Saccadic hypometria is compensation for and not a primary symptom of disease

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When asked to shift their gaze, healthy people often make a slightly hypometric saccade, particularly when gaze shift is of large amplitude. This primary saccade is usually followed by a corrective saccade to fixate the target. That is, it appears that the brain chooses to make a movement that misses a visual target, and relies on a second, corrective saccade to fixate it on the fovea. This behavior is not limited to healthy adults. Infants, older adults, and patients with disorders of the cerebellum (SCA[1,2], Williams syndrome[3]), basal ganglia (Parkinson Disease[4–6] and Huntington Disease[7–9]), and cortex (Alzheimer disease[10], Lewy Body dementia[6,11]) all have been shown to exhibit a more pronounced saccadic hypometria. Given the apparent ability of the oculomotor system to produce exquisitely precise eye movements, why does the brain of healthy adults and of patients select a policy that results in systematic errors and requires multiple eye movements to shift gaze?

We wondered if careful examination of patients with one movement disorder, ataxia-telangiectasia, would provide insight into this surprising but pervasive behavior. Ataxia-telangiectasia (A-T) is an autosomal recessive movement disorder, where affected individuals exhibit neurodegeneration, cerebellar atrophy, ocular and cutaneous telangiectasia, and immunodeficiency [12]. Among their neurologic symptoms are impairments in eye movement control – including saccadic eye movements – though they have normal visual acuity[13,14].

We asked people with A-T and control participants to shift their gaze to visual targets placed 10° to 40° apart, across the midline, on the horizontal axis. We observed that A-T subjects made a series of 2-6 sequential saccades to shift their gaze, typically moving only approximately halfway to the target with their first saccade, and tended to make more saccades with more pronounced hypometria when asked to shift gaze further (Fig. 1). Control subjects, however, made 1-2 saccades to the target, typically moving directly to, or near to, the target, and also exhibited more pronounced hypometria for larger gaze shifts.

Prior reports have hypothesized that the saccadic hypometria in patients with A-T may be due to impairment in the ability to execute saccades. Lewis et al[13] suggested that the eye movements of people with A-T are truncated prematurely due to inappropriate activation of the rostral pole of the superior colliculus by cerebellar output neurons. To test this hypothesis, we examined the trajectory of saccades made by participants in both groups (Fig. 2). We found that the velocity profiles of the eye movements made by the A-T subjects appeared neither truncated nor abnormal, with no evidence of premature termination. The relationships between the amplitude, duration, and peak velocity of saccades were all similar between control and A-T subjects, and inconsistent with premature termination of eye movements.

We next wondered if A-T subjects made their specific pattern of hypometric saccades as a strategy to cope with the deleterious effect of increased noise within their oculomotor system. We hypothesized that if A-T subjects exhibited greater signal dependent noise, employing a series of saccades instead of a single large saccade would be an effective compensatory response. To test this idea, we first quantified signal-dependent noise in the saccades of both control and A-T subjects (Fig 3). We found that A-T subjects exhibited a 4-fold greater noise. Using an optimal feedback controller to formalize our hypothesis incorporating costs of time and accuracy, we found that the optimal policy in the presence of this signal dependent noise was to make a sequence of hypometric saccades, particularly for large amplitude movements. Using the noise model, we predicted what the gain of saccades should be for each healthy and A-T subject (Fig. 4). We found that the increased number and reduced gain of saccades of patients with A-T were well predicted by the signal dependent noise. In fact, control subjects who manifested larger signal dependent noise also exhibited a reduced saccadic gain, although more subtle than that of subjects with A-T, in agreement with the predictions of our model (Fig. 4). Our analysis of previously published data also found that in a number of other neurological disorders (Huntington disease, Williams syndrome, and Parkinson disease), the changes in saccade gain were consistent with the model predictions, given only the measured increase in saccadic signal dependent noise.

Overall, our results suggest that saccadic hypometria in healthy and patient populations is a compensatory adaptation to the signal dependent noise properties of the oculomotor system, and not a primary deficit associated with the disease. Individuals with A-T as well as healthy controls have altered the planning of their saccades to match the characteristics of the bodies they control.

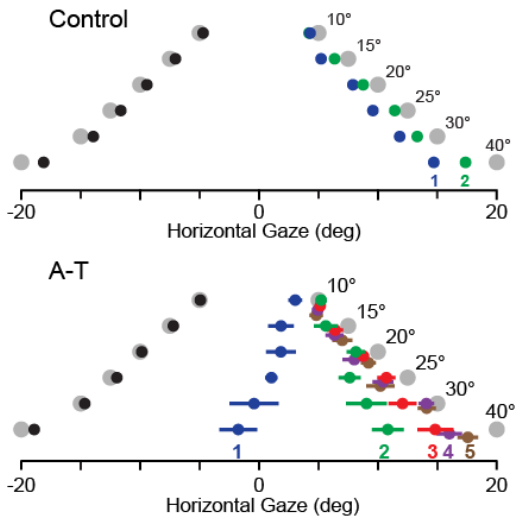

Fig. 1. A-T subjects made a sequence of saccades to the target, rather than a single saccade. The starting eye position (black) and endpoints of each saccade (colors) are shown. Targets (gray) are to scale. Data are mean ± SEM across subjects. Control subjects made 1-2 eye movements to shift their gaze, while A-T subjects made 2-6 movements.

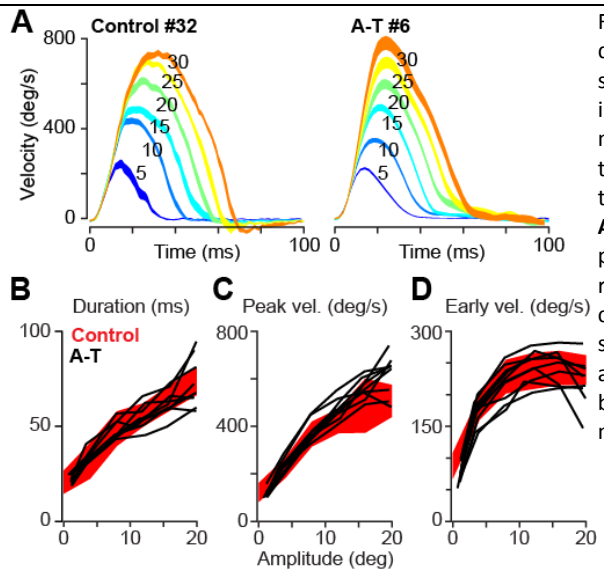

Fig. 2. Saccade dynamics of A-T subjects did not indicate midflight termination of the movement. **A**, velocity profiles for representative control and A-T subjects, averaged in 5° bins. Data are mean ± SEM. The relationship between the saccade amplitude and **B**, Saccade duration, **C**, Peak velocity of saccades, and **D,** Early saccade velocity, 10 ms after onset. Control subjects are red (mean ± 1SD), and each black line is an A-T subject. The saccade trajectories of A-T subjects were similar to those of control participants; we found no evidence of a deficit in saccade execution or midflight termination of eye movements.

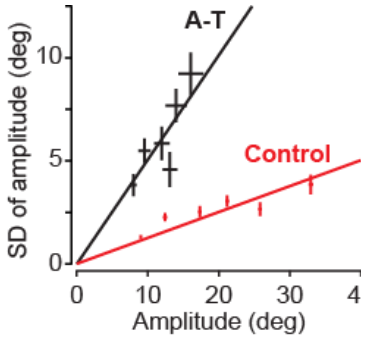

Fig 3. Both control and A-T subjects exhibited signal-dependent noise in the control of their saccades. However, A-T subjects had 4-fold greater noise for movements of the same amplitude.

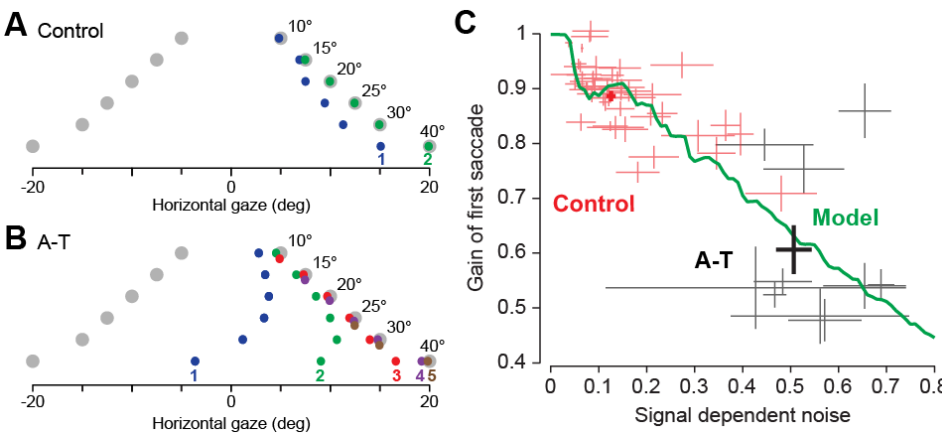

Fig 4. An optimal feedback controller accounts for saccadic hypometria, especially for large amplitude gaze shifts in both control subjects (**A**), and A-T subjects (**B**). (**C**) Each data point is a control or A-T subject. Individuals with greater noise exhibit greater hyperometria.

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