The role of a virtual avatar in attention and memory tasks in Rett Syndrome

Rosa Angela Fabio
Department of Clinical and experimental Medicine, University of Messina
Giorgia Pergolizzi
Department of Clinical and Experimental Medicine University of Messina
Andrea Nucita
Department of Cognitive, Psychological, Educational and Cultural Studies Sciences, University of Messina
Giancarlo Iannizzotto
Department of Cognitive, Psychological, Educational and Cultural Studies, University of Messina
Tindara Caprì (tcapri@unime.it)
University of Messina https://orcid.org/0000-0002-6395-9441

Research article

Keywords: Rett Syndrome, avatar, attention, memory, over-selectivity

Posted Date: February 3rd, 2020

DOI: https://doi.org/10.21203/rs.2.22464/v1

Version of Record: A version of this preprint was published at BMC Neurology on June 14th, 2021. See the published version at https://doi.org/10.1186/s12883-021-02212-w.

Abstract

Background

Since patients with Rett syndrome (RTT) focus their attention mainly on the faces of people with whom they interact, in this study the role of a human-like avatar in enhancing cognitive processes was examined. More in depth, this study examined patients with RTT performing attention and memory tasks with and without a virtual avatar.

Methods

Thirty-six girls with RTT participated in the study. They were matched for mental age and randomly submitted to two conditions (with and without virtual avatar) with two tasks (over-selectivity and memory paradigms).

Results

Results indicated that the RTT group exposed to the virtual avatar condition, presented better attention and memory abilities than the matched RTT group without the avatar condition.

Conclusions

Results were discussed in light of the relationship between motivation, attention and memory RTT.

Background

Because of the specific characteristics of the syndrome, patients with Rett syndrome (RTT) often use their eyes to communicate. As is known in scientific literature [1–4], they focus attention mainly on the faces of people with whom they interact [5, 6]. Social-valence related to faces increased attention also in Rett syndrome cynomolgus monkeys as demonstrated by a recent eye-tracking study [7].

New promising approaches have recently shown that technology-aided programs for patients with severe/profound and multiple disabilities are useful in enabling performance of daily tasks and improving cognitive abilities [8]. Typically, the technological devices promote forms of adaptive responses by bridging the gap between the person's behavioral repertoire and the abilities required for the adaptive response target. Spaghero [9], in a study in which he showed objects through virtual reality, demonstrated that subjects with intellectual disabilities can present a marked improvement in attention if solicited by audio and video presentations, since virtual reality offers the opportunity to interact with virtual objects and events. Therefore, this new approach has been recognized, as it provides a safe environment in which any individual can enjoy pleasurable activities [9] both with music [10], and communicating with the family [11]. Nevertheless, another major advantage in using technology-aided interventions is the possibility to acquire huge amounts of data, essential for advanced data analysis such as predictive analysis [12].

A new trend in current technologies is the presentation of a virtual environment to patients through an avatar that gives positive feedback to the subjects on the correction completion of a task, thereby improving motivation. This has highlighted an inherent interest in the technology on the part of researchers [13–16]. Avatars, i.e., graphical characters able to show human-like facial expressions and gestures, to speak and even react to users' interaction by interpreting gestures, emotional states and speech, have been exploited for several applications in the past [17]. Furthermore, virtual environments have often been combined with advanced human-computer interaction (HCI) technologies to facilitate user interaction in complex tasks [18].

The use of avatars has been shown to be an effective instrument in increasing attention in various disabilities [19, 20], however, the use of virtual avatars for people with RTT has not yet been explored. In the study by Mantziou, Vrellis, Tassos, and Mikropoulus [21] instead, the possibility of recognizing emotions in subjects with autism was investigated, thanks to the use of an avatar, able to recreate facial expressions inherent to specific emotions (anger, fear, happiness, surprise). Further evidence was provided by studying the use of an avatar [22, 23] in Attention Deficit/Hyperactivity Disorder (ADHD) [24–27]. These studies suggest that an avatar can be used as a computerized pedagogical agent with realistic characteristics; for example, it can appear on a computer screen and guide users through multimedia learning environments, designed to support learning and direct attention to relevant topics.

In the study by Mohammadhasani [22], the creation of Koosha (a virtual avatar similar to a young male nerd) was very efficient and the computerized agent responsible for teaching ADHD patients provided options for solving mathematic and logic problems. Results reached through Koosha in patients with ADHD were positive, and these patients reached higher levels of solution of math problems. The results of the study are in line with the multimedia theory of Mayer [28]. The author suggests that multimedia learning provides a deeper acquisition of information, with the constant presence of multimedia agents who administer verbal information with the addition of gestures, eye contact and who can emulate facial expressions, as close as possible to human expressions. These results might suggest that it could be possible to elicit greater attention in intellectually disabled subjects and highlight how the presence of a pedagogical agent may improve the performance of subjects.

The role of a pedagogical agent is also supported by other theories. One of these is Computers Are Social Actors (CASA); according to this theory, humans tend to respond to the media in the same way they would respond to humans, so the avatar would become a real social model [29]. A theory developed by Wang, Wenjing and Heping [30] also states that people would learn better from multimedia programs on the screen in the presence of a pedagogical agent, recognizing social presence. For these reasons the use of the avatar becomes effective for students to structure the appropriate processes and improve attention and learning [31] strengthening their interests [32].

Other studies on the role of the virtual avatar were provided by an experimental work by Fabio, Caprı, Iannizzotto, Nucita and Mohammadhasani [20] in which subjects with ADHD were submitted to three experimental conditions. In the first condition, the avatar simply provided instructions; in the second condition the avatar presented the instructions and also provided feedback on the student's attention; in the third condition the avatar was not presented. Results showed that the presence of the virtual avatar increased the ability of problem-solving of the subjects. These benefits were also confirmed in the work of Shema-Shiratzky, Brozgol CornejoThumm [33]. Summarizing, avatars can become real tutors, coaches, motivators, mentors, models to emulate [34] they show behaviour which is very similar to that which human beings face daily [35].

This study aims to examine whether the use of an avatar can improve motivation and, subsequently, attention and memory processes in girls with RTT. The tasks were implemented through eye tracking technology. More in depth, the underlying logic is that the motivation process significantly affects some cognitive functions, such as attention and memory. In this study, attention and memory tasks were presented with two conditions:

In the first condition, the avatar gave the instructions and asked the patient to give the answer. In the second condition there was no avatar. A voice gave the instruction and solicited the replies. The hypothesis was open: on one hand it may be that the avatar, acting as a social motivational model [29] can induce girls with RTT to focus and memorize more efficiently; on the other hand, based on the redundancy theory of Mayer [28], since the avatar is a third element it may be that it acts like a distractor and, not necessarily improve attention and memory.

Furthermore, since the eye tracking methodology helps to distinguish the encoding phase (with the registration of the length of fixations) and the retrieval phases (with the number of items recalled), in this study we want to understand if the avatar is efficient in the encoding phase or in the retrieval phase or both. As shown in previous studies with ADHD children [24–27] we expect that, if the patients with RTT show a high level of length of fixation in the condition with the avatar, such a condition will produce benefits also in the retrieval phase.

Method

Participants

Forty-one patients with a diagnosis of RTT took part in the experiment. Forty were female and one was male. Their families had been contacted by the Italian association for Rett syndrome (AIRETT) that asked them to participate in the study. The families come from all over Italy. Five patients were excluded from the study since they were not able to focus on the stimuli of the monitor. For this reason, finally, 36 patients participated in the study. They ranged in age between 4–32 years. A general assessment was carried out by a psychologist through the Vineland Adaptive Behaviour Scale (VABS) [36] and the Rett Syndrome Rating Scale (RARS) [37]. Thirty-one girls and one male attended schools or socio-educational centres; four girls were assisted by an educator at home. All the girls were in the post-regression phase of the disorder: They were severely mentally retarded and only six were able to use verbal speech. All showed little or no purposeful hand use and pervasive hand stereotypies were striking. Ambulation was preserved in 19 girls. Table 1 shows the chronological age of the participants, the RARS scores as well as the VABS Scores.

Material

A Tobii Series-I eye-tracker was used to record the subject's visual scanning. This device records ocular movements such as the location and duration of ocular fixations (pause of eye movement on an object of interest) and saccadic movements (rapid movements between fixations). The participant was positioned at a distance of about 30 cm from the screen and the direction of the gaze was determined according to the Pupil Centre/Corneal Reflection Method in low-intensity infrared light. Passive gaze tracing (LC Technologies, Sao Paulo, Brazil) software was used to generate gaze data during visuals scanning. In addition, this device allows to define the areas of interest (AOI) within the images chosen for the statistical analysis of eye tracking. An AOI cluster refers to selected specific areas that are used for both attention and recalling details of the images.

The eye-tracker was used for both the overselectivity paradigm and the memory paradigm. The avatar was created using an educational platform "Voki for Education" (https://www.voki.com/). Voki is a free collection of customizable speaking avatars for teachers and educators that allows users to create a precise profile of a talking character. Voki is created by Oddcast and can be customized to look like humans, cartoons, and/or animals.

The characteristics selected for the creation of the avatar were chosen through a pre-calibration, carried out during the 2018 Airett Campus in which several patients with RTT spent their holidays with family and educators. The pre-calibration was fundamental as it allowed to include the avatar that the RTT patients prefer. Following, the materials of both paradigms will be presented.

Memory Paradigm

The memory test was implemented. The story-cartoon presented with Tobii eye-tracker was easy to understand and remember, and the descriptions of facts were presented in a logical order. The cartoon sequences were extracted from “La Pimpa” and they were: “ant Bibi” and “Pimpa on the beach”. They were chosen out of seven cartoon sequences presented to 31 3-year-old children and calibrated on the basis of their comprehension of the story (> 90%) and on the basis of their recalling indices (> 90%). Each cartoon sequence contained 8 significant memory indices (Table 2). Both cartoon sequences “Ant Bibi” and “Pimpa on the Beach” lasted 2:30 minutes.

The test was carried out for each patient. After each cartoon was presented through the eye-tracker, the participants were asked to perform immediate recall of the cartoon with a recognition test with 8 questions regarding the story (Table 3).

For each of the relevant indexes two cards were presented on the screen, the correct answer and the distractor answer (Fig. 1). The scoring standard used in the present study involved giving 1 point for choosing the correct answer, and 0 point for choosing the distractor.

Overselectivity Paradigm

In this paradigm, 2 cards of 10 cm x 30 cm, each one reporting a different complex stimulus composed of three familiar objects shown in black and white, were presented on the screen of the Tobii eye-tracker. In the second phase, individual stimuli, consisting of cards of about 10 cm x 10 cm, were presented on the screen. Each card represented a single familiar object previously included in the target complex stimulus (Fig. 2). The cards were calibrated in a previous study [38].

In the condition with virtual avatar, the avatar presented both the complex stimuli and the individual stimuli between which the participant had to choose (Fig. 3, phase 1 and 2). In the condition without virtual avatar, no avatar was presented to participants.

Procedure

The experiment was carried out in a quiet room during the 2019 Rett summer campus of the AIRETT. The examiner administered the VABS and the RARS through an interview with the parents of the subjects with RTT and the educators. Participants sat in a dimly lit room of the association in front of the eye-tracker screen at a distance of 30 cm. The eye tracker was positioned in such a way that ambient lighting did not affect the recordings. The eye tracking equipment was calibrated for each participant at the beginning of the experiment. Gaze fixations of at least 1000 ms within a region of 2°– 3° around each calibration point were considered accurate. All participants were tested in the morning from 9.00 to 12.00 a.m.

The two tasks of this experiment were presented randomly. With reference to the memory task, in the condition with the avatar, the avatar appeared initially on the whole screen of the Tobii I-15 and said "Hi, my name is Giorgio. Watch this cartoon with me!" Then the avatar became smaller and moved to the lower left part of the screen. During the cartoon, it only moves its eyes and head in a stereotyped way to make the avatar seem alive. After watching the first cartoon, the avatar appeared again and says "Hello, we will play together now!” Then the avatar started by asking the participant the 8 questions mentioned above (Table 3). The participant had to choose the correct answer with their eyes and avoid focusing on the distractor. Then the avatar appeared again and repeated the process with a second video. As can be seen in Table 2, the questions have various levels of difficulty, from simple recognition of the main character of the story, to recognition of the emotional states of the characters, to identification of the actions within the story.

With reference to the overselectivity procedure, the examiner presented a pair of complex stimuli on the screen, placed to the right and left sides. The positioning of the images on the right or on the left took place in a random order. The images were placed 40 cm from each other. In this way, both images were easily observable and within easy reach and grasp of the patients who can use the hands. The task was carried out in two phases.

During the first phase, two images reporting complex stimuli (ABC, correct stimulus; XYZ, incorrect stimulus, see Fig. 2) were presented. The examiner presented each subject with the correct complex stimulus described as the “correct one”; both the correct and incorrect cards were then presented on the screen in front of each subject who was subsequently asked: “Which is the correct one?” Forty-five seconds were allowed to answer the question. The subjects could answer by grasping an image or by looking at it. If the subject chose the correct card (ABC) during the 45 sec, the examiner gave them a verbal reinforcement (e.g. "Great!" “Very good!”). If the subject chose the incorrect image (XYZ) or did not choose any image during 45 sec, both were removed, and the ‘no’ answer was coded, and a new possibility of choice started after 10 seconds.

In a second phase, the examiner used the cards reporting individual objects (Fig. 2, second phase) extracted both by correct and incorrect complex stimuli by devising 9 different pairs of individual stimuli from the combination of A with Y, B with X etc. The examiner asked every participant to choose the correct stimulus.

Measures

Memory task: two parameters were considered: fixation length (FL) of the correct stimuli related to the significant memory indices during the vision of the cartoon (Table 2) and the number of the recalled correct indexes. FL refers to the amount of time (seconds) spent by the subject when looking at the correct stimulus. Total fixation length refers to the sum of the time spent in looking at each significant index during the vision of the cartoon. Fixations were extracted using a threshold of 100 ms.

Overselectivity task: two parameters were considered: FL of the complex correct stimulus and the number of the individual correct recalled images

Statistical Analyses

The data were analysed using SPSS version 22.0 for Mac. The descriptive statistics of the dependent variables were tabulated and examined. Alpha level was set to 0.05 for all statistical tests. In the case of significant effects, the effect size of the test was reported. The relationship between continuous variables was evaluated by determining Pearson’s r; group comparisons were conducted using t-test for paired samples.

Results

The results are discussed firstly with reference to the memory paradigm and then with reference to the overselectivity paradigm.

A preliminary analysis showed that the two cartoons “Ant Bibi” and “Pimpa on the Beach” showed no statistical differences either with reference to fixation length of the total correct stimuli ($t(35) = 1.1$, $p = .43$) or the number of the correct recalled indexes ($t(35) = 0.76$, $p = .67$); for this reason in the following statistical analysis the mean of indexes of both cartoons is used. Table 4 shows means and standard deviations of the two conditions of the memory paradigm.

With reference to the length of the total correct stimuli results show significant differences, $t(34) = 4.55$, $p < 0001$. This means that the time spent in looking at each significant index during the vision of the cartoon was higher when the avatar helped the patients than when the avatar was not present. With reference to the number of the recalled correct indexes, again results show significant differences, $t(29) = 6.02$, $p < .0001$. Patients with Rett syndrome recall more significant indexes when the avatar is present than when it is absent.

With reference to the overselectivity paradigm, Table 5 shows means and standard deviations of the two conditions (with and without avatar).

Regarding fixation length (FL) of the complex correct stimulus, results show significant differences, $t(35) = 6.61$, $p < .001$. This means that the time spent in looking at the correct complex stimulus was higher when the avatar was present than when the avatar was not present. With reference to the number of the individual correct recalled images, again results show significant differences, $t(29) = 7.01$, $p < .0001$. Patients with RTT recall more significant indexes when the avatar is present than when it is absent.

With reference to the second question here addressed, the avatar helps both encoding and retrieval phases. Pearson's coefficient r was chosen as the measure of the strength of correlation. With reference to the memory paradigm the relationship between fixation length (FL) of the correct stimuli related to the significant memory indexes during the vision of the cartoon and the number of the recalled correct indexes is very high, $r(35) =. 678$, $p < .001$. With reference to the overselectivity task, again, the relationship between fixation length (FL) of the complex correct stimulus and the number of the individual correct recalled images is high, $r(35) = .52$, $p < .001$.

Discussion

In this study the first question addressed was if the avatar can act as a social motivational model [29] and improve attention and memory or if it is redundant [28] acting like a distractor and disrupting attention and memory. Both results, related to the two paradigms here analysed show that the avatar acts as a cognitive strengthener. The second question here addressed is if both phases (encoding and recalling) were empowered through the avatar. Results indicate that patients with RTT show a high level of length of fixation in the condition with the avatar and this produces benefits also in the retrieval phase.

Our results support the role of the avatar in learning environments and emphasizes the social aspect in the attention process. These results are in line with the CASA theory. According to this theory, humans tend to respond to the media in the same way they would respond to humans, so the avatar could become a real social model [29]. Wang's theory also states that people would learn better from multimedia programs on the screen in the presence of a pedagogical agent, recognizing social presence [30]. For these reasons, the use of the avatar becomes effective for patients with RTT, to structure the appropriate processes and improve their attention and their learning [31, 39–45].

In line with this [46–48], our avatar not only gives instructions on the relevant aspects of the coding phase but also helps the patients to better recall the contents. Hence, our results indicate that an interactive avatar that helps intellectually disabled patients to better direct their attention can concretely improve cognitive performance. We consider the findings reported in this article a relevant contribution to the introduction of a new generation of embodied interactive virtual agents (interactive avatars) aimed at supporting intellectually disabled patients in their everyday activities [49, 50]. These findings can help families and educators to identify what sort of software can be effectively used to help patients with RTT, and also software designers to make good evidence-based choices to offer more focused software, capable of giving significant performance improvements [51, 52].

A limitation of this research is that the graphical, behavioural, and technological characteristics of the avatar were not discussed. However, in principle it might be argued that they can influence the effectiveness of the avatar in improving the performance of the patients. Another limitation of this study may also be related to the size of the sample. In this study, the sample size is small and there may be constraints to the generalizability of the results. However, the effect size is adequate; consequently, the results from groups can be considered reliable. More in general, future research is needed to understand the conditions under which an avatar can enhance learning abilities and learning process.

Declarations

Ethics Approval and Consent to Participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

The Human Ethics Committee of the University of Messina approved the study.

Written informed consent was obtained from all parents of participants included in the study.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

R.A.F., G.P., A.N., G.I. and T.C. contributed to the conception and design of the work, the acquisition, analysis, and interpretation of data; R.A.F., G.P., A.N., G.I. and T.C. drafted the work and revised it critically for important intellectual content; all authors have read and approved the manuscript.

Funding

The authors declare no funding for this study.

Availability of data and material

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Acknowledgements

The authors want to thank the Italian Rett Syndrome Association, the participants and their families.

Abbreviations

Areas of interest (AOI)

Attention Deficit/Hyperactivity Disorder (ADHD)

Computers Are Social Actors (CASA)

Fixation length (FL)

Human-computer interaction (HCI)

Italian association for Rett syndrome (AIRETT)

Rett syndrome (RTT)

Rett Syndrome Rating Scale (RARS)

Vineland Adaptive Behaviour Scale (VABS)

References

1. Djukic A, Rose SA, Jankowski JJ, Feldman JF. Rett syndrome: recognition of facial expression and its relation to scanning patterns. Pediatr Neurol 2014;51:650-656.

2. Fabio RA, Giannatiempo S, Caprì, T. Attention and identification of the same and the similar visual stimuli in Rett Syndrome. Life Span Disabil 2019; XXII(1):113-127.
3. Fabio RA, Giannatiempo S, Oliva P, Murdaca AM. The increase of attention in Rett Syndrome. A pretest-post test research design. J Dev Phys Disabil 2011;23:99-111.
4. Romano A, Caprì T, Semino M, Bizzego I, Di Rosa G, Fabio RA. Gross Motor, Physical Activity and Musculoskeletal Disorder Evaluation Tools for Rett Syndrome: A Systematic Review. Dev Neurorehab 2019 DOI: 10.1080/17518423.2019.1680761
5. Fabio RA, Caprì, T, Nucita A, Iannizzotto G, Mohammadhasani N. Eye gaze digital games to improve motivational and attentional ability in Rett Syndrome. J Spec Educ Rehab 2018;9(3-4):105-126. DOI: 10.19057/jser.2019.43
6. Fabio RA, Caprì T, Buzzai C, Pittalà V, Gangemi A. Auditory and Visual Oddball Paradigm Evaluated Through P300 in Five Girls with Rett Syndrome. Neuroquant 2019;17: 40-49. doi: 10.14704/nq.2019.17.07.2591
7. Zhang, B, Zhou, Z, Zhou, Y, Zhang, T, Ma, Y, Niu Y, Chen, Y. Social-valence-related increased attention in rett syndrome cynomolgus monkeys: An eye-tracking study. Autism Res 2019:1585-1597.
8. Lancioni G, Singh N, O'Reilly M, Sigafoos J, Boccasini A, La Martire ML, et al. People with multiple disabilities use assistive technology to perform complex activities at the appropriate time. Int J Disabi Hum Dev 2016;15:261–6. doi: 10.1515/ijdhd-2015-0012
9. Spanghero F, Ferrari V, Pozzobon V , Rebellato. F Tecnologie per l’inclusione robotica. Tecnologie per l’inclusione, 2016;17:37-39
10. Fabio RA, Iannizzotto G, Nucita A, Caprì T. Adult listening behaviour, music preferences and emotions in the mobile context. Does mobile context affect elicited emotions? Cogent Eng 2019;6:1-17. Doi: 10.1080/23311916.2019.1597666
11. Caprì T, Gugliandolo MC, Iannizzotto G, Nucita A, Fabio RA. The influence of media usage on family functioning. Cur Psyc 2019;1(23):1-10. DOI 10.1007/s12144-019-00204-1
12. Nucita A, Bernava GM, Giglio P, Peroni M, Bartolo M, Orlando S, Marazzi MC, Palombi L. Lecture Notes in Computer Science. International Conference on Model and Data Engineering, MEDI 2013; 8216:225-2363.
13. Annaz D, Campbell R, Coleman M, Milne E, Swettenham J. Young children with autism spectrum disorder do not preferentially attend to biological motion. J Aut Dev Disord 2011;42:401–408. doi: 10.1007/s10803-011-1256-3.
14. Diehl JJ, Schmitt LM, Villano M, Crowell CR. The clinical use of robots for individuals with autism spectrum disorders: A critical review. Res Aut Spect Disord 2012;6:249–262. doi: 10.1016/j.rasd.2011.05.006.
15. Kumazaki H, Warren Z, Swanson A, et al. Brief Report: Evaluating the Utility of Varied Technological Agents to Elicit Social Attention from Children with Autism Spectrum Disorders. J Autism Dev Disord. 2019;49(4):1700–1708. doi:10.1007/s10803-018-3841-1

16. Pierno AC, Mari M, Lusher D, Castiello U. Robotic movement elicits visuomotor priming in children with autism. Neuropsychologia 2008;46:448–454.
17. Iannizzotto G, Lo Bello L, Nucita A, Grasso GM. A vision and speech enabled, customizable, virtual assistant for smart environments. Proceedings 11th International Conference on Human System Interaction 2018:50-56.
18. Iannizzotto G, La Rosa F, Costanzo C, Lanzafame P. A multimodal perceptual user interface for collaborative environments. Lecture Notes in Computer Science LNCS 2005; 3617 :115-122
19. Dautenhahn K. Socially intelligent robots: dimensions of human-robot interaction. Philos Trans R Soc Lond B Biol Sci 2007;362(1480):679–704. doi:10.1098/rstb.2006.2004
20. Fabio RA, Caprì T, Iannizzotto G, Nucita A, Mohammadhasani N. Interactive Avatar Boosts the Performances of Children with Attention Deficit Hyperactivity Disorder in Dynamic Measures of Intelligence. Cyberpsychol Behav Soc 2019; 22(9):588-596. https://doi.org/10.1089/cyber.2018.0711
21. Mantziou O, Vrellis I, Mikropoulos TA. Do Children in the spectrum of autism interact with real-time emotionally expressive human controlled avatars? Procedia Comput Sci 2015;241-251.
22. Mohammadhasani N, Fardanesh H, Hatami J, Mozayani N, Fabio RA. The pedagogical agent enhances mathematics learning in ADHD students. Educ Info Tech 2018; 23:1–11.
23. Mohammadhasani N, Fabio RA, Fardanesh H, Hatami J. The link between visual attention and memory in ADHD and normally developing students: seeing is remembering? Reti, Saperi e Linguaggi Ita J Cogn Scie 2015;1(2):89-102.
24. Fabio RA. The study of automatic and controlled processes in ADHD: A reread and a new proposal. Med J Clin Psy 2017;5:1-8.
25. Martino G, Caprì T, Castriciano C, Fabio RA. Automatic deficits can lead executive deficits in ADHD. Mediterranean Journal of Clinical Psychology 2017;5(3):1-32. DOI: 10.6092/2282-1619/2017.5.1669
26. Fabio RA, Caprì T, Mohammadhasani N, Gangemi A, Gagliano A, Martino G. Frequency bands in seeing and remembering: comparing ADHD and typically developing children. Neuropsychol Trends 2018;24:97-116. DOI: 10.7358/neur-2018-024-fabi
27. Fabio RA. Caprì T. Automatic and controlled attentional capture by threatening stimuli. Heliyon 2019;5:17-52. https://doi.org/10.1016/j.heliyon.2019.e01752
28. Mayer RE. Cognitive theory of multimedia learning. In Mayer R, ed. The Cambridge handbook of multimedia learning. New York, NY: Cambridge University Press, 2014 , 34–71.
29. Kim Y, Baylor. A social-cognitive framework for pedagogical agents as learning companions. Educ Tec Res Dev 2007;54:569–596.
30. Wang F, Wenjing LI, Heping XIE, et al. Is pedagogical agent in multimedia learning good for learning? A metaanalysis. Adv Psyc Scie 2017;25:12.
31. Kinnebrew J, Biswas G, Sulcer B, et al. Investigating self-regulated learning in teachable agent environments. In Azevedo R, Aleven V, editors. International handbook of metacognition and learning technologies. Amsterdam: Springer; 2013. p. 451–470.

32. Lusk MM, Atkinson R. Animated pedagogical agents: does their degree of embodiment impact learning from static or animated worked examples? Appl Cogn Psychol 2007; 21:747–764.
33. Shema-Shiratzky S, Brozgol M, Cornejo-Thumm P, et al. Virtual reality training to enhance behavior and cognitive function among children with attention-deficit/hyperactivity disorder: brief report. Dev Neuroreha habil 2019; 22:431–436.
34. Schroeder N, Adesope OO. A case for the use of pedagogical agents in online learning environments. J Teac Lea Tech 2012;1:43–47.
35. Veletsianos G, Russell GS. Pedagogical agents. In Spector JM, editors. Handbook of research on educational communications and technology. New York: Springer Science + Business Media;2013. p. 759–769.
36. Sparrow SS, Cicchetti DV, Balla DA. Vineland adaptive behavior scales: Second edition (Vineland II), The expanded interview form. Livonia, MN: Pearson Assessments; 2008.
37. Fabio RA, Martinazzoli C, Antonietti A. Costruzione e standardizzazione dello strumento “R.A.R.S.” (Rett Assessment Rating Scale). Ciclo Evol Disabil 2005;8:257-381.
38. Fabio RA, Giannatiempo S, Antonietti A, Budden S. The role of stereotypies in overselectivity process in Rett syndrome. Res Dev Disabil 2008;30(1):136-145.
39. Antonietti A, Fabio RA, Boari G, Bonanomi A. The“Style of learning and thinking” (SOLAT) Questionnaire: Psychometric data for reliability and validity of Italian Version. Testing Psy Method 2005;4:299-316.
40. Castelli I, Antonietti A, Fabio RA, Lucchini B, Marchetti A. Do Rett syndrome persons possess Theory of Mind? Some evidence from non-treated girls. Life Span Disab 2013; 2:157-168.
41. Fabio RA. Attention measures of patients with rett syndrome need to overcome the challenges in evaluating the oculomotor function using electronystagmography.Eur J Paediatr Neurol 2019; 23(2):232. doi:10.1016/j.ejpn.2019.02.008
42. Fabio RA, Billeci L, Crifaci G, Troise E, Tortorella G, Pioggia, G. Cognitive training modifies frequency EEG bands and neuropsychological measures in Rett Syndrome. Res Dev Disabil 2016;73–85.
43. Fabio RA, Gangemi A, Caprì T, Budden S, Falzone, A. Neurophysiological and cognitive effects of Transcranial Direct Current Stimulation in three girls with Rett Syndrome with chronic language impairments. Res Dev Disabil 2018;76:76–87.
44. Fabio RA, Magaudda C, Caprì T, Towey G, Martino G. Choice Behavior in Rett Syndrome, the consistency parameter. Life Span Disabi 2018;XXXI(1):47-62.
45. Fabio RA, Martino G, Caprì T, et al. Long chain poly-unsaturated fatty acid supplementation in Rett Syndrome: a randomized placebo-controlled trial. Asian Clin Nutr 2018;10:37-46. DOI: 10.3923/ajcn.2018.37.46
46. Heidig S, Clarebout G. Do pedagogical agents make a difference to student motivation and learning? Educ Res Rev 2011;6:27–54.

47. Kim Y, Baylor A. Simulating instructional roles through pedagogical agents. I J Arti Intell Educa 2005;15:95–115.
48. Payr S. The virtual university's faculty: an overview of educational agents. Appl Arti Intell An 2003;17:1–19.
49. Gangemi A, Caprì T, Fabio RA, Puggioni P, Falzone AM. Martino G. Transcranial Direct Current Stimulation (tDCS) and Cognitive Empowerment for the functional recovery of diseases with chronic impairment and genetic etiopathogenesis. In Kevin V. Urbanoeditors. Advances in Research. New York: Nova Science Publisher; 2018. ISBN: 978-153613265-6;978-153613264-9
50. Fabio RA, Caprì T, Lotan M, Towey GE, Martino G. Motor abilities are related to the specific genotype in Rett Syndrome. In Kevin V. Urbano Editors. Advances in Genetics Research. New York: Nova Science Publisher; 2018. ISBN: 978-153613265-6;978-153613264-9.
51. Prosperi, M., Min, J.S., Bian, J. et al.Big data hurdles in precision medicine and precision public health. BMC Med Inform Decis Mak18, 139 (2018). https://doi.org/10.1186/s12911-018-0719-2.
52. Parker, J., Mawson, S., Mountain, G. et al.Stroke patients' utilisation of extrinsic feedback from computer-based technology in the home: a multiple case study realistic evaluation. BMC Med Inform Decis Mak14, 46 (2014). https://doi.org/10.1186/1472-6947-14-46.

Tables

Table 1

Descriptive characteristics of the patients with Rett yndorme

	Name	Clinical stage	Age	MeCP2 Mutation	RARS[1] Point score	Level 1 of severity	VABS[2] score
1	A.L.R.	III	13	c.1063-1326 del264+insTGCG	63,5	Moderate	110
2	A.C.	IV	36	T158M	59	Moderate	63
3	A.S.	III	13	c.1566_1197 del41	76,5	Moderate	92
4	S.B.	III	12	c.916C>T	69	Moderate	88
5	D.O.	IV	29	R255C	72	Moderate	86
6	G.V.	III	8	/	48,5	Mild	121
7	S.B.	IV	31	R255C	59,5	Moderate	165
8	S.C.	III	16	T158M	71	Moderate	92
9	A.I.	III	22	c.1164-1189 de 26	66,5	Moderate	84
10	M.M.	II	4	C.916C>T	66,5	Moderate	83
11	A.B.	III	11	R255X	66	Moderate	83
12	G.T.	III	14	/	56	Moderate	58
13	K.C.	II	4	c.763 C>T	80,5	severe	40
14	C.A.	II	4	PT158M	52,5	Moderate	60
15	M.M.	III	26	R270X	56,5	Moderate	65
16	V.A.	III	5	R294X	66,5	Moderate	80
17	E.M.	III	14	R270X	61,5	Moderate	76
18	E.P.	IV	29	P.R135C	39	Mild	168
19	M.L.	III	5	p.Pro322Leu	58,5	Moderate	75
20	C.T.	III	7	/	47,5	Moderate	60
21	A.M.	III	20	CDLK5	61	Moderate	56
22	S.L.	III	8	p.R133C	35	Mild	140
23	L.G.	III	10	FOXG1	86,5	severe	35
24	M.G.	III	17	arg168stop	37	Mild	121
25	V.A.	IV	35	/	47	Mild	118
26	G.S.	II	4	C.916C>T	74	Moderate	50

27	A.L.	III	10	T158M	81	Severe	33
28	A.C.	II	4		71,5	Moderate	56
29	S.P.	III	16	168RX	62	Moderate	131
30	R.E.	III	18	/	67,5	Moderate	107
31	V.A.	III	7	R168X	51,5	Moderate	82
32	D.C.N.	III	12	R306C	59	Moderate	84
33	V.S	III	16	R133C	64,5	Moderate	110
34	Z.F	III	14	P322A	52,5	Moderate	86
35	G.S.	III	19	R255C	74,5	Moderate	84
36	D.G. (male)	III	20	c.964 C>T	58,7	Moderate	105

Table 2.

Significant indexes of cartoon sequence

Ant Bibi	Pimpa on the Beach
Main character	Main character
Secondary character	Action of Pimpa
Colour of main character	Secondary character
Ant character	Action on the beach
Action of Pimpa	Emotions of Pimpa
Underground	Crayfish character
Emotions of Pimpa	Underground
Final action	Final action

Table 3

Questions related to the significant indexes of the cartoon sequence

Ant Bibi	Pimpa on the Beach
1.Who was the main character of the story?	1. Who was the main character from the story?
2. Who met Pimpa at the beginning of the story?	2. What was Pimpa doing?
3. What colour was Pimpa?	3. Did Armando want to play with Pimpa?
4. Who met Pimpa?	4. Who did Pimpa play with on the beach?
5. What was Pimpa taking, the sack or the bucket?	5. Was Pimpa sad or happy?
6. Were there clouds or stars?	6. Who did you meet after the Pimpa?
7. How happy or sad was Pimpa?	7. Were there sun or stars?
8. What did Pimpa do at the end of the story?	8. What did Pimpa do in the end?

Table 4

Means and Standard deviations of the parameters of the memory task

Conditions	Means (standard deviation)
With Avatar	
fixation length of the total correct stimuli	26.37 (12.95)
number of the recalled correct indexes	5.23 (1.10)
Without Avatar	
fixation length of the total correct stimuli	15.95 (11.82)
number of the recalled correct indexes	3.23 (1.99)

Table 5

Means (and Standard deviations) of the parameters of the overselectivity task

Conditions	
With Avatar	
fixation of the complex correct stimuli	28.51 (9.22)
number of correct individual stimuli recalled	6.19 (2.33)
Without Avatar	
fixation of the complex correct stimuli	18.32 (11.01)
number of the recalled correct indexes	3.72 (0.99)

Figures

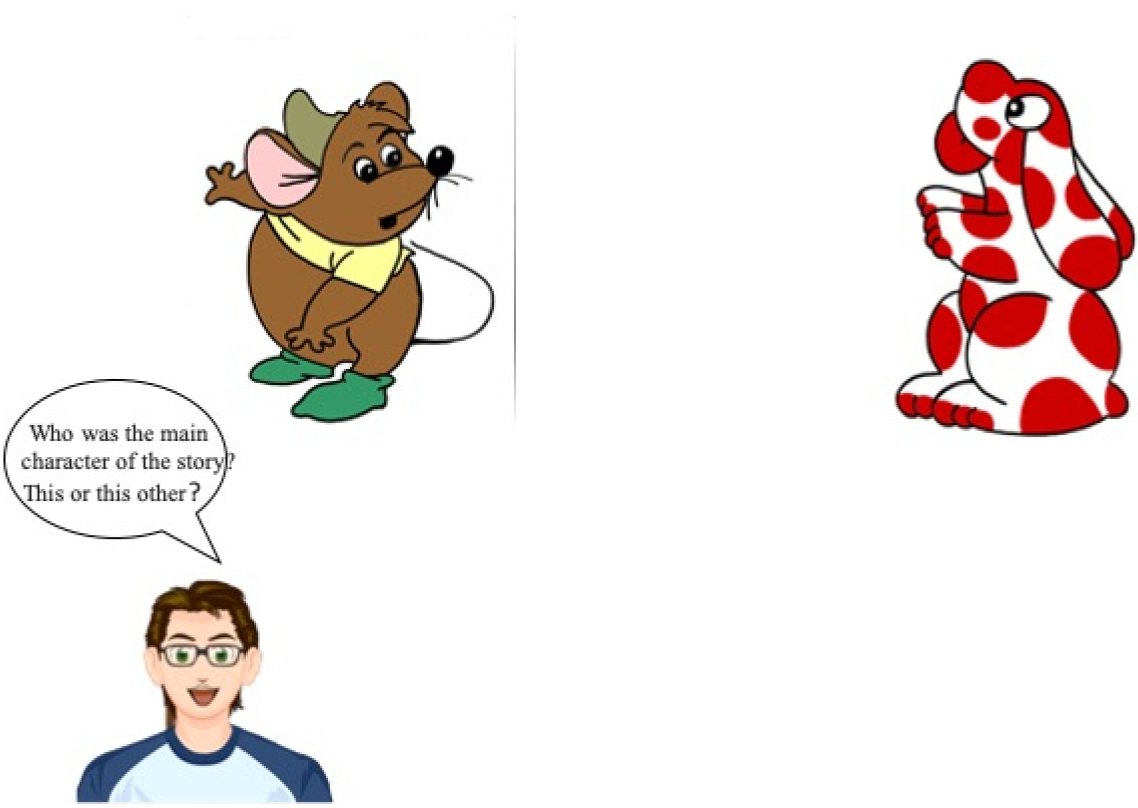

Figure 1

Recognition test: target and distractor

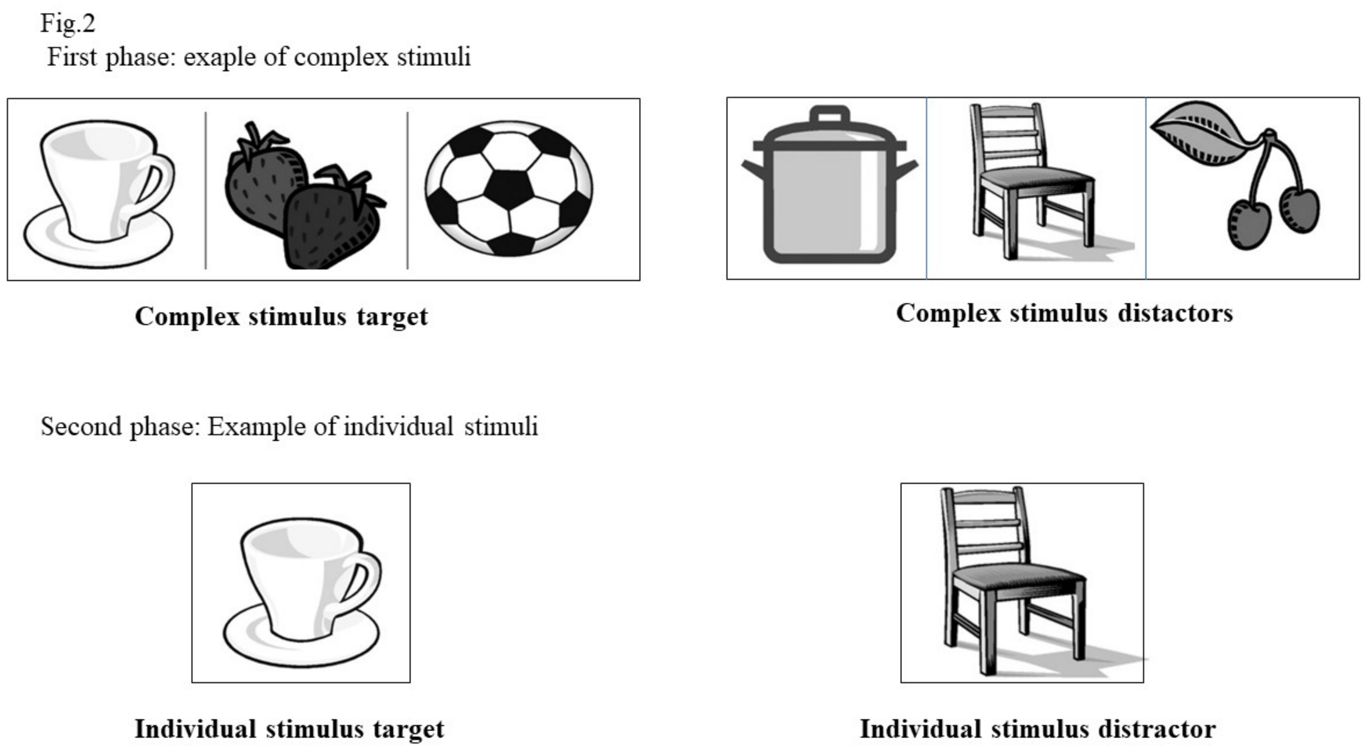

Figure 2

Overselectivity stimuli

Figure 3