Working Memory Deficits and its Relationship to Autism Spectrum Disorders

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Abstract

Background: There is a wealth of research done in developed countries on the investigation of the working memory (WM) performance in people with high-functioning Autism Spectrum Disorders (ASD) (IQ>70), with different reported findings. There is a dearth of similar studies in developing countries. In addition, the findings suggest that WM is possibly influenced by culture. The present study investigated WM performance and its relationship with the symptoms of ASD and Attention Deficit Hyperactivity Disorder (ADHD).

Methods: The present study is a cross-sectional comparative study between two groups of participants with high-functioning ASD, aged 8-16 years (n=30) and typically developing (n=30). This study was conducted in 2016-2017 in Tehran (Iran). The Multivariate Analyses of Variance (MANOVA) was used to compare the between-group differences on WM tasks. In addition, Pearson’s correlation coefficient was used to examine the relationship between the ASD and ADHD symptoms with WM performance. The data were statistically analyzed using the Statistical Package for the Social Sciences (SPSS), version 16.

Results: It was found that in general, WM was impaired in the people with ASD. Unexpectedly, in the present study, two subscales of Social interaction and Stereotyped Behaviors of the Gilliam Autism Rating Scale-Second Edition showed a significant positive correlation respectively with a score of two WM tasks, i.e. Visual Digit Span and Digit Span Forward.

Conclusion: These results showed that WM was impaired in individuals with ASD and that could have implications for intervention, but it is necessary that therapists be careful in choosing the appropriate tasks for intervention.

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Introduction

Autism spectrum disorders (ASD) are heterogeneous neurodevelopmental disorders characterized by deficits in social interaction and communication, and by the presence of repetitive and restricted behaviors/interests. The essential features of autism spectrum disorder are present in early childhood and limit or impair everyday functioning.1 There is no single explanation for this diagnosis.2 To account for these symptoms, a number of theories
have been proposed at the cognitive level. One of these theories is executive dysfunction. Executive function is an umbrella term that includes several skills such as planning, initiating, shifting, working memory (WM), problem-solving, monitoring, inhibition, and self-control. WM is an important component of executive function, which plays a role in daily functioning.

There is a considerable wealth of research done in developed countries to investigate the WM performance in people with high-functioning ASD, with varying findings reported. Some research showed weaknesses in WM and some did not find a difference in the WM of individuals with ASD compared to typically developing controls. In 2017, the results of the meta-analysis of 28 studies in the time period from 1986 to 2014 (819 individuals with ASD and 875 typically developing controls) showed that people with ASD exhibited general impairments in the WM, and spatial WM was more impaired in them compared to Verbal WM. In all those 28 studies, various tasks were used to evaluate the WM performance, such as Digits span, CANTAB Spatial WM task, Letter-Number Sequencing, Digit recall task, Self-ordered pointing, Corsi block-tapping test task, Benton visual retention test, etc.

One of the most comprehensive cognitive tools for measuring short-term and WM is the Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV) Integrated. The WISC-IV Integrated is the combination of the standard WISC-IV battery and 16 supplemental process subtests (in WISC-IV Integrated subtests are referred to as Process Subtests) that measures four domains (Verbal, Perceptual, WM, and Processing Speed). These supplemental process subtests are the variants of Core and Supplementary Subtests of the WISC-IV or the new tasks that expand the pool of cognitive capacities assessed by the WISC-IV. In the WM domain, the WISC-IV Integrated, compared to standard WISC-IV, renders a more in-depth assessment and provides a comparison among different aspects of WM. In several studies, WISC-V subtests have been used to measure the WM in individuals with ASD. But apart from the preliminary data reported in the WISC-IV Integrated technical manual, no data have yet been published on the WISC-IV Integrated in children with ASD. Wechsler administered the WISC-IV Integrated to 14 people with autism aged 7-16 (full scale IQ [FSIQ]>60) and 22 children with Asperger diagnosis aged 9-16 (FSIQ>70) Compared to typically developing control group. The results of the Wechsler study indicated that the Mean differences in children with autism, compared to the control group, in all of the WM process subtests produced larger effect size; in the Asperger group, this Mean difference produced a larger effect size for Spatial Span Backward (SSpB).

Bearing in mind the impact of culture on the WM in typically developing individuals and the lack of any study that has compared the cognitive phenotypes of children with ASD with different socio-cultural backgrounds and also a dearth of similar studies in developing countries, the first aim of this study was to measure WM in subjects with high-functioning ASD compared to the typically developing subjects. This was done by using the WM subtests of the WISC-IV and the WM process subtests of the WISC-IV Integrated in a developing country to detect any possible difference or similarity.

Given the relationship between the WM and social communication skills and repetitive and restrictive patterns of behavior and interests in earlier studies, it seems that the relationship between the WM performance and clinical symptoms can offer useful information. Moreover, according to the reports, there is a likelihood of 37% to 85% prevalence of Attention Deficit Hyperactivity Disorder (ADHD) symptoms in individuals with ASD; it has also been found that individuals with ADHD are performing poorly in WM. Moreover, the relationship between the severity of ADHD symptoms and its correlation with WM performance is an important consideration.

In sum, the aims of the present study could be summarized as follows:

- Investigating the WM performance and different aspects of WM in a sample with high-functioning ASD and typically developing, using WM tasks of WISC-IV and WISC-IV Integrated;
- Investigating the possible relationship between ASD symptoms (measured by Gilliam Autism Rating Scale-Second Edition [GARS-2]) and the WM performance in a sample with high-functioning ASD;
- Investigating the possible relationship between ADHD symptoms (measured by Conners' Parent Rating Scale-Revised (Short) (CPRS-RS) and the WM performance in a sample with high-functioning ASD.

Materials and Methods

The present study was a cross-sectional, comparative study between two groups of participants with high-functioning ASD (n=30) and typically developing control group (n=30).

Participants with High-Functioning ASD
Participants were recruited from...
individuals, aged 8 to 16 years, with a confirmed diagnosis of high-functioning ASD. They were referred to the first author by the special centers (the Iranian Special Education Organization, the Autism Charity, Roozbeh Psychiatric Hospital, the specialized clinics of schools of rehabilitation sciences, and 10 specialized clinics for children with autism). The following exclusion criteria, which were explored at a meeting with the participants’ family presenting the medical records of their children prevented individuals from entering the study.

- Conditions such as metabolic and genetic disorders;
- History of neurological diseases such as stroke, brain lesions, tumors, epilepsy, Tourette syndrome or simply Tourette’s and trauma;
- Different diseases and conditions that can affect cognition and comorbid mental disorders, such as schizophrenia or bipolar disorder;
- Visual, hearing or motor problems that could interfere with the test performance.

To confirm the diagnosis at the time of the study and estimate the severity of ASD symptoms and FSIQ, GARS-2 was used to predict the severity of ASD; moreover, to determine FSIQ score, WISC-IV was performed by trained professionals. The participants who obtained the cut-off score of GARS-2 and FSIQ standard score of 70 or higher on the WISC-IV were included in the study.

Finally, 30 (25%) subjects (27 men and 3 women) with a diagnosis of high-function ASD who had the conditions for entering the study were recruited as the participants in Tehran, Iran. The mean age of participants was 11.09 years (133.17±33.12 months). The participants’ mothers provided the information requested in the CPRS-RS. The age of the mothers with ASD in this study was between 32 and 54 years old (41.4±5.56). Subsequently, the WM process subtests of WISC-IV were performed by a trained evaluator for these 30 participants. The sample size was calculated by the following formula: 

\[ n = \frac{16}{\text{effect size}^2} \]

Effect size=0.8 and n=25

As this calculation is based on 'anticipated' values, the calculated sample size should be rounded upwards sensibly. Thus, in the present study, 30 participants per group was considered appropriate.

Typically Developing Participants

The control group consisted of 30 normally developing children (27 boys and 3 girls) matched on age and sex, with a mean age of 11.2 years (134.43±32.06 month). They were recruited through cluster sampling from a public primary and secondary school in Tehran. None of them had obvious behavioral problems or a history of relevant diseases according to the Strengths and Difficulties Questionnaire (SDQ), which will be described in the Research Tools section, and a semi-structured interview. Those with a personal or family history of psychiatric, neurological, or other medical conditions affecting brain development were identified and excluded from the sample. Typically developing children in this sample had a typical academic background. Their intellectual levels and WM performance were evaluated using WISC-IV and the WM process subtests of WISC-IV Integrated.

This study was conducted in 2016-2017 and approved by the Ethics committee of the Iran University of Medical Sciences (ir.iums.rec.1394.9211363204). Written and signed consent form was obtained from the parents of the participants, and verbal consent was obtained from the participants themselves. Additionally, all parents of the participants in the study were assured that their information would remain confidential and that researchers would only report the group results of the study. Children who did not cooperate with the examiner were eliminated from the study.

Research Tools

The Persian version of the Wechsler Intelligence Scale-Fourth Edition (WISC-IV)

The WISC-IV is an individually-administered clinical instrument for assessing intelligence ability of children (age range: 6:00-16:11). Two core subtests of WISC-IV (Digit Span, which includes Digit Span Forward [DSF] and Digit Span Backward [DSB], and Letter-Number Sequencing [LNS]) measured WM. The present study used the Persian version of the WISC-IV. The results showed that the overall Test-retest reliability coefficients of FSIQ in Persian version of the WISC-IV was 0.91, while the Test-retest reliability coefficients of core subscales ranged from 0.65 (Picture Concept subscale) to 0.94 (vocabulary subscale).

Working Memory Process Subtests of WISC-IV Integrated

The WISC-IV Integrated includes six WM Domain Process Subtests. These subtests are as follows: Visual Digit Span (VDS), Spatial Span (which includes Spatial Span Forward [SSpF] and SSpB), Letter Span (which includes Letter Span Rhyming [LSR] and Letter Span
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The Self-Administered Demographic and Economic Data Gathering Form

This form contains questions about children’s demographic information along with parental data, including their employment status, annual income, and level of education.

Statistical Analysis

The data were statistically analyzed using the Statistical Package for the Social Sciences (SPSS), version 16. The Mean and standard deviation were used for the descriptive part of the analysis. For the analytical part, the Kolmogorov-Smirnov test was used to ensure the normal distribution of the data. The Multivariate Analyses of Variance (MANOVA) was used to investigate the intra-group comparisons on Memory Components and WM tasks of WISC-IV and WISC-IV Integrated. To control the effect of FSIQ on the WM tasks, the Multivariate Analyses of Covariance (MANCOVA) were used. The Partial Eta Squared was used to estimate the effect size for the MANOVA and MANCOVA. The Cohen’s d, the difference of the two test means divided by the square root of the pooled variance, was reported so that it could be used to determine the effect size in the subtests, process subtests of WM, and memory components between the two groups.

Pearson’s correlation coefficient was used to examine the relationship between the GARS-2 and CPRS-RS subtests with WM subtests of WISC-IV, and WM process subtests of WISC-IV Integrated. The level of the statistical significance was set at 0.05 (5%) with confidence intervals of 95% for all statistical tests.

Results

In the present study, the results of the two groups of participants, including high functioning ASD (n=30) and typically developing individuals (n=30), were compared. The characteristics of the participants’ parents with high-functioning ASD (including Marital Status, Education [Mothers], Socioeconomic Status, and Bilingualism) are shown in table 1 and the characteristics of the participants (age, gender, and FSIQ in two groups and the results of the GARS-2 and CPRS-RS in participants with ASD) are presented in table 2.

As shown in table 2, the two groups were not significantly different in terms of age and gender, but they were in terms of the FSIQ. Since the issue of using FSIQ as a covariate in analyses of data in children with psychiatric disorders has not yet been fully resolved, the analyses were performed both with and without FSIQ as a covariate.
Comparing the WM Performance and Different Aspects of WM in Participants with High-Functioning ASD and Typically Developing

The comparison of the WM tasks between the high-functioning ASD (n=30) and typically developing control groups (n=30) showed a significant difference on the combined dependent variable of WM subtests and process subtests ($F_{11, 48} = 9.41$, $P = 0.001$, Wilk’s Lambada=0.294, Partial $\eta^2 = 0.70$) and memory components ($F_{5, 53} = 13.08$, $P = 0.001$, Wilk’s Lambada=1.21, Partial $\eta^2 = 0.54$). Analysis of each of the dependent variables, as shown in table 3, revealed that participants with ASD were weaker than typically developing participants in all memory components, and most of the WM tasks, except for the DSF and LSN tasks showed no significant differences between groups. After covarying the FSIQ, the effect of group on the combined dependent variable of WM subtests and process subtests ($F_{10, 48} = 3.04$, $P = 0.005$, Wilk’s Lambada=0.61, Partial $\eta^2 = 0.38$) and memory components ($F_{5, 53} = 2.68$, $P = 0.03$, Wilk’s Lambada=0.798, Partial $\eta^2 = 0.20$) was still found to be statistically significant (two subtests [LNPA and WA] did not enter into analysis due to the lack of homogeneity of variance). Analysis of each of the dependent variables revealed that the participants with ASD were significantly weaker than typically developing participants in

### Table 1: Characteristics of high-functioning ASD participants' parents (Marital Status, Education [Mothers], socioeconomic status, and Bilingual)

| Items                      | N (%) |
|----------------------------|-------|
| Marital Status             |       |
| Married                    | 27 (90.00) |
| Divorced                   | 2 (6.67)  |
| Widowed                    | 1 (3.33)   |
| Education (Mothers)        |       |
| Illiterate                 | 0 (0)  |
| Primary and Secondary School | 2 (6.67) |
| Diploma                    | 15 (50.00) |
| BS                         | 11 (36.67) |
| MS and PhD                 | 2 (6.66)  |
| Socioeconomic status       |       |
| Upper Class                | 1 (3.33)   |
| Upper Middle Class         | 9 (30.00)  |
| Middle Class               | 7 (23.34)  |
| Lower Middle Class         | 9 (30.00)  |
| Lower Class                | 4 (13.33)  |
| Bilingual                  |       |
| Yes                        | 5 (16.66) |
| No                         | 25 (83.34) |

### Table 2: Characteristics of the participants with high-functioning ASD (n=30) and Typical Developing group (n=30)

| Items                  | Autism Spectrum Disorders | Typical Development | Statistics ASD VS Typical Development |
|------------------------|----------------------------|---------------------|---------------------------------------|
| Age (months)           | 133.17±33.12               | 134.43±32.06        | t=-0.15, $P=0.881$                    |
| FSIQ (Wechsler Intelligence Scale for Children-Fourth Edition) | 85.63±12.51               | 111.87±9.62         | t=-9.1, $P=0.001$                     |
| Sex (male: female)     | 27:3                       | 27:3                |                                       |
| Gilliam Autism Rating Scale-Second Edition- Stereotyped Behaviors | 6.10±2.66                 |                     |                                       |
| Gilliam Autism Rating Scale-Second Edition-Communication | 4.20±1.38                 |                     |                                       |
| Gilliam Autism Rating Scale-Second Edition-Social interaction | 6.10±1.56                 |                     |                                       |
| Gilliam Autism Rating Scale-Second Edition-Autism Index | 74.16±11.85               |                     |                                       |
| Conners' Parent Rating Scale-Revised (Short)-Oppositional | 54.97±9.7                 |                     |                                       |
| Conners' Parent Rating Scale-Revised (Short)-Cognitive Problems/Inattention | 60.40±9.03                |                     |                                       |
| Conners' Parent Rating Scale-Revised (Short)-Hyperactivity | 64.23±11.59               |                     |                                       |
| Conners' Parent Rating Scale-Revised (Short)-ADHD Index | 60.83±7.28                |                     |                                       |
Visuospatial STM (F(1, 57) = 4.28, P = 0.04, Partial η² = 0.07) and significantly stronger than typically developing control group in the DSF subtest (F(1, 57) = 6.05, P = 0.01, Partial η² = 0.09).

The Correlations between WM Performance and ASD Symptoms in Participants with High-Functioning ASD

Investigate the correlation between the WM tasks of WISC-IV and WISC-IV Integrated and the subtests of the GARS-2, using Pearson's correlation coefficient, showed a significant positive correlation between the Social interaction-standard score of the GARS-2 and the DSF subtest (r = 0.46, P = 0.01).

There was also a significant positive correlation between the VDS process subtest and standard score (r = 0.41, P = 0.02) and percentage score of the Stereotyped Behaviors of the GARS-2 scale (r = 0.45, P = 0.01).

The Correlations between WM Performance and ADHD Symptoms in Participants with High-Functioning ASD

Assessing the correlation between the WM tasks of WISC-IV and WISC-IV Integrated, and the CPRS-RS subtests, using Pearson’s correlation coefficient showed a significant negative correlation, between Cognitive problems/inattention subtest of the CPRS-RS and the some process subtests of Executive WM (ARPA-B [r = -0.36, P = 0.04], ARPA-A [r = -0.36, P = 0.03] and DSB [r = -0.46, P = 0.01]) and the process subtests of Phonological STM.
The comparison of scores of the memory components, the WM tasks of WISC-IV, and WISC-IV Integrated without controlling of FSIQ showed significant differences between groups in all of the memory components, WM tasks of WISC-IV, and WISC-IV Integrated except for the DSF subtest and LSR process subtest. Some studies did not report significant differences between the ASD and typically developing control groups in the DSF subtest. Minshew and Goldstein showed that individuals with ASD had a significant negative correlation with the cognitive problems/inattention index of the CPRS-RS.

Comparing the WM Performance and Different Aspects of WM in a Sample with High-Functioning ASD and Typically Development

The comparison of scores of the memory components, the WM tasks of WISC-IV, and WISC-IV Integrated without controlling of FSIQ showed significant differences between groups in all of the memory components, WM tasks of WISC-IV, and WISC-IV Integrated except for the DSF subtest and LSR process subtest. Some studies did not report significant differences between the ASD and typically developing control groups in the DSF subtest. Minshew and Goldstein showed that individuals with ASD had a significant negative correlation with the cognitive problems/inattention index of the CPRS-RS.

Discussion

Generally, it can be concluded that in the recruited sample for this study:

- WM was impaired in individuals with ASD compared to typically developing control group even if the effect of FSIQ were controlled.
- Some WM tasks (VDS and DSF) had a significant positive correlation with social interaction and stereotyped behavior subscales of GARS-2.
- Some WM tasks (ARPA-A, ARPA-B, DSB, DSF, LSR, and LSN) had a significant negative correlation with the cognitive problems/inattention index of the CPRS-RS.
- The correlations between WM performance and different aspects of WM in a sample with high-functioning ASD and typically developing ASD showed a significant positive correlation with VDS. In other words, the parents reported more anti-social and Stereotyped Behaviors, while the score of individuals was higher in the VDS and DSF. This result was in disagreement with that of other studies that had found a negative relationship between ASD symptoms and WM performance. Clearly, these studies used other tasks to measure WM performance. A meaningful point in these two tasks is that the numerical nature is visually in one task and it is orally in the other. Klin and colleagues investigated the circumscribed interests in people with high-functioning ASD and noted that a third of their sample displayed a fascination.
with circumscribed interests might play an important role in the way that children spent their time by themselves and could determine the nature of contact that they had with others. Understanding the possible impact that this phenomenon could have on shaping and determining children’s means of understanding the social and personal world around them deserves more investigations and systematic attention.34 Perhaps engaging with numbers, which are part of the interest of a considerable group of children with ASD makes them stronger in these tasks but keeps them out of the social world.

The Correlations between WM Performance and ADHD Symptoms in Participants with High-Functioning ASD

The cognitive problems/inattention index of the CPRS-RS showed a significant negative correlation with the arithmetic, Digit Span, and Letter Span subtests. But there was no significant correlation between Oppositional, Hyperactivity, and ADHD index of the CPRS-RS with WM subtests of WISC-IV or WM process subtests of WISC-IV Integrated. While some researchers have found that children with high-functioning ASD plus ADHD have a poorer performance in WM tasks than children with high-functioning ASD alone,35 others have not reported any difference.36 Oliveras-Rentas and colleagues did not find a significant correlation between WISC-IV subtests and ADHD index in children with ASD.37

The current research is the first of its kind in developing countries that compares the WM performance in participants with ASD and typically developing children. In the present study, a comprehensive instrument was used for assessing WM performance. This instrument allowed researchers to compare different WM components in children with ASD in comparison with typically developing participants. Findings of the present study should be considered with respect to its limitations. Findings might be different if a larger sample size was used. Since the present study was considered to be a groundbreaking study in its field, one of its limitation was that the lack of any prior research in other developing countries relevant to the topic investigated in this study made it almost impossible to lay a foundation for understanding the research problem as examined in this study. Another limitation was the difference between the two groups in terms of their FSIQ. Since the intellectual abilities of participants with ASD are mostly lower than those of their age-matched typically developing control group, matching the FSIQ of the two groups was rather difficult.38 Therefore, in this study, and similar earlier studies conducted in this area that the two groups could not be matched for FSIQ from the baseline,34, 29, 39 statistical analysis was used to control the effect of FSIQ.

Conclusion

The results of the present study showed that compared to typically developing control group, the participant with high-functioning ASD group exhibited impairment in WM ability. In addition, the findings indicated a significant positive correlation between the GARS-2 social interaction and stereotyped behaviors with the DSF and VDS tasks. These results bring this question to the fore that whether the enhancement of these tasks can actually increase these core symptoms in individuals with high-functioning ASD. The results of previous studies revealed that some WM tasks had a significant negative correlation with restricted repetitive symptoms and social functioning. Therefore, WM training could possibly reduce these core symptoms if appropriate WM tasks for training are selected. In this research, no significant correlation was found between WM tasks and ADHD index in children with high-functioning ASD.

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