ARTICLE ORIGINAL

Working memory training in autism: Near and far transfer

Entraînement de la mémoire de travail dans l'autisme: Transfert proche et éloigné

Safae Sedjari[1], Mohammed El-Mir[2], Zouhayr Souirti[3]

1. Department of Psychology, Faculty of Letters and Human Sciences Dhar El Mahraz, university Sidi Mohamed Ben Abdellah, Fes, Morocco.
2. Psychological, Sociological and Cultural Studies Lab (PSOCUSL), Department of Psychology, Faculty of Letters and Human Sciences, Dhar El Mahraz, Sidi Mohamed Ben Abdellah University, Fes, Morocco. Editor-in-Chief of Arab Journal of Psychology
3. Neurology Department, Sleep Medicine Center, Hassan II University Hospital of Fez, Morocco. Head of the Outpatient Center, Hassan II University Hospital of Fez, Morocco. Clinical Neurosciences Laboratory, Faculty of Medicine and Pharmacy, University of Sidi Mohammed Ben Abdellah, Fez, Morocco

Abstract

Introduction: The autistic population is expanding. It is generally recognized that executive function deficits (EFs) are at the core of this disorder. Working memory (WM) is considered a critical element in executive functioning. WM training is regarded as a promising new therapy that can improve EFs and reduce symptoms of autism by targeting WM through repetitive exercises.
Aim: To investigate the impact of WM training on WM, cognitive flexibility, planning, and clinical symptoms. Also, to examine whether age influences the remediation effects.
Methods: Only one group of 20 verbal autistic participants aged 6 to 21 years was included. They received 40 training sessions. The program used is called «Cogmed». Neuropsychological measures were administered before and after the intervention to assess the three EFs. The Social Communication Questionnaire (SCQ) was exploited to evaluate its effects on clinical symptoms.
Results: Only 17 participants have completed the training. They showed significant and large improvements in WM subtests ($p<0.01$, $\eta^2>0.06$), cognitive flexibility ($p<0.05$, $\eta^2>0.06$), planning ($p<0.01$, $\eta^2>0.06$), and symptoms ($p<0.01$, $\eta^2>0.06$). Also, the ANOVA test revealed that the age and the intervention effects are not correlated in our sample ($p>0.05$).
Conclusion: WM training influences EFs positively in autism and reduces the severity of its clinical characteristics. Thus, it's an effective therapy that can be added to the management of this disorder.

Key words: Autism; Working memory; Working memory training; Cognitive flexibility; Planning; Autistic symptoms.

Résumé

Introduction: La population autistique est en expansion. Il est reconnu que les déficits des fonctions exécutives (FEs) sont au centre de ce trouble. La mémoire de travail (MT) est un élément crucial dans le fonctionnement exécutif. L'entraînement de la MT est considéré comme une nouvelle thérapie prometteuse qui peut améliorer les FE et réduire les symptômes de l'autisme en ciblant la MT par des exercices répétitifs.
Objectifs: Étudier l'impact de l'entraînement de la MT sur la MT, la flexibilité cognitive, la planification et les symptômes cliniques. Examiner aussi si l'âge influence les effets de la remédiation.
Méthodes: Un seul groupe de 20 participants autistes verbaux âgés de 6 à 21 ans a été inclus. Ils ont bénéficié de 40 sessions d'entraînement. Le programme utilisé est appelé «Cogmed». Des mesures neuropsychologiques ont été administrées avant et après l'intervention pour évaluer les trois FEs. Le questionnaire de communication sociale a été utilisé pour évaluer ses effets sur les symptômes.
Résultats: Seulement 17 participants ont terminé l'entraînement. Ils ont montré une importante amélioration de la MT ($p<0,01$, $\eta^2>0,06$), la flexibilité cognitive ($p<0,05$, $\eta^2>0,06$), la planification ($p<0.01$, $\eta^2>0.06$) et les symptômes ($p<0,01$, $\eta^2>0,06$). Le test d'ANOVA a révélé que l'âge et les effets de l'intervention ne sont pas corrélés dans notre échantillon ($p>0,05$).
Conclusion: L'entraînement de la MT influence positivement les FEs dans l'autisme et réduit la sévérité de ses caractéristiques cliniques. Ainsi, c'est une thérapie efficace qui peut être ajoutée à la prise en charge de ce trouble.

Mots clés: Autisme; Mémoire de travail; Entraînement de la mémoire de travail; Flexibilité cognitive; Planification; Symptômes autistiques.

Correspondance
Safae Sedjari
Department of Psychology, Faculty of Letters and Human Sciences Dhar El Mahraz, university Sidi Mohamed Ben Abdellah, Fes, Morocco.
Email: safae.sedjari@usmba.ac.ma

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INTRODUCTION

According to the Diagnostic and Statistical Manual of Mental Disorders (1), autism or autism spectrum disorder (ASD) is a neurodevelopmental condition that affects males four times more than females, and it's characterized by insistent deficits in social communication and interaction in different contexts associated with restricted and repetitive behaviors, interests, or activities. The prevalence of this disorder has almost reached 1% of the population in the past few years (1). The increasing autistic population is both alarming and challenging in terms of patient care, which requires more importance and supplemental interventions to alleviate its severity. One of the major cognitive theories in autism suggests that executive function deficits might be a logical theoretical explanation of autistic symptoms (2-4). EFs refer to superior cognitive processes used in the control of thoughts and actions (5) to adapt to new environmental stimuli (6). The deficit of EFs alters the daily life of the individual, his behaviors, and his social interactions (7). Some studies have suggested a strong correlation between impaired executive functioning and either social or non-social ASD clinical symptoms (8-13). WM is considered a crucial component of executive functioning that allows the temporary maintenance and manipulation of information to perform complex cognitive activities. It was associated with language skills and symptom severity (14) and also correlated to social functioning in the autistic population (15,16). Several studies have suggested that training through repetitive exercises can increase the capacity of WM (17-20). Moreover, a growing body of literature has indicated that WM training can be promising in many populations with neurodevelopmental disorders (21-25). However, there is a paucity of scientific research examining the effects of this therapy on ASD, and outcomes relating to either near transfer (enhancement of the trained domain) or far transfer (enhancement of the untrained domain) are controversial. For instance, some studies have reported important near transfer to WM (26-31), far transfer to autistic symptoms (29), and far transfer to other non-trained tasks (30), However, the meta-analyses of Melby-Lervåg and Hulme (18) showed the absence of transfer effects of WM training to further untrained tasks. Wagle and colleagues (32) have noticed the absence of either a near transfer to WM or a far transfer to clinical symptoms after a short-term intervention. de Vries and colleagues (33) have revealed that WM training leads to only marginal near transfer to WM but has no effect on social behavior. To our knowledge, there has been no research conducted about the far transfer of the WM training effect to EFs in autism; nevertheless, some studies adopting cognitive remediation programs containing the WM module, among others, have reported amelioration of EFs (34-38) and autistic symptoms (35,37-39). In effect, we cannot consider that these improvements are the results of WM training, but we presuppose this therapy can contribute to EFs and autistic symptom enhancement. Then, the effects of WM training on ASD are not clear, which necessitates more scientific studies relating to this area.

METHODS

Study and participants

This study is a pilot study of a single-group open-label trial. Participants are aged 6 to 21 and affiliated with an association specializing in autism. A written consent was required from their parents. Twenty verbal participants with ASD (level 1, 2, or 3) met the eligibility criteria, predominantly male and all Moroccan. Only 17 have completed the remediation, 16 male and one female. The dropout rate was 15%. Eight participants presented comorbidity (ADHD). The group included children aged 6 to 11 (n = 6), adolescents aged 12 to 17 (n = 8), and adults aged 18 to 20 (n = 3). They were diagnosed according to the DSM-5-TR by pediatricians, psychologists, or pediatric psychiatrists. All participants had to be able to recognize letters and numbers from one to nine in French, seeing that the program was administered in French. They also had to be able to use a laptop, digital tablet, or iPad since the program of remediation is computerized. They all needed to complete 40 training sessions; every session lasted 25 minutes. None of the participants used drug treatment. Most of them (n = 13) attended primary school, and four were in middle school. The only exclusion criterion was starting or stopping a drug treatment, such as psychotropic medication, that can influence the cognitive processing of the participant to avoid confusion concerning the effects of the intervention. All participants were examined twice with neuropsychological measures by the same neuropsychologist in a dedicated assessment site at the headquarters of the association. The first evaluation was to assess baseline cognitive functioning, and the second was to evaluate the remediation effects. A questionnaire was administered to the participant's parent or assistant before and after training to examine changes in autistic symptoms.

Measures

Measures included two kinds of tasks: near transfer to WM and far transfer to cognitive flexibility, planning, and ASD symptoms.

The tests used to evaluate the three components of WM are the forward digit span task to measure the phonological loop's capacity, the Corsi block test to measure the visuospatial sketchpad's capacity, the back digit span task, and the modified one to evaluate the central executive. The computerized version of the Wisconsin Card Sorting Test (WCST) was used to assess cognitive flexibility; the Tower of London Test (TLT) was used to evaluate planning; and symptoms of ASD were assessed using the Social Communication Questionnaire (SCQ). In addition to these measures, we adopted Cogmed Working Memory Training (CWMT) as a training program.

Near transfer to WM tasks

Forward digits span task

This task, from the Wechsler Adults Intelligence Scale (WAIS) and the Wechsler Memory Scale (WMS), is used to measure the phonological loop's capacity. It consists of the oral presentation of eight series of digits, from two digits up to nine digits, at the rate of one item per second. The participant must memorize and retrieve numbers in the order in which they are presented. He can try two attempts for each series; if he fails the first, the examiner gives him the second, but if he fails both attempts, the test stops.

The capacity of the phonological loop corresponds to the number of elements of the longest series reproduced without error.

Corsi block task

This test was developed by Corsi (40) and applied to measure the visuospatial sketchpad's capacity. The participant has to retain and reproduce the visuospatial sequences carried

out by the examiner using his index finger on a wooden board with nine small blocks distributed irregularly and asymmetrically, with a pointing frequency between 1 and 3 seconds. The number of blocks increases progressively. If the participant fails the first attempt, he must try a second one. When two attempts at the same level fail, the test stops.
The longest sequence that the participant remembered and was able to successfully reproduce, in one of the two attempts, coincides with the sequential visuospatial span.

Backward digit span task
This task, from the Wechsler Intelligence Scale for Children (WISC-V), is used to evaluate the central executive. It comprises eight series of numbers presented at the rate of one item per second, which the participant had to recall immediately and inversely. The number of digits increased, and each series had two tries. If the participant succeeds in the first attempt, the examiner presents the series for the next level; if not, he tries the second attempt, and in the event of failure, the test stops.
The reverse digit span corresponds to the longest series that the participant was able to memorize and retrieve correctly in reverse order.

Modified digit span task
It's also applied to evaluate the central executive; it involves a series of letters ending in a number, ranging from two to eight series, which must be presented at the rate of one item per second. The participant must retrieve digits according to the order of the presentation and omit the letters. He can make two trials; if he succeeds in the first, he passes to the next level. If he fails, he can try another time. The test stops if he fails both trials.
The modified digit span is the number of digits correctly retrieved by the participant.

Far transfer to flexibility task

Wisconsin Card Sorting Test (WSCT)
The version of WSCT used in this study is computerized and available at (www. psytoolkit.org). There are 60 trials in this test. Four stimulus cards are presented at the top of the screen, each containing one red circle, two green triangles, three blue crosses, or four yellow stars. The participant should match a card to one of the four others following one of the three rules: the color, the number, or the shape that changed now and then. He gets feedback; if his choice is not correct, he needs to change the rule.
At the end of the test, we get the number of errors and perseveration errors that refer to the number of times the participant had to change the rule, but he did not.

Far transfer to planning task

Tower of London Test
This test was created by Shallice (41). It necessitates two models, each with three rods of 1 cm in diameter fixed on a base. The rods are respectively at heights of 13, 8.5, and 4 cm, and they are separated from each other by 4 cm (42). The participant must use three balls of different colors (red, green, and blue) with a diameter of 4 cm to arrange an initial configuration. The complexity of the test increases by increasing the minimum number of moves necessary to complete the model (43).

Far transfer to ASD symptoms

Social Communication Questionnaire
The SCQ is a binary rating scale used in the diagnostic process for ASD and is relevant to individuals aged more than 4 years with a mental age of at least 2 years. It contains 40 items targeting the three basic domains: the domain of reciprocal social interaction, the domain of communication, and the domain of restricted repetitive and stereotyped behaviors. The questionnaire is taken from the Autism Diagnostic Interview-Revised (ADI-R) and has two forms: the lifetime form and the current form (44). The form used in this study is the current one that can be completed by the parents or the principal caregiver concerning the individual's behavior all through the latest 3-month period. The current form can provide outcomes relating to the level of severity of ASD symptomatology over time and evaluate the effects of therapeutic or educational interventions (44).
Before utilization, the SCQ was translated into Arabic and validated for the Moroccan population.

WM training program
The training program adopted in this study is «Cogmed," or Cogmed Working Memory Training (CWMT). It's a computerized cognitive remediation program founded in 2001 by Torkel Klingberg. This program targets the components of the WM according to the Baddeley and Hitch model through repeated exercises in verbal, visuospatial, or bimodal modality (https://www.cogmed.com). The version used in this study is «standard,» with 11 exercises. Participants should carry out five sessions a week, with three exercises per session lasting 25 minutes. An optional reward game is presented at the end of each session to reinforce the user.

Statistical analysis
All data analyses were performed using the Statistical Package for Social Sciences (SPSS, version 25). The means and standard deviations were determined, and the paired t-test was applied to compare pre- and post-evaluations to examine whether participants improved in WM, cognitive flexibility, planning, and ASD symptomatology. The eta square test was conducted to determine the effect size of the intervention on the three EFs and autism symptoms. Additionally, an ANOVA test was used to verify whether there is a correlation between age and training effects. Participants were divided according to three age ranges: 6 to 11, 12 to 17, and 18 to 20.

Ethical Approval
The study was approved by the research ethics committee of the clinical neuroscience laboratory at the Faculty of Medicine, University Sidi Mohamed Ben Abdellah.

RESULTS

The statistical analysis included only the 17 participants who completed 40 training sessions, excluding those who dropped out of the study.
Table 1 reports a comparison of each neuropsychological test and the SCQ results before and after intervention. We used the number of perseverative errors as the criterion measure in WCST. In the SCQ, we have grouped the two domains of communication and social interaction in the same domain to be in line with the diagnostic criteria of ASD according to DSM-5-TR.
The table reveals there are statistically significant differences at 0.01 and 0.05 levels between pre- and post-evaluations of WM and cognitive flexibility, respectively. Differences were in favor of post-evaluation. Therefore, participants showed significant amelioration in the near transfer to WM subtests, and they also significantly improved in the far transfer to cognitive flexibility test.

The table shows there are also statistically significant differences at the 0.01 level between the pre- and post-test of the Tower of London. Differences were in favor of the post-test for the planning score while they were in favor of the pre-test concerning the number of moves and total time, which means the planning score was higher in the post-test while the number of moves and total time decreased after intervention. Hence, there is a significant amelioration between pre- and post-intervention scores in the transfer to planning task. Concerning the SCQ results, there are statistically significant differences at the 0.01 level between the pre- and post-evaluations in the total score as well as in the SCI and the RRSB domains. The differences were in favor of the pre-evaluation. Thus, participants showed a notable diminution in ASD symptoms.

Table 1. results of the paired t-test relating to pre- and post-evaluations

	Pre-evaluation (n=17)		Post-evaluation (n=17)				
Measures	**Mean**	**SD**	**Mean**	**SD**	**DF**	**t**	**p**
WM tests							
Forward digit span task	2.6471	1.80074	3.4118	1.66053	16	-4,19	0.001
Corsi block task	2.8824	1.72780	4.8824	2.39485	16	-5.090	0.000
Backward digit span task	1.5294	1.77192	2.8235	1.91165	16	-4.600	0.000
Modified digit span task	0.9412	1.59963	2.0588	2.07577	16	-3.271	0.005
WCST							
Perseverative errors	19.5882	5.79934	15.8824	3.14011	16	2.384	0.030
TLT							
Planning score	5.1176	4.60818	10.0588	3.97603	16	-4.915	0.000
Number of moves	70.1176	13.49946	57.7059	11.08921	16	4.458	0.000
Total time (s)	412.4118	272.53464	213.0588	223.06739	16	3.592	0.002
SCQ							
Total score	17.7059	6.14171	6.5882	3.04259	16	7.462	0.000
Domain of SCI	12.8824	4.70216	5.5294	2.96052	16	6.911	0.000
Domain of RRSB	4.8235	2.55527	1.0588	1.29762	16	6.001	0.000

WM: Working Memory; WCST: Wisconsin Card Sorting Test; TLT: Tower of London Test; SCQ: Social Communication Questionnaire; SCI: Social Communication and Interaction; RRSB: Restricted Repetitive and Stereotyped Behaviours

Table 2 shows the eta-squared values and the effect sizes of the intervention on the scores of each assessment. These values range from 0.26 to 0.80 ($\eta^2 \geq 0.06$), which indicates that the effect of the intervention on all post-measure outcomes is large.

Table 2. Eta squared values and effect size of the intervention on working memory, mental flexibility, planning, and ASD symptoms.

Measures	r	t	DF	η²	Size effect
WM tests					
Forward digit span task	0.909	-4.190	16	0.52	Large
Corsi block task	0.737	-5.090	16	0.62	Large
Backward digit span task	0.804	-4.600	16	0.57	Large
Modified digit span task	0.735	-3.271	16	0.40	Large
WCST					
Perseverative errors	0.066	2.384	16	0.26	Large
TLT					
Planning score	0.542	-4.915	16	0.60	Large
Number of moves	0.579	4.458	16	0.55	Large
Total time (s)	0.590	3.592	16	0.45	Large
SCQ					
Total score	0.247	7.462	16	0.77	Large
Domain of SCI	0.418	6.911	16	0.75	Large
Domain of RRSB	0.230	6.001	16	0.69	Large

ASD: Autism Spectrum Disorder; WM: Working Memory; WCST: Wisconsin Card Sorting Test; TLT: Tower of London Test; SCQ: Social Communication Questionnaire; SCI: Social Communication and Interaction; RRSB: Restricted Repetitive and Stereotyped Behaviors

In Table 3, the p-values obtained from the one-way ANOVA F-test assessing the correlation between age and the training effects were greater than 0.05 in all tests. Based on the analysis, we did not find sufficient evidence to conclude that age has a statistically significant impact on the outcomes of the intervention. This means that in our sample, age and the intervention's effect are not correlated.

Table 3. Results of the ANOVA F-test relating to the significance of post-measures means according to age

Post-evaluation	Age	N	Mean	SD	F	P
WM tests						
Forward digit span task	6-11	6	3.0000	1.67332	0.617	0.553
	12-17	8	3.3750	1.59799		
	18-20	3	4.3333	2.08167		
Corsi block task	6-11	6	5.3333	2.16025	0.282	0.758
	12-17	8	4.8750	2.85044		
	18-20	3	4.0000	2.00000		
Backward digit span task	6-11	6	1.5000	1.97484	2.735	0.099
	12-17	8	3.6250	1.68502		
	18-20	3	3.3333	1.15470		
Modified digit span task	6-11	6	1.3333	2.42212	0.540	0.594
	12-17	8	2.5000	1.92725		
	18-20	3	2.3333	2.08167		
WCST						
Perseverative errors	6-11	6	15.3333	2.33809	0.265	0.771
	12-17	8	16.5000	4.00000		
	18-20	3	15.3333	2.51661		
TLT						
Planning score	6-11	6	9.0000	4.81664	0.434	0.656
	12-17	8	10.2500	4.16619		
	18-20	3	11.6667	0.57735		
Number of moves	6-11	6	58.6667	13.70645	0.184	0.834
	12-17	8	58.3750	11.62433		
	18-20	3	54.0000	4.00000		
Total time (s)	6-11	6	255.3333	258.50932	0.182	0.835
	12-17	8	178.875	225.9275		
	18-20	3	219.6667	205.55372		
SCQ						
Total score	6-11	6	7.1667	2.92689	0.181	0.836
	12-17	8	6.1250	3.09089		
	18-20	3	6.6667	4.16333		
Domain of SCI	6-11	6	6.1667	3.12517	0.342	0.716
	12-17	8	4.8750	2.94897		
	18-20	3	6.0000	3.46410		
Domain of RRSB	6-11	6	1.0000	1.09545	0.207	0.815
	12-17	8	1.2500	1.58114		
	18-20	3	0.6667	1.15470		

WM: Working Memory; WCST: Wisconsin Card Sorting Test; TLT: Tower of London Test; SCQ: Social Communication Questionnaire; SCI: Social Communication and Interaction; RRSB: Restricted Repetitive and Stereotyped Behavior

DISCUSSION

The main focus of the current study was to examine three questions. First, whether WM training has a positive effect on its three components (near transfer); second, whether this effect can reduce the severity of ASD symptomatology and be generalized to other EFs, mainly cognitive flexibility and planning, that are not trained (far transfer); and third, whether there is a relationship between age and remediation effects. Outcomes of statistical analysis demonstrated large improvements in WM, cognitive flexibility, planning tasks, and symptoms. Hence, WM training leads to near transfer to WM and induces far transfer to other EFs in addition to clinical symptoms, but no association was detected between age and training effects.

Our findings are consistent with previous research; a near transfer of WM training in autism was reported in other studies (26-31), but not far transfer to cognitive flexibility and planning. As far as we know, no study focused on the effect of WM training on these two aspects of EFs. The far transfer to cognitive flexibility was found in neurotypical groups (45-47). Whereas the effect on planning was explored in other populations, such as children with ADHD and pediatric bipolar disorder (48). Some authors have noticed a diminution in clinical symptoms in ASD patients using the Frontal Executive Program, which targets not only WM but also cognitive flexibility and planning (34,38,39). So, training in these three processes induced an improvement in autistic symptoms. The current study confirms that WM training led to a far transfer to cognitive flexibility, planning, and ASD symptoms. In light of the two conclusions, we could put forward that WM training can contribute to the improvement of the clinical symptoms of autism. Even though there is a lack of studies exploring the effects of WM training in the autistic population, the results of the present work follow literature relating to WM. There is a strong relationship between WM and EFs (48). The central executive links between them even if they are disassociated (49). Transfer to other EFs is evident as training enlarges the WM capacity (23,50). The improvement is generalized (51) because of the key role of the WM capacity in the performance of many cognitive functions (52,53-55). More precisely, it has been shown that cognitive flexibility depends strongly on the phonological loop in the Baddeley and Hitch model. There exists a negative correlation between this function and verbal WM (56,57). Likewise, people with high WM capacity perform significantly better in tasks classically used to evaluate planning; the Hanoi Tower Task (58,59) and its variant, the TLT (60). Altagassen and colleagues (61) revealed that each of the three elements of WM was related to the planning task in healthy people. Furthermore, the remediation program adopted in this study targets all components of WM that may contribute to the generalization of training's effect (62,63). Also, it may be related to other moderating factors, such as parental support or the motivation of subjects (64,65). Unfortunately, our study did not investigate any of these moderators.

From an anatomical perspective, many neuroimaging studies have indicated that EFs are connected through an active, flexible network. The same prefrontal regions mediate different aspects of executive functioning (66). Tasks involving EFs and WM activate the same brain regions, namely the prefrontal regions and the frontal and posterior association cortex areas (67). A meta-analysis of 193 neuroimaging studies has shown that the network comprising prefrontal, dorsal anterior cingulate, and parietal cortices was constantly activated in all executive domains examined, including WM, cognitive flexibility, and planning (68). Thus, functions that share neural substrates with WM could be affected by WM training.

As to the correlation between age and benefits, it is noted that early intervention is beneficial for people with autism. Pasco (69) indicates that empirical research relating to this perspective is limited, but some research has identified the major importance of this process at an early age (70). Early intervention can increase effects (71,72). For example, in WM training, Melby-Lervåg and Hulme (18) found that larger benefits were noted in younger children than in older children. Nevertheless, we did not take notice of any correlation between age and training gains in the current study. This could be attributed to the restricted size of the sample adopted.

It is interesting to note that the present study has two limitations, which should be further examined in future research. The first limitation is related to the limited sample size of the study. The small sample size was appropriate for a pilot study; however, it should be expanded in future studies to get reliable results that can be generalized. The second limitation is the absence of a control group. Next research should include a control group that allows for obvious deductions about the effectiveness of the intervention. A follow-up investigation is also needed to examine the persistence of the training effects on WM, cognitive flexibility, planning, and ASD symptoms.

CONCLUSION

To summarize, the results of the present study demonstrate that WM training using CWMT shows a robust effect on WM, cognitive flexibility, planning, and ASD symptoms, but they do not show any relationship between age and training effect. These findings provide evidence that WM training can be promising to improve other EFs and reduce the severity of autism's symptoms. Thus, this therapy can be a favorable supplement in the therapeutic plan of people with ASD and contribute to the amelioration of their quality of life.

List of abbreviations

ADHD: Attention Deficit Hyperactivity Disorder
ADI-R: Autism Diagnostic Interview-Revised
ASD: Autism Spectrum Disorder
CWMT: Cogmed Working Memory Training
DSM-5-TR: Diagnostic and Statistical Manual of Mental Disorders 5th ed., Text Revised
EFs: Executive Functions
RRSB: Restricted Repetitive and Stereotyped Behaviours
SCI: Social Communication and Interaction
SCQ: Social Communication Questionnaire
SPSS: Statistical Package for Social Sciences
TLT: Tower of London Test
WAIS: Wechsler Adults Intelligence Scale
WCST: Wisconsin Card Sorting Test
WISC: Wechsler Intelligence Scale for Children
WM: Working Memory
WMS: Wechsler Memory Scale

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