Title: A Comparison of Remediation and Compensatory Cognitive Interventions on Executive Functions and Theory of Mind Skills in Preschoolers with High Functioning Autism: Study Protocol for a Randomized Controlled Trail

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To appear in: **Basic and Clinical Neuroscience**

Received date: 2022/12/03

Revised date: 2023/03/04

Accepted date: 2023/03/04

Please cite this article as:

Abadi, F., Moradi, A.R., Zarafshan, H., Mohamadi, M.R., Sadeghi, M. (In Press). A Comparison of Remediation and Compensatory Cognitive Interventions on Executive Functions and Theory of Mind Skills in Preschoolers with High Functioning Autism: Study Protocol for a Randomized Controlled Trail. Basic and Clinical Neuroscience. Just Accepted publication Jul. 10, 2023. Doi: http://dx.doi.org/10.32598/bcn.2023.3612.2

DOI: http://dx.doi.org/10.32598/bcn.2023.3612.2

Abstract

Background: interventions using 'hybrid' remediation/ compensatory cognitive interventions may be beneficial to improving socio- cognitive functioning of children with autism spectrum disorder (ASD). Previous studies have showed neurocognitive impairments in executive function (EF) and theory of mind (TOM) are specifically associated with ASD.

Aim: the primary aim of the study is to determine the impact of the remediation and compensatory cognitive intervention on executive functions and theory of mind abilities. The secondary aim is to evaluate TOM and EF behavioral domains as result of the remediation and compensatory cognitive intervention.

Methods/ Design: 75 children aged 4 to 7 diagnosed high- functioning autism and their parents will be recruited to this double-blind, multicenter, multi-arm randomized controlled trial. The primary outcome is executive functions and theory of mind as measured by the shape school, shape span test, TOM scale, TOM story books, TOM assessment checklist, and EFs assessment checklist. The secondary outcome is EFs and TOM behavioral domains as measured by TOM behavior checklist, and brief-preschool version at baseline (T0), post-treatment (T1), one-month follow-up (T2) and three-month follow-up (T3). Primary and secondary outcomes will be analyzed using repeated mesesure Analysis of Variance (ANOVA) and mixed model.

Discussion: the study will assess whether the cognitive intervention program effect not only on neuropsychological functioning of children with ASD but also on daily functioning. If the current trial shows that either the remediation approach and compensatory approach, or both are effective in improving socio-cognitive functioning, the trial would reveal a 'hybrid' remediation/ compensatory approach.

Keywords: Theory of mind, Executive function, Remediation cognitive intervention, Compensatory cognitive intervention, Autism.

Trial registration: This trial was registered in the Iranian Registry of Clinical Trials on the 1st of November, 2021. Registry NO. IRCT20210619051618N1

1. Introduction

Autism spectrum disorder is a neurological developmental condition characterized by a deficit in social interactions, verbal and nonverbal communications, restricted and repetitive patterns of activities and interests (American Psychiatric Association, 2013). This research focuses only on Autism with High-Functioning (HFA). Despite having average and high cognitive abilities, a child with HFA has significant deficits in other domains, such as executive functions (EFs) and theory of mind (TOM; American Psychiatric Association, 2013; Alvares et al., 2020; Devine, White, Ensor, & Hughes, 2016). Executive functions refer to higher – order cognitive processes that is critical goal-directed and adaptive behaviors (Carlson, 2005; Zelazo, 2015), which are closely related to social-emotional functions such as ToM. (Carlson, Claxton, & Moses, 2015; ozonoff & Miller, 1999). TOM is the social-cognitive capacity of humans to attribute mental states to themselves and others to anticipate and interpret behavior (Baron- Cohen, Leslie, & Frith, 1985; Leslie, 1987; Wellman & Liu, 2004). Longitudinal studies have demonstrated reciprocal relation between TOM and core components of EFs, including working memory, inhibitory control and cognitive flexibility (Carlson, Mandell, & Williams, 2004; Perner & Lang, 1999). There are some reasons of an association between TOM and EFs: First, both cognitive functions have a common developmental timeline: both TOM and EFs develop in preschool period. Second, TOM and EFs covered by a common brain region. Third, autistic individuals have impairments in TOM and EFs (Carlson, Moses,& Breton, 2002). Because of the critical role EFs and TOM in every aspects of human life and academic achievement(bets et al., 2011), several empirical evidence have been focused on cognitive interventions aimed at enhancing TOM and EFs in preschoolers (Steernman, Jackson, Pelzer, & Muris, 1996; Wellman et al., 2002; Begeer et al., 2011,2015; Scionti, Cavallero, Zogmaister, & Marzocchi, 2020). As a result, development and effectiveness of cognitive training programs for improving TOM and core executive functions may help produce treatment protocols that promote social interactions and quality of life from childhood to adulthood (Beeger et al., 2011; Beeger et al., 2015; de Veld, 2017).

Over the last few years, a large number of studies focused on the remarkable effects of cognitive interventions (Rossignoli-Palomeque et al., 2019; Scionti et al., 2020; Macoun, et al., 2021; Pasqalotto et al., 2021). Cognitive interventions most commonly use two approaches for promote and remedy of cognitive dysfunction: a process-based approach and a strategy-based approach; The process-based approach points to remediation cognitive

interventions (Kleim & Jones, 2008; Sohlberg et al., 2003). while the strategy-based approach is related to compensatory cognitive interventions (Ylvisaker, 1998; Wykes et al., 2011).

remediation approaches use a wide range of cognitive tasks and standard set of exercises to restore impairment cognitive functions. Some remediation programs aim to promote a specific cognitive function (e.g., inhibitory control), while others are extended-based, comprising multiple domains (Kleim & Jones, 2008; Mishra & Gazzaley, 2014). In contrast, the Compensatory Strategies are modifications and behavioral strategies aim to circumvent cognitive and motivational challenges (Horn & lewis, 2014; Ylvisaker et al., 2007).

Both approaches have potential and unique benefits, consequently, more recent studies suggested that a combination of compensatory and remediation cognitive intervention can be used in cognitive training programs (Cicerone et al., 2011; partanen, Jansson, Lisspers, & Sundin, 2015).

According to research evidence, it seems that hybrid remediation and compensatory interventions leads to generalized improvements trained and untrained cognitive functions (i.e., executive skills) than training each of these alone (Macoun, et al., 2021; Cicerone et al., 2011; partanen, Jansson, Lisspers, & Sundin, 2015). As a result, combining process-based and strategy-based approaches can be useful in significant change and the near- and far- transfer (Macoun, et al., 2021). Although, a large number of studies to date have focused on cognitive training programs to be successful to improve impaired functioning. Nevertheless, a closer look at the literature on cognitive interventions reveals several gaps and insufficiencies.

In children with ASD, intervention and rehabilitation programs to improve executive functions are far less than the theory of mind interventions (Fisher & Happe, 2005; Kenworthy et al., 2014; de Vries, Prins, Schmand, & Geurts, 2015). Even though there is reciprocal correlation between theory of mind and executive function. Yet, no specific hybrid training program for enhancing both executive functions and theory of mind has been developed.

A large number of cognitive interventions especially interventions aimed to improving theory of mind and executive functions were carried out for school-aged children with ASD (begger et al., 2011; Hoddenbach et al., 2012; de Veries et al., 2015; de Veld et al., 2017; Caputi, Cugnata, & Brombin, 2012; Spaniol et al., 2021). Whereas, cognitive interventions in preschool children with ASD are very limited (Fisher & Happe, 2005; Gulsrud, Kasari, Freeman,

& Paparella, 2007; Macoun et al., 2020). Since, TOM and EF development milestones are in preschool periods. Therefore, focusing on improving and promoting impaired cognitive functions (EFs and TOM) during the preschool periods will have a lasting effect on social and cognitive functions at school age (Gibb et al., 2021; Scionti, Cavallero, Zogmaister, & Marzocchi, 2020; Diamond & Lee, 2011).

The majority of studies have shown that impaired executive function and theory of mind have negative and substantial outcomes for academic performance, psychosocial adjustment and everyday behavior. On the other hand, neuropsychological assessments don't provide reliable and comprehensive information about executive function and theory of mind behavioral features in real world situation. Therefore, to evaluation of the effectiveness of cognitive intervention on broad domains of behaviors in natural environment, must be use behavioral rating measures of theory of mind and executive function.

In the present trial, the intervention program will be designed to address some of the limitations of previous cognitive interventions in children with ASD. a remediation-based intervention will be carried out to improve cognitive functions, such as EFs and TOM. Compensatory-based interventions will be carried out to manage disruptive behaviors, communication and social interaction. As a result, the goal of present study is to evaluate executive function and theory of mind via both cognitive and behavioral assessments.

1.1 Aims and objectives

This research aims to compare the effects of remediation and compensatory cognitive interventions on EFs and TOM skills in preschool children with autism. We are interested in surveying transfer effects from the cognitive intervention to an untrained domain of TOM and EF (i.e., measures of behavioral outcome).

1.2 Primary objective

1. To assess the effectiveness of remediation and compensatory cognitive intervention and hybrid remediation and compensatory cognitive intervention on TOM skills.
2. To assess the effectiveness of remediation and compensatory cognitive intervention and hybrid remediation and compensatory cognitive intervention on EF components (working memory, inhibitory control, cognitive flexibility).

1.3 Secondary objective

1. To assess the effectiveness of remediation and compensatory cognitive intervention and hybrid remediation and compensatory cognitive intervention on TOM behavioral domains.
2. To assess the effectiveness of remediation and compensatory cognitive intervention and hybrid remediation and compensatory cognitive intervention on EF behavioral domains.

2. Methods/ Design

2.1 Trial design

A multicenter, multi-arm, double-blinded, randomized controlled trial will be conducted to compare the effectiveness of remediation and compensatory cognitive interventions. The proposed trial will have parallel, three-groups with random allocation of participants to each group (1:1:1ratio): remediation cognitive intervention, compensatory cognitive intervention or (active control group), and 'hybrid' cognitive intervention (remediation + compensatory). All three arms will be examined four times: T0 (pre-test, baseline), T1 (post-test), T2 (1-month follow-up), and T3 (3-months, follow-up) point. The protocol was specified before the start of the trial (www.irct.ir, registration cod: IRCT20210619051618N1) and published before the data collection was finished. Full details of the trail protocol are available at www.irct.ir. Figure 1 outline the CONSORT (Consolidate Standard of Reporting Trail) flow diagram of this trail.

2.2 Participants and Eligibility criteria

Parents of preschoolers with ASD, ages 4 to 7, are invited to participate. The Diagnosis and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) is used to make the diagnosis of autism spectrum disorder; a multidisciplinary professional team has assessed all children and received a diagnosis of autism spectrum disorder. Inclusion criteria will be as follow: i) Child aged between 4- 7 years old; ii) preliminary diagnosis of autism spectrum disorders (according to psychiatrist criteria from the DSM 5th edition); iii) A full intelligence quotient (IQ) of at least 70 as measured by the version of the Persian Wechsler Intelligence Scale for children (WISC- III); iv) parental consent to participate in research; v) availability to participate in the research for six month; Exclusion criteria will be as follow: i) Participate in a similar rehabilitation and psychological intervention; ii) Refusal/ withdrawal to participate in this trial; iii) severe sensory motor impairment condition associated with ASD; iv) absence

more than three times during intervention period; v) inaccessibility to the internet at home; vi) Low intrinsic motivation to participate.

2.3 Ethics and dissemination

The study protocol was approved by the Human Research Ethics Committee of the Institute of Cognitive Science Studies and Institutional Research Ethics Committee (IR.UT.IRICSS.REC.1399.011). All of the Participants voluntarily will be joined in the present study and they are asked to fill written informed consent. Participants data will be detected by the code number. research records will be retained for three years after the completion of the research. Participants will be provided the opportunity to fill out questionnaires and checklists and they are asked to call principal investigator with any question and ambiguity.Training sessions may be recorded on video or photographed and used to educate or present, but the faces of the children will be obscured in both cases. Each participant will be notified of the risk and potential benefits of taking part in this trial.

2.4 Recruitment procedure

The principal investigator will be given the details of the study over the phone and via WhatsApp to the parents/caregivers of the children who meet the inclusion criteria. Obviously, individuals may submit an opt-out form if they do not want to be contacted again for research purposes. The principal investigator will be contacted the participants about two weeks later. The research assistant explains the details of the research to the parents, such as length of the sessions and the content of the intervention. Then, they will acquire written permission from the parents to complete questionnaires and checklists during the intervention and follow-up. All intervention and assessment sessions will be conducted using an online skype meeting app.

2.5 Sample size calculation

The sample size for this study will be performed by power calculations using G* power 3.1.9.7 (Faul, Erdfelder, Lang, Buchner, & 2007). Because there are two primary outcomes, so compute separately the sample size for each primary outcome and will use the greatest obtained sample size. A previous study indicates that theory of mind intervention for children with ASD generally has a medium effect size (Cohen's *f*=0.260), and previous studies indicate that executive function training in preschoolers overall has a medium effect size (Cohen's *d=0.498)*. The required sample size per arm is 22 (Begeer et al., 2011; Ryan & Charragain; 2010; Re, Capodieci, & Cornoldi, 2015; Joekar et al., 2017; Volkaert & Noel, 2015). according

to our experience in the previous study, it is assumed a drop-out rate of %15, so the sample size will be determined at 25 participants in each group: remediation group (n=25), remediation + compensatory (n=25), and active control group (n=25).

2.6 Randomization and Blinding

2.6.1 Sequence Generation

After receiving informed consent, all eligible participants will be randomly assigned to one of the three arms using randomized permuted blocks of length 3 in a ratio of 1:1:1. Participants will be randomly allocated and enrolled to Arm A, Arm B, or Arm C. The assignment list will be carried out by a co-principal investigator who is not involved in the present study.

2.6.2 Allocation Concealment Mechanism

Randomization will be generated by a web-based randomization program (http://www.randomization.com). The allocation concealment will be guaranteed, as the arm allocation and randomized sequence list will be provided by the co-principal investigator and will be quite concealed from the research team until the end of the registration period. So assignment list will be kept by a responsible person.

2.6.3 Blinding

Research team expect principal investigator (who is the intervention provider), parents, outcome assessors, and data analyst will be blind to participant group for the baseline, post-test and 1, 3-month follow-up visit. The research team will not be involved in the randomization process or intervention delivery.

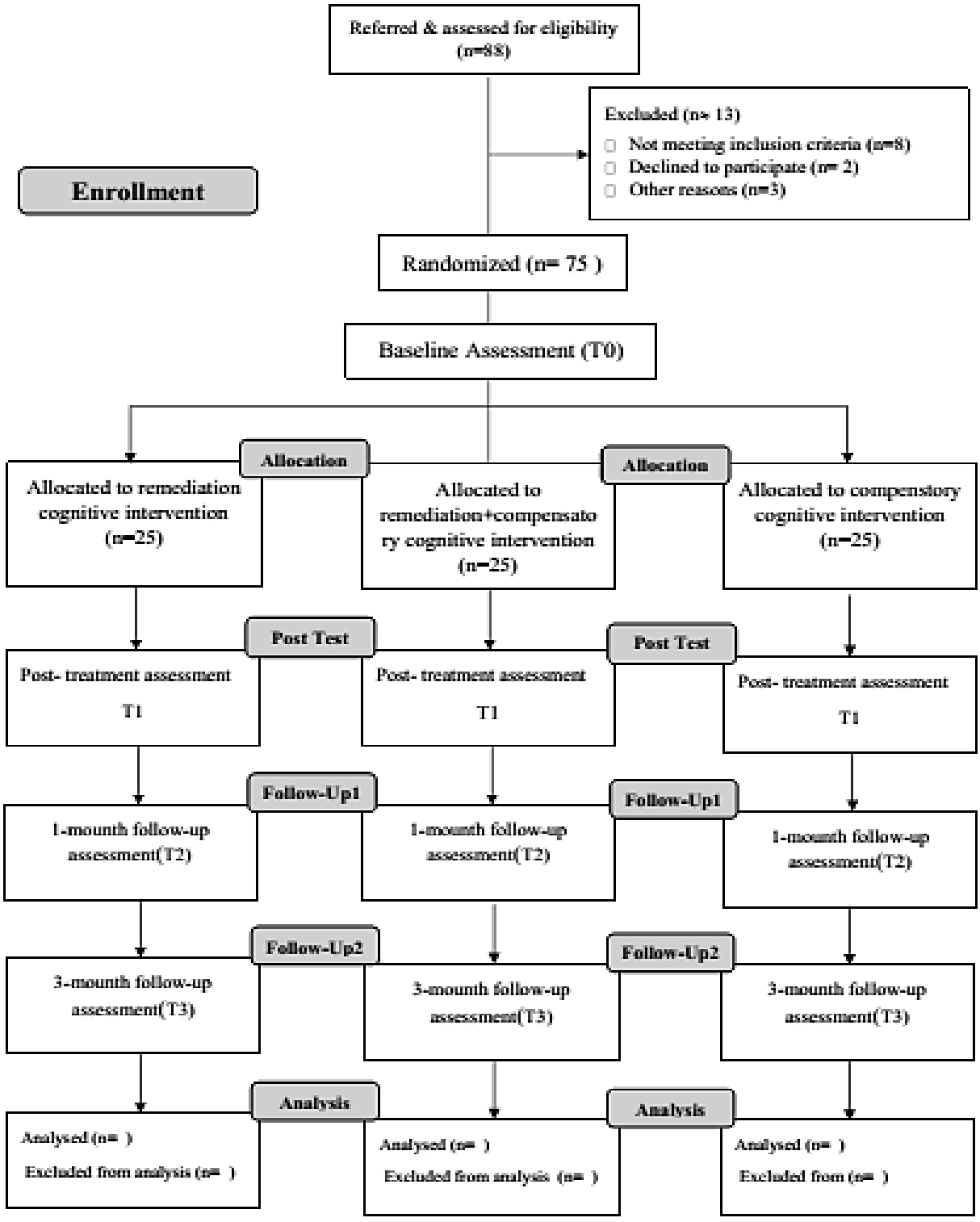

Figure 1. Enrollment, randomization, allocation, post-test, and follow-up on a CONSORT diagram

2.7 Outcome measures

2.7.1 Primary outcome measures

2.7.1.1 Inhibitory Control and Cognitive Flexibility Assessment

The Shape school is intended to evaluate preschoolers' executive skills, such as cognitive flexibility and inhibitory control. It is to orally assess inhibition and switching both independently and concurrently. The Shape school is designed in a storybook format with attractive stimuli. The story continues with the pupils " lining up " in the playground and it comprises four conditions: In control conditions, the child is asked to name the figures' color (i.e., a red circle, a yellow square, or a blue one). In inhibit conditions, shapes have two distinct emotional states. The child is asked to identify pupils who are ready for lunch (happy faces) but not those who are not (sad faces) .The inhibit condition use to evaluate prepotent response suppression. In the switch condition, some pupils are wearing hats, while others are not. In the third condition, every pupil has a neutral face. The child is asked to identify the shape of the pupils wearing hats and the color of the pupils without hats. The switch condition use to assess cognitive shifting. The fourth condition, inhibition and switching include pupils with happy and sad face, as well as those with and without hats. The child is instructed that not all pupils are prepared to paint. The child is asked to identify the happy pupils who are prepared to paint (e.g., color or shape) but not those with a sad face. In the last condition, response inhibition and cognitive switching are evaluated simultaneously. Efficiency score was calculated (the number of correct- the number of error / total time; Espy, 1997). The shape school does not have a Persian version. Therefore, their validity and reliability will be calculated.

2.7.1.2 Working Memory Assessment

Shape span was used to measure working memory in preschool children. The task was carried out similarly as digit-span forward and backward, except that instead of a digit, line drawing shapes (e g., animal or fruits) are presented to the child. The digit span was introduced and scored as recommended in the WISC-III manual. In shape span, participants were asked to name a picture of each animal before carrying test. If the participant does not identify the animal, the animal was not included in the test. In the beginning, two shapes (one small and one big) are shown to the participant. The participant then is asked to recall the shape from small to large. An image is added at each step to reach nine images. During the

task, the shape of any animal was used only once. The total score is acquired based on the number of correct answers in each trials(Carlson, 2005). The shape span does not have a Persian version. Therefore, their validity and reliability will be calculated.

2.7.1.3 TOM Scale

Wellman & Liu designed the TOM scale to measure some of the theory of mind's components. We will use a Persian adaptation of the TOM scale, which consists of six tasks: Diverse Desire (DD), Diverse Belief (DB), Knowledge Access, Explicit False Belief (EFB), Hidden Emotion (HE), and Content False Belief (CFB) (EFB). These five tasks comprise the standard 5-item scale, which is commonly administered to children aged 3 to 7 years. Each task contains a warm-up or control question in addition to its target question. The process of translation and adaptation of TOM scale into the persion version comprises the following steps: forward translation, back translation, revision by an expert panel and pre-testing. Total TOM score is ranging between 0 and 6 (Wellman & Liu, 2004). TOM scale does not have a Persian version. Therefore, their validity and reliability will be calculated.

2.7.1.4 Theory of Mind Story Book (TOMSB)

The TOMSB has been chosen to evaluate the TOM qutiont of children aged 3 to 11 years. There are 34 tasks with a total of 95 questions, including 77 test questions and 18 justification questions. There are a total of 6 stories: How does Sam feel? Sam goes to the park, Sam goes swimming, and Sam visits his grandparents, Sam on the farm, for his birthday celebration. The TOMSBs tasks are based on tasks from previous research, such as emotion recognition, emotion-based desire, mental-physical differentiation, perceptual knowledge, emotion-based belief, and first-order false belief (unexpected transfer and unexpected content task). The process of translation and adaptation of TOM qutiont into the persion version comprises the following steps: forward translation, back translation, revision by an expert panel and pre-testing. Answers are encoded as correct or incorrect. Internal consistency of the TOM qutiont in Dutch sampels was good (Cronbach's alpha = 0.90; Blijd-Hoogewys, Van Geert, Serra, & Minderaa, 2008). Theory of mind qutiont does not have a Persian version. Therefore, their validity and reliability will be calculated.

2.7.2 Secondary outcome measures

2.7.2.1 TOM Behavior Checklist (TOMBC)

TOMBC is chosen to evaluate TOM behaviors. The TOMBC is a parent questionnaire meant to examine parental observations of their child's theory of mind-related behaviors. Parents were asked to rate the frequency of eight behavioral domains (empathizing with others, inquiring about others' feelings, apologizing for mistakes, paying attention to what others are saying, unconsciously complimenting others, expressing interest and enthusiasm in what others are saying, asking interesting questions, and understanding jokes) over the previous week (0-never to 5-always). These behaviors were chosen based on information supplied by parents during earlier intervention evaluation sessions. Internal reliability of the TOMBC in Dutch sampels was 0.81(begeer et al., 2011). Theory of mind behavior checklist does not have a Persian version. Therefore, their validity and reliability will be calculated.

2.7.2.2 BRIEF-Preschool Version

This questionnaire is used to assess the different aspects of ececutive functions in preschool children 2 to 5 years and 11 months in everyday life situations. The preschool version of the Behavior Assessment Test (BAT) in the field of EF has 63 questions. EFs in this questionnaire are divided into 9 items. Inhibit, Shift, Emotional Control, Working Memory, and Planning / Organizing are its five clinical scales. Its three principal clinical signs are the result of a complex interaction of critical components such as Inhibitory Self-Control, Flexibility, and Emergent Metacognition. Internal consistency and content validity of the BRIEF in persion sampels was good (Cronbach's alpha: 0.93; Gioia, Isquith, Guy, & Kenworthy, 2000).

2.7.3 Other measures - diagnostic assessments

2.7.3.1 ATEC Evaluation Structure

The Autism Treatment Evaluation Checklist (ATEC) is a questionnaire given by parents, teachers, and caregivers to assess changes in the severity of ASD in response to treatment. This comprises the overall score (77) as well as the four subscale scores, which are Speech / Language Communication (14 questions), Sociability (20 items), Sensory / Cognitive Awareness (18 items), and Health / Physical / Behavioral Awareness (18 things) (25 items). A lower score indicates less severe ASD symptoms and a higher score is associated with more severe ASD symptoms. ATEC is practical tool to evaluate the effectiveness of various autism treatment. In adition to, it is a diagnostic tool in the evaluation of children's autism symptoms. Many parents and teachers use ATEC to monitor their child's performance over

time. Internal consistency and content validity of the ATEC in persion sampels was good (Cronbach's alpha: 0.86 -0.93; Memari et al., 2013).

2.7.3.2 Wechsler Preschool and Primary Scale

For preschool-aged children, the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III) is an international multidimensional measure of intelligence (from 2 years and 6 months to 7 years and 3 months). The Iranian children will be measured by the Persian Wechsler Intelligence scale revised (Wechsler & Kort 2005). The reliability for Persian version is (r=83), (r=90), and (r=.88) for verbal IQ, performance IQ and full-scale IQ (Wechsler, 1991; Shahim, 2006).

2.8 Intervention Description

2.8.1 Remediation Cognitive Intervention

Autism Yar is a paper and pencil cognitive rehabilitation program. Autism Yar program introduces a set of tasks and activities that build and enhance executive functions and social cognition skills enjoyably and interactively. Executive function and memory pack comprise the following workbooks: working memory, inhibitory control, cognitive flexibility, visual memory, visual-spatial memory, visual-sequential memory, auditory memory, and auditory comprehension. The social cognition pack includes the following workbooks: emotion comprehension (emotion recognition, situation-based emotion, external cause of emotion, desire-based emotion, belief-based emotion, reminder of emotion, emotion regulation, hidden emotion, mixed emotion, multiple emotion, emotion caused by moral and immoral factors), appearance-reality distinction, mental physical distinction, diverse desire and diverse belief, informational state (simple visual perspective taking, complex visual perspective taking, seeing leads to knowing, action based knowledge, false belief), and empathy.

The Autism Yar program is a 42-session individual or group based intervention for children with autism. Due to the COVID-19 pandemic, the intervention will be carried out online by one of the researchers, who will provide training to intervention groups. The online format as group will be held during 45 sessions (3 days a week) for parents of children with autism. In each online group, there will be about 25 people (see table 1).

Table 1. Overview of sessions- remediation cognitive intervention

SESSIONS	MAIN DOMAIN TOM TASK	MAIN DOMAIN EFS TASK	INTERVENTION SESSIONS IN WEEK
SESSION 1 **SESSION 2**	Appearance- reality distinction (Material, size color, identity)	**WM** - shapes span recalling two& three shapes (smallest to largest)	Week 1
SESSION 4 **SESSION 5**	mental- physical distinction (identity)	**WM** - shapes span recalling four & five shapes (smallest to largest)	Week 2
SESSION 7 **SESSION 8**	Diverse desire- diverse belief	Simon says with multiple instruction	Week 3
SESSION 10 **SESSION 11**	emotion recognition	Which is shape missing	Week 4
SESSION 13 **SESSION 14**	external cause of emotion	**WM** recalling six & seven shapes(smallest to largest)	Week 5
SESSION 16 **SESSION 17**	desire- based emotion	**WM** Match picture pairs	Week 6
SESSION 19 **SESSION 20**	belief- based emotion	**inhibitory control** identification of size, shape, number-color, animal- color, direction- color, fruit- color and inhibition of other stimuli	Week 7
SESSION 22 **SESSION 23**	emotion regulation	**inhibitory control** find hidden shape	Week 8
SESSION 25 **SESSION 26**	hidden emotion	**inhibitory control** distinguish one stimulus from other stimuli that are similar	Week 9
SESSION 28 **SESSION 29**	simple perspective taking	**inhibitory control** distinguish one stimulus from other stimuli that are similar	Week 10
SESSION 31 **SESSION 32**	complex perspective taking	**inhibitory control** inhibition of conventional color and identification of unconventional color	Week 11
SESSION 34 **SESSION 35**	seeing leads to knowing	**cognitive flexibility** tracing stimuli	Week 12
SESSION 37 **SESSION 38**	predicting actions of person's knowledge	**cognitive flexibility** shifting attention and trail making task	Week 13
SESSION 40 **SESSION 41**	understanding first order false belief (unexpected transfer/ unexpected content false belief).	**cognitive flexibility** Shape and movement, similarity of shapes, sorting by dimensional change	Week 15

10 sessions (3,6,9,18,21,24,27,30,33,36,39, 42) out of the total sessions will be dedicated to answering parents' questions. Also, the therapist will do the exercises in the presence of the parents with one of the children who will be chosen as a model so that they can be trained.

2.8.2 Compensatory cognitive intervention

Compensatory cognitive intervention is based on parent education programs (PEP) and Project ImPACT (Improving Parents as Communication Teachers). PEP and Project ImPACT focus on the core symptom area of ASD (such as behavioral difficulties, socialization, and communication). This program will be conducted and managed by a psychologist (a member of the research team) and consisted of 12 (60- 90 minutes) core sessions. The structured PEP sessions can be administered either in individually or groups to the parent using direct strategies, role play, filling out the daily activity schedule, video examples, and homework assignments. Parents are instructed on the underlying causes of autism disorder, the behavioral problems, how to improve the child's impaired social and cognitive functions, and also behavior management skills. Ingersoll and Dvortcsak detail the intervention strategies and training programs for parents in great detail (Ingersoll & Wainer, 2013). Furthermore, the parents during the sessions will be taught about making use of positive behavior support techniques to manage maladaptive behaviors and support the improvement of their child's communication skills, play skills, and social functioning (see table 2; Brereton & Tonge, 2005).

Table 2. Overview of sessions- compensatory cognitive intervention

GROUP SESSIONS	CONTENTS
SESSION 1	Overview of project ImPATC and set up your home
SESSION 2	Develop goals for your child
SESSION 3	Focus on your child and adjust your communication
SESSION 4	Create opportunities
SESSION 5	Teach new communication skills
SESSION 6	Teach play skills
SESSION 7	Shape the interaction and plan for continued success
SESSION 8	Review of shape the interaction and update your child's goals
SESSION 9	**Self- regulation: the key to making it through the day** The case for self-regulation Why do autistic children have difficulty self-regulating?
SESSION 10	**Setting children up for success** Adjust learning experiences and the environment Emphasize structure and consistency
SESSION 11	**Social skills** Teaching social thinking Teaching conversational skills
SESSION 12	**Encouraging imaginative play** Teaching play and building imagination Facilitating play with peers Maintaining play and coping with resistance

2.8.3 Hybrid cognitive intervention (Compensatory cognitive intervention remediation cognitive intervention

This group of children will receive combination of the Autism Yar program, parent education programs (PEP) and Project ImPACT over 14 weeks(4 days a week). Participants will receive the Autism Yar program at 3 days a week and the PEP will receive one day per week.

2.9 Data analysis

Before analysis, the normality of the raw data will be tested for all of the key variables. Analysis all of the primary outcomes and secondary outcomes will be carried out using repeated measures analysis of variance (ANOVA) and mixed models as the primary design. Multiple imputations will be used for missing observations at post-intervention, 1- month, and 3-month follow-up. Pretest differences in demographic characteristics (age, gender, Total IQ, verbal IQ, performance IQ, parental education, parental age) will be investigated with chi-square tests and analyses of variance. Both within (changes within person across time) and between-subject (changes between persons in the intervention condition versus the control conditions) impacts will be investigated to determine the efficacy of the remediation and compensatory cognitive intervention. Within-subject variable "time" has four levels: T0 (pre-intervention), T1 (post-intervention), T2 (1-month follow-up), and T3 (3-months follow-up). between-subject variable "condition" has two levels: intervention conditions and control conditions. The eta-square statistic ($\eta 2$) will be computed to estimate the effect size to recognize the practical significance of the results. Secondary outcomes investigated in a same method to the primary outcomes analisis. Statistical analyses are performed using SPSS 22.0 statistical software (SPSS) and are two-sided, with a level of significance of $\alpha = 0.05$.

3. Discussion

The aim objective of this trial is to determine the effectiveness of an Autism Yar rehabilitation program for improving EFs and TOM skills in preschoolers with ASD. The Autism Yar can also be used as an educational and rehabilitation tool for teachers and parents by providing them with strategies to create regular and continuous learning opportunities for their children daily at home and school. Overall, the Autism Yar has the potential to intensify the positive impact of any developmental, social and behavioral program for the treatment of ASD children.

The results of this trial will provide evidence to assess the feasibility of parents becoming a therapist for their children with ASD through a rigorous and yet pragmatic

evaluation process. It will also provide evidence for the effectiveness of the Autism Yar program in improving trajectories for children with autism at school age.

One of the strengths of the current trial, our study is the Multicenter, randomization, double-blinded, treatment-as-usual to control group, parallel-group trial for the comprehensive evaluation and effectiveness of a dimensional rehabilitation program in preschoolers with autism. Another strength is using the multiple outcome assessment tools to obtain information from a variety of reporters.

Three potential limitations of the present trial should be mentioned. First, trained parents will do the intervention. In order to confirm the effectiveness and generalizability of the rehabilitation program, the training implemented by teachers should be evaluated. Second, it will not address whether the rehabilitation group's TOM and EF gains were sustained or whether the rehabilitation program was associated with greater academic achievement and school readiness at the end of Kindergarten and Grade 1. It is necessary to focus future studies on the effectiveness of TOM and EFs training on academic achievement and social communication.

Third, although having an active control group is better than an inactive control group, the number of intervention sessions in the active control group (12 sessions) is not the same as the intervention groups (one of them received 42 sessions and the other received 54 sessions). Therefore, the improvement in performance and changes in brain activity in the intervention groups are probably partially explained by the difference in the amount of intervention between the three groups. So, it is better that the groups receive the same intervention sessions in future studies.

Conflict of Interest

The authors report no conflict of interest.

Acknowledgment

The research team would like to Special thanks to rehabilitation centers for referring their patients to principal researcher in this study.

Funding

This study has received funding from the Cognitive Science and Technologies Council for conducting parenting workshops, designing the trial, collection and analysis and interpreting of data, and developing and designing the AutismYar rehabilitation program.

Author's contributions

FS, AM, HZ, MM, and MS contributed to the design of the trial. AM supervised the development of the study protocol. HZ, FA, and MA jointly designed checklists. FA is a Ph.D. student and supervises the process of participant recruitment, parent training, and drafting the manuscript. MS planned the statistical analysis.

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CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	Title and abstract page 1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	Title and abstract page 1
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	2- 5
	2b	Specific objectives or hypotheses	6
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6,7
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	n/a
Participants	4a	Eligibility criteria for participants	7
	4b	Settings and locations where the data were collected	8
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	17, 18

Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	11-16
	6b	Any changes to trial outcomes after the trial commenced, with reasons	n/a
Sample size	7a	How sample size was determined	8,9
	7b	When applicable, explanation of any interim analyses and stopping guidelines	n/a
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	9
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	9
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	9
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	9
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	9
	11b	If relevant, description of the similarity of interventions	n/a
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	18,19
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	18,19
Results			
Participant flow (a diagram is	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	n/a

strongly recommended)	13b	For each group, losses and exclusions after randomisation, together with reasons	
Recruitment	14a	Dates defining the periods of recruitment and follow-up	
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	n/a
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	n/a
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	19
Other information			
Registration	23	Registration number and name of trial registry	2,7
Protocol	24	Where the full trial protocol can be accessed, if available	2,7

Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	20

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.