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CONCEPTS OF COLOR, SHAPE, SIZE AND POSITION IN TEN CHILDREN WITH RETT SYNDROME

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Abstract – Individuals with Rett syndrome (RS) present severe motor, language and cognitive deficits, as well as spontaneous hand movement loss. On the other hand, there are strong evidence that these individuals use the eyes with intentional purpose. Ten girls aged 4y8m to 12y10m with RS were assessed with a computer system for visual tracking regarding their ability of indicating with eyes the recognition of concepts of color (red, yellow and blue), shape (circle, square and triangle), size (big and small) and spatial position (over and under) to which they were first exposed to. Results from comparing the time of eyes fixation on required and not required concepts did not differ significantly. Children did not show with eyes the recognition of the required concepts when assessed with eye tracking system.

KEY WORDS: Rett syndrome, cognition, eye movement measurements, eye movements.

Conceitos de cor, forma, tamanho e posição em dez crianças com síndrome de Rett

Resumo – Pessoas com síndrome de Rett (SR) apresentam severos prejuízos psicomotores, verbais, cognitivos e perda das habilidades manuais proposicionais que impedem o conhecimento de suas reais aquisições intelectuais. Entretanto, estudos relatam que essas pessoas utilizam o olhar com finalidade intencional. O objetivo deste estudo foi avaliar se crianças com SR, após terem sido expostas aos conceitos de cor (vermelho, amarelo e azul), forma (círculo, quadrado e triângulo), tamanho (grande e pequeno) e posição espacial (em cima e em baixo), manifestam o reconhecimento desses conceitos com o olhar, avaliado com equipamento computadorizado de rastreamento ocular. Foram avaliadas dez crianças com diagnóstico de SR, com idades entre 4 anos e 8 meses e 12 anos e 10 meses. Os resultados não indicaram diferenças significativas no tempo de fixação do olhar das crianças quando comparados os conceitos solicitados e os não solicitados. Concluiu-se que, com o método utilizado, as crianças não reconheceram os conceitos avaliados.

PALAVRAS-CHAVE: síndrome de Rett, cognição, medições dos movimentos oculares, movimentos oculares.

Rett syndrome (RS) is considered a disorder linked to a dominant X chromosome, lethal in the male gender and for this reason is only studied in females[1]. Today, it is known that there are some cases where men can be affected: boys having Klinefelter syndrome comorbidity, boys presenting severe encephalopathy, and brothers having affected sisters who were born with severe neurological disorders, generally evolving into premature death[1-3]. In 1999, Amir et al.[4] described mutations of the *MECP2* gene in patients with RS, classifying it as a genetic alteration, in fact linked to a dominant X chromosome. The *MECP2* gene codifies the MeCP2 protein which operates as a global transcribing repressor and acts in different locations. The different mutations that have already been identified can be responsible for the various phenol-typical patterns observed[5].

RS is a condition that evolves with progressive acquisition loss of psychomotor development (motor and cognitive acquisitions), deceleration of cranial perimeter growth and verbal communication inability. Nevertheless, spontaneous stereotypical hand movement is strongly suggestive of this syndrome, with loss of voluntary hand functions, once acquired. These people tend to lock their hands and hold them in front along the central part of the body displaying the stereotypical movement of "washing their hands", rocking the hands in front of the face, putting them in the mouth and, occasionally, even biting them[6]. According to the Diagnostic and Statistical Manual of Mental Disorders – DSM-IV[7], RS is classified as an pervasive developmental disorder, for which incidence is estimated at 1:15.000 girls. There is little research and little documented information about the cognitive potential

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of people with RS. Most of the studies are in agreement that, before the onset of the regression and the diagnosis, they follow typical developmental phases, even though, when seen retrospectively, these phases can be considered incomplete or delayed[8]. The evaluation of cognitive functions almost always depends on verbal or gesture responses, and the motor and communication impairment specific to RS impede the evaluation of cognitive skills in this population, which provokes the researcher to reflect about other strategies of evaluation. Baptista[9] and Amorosino[10] used a computerized ocular tracking system to demonstrate that girls with RS truly seemed to have an intentional look, objectively corroborating many qualitative reports that these girls use their eyes with intentional purpose. The fixed and intense stare as a form of communication or as an expression of desire, allows it to be used as a means of evaluating cognitive aspects[8,11,12].

The objective of this study was to evaluate recognition of concepts of color (red, yellow and blue), shape (circle, square and triangle), size (big and small) and spatial position (over and under) in 10 children with RS, using the computerized ocular tracking equipment.

METHOD

Ten girls clinically diagnosed with RS (clinical stage III or IV), aged between 4 years 8 months and 12 years 10 months, having different schooling levels participated in this study (Table). All of the children were submitted to a genetic examination for mutations of the *MECP2* gene; 8 of them tested positive and 2 received negative results, suggesting that the exam be reapplied.

The severity of the girls' clinical condition was characterized by applying the Kerr et al.[13] standardized scale. This scale is composed of 20 items with scoring of 0, 1 or 2. The maximum score on the scale is 40 points. The greater the score obtained by the girl, the more severe her RS condition. The total scores for each child can be found in Table. The scale was applied to the parents or caregivers on the day of the evaluation.

The incapacity of the children to adapt to the evaluating instrument as well as the presence of severe visual compromise that could negatively affect the answers to the proposed stimuli was considered as exclusion criteria.

The 10 children evaluated underwent specialized attendance including physiotherapy, speech-therapy, music therapy and pedagogic stimulation. The three eldest girls were attended at the Brazilian Association of Rett Syndrome in São Paulo (Abre-Te/SP – *Associação Brasileira de Síndrome de Rett de São Paulo*), and the other seven children, due to their ties to the referred-to institution, participated in this study.

Initially, the technical coordinator of Abre-Te/SP and the parents or caregivers had received explanations about the project and an informative letter about the study, which occurred after having given their consent.

This study was approved by the Research Ethics Committee of Presbyterian Mackenzie University – Universidade Presbiteriana Mackenzie (process CEP/UPM 967/03/07 e CAAE – 0017.0.272.000-07).

Before the evaluation, in two 30-minute weekly sessions, for 30 days, the professionals that worked with the children participating in the study presented to them the primary colors "red", "blue" and "yellow"; the shapes "square", "circle" and "triangle"; the sizes "big" and "small"; and the positions "over" and "under", naming these concepts, in a manner that assured the researcher that the children had already been exposed to the concepts being evaluated. The concepts were introduced to the children on boards supplied by the researcher, using the same model that would be presented later in the evaluation.

After this period, all of the evaluations were submitted to the Interdisciplinary Research Laboratory of the Post-graduation Program in Developmental Disorders at *Universidade Presbiteriana Mackenzie*, using the *Tobii 1750* computerized equipment and the *ClearView software (Tobii Technology,* 2005), developed to evaluate and register an individual's visual scan in the face of a visual stimulus projected onto the computer screen. The equipment is capable of detecting various parameters during eye movement, such as fixation (stopped) and saccadic (moving rapidly).

The equipment is composed of a 17" TFT 1.280 x 1.024 pixels monitor, with two high-resolution cameras built into the lower part. To generate brilliance and reflection of the subject's eye, the equipment has built-in diodes that emit an infra-red ray (*Near Infra-Red Light-Emitting Diodes – NIR-LEDs)*. This instrument does not offer any risk to the individual.

It is necessary to calibrate the equipment before the application of any task. To do this, the subject, while sitting in front of the monitor, must focus her look at a point on the screen that is being moved in all directions. After the equipment is calibrated, the stimuli relative to each concept were displayed on the computer screen in a manner such that the child would, with her eyes, indicate the concept that had been solicited by a simple verbal command.

The background of the displayed boards was black, in order that no stimulus other than the desired one, could influence the answers.

The images were presented by semantic group. Firstly, they were presented on a board that exhibited, inside circles, the three colors that the children had been exposed to and a different color ("green"). The child was then asked to indicate a determinate color. The color "green" was used to complete four stimuli, so that the figures would be well-distributed on the computer screen and, thereby, avoid any type of attention-calling focus distracter. The same board was presented three times, until all of the colors had been solicited. The order of the stimuli presented on the board remained unaltered to avoid a random indication that could place the child's answer into doubt. Thereafter, the board contained the three shapes to which the children had been exposed and a different one ("cross"), once again in order to complete the four stimuli on the screen. This board

Table. Characterization of the sample.

Subject	Current age	Date of birth	Age of clinical diagnosis	Clinical stage	Mutation in *MECP2*	Specialized therapies	Schooling	Total score on Kerr et al. scale
1	4y8m	23.01.03	1a6m	III	Negative*	Speech therapy Physiotherapy Pedagogy Horse therapy Acupuncture	Pre I (regular school)**	24
2	6y	06.10.01	3a	III	Positive	Speech therapy Occupational therapy Hydrotherapy	Kindergarten (regular school)**	19
3	7y5m	05.05.00	2a	III	Positive	Speech therapy Physiotherapy Occupational-therapy Music-therapy Pedagogy	Special room (regular school)**	27
4	7y10m	10.12.99	1a6m	III	Positive	Speech therapy Physiotherapy Occupational therapy Horse therapy	Special school**	21
5	7y11m	16.11.99	4a	III	Positive	Speech therapy Physiotherapy Occupational therapy	Pre I (regular school)**	18
6	8y8m	20.02.99	2a	III	Positive	Speech therapy Physiotherapy Occupational therapy Horse therapy	1st grade (regular school)**	17
7	8y11m	26.11.98	2a6m	III	Negative*	Speech therapy Physiotherapy Occupational therapy	1st grade (regular school)**	21
8***	10y8m	02.02.97	2a8m	III	Positive	Speech therapy Physiotherapy Music therapy Psycho-pedagogy	–	25
9***	12y9m	05.01.95	5a	IV	Positive	Speech therapy Physiotherapy Music therapy Psycho-pedagogy	–	22
10***	12y10m	08.12.94	1a9m	IV	Positive	Speech therapy Physiotherapy Music therapy Psycho-pedagogy	–	20

*Exam will be done; **With private pedagogic stimulation; ***Child frequented the Reference Center AbreTe/SP – Brazilian Association of Rett Syndrome of São Paulo.

was presented three times, until all three shapes had been solicited. The boards evaluating concepts of size and position were composed of two circles. On the board relative to size, there was a larger and a smaller circle and, on the board relative to position, there was one circle above and one below.

During the evaluation, prior to presenting the first and between each stimulus, a board with a central circle was displayed so that the child would return her attention to the center of the screen, thus avoiding that she keep her eyes on the same field of the previous stimulus screen.

The evaluation included 10 verbal commands given to the children in the following order: "Look at: yellow, red, blue, triangle, square, circle, big, small, over, under".

In this study, we decided to use a permanence of three seconds for the mediator boards and four seconds for the boards that contained the solicited concepts.

The fields on the screen that contained figures-concepts were selected, and the results were analyzed based on the fixation time on the alternatives, expressed in milliseconds. These data were analyzed with the application of non-parametric statistical tests, constructing confidence intervals of 95% and adopting a hypothesis rejection probability of 90% (p≤0.01).

RESULTS

In the "colors" and "shapes" categories, the average percentages of eye fixation on each figure-concept were compared to each command given. The Friedman test demonstrated that, on the "blue" command, the tendency for eye fixation time on the color "blue" was significantly greater (p=0.109); however, there was no difference observed in this time for any of the other commands relative to colors and shapes.

In turn, the Wilcoxon test revealed a significantly greater fixation time on the "non- red" stimulus when soliciting "red" (p=0.067), and on the "non-square" stimulus when requesting "square" (p=0.066). Using the same statistical technique, a greater fixation time was observed on the "non-yellow" stimulus when the command was "yellow" (p=0.125) and on the "non-circle" stimulus when soliciting "circle" (p=0.102).

To compare the average percentages of fixation time when concepts of size and spatial position were solicited and in the other groups not solicited, the Wilcoxon test identified a significantly greater fixation time on the stimulus "big" when the request was "small" (p=0.046), and with the stimulus "over" when "under" (p=0.034) was requested.

In the correlation analysis between the age of the girl with RS and fixation time in all of the stimuli, Spearman's correlation coefficient validated by the correlation test indicated that: greater eye fixation time on the "blue" stimulus when "blue" was solicited was significantly correlated to a greater age (p=0.024); greater eye fixation time on the "yellow" stimulus when "red" was solicited was significantly correlated to a lesser age (p=0.082); and greater eye fixation time for the stimulus "triangle" to the command "triangle" was significantly correlated to a lesser age (p=0.074).

The percentages of each girl's hits and misses for all of the commands were analyzed, in which the test of dual proportion equality indicated a percentage of errors significantly greater than correct answers (p≤0.01 in all cases) for nine girls; and only one girl presenting an equal percentage of correct and incorrect responses.

DISCUSSION

Studies about cognitive aspects in individuals with RS agree that these children present severe intellectual impairment[1,6,14], although the evaluation of these aspects in this population is practically rendered impossible due to the presence of great motor inability and severe verbal communication alterations[8,14,15]. The degree of severity in this condition is such that the constitution of a control-group for the study would be arbitrary.

Many studies refer to RS children using the eye as a form of communication[8,12]. Parents or caregivers of children with RS state that their understanding surpasses their ability to communicate, and that this is expressed through the eye[11]. Nonetheless, our results question these affirmations, at least in that which refers to the acquisition of basic concepts, at the same time that the conclusions of Tetzchner et al.[12] are ratified: that the fixed look of these children may not necessarily signify an indication of possible cognitive capacity superior to what they seemingly have, but rather that the persistent look may constitute an indication of momentary interest and a demonstration of great social interaction.

The concepts evaluated in this study (colors, shapes, sizes and spatial positions) were selected within the patterns expected for the adequate development of children between three and six years of age.

The knowledge of colors can be acquired between two and six years of age[16], and there are studies reporting that, at two years of age, children demonstrate a vast ability to name colors[17,18]. Through these data, studies have shown that at three years and three months of age children already know most of the colors[19]. It is expected that children acquire the concepts of the shapes presented with three years of age[20,21]. At three or three-and-a-half years of age children already know the concepts of space and size presented[22]. Therefore, children with adequate development acquire the concepts used in the proposed evaluation, at a maximum, between two and six years of age.

Many studies have stressed the importance of the motor-sensory exploration of children in their world and of the things they have yet to acquire, the conceptual aspects[20,23]. It is known that babies at age four to six months can perceptually discriminate objects by color and shape[24] and that babies at the age of 10 to 14 months can distinguish spatial representations[25,26].

The RS children in our study varied in age from 4 years 8 months to 12 years 10 months, and 9 of them were 6 years old or older. During the calibration, the children being evaluated would look at the computer screen, following the circle that moved inside, indicating that they have visual perception. Considering that other similar studies using the same eye tracking equipment have demonstrated that these children possess an intentional eye[9,10], our results, however, indicated that the eye of the children being evaluated did not manifest recognition of the solicited concepts, suggesting the non-acquisition of these same. The children looked, many times, at the same stimulus-concept throughout all of the different solicitations, placing their response in doubt.

The two oldest children looked at two concepts correctly, and "blue" was commonly correct for the two. These data raise the hypothesis that, although with great lag, some RS children can learn some concepts. However, another significant correlation was that, with the increase of age, there was less eye fixation time for "triangle", when the command was to look at the "triangle". This observation contradicts the assertion that there may be more correct answers as the age of RS children advances.

Our small sample, composed of 10 children, limits the possibility of generalizing our results, but the fact that these children receive specialized attendance must be taken into account, as they are constantly stimulated and exposed to cognitive concepts, and the greater part of them are also inserted in the regular schooling process which, in and of itself, somewhat differentiates this group.

There is another methodological factor that could have possibly interfered with the results. Many researchers, concerned with evaluating the cognitive skills in RS individuals, refer to the importance of considering the amount of time these children need to respond to a stimulus[8,11,12]. Nonetheless, there is no report about the objective measuring of this delay in the response time. Thus, we can place into discussion whether the four-second-span during which the concept boards were displayed to the children was insufficient, due to the difficulty of articulating eye movement and thought in conventional time.

Effective interventions presuppose strategies and techniques that stimulate skills that could be developed while, simultaneously, could please the children (in RS, for example, music is an instrument of immense pleasure). Within the possibilities of these children, the introduction and development of concepts capable of generating better life-quality and which can be used in their daily routines should be considered. Therefore, this study suggests that the pedagogic tasks now being used should be rethought, in such a way that, in fact, the passive development skills of RS children are stimulated.

The data obtained by tracking the eye of the 10 children with RS indicated that the eye does not recognize the concepts relative to the colors "red", "yellow" and "blue"; the shapes "square", "circle" and "triangle"; the sizes "big" and "small"; and the spatial positions "over" and "under".

It seems appropriate to recommend an increase of objective studies to evaluate, through visual tracking, cognitive concepts in children with RS, using new interventions and re-evaluations.

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