

Oculomotor function in individuals with Rett Syndrome

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Original Articles

Oculomotor Function in Individuals With Rett Syndrome

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ABSTRACT

BACKGROUND: Individuals with Rett syndrome (RTT) are notoriously reliant on the use of eye gaze as a primary means of communication. Underlying an ability to communicate successfully via eye gaze is a complex matrix of requirements, with an intact oculomotor system being just one element. To date, the underlying neural and motor pathways associated with eye gaze are relatively under-researched in RTT.

PURPOSE: This study was undertaken to plug this gap in knowledge and to further the understanding of RTT in one specific area of development and function, namely oculomotor function.

MATERIAL AND METHODS: The eye movements of 18 girls and young women with RTT were assessed by electronystagmography (ENG). This tested their horizontal saccadic and smooth pursuit eye movements as well as optokinetic nystagmus and vestibulo-ocular reflex. Their results were compared with normative data collected from 16 typically developing children and teenagers.

RESULTS: Overall, the individuals with RTT demonstrated a range of eye movements on a par with their typically developing peers. However, there were a number of difficulties in executing the ENG testing with the RTT cohort which made quantitative analysis tricky, such as reduced motivation and attention to test materials and low-quality electrode signals.

CONCLUSIONS: This study suggests that individuals with RTT have an intact oculomotor system. However, modifications should be made to the ENG assessment procedure to combat problems in testing and add strength to the results. Further investigation into these testing difficulties is warranted in order to inform such modifications.

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Introduction

Individuals with Rett syndrome (RTT, OMIM 312750) are notoriously reliant on the use of eye gaze as a primary means of communication. Underlying an ability to communicate successfully via eye gaze is a complex matrix of requirements, with an intact oculomotor system being just one element. To date, however, the

underlying motor pathways associated with eye gaze are relatively under-researched in RTT. This study was undertaken in order to plug this gap in knowledge and to further our understanding of RTT in this specific area of development and functioning.

Rett syndrome is a complex neurological disorder usually resulting from a *de novo* mutation in the gene encoding Methyl-CpG-binding protein 2 (*MECP2*), a transcriptional regulator¹⁻³ primarily, although not exclusively⁴ expressed in neurons. The syndrome predominantly affects females and is typified by seemingly near normal development in the first six to 18 months of life followed by a deceleration in head growth and stagnation and regression in acquired skills, particularly loss of spoken language and purposeful hand use,⁵⁻⁷ accompanied by stereotypic hand movements and gait abnormalities.⁸⁻¹⁰ Many studies have been conducted, utilizing animal models as well as humans and human cell lines, in an attempt to better understand and explain the biology of RTT.¹¹⁻²³ Neuroimaging of the brain has revealed an overall reduction in cerebral volume and decreased dendritic arborization, in line with the noted microcephaly, with diffuse reductions in white matter and more focal reductions in gray, for example, the frontal lobe and cortex and the anterior temporal and dorsal parietal regions.²²⁻²⁴ In contrast, however, the occipital cortex²³ and the tracts associated with visual function, specifically those within the posterior corona radiata²¹ are relatively preserved.

Some studies have focused on the expression and distribution of *MECP2* in the brain and found it to be reduced in certain areas, with the brainstem and thalamus exhibiting the greatest reductions in *MECP2* protein expression.²⁵ These findings accord with the fact that many of the secondary features associated with RTT, such as cardiorespiratory and sleep disturbances, problems with cardiovascular and sensory regulation, and apraxia and/or dyspraxia, arise from disruptions in brainstem functioning. Features such as epilepsy, dystonia and other movement disorders, and orthopedic problems are more related to disturbances at a cortical or extrapyramidal level²⁶ and can be at least partly explained by the structural studies reported above which have found reductions in white and gray matter, with reduced synaptic development and neuronal connectivity.

Alongside these areas of deficit, however, one of the most frequently reported observations is the use of “intense eye communication – ‘eye pointing’”^{8,26} by individuals with RTT who otherwise struggle to communicate through more conventional means. The complex interaction of dyspraxia, dystonia, ataxia, and other motor features affects the speed, reliability, control, and coordination of movements. Yet individuals with RTT are usually thought to demonstrate good functional use of “eye pointing” or eye gaze for communication,^{6,27} which opens the question of whether the neural and motor movements associated with eye gaze are (relatively) less affected than other pathways. This has been evidenced to some extent by studies described above,^{23,21} in addition to which there have been a number of studies examining visual evoked potentials and aspects of visual acuity in

individuals with RTT as a measure of brain function.²⁸⁻³⁴ Such studies have investigated the afferent or peripheral visual pathways which convey visual signals from the retina to the brain and have found these pathways to be intact, although there are indications of disruption to visual processing at a higher, cortical level, which may deteriorate with age. At another level of analysis, Jain et al.³⁵ examined, postmortem, the eyes of two individuals with RTT and reported no gross or microscopic changes when compared with controls. They also tentatively explored the role of *MECP2* in vision, by comparing the levels of *MECP2* to be found in the retinas of the individuals with RTT versus the controls and concluded that “the normally limited expression of *MECP2* in visual pathway neurons may underlie the intact vision observed in RTT.” However, studies focusing on the efferent visual pathways in RTT, involving the oculomotor system, are much rarer. Koslowe et al.²⁹ did consider visual tracking as one parameter and concluded that although the optic nerve appeared to be normal in RTT, the individuals in their study demonstrated significant deficits in their visual tracking skills. It is this gap in knowledge—of the efferent visual system of individuals with RTT—that the current study seeks to fill.

Eye movements and the oculomotor system

Five different types of eye movements—both voluntary and reflex—have been identified.^{36,37} Four of these can be described as visual-ocular responses (provoked by images moving across the visual field).³⁸ These are: saccades, smooth pursuit (SP), optokinetic nystagmus (OKN), and vergence. The fifth, or vestibulo-ocular reflex (VOR), is in response to movement of the head which is detected by the vestibular system.³⁹⁻⁴¹ These five movements share the common aim of stabilizing images on the retina (specifically on the fovea, the part of the retina with the sharpest visual acuity), either by holding gaze and image steady or by shifting gaze to bring images to the fovea independent of any head movement. In essence, saccades could be said to be gaze shifting while SP, OKN, vergence, and VOR are gaze holding mechanisms.^{38,42} In addition, some researchers^{37,42-46} describe the process of fixation—the act of holding an image on the fovea to allow time for visual analysis of the image. The study we report in this article, conducted with individuals with RTT, focuses on examination of saccades, SP, OKN, and VOR.

Eye tracking and Rett syndrome

In recent years, eye tracking technology has been increasingly used by individuals with RTT as a way of accessing communication and developing a means of self-expression. Eye tracking technology has also been used as a medium for assessing the cognitive and receptive language skills of individuals with RTT.⁴⁷⁻⁵⁷

Most common eye tracking systems used for communication depend upon a camera measuring the reflection of near infrared light on the cornea and pupil of each eye to determine where the gaze is directed on screen.⁵⁸

Grids or "pages" of pictures and/or words are presented and selected by the user fixing his or her gaze on an item of choice for a specified length of time ("dwell time"). In this, saccades, SP, and fixation come into play, as does the VOR if the head moves or tilts. Visual attention is also a factor in how an individual directs his or her gaze.

There is a presumption that eye tracking technology is pertinent for individuals with RTT because of their ability to communicate with their eyes in the context of loss of purposeful hand movement.^{59–61} Yet little research has been conducted into the functioning of the oculomotor system in RTT. For example, to consider whether this system is affected by apraxia and delayed reaction time in the same way that other body movements are affected. Research has been conducted into oculomotor apraxia in other client groups⁶² and into the relationships between other clinical disorders and eye movements,^{63,64} but these findings cannot necessarily be extrapolated to RTT, neither can results from neurotypically developing individuals be presumed to apply. Research into the mechanisms underlying successful use of eye gaze in individuals with RTT is warranted to better our understanding of this complex rare disease.

Electronystagmography

Examination of eye movements may be performed through direct observation, for example, by the examiner moving a finger or penlight in front of the participant's gaze to test saccades or SP, or spinning the participant in a chair before bringing them to a sudden halt to test VOR. The tests can also be conducted more objectively through electronystagmography (ENG).⁶⁵ This involves the placement of electrodes around the eyes (usually above, below and to the sides, with a ground electrode on the forehead) so that electrical activity in the eyes can be detected, fed into a computer where the signal is amplified and recorded, and charts can be produced—if desired—which graphically illustrate the various oculomotor movements. Electrical activity is registered by detecting the corneo-retinal potential. In this the retina acts as the negative pole and the cornea as the positive.

The Department of Otorhinolaryngology (ENT) at Maastricht University Medical Center (MUMC+)—an international center specializing in central and peripheral vestibular disorders and disorders of the oculomotor system—regularly conducts oculomotor assessments through ENG. By applying these tests to the individuals with RTT who were coming into the hospital, therefore, we aimed to discover more about the impact (if any) that disturbances in *MECP2* may exert on the oculomotor system of individuals with RTT.

Materials and Methods

The study was conducted as a collaborative venture between the Rett Expertise Centre Netherlands—GKC and the ENT Department at MUMC+. It was performed in accordance with institutional guidelines and the 1964 Declaration of Helsinki. Ethical approval for conducting oculomotor research with individuals with Rett syndrome

was granted by the MUMC+ Medical Ethics Research Committee (NL57673.068.16 / METC162027) and written informed consent was obtained from the participants and/or parents for use of their anonymized data.

Tests of SP eye movement, saccades, and OKN were performed. In addition the VOR was tested.

Participants

The RTT cohort were recruited from individuals with Rett syndrome admitted to MUMC+'s Pediatric Intensive Care Unit (PICU) for three-day evaluation of brainstem functioning; the oculomotor assessments took place in the ENT department during their hospital stay.

The control groups were recruited from families of hospital employees as part of a larger, separate hospital study collecting normative ENG data for children and teenagers.

Test conditions, preparation, and procedure

The early assessments were performed using the BalanceLab Vestibular Research Laboratory, Version 2.3.0, build 969; during the course of the study, this system was upgraded to KingsLab, Version 1.6.1, build 740 (Maastricht University 2015). Standard procedure involved placing nine disposable Ambu Blue Sensor electrodes (children NF-50-K/W/12, adults N-50-K/25) above, below, and to the sides of each eye (temporal, nasal, supra-, and infraorbital) with a ground electrode on the forehead. During the study this was modified to three electrodes: two placed temporally (at the lateral canthus of each eye) and one on the forehead. In order to ensure good adherence and impedance, the skin around each participant's eyes, nose, and cheeks was cleansed with a fat-solvent petroleum ether and gently scoured with a skin rasp before electrode fixation. These preparations were performed in an outer room before proceeding into the test room proper. Testing with electrodes was selected as the preferred medium for the study rather than, for example, using video goggles, as professional experience indicated that electrodes would give a signal even if the participant's eyes were not fully open and fewer instructions would be required to complete the assessments.

All tests were conducted by a well-trained examiner in a semi-darkened room with the only illumination being the beamer, which projected the images onto the wall during the three oculomotor tests. The beamer was turned off for the final test, the rotatory chair (torsion swing) test, so that the room was then in total darkness. Participants were seated on a fixed chair in the center of the room, at a distance of 165 to 170 cm from the wall onto which the images were projected. Once seated, they were secured by a safety belt and the electrodes were plugged into a small transducer worn around the participant's neck which acted as an interface to connect to the computer. Any participants who were unable to sit independently were seated on their parent's lap and, to minimize any head movements, the parent was asked to hold their child's head.

The examiner remained in the outer room from where he and/or she operated the computer system controlling the tests; an infrared video camera and two-way speaker system allowed for constant monitoring and communication between the examiner and participants. Minimal verbal instruction was given, with the participants told simply to look at the pictures that would appear on the wall. At all times, at least one parent and a medical professional were present in the test room to provide reassurance and give additional instruction or encouragement if necessary. For example, parents might give a simple commentary on the images as they appeared ("oh, there's dad," "I can see a white horse, a bird, a dog").

Test components and data analysis

Where possible, signals from both eyes were recorded and combined after amplification. The four ENG tests were conducted in sequence in a single session, with calibrations measured at the start and in between the tests. Where only three electrodes were used,

the signals were recorded on one channel only, either using the right side channel (OD) or the left (OS). In the first instance, the RTT cohort and control group values were plotted against commonly used adult reference norms and then compared with each other, as the control group values were being used to set a new normative reference for a younger population.

Calibrations were performed by asking each participant to follow a single image moving in a saccadic pattern with 10° intervals from the center to the left and to the right in a horizontal plane (a total movement of 20°). Where calibration proved difficult on the first attempt, it was repeated, sometimes several times. Calibrations were deemed to be of a good or high quality if the signals gave clear recordings for both eyes in both vertical and horizontal planes, and were in the expected direction and time frame with minimal drift (less than 5°/second). They were said to be of poor or low quality if there was a nil response, a signal was recorded for only one eye or in one direction, or there was too much drift (greater than 5°/second) due to the signal to noise ratio (i.e., signal fluctuation in the absence of eye movements). Continuing poor calibrations did not automatically lead to abandonment of testing. If the quality of signals was too poor or unreliable to yield quantitative results that could be analyzed automatically by the computer, qualitative judgments were made from observation and visual inspection of the data by the examiners. Each type of eye movement was judged to be present or absent where there was a clear and readable signal or marked as "unsure" if (1) a good calibration had not been achieved previously and/or (2) the trace on a particular test could not be read due to a nil response or too much drift despite a previously good calibration. All judgments were reached through consensus, with at least two, usually three, examiners working together.

Smooth pursuit eye movements were tested by asking each participant to follow a single image moving horizontally to the right at a frequency of 0.2 Hz and a constant speed of 11.3°/second until it reached 10° eccentricity, at which point it abruptly changed direction and began moving to the left. The parameters of interest were: (1) presence of SP eye movements, (2) if present, whether SP was completely smooth, and (3) the percentage "gain." A valid SP movement was defined as an eye movement with its direction and phase corresponding to the stimulus, with a gain falling between 85% and 105% (the adult reference value). SP was judged to be completely smooth if there were no catch up saccades or drift noted.

Horizontal saccades were tested by asking each participant to look at a single image moving abruptly at random intervals, 10° to the left and right of center. The parameters of interest were: (1) presence of saccadic eye movements to both sides, (2) dysmetria (eyes not moving far enough to place the image on the fovea at first attempt so needing to make a minor correction saccade), (3) latency (time delay between stimulus and response), and (4) maximum velocity (maximum speed of movement, comparing between both eyes and between stimuli to the right and left, where possible). In addition, the examiner made a judgment about whether the eye movements were conjugate. A valid saccade was defined as eye movement in the same direction as the moving image, occurring in under 249 ms and with a maximum velocity below 235°/second to both the right and the left (the adult reference values).

Optokinetic nystagmus was tested by asking each participant to look at a pattern of images that filled the wall and moved alternately to the right and to the left, at speeds that increased from 5 to 48°/second at 4.72° intervals. The parameters of interest were: (1) presence of OKN, (2) whether OKN was "correct" (fell within the expected gain range), and (3) mean maximum slow component velocity (SCV) (also known as slow phase velocity). A valid OKN was defined as a nystagmus moving in the opposite direction to the moving images, with a mean maximum SCV to both the right and the left of below 23°/second (the adult reference value).

Vestibulo-ocular reflex was conducted through a sequence of bidirectional halfway rotations of the chair on which the participant was

seated, while in complete darkness. This is also known as the *torsion swing test* and stimulates the vestibular system in order to evoke a horizontal nystagmus. The tests were performed using sinusoidal rotation with a frequency of 0.1Hz and a peak velocity of 100°/second during one minute. The parameters of interest were: (1) presence of VOR, and (2) percentage "gain." A valid VOR was defined as a series of consecutive nystagmuses in the same direction as the movement of the chair and the head, within a gain range of 30% to 65% (the adult reference value).

During the calibrations, and tests of SP and saccades, single images of faces were projected onto the wall. For the RTT cohort, the faces were those of the participant's parents or other close family members, supplied as a digital image by the family before the test; for the control group, familiar cartoon characters were used (e.g., Bert and Ernie from Sesame Street). For the OKN test, cartoon images of animals were used across both groups.

Statistical evaluation

Descriptive analyses of data were performed using IBM SPSS version 24. More rigorous statistical analyses were not undertaken in order to avoid bias, as there were large gaps in quantitative data for the RTT cohort. Further details—and potential explanations—for this will be given below.

Results

The RTT cohort consisted of 18 girls and young women aged between two years seven months and 25 years 11 months (mean age nine years seven months, SD 6:5), all of whom had a clinical and genetic diagnosis of Rett syndrome.

The control group consisted of 16 children aged between three years six months and 18 years seven months (mean age seven years eight months, SD 4:0), nine males and seven females, all of whom had a normal clinical evaluation (Table 1).

ENG findings

Five children in the control group were assessed using nine electrodes. Their results are based on their ODS (combined right and left channel) scores. Eleven in the control group were tested with only three electrodes. Of these, 10 of 11 were recorded on the right side channel (OD) and one of 11 on the left (OS).

Seventeen of the RTT cohort were assessed using nine electrodes. For three of 17, the signals could not be read for the right eye so the results are based on the recording of their left eye only; for the remaining 14 of 17, the analysis is based on the combined ODS score where possible. One child from the RTT cohort was tested with three electrodes only, with her results recorded on the OD channel.

TABLE 1. Participant Overview

Group	Mean Age (years: months)	Range (years: months)	SD
RTT n = 18	9:7	2:7-25:11	6:5
Control n = 16	7:8	3:6-18:7	4:0

TABLE 2. Overview of Main ENG Findings

Group		Smooth Pursuit		Saccades		OKN		VOR Present
		Present % (n/N)	Completely smooth	Present	Dysmetria	Present	Correct	
RTT n = 18	Yes	67% (12/18)	58% (7/12)	72% (13/18)	–	83% (15/18)	60% (9/15)	86% (12/14*)
	No	–	17% (2/12)	–	85% (11/13)	–	–	–
	Unsure	33% (6/18)	25% (3/12)	28% (5/18)	15% (2/13)	17% (3/18)	40% (6/15)	14% (2/14*)
Control n = 16	Yes	100% (16/16)	75% (12/16)	100% (15/15)†	–	100% (16/16)	100% (16/16)	100% (16/16)
	No	–	25% (4/16)	–	100% (15/15)†	–	–	–
	Unsure	–	–	–	–	–	–	–

* Only 14 of 18 of the RTT cohort were tested for VOR on torsion swing.

† Only 15 of 16 of the control group were tested for saccades.

Calibration

All of the control group achieved a good calibration at the start of the session; these were repeated again before the torsion swing tests.

Calibration proved more difficult with the RTT cohort. For only four of 18 was the calibration deemed to be good or of high quality; for two of 18 horizontal calibration was better than vertical, and for three of 18 calibration was only possible on one eye. For the remaining nine of 18, the calibrations were regarded as poor or of low quality, giving unreadable signals. In one or two cases a better calibration was achieved with repetition.

An overview of the main ENG findings—especially the presence or absence of the four assessed movements (SP, saccades, OKN, and VOR)—is given in Table 2, while more detailed aspects pertaining to these movements are presented in Table 3.

The ENG results were also grouped according to each type of assessed eye movement, details of which are presented below.

Smooth pursuit

As shown in Table 2 and Fig 1, SP was present in all of the control population. However, it could not be reliably determined in a third of the RTT cohort. In all unclear cases, a coding of "unsure" was given rather than "no" (not present) because none of these cases achieved a good calibration before the test of SP. One of the six

achieved a better calibration following the SP test, before the test of saccades. Potential reasons for the poor calibrations and variability within samples will be explored in the Discussion section.

Judgments of whether SP was completely smooth could only be made in cases where SP was detected as present, that is, a decision could be made for all 16 of the control subjects but for only 12 of the RTT cohort. A portion of both the control and RTT groups was found not to have smooth movements even though SP was present (Fig 2). In some cases, one or two "good" SP traces could be found within a longer sample which, if taken overall, would not have been deemed "good." This required a well-trained examiner to analyze, and where possible, clean up the signals to remove extraneous "noise." In Fig 3, several focused SP eye movements are demonstrated in the middle of the recording although these are not smooth.

Likewise, a calculation of percentage gain could only be made if SP was judged to be present and, even then, the signal was not always good enough to give clear or reliable quantitative data. Gain could be calculated for all of the control group but for only two thirds of the RTT cohort for whom SP was deemed to be present (Table 3 and Fig 4).

Saccades

All of the control subjects who were tested for saccades demonstrated reliable saccades with no dysmetria.

TABLE 3. Scores on Individual ENG Parameters

Group		Smooth Pursuit		Saccades		OKN		VOR Gain† (30-65%)
		Gain‡ (85-105%)	Latency‡ (<249 ms)	Max velocity to R‡ (>235°/sec)	Max velocity to L‡ (>235°/sec)	Mean max SCV to R‡ (>23°/sec)	Mean max SCV to L‡ (>23°/sec)	
RTT n = 18*	N	8	9	8	8	10	10	7
	Min-Max	83-104	160-356	352-884	299-1433	13-53	10-48	42-90
	Mean	96	203	509	552	32	32	65
	SD	8.04	59.13	185.28	369.59	11.63	10.99	19.34
Control n = 16†	N	16	15	15	15	16	16	16
	Min-Max	79-111	104-140	321-640	315-578	24-51	29-45	26-119
	Mean	94	120	466	459	41	39	71
	SD	9.59	11.72	87.36	91.92	7.81	4.65	22.84

* As quantifiable results could not be obtained for all of the RTT cohort, the results in this table are not always based on n = 18 but vary for each test.

† Only 15 of 16 children in the control group were tested for saccades; one child was not.

‡ The commonly used adult reference values are given for comparison.

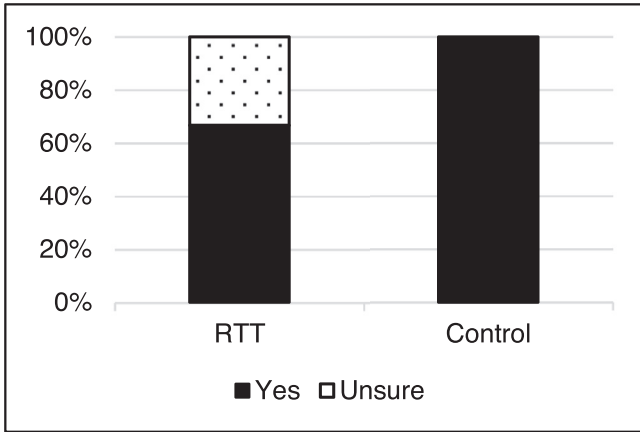


FIGURE 1. Smooth pursuit present. Key: This shows % of total N for each group. RTT n = 18, Control n = 16.

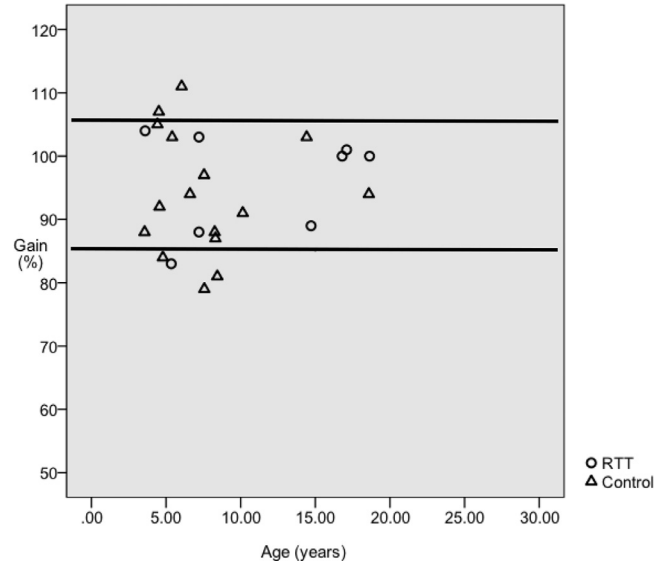


FIGURE 4. Smooth pursuit percentage gain. Key: n = Participants in each group for whom gain could be measured. RTT n = 8, Control n = 16. The two solid black lines indicate the minimum and maximum adult reference values (85% to 105%).

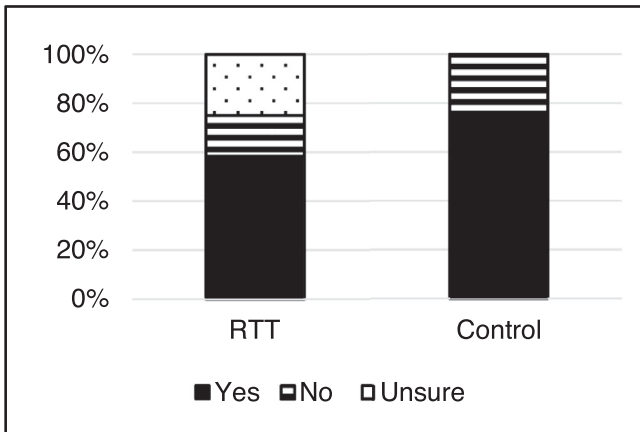


FIGURE 2. Smooth pursuit completely smooth. Key: n = Participants in each group for whom SP is present. RTT n = 12, Control n = 16.

One participant was not tested due to fatigue and reduced cooperation. All of the RTT cohort were tested but neither judgment could be reliably determined for a portion of this group (Table 2; Fig. 5 and 6). Latency and velocity could only be calculated where saccades were deemed to be present. Although the signals were not

clear enough in all cases to yield quantitative results, it did appear from visual inspection that the RTT cohort tended toward a longer latency than the control group (Table 3; Fig. 7 and 8).

Conjugation

This was difficult to assess in cases where only one eye was measured, but from observation by a trained examiner, and/or where two eyes were measured, all participants (RTT and control group) were judged to demonstrate conjugate eye movements.

Optokinetic nystagmus

All of the control group demonstrated OKN, which in all cases was also judged to be correct in that it fell within the expected gain range. As with the previous

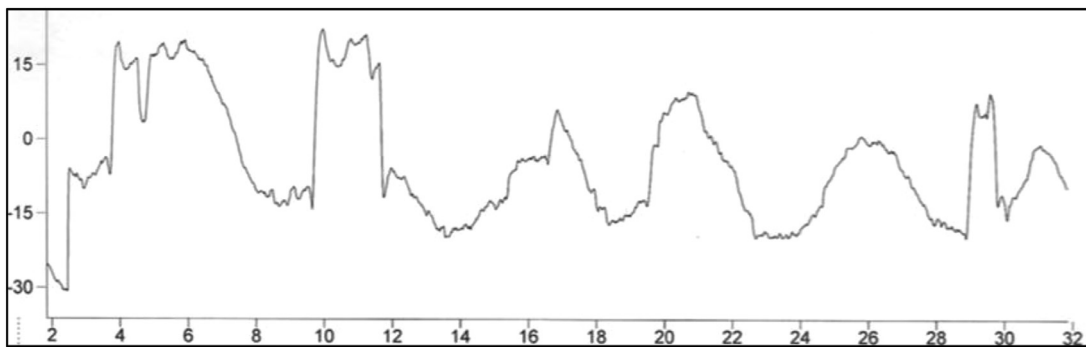


FIGURE 3. Trace recording of smooth pursuit eye movement.

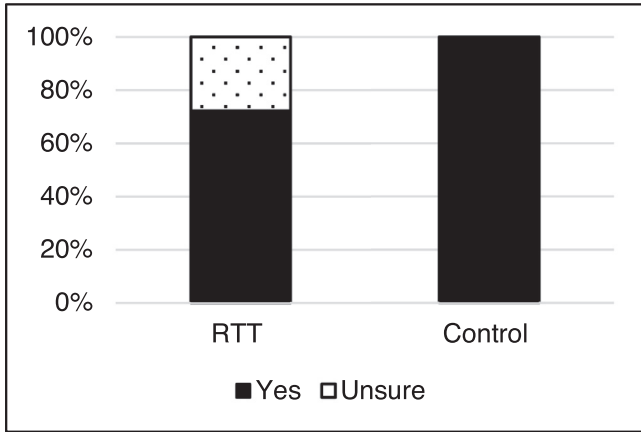


FIGURE 5. Saccades present (to R & L). Key: This shows % of total N for each group. RTT n = 18, Control n = 15.

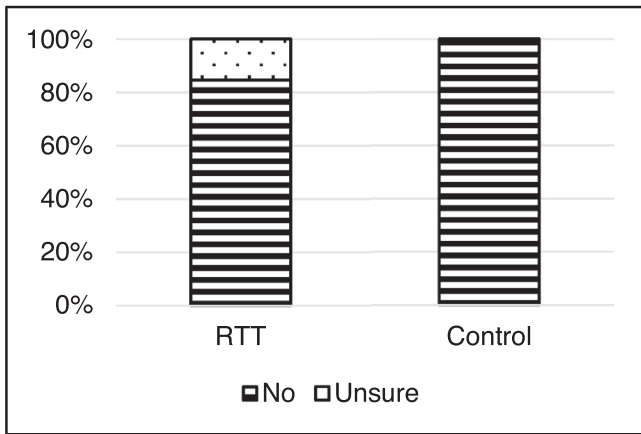


FIGURE 6. Dysmetria present. Key: n = Participants in each group for whom saccades are present. RTT n = 13, Control n = 15.

oculomotor tests, it was not possible to determine whether a portion of the RTT cohort had OKN. This type of eye movement could, however, be provoked in a higher number of cases than for SP or saccades, even if the signal response did not yield clear quantitative data for analysis (Table 2; Figs. 9 to 11). In two of the RTT cohort, the OKN was only elicited at lower velocities but nonetheless judged to be present, in three other RTT participants the OKN gain was relatively low and classified as "correct" though borderline, and one further participant demonstrated a small asymmetry, with a lower frequency OKN and a negative exponential slow phase.

Vestibulo-Ocular reflex

All of the control group demonstrated the presence of VOR with a measurable gain. Four of the RTT cohort were not tested as their parents declined the torsion swing. However, this test did produce the highest set of positive responses in the RTT cohort with VOR detected in 85% of those tested, even though the gain could only be quantified in half of these cases (Tables 2

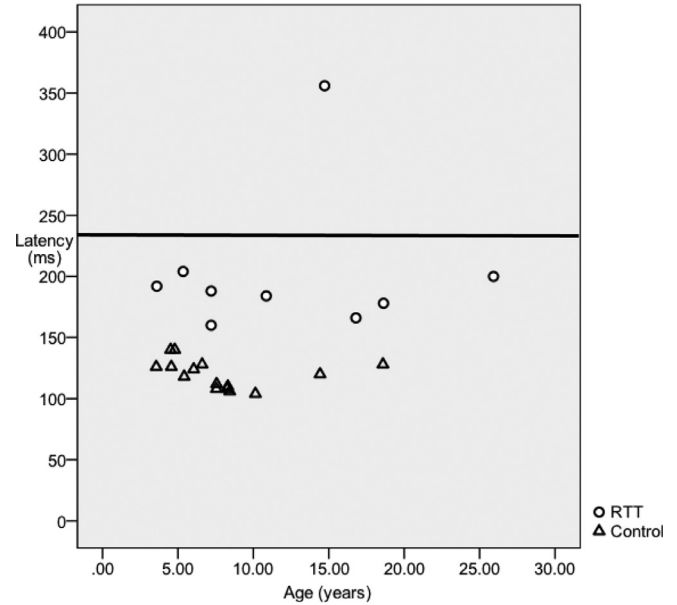


FIGURE 7. Latency of saccades. Key: n = Participants in each group for whom latency could be measured. RTT n = 9, Control n = 15. The solid black line indicates the adult reference value (<249 ms).

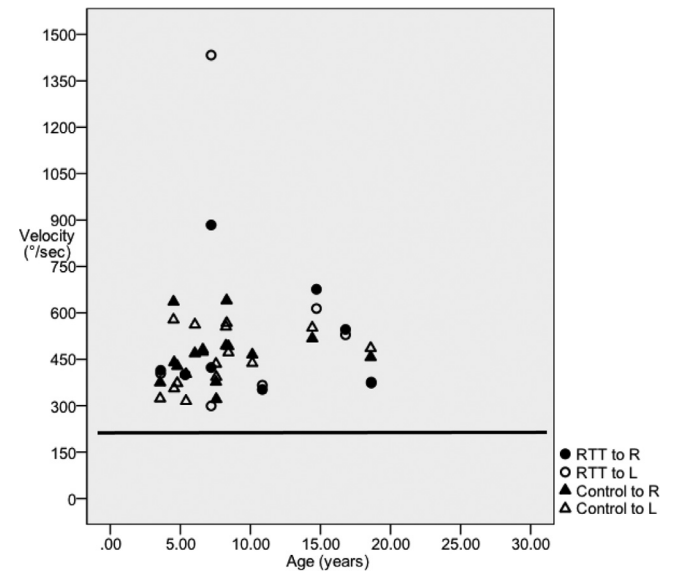


FIGURE 8. Maximum velocity of saccades to R and to L. Key: n = Participants in each group for whom maximum velocity could be measured. RTT n = 8, Control n = 15. The solid black line indicates the adult reference value (>235°/second).

and 3; Fig. 12 and 13). In five of the RTT participants, the fast phase velocity was noted, incidentally, to be relatively slow.

Discussion

This study investigated the oculomotor function of girls and young women with Rett syndrome. The results of

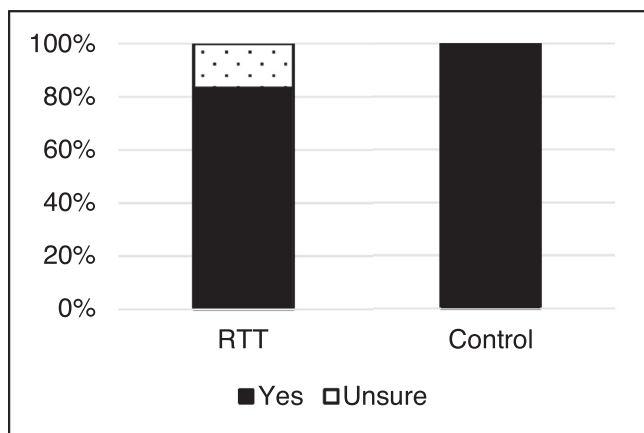


FIGURE 9. OKN present. Key: This shows % of total N for each group. RTT n = 18, Control n = 16.

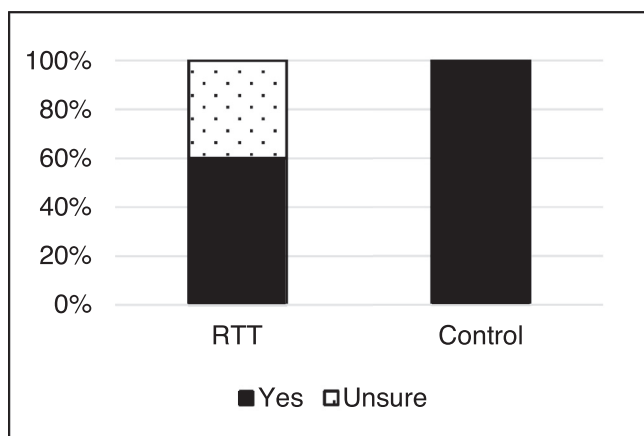


FIGURE 10. OKN correct. Key: n = Participants in each group for whom OKN is present. RTT n = 15, Control n = 16.

their assessments were compared with those of a similarly aged neurotypical control group, against a background of the commonly used adult normative values.

Overall, where their responses could be observed and/or measured, the individuals with RTT demonstrated a range of eye movements on a par with their neurotypical peers. For example, all of the control group and the majority of girls with RTT who gave a measurable result showed that they possessed SP and saccadic eye movements, OKN, and VOR. When the scatter plots were inspected visually, no major differences between the two groups were immediately apparent across most of the quantifiable measures (SP gain, saccades velocity, OKN mean maximum SCV, and VOR gain), except for occasional outliers, when compared with the adult reference norms. Likewise, both groups included individuals for whom SP was not smooth. This phenomenon was not restricted to the RTT population, and is something often considered to be an artifact of variable attention, especially when testing children. Two areas of potential difference are: (1) saccades latency, where the RTT cohort seemed to exhibit a longer latency, and (2) VOR, where it was noted

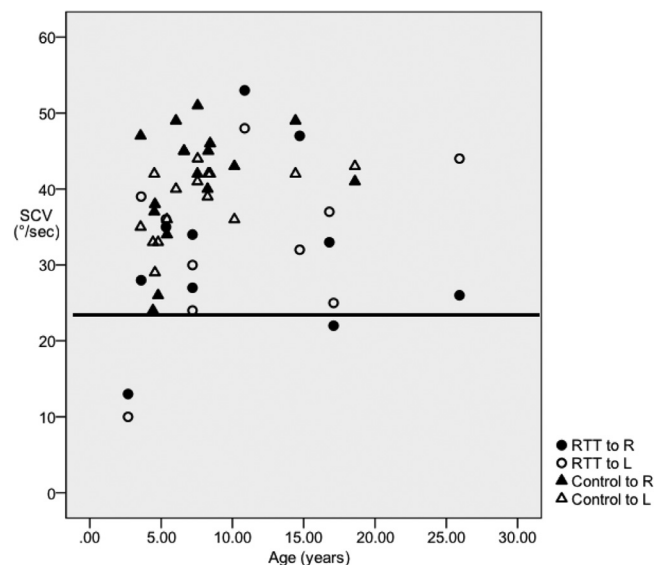


FIGURE 11. Mean maximum SCV. Key: n = Participants in each group for whom mean maximum SCV could be measured. RTT n = 9, Control n = 15. The solid black line indicates the adult reference value (>23°/second).

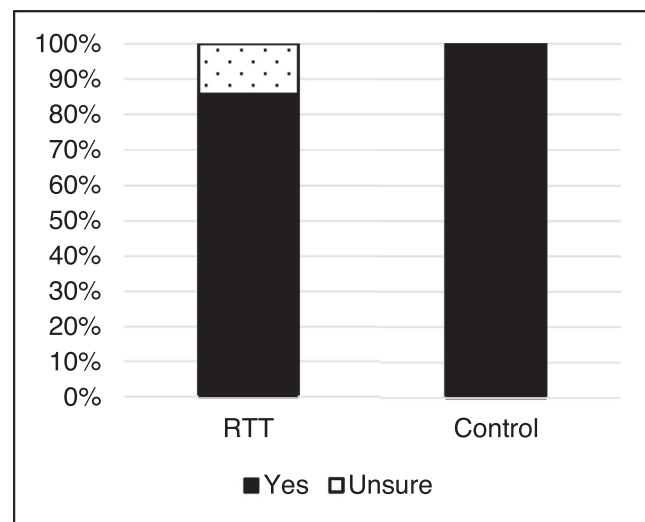


FIGURE 12. VOR present. Key: This shows % of total N tested on torsion swing for each group. RTT = 14, Control = 16.

incidentally that the RTT group demonstrated a somewhat slower fast phase velocity. As the power was so low, however, this difference could not be tested for significance, and the VOR test itself was brought into question by the unusually broad range of VOR gain recorded across both groups, which pointed toward possible errors in recording or calibration for this specific test. Longer saccades latency could be of relevance, however, and should be investigated further in the future.

The real difference between the two groups, though, lay in the high number of RTT individuals whose responses could not be quantified or classified as present and/or

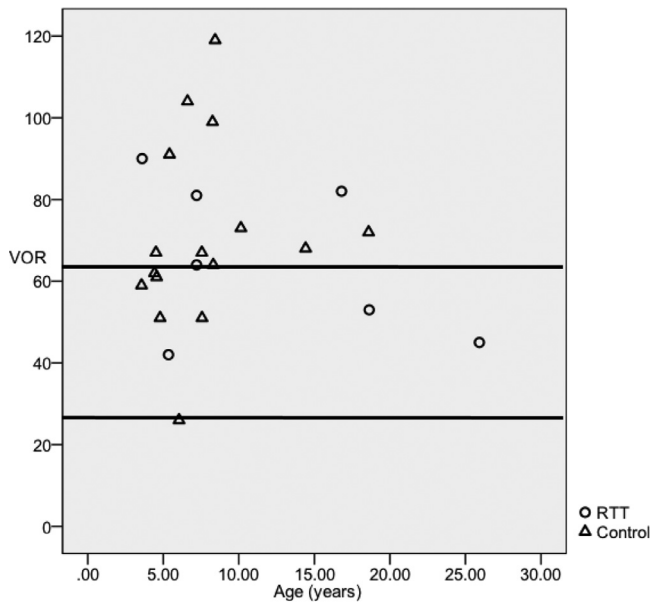


FIGURE 13. VOR gain. Key: n = Participants in each group for whom VOR could be measured. RTT n = 7, Control n = 16. The two solid black lines indicate the minimum and maximum adult reference values (30% to 65%).

absent with any certainty. In this respect the difficulties in executing the ENG testing with the RTT cohort were highlighted and the resulting low powers and risk of bias meant that no statistical analyses were performed. Poor signal to noise ratios, with a lot of drift, interfered with the quality of the recordings such that the signals were not clean and were difficult to read. In many cases taking a whole signal yielded poor average values, but, with an experienced tester, it was often possible to isolate one or two good responses from a longer trace. Wherever a couple of good responses could be observed then that was taken as an indication of whichever target movement was in question. Many of the RTT cohort struggled to achieve a good calibration, only managing this in one eye in some cases or after repeated attempts. If a calibration was achieved, however, this was an indication that saccadic eye movement was possible even if they were unable to perform consistently well on the test of saccades itself. In all cases where saccades were recorded, these were present to the right and to the left in both the RTT and control groups.

At face value the problems in achieving a good calibration and in testing in general seemed to relate to multiple factors, including blinking and/or extraneous head movements, participants touching or pulling at the electrodes which loosened them and led to poor connectivity, and reduced motivation, interest in and attention to the test materials. Indeed, the variability in performance exhibited by some individuals would typically be seen as indicative of an attentional issue in neurotypical children. Attention plays an important role in OKN especially, and, if VOR is shown to be intact following a nil or unclear OKN response, this can confirm that attention was likely the issue as VOR is evoked without a visual stimulus. One

further factor to be considered, though, is that the need for speed in preparation of the skin and attachment of the electrodes, to reduce the possibility of irritation and discomfort, may have led to reduced adherence of the electrodes and hence conduction of the signals was impeded. During the study period, there was an attempt to address this issue by reducing the number of electrodes from nine to three. In this way, recording was necessarily reduced to one channel only (either OS or OD). Whether this is an effective remedy, or whether alternative forms of testing which do not require electrodes will yield more complete and reliable results, remains to be seen with continued testing of a larger cohort.

The need for an intact oculomotor system is but one element of the jigsaw when considering the use of eye pointing or eye gaze for communication. Sargent et al.⁶⁶ offer a useful working definition of eye pointing, suggesting that it is the “context-relevant, controlled and intentional use of gaze in order to direct one or more partner’s visual attention to any item or object for a deliberate communicative purpose.” They further conclude that “eye-pointing can be seen as the integrated outcome of a combination of visual, social, cognitive and motor skills,” and that careful evaluation of this matrix of skills is required if we are to reach a common understanding of all that is involved in successful use of eye pointing, or eye gaze, for communication. The starting point is that of assessing whether an individual can maintain and shift fixation of static and moving targets. It is at exactly this level of basic oculomotor skill that our study was aimed.

Where any individual with RTT appears to be “failing” or struggling to use eye gaze, or eye tracking technology, for communication, an assessment of their oculomotor system is a starting point for unraveling where the point of breakdown may lie. To ensure a valid and helpful result, however, traditional ENG testing procedures need to be adapted, and new methods of assessment should be developed. Reasons for the difficulties encountered in the ENG assessments undertaken in this study and possible options for change will be explored in phase two of the study.⁶⁷

Conclusion

The data obtained from this study indicate that individuals with RTT have largely intact oculomotor functioning but their responses on traditional ENG assessment are hindered by issues such as poor attention.

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