compare the effectiveness of the hybrid strategy versus a non-strategy approach to CR. As Medalia and Saperstein (2013) noted, without a non-strategy coaching component, it is difficult to ascertain whether it was the cognitive coach or the strategy itself that contributed to cognitive gains among participants. Strain and Bovey (Strain and Bovey, 2011) emphasized that an ample amount of time is actually needed to reach optimal fidelity. While our study limited evaluation of fidelity to post-hoc analysis, fidelity may be improved in future studies by incorporating fidelity checks throughout the intervention. Future research involving a randomized, experimental design with a no strategy/no coaching control group might serve to clarify the associations among age, the type of interventions available, strategies offered and value of cognitive coaching in the delivery and effectiveness of CR to adolescents with 22q11DS.

4.7. Study implications

Despite the aforementioned limitations, our study contributes to the CR literature on adolescents with 22q11DS in unique and potentially significant ways. Our novel approach, using videoconferencing software and utilizing a hybrid strategy approach delivered by cognitive coaches was feasible, accessible and initial findings suggested that it was effective in improving the cognitive skills of a range of adolescents with 22q11DS throughout the country. If replicated with a randomized, controlled trial, this could have implications for service delivery among youth with the disorder who may not otherwise have access to service professionals or treatment. Moreover, results suggested that CR can be used successfully with 22q11DS adolescents with intellectual disability and lower IQ. Based on preliminary findings, a hybrid strategy approach to CR, using a cognitive coach can improve executive processes related to working memory, shifting attention and cognitive flexibility tasks. Findings indicated that older participants progressed more successfully through the intervention than their younger counterparts. This is potentially valuable to parents and clinicians involved with planning as adolescents with 22q11DS transition into post-secondary or work environments. Finally, this was one of the first studies to examine and report fidelity of the hybrid strategy/cognitive coaching technique for CR with 22q11DS youth. As such, we have provided groundwork for replication studies and shed light on the delivery of CR to adolescents with 22q11DS.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Demographics.

Gender	
Males	9
Females	12
Age	
Mean (S.D.)	14.61 (1.28)
Range	12.2-16.9
Parent SES[a]	
Mean (S.D.)	45.74 (12.66)
Range	23-66
FSIQ	
Mean (S.D.)	76.85 (8.98)
Range	63-94
Academic status	
Percent of participants in regular classroom	52%
Percent of participants in regular classroom with resources	43%
Percent of participants in self-contained classroom	5%
Services	
Percent of participants receiving speech therapy	33%
Percent of participants receiving occupational therapy	14%
Percent of participants receiving behavioral therapy	10%

[a]Hollingshead (1975).

Table 2

BASC-2 PRS[a] Behavior Function Scores.

	Baseline (T1)	Pre-treatment (T2)	Post-treatment (T3)
Externalizing problems			
Mean (S.D.)	54.00 (12.34)	55.00 (12.23)	52.11 (12.31)
Range	38-93	40-86	38-83
Internalizing problems			
Mean (S.D.)	59.30 (14.15)	61.95 (13.72)	59.37 (14.07)
Range	37-86	44-86	41-98
Behavior symptoms index			
Mean (S.D.)	60.70 (13.88)	62.95 (12.88)	60.16 (12.96)
Range	37-94	41-87	38-87
Adaptive skills			
Mean (S.D.)	38.05 (6.80)	36.24(6.69)	39.42 (7.37)
Range	24-53	26-48	26-54

[a]Behavior Assessment System for Children-Parent Rating Scales, Second Edition (Reynolds and Kamphaus, 2004).

Table 3

Challenging our Minds (COM) domains and task example.

Track (number of tasks)	Type of tasks within track[a]
Attention (10):	Participants respond as quickly as possible to colors, sounds and images as they appear and/or move across the screen
Executive function (11):	Participants differentiate and organize data and information by categorizing shapes, colors, words and numbers
Memory (8):	Participants remember locations of colors and images, recall the facts associated with a phone message, recall series of up to 5 numbers forward, backwards and after a 15 second delay.
Visual spatial skills (9)	Participants complete complex puzzles and designs, identify and recognize shades of light/dark, complex patterns angles, and spatial relationships among different objects.
Problem solving (10):	Participants organize information and use deductive and inductive reasoning to come to conclusions and solve problems.
Communication (5):	Participants complete tasks focusing on auditory discrimination, verbal comprehension, reading and following both written and verbal instructions.

[a]Due to space limitations, a subset of tasks are described for each track

Table 4

Composite Scaled Scores[a] on CNS-VS from baseline to post-treatment

Composites	Baseline scores (T1): Mean (S.D.)	Pre-treatment scores (T2): Mean (S.D.)	Post-treatmentscores (T3): Mean (S.D.)	Repeated measures ANOVA			t-test: T1:T2[c]		t-test: T2:T3[c]	
				Wilks' Lambda	p-Value[b]	Effect size (η^2)	t	p-Value	t	p-Value
Cognitive flexibility	64.6 (18.1)	72.7 (20.5)	80.7 (15.9)	**0.30**	**0.0001**	0.697	–2.25	0.036	–2.83	0.010
Executive function	67.4 (17.0)	75.0 (20.8)	83.7 (14.5)	**0.30**	**0.0001**	0.702	–2.20	0.039	–2.72	0.013
Reaction time	67.2 (18.7)	68.9 (20.6)	81.0 (17.1)	**0.47**	**0.001**	0.534	–0.53	0.602	–4.44	0.001
Working memory	69.1 (18.9)	79.3 (17.1)	87.2 (17.2)	0.45	**0.001**	0.550	–3.43	0.003	–2.26	0.035
Complex attention	70.8 (24.0)	76.7 (22.1)	86.0 (22.6)	**0.53**	**0.002**	0.472	–1.30	0.210	–2.55	0.012
Sustained attention	77.4 (16.9)	85.4 (14.2)	89.6 (16.4)	0.64	0.013	0.365				
Processing speed	77.0 (12.0)	79.7 (11.6)	82.4(13.2)	0.68	0.026	0.318				
Composite memory	80.9 (23.3)	83.4(20.3)	80.1 (26.3)	0.94	0.563	0.059				
Verbal memory	87.5 (23.6)	89.5 (21.2)	87.7 (25.2)	1.0	0.882	0.0				
Visual memory	82.8 (19.2)	85.0 (20.5)	81.1 (21.9)	0.9	0.574	0.1				

[a]Standardized scores were used for analysis.

[b]Bonferroni-corrected p-values were ≤ 0.005.

[c]Follow-up comparisons for composite scores of which Wilks' Lambda was significant.

Table 5

Scaled scores[*] on CNS-VS subtests[a] from baseline to post-treatment

Subtests	Baseline scores (T1): Mean (S.D.)	Pre-treatment scores (T2): Mean (S.D.)	Post-treatment scores (T3): Mean (S.D.)	Repeated measures ANOVA			t-test: T1:T2		t-test: T2:T3	
				Wilks' Lambda	p-Value[b]	Effect size (η^2)	t	p-Value[c]	t	p-Value[c]
Continuous performance task: commission errors[d]	90.7 (22.6)	95.4 (18.1)	89.5 (25.8)	0.90	0.354	0.104				
Continuous performance task: omission errors	85.0 (23.6)	84.4 (26.2)	88.4 (22.1)	0.95	0.628	0.048				
Working memory[e], 2-back: correct responses	81.1 (16.2)	81.6 (14.5)	90.8 (15.1)	0.64	**0.014**	0.363	–0.10	0.922	–3.24	**0.004**
Working memory, 2-back: incorrect responses[d]	81.7 (28.1)	87.4 (23.6)	90.3 (20.4)	0.90	0.349	0.105				
Shifting attention task: correct responses	62.3 (15.1)	70.5 (18.6)	77.4 (15.2)	**0.30**	**0.0001**	0.698	–2.76	0.012	–2.29	0.033
Shifting attention task: errors	79.7 (19.4)	85.6 (22.9)	97.3 (15.5)	**0.45**	**0.001**	0.547	–1.49	0.151	–2.91	**0.009**
Stroop: commission errors	79.2 (21.8)	83.0 (19.9)	81.4 (20.3)	0.98	0.793	0.024				
Stroop: congruent condition, reaction time[d] to correct responses	66.7 (16.14)	70.4(20.1)	79.7 (18.5)	**0.58**	**0.006**	0.419	–1.16	0.261	–3.06	**0.006**
Stroop: incongruent condition, reaction time to correct responses	73.7 (21.9)	72.5 (21.1)	85.9 (16.7)	**0.57**	**0.004**	0.434	0.29	0.773	–3.77	**0.001**

[*] Standardized scores were used for analysis.

[a] We reported subtests that comprised Bonferroni-corrected significant composite scores as described in Table 4.

[b] p-Value ≤ .05.

[c] Bonferroni-corrected p-values ≤ .01.

[d] As raw scores for errors/incorrect responses/reaction time decreased, scaled scores increased.

[e] For clarity, we are referring to the CNS-VS, Four-Part CPT, as Working Memory since only the subtest score which measured Working Memory specifically, comprised the Working Memory domain.