SIMULATION OF ABNORMAL EYE MOVEMENTS IN CEREBELLAR DISEASE

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ABSTRACT

We have recorded eye movements from patients with cerebellar disease using an accurate infrared photoelectric technique. Abnormally large eye movements occurred when these patients attempted to make a refixation to a new point of regard; that is, during the time optimal "flick of an eye" called a saccade. Two classes of abnormal behavior from two groups of patients were analyzed. In the first, saccadic overshoot dysmetria, the patient's eye continually overshot the point of intended regard in a convergent fashion until they arrived sufficiently close to the target and stopped. In the second, macrosaccadic oscillation, the patient's eyes continually overshot the target in a divergent fashion until they were making large, 40° saccades across the field of view; and only then began to converge onto the point of intended regard.

We simulated these abnormal movements by increasing the feed-forward gain in Young and Stark's sampled data model for saccades (1963). This nonlinear, discontinuous control system model was implemented using the ISL analog simulation language on a DEC PDP-12 digital computer. In the model, at a gain of 1.0 the eyes will jump precisely to the target; at a gain between 1.0 and 2.0 each saccade will overshoot the target but the eyes will eventually converge onto the intended position; at a gain of 2.0 the eyes will oscillate perpetually; and at higher gains the ocular oscillation will be divergent. These gain relationships were used to quantitatively duplicate the observed behavior. We thus suggest that an effect of cerebellar disease in these patients was to permit alteration of gain of the oculomotor control system and that the resulting abnormal gain can be considered as a manifestation of the disease process.

INTRODUCTION

We report here on the simulation of saccadic dysmetria observed in patients with acute and chronic cerebellar disease. The model for this simulation is a modification of Young and Stark's sampled data model of conjugate eye movements (1963). A saccade is the time optimal, conjugate, refixation movement of the eyes. In normal subjects it is a discrete movement which is programmed in the brain from visual information received 125 to 200 ms. previously. Its peak velocity, which ranges from 10 to 900°/sec, is a function of the magnitude of the movement. Saccades can show errors of form (dissociation), velocity (slowing), and metrics (over- or undershooting). In the latter case, dysmetria, the error will be corrected by another saccade occuring 125 to 150 ms. after new position information is received.

Hsu, Krishnan, and Stark (in preparation) simulated the pattern of overshooting saccadic movements found in our cerebellar patients (of the Young-Stark model) by raising the forward saccadic gain. This paper reports on further results of that simulation.

EXPERIMENTAL METHODS

Eye movements were recorded by reflecting infrared light off of the eye and onto a pair of phototransistors aimed at each scleral-iris border on the horizontal plane. More light is reflected from the white sclera than from the colored iris. The difference between the photocurrents from the two sensors is proportional to the instaneous position of the eye within a range of 30° (Bahill, Clark, and Stark, 1975). The frequency response of the recording system is 0 to 60 Hz. (-3 dB) and position resolution is within one degree of arc.

As the stimulus to eye movements, a spot of light was reflected by a mirror galvanometer onto a viewing screen placed one meter in front of the patient.

OBSERVATIONS

Two classes of abnormal oculomotor behavior will be reported here. In the first, saccadic overshoot dysmetria, the patient's eyes continually overshot the point of intended regard in a convergent fashion until they arrived sufficiently close to the target. In the second, macrosaccadic oscillation, the patient's eyes continually overshot the target in a divergent fashion until they were making 40° saccades across the field of view, and only then began to converge onto the point of intended regard.

Examples of saccadic overshoot dysmetria are shown in Figure 1. This phenomenon occurred in nine patients from a group of twenty consecutively measured, documented cases of cerebellar disease, recorded over a seven month period. Four features define saccadic overshoot dysmetria: i) each saccade overshoots the target to form a series of sequentially smaller saccades, ii) all saccades have normal form and velocity, iii) there are no systematic drifts during the intersaccadic interval, iv) the period from one saccade to the next is consistent with visually guided movements and the phenomenon does not occur with saccades in the dark. This effect is quite variable; in some patients it occurs infrequently and not necessarily in both directions; in others it occurs on every saccade.

Over a period of several years four patients with acute cerebellar disease were found to exhibit macrosaccadic oscillation. Accurate eye movement recordings were made on the most recent of these patients. Figure 2 shows several features of this disorder: i) there are bursts of increasing and then decreasing saccadic oscillation, ii) saccades have normal form but are somewhat slow, iii) there are no systematic drifts during the intersaccadic interval, iv) the period from one saccade to the next is consistent with visually guided movements and the

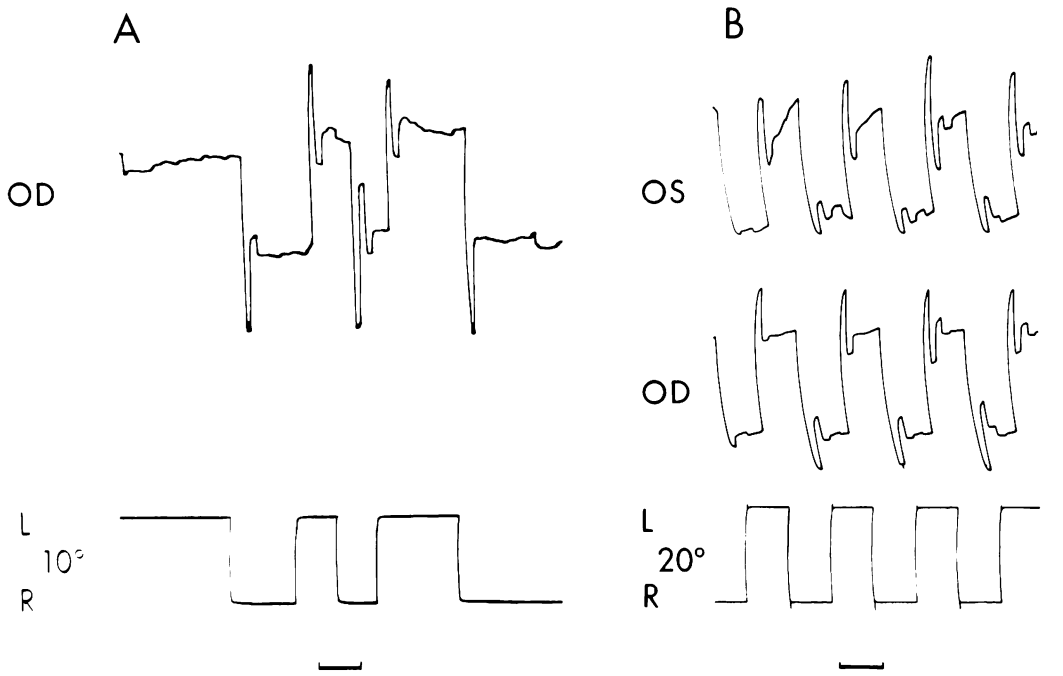

Fig. 1 - Saccadic overshoot dysmetria from two patients with cerebellar tumors. OS and OD signify right eye and left eye respectively. The stimulus position is shown in the bottom trace. Time bars indicate one second.

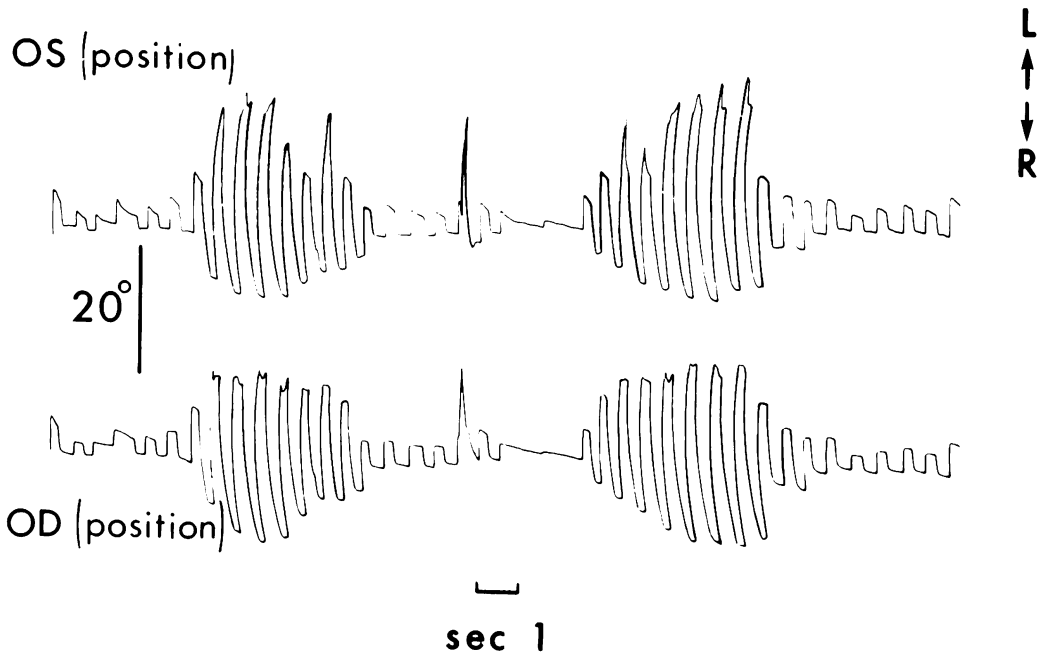

Fig. 2 - Macrosaccadic oscillation from a patient with a large midline cerebellar tumor. The patient was attemptimg to fixate in the central position. The photocell recording system became saturated in the extreme left position.

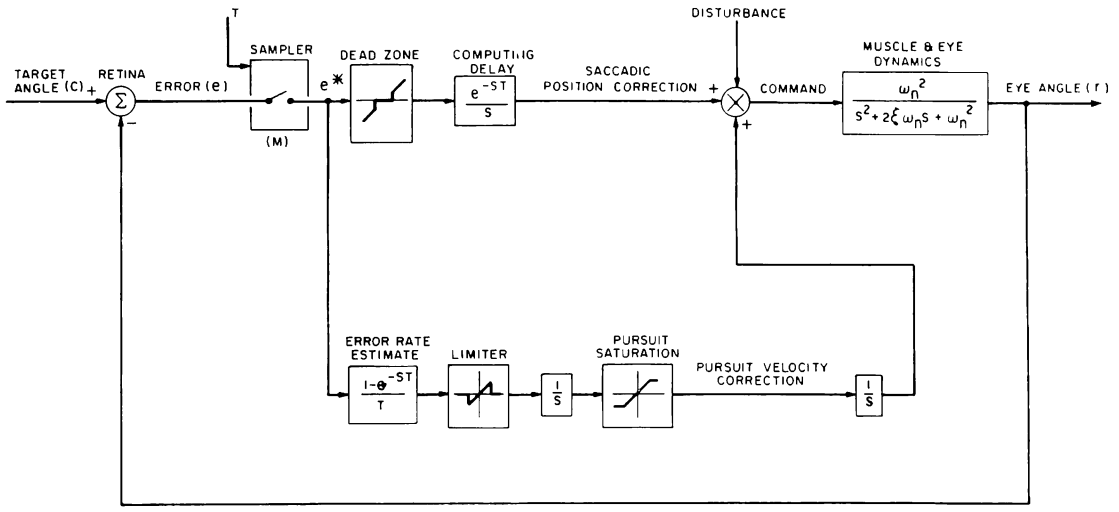

Fig. 3 - The Young-Stark sampled data model. The upper feed-forward path controls saccadic eye movements and the lower feed-forward path (not simulated for this study) controls smooth pursuit movements.

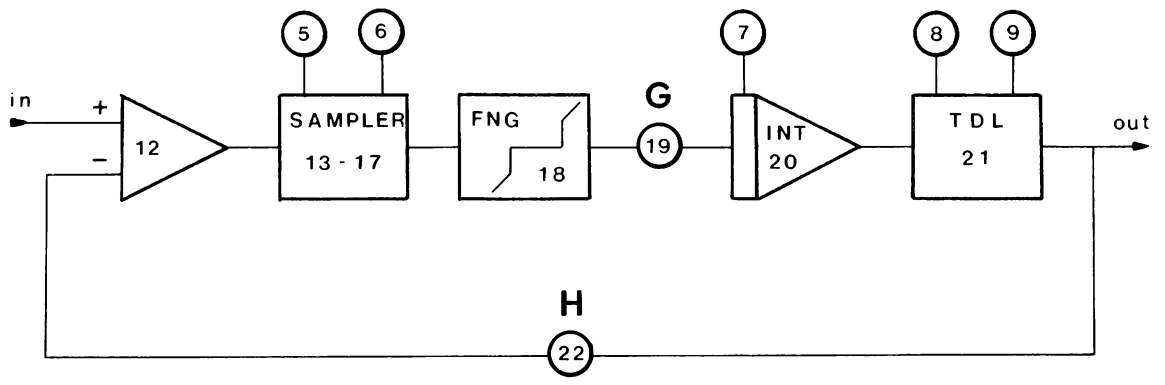

Fig. 4 - ISL flow chart for the saccadic branch of the Young-Stark model. See Appendix for program details.

phenomenon does not occur in the dark. The exact time course is variable, showing short periods of steady fixation, low amplitude saccadic oscillation, and variable duration bursts of macrosaccadic oscillation.

SIMULATION AND ANALYSIS

Although saccadic overshoot dysmetria and macrosaccadic oscillation appear quite different to an observer, they can be explained with a single model. The main difference, in both medical and system analytic terms is the magnitude of the defect.

The model for this simulation is a modification of Young and Stark's (1963) sampled data model of conjugate eye movements (Figure 3). This is a dual-mode controller having two feed-forward paths. The upper path represents the saccade system. The feedback path is strictly visual; the error signal being the retinal distance between the central fovea and the image of the target. Although the brain receives continuous sensory information from the eyes, it is intermittently sampled to drive the saccadic controller. This can be shown by stepping a target between two points with less than a 180 ms. pause on the first point. The eye will attempt to follow the target but will do so with an average pause of 180 ms. In Figure 3 the saccadic system is modeled with a fixed interval sampler, a dead zone (representing the fovea), a zero order hold, and a fixed delay (representing the computation and information transport time). The pursuit system which serves to hold the eyes on a moving target (lower feed-forward path in Figure 3) is not involved in saccadic dysmetria and was omitted from the simulation. The second order process representing muscle dynamics was also omitted for the purpose of this study. In any case, this first approximation of muscle dynamics could be replaced by the sixth order homeomorphic model of Clark and Stark (1975) or as modified by Collins (1976)

The Young-Stark model was programmed using the ISL Analog Simulator Language on a Digital Equipment Corporation PDP-12 digital computer (Figure 4 and Appendix). ISL is an easy language to use, however, caution must be exercised when dealing with discontinuous (sampled) signals. In particular, the delay function is simulated using 20 words of core, and the input signal is subsequently recreated by interpolation between the points. Discontinuities will be dispersed by this operator but the full amplitude will be maintained. This dispersion will yield an apparent tenfold increase in gain when a pulse of one step width is integrated. The problem was circumvented by placing the delay element after the integrator, insuring that the delayed signal was, at least, piecewise continuous. Dispersion effects at the leading edge of a saccade occur between samples and are thus inconsequential.

The sampler was simulated using the ISL "CNT" block (see program in Appendix, Lines 5, 6, 13-17). Every 200 steps, CNT causes the input to be placed into an output hold register (Line 6), which is otherwise zero. With this procedure, it is necessary to change the CNT index when the step size is changed. Alternatively, an IRL block could be driven with a periodic function, however, this procedure induces sample time errors (jitter). In the ISL model the dead zone nonlinearity was $\pm 0.5^{o}$, the sample interval was 200 ms., and the delay was 160 ms. Note that the control system becomes unstable when the delay is greater than the sample interval.

Gain is here defined as the ratio of an output response to an input stimulus. In the model (Figure 4) feed-forward and feedback gains are controlled with elements 19 and 22, which normally have the value of 1.0. We experimentally varied the feedback (external-visual) gain for a normal subject by combining a fraction of his eye position with the input command, yielding a target which moved in a controlled fashion as the subject tried to achieve fixation. The result of this experiment and its simulation are in good agreement (Figure 5). Although this eye movement pattern is somewhat similar to saccadic overshoot dysmetria, it is the internal feed-forward gain which will be affected by disease of the brain. Figure 6 shows a family of curves simulating oculomotor response to a 2^{o} step stimulus with the feed-forward gain varied between 1.0 and 2.25. At a gain of 1.0 the response is accurate, at a gain between 1.0 and 2.0 each saccade overshoots the target but the output of the model eventually converges onto the target (i.e., within the error defined by the dead zone), at a gain of 2.0 the overshoot equals the original error and the output oscillates perpetually, and at even higher gains the oscillation is divergent.

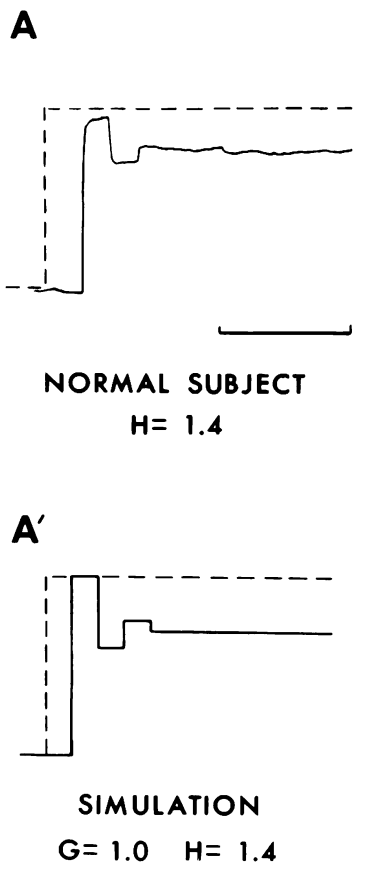

Fig. 5 - Comparison of experimentally altered feedback gain with model. A) Recording from a normal subject under conditions of experimentally altered feedback gain (see text). The dotted line indicates a 10^{o} stimulus step to the subject-feedback system. A') Simulation of experiment in A.

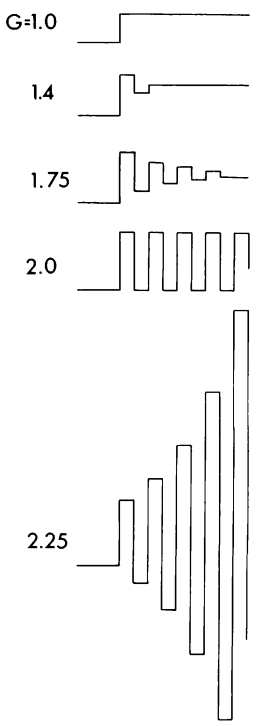

Fig. 6 - Simulation of Young-Stark model with various feed-forward gains. The input stimulus was a 4^{o} step.

The description of saccadic overshoot dysmetria suggests a feed-forward gain between 1.0 and 2.0. In Figure 7 we present a recording of the disturbed eye movement and a simulation of the phenomenon. The agreement between the two figures indicates that saccadic overshoot dysmetria is a disorder of elevated gain in the oculomotor controller.

In a similar fashion, bursts of macrosaccadic oscillation appear to arise from an initial feed forward gain which is greater than 2.0 and then which falls to a value between 1.0 and 2.0. In Figure 8 we present a recording of the disturbed eye movement and a simulation of the phenomenon. Again, the two figures are in essential agreement. The minor differences are instructive. The low amplitude square wave oscillation before and after the burst indicates a steady gain of 2.0 in these regions. The smooth envelope of the phenomenon may suggest a slowly varying gain change rather than the abrupt change of our simulation.

CONCLUSION

The clinical findings of cerebellar disease in both of these disorders manifesting high saccadic gain lead us to view the cerebellum as an organ which serves to calibrate the gain of the underlying oculomotor nuclei in the brainstem in a parametric fashion. Disruption of cerebellar function allows the gain of the saccadic control system to increase, resulting in saccadic overshoot dysmetria or, in more severe cases, macrosaccadic oscillation.

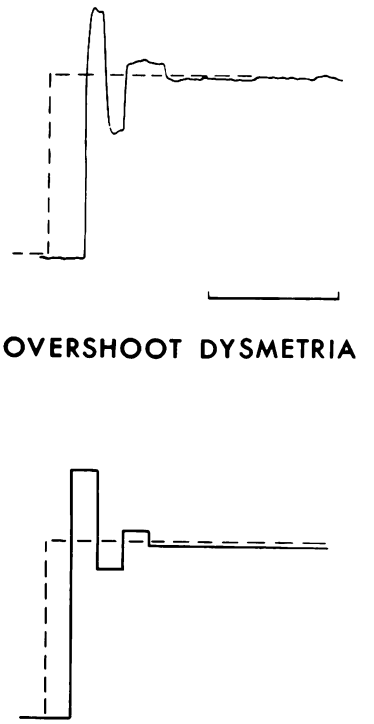

Fig. 7 - Comparison of saccadic overshoot dysmetria with model. A 20^{o} stimulus is shown by the dotted line. Time bar is 1 second.

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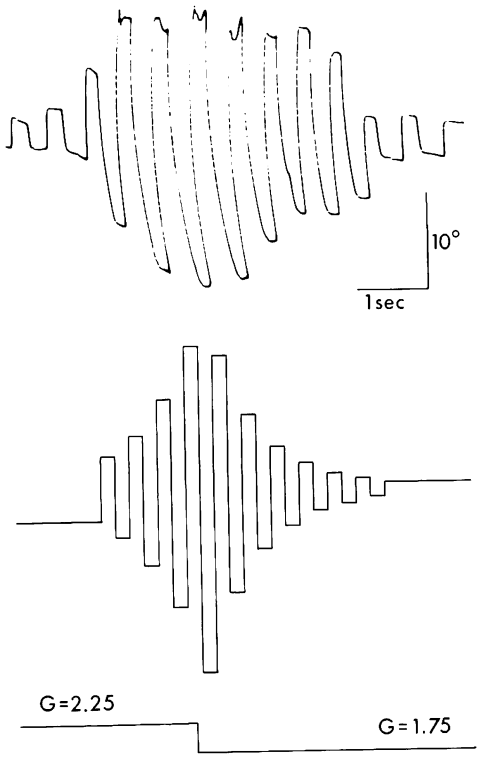

Fig. 8 - Comparison of macrosaccadic oscillation with model. The model was initially on target and then stimulated with a 2^{0} step, starting the oscillation. The gain in the model was abruptly lowered as shown in the lower line.

APPENDIX

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0    CON  0                =  0.000E 0    0
1    CON  1                =  1.000E-3    1
2    CON  2                =  1.000E-1    2
3    CON  3                =  5.000E 0    3
4    CON  4                =  0.000E 0    4
5    CON  5                =  0.000E 0    5
6    CON  6                =  0.000E 0    6
7    CON  7                =  0.000E 0    7
8    CON  8                =  1.000E 0    8
9    CON  9                =  8.000E 0    9
10   INT  0, 1             =  1.000E-2    10
11   IFL  10, 2, 3, 4      =  0.000E 0    11
12   ALD  11,-22           =  0.000E 0    12
13   CNT  200              = -0.930E-1    13
14   GTO  17               =  0.000E 0    14
15   EQT  12, 6            =  0.000E 0    15
16   GTO  18               =  0.000E 0    16
17   EQT  5, 6             =  0.000E 0    17
18   FNG  6                =  0.000E 0    18
      -1.000E 5      -1.000E 5
      -1.000E 3      -1.000E 3
      -1.000E 1      -1.000E 1
      -1.000E 0      -1.000E 0
      -5.010E-1      -5.010E-1
      -5.000E-1       0.000E 0
       5.000E-1       0.000E 0
       5.010E-1       5.010E-1
       1.000E 5       1.000E 5
19   POT  18, 1.000E 0 =  0.000E 0    19
20   INT  7, 19            =  0.000E 0    20
21   TDL  20, 8, 9         =  0.000E 0    21
22   POT  21, 1.000E 0 =  0.000E 0    22
23   TME  23               =  1.000E 1    23
24   CON  24               =  1.000E 3    24
25   ADE  IN11  , OUT21
26   PRI  11, 21           =  0.000E 0    26
27   FIN  23, 24           =  0.000E 0    27
28   END  28               =  0.000E 0    28

*I
S=1.E0,   T=20
```